Glycosyl cations in glycosylation reactions

Hansen, T.

Glycosyl Cations in Glycosylation Reactions Thomas Hansen

Glycosyl Cations in Glycosylation Reactions

Thomas Hansen

Universiteit Leiden

Glycosyl Cations in Glycosylation Reactions

PROEFSCHRIFT

ter verkrijging van
de graad van Doctor aan de Universiteit Leiden,
op gezag van Rector Magnificus prof. mr. C. J. J. M. Stolker,
volgens besluit van het College voor Promoties
te verdedigen op woensdag 25 november 2020
klokke 15:00 uur

door

Thomas Hansen

Geboren te Leiden in 1992

Promotiecommissie

Promotor:	Prof. dr. J. D. C. Codée
Co-promotor:	Prof. dr. G. A. van der Marel
Overige commissieleden:	Prof. dr. H. S. Overkleeft (Voorzitter) Prof. dr. J. Brouwer (Secretaris) Dr. D. V. Filippov Prof. dr. F. M. Bickelhaupt, VU Amsterdam Dr. M. T. C. Walvoort, Rijksuniversiteit Groningen Prof. dr. K. A. Woerpel, New York University

Printed by Ridderprint
ISBN 978-94-6416-235-6

The cover depicts the conformational energy landscape of the elusive glycosyl cation, which is one of the key reactive intermediates in glycosylation reactions.

Adapted from Hansen *et al.*, *ACS Cent. Sci.* **2019**, 5 (5).

Table of contents |

Ac	acetyl
AIBN	2,2'-azobis(2-methyl-propionitrile)
All	allyl
APT	attached proton test
aq.	aqueous
Ar	aryl
Ara	arabinose
Arom	aromatic
ASM	activation strain model
B	boat
B3LYP	Becke, 3-parameter, Lee-Yang-Parr
BAIB	(diacetoxyiodo)benzene
Bn	benzyl
bs	broad singlet
BSP	1-benzenesulfinylpiperidine
Bu	butyl
Bz	benzoyl
C	chair
cal	calorie
calcd	calculated
Car	caryophyllose
cat.	catalytic
CBz	carboxybenzyl
CDI	carbonyldiimidazole
CEL	conformational energy landscape
CID	collision induced dissociation
CIP	contact ion pair
COSY	correlation spectroscopy
C_q	quaternary carbon atom
CSA	camphor-10-sulfonic acid
Cy	cyclohexyl
δ	chemical shift
d	doublet
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCE	1,2-dichloroethane
DCM	dichloromethane
dd	double doublet
ddd	doublet of double doublets
dddd	double doublet of double doublets
ddt	doublet of double triplets
DEAD	diethyl azocarboxylate
DFE	difluoroethanol
DFT	density function theory
DiPEA	diisopropylethylamine
DMAP	4-dimethylaminopyridine
DMF	dimethylformamide
DMNPA	2,2-dimethyl-2-(*ortho*-nitrophenyl)
DMP	Dess-Martin periodinane
DMSO	dimethylsulfoxide
DPS	diphenylsulfoxide
dq	double quartet
dt	double triplet
dtd	doublet of triple doublets
DTBMP	2,6-di-*tert*-butyl-4-methylpyridine
DTBS	di-*tert*-butylsilylidene
E	energy
E	envelope
EDA	energy decomposition analysis
eq.	molar equivalent
Et	ethyl
E-X	electrophilic activator system
Fuc	fucose
FT	Fourier transform
gg	*gauche-gauche*
gt	*gauche-trans*
GATED	proton decoupling applied only during relaxation
Gal	galactose
Glc	glucose
GlcA	glucuronic acid
$GlcN_3$	2-azido-2-deoxy glucose
h	hour(s)
H	half-chair
HATU	1-[bis(dimethylamino)methylene]-1*H*-1,2,3-triazolo[4,5-*b*]pyridinium 3-oxide hexafluorophosphate
HFIP	hexafluoro-*iso*-propanol
HMBC	heteronuclear multiple-bond correlation spectroscopy
HOMO	highest occupied molecular orbital
HPLC	high performance liquid chromatography
HRMS	high-resolution mass spectroscopy
HSQC	heteronuclear single quantum coherence
IDCP	iodonium dicollidine perchlorate
IR	infrared
IRIS	infrared ion spectroscopy
IRC	intrinsic reaction coordinate
J	coupling constant
KIE	kinetic isotope effect
KS-MO	Kohn-Sham molecular orbital theory
LC-MS	liquid chromatography mass spectrometry
LG	leaving group
LOS	lipooligosaccharides
LTQ	linear trap quadropole
LUMO	lowest unoccupied molecular orbital

LRP	long-range participation
Lyx	lyxose
M	molar
m	multiplet
M.	*Mycobacterium*
m.s.	molecular sieves
MS^2	tandem-mass spectrometric
m/z	mass over charge ratio
min	minute(s)
Man	mannose
ManA	mannuronic acid
Me	methyl
MFE	monofluoroethanol
MM	molecular mechanics
M.S.	molecular sieves
Nap	2-methylnaphthyl
NBS	*N*-bromosuccinimide
NIS	*N*-iodosuccinimide
NGP	neighboring group participation
NMR	nuclear magnetic resonance
NOESY	nuclear Overhauser effect spectroscopy
Nuc	nucleophile
p	*para*
P	protection group
PC	product complex
PCM	polarizable continuum model
Ph	phenyl
PMB	4-methoxybenzyl
ppm	parts per million
q	quartet
qd	quartet of doublets
QM	quantum mechanics
RC	reaction complex
R_f	retention factor
Rib	ribose
RRV	relative reactivity value
rxn	reaction
s	singlet
S	skew boat
sat.	saturated
SCF	self-consistent field
S_N1	uni-molecular nucleophilic substitution
S_N2	bi-molecular nucleophilic substitution
SSIP	solvent-separated ion pair
SAR	structure-activity-relationships
t	triplet
t	*tert*
T	twist
tg	*trans-gauche*
TBAF	tetrabutylammonium fluoride
TBAI	tetrabutylammonium iodide
TBS	*tert*-butyldimethylsilyl
TBDMS	*tert*-butyldimethylsilyl
TBDPS	*tert*-butyldiphenylsilyl
TES	triethylsilyl
TEMPO	2,2,6,6-tetramethylpiperidine 1-oxyl
TFA	trifluoroacetic acid
TFE	trifluoroethanol
Tf	triflyl; trifluoromethanesulfonyl
THF	tetrahydrofuran
TIPS	tri-*iso*-propylsilyl
TLC	thin layer chromatography
TMEDA	tetramethylethylenediamine
TMS	trimethylsilyl
TOCSY	total correlation spectroscopy
Tol	tolyl; 4-methylphenyl
TPP	triphenylphosphine
TPPO	triphenylphosphine oxide
Trt	trityl; triphenylmethyl
Ts	tosyl; 4-methylbenzene-1-sulfonyl
TS	transition state
td	triple doublet
tt	triple triplet
TPAP	tetrapropylammonium perruthenate
TTBP	2,4,6-tri-*tert*-butylpyrimidine
UDP	uridine diphosphate
UV	ultraviolet
VT	variable temperature
Xyl	xylose
YerA	yersiniose A
ZORA	zeroth order regular approximated
ZPE	zero-point energy

Chapter 1

General Introduction

Carbohydrates and glycoconjugates are the most diverse and abundant class of biomolecules occurring in all kingdoms of life. They are involved in a significant number of pathologies, including bacterial infections, cancer, and inflammatory diseases.[1] They fulfill an indispensable role as structural components, in energy housekeeping, and as signaling molecules. The study of carbohydrates and the development of carbohydrate-based medication (*e.g.*, antibacterials, anticancer agents, and vaccines) has been challenging because these molecules are often present in nature as heterogenic mixtures, which complicates their isolation from these sources.

Synthetic chemistry is one of the most important suppliers of well-defined and single molecule carbohydrates and glycoconjugates. Several synthetic analogs have found their way into the clinical use, including the anticoagulant Fondaparinux (Arixtra®) and the antiviral medication Oseltamivir (Tamiflu®). Notwithstanding these advances, the construction of complex carbohydrates and glycoconjugates remains an exceptionally difficult task as there has been no general solution for the stereoselective synthesis of glycosidic linkages.[2–7] To date, the majority of carbohydrate syntheses have been target-oriented, delivering a solution for a single problem. In contrast to these studies, this thesis describes an investigation to the intrinsic reactivity of carbohydrate building blocks as a function of the substitution pattern on the carbohydrate ring. It maps how the combination of the building block reactivities (*i.e.*, the donor and acceptor that are connected in the glycosylation reaction) impacts the mechanism of the glycosylation reaction to shape the outcome of the reaction.

The chemical glycosylation reaction

The central reaction in glycochemistry is the glycosylation reaction, in which two – often expensive – building blocks are united to form more complex (oligo)saccharides. Insufficient knowledge of this reaction thwarts the routine assembly of these materials. In essence, the glycosylation reaction is a substitution reaction between a nucleophile and an electrophile. Figure 1 depicts the general mechanism for the glycosylation reaction, in which the first step consists of the activation of a donor molecule by a promotor system.[4,5,8,9] This activation leads to an array of reactive intermediates, including covalent species, which can undergo S_N2-like substitutions, while cationic intermediates can partake in S_N1-like reactions. The true S_N2- and S_N1-pathways can be found at the extremes of a substitution reaction mechanism continuum that fills the space between these two archetypal reaction mechanisms. Where along the continuum a given glycosylation reaction will take place is heavily influenced by the nature of both reaction partners, the acceptor (*i.e.*, nucleophile) and the donor (*i.e.*, electrophile). The configuration, conformation, and stereoelectronic effects of the ring substituents of both reactants are of all-importance to the reaction mechanism. External factors such as the temperature, concentration and solvent can also change the course of the glycosylation reaction.[2,7–9]

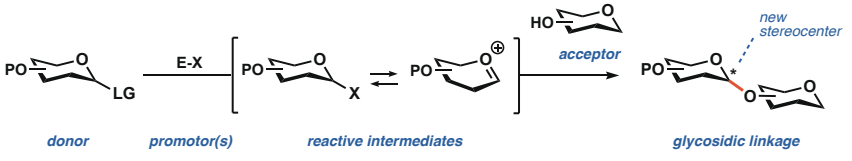


Figure 1. General overview of the glycosylation reaction. Glycosylation reactions are best considered as taking place at a continuum between two formal extremes of the mechanisms, the S_N1- and S_N2-mechanism.

Glycosyl cations: reactivity

Glycosyl cations, also known as oxocarbenium ions, are essential reactive intermediates in glycosylation reactions. These highly reactive intermediates have a short but significant lifetime in aqueous solution, while in less polar organic solvents these species are substantially less stable.[10] The stability of the glycosyl cation is influenced by the substituents present on the carbohydrate ring. Electron-withdrawing substituents (*e.g.* oxygen- or nitrogen-based) have a destabilizing effect on the glycosyl cation. The stability is also affected by the position and orientation of the substituent on the ring. The combined effect of all substituents on the ring determines the stability of the glycosyl cation. The stability of the glycosyl oxocarbenium ions translates to the reactivity of glycosyl donors. The functional groups on glycosyl donor molecules (most commonly hydroxyl and amino groups) are generally protected to reduce unwanted side reactions. It has long been known that the nature of the protecting groups can have a profound effect on the reaction rate and the stereochemical outcome of a glycosylation reaction. In 1982 the group of Paulsen noted that glycosyl halide donors carrying acyl protecting groups were significantly more stable than the corresponding alkylated donors.[11,12] Later, Fraser-Reid and co-workers

conceptualized this reactivity difference in the development of armed-disarmed glycosylation reactions (Figure 2A).[13–15] They showed that *O*-pentenyl glycosides that bear alkyl protecting groups can be selectively activated over *O*-pentenyl glycosides, featuring electron-withdrawing acyl groups. The electron-withdrawing effect of the acyl groups retards the development of positive charge at the anomeric center upon expulsion of the activated anomeric leaving group. The synthesis of trisaccharide **6** shows the applicability of the armed-disarmed concept. In the presence of disarmed pentenyl glycoside **2**, armed donor **1** selectively reacts with the mild activator, iodonium dicollidine perchlorate (IDCP) to furnish the pentenyl disaccharide. Changing the acyl protecting groups in the resulting disaccharide to benzyl ethers 'arms' the disaccharide setting the stage for a second IDCP mediated glycosylation reaction to deliver the trisaccharide.

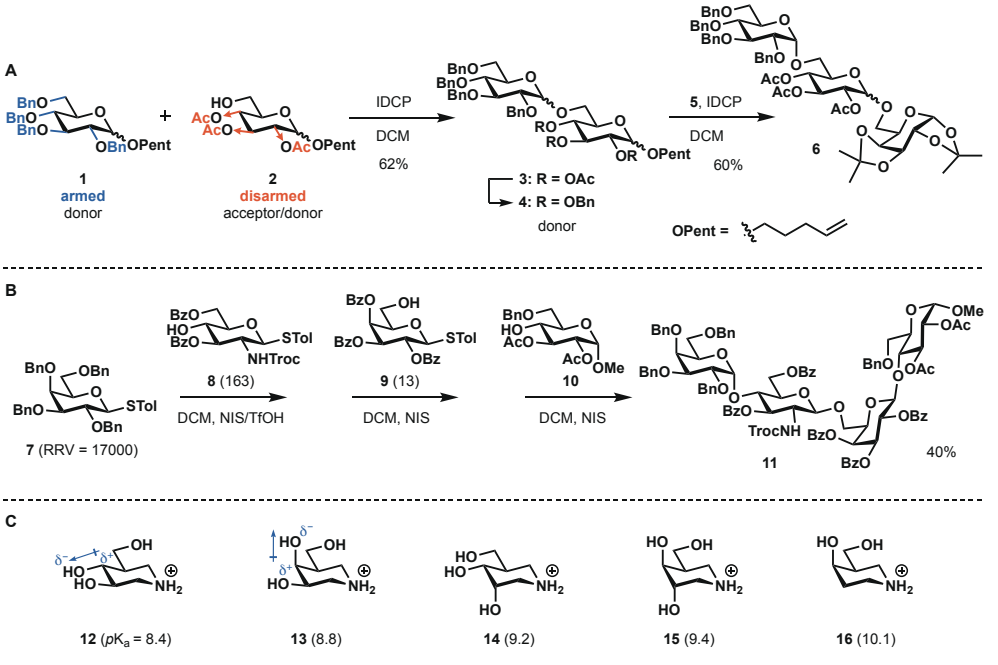


Figure 2. (A) Trisaccharide synthesis of the group Fraser-Reid using the armed-disarmed concept; (B) Tetrasaccharide synthesis of the group of Wong illustrating the continuum of reactivities of the donor molecules; (C) pK_a trends found for substituted piperidines by the group of Bols.

Later, it became apparent that the reactivity of donor glycosides should not be viewed as either armed or disarmed but rather as a continuum of reactivity, and that the nature of the protection groups, the configuration and type of carbohydrate donor all influence the reactivity. Ley and co-workers, followed closely by Wong and co-workers, set out to quantify donor reactivity using a broad range of donor glycosides. Wong and co-workers have compiled large donor reactivity data sets, showing relative donor reactivity to span over eight orders of magnitude. With these data, clear structure-reactivity relationships could be defined for these donors.[16–18] This has enabled the rational design of reactivity-based one-pot glycosylation strategies, an example of which is depicted in Figure 2B.

Galactosyl donor **7**, bearing solely benzyl ethers, has a relative reactivity value (RRV) of 17000, and can be activated selectively over trichloroethoxy carbamate protected glucosamine **8** (RRV = 163) using *N*-iodosuccinimide and triflic acid to provide the galactose-glucosamine disaccharide. Addition of galactose building block **9** (RRV = 13), and additional NIS than leads to the formation of the intermediate trisaccharide which can react with glucose acceptor **10** to deliver tetrasaccharide **11** in 40% yield.

The group of Bols has drawn the parallel between glycosyl donor reactivity and the pK_a-value of iminosugars (Figure 2C).[19,20] They found that the galactose configured iminosugar **13** is 0.4 pK_a units more basic compared to the corresponding gluco-configured piperidine **12**.[19] With a broad panel of different iminosugars they were able to relate the established pK_a-differences to differences in charge-dipole interactions of axially and equatorially oriented hydroxyl groups. They concluded that equatorially oriented hydroxyls are more electron withdrawing than their axially oriented counterparts.[21,22]

Glycosyl cations: stability, selectivity and shape

To investigate the influence of glycosyl substituents on the stereoselectivity of glycosylation reactions proceeding at the S_N1-side of the reaction continuum, the group of Woerpel has systematically studied *C*-glycosylation reactions of a set of furanosyl and pyranosyl donors.[23–32] Their studies in the furanose series are summarized in Figure 3A. They found that the alkoxy groups at the C2- and C3-position have a strong influence on the stereochemical outcome of the reaction, providing the *cis*-products, while the alkoxy group at the C5-position appears to have less effect on the stereoselective outcome.[23,25]

To account for these stereodirecting substituent effects, they devised a model (Figure 3B) that takes into account the equilibrium between two possible envelope oxocarbenium ion conformers (^3E and E_3).[25] In the ^3E and E_3 the flat C2-C1=O4$^+$-C4 system allows for stabilization of the electron depleted anomeric carbon by the C4-oxygen. Nucleophilic addition to these furanosyl cation conformers occurs from the 'inside' of the envelopes, which avoid unfavorable eclipsing interactions between the C1-*H* and the *pseudo*-equatorial substituent at the C2-position. Additionally, it also avoids unfavorable interaction between the incoming nucleophile and the axial C2-substituent.

The spatial orientation of the alkoxy groups influences the shape and stability of furanosyl cations. A *pseudo*-equatorial position of the C2-substituent enables hyperconjugative stabilization of the furanosyl cation by the *pseudo*-axially oriented C2-H2 bond (Figure 3C). Stabilization of the furanosyl cation featuring a C3-alkoxy group is achieved by placing the electronegative substituent in an axial fashion, thereby providing a stabilizing electrostatic interaction (Figure 3C). With these spatial substituent preferences, the stereochemical outcome of the *C*-glycosylation reactions in Figure 3A can be explained. Activation of the C2-benzyloxy furanosyl acetate **17** provides a furanosyl cation intermediate that preferentially adopts a ^3E conformation. Nucleophilic addition on this conformer takes place in an inside fashion that leads to the 1,2-*cis* product. By a similar mechanism, inside nucleophilic addition on the ^3E conformer of the C3-benzyloxy

furanosyl cation, derived from furanosyl acetate **18**, accounts for the stereochemical outcome of the *C*-glycosylation. The oxocarbenium ion derived from C4-benzyloxy protected **19** has no clear conformational preference, which results in a stereochemical mixture of products.

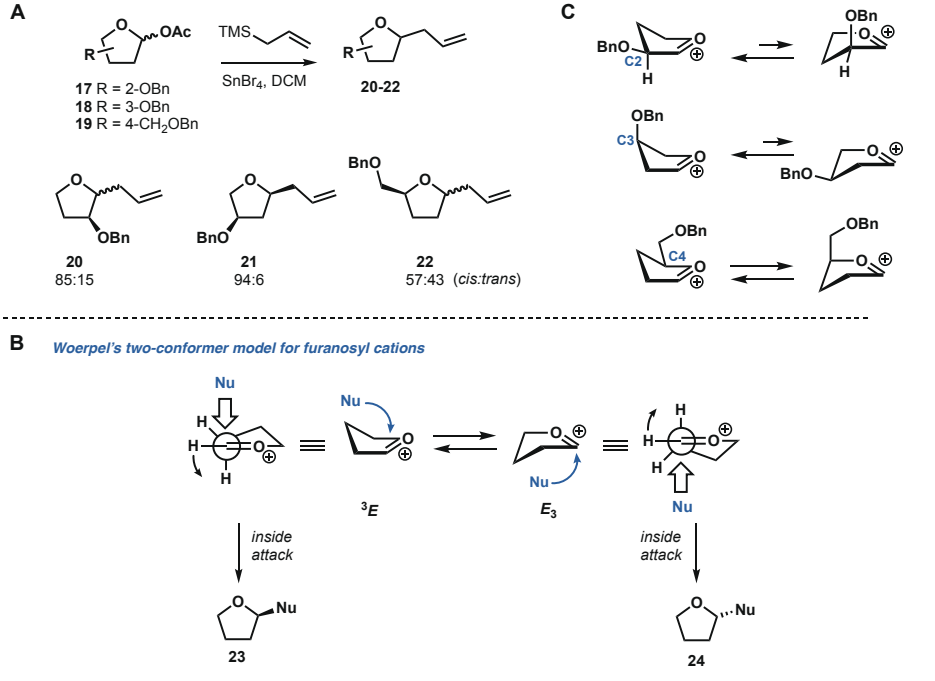


Figure 3. Stereochemical preference of furanosyl cations. (A) Stereochemical outcome of *C*-glycosylation of a set of mono-substituted furanosyl acetates, in which the *cis*:*trans* ratio is expressed as the relationship between the substituent and the coupled nucleophile; (B) Two-conformer model proposed by the group of Woerpel; (C) Conformational preference of mono-substituted furanosyl cations.

To analyze the combined effect of multiple substituents on the furanosyl cation, van Rijssel *et al.*[33–36] adopted a computational method, initially developed by Rhoad and co-workers.[37] This computational method calculates the energy of all furanosyl oxocarbenium ion conformers, which can be plotted on the pseudorotational circle introduced by Altona and Sundaralingam (Figure 4C). The conformational energy landscapes (CEL) of four fully decorated diastereoisomeric furanosyl oxocarbenium ions were generated, revealing the lowest energy conformers for the ribo-, arabino-, xylo- and lyxo-configured furanosyl oxocarbenium ions (Figure 4B). Based on the computed CEL maps, the stereoselectivity of S_N1-type glycosylation reactions of the four diastereoisomeric furanosyl acetates **25-28** could be explained (Figure 4A). All four furanosides reacted in a 1,2-*cis* selective fashion when activated by TMSOTf in the presence of triethylsilane-*d* (TES-*d*), and only xylofuranosyl acetate **27** provided some of the 1,2-*trans* product. The erosion of stereochemistry for the xylofuranosyl cation could be related to the relative stability of the ^3E furanosyl cation intermediate (ΔE = 1.0 kcal mol^{-1}).

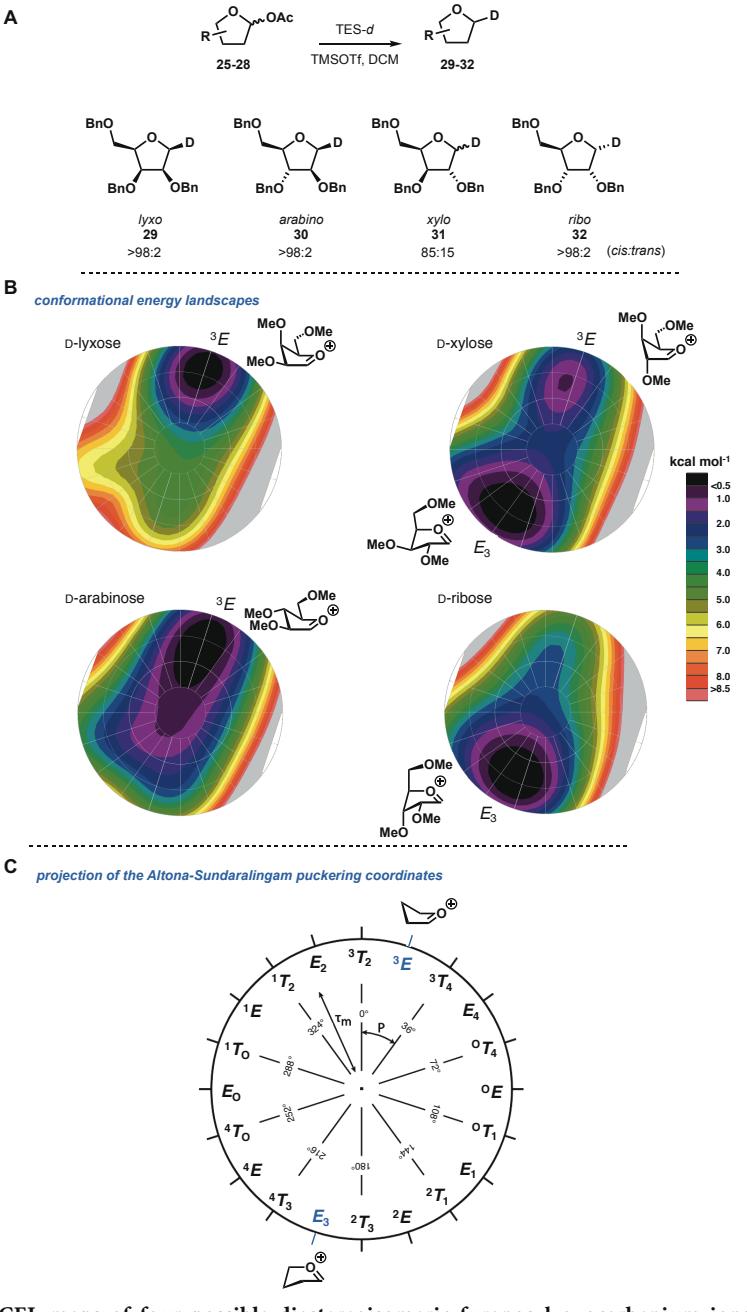


Figure 4. CEL maps of four possible diastereoisomeric furanosyl oxocarbenium ions and the diastereoselective reductions of furanosyl acetates. (A) Experimentally found stereoselectivities of model glycosylation reactions with TES-*d* as nucleophile; (B) CEL maps in which the local minima are shown. All energies are as computed at PCM(CH_2Cl_2)-B3LYP/6-311G(d,p) and expressed as the solution-phase electronic energy; (C) The pseudorotational circle describing the complete conformational space a five-membered ring can occupy. The pseudorotational phase angle (P) in combination with the puckering amplitude (τ_m) defines the ring conformation.

The above-described substituent effects can also be found in related, charged or strongly polarized six-membered ring systems, as illustrated in Figure 5.[38–40] Figure 5A depicts that an electronegative groups at C4 of a cyclohexanone takes up an axial position to maximize electrostatic stabilization of the electron poor ketone carbon, lowering the total energy of the system.[29,30,41,42] This is also the case for the glycosidase inhibitor depicted in Figure 5B, which adopts an "all-axial" conformer to maximize the electrostatic stabilization of the sulfonium cation.[43] Even though this introduces a significant amount of steric interactions, this is not sufficient to override the electrostatic stabilization. Substituents at a position next to an electron depleted carbon (*i.e.*, C2-position) will preferentially adopt an orientation to allow for optimal hyperconjugative stabilization (Figure 5C).[32,44] In cyclohexanone **37**-**38**, the C-F bond is a much weaker σ-donor than the C-H bond, and therefore the C-F is placed in a *pseudo*-equatorial position. In contrast, the C-I bond is a significantly stronger σ-donor than the C-H bond, and therefore C-2-iodo cyclohexanone **40**, having C-I bond in a *pseudo*-axial orientation, is more stable than conformer **39**.

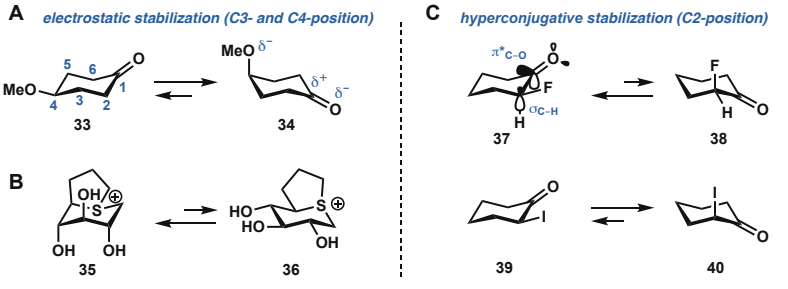


Figure 5. Electrostatic and hyperconjugative stabilization can have a dramatic effect on the conformational preferences of charged or strongly polarized six-membered rings. (A) Electronegative groups on the C3- and C4-position of cyclohexanone favor a *pseudo*-axial position; (B) Glycosidase inhibitor adopts an all-axial conformation as a result of stabilizing electrostatic interactions; (C) Hyperconjugation capacity gives rise to a clear conformational trend when comparing different halides present on the 2-position of cyclohexanones.

In parallel to the stereoelectronic substituent effects found in the 5-membered ring series, the group of Woerpel and others investigated 6-membered ring systems.[26–28,45,46] In line with the effects observed in the 5-membered ring series, the stability of these cations benefits from a *pseudo*-equatorial orientation of the alkoxy group on the C2-position (allowing for hyperconjugative stabilization by the $\sigma_{C2\text{-}H2}$ bond), and an axial orientation of the alkoxy groups on the C3- and C4-positions.[28] The alkoxymethylene group on the C5-position has a preference for an equatorial position for steric reasons.[26] The group of Woerpel reasoned that pyranosyl cations preferentially adopt a $^{3}H_{4}$ or $^{4}H_{3}$ half-chair structure to accommodate the flat C2-C1=O5^{+}-C5 oxocarbenium ion moiety (Figure 6B).[28] The addition reactions to these half-chair intermediates by incoming nucleophiles preferentially follow a trajectory that leads to a chair-like transition state. Thus, the addition to a $^{3}H_{4}$ half-chair occurs from the top-face, whereas addition to the opposite $^{4}H_{3}$ half-chair

leads to the bottom-face product. With the above described spatial substituent preferences and mode of nucleophilic addition, the stereochemical outcome in the *C*-glycosylation reactions shown in Figure 6A can be accounted for. The C2-OBn is *cis*-directing, where the C3-OBn forms in excellent selectivity the *cis*-product, and the C4-OBn forms exclusively the *trans*-product.

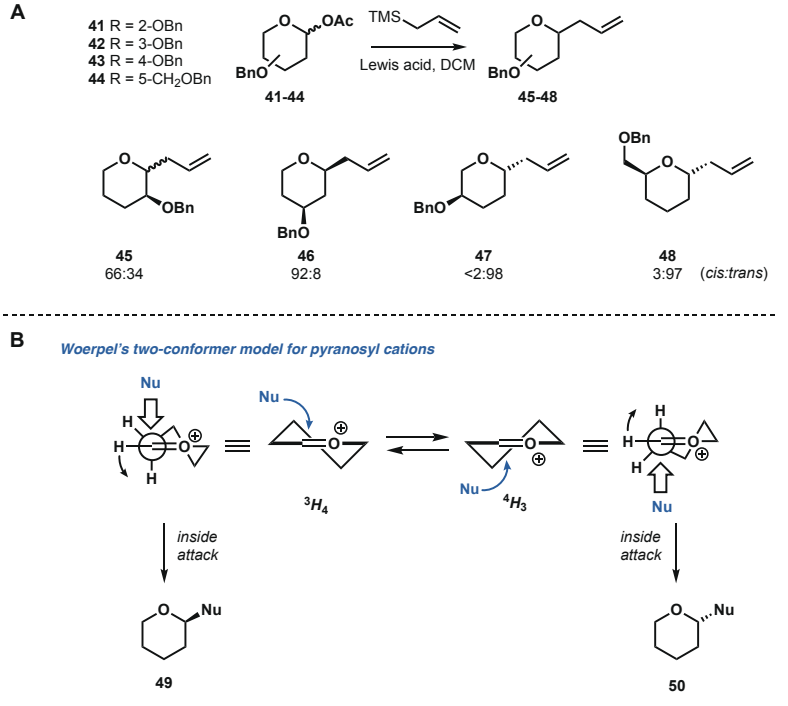


Figure 6. Stereochemical preference of pyranosyl cations. (A) Stereochemical outcome of *C*-glycosylations of a set of mono-substituted pyranosyl acetates, in which the *cis*:*trans* ratio is expressed as the relationship between the substituent and the coupled nucleophile; (B) Two-conformer model proposed by the group of Woerpel.

To accurately gauge the combined substituent effects on the conformational behavior, reactivity and stability of pyranosyl oxocarbenium ions, several computational studies have been undertaken (see Figure 7B).[47–53] The conformational space of pyranosyl oxocarbenium ion can be visualized by the use of the Cremer–Pople sphere (Figure 7C), and all possible conformations can be plotted on this "sphere". Whitfield and co-workers have investigated the conformational preference of tetra-*O*-methyl-gluco- and tetra-*O*-methyl-mannopyranosyl oxocarbenium ions (**59** and **60**) as well as their 4,6-*O*-benzylidene analogs (**61** and **62**). They studied the conformational behavior of the oxocarbenium ions, formed upon dissociation of the triflate leaving group.[50] In these studies a lithium cation was used to stabilize the anionic leaving group upon departure. These computations revealed that dissociation of the tetra-*O*-methyl gluco- and tetra-*O*-methyl-mannopyranosyl α-triflates initially provides the $^4H_3$ oxocarbenium ion for both pyranosides (Figure 7B).

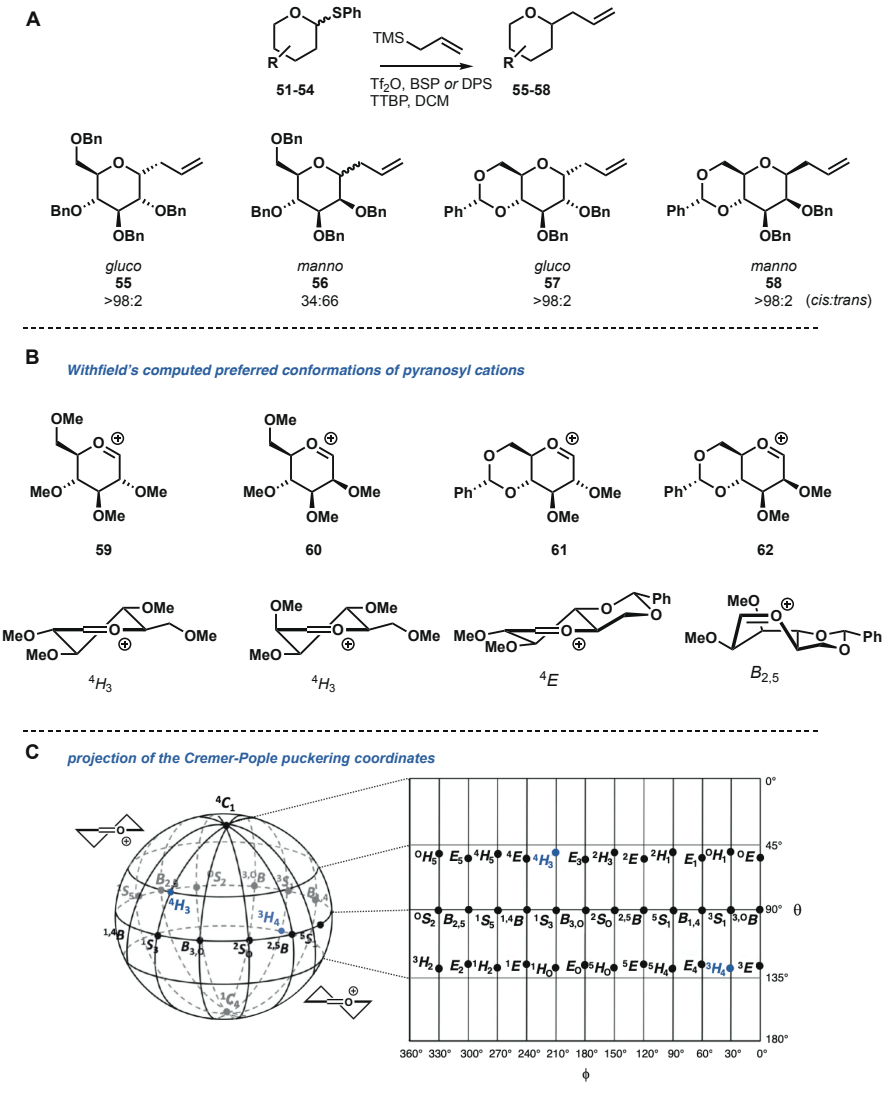


Figure 7. Computational data of selected pyranosyl oxocarbenium ions and the diastereoselective *C*-glycosylations of pyranosyl donors. (A) Experimentally found stereoselectivities for model glycosylation reactions with allyltrimethylsilane as nucleophile; (B) Selection of oxocarbenium ions and their computed solution-phase energies by density functional theory (DFT); (C) Cremer–Pople sphere which is a spherical representation describing all possible conformations a six-membered ring can adopt.

Dissociation of the triflate from the β-stereoisomers requires a conformational change, where the glucose and mannose pyranosyl rings distort to a $^{1}S_{3}$-like structure.[50] In this geometry, the anomeric leaving group can be dissociated by assistance of the ring oxygen leading to a ^{4}E (for the glucose case) or $^{4}H_{3}$ half chair (for the mannose case).

Similar itineraries have been established to be operational in glycosyl hydrolases. The group of Rovira has found for retaining glucosyl hydrolases, that hydrolysis of β-glucosides proceeds via a trajectory in which the substrate is first placed in a $^{1}S_{3}$ conformation which allows for dissociation of the aglycon.[54,55] After passing through a $^{4}H_{3}$-like transition state, the $^{4}C_{1}$ product (the covalent enzyme-glucose adduct) is formed. This catalytic itinerary was established using a combination of X-ray crystallography, free energy landscape mapping, and QM/MM simulations.

The Whitfield group showed that the 4,6-*O*-benzylidene glucose oxocarbenium ion **61** preferentially take up a ^{4}E conformer, while the corresponding benzylidene-mannose structure **62**, takes up a $B_{2,5}$ conformation.[50] In the latter structure, both the electrostatic interaction by the C3-OMe and hyperconjugative stabilization of the $\sigma_{C2\text{-}H2}$ bond contributes to the stability of the mannosyl cation. Based on the computed preferred conformations, the stereoselectivity of the *C*-glycosylation reactions of a set of glucosyl- and mannosyl donors (**51**-**54**) could be explained (Figure 7A).[45,56] The glucosyl derivatives (**51** and **53**) both form exclusively the 1,2-*cis* product, which could be explained by a bottom-face addition of the nucleophile to the $^{4}H_{3}$-like structure. For mannosyl donor **52** a 1,2-*trans* preference was found, which could be explained by a bottom-face addition on the $^{4}H_{3}$, while for mannosyl donor **54** a top-face addition on the $B_{2,5}$ structure results in exclusive formation of the 1,2-*cis* product.

Glycosyl cations: experimental observation

To date, many anomeric triflates, the reactive intermediates on the S_N2-side of the glycosylation reaction mechanism manifold, have been spectroscopically characterized by variable temperature NMR experiments. In contrast, the intrinsic high reactivity of glycosyl cations hampers their straightforward detection. The group of Woerpel have used pyranosyl dioxocarbenium ions (Figure 8A) as a stabilized analogue of the corresponding oxocarbenium ion.[30] They computed the expected conformational preference and correlated this with the experimentally determined $^{3}J_{H\text{-}H}$ NMR coupling constants. This supported the proposed axial preference of alkoxy-substituents at the C3- and the C4-position.

The group of Blériot reported the generation and spectroscopic investigation of glycosyl cations by the use of a superacid medium (*i.e.*, HF/SbF_5).[57,58] The cations, generated in this non-nucleophilic solvent proved to be stable for several hours at −40 °C in the superacid medium, which allowed the full characterization of these species. Figure 8B shows the conversion of 2-deoxy-glucosyl donor **65** into the glycosyl cation adopting a ^{4}E conformation. The conformation of the cation was deduced from the $^{3}J_{H\text{-}H}$ coupling constants and supported by DFT computations and simulated spectra. Trapping of the glycosyl cation **66** by cyclohexane-d_{12} resulted in the selective formation of an α-deuterated 2-deoxy-glucoside. The formation of this product can be accounted for using the found ^{4}E conformer, which forms the α-product through a chair-like bottom-face addition reaction.

Obviously, the solvent system used in these NMR experiments deviates significantly from the conditions used in normal glycosylation reactions, and therefore, care should be taken in the translation of the results obtained in the superacid medium. Nonetheless, this study has provided fundamental information on the conformational preference of glycosyl cations.

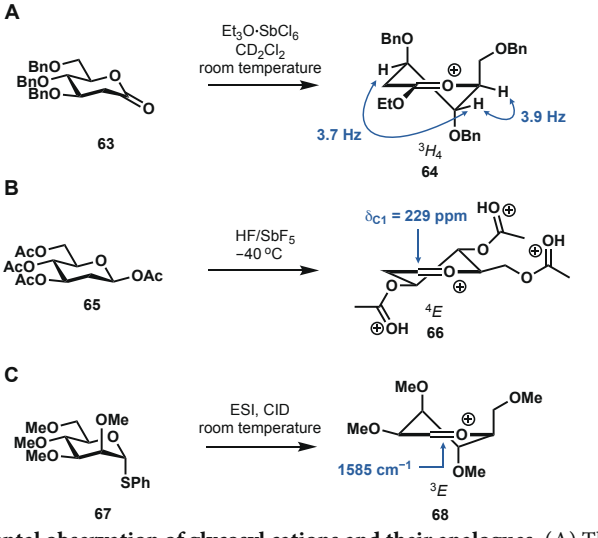


Figure 8. Experimental observation of glycosyl cations and their analogues. (A) The formation of a dioxocarbenium ion by treating a lacton with Meerwein's salt; (B) Generation of a 2-deoxy-glucosyl cation in HF/SbF_5; (C) The formation of a mannosyl cation by the use of collision induced dissociation tandem mass spectrometry.

Recently, also the groups of Boltje and Pagel reported on the formation and analysis of glycosyl oxocarbenium ions (Figure 8C).[59–61] They used collision induced dissociation tandem mass spectrometry, which generates glycosyl cations in the gas-phase followed by infrared ion spectroscopy. The experimentally observed IR spectra were compared with DFT computed spectra, enabling the detailed structural elucidation of the glycosyl cations. For mannose donor **67**, mannosyl cation **68** with a ^3E conformation was established. Also, with this method care should be taken in the translation of the results obtained in the gas-phase at room temperature to experimental glycosylation reactions taking place in an organic reaction medium, often at low temperatures.

Glycosyl cations: product-forming reactive intermediates

The group of Crich used kinetic isotope effect (KIE) experiments to generate proof for glycosyl cations as product-forming intermediates.[62,63] Using natural abundance ^{13}C primary KIEs, in combination with DFT calculations, they analyzed the amount of carbocation character that builds up in the transition state of the reactions shown in Figure 9A. The systems that were studied included glycosylations of 2-propanol with either a benzylidene protected mannosyl **69** or glycosyl donor **76**.[62] From the experimental and

computed KIE values, it was deduced that the β-mannosyl product was formed through an associative pathway, in which the S_N2-like transition state passes through a $B_{2,5}$ conformation. In contrast, the α-mannosyl product originated from a more dissociative mechanism, involving a mannosyl cation. The DFT calculations suggested a $^4E/^4H_3$-like conformation for the intermediate mannosyl cation.

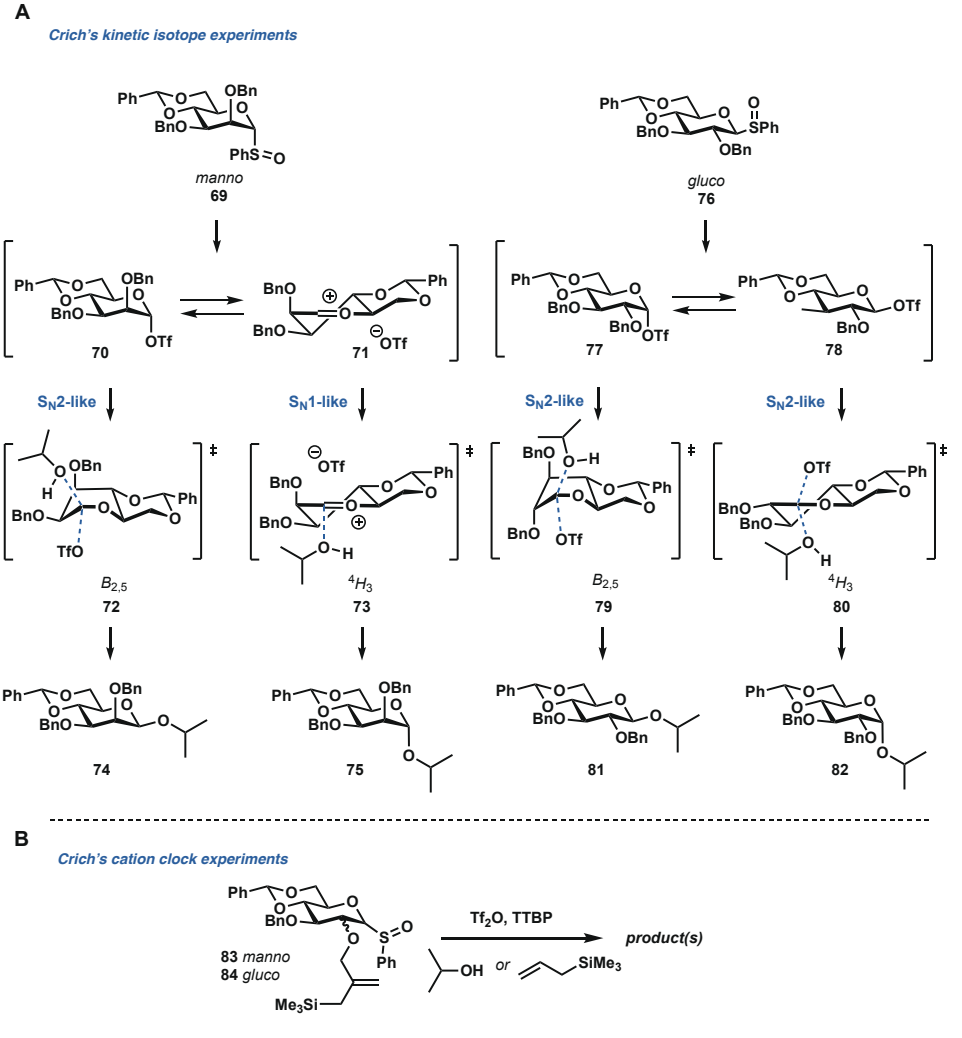


Figure 9. Product forming pathways for benzylidene mannosylations and glucosylations. (A) Reaction mechanistic results based on natural abundance ^{13}C primary kinetic isotope effects; (B) Reaction mechanistic results based on the cation clock method.

For the benzylidene glucose system, it was found that both the α- and β-products were formed through an associative S_N2-like mechanism.[62]

In parallel, the group of Crich developed cation clock methodology, which is shown in Figure 9B.[64,65] In this method external nucleophiles (*i.e.*, 2-propanol or allyltrimethylsilane) are used to compete with an intramolecular nucleophilic cyclization reaction. Using mannosyl and glucosyl donors **83** and **84**, they showed that the *O*-glycosylations are more concentration dependent than the *C*-glycosylation reactions.[64,65] Using this method, they found that the formation of the *O*-mannosyl α- and β-products results from different mechanistic pathways. For the α-product an S_N1-like pathway was found, while the β-products were formed through an S_N2-like pathway. When allyltrimethylsilane was employed as a nucleophile, only the β-*C*-allyl mannosyl and α-*C*-allyl glucosyl products were obtained in a reaction that was relatively independent of the concentration of the nucleophile, indicating the presence of significant S_N1-like character in these reactions.

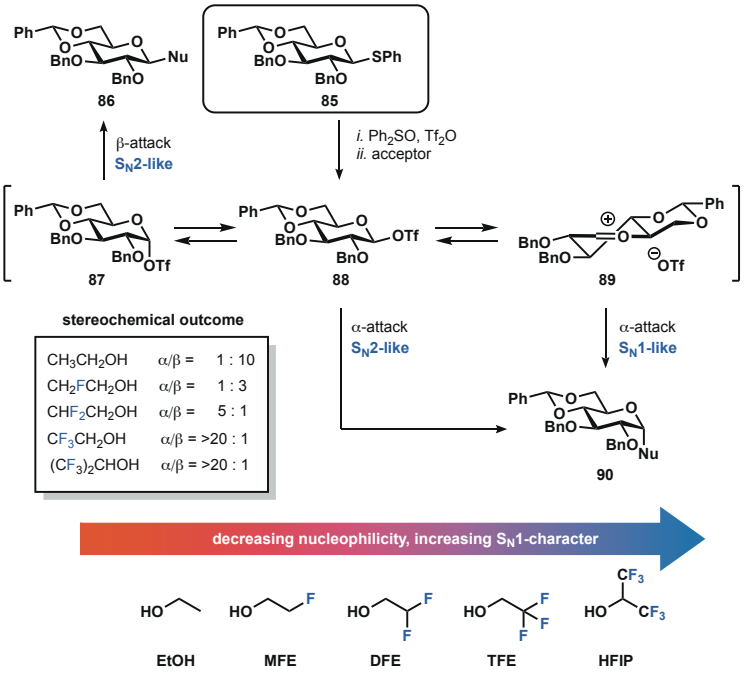


Figure 10. Found mechanistic continuum operational during the glycosylation of donor **73** with a set of model nucleophiles.

Van der Vorm *et al.* also provided evidence for the involvement of glycosyl cation-like species in *O*-glycosylation reactions (Figure 10).[45,46,66] They performed an array of glycosylation reactions with a set of model (fluorinated) alcohol nucleophiles (*i.e.*, EtOH, MFE, DFE, TFE and HFIP) of gradually decreasing nucleophilicity. This revealed that the stereoselectivity in glycosylations of benzylidene protected glucose donors are very

susceptible to acceptor nucleophilicity. Reactions of this donor proceeded with stereoselectivity, ranging from complete β-selectivity to the exclusively formation of the α-product (Figure 9). They related this reactivity-selectivity relationship to changes from an S_N2-type substitution of the covalent intermediate (*e.g.*, α-glycosyl triflate) for the most nucleophilic alcohols to reactions involving more oxocarbenium character for the poorest nucleophiles (*i.e.*, TFE and HFIP).

Summary and thesis outline

Glycosyl cations are essential reactive intermediates in glycosylation reactions. Although significant progress has been made in the field, studying these highly reactive intermediates remains a major challenge and lies at the forefront of current efforts to advance glycosylation knowledge. The research described in this thesis aims to gain more fundamental insight into the mechanisms of chemical glycosylation reactions and their reactive intermediates. Chapter 2 introduces a novel computational approach to study the shape of glycosyl cations as a function of their substitution pattern. More than 30 different glycosyl donors with varying substituents are evaluated. To connect the computational efforts to experimental results, all studied cations are subjected to a set of model S_N1-glycosylations. Selected glycosyl cations are also generated under superacid conditions, which allowed the direct observation of these highly reactive intermediates. Chapter 3 expands on Chapter 2 focusing on the transition state of the addition reaction between the glycosyl cation and the acceptor. Using typical S_N1-nucleophiles, it is found that the course of the addition reaction to some cations is very susceptible to the nature of the used nucleophile, with an opposite stereochemical outcome found for different nucleophiles. Using computational methods, Curtin-Hammett kinetic scenarios are dissected to account for the observed results. The subject of Chapter 4 covers the possible formation of dioxolenium ions through remote acyl groups present on donor molecules, which can result in long-range participation and steering of the stereochemical outcome of glycosylation reactions. This chapter reports an integrated approach, using infrared ion spectroscopy, DFT calculations and a systematic series of glycosylation reactions to probe these ions and their relevance for the glycosylation reaction. The research described in Chapter 5 implements the fundamental insight gained in the previous chapters in the assembly of a biologically relevant complex mycobacterial glycolipid, built up from (amongst others) rare and complex monosaccharides, featuring tertiary stereocenters. By using variable-temperature NMR, DFT computations, and model glycosylations, the rational design of caryophyllose acceptor and donor molecules with the desired properties was possible. This enabled the assemble of a fragment of the LOS-IV lipooligosaccharide and related shorter fragments, present in *Mycobacterium marinum*, a closely related bacterium to *Mycobacterium tuberculosis*. Chapter 6 provides a summary of the results described in this thesis, as well as an outlook for further investigations to unravel the details of the glycosylation mechanism.

References

(1) Seeberger, P. H.; Werz, D. B. Synthesis and Medical Applications of Oligosaccharides. *Nature* **2007**, *446* (7139), 1046–1051.

(2) A. V. Demchenko. *Handbook of Chemical Glycosylation: Advances in Stereoselectivity and Therapeutic Relevance*; Wiley, **2008**.

(3) Zhu, X.; Schmidt, R. R. New Principles for Glycoside-Bond Formation. *Angew. Chem. Int. Ed.* **2009**, *48* (11), 1900–1934.

(4) Bohé, L.; Crich, D. A Propos of Glycosyl Cations and the Mechanism of Chemical Glycosylation; the Current State of the Art. *Carbohydr. Res.* **2015**, *403*, 48–59.

(5) Bohé, L.; Crich, D. A Propos of Glycosyl Cations and the Mechanism of Chemical Glycosylation. *Comptes Rendus Chimie* **2011**, *14* (1), 3–16.

(6) Boltje, T. J.; Buskas, T.; Boons, G.-J. Opportunities and Challenges in Synthetic Oligosaccharide and Glycoconjugate Research. *Nat. Chem.* **2009**, *1* (8), 611–622.

(7) Nigudkar, S. S.; Demchenko, A. V. Stereocontrolled 1,2-*Cis* Glycosylation as the Driving Force of Progress in Synthetic Carbohydrate Chemistry. *Chem. Sci.* **2015**, *6* (5), 2687–2704.

(8) Adero, P. O.; Amarasekara, H.; Wen, P.; Bohé, L.; Crich, D. The Experimental Evidence in Support of Glycosylation Mechanisms at the S_N1–S_N2 Interface. *Chem. Rev.* **2018**, *118* (17), 8242–8284.

(9) Mydock, L. K.; Demchenko, A. V. Mechanism of Chemical *O*-Glycosylation: From Early Studies to Recent Discoveries. *Org. Biomol. Chem.* **2010**, *8* (3), 497–510.

(10) Amyes, T. L.; Jencks, W. P. Lifetimes of Oxocarbenium Ions in Aqueous Solution from Common Ion Inhibition of the Solvolysis of α-Azido Ethers by Added Azide Ion. *J. Am. Chem. Soc.* **1989**, *111* (20), 7888–7900.

(11) Paulsen, H. Advances in Selective Chemical Syntheses of Complex Oligosaccharides. *Angew. Chem. Int. Ed.* **1982**, *21* (3), 155–173.

(12) Paulsen, H. Fortschritte bei der selektiven chemischen Synthese komplexer Oligosaccharide. *Angew. Chem.* **1982**, *94* (3), 184–201.

(13) Fraser-Reid, B.; Udodong, U. E.; Wu, Z.; Ottosson, H.; Merritt, J. R.; Rao, C. S.; Roberts, C.; Madsen, R. *N*-Pentenyl Glycosides in Organic Chemistry: A Contemporary Example of Serendipity. *Synlett* **1992**, *1992* (12), 927–942.

(14) Mootoo, D. R.; Konradsson, Peter.; Udodong, Uko.; Fraser-Reid, Bert. Armed and Disarmed *N*-Pentenyl Glycosides in Saccharide Couplings Leading to Oligosaccharides. *J. Am. Chem. Soc.* **1988**, *110* (16), 5583–5584.

(15) Fraser-Reid, B.; Wu, Z.; Udodong, U. E.; Ottosson, H. Armed/Disarmed Effects in Glycosyl Donors: Rationalization and Sidetracking. *J. Org. Chem.* **1990**, *55* (25), 6068–6070.

(16) Zhang, Z.; Ollmann, I. R.; Ye, X.-S.; Wischnat, R.; Baasov, T.; Wong, C.-H. Programmable One-Pot Oligosaccharide Synthesis. *J. Am. Chem. Soc.* **1999**, *121* (4), 734–753.

(17) Mong, K.-K. T.; Wong, C.-H. Reactivity-Based One-Pot Synthesis of a Lewis Y Carbohydrate Hapten: A Colon–Rectal Cancer Antigen Determinant. *Angew. Chem.* **2002**, *114* (21), 4261–4264.

(18) Hsu, C.-H.; Hung, S.-C.; Wu, C.-Y.; Wong, C.-H. Toward Automated Oligosaccharide Synthesis. *Angew. Chem. Int. Ed.* **2011**, *50* (50), 11872–11923.

(19) Jensen, H. H.; Lyngbye, L.; Jensen, A.; Bols, M. Stereoelectronic Substituent Effects in Polyhydroxylated Piperidines and Hexahydropyridazines. *Chem. Eur. J.* **2002**, *8* (5), 1218–1226.

(20) Jensen, H. H.; Bols, M. Synthesis of 1-Azagalactofagomine, a Potent Galactosidase Inhibitor. *J. Chem. Soc., Perkin Trans. 1* **2001**, No. 8, 905–909.

(21) Pedersen, C. M.; Nordstrøm, L. U.; Bols, M. "Super Armed" Glycosyl Donors: Conformational Arming of Thioglycosides by Silylation. *J. Am. Chem. Soc.* **2007**, *129* (29), 9222–9235.

(22) Pedersen, C. M.; Marinescu, L. G.; Bols, M. Conformationally Armed Glycosyl Donors: Reactivity Quantification, New Donors and One Pot Reactions. *Chem. Commun.* **2008**, No. 21, 2465–2467.

(23) Larsen, C. H.; Ridgway, B. H.; Shaw, J. T.; Woerpel, K. A. A Stereoelectronic Model To Explain the Highly Stereoselective Reactions of Nucleophiles with Five-Membered-Ring Oxocarbenium Ions. *J. Am. Chem. Soc.* **1999**, *121* (51), 12208–12209.

(24) Shaw, J. T.; Woerpel, K. A. Divergent Diastereoselectivity in the Addition of Nucleophiles to Tetrahydrofuran-Derived Oxonium Ions. *Tetrahedron* **1999**, *55* (29), 8747–8756.

(25) Larsen, C. H.; Ridgway, B. H.; Shaw, J. T.; Smith, D. M.; Woerpel, K. A. Stereoselective *C*-Glycosylation Reactions of Ribose Derivatives: Electronic Effects of Five-Membered Ring Oxocarbenium Ions. *J. Am. Chem. Soc.* **2005**, *127* (31), 10879–10884.

(26) Lucero, C. G.; Woerpel, K. A. Stereoselective *C*-Glycosylation Reactions of Pyranoses: The Conformational Preference and Reactions of the Mannosyl Cation. *J. Org. Chem.* **2006**, *71* (7), 2641–2647.

(27) Romero, J. A. C.; Tabacco, S. A.; Woerpel, K. A. Stereochemical Reversal of Nucleophilic Substitution Reactions Depending upon Substituent: Reactions of Heteroatom-Substituted Six-Membered-Ring Oxocarbenium Ions through Pseudoaxial Conformers. *J. Am. Chem. Soc.* **2000**, *122* (1), 168–169.

(28) Ayala, L.; Lucero, C. G.; Romero, J. A. C.; Tabacco, S. A.; Woerpel, K. A. Stereochemistry of Nucleophilic Substitution Reactions Depending upon Substituent: Evidence for Electrostatic Stabilization of Pseudoaxial Conformers of Oxocarbenium Ions by Heteroatom Substituents. *J. Am. Chem. Soc.* **2003**, *125* (50), 15521–15528.

(29) Chamberland, S.; Ziller, J. W.; Woerpel, K. A. Structural Evidence That Alkoxy Substituents Adopt Electronically Preferred Pseudoaxial Orientations in Six-Membered Ring Dioxocarbenium Ions. *J. Am. Chem. Soc.* **2005**, *127* (15), 5322–5323.

(30) Yang, M. T.; Woerpel, K. A. The Effect of Electrostatic Interactions on Conformational Equilibria of Multiply Substituted Tetrahydropyran Oxocarbenium Ions. *J. Org. Chem.* **2009**, *74* (2), 545–553.

(31) Beaver, M. G.; Woerpel, K. A. Erosion of Stereochemical Control with Increasing Nucleophilicity: *O*-Glycosylation at the Diffusion Limit. *J. Org. Chem.* **2010**, *75* (4), 1107–1118.

(32) Billings, S. B.; Woerpel, K. A. Nucleophilic Substitution Reactions of Sulfur-Substituted Cyclohexanone Acetals: An Analysis of the Factors Controlling Stereoselectivity. *J. Org. Chem.* **2006**, *71* (14), 5171–5178.

(33) van Rijssel, E. R.; van Delft, P.; Lodder, G.; Overkleeft, H. S.; van der Marel, G. A.; Filippov, D. V.; Codée, J. D. C. Furanosyl Oxocarbenium Ion Stability and Stereoselectivity. *Angew. Chem. Int. Ed.* **2014**, *53* (39), 10381–10385.

(34) van Rijssel, E. R.; van Delft, P.; van Marle, D. V.; Bijvoets, S. M.; Lodder, G.; Overkleeft, H. S.; van der Marel, G. A.; Filippov, D. V.; Codée, J. D. C. Stereoselectivity in the Lewis Acid Mediated Reduction of Ketofuranoses. *J. Org. Chem.* **2015**, *80* (9), 4553–4565.

(35) Madern, J. M.; Hansen, T.; van Rijssel, E. R.; Kistemaker, H. A. V.; van der Vorm, S.; Overkleeft, H. S.; van der Marel, G. A.; Filippov, D. V.; Codée, J. D. C. Synthesis, Reactivity, and Stereoselectivity of 4-Thiofuranosides. *J. Org. Chem.* **2019**, *84* (3), 1218–1227.

(36) van der Vorm, S.; Hansen, T.; van Rijssel, E. R.; Dekkers, R.; Madern, J. M.; Overkleeft, H. S.; Filippov, D. V.; van der Marel, G. A.; Codée, J. D. C. Furanosyl Oxocarbenium Ion Conformational Energy Landscape Maps as a Tool to Study the Glycosylation Stereoselectivity of 2-Azidofuranoses, 2-Fluorofuranoses and Methyl Furanosyl Uronates. *Chem. Eur. J.* **2019**, *25* (29), 7149–7157.

(37) Rhoad, J. S.; Cagg, B. A.; Carver, P. W. Scanning the Potential Energy Surface of Furanosyl Oxocarbenium Ions: Models for Reactive Intermediates in Glycosylation Reactions. *J. Phys. Chem. A* **2010**, *114* (15), 5180–5186.

(38) Smith, D. M.; Woerpel, K. A. Electrostatic Interactions in Cations and Their Importance in Biology and Chemistry. *Org. Biomol. Chem.* **2006**, *4* (7), 1195–1201.

(39) Dibble, D. J.; Ziller, J. W.; Woerpel, K. A. Spectroscopic and X-Ray Crystallographic Evidence for Electrostatic Effects in 4-Substituted Cyclohexanone-Derived Hydrazones, Imines, and Corresponding Salts. *J. Org. Chem.* **2011**, *76* (19), 7706– 7719.

(40) Baghdasarian, G.; Woerpel, K. A. Electrostatic Effects on the Reactions of Cyclohexanone Oxocarbenium Ions. *J. Org. Chem.* **2006**, *71* (18), 6851–6858.

(41) Stolow, R. D.; Giants, T. W. Predominance of the Axial Conformation of 4-Methoxycyclohexanone. *J. Chem. Soc. D* **1971**, No. 11, 528–529.

(42) Baldry, K. W.; Gordon, M. H.; Hafter, R.; Robinson, M. J. T. Conformational Effects in Compounds with 6-Membered Rings—XI : Study of a Conformational Equilibrium in the Gas Phase and in Solvents Ranging from Non-Polar to Water: 4-Methoxycyclohexanone. *Tetrahedron* **1976**, *32* (21), 2589–2594.

(43) Szczepina, M. G.; Johnston, B. D.; Yuan, Y.; Svensson, B.; Pinto, B. M. Synthesis of Alkylated Deoxynojirimycin and 1,5-Dideoxy-1,5-Iminoxylitol Analogues: Polar Side-Chain Modification, Sulfonium and Selenonium Heteroatom Variants, Conformational Analysis, and Evaluation as Glycosidase Inhibitors. *J. Am. Chem. Soc.* **2004**, *126* (39), 12458–12469.

(44) Basso, E. A.; Kaiser, C.; Rittner, R.; Lambert, J. B. Axial/Equatorial Proportions for 2-Substituted Cyclohexanones. *J. Org. Chem.* **1993**, *58* (27), 7865–7869.

(45) Vorm, S. van der; Hansen, T.; Overkleeft, H. S.; Marel, G. A. van der; Codée, J. D. C. The Influence of Acceptor Nucleophilicity on the Glycosylation Reaction Mechanism. *Chem. Sci.* **2017**, *8* (3), 1867–1875.

(46) Hagen, B.; Ali, S.; Overkleeft, H. S.; van der Marel, G. A.; Codée, J. D. C. Mapping the Reactivity and Selectivity of 2-Azidofucosyl Donors for the Assembly of *N*-Acetylfucosamine-Containing Bacterial Oligosaccharides. *J. Org. Chem.* **2017**, *82* (2), 848–868.

(47) Hosoya, T.; Takano, T.; Kosma, P.; Rosenau, T. Theoretical Foundation for the Presence of Oxacarbenium Ions in Chemical Glycoside Synthesis. *J. Org. Chem.* **2014**, *79* (17), 7889–7894.

(48) Hosoya, T.; Kosma, P.; Rosenau, T. Contact Ion Pairs and Solvent-Separated Ion Pairs from D-Mannopyranosyl and D-Glucopyranosyl Triflates. *Carbohydr. Res.* **2015**, *401*, 127–131.

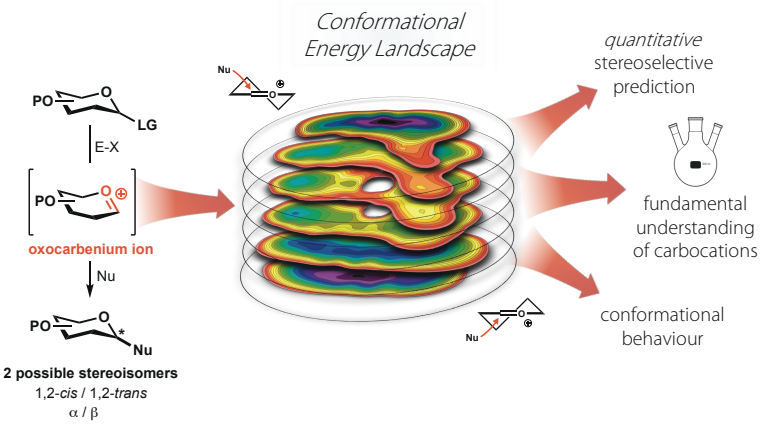
(49) Hosoya, T.; Kosma, P.; Rosenau, T. Theoretical Study on the Effects of a 4,6-*O*-Diacetal Protecting Group on the Stability of Ion Pairs from D-Mannopyranosyl and D-Glucopyranosyl Triflates. *Carbohydr. Res.* **2015**, *411*, 64–69.

(50) Whitfield, D. M. DFT Studies of the Ionization of Alpha and Beta Glycopyranosyl Donors. *Carbohydr. Res.* **2007**, *342* (12–13), 1726–1740.

(51) Whitfield, D. M. Plausible Transition States for Glycosylation Reactions. *Carbohydr. Res.* **2012**, *356*, 180–190.
(52) Whitfield, D. M. In a Glycosylation Reaction How Does a Hydroxylic Nucleophile Find the Activated Anomeric Carbon? *Carbohydr. Res.* **2015**, *403*, 69–89.
(53) Satoh, H.; Nukada, T. Computational Chemistry on Chemical Glycosylations. *Trends in Glycoscience and Glycotechnology* **2014**, *26* (147), 11–27.
(54) Ardèvol, A.; Biarnés, X.; Planas, A.; Rovira, C. The Conformational Free-Energy Landscape of β-D-Mannopyranose: Evidence for a $^{1}S_{5} \rightarrow B_{2,5} \rightarrow {}^{O}S_{2}$ Catalytic Itinerary in β-Mannosidases. *J. Am. Chem. Soc.* **2010**, *132* (45), 16058–16065.
(55) Davies, G. J.; Planas, A.; Rovira, C. Conformational Analyses of the Reaction Coordinate of Glycosidases. *Acc. Chem. Res.* **2012**, *45* (2), 308–316.
(56) Crich, D.; Sharma, I. Is Donor–Acceptor Hydrogen Bonding Necessary for 4,6-*O*-Benzylidene-Directed β-Mannopyranosylation? Stereoselective Synthesis of β-*C*-Mannopyranosides and α-*C*-Glucopyranosides. *Org. Lett.* **2008**, *10* (21), 4731–4734.
(57) Martin, A.; Arda, A.; Désiré, J.; Martin-Mingot, A.; Probst, N.; Sinaÿ, P.; Jiménez-Barbero, J.; Thibaudeau, S.; Blériot, Y. Catching Elusive Glycosyl Cations in a Condensed Phase with HF/SbF_5 Superacid. *Nat. Chem.* **2016**, *8* (2), 186–191.
(58) Lebedel, L.; Ardá, A.; Martin, A.; Désiré, J.; Mingot, A.; Aufiero, M.; Aiguabella Font, N.; Gilmour, R.; Jiménez-Barbero, J.; Blériot, Y.; Thibaudeau, S. Structural and Computational Analysis of 2-Halogeno-Glycosyl Cations in the Presence of a Superacid: An Expansive Platform. *Angew. Chem. Int. Ed.* **2019**, *58* (39), 13758–13762.
(59) Elferink, H.; Severijnen, M. E.; Martens, J.; Mensink, R. A.; Berden, G.; Oomens, J.; Rutjes, F. P. J. T.; Rijs, A. M.; Boltje, T. J. Direct Experimental Characterization of Glycosyl Cations by Infrared Ion Spectroscopy. *J. Am. Chem. Soc.* **2018**, *140* (19), 6034–6038.
(60) Elferink, H.; Mensink, R. A.; Castelijns, W. W. A.; Jansen, O.; Bruekers, J. P. J.; Martens, J.; Oomens, J.; Rijs, A. M.; Boltje, T. J. The Glycosylation Mechanisms of 6,3-Uronic Acid Lactones. *Angew. Chem. Int. Ed.* **2019**, *58* (26), 8746–8751.
(61) Mucha, E.; Marianski, M.; Xu, F.-F.; Thomas, D. A.; Meijer, G.; von Helden, G.; Seeberger, P. H.; Pagel, K. Unravelling the Structure of Glycosyl Cations via Cold-Ion Infrared Spectroscopy. *Nat. Commun.* **2018**, *9* (1), 1–5.
(62) Huang, M.; Garrett, G. E.; Birlirakis, N.; Bohé, L.; Pratt, D. A.; Crich, D. Dissecting the Mechanisms of a Class of Chemical Glycosylation Using Primary ^{13}C Kinetic Isotope Effects. *Nat. Chem.* **2012**, *4* (8), 663–667.
(63) Crich, D.; Chandrasekera, N. S. Mechanism of 4,6-*O*-Benzylidene-Directed β-Mannosylation as Determined by α-Deuterium Kinetic Isotope Effects. *Angew. Chem.* **2004**, *116* (40), 5500–5503.
(64) Adero, P. O.; Furukawa, T.; Huang, M.; Mukherjee, D.; Retailleau, P.; Bohé, L.; Crich, D. Cation Clock Reactions for the Determination of Relative Reaction Kinetics in Glycosylation Reactions: Applications to Gluco- and Mannopyranosyl Sulfoxide and Trichloroacetimidate Type Donors. *J. Am. Chem. Soc.* **2015**.
(65) Huang, M.; Retailleau, P.; Bohé, L.; Crich, D. Cation Clock Permits Distinction Between the Mechanisms of α- and β-*O*- and β-*C*-Glycosylation in the Mannopyranose Series: Evidence for the Existence of a Mannopyranosyl Oxocarbenium Ion. *J. Am. Chem. Soc.* **2012**, *134* (36), 14746–14749.
(66) Vorm, S. van der; Hansen, T.; Hengst, J. M. A. van; S. Overkleeft, H.; Marel, G. A. van der; C. Codée, J. D. Acceptor Reactivity in Glycosylation Reactions. *Chem. Soc. Rev.* **2019**, *48* (17), 4688–4706.

Chapter 2

Defining the S_N1 Side of Glycosylation Reactions: Stereoselectivity of Glycopyranosyl Cations



Abstract | The broad application of well-defined synthetic oligosaccharides in glycobiology and glycobiotechnology is largely hampered by the lack of sufficient amounts of synthetic carbohydrate specimens. Insufficient knowledge of the glycosylation reaction mechanism thwarts the routine assembly of these materials. Glycosyl cations are key reactive intermediates in the glycosylation reaction but their high reactivity and fleeting nature have precluded the determination of clear structure-reactivity-stereoselectivity principles for these species. This chapter describes a combined experimental and computational method that connects the stereoselectivity of oxocarbenium ions to the full ensemble of conformations these species can adopt, quantitatively mapped in conformational energy landscapes (CEL). The detailed description of stereoselective S_N1-type glycosylation reactions firmly establishes glycosyl cations as true reaction intermediates and will enable the generation of new stereoselective glycosylation methodologies.

Published | Hansen, T.; Lebedel, L.; Remmerswaal, W. A.; van der Vorm, S.; Wander, D. P. A.; Somers, M.; Overkleeft, H. S.; Filippov, D. V.; Désiré, J.; Mingot, A.; Bleriot, Y.; van der Marel, G. A.; Thibaudeau, S.; Codée, J. D. C. *ACS Central Science* **2019**, 5 (5), 781–788.

Introduction

Carbohydrates play numerous roles in living organisms, as key players in energy housekeeping, structural components, and signaling molecules. To unravel the role carbohydrates play in biological processes, well-defined single molecules are indispensable and organic synthesis has been one of the major suppliers for pure oligosaccharide specimens to fuel glycobiological and glycomedical research. Although significant progress has been made in the field, the generation of sufficient amounts of synthetic (complex) oligosaccharides remains a difficult and time-consuming undertaking.[1–5] The main obstacle in the construction of oligosaccharides is the stereoselective construction of 1,2-*cis*-glycosidic linkages.[6,7] While 1,2-*trans* linkages can be reliably installed using a neighboring group participation approach, there is no general solution for the construction of 1,2-*cis* linkages. Different reaction pathways can be followed during a glycosylation reaction and these can lead to different diastereomeric products. Figure 1 depicts the current understanding of the continuum of mechanisms that is operational during a glycosylation reaction.[8–10]

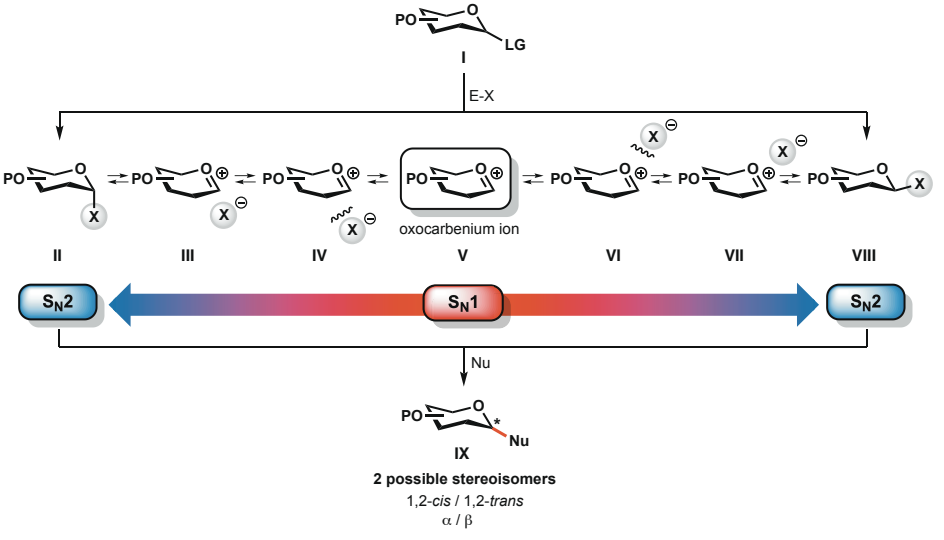


Figure 1. The reaction mechanism continuum operational during glycosylation reactions. Glycosylation reactions are best considered as taking place at a continuum between two formal extremes of an S_N1- and S_N2 mechanism; **I**: donor substrate; **II**: reactive covalent α-intermediate; **III**: contact ion pair, with the leaving group associated at the α-face; **IV**: solvent separated ion pair, with the leaving group that has departed from the α-face; **V**: solvent separated oxocarbenium ion; **VI**: solvent separated ion pair, with the leaving group that has departed from the β-face; **VII**: contact ion pair, with the leaving group associated at the β-face; **VIII**: reactive covalent β-intermediate; **IX**: addition product; LG = leaving group; P = protection group; E-X = promoter system; Nu = nucleophile.

The activation of a donor glycoside (**I**) leads to an array of reactive (electrophilic) intermediates (**II** – **VIII**), formed from the donor glycoside and the activator derived counterion. In case a participating group is present at the C2 (such as an *O*-acyl functionality) these reactive intermediates are intramolecularly trapped to provide a relatively stable dioxolenium ion, that is stereoselectively substituted from the opposite side of the ring to deliver the 1,2-*trans* glycoside product. In the absence of a C2-participation functionality, the situation is more complex and it has been proposed that both covalent reactive intermediates (**II** and **VIII**) and reactive oxocarbenium ion (like) species (**III** – **VII**) can be the product forming intermediates. The covalent intermediates on the S_N2-side of the reaction mechanism continuum can be studied using low-temperature NMR techniques and over the years hundreds of reactive intermediates (triflates, oxosulfonium ions, amongst others) have been characterized.[11–18] The substitution of these species with reactive nucleophiles (such as primary carbohydrate alcohols) defines the S_N2-side of the reaction mechanism continuum. In contrast, the oxocarbenium ions on the S_N1-side of the continuum remain ill-understood and the intermediacy of these species in glycosylation reactions is heavily debated.[19–36] Because the lifetime of these intermediates in conventional reaction media is extremely short, there is currently no (spectroscopic) technique available to study these species in a direct manner and assess their behavior.[37–39] It is clear that the substitution pattern on the carbohydrate ring plays an all-important role in determining the stability and reactivity of these species but it has been impossible to establish clear structure-reactivity-stereoselectivity relationships because of the conformational freedom and short life-time of these reactive intermediates in classical solutions. Thus, the course of S_N1-type glycosylation can at present not be properly understood (let alone predicted) leaving a major gap in the mechanistic conceptualization of glycosylation reactions.

To investigate the stability and reactivity of glycosyl oxocarbenium ions as product forming intermediates in glycosylation reactions, in this chapter the development of a computational method is reported that maps the stability of these species as a function of their overall shape. It is shown that the stereoselectivity of glycosylation reactions employing weak nucleophiles can be directly related to the conformational energy landscape (CEL) of the glycosyl oxocarbenium ions, as mapped *in silico*, and in doing so the S_N1-side of the glycosylation reaction mechanism continuum is defined. Direct spectroscopic evidence for the computed conformers is obtained by generation of the oxocarbenium ions under superacid conditions and it is revealed that fully substituted glycopyranosyl oxocarbenium ions react in a highly stereoselective 1,2-*cis* manner.

Results and discussion

The energy of glycopyranosyl oxocarbenium ions has been mapped as a function of their shape to understand the reactivity of these species following the strategy outlined in Figure 2. To generate the CEL maps, plotted on the Cremer-Pople sphere (a spherical representation describing all possible conformations a six-membered ring can adopt), a

suite of conformations was generated, by scanning the three dihedral angles (C1-C2-C3-C4, C3-C4-C5-O5, and C5-O5-C1-C2) from −60° to 60° in 15° increments, to fill the complete conformation space (Figure 2-1). The geometry of all these conformers was optimized and the associated energies computed by utilizing DFT as the level of theory, B3LYP as hybrid functional[40] and 6-311G(d,p) as the basis set. Solvation of CH_2Cl_2 was taken into account using a polarizable continuum model and energies are expressed in Gibbs free energy (For more information see Supplementary Information).[41] The energy landscapes were then generated by visualizing the relative energy in contour plots on "slices" of the pseudo rotational sphere.[42]

Inspection of the generated energy maps revealed that two families of structures are most relevant: the continuum of (^3E, $^3H_4$, E_4, and $B_{2,5}$)-like structures are grouped on the north-east side of the spheres and these form an ensemble of structures that are preferentially attacked from the top face. The 'opposite' family of structures, located on the south-west side of the sphere, is composed of the range of (^4E, $^4H_3$, E_3, and $^{2,5}B$)-like conformers, which are likely be approached by an incoming nucleophile from the bottom face (see Figure 2 and Supplementary Information).[20,43] The relative population of all conformational states can be calculated, based on their relative energies as computed above, utilizing the Boltzmann equation (see Supplementary for more information). Accordingly, the population of the top- and bottom face selective families was determined, which should be a measure for the relative stereoselectivity of addition reactions with weak nucleophiles to the glycosyl oxocarbenium ions.

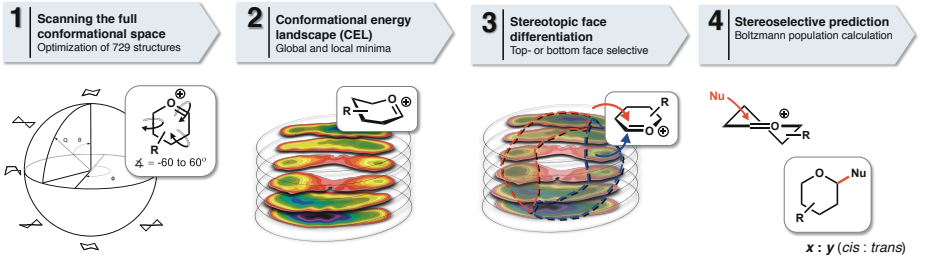


Figure 2. Overview of the workflow to map the conformational and stereoselective preference of pyranosyl oxocarbenium ions. (1) The complete conformational space of a six membered ring was scanned by computing 729 pre-fixed structures; A few canonical conformations (chair, half-chair, envelope and boat) are depicted; (2) The associated energies were graphed on slices dividing the Cremer-Pople sphere; (3) Top- and bottom face selective conformers lie in separate areas of the sphere. The family of top face-selective (^3E, $^3H_4$, E_4 and $B_{2,5}$)-like structures are found in the area contoured with the red dashed line, while the bottom face-selective family of (^4E, $^4H_3$, E_3, and $^{2,5}B$)-like conformers is found on the opposite side of the sphere, grouped within the blue dashed line; (4) Based on the Boltzmann distribution of the top- and bottom-face selective structures the stereochemical outcome of nucleophilic addition reactions to pyranosyl oxocarbenium ions can be computed.

To put this workflow to practice, a set of 13 mono-substituted pyranosyl oxocarbenium ions was investigated, differing in the nature of the substituent (BnO–, TBDPSO–, N_3–, F–, Cl–, Br–, I–, PhS–, MeS– and Me–) as well as the position on the ring. Their structures, the computed theoretical reaction stereoselectivity and the experimentally determined stereoselectivity obtained in reactions with classical S_N1-nucleophiles, triethylsilane-*d* (TES-*d*)[19,44–46] or allyltrimethyl silane (allyl-TMS), are summarized in Table 1 (Entry 1-13). The CEL maps (see Figure 3A for three representative examples, all other CEL maps are provided in Figures SI S3-S8) revealed that only a limited region of the full conformational space is accessible for the monosubstituted ions, in which local minima are found at both "poles", centered around the $^3H_4$- and the $^4H_3$-like conformations. Depending on the nature of the substituents, one of these families is favored, placing the substituent either axially or equatorially. At the C4-position, electronegative substituents (BnO–, F–, TBDPSO–, N_3–, Cl–, and Br–) favor an axial position to stabilize the oxocarbenium ion by through space electrostatic interactions, preferentially adopting the $^4H_3$-like conformation.[31,32,47–49] Decreasing electronegativity and increasing size of the substituent (I–, PhS–, MeS– and Me–) translates to a preference to adopt an equatorial position (*i.e.*, $^3H_4$-like conformations) to minimize steric interactions (Figure 3A). This trend is similar for substituents at the C3-position. An electronegative BnO-substituent at C2-position is preferentially placed in a *pseudo*-equatorial position as this enables the hyperconjugative stabilization of the oxocarbenium ion by the *pseudo*-axial C2-H2 bond. When the population of the conformational families, as revealed in the CEL maps, are translated to a calculated stereoselectivity and compared to the stereoselectivity obtained in the experiments[31,32,50] it becomes apparent that there is excellent agreement between theory and practice. Importantly, not only highly stereoselective glycosylations can be reliably predicted from the CEL maps, but also the condensation reactions that proceed with moderate selectivity (*e.g.*, Table 1, Entries 6, 7 and 13) are accurately matched by the computed data.

Next, CEL maps of multi-substituted pyranosyl oxocarbenium ions were generated and the theoretical stereoselectivity of these species computed. The results of these studies are summarized in the second half of Table 1 (Entry 14-32). A selection of CEL maps is depicted in Figure 3B (All CEL maps are provided in Figures SI S3-S9). Table 1 also reports the experimental stereoselectivity and yield of the reactions of the thioglycoside donors, obtained by pre-activation of the donors using the diphenyl sulfoxide (Ph_2SO)/triflic anhydride (Tf_2O) activator[51] and TES-*d* as the nucleophile.[52] Again, excellent agreement is found for the calculated and experimentally obtained stereoselectivity. The stereoselectivity of all these condensation reactions can now be traced back to the families of low-energy conformers of the oxocarbenium ions as revealed by the CEL maps. Some maps show a very localized energy minimum for a particular conformational family, such as the CEL map for the L-fucosyl oxocarbenium ion **19** (Figure 3B).

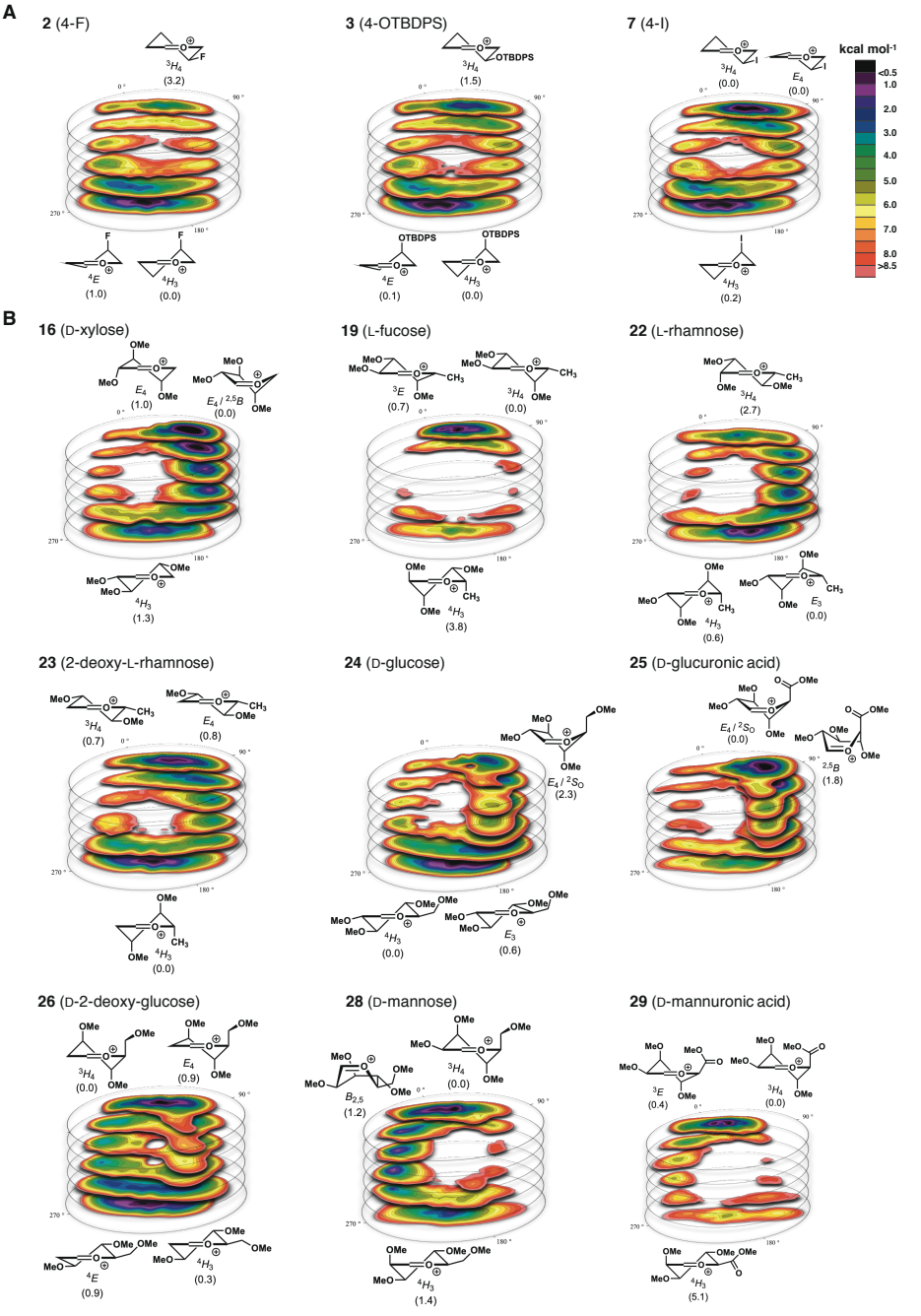


Figure 3. CEL maps of selected pyranosyl oxocarbenium ions in which the found local minima are indicated with their respective energy. (A) CEL map of mono-substituted-pyranosyl oxocarbenium ions **2**, **3** and **7**; (B) CEL map of multi-substituted-pyranosyl oxocarbenium ions **16**, **19**, **22**-**26** and **28**-**29**. All energies are computed at PCM(CH_2Cl_2)-B3LYP/6-311G(d,p) at T=213.15 K and expressed as solution-phase Gibbs free energy.

Table 1. Computed and experimentally found stereoselectivity for glycosylation reactions on mono- and multi-substituted pyranosyl oxocarbenium ions.[56] For the mono-substituted pyranosides (Entry 1-13) the *cis*:*trans* ratio is expressed as the relationship between the substituent and the coupled nucleophile; for the 2-deoxy-glycosides (Entry 17, 20, 23 and 32) the *cis*:*trans* ratio is expressed as the relationship between the substituent on C3-position and the coupled nucleophile; for the other glycopyranosides (Entry: 14-16, 18-19, 21-22 and 27-31) the *cis*:*trans* ratio is expressed as the relationship between the substituent on C2-position and the coupled nucleophile. The names in the table relate to the carbohydrate studied. For the computational studies, per-*O*-methylated oxocarbenium ions are used, where the experimental glycosylation use per-*O*-benzylated substrates.[57] Entries 1-13 are experimentally performed with allyl-TMS by the group Woerpel,[31,32] while Entries 14-32 are done with TES-*d*.

Entry	oxocarbenium ion	computed selectivity (*cis*:*trans*)	experimental selectivity (*cis*:*trans*)	yield (%)
1	**1** (4-OBn)	<2:98	<2:98	75
2	**2** (4-F)	<2:98	4:96	45
3	**3** (4-OTBDPS)	8:92	6:94	99
4	**4** (4-N_3)	12:88	12:88	95
5	**5** (4-Cl)	10:90	14:86	90
6	**6** (4-Br)	32:68	29:71	87
7	**7** (4-I)	73:27	72:28	90
8	**8** (4-SPh)	81:19	78:22	87
9	**9** (4-SMe)	88:12	84:16	75
10	**10** (4-Me)	95:5	94:6	74
11	**11** (3-OBn)	90:10	92:8	95
12	**12** (3-Me)	4:96	3:97	41
13	**13** (2-OBn)	66:34	66:34	85
14	**14** (D-lyxose)	>98:2	>98:2	81
15	**15** (D-arabinose)	>98:2	>98:2	79
16	**16** (D-xylose)	>98:2	>98:2	86
17	**17** (2-deoxy-D-xylose)	>98:2	>98:2	74
18	**18** (D-ribose)	>98:2	>98:2	69
19	**19** (L-fucose)	>98:2	>98:2	74
20	**20** (2-deoxy-L-fucose)	<2:98	<2:98	89
21	**21** (2-azido-L-fucose)	>98:2	>98:2	65
22	**22** (L-rhamnose)	>98:2	>98:2	79
23	**23** (2-deoxy-L-rhamnose)	71:29	66:34	96
24	**24** (D-glucose)	>98:2	>98:2	70
25	**25** (D-glucuronic acid)	>98:2	>98:2	43
26	**26** (2-deoxy-D-glucose)	52:48	52:48	76
27	**27** (2-azido-D-glucose)	>98:2	>98:2	52
28	**28** (D-mannose)	97:3	97:3	93
29	**29** (D-mannuronic-acid)	>98:2	>98:2	76
30	**30** (2-azido-D-mannuronic-acid)	>98:2	>98:2	53
31	**31** (D-galactose)	>98:2	>98:2	86
32	**32** (2-deoxy-D-galactose)	<2:98	<2:98	91

In the most favorable $^{3}H_{4}$-, ^{3}E- and E_{4}-like conformations of this ion, the ring substituents at C2 and C4 take up an electronically favorable orientation, leading to the localized energy minimum around the $^{3}H_{4}$-pole. Nucleophilic addition to these conformers stereoselectivity provides the 1,2-*cis*-linked products and the generated CEL map thus provides an explanation for the high 1,2-*cis*-selectivity generally observed with fucosyl donors.[53–55]

Similarly, the mannosyl oxocarbenium ion **28** can place its C2, C3 and C4 substituents in stabilizing positions when adopting a $^{3}H_{4}/^{3}E$-like structure (Figure 3B) as alluded to by Woerpel and co-workers.[24] These structures are selectively substituted from the top face to provide the β-mannosyl product, a result that is indeed born out in the glycosylation experiment (Table 1, Entry 28). Glycosylations of mannuronic acid ester **29** proceed with exceptional 1,2-*cis* stereoselectivity and the generated CEL map (Figure 3B) provides an adequate explanation for this reaction outcome as a very localized energy minimum is determined for the $^{3}H_{4}$-like conformational family. The additional stabilization from the axial C5-CO_2Me in **29** with respect to the axial C5-CH_2OMe group in the mannosyl oxocarbenium ion (**28**) becomes very clear from the comparison of the CEL maps of **28** and **29**.

The CEL maps of pyranosyl oxocarbenium ions bearing substituents, that have "conflicting positional interests" reveal that non-canonical conformations can become important and that broader conformational families or families around the different poles can become equally relevant. For example, the D-xylosyl oxocarbenium ion **16** preferentially adopts a non-canonical flattened (skew)-boat-like structure (see Figure 3B). The CEL map for the 2-deoxy-L-rhamnose ion **23** reveals two conformational families of similar energy, leading to a mixture of α- and β-products in the condensation reaction (Table 1, Entry 23). The CEL maps in the *gluco*-series illustrate how point mutations in the structure of the parent donor translate to differently shaped oxocarbenium ions and a different stereochemical outcome in the glycosylation reactions. The glucopyranosyl cation **24** is most stable when adopting a $^{4}H_{3}/E_{3}$-like shape, while its glucuronic acid counterpart (**25**), bearing a C5-carboxylic acid ester prefers to adopt a structure in between the $E_{4}/^{2}S_{O}$-conformations. Both ions are preferentially attacked from the bottom face to selectively provide the α-product (Table 1, Entry 24 and 25). For 2-deoxyglucose **26**, two families of oxocarbenium ion conformers are equally stable and the populations of $^{4}H_{3}/^{4}E$-like and $^{3}H_{4}/E_{4}$-like states point to an unselective addition reaction leading to the formation of α- and β-products in almost equal amounts. Overall, there is excellent agreement between the calculated and experimentally established α/β-selectivity of the multi-substituted glycosides, providing very compelling evidence for (families of) glycopyranosyl oxocarbenium ion conformers as product forming intermediates in the substitution reactions, thereby defining the S_N1-side of the glycosylation reaction mechanism manifold.

To obtain direct experimental support for the conformations computed using the CEL mapping method two 2-deoxy diacetylated oxocarbenium ions derived from L-fucose **33** and L-rhamnose **34** were studied in "non-nucleophilic" super acidic media (Figure 4A).[37]

The choice of acetyl groups and a 2-deoxy position is guided by the fact that methoxy groups are prone to elimination and the presence of a C2-substituent results in by-products. As the acetyl groups at C3- and C4-position of the oxocarbenium ions generated from donors **33** and **34** will be protonated under the superacid conditions used, polycationic oxocarbenium ions **35** and **36** were subjected to the CEL mapping method. The CEL map for 2-deoxy-fucosyl oxocarbenium ion **35** (Figure 4C) shows a strong preference for the $^3H_4$ and closely related E_4 conformations. The CEL map for the 2-deoxy-rhamnosyl oxocarbenium ion **36**, on the other hand, features multiple local minima and both the $^3H_4$ and the $^4H_3$-family are relatively low in energy resulting in a conformational mixture in solution. In parallel, 2-deoxy-L-fucose and 2-deoxy-L-rhamnose acetates **33** and **34** were dissolved in HF/SbF_5 to generate the polycationic structures **35** and **36**, of which the NMR spectra (Figure 4B) clearly indicated the presence of an oxocarbenium ion as the main species (carboxonium signal **35**: δ_{C1} = 224.2 ppm and δ_{H1} = 8.76 ppm; **36**: δ_{C1} = 223.4 ppm and δ_{H1} = 8.84 ppm).[37,58]

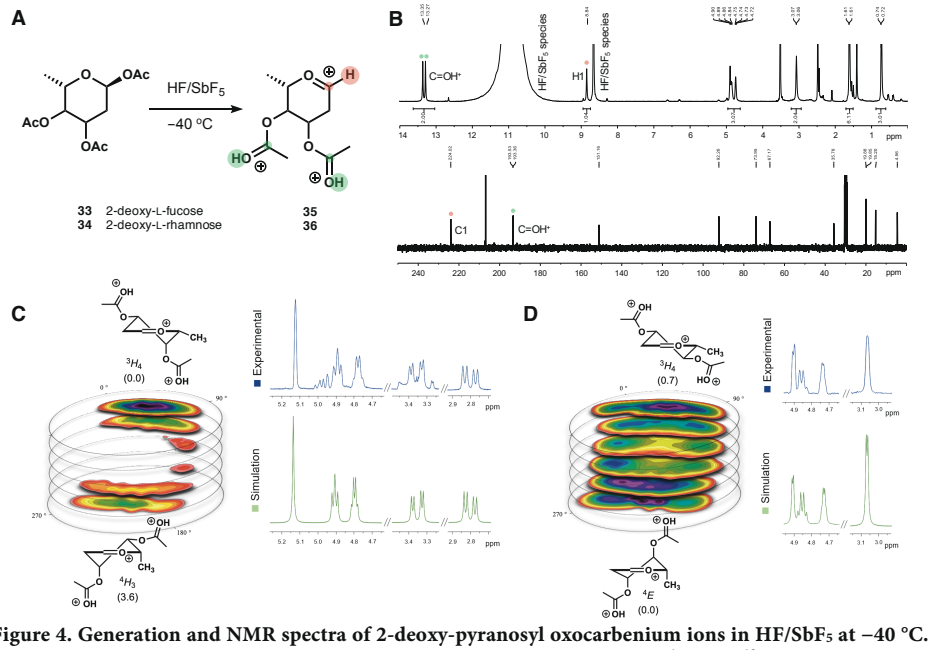


Figure 4. Generation and NMR spectra of 2-deoxy-pyranosyl oxocarbenium ions in HF/SbF_5 at −40 °C. (A) Generation of oxocarbenium ion **35** and **36** in HF/SbF_5; (B) Experimental ^{1}H- and ^{13}C DEPT NMR of 2-deoxy-L-rhamnose oxocarbenium **36**; (C) The generated ^{1}H-NMR spectrum of the oxocarbenium **35** compared to the simulated spectrum based on the computed CEL; (D) The generated ^{1}H-NMR spectrum of the oxocarbenium **36** compared to the simulated spectrum based on the computed CEL.

Both ester groups were indeed protonated as revealed by the presence of two proton singlets at δ_H = 13.28 ppm and 13.35 ppm). Because of the sufficient lifespan of **35** and **36** in the superacid media, full conformational characterization of these species could be

performed (see SI for more information). The coupling constants of the ring protons of **35** indicate that it adopts a $^{3}H_{4}$-like conformation. The NMR spectrum of 2-deoxy-L-rhamnosyl oxocarbenium **36** (Figure 4D) on the other hand showed significant line broadening as a result of the conformational flexibility of this species. Using the relevant conformations, obtained from the CEL maps for these ions, the NMR spectrum was reconstituted using the Boltzmann weighted averaged coupling constants of ions **35** and **36**. Perfect agreement between the experimental NMR spectra for these per-*O*-acetylated polyprotonated glycosyl cations and their simulated spectra show that the conformational dynamics of these ions are well captured by the CEL mapping method.

Conclusion

In conclusion, this chapter has benchmarked the S_N1-side of the glycosylation reaction mechanism. The stability, reactivity and conformational mobility of glycosyl oxocarbenium ions can be fully understood by mapping the complete conformational energy landscape of these ions and the preference of the cations can be directly related to the experimental stereochemical outcome of addition reactions to these. The maps show in detail how the stereoelectronic effects of various ring substituents (halogens, chalcogens, azides, and carbon-based substituents) determine the overall shape of the cations and thereby the stereochemical course of the reactions. In addition, the simulated NMR spectra of selected ions, reconstituted by using the Boltzmann weighted averaged coupling constants determined by the CEL mapping method, perfectly fit with the experimental ones observed by low-temperature NMR in superacid. Where glycosyl oxocarbenium ions were previously thought to be at the basis of non-selective coupling reactions because of their high reactivity, this chapter shows that these species – including the ions derived from L-fucose, L-rhamnose, D-glucose, D-mannose and D-galactose – have an intrinsic preference to generate the challenging 1,2-*cis*-linkages. This will enable the stereoselective synthesis of *C*-glycosides and open up new avenues to develop stereoselective *O*-glycosylation reactions.[59] The mechanistic insight offered here will be instrumental in the interpretation of future glycosylation results and serve as the basis to further explore the glycosylation reaction mechanism. The uncovered stereoelectronic substituent effects will be relevant in many other transformations involving carbocationic intermediates, and the strategy developed to grasp the full conformational space of these flexible intermediates can be a blueprint for the study of other flexible reactive intermediates.

Supporting information

DFT calculations

General procedure I: conformational energy landscape calculation of glycosyl cations • To keep the calculation time manageable, the *O*-Bn protection groups were substituted with electronically comparable smaller groups (*i.e.*, *O*-Me). The initial structure for the conformational energy landscape (CEL) was optimized by starting from a 'conformer distribution search' option included in the Spartan 10 program by utilizing DFT as the level of theory and the hybrid functional B3LYP in gas phase with 6-31G(d) as the basis set. All generated gas-phase geometries were re-optimized with Gaussian 09 rev D.01 by using B3LYP/6-311G(d,p), after which a vibrational analysis was computed to obtain the thermodynamic properties. The gas-phase structures were then solvated by using the PCM implicit solvation model, with CH_2Cl_2 as solvent (or in selected cases Et_2O or MeCN). Solvent effects were explicitly used in solving the SCF equations and during the optimization of the geometry. For heavy elements, including iodine, a combination of LANL2DZ and 6-311G(d,p) was used as basis set by utilizing the keyword "genecp". The geometry with the lowest solvated energy was selected as the starting point for the CEL map. A complete survey of the possible conformational space was done by scanning three dihedral angles ranging from –60° to 60°, including the C1-C2-C3-C4 (D1), C3-C4-C5-O (D3) and C5-O-C1-C2 (D5). The resolution of this survey is determined by the step size which was set to 15° per puckering parameter, giving a total of 729 pre-fixed conformations per six-membered oxocarbenium ion spanning the entire conformational landscape. All other internal coordinates were unconstrained. With the exception of a C2-substituent being present on the oxocarbenium ring of interest, then the C2-H2 bond length was fixed based on the optimized structure to counteract rearrangements occurring for higher energy conformers. The 729 structures were computed with Gaussian 09 rev D.01 again with a two-step procedure. First, the structures were optimized in the gas-phase with B3LYP/6-311G(d,p), after which a vibrational analysis was computed to obtain the thermodynamic properties. The gas-phase structures were then solvated by using the PCM implicit solvation model, with CH_2Cl_2 as solvent (or in selected cases Et_2O or MeCN). Solvent effects were explicitly used in solving the SCF equations and during the optimization of the geometry. For pyranosyl oxocarbenium ions bearing a C5-C6 substituent, three staggered rotamers (*i.e.*, *gg*, *gt*, *tg*) of the O5-C5-C6-O6 dihedral angle (*i.e.*, –65°, 65°, 175°) were considered. Earlier work showed the importance of these rotamers and their crucial impact on the selectivity and reactivity of the ion.[60] The CEL maps were computed separately and the starting geometry was obtained from the method described above in which the lowest, ZPE corrected, solvated energy generated rotamers were used. The three C5-C6 bond rotamers (not constrained) bring the total conformations for each pyranosyl oxocarbenium ion configuration to 2187 geometries. The final denoted free Gibbs energy was calculated using Equation S1 in which ΔE_{gas} is the gas-phase energy (electronic energy), $\Delta G^{T}_{gas,QH}$ (T = reaction temperature and p = 1 atm.) is the sum of corrections from the electronic energy to free Gibbs energy in the quasi-harmonic oscillator approximation also including zero-point energy (ZPE), and ΔG_{solv} is their corresponding free solvation Gibbs energy. The $\Delta G^{T}_{gas,QH}$ were computed using the quasi-harmonic approximation in the gas phase according to the work of Truhlar.[61]

$$\Delta G^{T}_{CH_2Cl_2} = \Delta E_{gas} + \Delta G^{T}_{gas,QH} + \Delta G_{solv} \qquad \text{(Eq. S1)}$$

$$= \Delta G^{T}_{gas} + \Delta G_{solv}$$

The quasi-harmonic approximation is the same as the harmonic oscillator approximation except that vibrational frequencies lower than 100 cm^{-1} were raised to 100 cm^{-1} as a way to correct for the breakdown of the harmonic oscillator model for the free energies of low-frequency vibrational modes. All optimized structures were checked for the absence of imaginary frequencies. To visualize the energy levels of the conformers on the Cremer-Pople sphere, slices were generated dissecting the sphere that combine closely associated conformers (Figure S1). The OriginPro software was employed to produce the energy heat maps, contoured at 0.5 kcal mol^{-1}. For ease of visualization, the Cremer-Pople globe is turned 180° with respect to its common representation and both poles (*i.e.*, the $^4C_1$ and $^1C_4$ structures) are omitted as these conformations are very high in energy. Visualization of conformations of interest was done with CYLview.

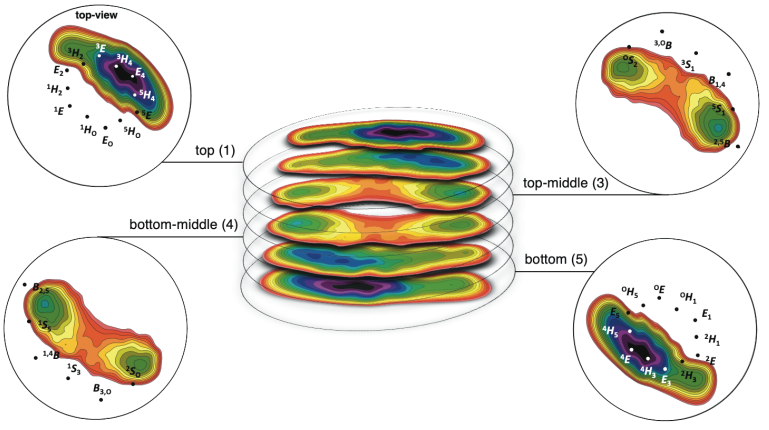


Figure S1. "Deconvolution" of the CEL map showing a top view of the most important slices that have been combined to generate the full CEL map.

General procedure II: stereochemical preference based on the computed CEL • To convert the relative energies of the continuum of conformers into the stereoselectivity of reactions the Boltzmann equation was used (Equation S2). The temperature used in the Boltzmann equation was equal to the reaction temperature. Inspection of the generated conformational energy maps led to the realization that two families of structures are most relevant: the continuum of (^3E, $^3H_4$, E_4 and $B_{2,5}$)-like structures and the 'opposite' family of structures, composed of the range of (E_3, $^4H_3$, ^4E and $^{2,5}B$)-like conformers.

$$\frac{N_i}{N_{total}} = \frac{e^{-E_{rel}/RT}}{\sum_{k=1}^{N_{total}} e^{-E_k/RT}} \qquad \text{(Eq. S2)}$$

To discriminate both families, a selection criterion was set to separate both conformational families. This selection was based on the H2$_{a/b}$-C2-C1-O5 dihedral angle of the oxocarbenium of interest (Figure S2). For the top-half of the CEL map, conformations with an H2$_a$-C2-C1-O5 angle larger than 105° were regarded as top face-selective, while a smaller angle was considered as bottom face-selective and vice versa for the bottom of the CEL map, but with the H2$_b$-C2-C1-O5 dihedral angle. This yields a top face- and bottom face-selective group with a corresponding fractional population, which was considered as the computed stereoselectivity of the computed oxocarbenium. Only calculated structures with a relative energy of < 5 kcal mol^{-1} were taken into account for calculating the Boltzmann distribution.

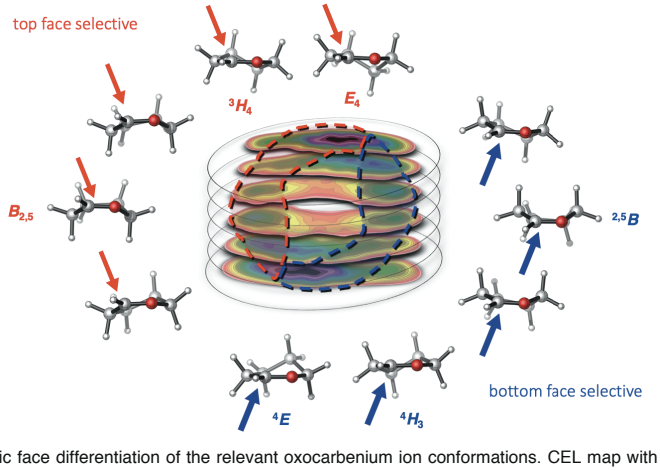


Figure S2. Stereotopic face differentiation of the relevant oxocarbenium ion conformations. CEL map with marked areas for the top- and bottom face-selective family of conformations.

General procedure III: simulation of NMR spectra based on the computed CEL map • To convert the relative energies of the continuum of conformers into simulated NMR spectra the Boltzmann equation was used (Equation S2). Based on all relevant geometries ($\Delta G^{T}_{gas/solution}$ < 2 kcal mol^{-1}) the spin-spin coupling constants were calculated according to the work of Rablen and Bally with the use of 6-311g(d,p) u+1s as basis set and a scaling factor of 0.92.[62] The computed total nuclear spin-spin coupling terms were used as calculated spin-spin coupling constants. Spectra were simulated with the use of MestReNova 9 with a line width of 4.0 Hz. The used chemical shift in the simulated spectra was acquired from the experimental spectra.

CEL maps • All CEL maps that are described in this chapter are summarized in the following section. The displayed CEL maps are based on the $\Delta G^{T}_{gas/solution}$ and relevant structures are added with their respective relative energy.

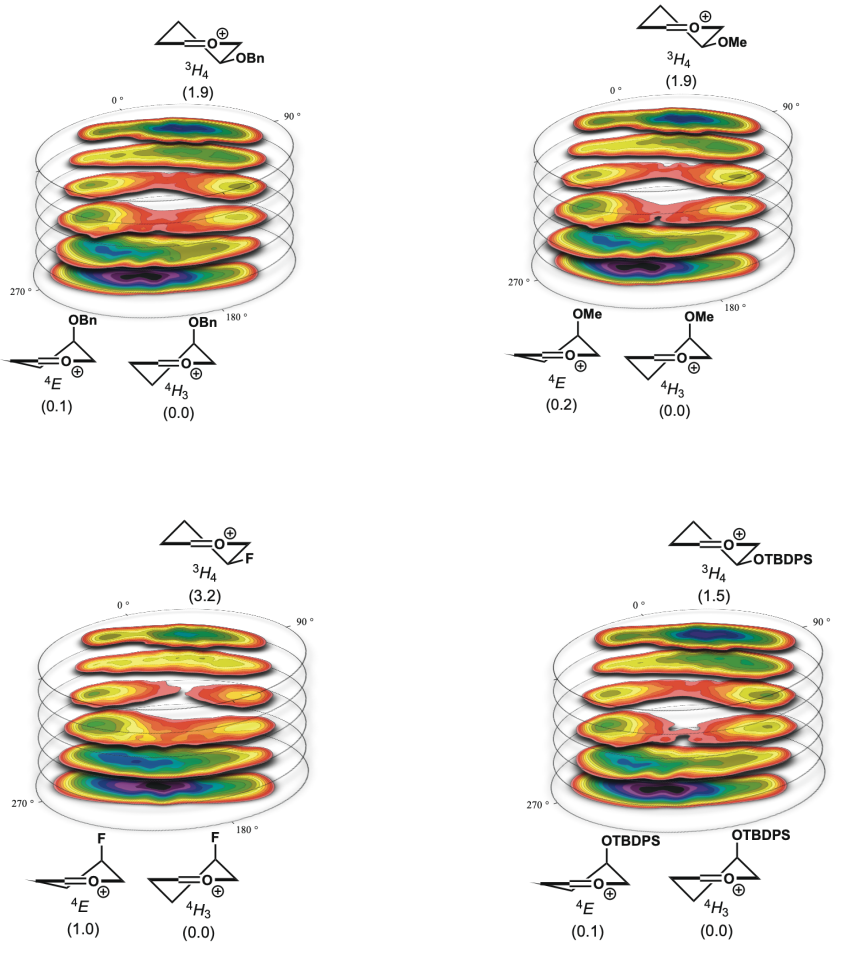


Figure S3. CEL maps of **1**, **S1**, **2** and **3**.

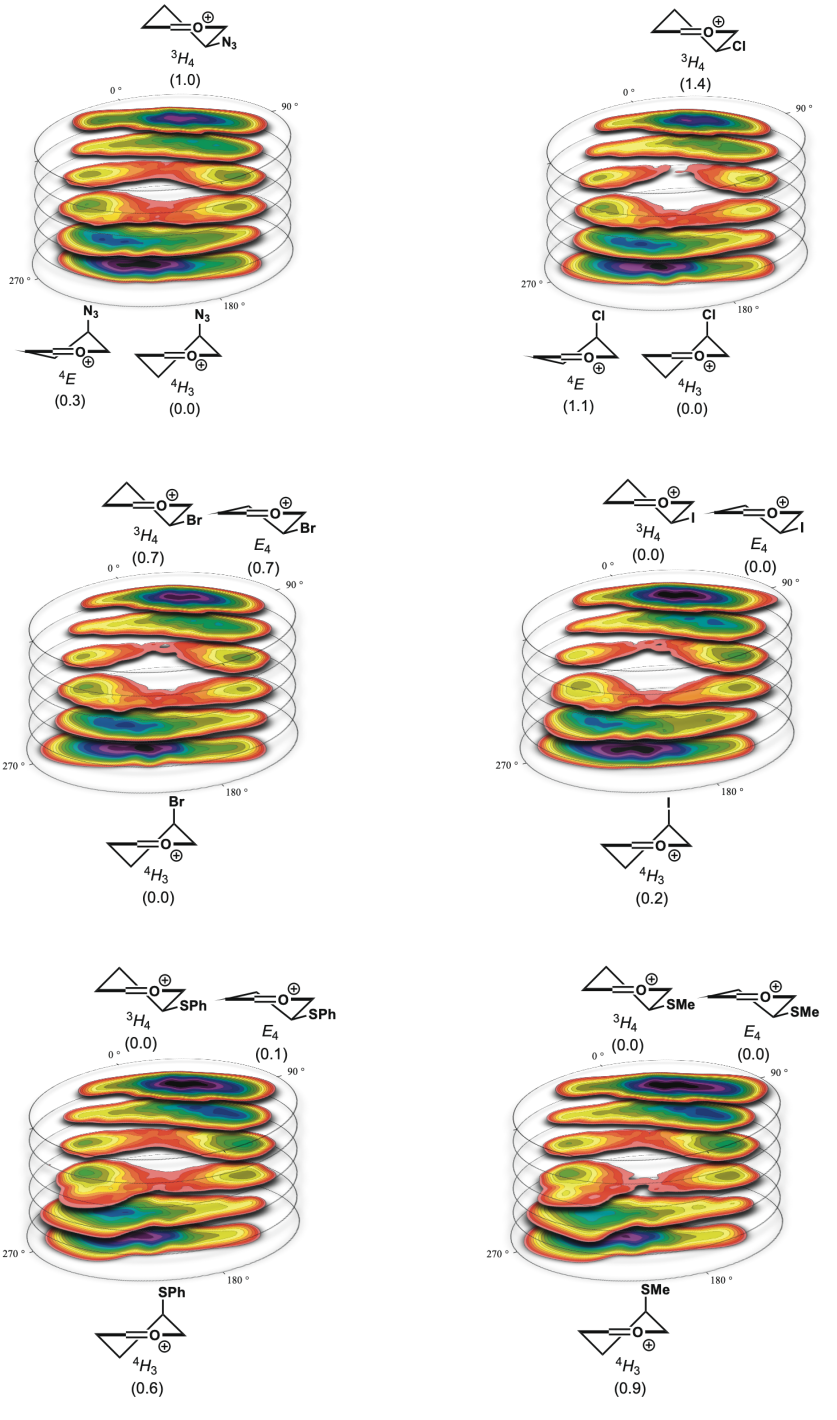


Figure S4. CEL maps of **4**, **5**, **6**, **7**, **8** and **9**.

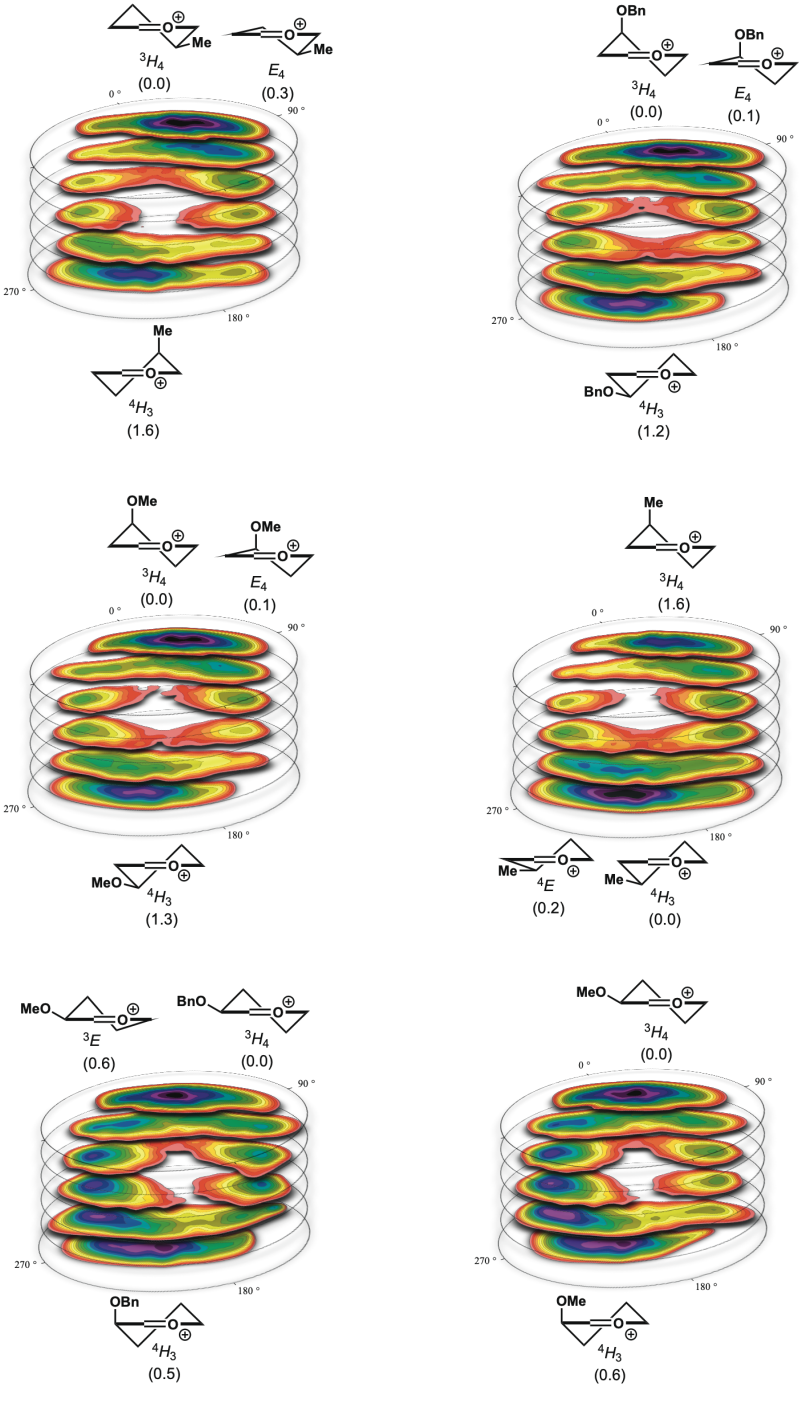


Figure S5. CEL maps of **10**, **11**, **S2**, **12**, **13** and **S3**.

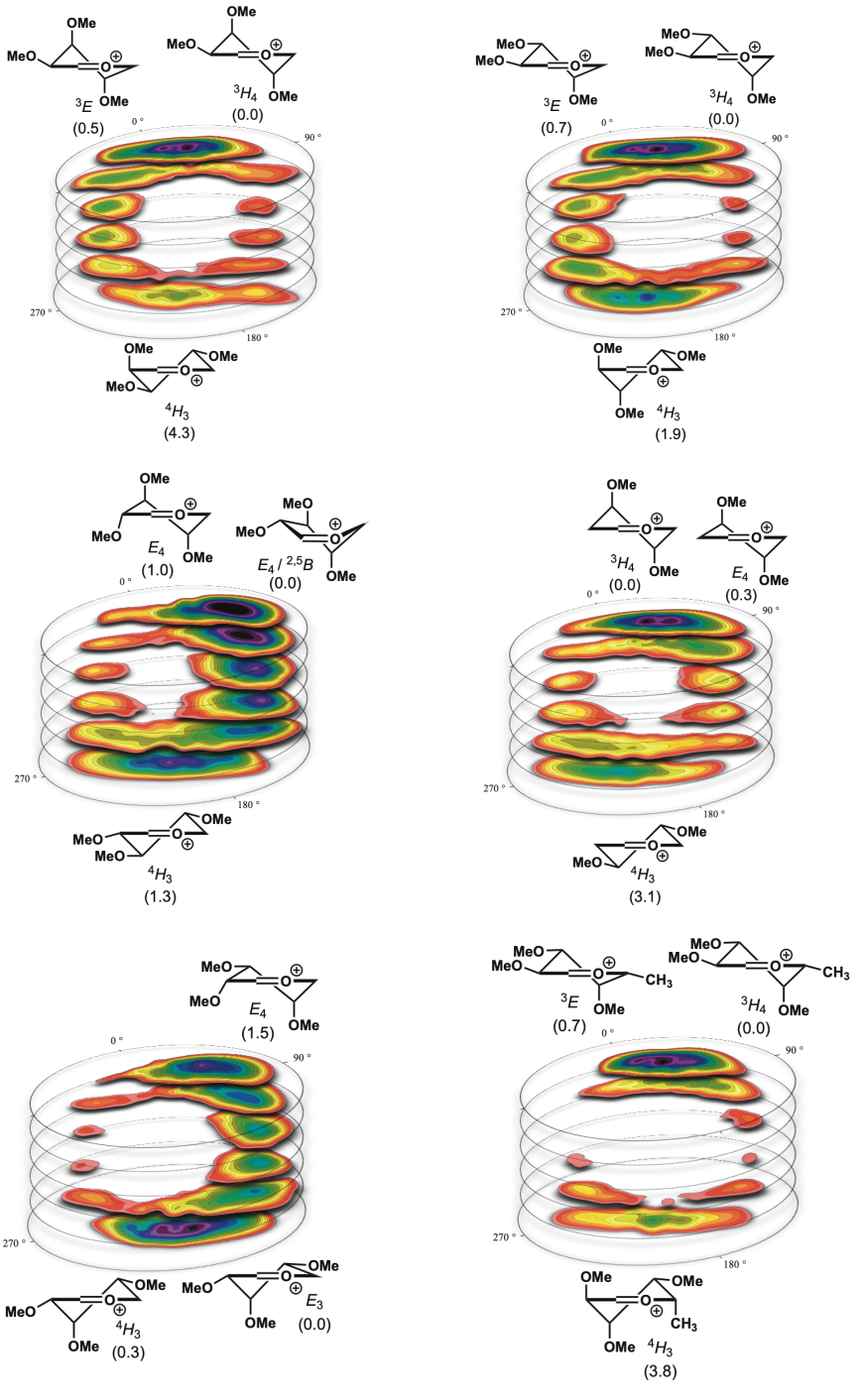


Figure S6. CEL maps of **14**, **15**, **16**, **17**, **18** and **19**.

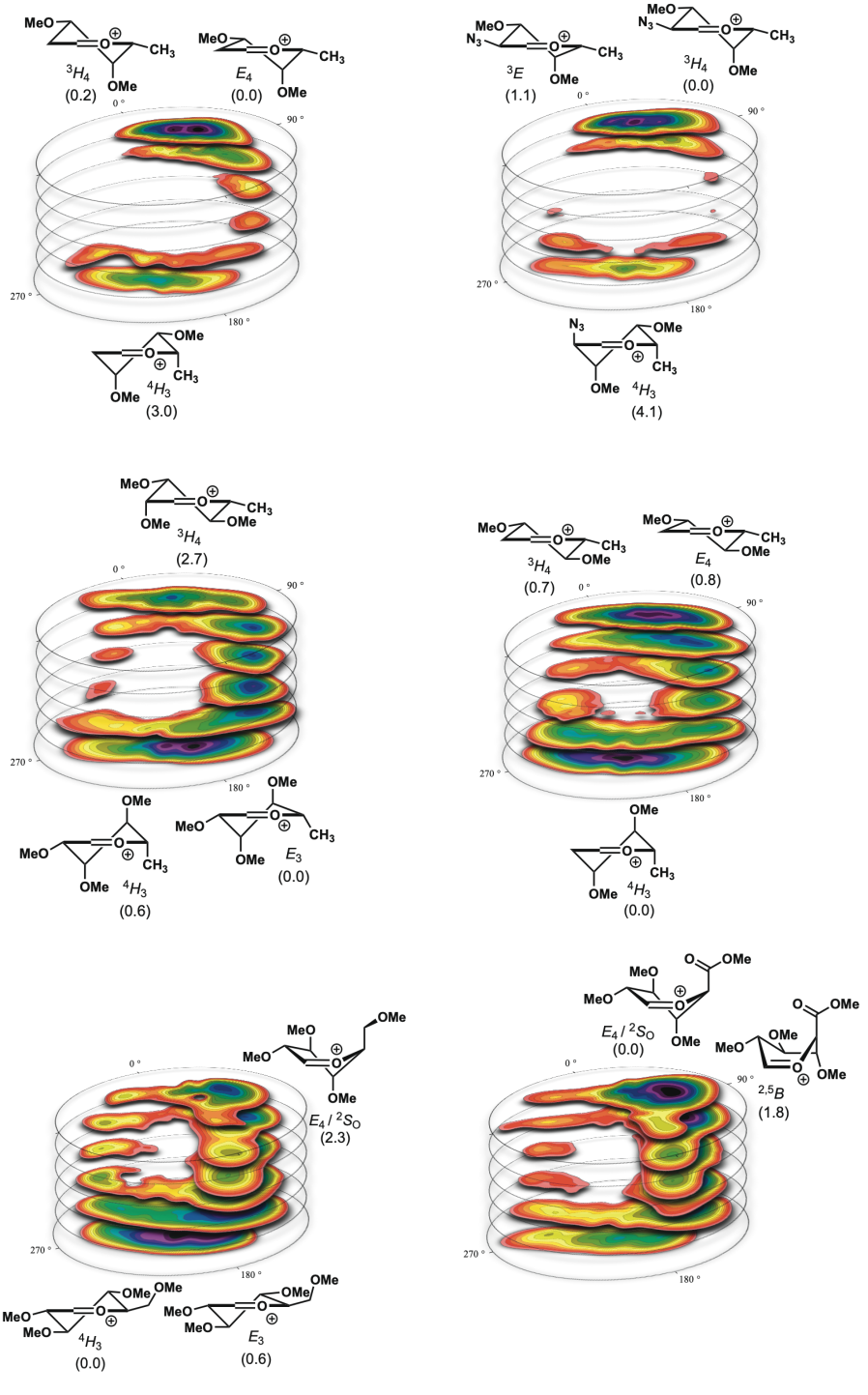


Figure S7. CEL maps of **20**, **21**, **22**, **23**, **24** and **25**.

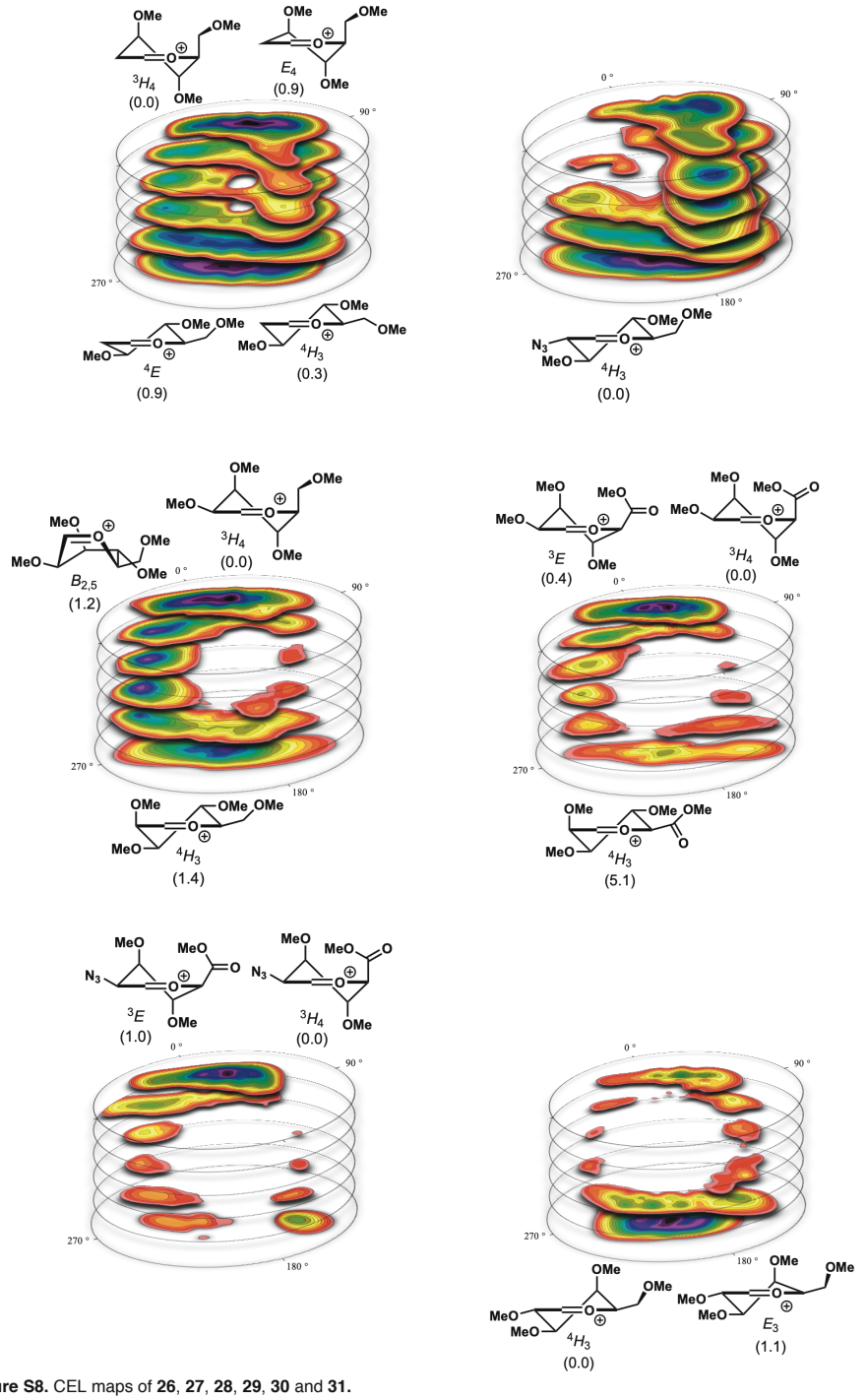


Figure S8. CEL maps of **26**, **27**, **28**, **29**, **30** and **31.**

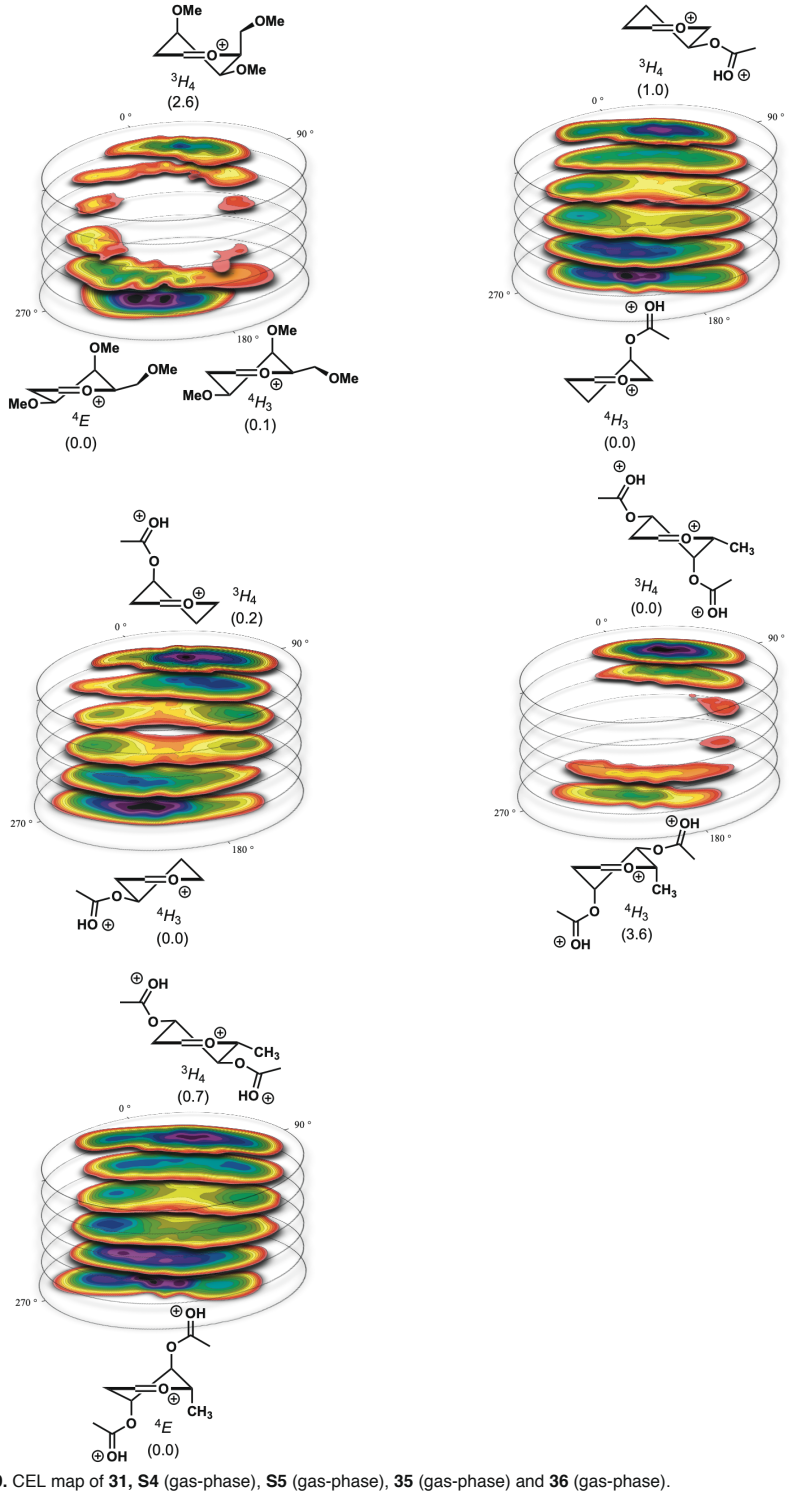


Figure S9. CEL map of **31, S4** (gas-phase), **S5** (gas-phase), **35** (gas-phase) and **36** (gas-phase).

Influence of the substituent orientation on the oxocarbenium ion stability • To investigate whether the orientation of the substitutions on the ring has an effect on the stability of the oxocarbenium ion, DFT computations were done in which the dihedral angle of the substituent was systematically rotated (Figure S10). Two important conformations were selected as starting point, including the $^{3}H_{4}$ and $^{4}H_{3}$, obtained from CEL maps. The ring dihedral angles were fixed to counter any conformational changes and the dihedral angle of interest was rotated from 0−360° with increments of 20°. All calculations were performed with Gaussian 09 rev. D.01 by using PCM(CH_2Cl_2)-B3LYP/6-311G(d,p).

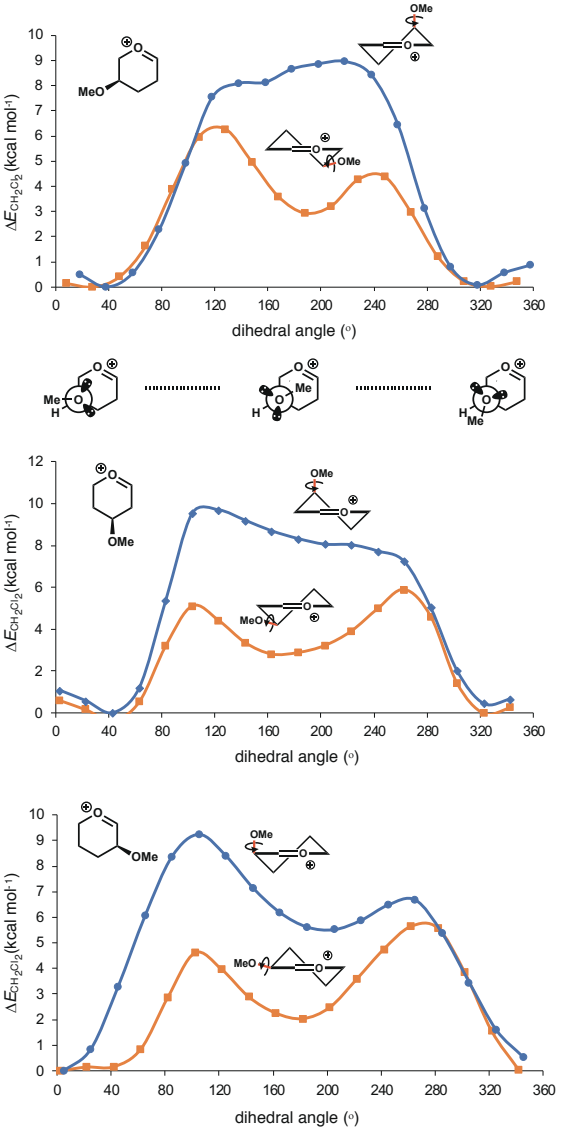
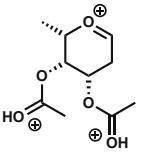


Figure S10. Probing the influence of the orientation of the C4-, C3- and C2-OMe substituent on the oxocarbenium ion stability. Energies are expressed as $\Delta E_{CH_2Cl_2}$; blue line = $^{4}H_{3}$ and orange line = $^{3}H_{4}$.

Superacid NMR experiments

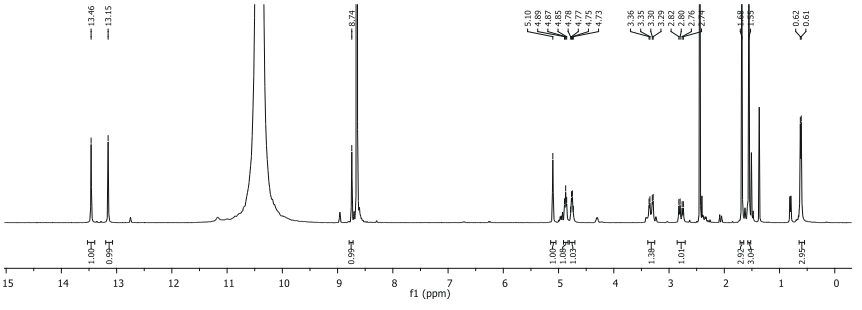
General procedure IV: NMR experiments in super acidic media • The authors want to draw the reader's attention to the dangerous features of super acidic chemistry. Handling of hydrogen fluoride and antimony pentafluoride must be done by experienced chemists with all the necessary safety arrangements in place. Experiments performed in superacid were carried out in a sealed Teflon® flask with a magnetic stirrer. No further precautions have to be taken to prevent reaction mixture from moisture (test reaction performed in anhydrous conditions leads to the same results). ^{1}H and ^{13}C NMR were recorded on a 400 MHz Bruker Advance DPX spectrometer using CD_3COCD_3 as an external reference. To get better resolution of signals with small coupling constants or overlapping signals a gaussian window function (LB = ± −1 and GB = ± 0.5) was used on the ^{1}H NMR spectrum. COSY and HSQC experiments were used to confirm the NMR peak assignments. To a magnetically stirred mixture of HF/SbF_5 (1 mL, SbF_5 22 mol%) maintained at −40 °C, was added substrate. After 5 min, the mixture was introduced in a Teflon® NMR tube which was inserted into a classical glass NMR tube containing acetone-d_6 as external standard.

Protonated pyranosyl oxocarbenium ions

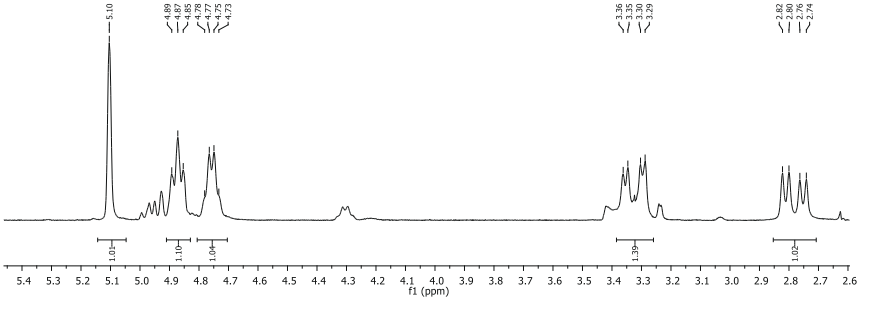


Protonated 2-deoxy-3,4-di-*O*-acetyl-fucose-L-pyranosyl oxocarbenium ion (35). The ion **35** was obtained from glycosyl donor **33** according to general procedure IV. ^{1}H NMR (400 MHz, Acetone-d_6): δ 13.46 (s, 1H, H'), 13.15 (s, 1H, H'), 8.74 (s, 1H, H-1), 5.10 (d, J = 3.0 Hz, H-4), 4.87 (t, J = 8.5 Hz, 1H, H-3), 4.76 (q, J = 6.4 Hz, 1H, H-5), 3.33 (dd, J = 23.7, 6.8 Hz, 1H, H-2b), 2.78 (dd, J = 23.7, 9.8 Hz, 1H, H-2a), 1.68 (s, 3H, CH_3Ac), 1.55 (s, 3H, CH_3 Ac), 0.62 (d, J = 6.5 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, Acetone-d_6): δ 224.8 (CH, C-1), 194.2 (C=O), 193.3 (C=O), 94.7 (CH, C-5), 75.8 (CH, C-4), 69.6 (CH, C-3), 35.6 (CH_2, C-2), 19.6 (CH_3 Ac), 19.5 (CH_3 Ac), 13.0 (CH_3).

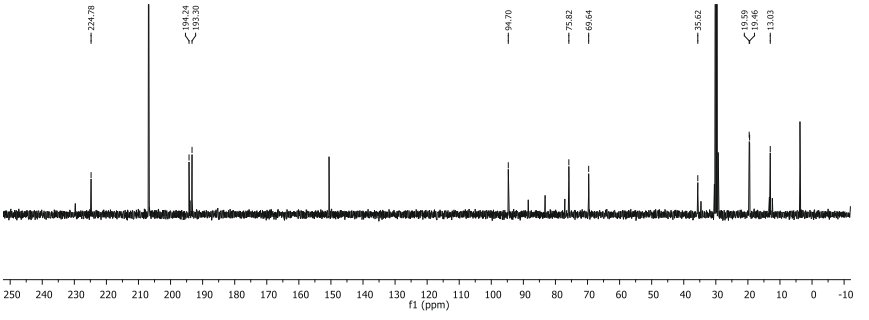
^{1}H NMR, acetone-d_6 of oxocarbenium ion **35**



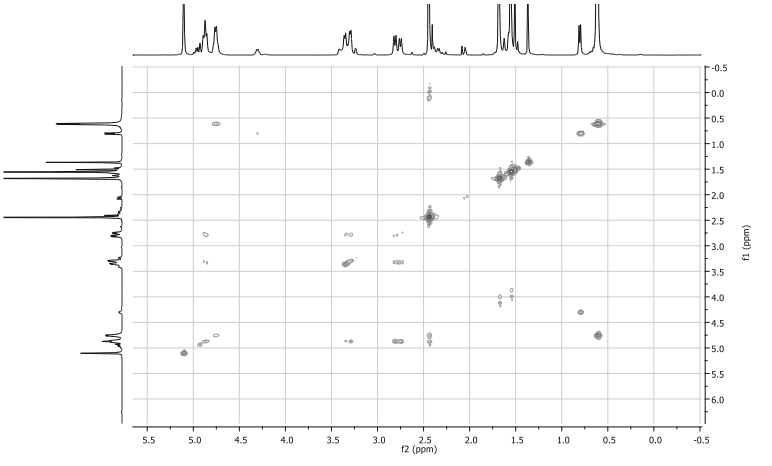
^{1}H NMR, acetone-d_6 of oxocarbenium ion **35** (cropped)



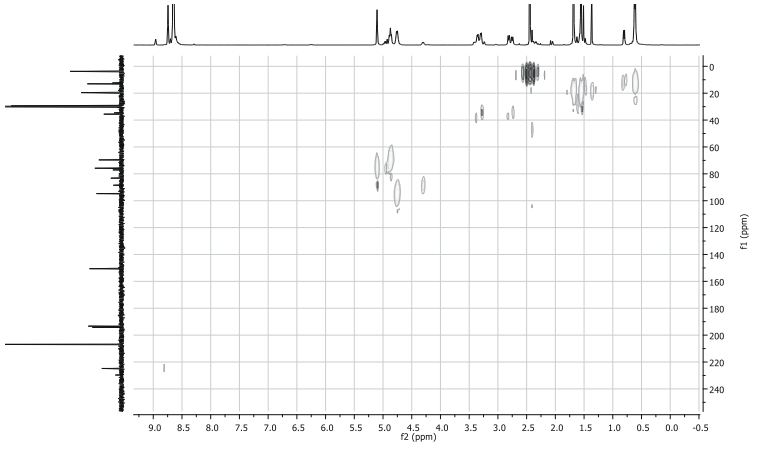
^{13}C NMR, acetone-d_6 of oxocarbenium ion **35**

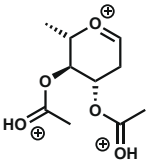


COSY NMR, acetone-d_6 of oxocarbenium ion **35**



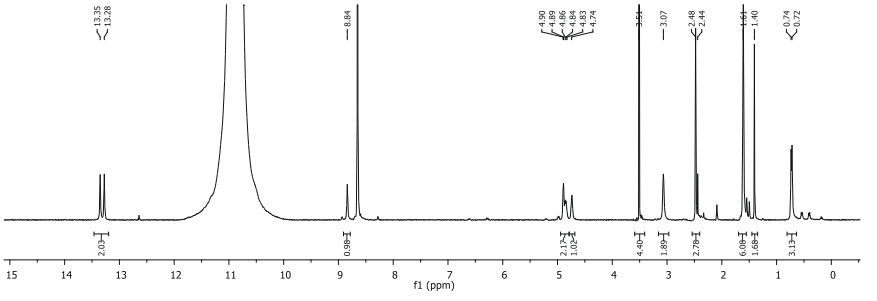
HSQC NMR, acetone-d_6 of oxocarbenium ion **35**



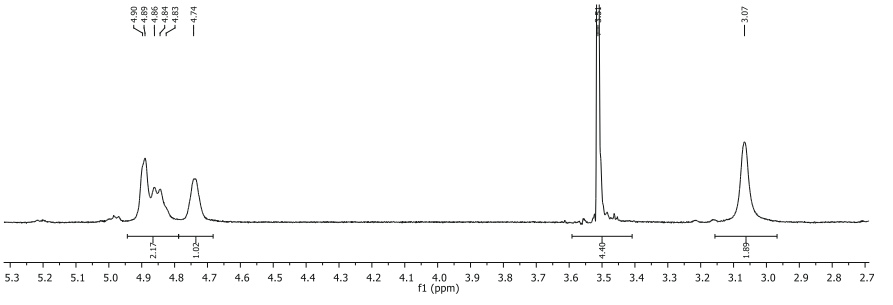


Protonated 2-deoxy-3,4-di-*O*-acetyl-rhamnose-L-pyranosyl oxocarbenium ion (36). The ion **36** was obtained from glycosyl donor **34** according to general procedure IV. ^{1}H NMR (400 MHz, Acetone-d_6): δ 13.35 (s, 1H, H'), 13.28 (s, 1H, H'), 8.84 (s, 1H, H-1), 4.89 (d, J = 3.5 Hz, 1H, H-4), 4.85 (q, J = 7.5 Hz, 1H H-5), 4.74 (bs, 1H, H-3), 3.07 (bs, 2H, H-2), 1.61 (s, 6H, 2x CH_3 Ac), 0.73 (d, J = 6.8 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, Acetone-d_6): δ 224.0 (CH, C-1), 193.5 (C=O), 193.4 (C=O), 92.3 (CH, C-5), 73.5 (CH, C-4), 61.2 (CH, C-3), 35.8 (CH_2, C-2), 19.9 (CH_3 Ac), 19.8 (CH_3 Ac), 15.2 (CH_3).

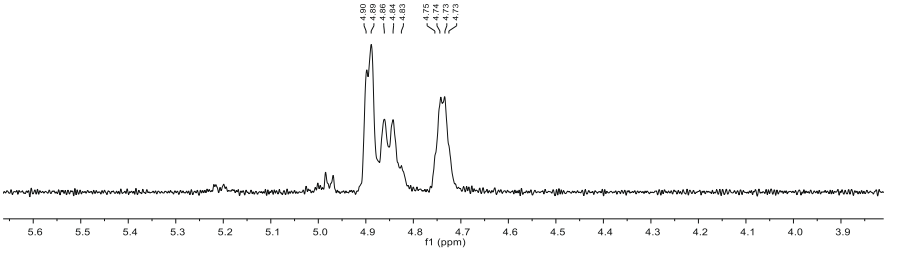
^{1}H NMR, acetone-d_6 of oxocarbenium ion **36**



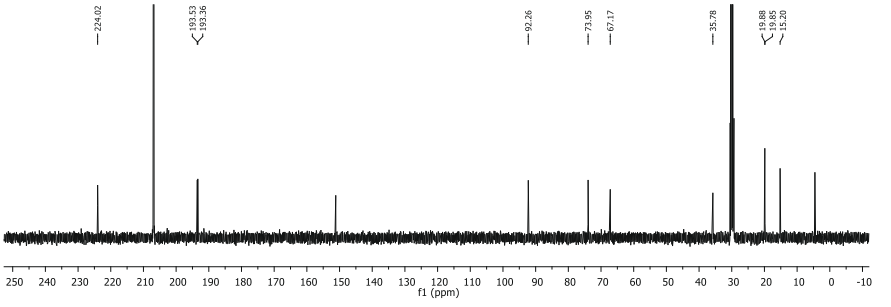
^{1}H NMR, acetone-d_6 of oxocarbenium ion **36** (cropped)



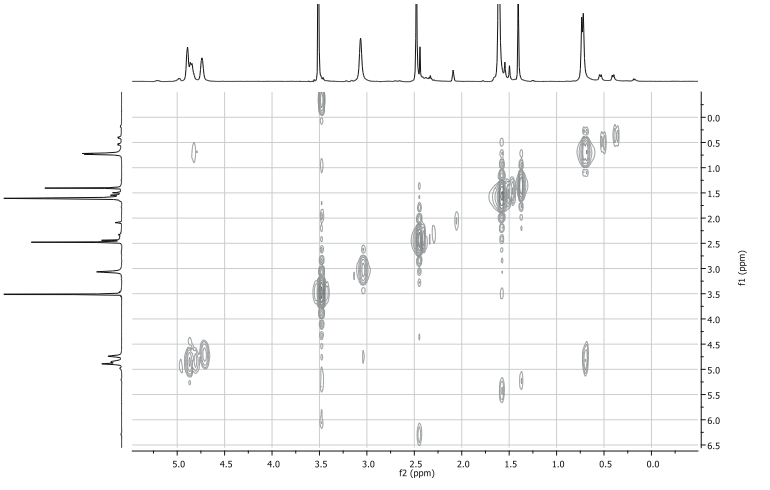
^{1}H NMR, acetone-d_6 of oxocarbenium ion **36** (cropped; LB = ± –2 and GB = ± 4)



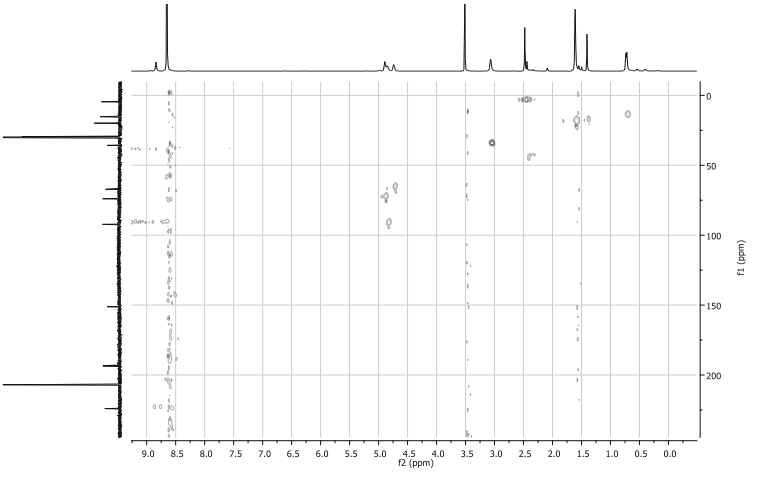
^{13}C NMR, acetone-d_6 of oxocarbenium ion **36**



COSY NMR, acetone-d_6 of oxocarbenium ion **36**



HSQC NMR, acetone-d_6 of oxocarbenium ion **36**



Organic synthesis

General experimental procedures • All chemicals (Acros, Fluka, Merck, and Sigma-Aldrich) were used as received unless stated otherwise. Dichloromethane was stored over activated 4 Å molecular sieves (beads, 8-12 mesh, Sigma-Aldrich). Before use traces of water present in the donor, diphenyl sulfoxide (Ph_2SO) and tri-*tert*-butylpyrimidine (TTBP) were removed by co-evaporation with dry toluene. The acceptor (triethylsilane-*d*) was stored in stock solutions (DCM, 0.5 M) over activated 4 Å molecular sieves. Trifluoromethanesulfonic anhydride (Tf_2O) was distilled over P_2O_5 and stored at −20 °C under a nitrogen atmosphere. Overnight temperature control was achieved by an FT902 Immersion Cooler (Julabo). Column chromatography was performed on silica gel 60 Å (0.04 – 0.063 mm, Screening Devices B.V.). Size exclusion chromatography was carried out on Sephadex™ (LH-20, GE Healthcare Life Sciences) by isocratic elution with DCM:MeOH (1:1, v:v). TLC-analysis was conducted on TLC Silica gel 60 (Kieselgel 60 F_{254}, Merck) with UV detection by (254 nm) and by spraying with 20% sulfuric acid in ethanol followed by charring at ± 150 °C or by spraying with a solution of $(NH_4)_6Mo_7O_{24}{\cdot}H_2O$ (25 g/l) and $(NH_4)_4Ce(SO_4)_4{\cdot}_2H_2O$ (10 g/l) in 10% sulfuric acid in water followed by charring at ± 260 °C. High-resolution mass spectra were recorded on a Thermo Finnigan LTQ Orbitrap mass spectrometer equipped with an electrospray ion source in positive mode (source voltage 3.5 kV, sheath gas flow 10, capillary temperature 275 °C) with resolution R=60.000 at m/z=400 (mass range = 150-4000). ^1H, ^2H and ^{13}C NMR spectra were recorded on a Bruker AV-400 NMR instrument (400, 61 and 101 MHz respectively), a Bruker AV-500 NMR instrument (500, 75 and 126 MHz respectively), or a Bruker AV-600 NMR instrument (600, 92 and 150 MHz respectively). For samples measured in $CDCl_3$ chemical shifts (δ) are given in ppm relative to tetramethylsilane as an internal standard or the residual signal of the deuterated solvent. Coupling constants (*J*) are given in Hz. To get better resolution of signals with small coupling constants or overlapping signals a gaussian window function (LB = ± −1 and GB = ± 0.5) was used on the ^1H NMR spectrum. All given ^{13}C APT spectra are proton decoupled. NMR peak assignment was made using COSY, HSQC. If necessary additional NOESY, HMBC and HMBC-GATED experiments were used to elucidate the structure. The anomeric product ratios were based on the integration of ^1H NMR. If the stereochemistry of the coupled product could not be confirmed a deprotection step was performed to verify the stereochemistry. IR spectra were recorded on a Shimadzu FTIR-8300 IR spectrometer with a resolution of 4 cm^{-1} and are reported in cm^{-1}. Specific rotations were measured on an MCP 100 Anton Paar polarimeter in $CHCl_3$ (10 mg/mL) at 589 nm unless stated otherwise.

General procedure V: synthesis of phenyl 2,3,4-tri-*O*-benzyl/methyl-1-thio-pentopyranoses • To a suspension of the corresponding pentose (10 mmol to 40 mmol) in pyridine (0.40 M), Ac_2O (12 eq.) was added dropwise at 0 °C. The mixture was allowed to warm to room temperature and stirred for 16 h. The reaction was quenched with sat. aq. $NaHCO_3$ and diluted with H_2O. The resulting product was extracted with DCM (3x). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was dissolved in DCM (0.15 M) and cooled to 0 °C. Hydrogen bromide (33 wt% in AcOH, 4.4 eq.) was added dropwise, and the reaction was allowed to warm to room temperature and stirred for an additional 16 h. Subsequently, the reaction mixture was concentrated under reduced pressure and co-evaporated with toluene (3x). To a solution of the crude product and thiophenol (1.05 eq.) in DMF (0.5 M), NaH (60% dispersion in mineral oil, 1.05 eq.) was added portion wise at 0 °C. After stirring for 16 h, the reaction was quenched by the addition of aqueous HCl (0.02 M) and diluted with H_2O. The resulting crude product was extracted with Et_2O (3x). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. Column chromatography yielded an inseparable pyranose/furanose mixture. To a solution of the crude product in MeOH (0.2 M), NaOMe (0.2 eq.) was added portion wise. The reaction mixture was stirred for 1 h after which Amberlite IR120 H^+ was added until pH 6 was reached. The resulting suspension was filtered, concentrated under reduced pressure and co-evaporated with toluene (3x). The crude product was dissolved in DMF (0.25 M) and cooled to 0 °C. NaH (60% dispersion in mineral oil, 4 eq.) was added, and the resulting mixture was stirred for 10 min. Subsequently, benzyl bromide (4 eq.) or methyl iodide (4 eq.) was added, and the reaction mixture was allowed to warm up to room temperature and stirred for an additional 16 h. The reaction was quenched with MeOH and diluted with H_2O, after which the resulting mixture was extracted with Et_2O (3x). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure.

General procedure VI: pre-activation Tf_2O/Ph_2SO based *d*-glycosylation • A solution of the donor (100 µmol), Ph_2SO (26 mg, 130 µmol, 1.3 eq.) and TTBP (62 mg, 250 µmol, 2.5 eq.) in DCM (2 mL, 0.05 M) was stirred over activated 3 Å molecular sieves (rods, size 1/16 in., Sigma-Aldrich) for 30 min under an atmosphere of N_2. The solution was cooled to –80 °C and Tf_2O (22 µl, 130 µmol, 1.3 eq.) was slowly added to the reaction mixture. The reaction mixture was allowed to warm to –60 °C in approximately 45 min, followed by cooling to –80 °C and the addition of the acceptor (200 µmol, 2 eq.) in DCM (0.4 mL, 0.5 M). The reaction was allowed to warm up to –60 °C and stirred for an additional 80 h at this temperature to ensure reaction completion. The reaction was quenched with sat. aq. $NaHCO_3$ at –60 °C and diluted with DCM (5 mL). The resulting solution was washed with H_2O and brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification by column chromatography yielded the corresponding *d*-coupled glycoside.

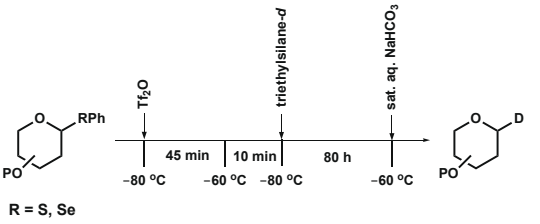


Figure S11. Schematic representation of the reaction procedure during pre-activation Ph_2SO/Tf_2O mediated glycosylation.

General procedure VII: debenzylation of *d*-coupled pyranoses • The *d*-coupled pyranose was dissolved in MeOH (0.02 M) under an atmosphere of N_2, and Pd/C (10 mol%) was added. Subsequently, H_2 was bubbled through the reaction mixture for approximately 15 min., and the reaction was stirred for an additional 32 h. The reaction was filtered over Celite® 545 (Sigma-Aldrich) and concentrated under reduced pressure. Purification by column chromatography yielded the corresponding deprotected *d*-coupled glycoside.

General procedure VIII: pre-activation Tf_2O/Ph_2SO based *d*-glycosylation in Et_2O or CH_3CN • A solution of the donor (100 µmol), Ph_2SO (26 mg, 130 µmol, 1.3 eq.) and TTBP (62 mg, 250 µmol, 2.5 eq.) in Et_2O (1.7 mL) or CH_3CN (1.7 mL) and DCM (0.7 mL) was stirred over activated 3 Å molecular sieves (rods, size 1/16 in., Sigma-Aldrich) for 30 min under an atmosphere of N_2. The solution was cooled to –80 °C and Tf_2O (22 µl, 130 µmol, 1.3 eq.) was slowly added to the reaction mixture. The reaction mixture was allowed to warm to –60 °C in approximately 45 min, followed by cooling to –80 °C and the addition of the acceptor (200 µmol, 2 eq.). The reaction was allowed to warm up to –60 °C and stirred for an additional 80 h at this temperature to ensure reaction completion. The reaction was quenched with sat. aq. $NaHCO_3$ at –60 °C and diluted with DCM (5 mL). The resulting solution was washed with H_2O and brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification by column chromatography yielded the corresponding *d*-coupled glycoside.

General procedure IX: TMSOTf activation based *d*-glycosylation • The imidate donor (100 µmol, 1 eq.) was co-evaporated twice with dry toluene and then dissolved in dry DCM (1 mL, 0.1 M). Activated 3 Å molecular sieves and the acceptor (200 µmol, 2 eq.) were added and the solution was stirred for 30 min at room temperature under an inert atmosphere.

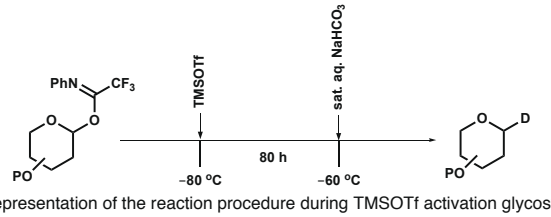
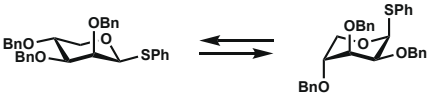


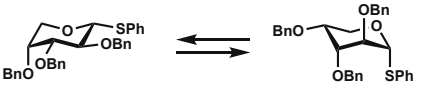
Figure S12. Schematic representation of the reaction procedure during TMSOTf activation glycosylation.

The reaction mixture was cooled to the –80 °C and a freshly prepared stock solution of TMSOTf in DCM (0.5 M) of was introduced via syringe (50 µL, 0.01 mmol, 0.1 eq.). The reaction was allowed to warm up to

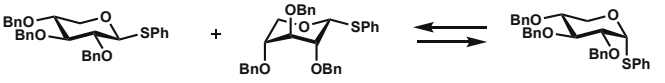
–60 °C and stirred for an additional 80 h, and was then quenched by the addition of sat. aq. $NaHCO_3$. The mixture was diluted with DCM and H_2O and twice extracted with DCM. The combined organic layers were dried with $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by column chromatography yielded the corresponding *d*-coupled glycoside.



Phenyl 2,3,4-tri-*O*-benzyl-1-thio-D-lyxopyranoside (S6). The title compound was prepared according to general procedure V from D-lyxose. Column chromatography (100:0 → 95:5, pentane:EtOAc) yielded compound **S6** (643 mg, 1.22 mmol, 52% over 5 steps, average of 88% per step, colorless solid). TLC: R_f 0.21 (pentane:EtOAc, 9.5:0.5, v:v); $[\alpha]_D^{20}$ –87.0°; IR (thin film, cm^{-1}): 693, 748, 1049, 1217, 1367, 1438, 1743; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC, HH-NOESY, HMBC-Gated): δ 7.54 – 7.15 (m, 20H, CH_{arom}), 5.30 (d, *J* = 4.0 Hz, 1H, H-1), 4.88 (d, *J* = 12.2 Hz, 1H, C*H*H Bn), 4.77 – 4.71 (m, 2H, CH_2 Bn), 4.68 (d, *J* = 12.2 Hz, 1H, CH*H* Bn), 4.55 (s, 2H, CH_2 Bn), 4.33 (dd, *J* = 12.3, 2.5 Hz, 1H, H-5), 4.18 (dd, *J* = 4.1, 2.5 Hz, 1H, H-2), 3.79 – 3.69 (m, 2H, H-3, H-4), 3.51 (dd, *J* = 12.2, 4.3 Hz, 1H, H-5); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC, HMBC-Gated): δ 138.6, 138.1, 137.5 ($C_{q\text{-}arom}$), 130.6, 128.9, 128.5, 128.5, 128.4, 128.1, 127.9, 127.8, 127.7, 127.7, 126.7 (CH_{arom}), 87.9 (C-1), 77.2 (C-3), 75.7 (C-2), 75.2 (C-4), 73.4, 72.9, 72.0 (CH_2 Bn), 62.1 (C-5); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 87.9 ($J_{C1\text{-}H1}$= 160 Hz, 1,2-*cis*); HRMS: $[M+NH_4]^+$ calcd for $C_{32}H_{36}NO_4S$ 530.23596, found 530.23568.



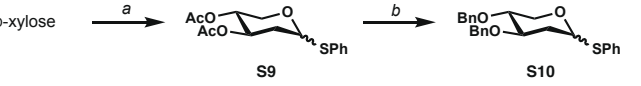
Phenyl 2,3,4-tri-*O*-benzyl-1-thio-D-arabinopyranoside (S7). The title compound was prepared according to general procedure V from D-arabinose. Column chromatography (100:0 → 95:5, pentane:EtOAc) yielded compound **S7** (2.21 g, 4.31 mmol, 50% over 5 steps, average of 87% per step, off-white solid). TLC: R_f 0.45 (pentane:EtOAc, 9.5:0.5, v:v); $[\alpha]_D^{20}$ –49.8°; IR (thin film, cm^{-1}): 731, 775, 1026, 1042, 1082, 1125, 1452, 2862; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC, HH-NOESY, HMBC-Gated): δ 7.56 – 7.19 (m, 20H, CH_{arom}), 4.91 (d, *J* = 6.1 Hz, 1H, H-1), 4.70 (d, *J* = 11.0 Hz, 1H, C*H*H Bn), 4.68 – 4.61 (m, 4H, CH_2 Bn, CH_2 Bn), 4.59 (d, *J* = 12.3 Hz, 1H, CH*H* Bn), 4.26 (dd, *J* = 12.0, 5.8 Hz, 1H, H-5), 3.94 (t, *J* = 6.5 Hz, 1H, H-2), 3.82 (dt, *J* = 5.8, 2.8 Hz, 1H, H-4), 3.67 (dd, *J* = 6.9, 3.1 Hz, 1H, H-3), 3.44 (dd, *J* = 12.0, 2.6 Hz, 1H, H-5); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC, HMBC-Gated): δ 138.3, 138.2, 138.1, 135.6 ($C_{q\text{-}arom}$), 131.3, 128.9, 128.5, 128.5, 128.4, 128.1, 127.9, 127.9, 127.9, 127.8, 127.1 (CH_{arom}), 87.3 (C-1), 78.6 (C-3), 77.4 (C-2), 74.3 (CH_2 Bn), 72.4 (C-4), 72.4, 71.2 (CH_2 Bn), 63.3 (C-5); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 83.3 ($J_{C1\text{-}H1}$= 158 Hz, 1,2-*trans*); HRMS: $[M+NH_4]^+$ calcd for $C_{32}H_{36}NO_4S$ 530.23596, found 530.23588.



Phenyl 2,3,4-tri-*O*-benzyl-1-thio-D-xylopyranoside (S8). The title compound was prepared according to general procedure V from D-xylose. Column chromatography (100:0 → 95:5, pentane:EtOAc) yielded compound **S8** (2.33 g, 4.40 mmol, 48% over 5 steps, average of 86% per step, yellow wax, 1,2-*cis*:1,2-*trans*; 23:77). TLC: R_f 0.42 (pentane:EtOAc, 9.5:0.5, v:v); IR (thin film, cm^{-1}): 694, 735, 1026, 1070, 1120, 1454, 2864, 3030; Data of the major stereoisomer (1,2-*trans* product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC, HH-NOESY, HMBC-Gated): δ 7.54 – 7.25 (m, 20H, CH_{arom}), 4.89 (d, *J* = 10.9 Hz, 1H, C*H*H Bn), 4.85 (d, *J* = 10.1 Hz, 1H, C*H*H Bn), 4.83 (d, *J* = 10.9 Hz, 1H, CH*H* Bn), 4.75 (d, *J* = 10.0 Hz, 1H, CH*H* Bn), 4.71 (d, *J* = 11.6 Hz, 1H, C*H*H Bn), 4.67 (d, *J* = 9.5 Hz, 1H, H-1), 4.62 (d, *J* = 11.6 Hz, 1H, CH*H* Bn), 4.09 – 4.02 (m, 1H, H-5_{eq}), 3.67 – 3.60 (m, 2H, H-3, H-4), 3.44 (t, *J* = 8.7 Hz, 1H, H-2), 3.24 (dd, *J* = 11.5, 9.6 Hz, 1H, H-5_{ax}); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC, HMBC-Gated): δ 138.6, 138.2, 133.8, 132.0 ($C_{q\text{-}arom}$), 129.1, 128.6, 128.5, 128.5, 128.3, 128.1, 128.0, 128.0, 128.0, 127.9, 127.7 (CH_{arom}), 88.5 (C-1), 85.4 (C-3), 80.5 (C-2), 77.8 (C-4), 75.8, 75.6, 73.4 (CH_2 Bn), 67.6 (C-5); ^{13}C-GATED NMR (126 MHz, $CDCl_3$): δ 88.5 ($J_{C1\text{-}H1}$= 157 Hz, 1,2-*trans*); Data of the minor stereoisomer (1,2-*cis* product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC, HH-NOESY, HMBC-Gated): δ 7.47 – 7.44 (m, 20H, CH_{arom}),

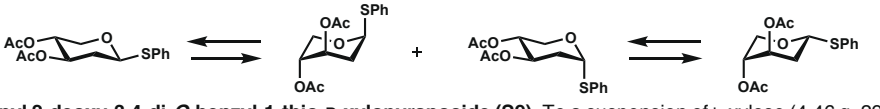
5.54 (d, *J* = 4.4 Hz, 1H, H-1), 4.93 (d, *J* = 10.8 Hz, 1H, C*H*H Bn), 4.76 (d, *J* = 10.6 Hz, 1H, C*H*H Bn), 4.63 (d, *J* = 11.7 Hz, 1H, CH*H* Bn), 3.82 – 3.78 (m, 2H, H-2, H-3), 3.71 – 3.66 (m, 2H, H-5, H-5). 3.61 – 3.53 (m, 1H, H-4); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC, HMBC-Gated): δ 138.8, 138.4, 137.9, 134.6 ($C_{q\text{-}arom}$), 131.7, 129.1, 128.6, 128.5, 128.2, 128.2, 127.9, 127.8, 127.2 (CH_{arom}), 87.5 (C-1), 81.8 (C-3), 79.6 (C-2), 77.7 (C-4), 75.9, 73.7, 72.8 (CH_2 Bn), 61.2 (C-5); ^{13}C-GATED NMR (126 MHz, $CDCl_3$): δ 87.5 ($J_{C1\text{-}H1}$= 165 Hz, 1,2-*cis*); HRMS: $[M+NH_4]^+$ calcd for $C_{32}H_{36}NO_4S$ 530.23596, found 530.23589.

Preparation of donor S10

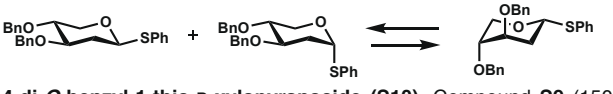


S9 **S10**

Scheme S1. Donor **S10** synthesis. *Reagents and conditions:* a) *i.* Ac_2O, pyridine; *ii.* HBr, AcOH, DCM; *iii.* Bu_3SnH, AIBN, toluene; *iv.* PhSH, $BF_3{\cdot}OEt_2$, DCM **S9**: 69%; b) *i.* NaOMe, MeOH, *ii.* BnBr, NaH, DMF, **S10**: 92%.

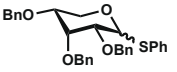


Phenyl 2-deoxy-3,4-di-*O*-benzyl-1-thio-D-xylopyranoside (S9). To a suspension of L-xylose (4.46 g, 29.7 mmol) in pyridine (72 mL), Ac_2O (34 mL, 356 mmol, 12 eq.) was added dropwise at 0 °C. After stirring for an additional 16 h at room temperature the mixture was concentrated *in vacuo* and co-evaporated three times with heptane. The crude product was dissolved in a mixture of DCM (55 mL) and Ac_2O (0.28 mL, 3.0 mmol, 0.1 eq.), HBr (33 wt% in AcOH, 23 mL, 127 mmol, 4.3 eq.) was added dropwise at 0 °C. The mixture was stirred for an additional 16 h at room temperature and subsequently concentrated under reduced pressure. The crude product was three times co-evaporated with toluene. The crude product was dissolved in toluene (1.2 L, 0.025 M) and AIBN (0.49 g, 2.97 mmol, 0.1 eq.) was added. The reaction was stirred at 80 °C for 30 min and Bu_3SnH (9.6 mL, 35.6 mmol, 1.2 eq.) was added dropwise over 16 h. The reaction mixture was concentrated and column chromatography (80:20 → 70:30, pentane:EtOAc) afforded the crude product. The crude product was dissolved in DCM (250 mL, 0.10 M) and cooled to −80 °C. Subsequently, thiophenol (3.4 mL, 32.7 mmol, 1.1 eq.) and $BF_3{\cdot}OEt_2$ (4.5 mL, 35.6 mmol, 1.2 eq.) were added dropwise to the solution and the reaction was allowed to warm up to room temperature in 4 h. The reaction mixture was quenched with sat. aq. $NaHCO_3$ and extracted with DCM (3x). The combined organic layers were dried with $MgSO_4$ and concentrated *in vacuo*. The residue was purified using column chromatography (pentane:EtOAc, 90:10 → 70:30) affording title compound **S9**. (6.36 g, 20.5 mmol, 69% over 4 steps, average of 91% per step, colorless oil, 1,3-*cis*:1,3-*trans*; 66:34). TLC: R_f 0.42 (pentane:EtOAc, 7:3, v:v); IR (thin film, cm^{-1}): 693, 743, 1026, 1049, 1220, 1368, 1736; Data of the major stereoisomer (1,3-*cis* product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.65 – 7.18 (m, 5H, CH_{arom}), 5.10 (dd, *J* = 7.4, 4.0 Hz, 1H, H-1), 5.00 (td, *J* = 7.5, 4.5 Hz, 1H, H-3), 4.85 (td, *J* = 7.0, 4.0 Hz, 1H, H-4), 4.36 (dd, *J* = 12.2, 3.9 Hz, 1H, H-5), 3.49 (dd, *J* = 12.2, 6.7 Hz, 1H, H-5), 2.52 (dt, *J* = 13.9, 4.3 Hz, 1H, H-2), 2.11 (s, 3H, CH_3 Ac), 2.08 (s, 3H, CH_3 Ac), 1.95 (dt, *J* = 13.9, 7.6 Hz, 1H, H-2); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 170.1, 170.1 (C=O), 134.4 ($C_{q\text{-}arom}$), 131.8, 129.1, 127.7 (CH_{arom}), 82.8 (C-1), 69.0 (C-3), 68.5 (C-4), 63.6 (C-5), 34.1 (C-2), 21.3, 21.1 (CH_3 Ac); Data of the minor stereoisomer (1,3-*trans* product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.33 (dd, *J* = 6.6, 3.9 Hz, 1H, H-1), 5.17 (td, *J* = 6.9, 4.2 Hz, 1H, H-3), 4.80 (td, *J* = 6.7, 4.1 Hz, 1H, H-4), 4.09 (dd, *J* = 12.2, 6.2 Hz, 1H, H-5), 3.89 (dd, *J* = 12.2, 3.7 Hz, 1H, H-5), 2.34 (ddd, *J* = 14.0, 6.6, 4.2 Hz, 1H, H-2), 2.09 (s, 3H, CH_3 Ac), 2.08 (s, 3H, CH_3 Ac); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 170.2, 169.8 (C=O), 134.2 ($C_{q\text{-}arom}$), 131.5, 127.7 (CH_{arom}), 82.2 (C-1), 68.3 (C-4), 68.2 (C-3), 63.1 (C-5), 33.9 (C-2), 21.2, 21.1 (CH_3 Ac); HRMS: $[M+Na]^+$ calcd for $C_{15}H_{18}NaO_5S$ 333.0767, found 333.0771.

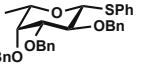


Phenyl 2-deoxy-3,4-di-*O*-benzyl-1-thio-D-xylopyranoside (S10). Compound **S9** (150 mg, 0.48 mmol) was dissolved in MeOH (4.8 mL, 0.1 M) and subsequently NaOMe (2.6 mg, 48 µmol 0.1 eq.) was added portionwise. The reaction mixture was stirred for 1 h after which Amberlite IR120 H^+ was added until pH 6 was reached. The resulting suspension was filtered, concentrated under reduced pressure and co-evaporated with toluene (3x). The crude product was dissolved in DMF (4.8 mL, 0.1 M) and cooled to 0 °C.

benzyl bromide (0.14 mL, 1.2 mL, 2.4 eq.) was added, and subsequently, NaH (60% dispersion in mineral oil, 46 mg, 1.2 mmol, 2.4 eq.) was added. The reaction mixture was allowed to warm up to room temperature and stirred for an additional 16 h. The reaction was quenched with MeOH and diluted with H_2O, after which the resulting mixture was extracted with Et_2O (3x). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. Column chromatography (95:5 → 85:15, pentane:EtOAc) gave the title compound **S10** (180 mg, 0.44 mmol, 92%, over 2 steps, average of 97% per step, colorless oil, 1,3-*cis*:1,3-*trans*; 62:38). TLC: R_f 0.31 (pentane:EtOAc, 8:2, v:v); IR (thin film, cm^{-1}): 694, 695, 735, 1026, 1077, 1089, 1206, 1440, 1454, 1480, 2846; Data of the major stereoisomer (1,3-*cis* product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.53 – 7.17 (m, 15H, CH_{arom}), 4.96 (dd, *J* = 8.9, 3.3 Hz, 1H, H-1), 4.72 (dd, *J* = 11.8, 3.3 Hz, 1H, C*H*H Bn), 4.65 – 4.55 (m, 3H, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.21 (dd, *J* = 11.9, 4.1 Hz, 1H, H-5_{eq}), 3.65 (ddd, *J* = 8.8, 7.1, 4.6 Hz, 1H, H-3), 3.51 (ddd, *J* = 14.2, 7.3, 4.0 Hz, 1H, H-4), 3.36 (dd, *J* = 11.9, 7.9 Hz, 1H, H-5_{ax}), 2.47 (ddd, *J* = 13.5, 4.6, 3.3 Hz, 1H, H-2_{eq}), 1.86 (dt, *J* = 13.5, 8.8 Hz, 1H, H-2_{ax}); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 138.4, 138.4, 135.0 ($C_{q\text{-}arom}$), 131.3, 129.0, 128.6, 128.6, 127.9, 127.9, 127.8, 127.8, 127.8, 127.7, 127.3, 127.2 (CH_{arom}), 83.2 (C-1), 77.1 (C-3), 76.5 (C-4), 72.8, 71.9 (CH_2 Bn), 65.5 (C-5), 35.2 (C-2); Data of the minor stereoisomer (1,3-*trans* product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.43 (t, *J* = 4.7 Hz, 1H, H-1), 4.04 (dd, *J* = 11.9, 7.4 Hz, 1H, H-5), 3.83 (dd, *J* = 11.9, 4.0 Hz, 1H, H-3), 2.35 (ddd, *J* = 13.7, 5.2, 4.3 Hz, 1H, H-2), 2.04 (ddd, *J* = 13.2, 8.6, 4.4 Hz, 1H, H-2); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 138.5, 138.5, 134.9 ($C_{q\text{-}arom}$), 83.0 (C-1), 76.3 (C-3), 75.6 (C-4), 72.5, 72.0 (CH_2 Bn), 63.1 (C-5), 34.9 (C-2); HRMS: $[M+Na]^+$ calcd for $C_{25}H_{26}O_3SNa$ 429.1495, found 429.1499.



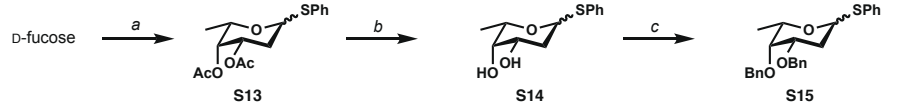
Phenyl 2,3,4-tri-*O*-benzyl-1-thio-D-ribopyranoside (S11). The title compound was prepared according to general procedure V from D-ribose. Column chromatography (95:5 → 90:10, pentane:EtOAc) yielded compound **S11** (1.02 g, 2.00 mmol, 25% over 5 steps, average of 76% per step yellow oil, 1,2-*cis*:1,2-*trans*; 32:68). TLC: R_f 0.39, 0.54 (pentane:EtOAc, 9.5:0.5, v:v); IR (thin film, cm^{-1}): 694, 735, 1026, 1060, 1087, 1454, 2873, 2926; Data of the major stereoisomer (1,2-*trans* product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC, HH-NOESY, HMBC-Gated): δ 7.55 – 7.19 (m, 20H, CH_{arom}), 5.22 (d, *J* = 9.0 Hz, 1H, H-1), 4.81 (s, 2H, CH_2 Bn), 4.61 – 4.54 (m, 4H, CH_2 Bn, CH_2 Bn), 4.13 (t, *J* = 2.5 Hz, 1H, H-3), 3.90 – 3.83 (m, 2H, H-5_{ax}, H-5_{eq}), 3.52 (ddd, *J* = 8.3, 5.9, 2.3 Hz, 1H, H-4), 3.33 (dd, *J* = 9.1, 2.5 Hz, 1H, H-2); ^{13}C NMR (101 MHz, $CDCl_3$): δ 138.9, 138.2, 137.9 ($C_{q\text{-}arom}$), 133.9, 131.8, 128.9, 128.6, 128.5, 128.3, 128.1, 128.0, 127.6 (CH_{arom}), 84.4 (C-1), 77.8 (C-2), 75.3 (C-4), 74.4 (C-3), 74.1, 72.4, 71.5 (CH_2 Bn), 64.6 (C-5); ^{13}C-GATED NMR (101 MHz, $CDCl_3$, HSQC, HMBC, HMBC-Gated): δ 84.4 ($J_{C1\text{-}H1}$ = 161 Hz); Data of the minor stereoisomer (1,2-*cis* isomer product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC, HH-NOESY, HMBC-Gated): δ 7.56 – 7.18 (m, 20H, CH_{arom}), 5.46 (d, *J* = 5.5 Hz, 1H, H-1), 5.03 (d, *J* = 12.4 Hz, 1H, C*H*H Bn), 4.89 (d, *J* = 12.5 Hz, 1H, CH*H* Bn), 4.71 (d, *J* = 11.9 Hz, 1H, C*H*H Bn), 4.61 (d, *J* = 11.7 Hz, 1H, C*H*H Bn), 4.51 (m, 1H, C*H*H Bn), 4.45 (d, *J* = 12.1 Hz, 1H, CH*H* Bn), 4.40 (t, *J* = 10.8 Hz, 1H, H-5_{ax}), 4.16 (d, *J* = 2.5 Hz, 1H, H-3), 3.70 (dd, *J* = 5.5, 2.2 Hz, 1H, H-2), 3.63 (dd, *J* = 10.9, 5.0 Hz, 1H, H-5_{eq}), 3.49 – 3.44 (m, 1H, H-4); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC, HMBC-Gated): δ 139.1, 138.6 , 138.2, 137.9 ($C_{q\text{-}arom}$), 131.1, 128.9, 128.6, 128.2, 128.0, 127.9, 127.9, 127.8, 127.8, 127.6, 127.6, 127.3, 126.8 (CH_{arom}), 87.0 (C-1), 77.0 (C-2), 74.4 (C-4), 74.0 (C-3), 74.0, 71.2, 70.9 (CH_2 Bn), 58.2 (C-5); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 87.0 ($J_{C1\text{-}H1}$ = 162 Hz); HRMS: $[M+NH_4]^+$ calcd for $C_{32}H_{36}NO_4S$ 530.23596, found 530.23579.



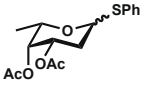
Phenyl 2,3,4-tri-*O*-benzyl-1-thio-β-L-fucopyranoside (S12). Compound **S12** was obtained from L-fucose, according to a literature procedure.[63] TLC: R_f 0.53 (pentane:Et_2O, 8:2, v:v); IR (thin film, cm^{-1}): 736, 868, 1043, 1053, 1059, 1441, 1479, 1584, 2855, 2897; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.65 – 7.16 (m, 20H, CH_{arom}), 5.01 (d, *J* = 11.6 Hz, 1H, C*H*H Bn), 4.79 (d, *J* = 10.2 Hz, 1H, CH*H* Bn), 4.75 – 4.64 (m, 4H, CH_2 Bn, CH_2 Bn), 4.60 (d, *J* = 9.6 Hz, 1H, H-1), 3.93 (t, *J* = 9.4 Hz, 1H, H-2), 3.64 (dd, *J* = 2.9, 0.9 Hz, 1H, H-4), 3.59 (dd, *J* = 9.2, 2.8 Hz, 1H, H-3), 3.53 (qd, *J* = 6.4, 1.0 Hz, 1H, H-5), 1.27 (d, *J* = 6.4 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 138.9, 138.5, 138.5 ($C_{q\text{-}arom}$), 134.5, 131.6, 128.9, 128.6, 128.5, 128.4, 128.3, 128.1, 127.8, 127.8, 127.7, 127.6, 127.1 (CH_{arom}), 87.7 (C-1), 84.7 (C-3), 77.3 (C-2),

76.8 (C-4), 75.7 (CH_2 Bn), 74.8 (C-5), 74.7, 73.0 (CH_2 Bn), 17.5 (CH_3); HRMS: $[M+H]^+$ calcd for $C_{33}H_{35}O_4S$ 527.22506, found 527.22479.

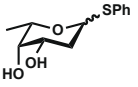
Preparation of donor S15



Scheme S2. Donor **S15** synthesis. *Reagents and conditions:* a) *i.* Ac_2O, pyridine; *ii.* HBr, AcOH, DCM; *iii.* Bu_3SnH, AIBN, toluene; *iv.* PhSH, $BF_3{\cdot}OEt_2$, DCM, **S13**: 61%; b) NaOMe, MeOH, **S14**: 97%; c) BnBr, NaH, DMF, **S15**: 92%.

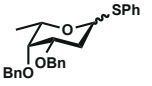


Phenyl 2-deoxy-3,4-di-*O*-acetyl-1-thio-L-fucopyranoside (S13). To a suspension of L-fucose (928 mg, 5.7 mmol) in pyridine (2.5 mL), Ac_2O (5 mL, 53 mmol, 12 eq.) was added dropwise at 0 °C. After stirring for an additional 16 h at room temperature the mixture was concentrated *in vacuo* and co-evaporated three times with heptane. The crude product was dissolved in a mixture of DCM (4 mL) and Ac_2O (0.25 mL, 2.6 mmol, 0.5 eq.), HBr (33 wt% in AcOH, 1.6 mL, 9.9 mmol, 1.8 eq.) was added dropwise at 0 °C. The mixture was stirred for an additional 4 h at room temperature and subsequently concentrated under reduced pressure. The crude product was dissolved in toluene (500 mL, 0.01 M) and AIBN (123 mg, 0.75 mmol, 0.1 eq.) was added. The reaction was stirred at 80 °C for 30 min and Bu_3SnH (3 mL, 11.3 mmol, 2 eq.) was added dropwise over 16 h. The reaction mixture was concentrated and column chromatography (90:10 → 80:20, pentane:EtOAc) afforded the crude product. The crude product was dissolved in DCM (40 mL, 0.15 M) and cooled to −80 °C. Subsequently, thiophenol (0.6 mL, 5.9 mmol, 1.05 eq.) and $BF_3{\cdot}OEt_2$ (0.79 mL, 6.2 mmol, 1.1 eq.) were added dropwise to the solution and the reaction was allowed to warm up to room temperature in 4 h. The reaction mixture was quenched with sat. aq. $NaHCO_3$ and extracted with DCM (3x). The combined organic layers were dried with $MgSO_4$ and concentrated *in vacuo*. The residue was purified using column chromatography (pentane:EtOAc, 90:10 → 70:30) affording title compound **S13**. (1.43 g, 3.4 mmol, 61% over 4 steps, average of 85% per step, colorless oil, 1,3-*cis*:1,3-*trans*; 20:80). TLC: R_f 0.45 (pentane:EtOAc, 8:2, v:v); IR (thin film, cm^{-1}): 884, 1024, 1060, 1224, 1366, 1440, 1480, 1742; Data of the major stereoisomer (1,3-*trans* product): ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.55 – 7.22 (m, 5H, CH_{arom} SPh), 5.74 (d, *J* = 5.7 Hz, 1H, H-1), 5.28 (ddd, *J* = 12.6, 4.9, 3.0 Hz, 1H, H-3), 5.23 (d, *J* = 3.1 Hz, 1H, H-4), 4.56 (dt, *J* = 7.5, 6.0 Hz, 1H, H-5), 2.46 (td, *J* = 12.9, 5.9 Hz, 1H, H-2), 2.16 (s, 3H, CH_3 Ac), 2.10 – 2.02 (m, 1H, H-2), 2.01 (s, 3H, CH_3 Ac), 1.15 (d, *J* = 6.5 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 170.8, 170.1 (C=O Ac), 131.1, 129.1, 127.3 (C_{arom} SPh), 83.8 (C-1), 69.8 (C-3), 67.4 (C-4), 65.9 (C-5), 30.7 (C-2), 20.9 (CH_3 Ac), 16.6 (C-6); Data of the minor stereoisomer (1,3-*cis* product): ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.55 – 7.22 (m, 5H, CH_{arom} SPh), 5.13 (d, *J* = 3.2 Hz, 1H, H-4), 5.01 (ddd, *J* = 10.1, 7.4, 3.1 Hz, 1H, H-3), 4.83 (dd, *J* = 8.3, 5.8 Hz, 1H, H-1), 3.73 (qd, *J* = 6.3, 0.9 Hz, 1H, H-5), 2.16 (s, 3H, CH_3 Ac), 2.12 – 2.02 (m, 2H, H-2, H-2), 2.00 (s, 3H, CH_3 Ac), 1.24 (d, *J* = 6.4 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 131.8, 129.0, 127.7 (CH_{arom} SPh), 82.5 (C-1), 73.4 (C-5), 70.0 (C-3), 68.7 (C-4), 31.5 (C-2), 21.1 (CH_3 Ac), 17.1 (CH_3); HRMS: $[M+Na]^+$ calcd for $C_{16}H_{20}NaO_5S$ 347.0929, found 347.0925.

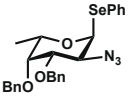


Phenyl 2-deoxy-1-thio-L-fucopyranoside (S14). Compound **S13** (243 mg, 0.75 mmol) was dissolved in MeOH (3 mL, 0.25 M), NaOMe (8 mg, 750 µmol, 0.1 eq.) was added portion wise to the stirred solution. After 4 h of stirring the reaction was quenched with Amberlite IR120 H^+. Filtration followed by column chromatography (50:50 → 20:80, pentane:EtOAc) afforded the title compound **S14** (0.78 g, 3.3 mmol, 97%, white solid, 1,3-*cis*:1,3-*trans*; 20:80). TLC: R_f 0.43 (pentane:EtOAc, 2:8, v:v); IR (neat, cm^{-1}): 733, 876, 968, 1092, 1165, 1373, 1585, 2882, 3348; Data of the major stereoisomer (1,3-*trans* product): ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.56 – 7.17 (m, 5H, CH_{arom}), 5.65 (d, *J* = 5.7 Hz, 1H, H-1), 4.03 (ddd, *J* = 12.1, 5.3, 3.2 Hz, 1H, H-3), 3.79 – 3.53 (m, 2H, H-4, H-5), 2.84 – 2.29 (m, 2H, 3-OH, 4-OH), 2.29 – 2.04

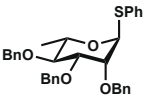
(m, 1H, H-2), 2.18 – 1.70 (m, 1H, H-2), 1.28 (d, *J* = 6.6 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 135.1 ($C_{q\text{-}arom}$), 131.6, 131.1, 129.1, 127.2 (CH_{arom}), 84.0 (C-1), 71.4 (C-4), 67.0 (C-5), 66.7 (C-3), 33.6 (C-2), 16.8 (CH_3). Data of the minor stereoisomer (1,3-*cis* product): ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.56 – 7.17 (m, 5H, CH_{arom}), 4.72 (dd, *J* = 12.0, 2.2 Hz, 1H, H-1'), 4.43 (q, *J* = 6.8 Hz, 1H, H-5'), 3.79 – 3.53 (m, 2H, H-3', H-4'), 2.84 – 2.29 (m, 2H, 3-OH, 4-OH), 2.29 – 2.04 (m, 1H, H-2), 2.18 – 1.70 (m, 1H, H-2), 1.35 (d, *J* = 6.5 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 134.0 ($C_{q\text{-}arom}$), 131.6, 129.1, 129.0, 127.6 (CH_{arom}), 82.5 (C-1), 74.8 (C-4), 70.6 (C-5), 69.8 (C-3), 34.7 (C-2), 17.3 (CH_3); HRMS: $[M+Na]^+$ calcd for $C_{12}H_{16}NaO_3S$ 263.0719, found 263.0717.



Phenyl 2-deoxy-3,4-di-*O*-benzyl-1-thio-L-fucopyranoside (S15). Compound **S14** (120 mg, 0.5 mmol) was dissolved in DMF (2.5 mL, 0.25 M) and cooled to 0 °C. NaH (60% dispersion in mineral oil, 44 mg, 1.1 mmol, 2.2 eq.) was added portion wise and the resulting mixture was stirred for 15 min. Subsequently, benzyl bromide (131 µL, 1.1 mmol, 2.2 eq.) was added and the reaction mixture was allowed to warm up to room temperature and stirred for an additional 16 h. The reaction was quenched with MeOH and diluted with H_2O, after which the resulting mixture was extracted with Et_2O (3x). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. Column chromatography (95:5 → 85:15, pentane:Et_2O) gave the title compound **S15** (194 mg, 0.46 mmol, 92%, white solid, 1,3-*cis*:1,3-*trans*; 39:61). TLC: R_f 0.42 and 0.62 (pentane:Et_2O, 9:1, v:v); IR (thin film, cm^{-1}): 691, 733, 957, 1026, 1057, 1099, 1362, 2866; Data of the major stereoisomer (1,3-*trans* product): ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.63 – 7.16 (m, 15H, CH_{arom}), 5.76 (d, *J* = 5.6 Hz, 1H, H-1), 4.98 (d, *J* = 11.7 Hz, 1H, C*H*H Bn), 4.71 (m, 1H, CH*H* Bn) 4.66 (d, *J* = 12.8 Hz, 1H, C*H*H Bn), 4.62 (d, *J* = 11.9 Hz, 1H, CH*H* Bn), 4.27 (q, *J* = 6.5 Hz, 1H, H-5), 3.91 (ddd, *J* = 12.3, 4.4, 2.5 Hz, 1H, H-3), 3.70 – 3.63 (m, 1H, H-4), 2.60 (td, *J* = 12.7, 5.8 Hz, 1H, H-2_{ax}), 2.16 (dd, *J* = 13.0, 4.5 Hz, 1H, H-2_{eq}), 1.19 (d, *J* = 6.5 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 138.9, 138.4, 135.7 ($C_{q\text{-}arom}$), 131.3, 130.6, 129.0, 128.8, 128.6, 128.4, 128.3, 127.8, 127.5 (CH_{arom}), 84.4 (C-1), 76.1 (C-3/C-4), 76.0 (C-3/C-4), 74.6 (CH_2 Bn), 70.6 (CH_2 Bn), 68.0 (C-5), 31.7 (C-2), 17.3 (CH_3); Data of the minor stereoisomer (1,3-*cis* product): ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.98 (d, *J* = 11.8 Hz, 1H, C*H*H Bn), 4.74 – 4.68 (m, 1H, H-1), 4.69 (d, *J* = 11.8 Hz, 1H, C*H*H Bn), 4.63 (d, *J* = 12.1 Hz, 1H, CH*H* Bn), 4.57 (d, *J* = 12.1 Hz, 1H, CH*H* Bn), 3.59 (ddd, *J* = 11.5, 4.6, 2.5 Hz, 1H, H-3), 3.54 (dt, *J* = 2.5, 1.2 Hz, 1H, H-4), 3.46 (q, *J* = 5.7 Hz, 1H, H-5), 2.28 (q, *J* = 11.9 Hz, 1H, H-2_{ax}), 2.20 – 2.10 (m, 1H, H-2_{eq}), 1.26 (d, *J* = 6.4 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 139.0, 138.4 ($C_{q\text{-}arom}$), 134.7, 131.3, 128.8, 128.6, 128.3, 128.2, 127.7, 127.5, 127.4, 127.1, 127.0, 126.8 (CH_{arom}), 82.7 (C-1), 79.0 (C-3), 75.1 (C-5), 74.6 (C-4), 74.3 (CH_2 Bn), 70.3 (CH_2 Bn), 68.0 (CH_2 Bn), 32.1 (C-2), 17.8 (CH_3); HRMS: $[M+Na]^+$ calcd for $C_{26}H_{28}NaO_3S$ 443.1657, found 443.1651.

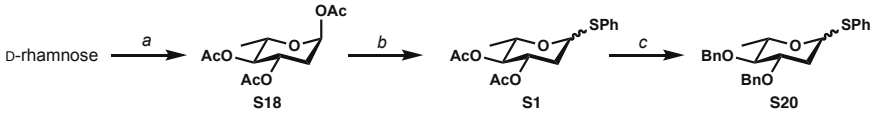


Phenyl 2-azido-2-deoxy-3,4-di-*O*-benzyl-1-seleno-β-L-fucopyranoside (S16). Compound **S16** was obtained from L-fucose, according to a literature procedure.[64] TLC: R_f 0.68 (pentane:Et_2O, 8:2, v:v); IR (thin film, cm^{-1}): 694, 737, 1064, 1105, 1454, 1744, 2106, 2855, 2922; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.63 – 7.18 (m, 15H, CH_{arom}), 5.93 (d, *J* = 5.3 Hz, 1H, H-1), 4.93 (d, *J* = 11.5 Hz, 1H, C*H*H Bn), 4.78 (d, *J* = 11.4 Hz, 1H, CH*H* Bn), 4.75 (d, *J* = 11.4 Hz, 1H, C*H*H Bn), 4.60 (d, *J* = 11.4 Hz, 1H, CH*H* Bn), 4.35 (dd, *J* = 9.9, 5.3 Hz, 1H, H-2), 4.22 (q, *J* = 6.5 Hz, 1H, H-5), 3.75 – 3.69 (m, 2H, H-3, H-4), 1.13 (d, *J* = 6.5 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 138.3, 137.6, 134.5 ($C_{q\text{-}arom}$), 129.1, 128.7, 128.4, 128.3, 128.2, 128.0, 127.9, 127.8 (CH_{arom}), 85.7 (C-1), 80.8 (C-3), 75.9 (C-4), 75.1, 72.7 (CH_2 Bn), 69.5 (C-5), 61.1 (C-2), 16.7 (CH_3); HRMS: $[M-N_2+NH_4]^+$ calcd for $C_{26}H_{28}NO_3Se$ 482.12289, found 482.12287.

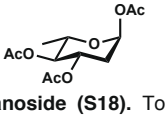


Phenyl 2,3,4-tri-*O*-benzyl-1-thio-β-L-rhamnopyranoside (S17). Compound **S17** was obtained from L-rhamnose, according to a literature procedure.[65] TLC: R_f 0.63 (pentane:Et_2O, 8:2, v:v); IR (thin film, cm^{-1}): 692, 732, 843, 908, 1024, 1070, 1082, 1205, 1452, 2868; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.48 – 7.10 (m, 20H, CH_{arom}), 5.49 (d, *J* = 1.6 Hz, 1H, H-1), 4.97 (d, *J* = 10.8 Hz, 1H, C*H*H Bn), 4.72 (d, *J* = 12.4 Hz, 1H, C*H*H Bn), 4.68 – 4.58 (m, 4H, CH_2 Bn, CH_2 Bn), 4.14 (dq, *J* = 9.3, 6.2 Hz, 1H, H-5), 3.99 (dd, *J* = 3.1, 1.7 Hz, 1H, H-2), 3.83 (dd, *J* = 9.3, 3.1 Hz, 1H, H-3), 3.68 (t, *J* = 9.3 Hz, 1H, H-4), 1.35 (d, *J* = 6.2 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 138.6, 138.3, 138.0, 134.8 ($C_{q\text{-}arom}$), 131.4, 129.1, 128.5, 128.5, 128.1, 128.1, 127.9, 127.9, 127.8, 127.4 (CH_{arom}), 85.9 (C-1), 80.6 (C-4), 80.1 (C-3), 76.6 (C-2), 75.6, 72.2, 72.2 (CH_2 Bn), 69.4 (C-5), 18.1 (CH_3); HRMS: $[M+H]^+$ calcd for $C_{33}H_{35}O_4S$ 527.22506, found 527.22483.

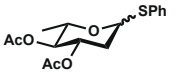
Preparation of donor S20



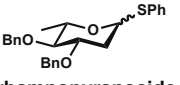
Scheme S3. Donor **S20** synthesis. *Reagents and conditions:* a) *i.* Ac_2O, pyr; *ii.* HBr, AcOH, DCM; *iii.* $CuSO_4{\cdot}5H_2O$, Ac_2O, NaOAc, AcOH, Zn; *iv.* Ac_2O, HBr, AcOH, **S18**: 60%; b) PhSH, $BF_3{\cdot}Et_2O$, DCM, **S19**: 97%; c) *i.* NaOMe, MeOH, *ii.* BnBr, NaH, DMF, **S20**: 95%.



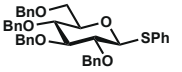
2-deoxy-1,3,4-tri-*O*-acetyl-α-L-rhamnopyranoside (S18). To suspension of L-rhamnose (4.5 g, 27.5 mmol) in pyridine (25 mL), Ac_2O (32 mL, 340 mmol, 12 eq.) at 0 °C. After stirring for an additional 16 h at room temperature the mixture was concentrated *in vacuo* and co-evaporated three times with heptane. The resulting colorless oil was used in the next step without further purification. The crude product was dissolved in DCM (18 mL), followed by the addition of Ac_2O (1.0 mL, 11 mmol, 0.4 eq.). To the solution HBr (33 wt% in AcOH, 8.5 mL, 55.0 mmol, 2.0 eq.) was added dropwise at 0 °C and stirred for an additional 4 h at room temperature The mixture was then concentrated under reduced pressure and the yellow oil was used as a crude product in the next step. Copper sulfate pentahydrate (0.88 g), Ac_2O (3.6 mL, 38 mmol, 1.4 eq.), sodium acetate (4.5 g, 55 mmol, 2 eq.), AcOH (3.2 mL) were suspended in acetonitrile (12 mL), and subsequently Zn (dust, 3.6 g, 55 mmol, 2 eq.) was added. After 45 min of stirring the rhamnosyl bromide was added in 60 mL acetonitrile via a dropping funnel over 40 min. The reaction was allowed to stir for an additional 2 h. After reaction completion the mixture was diluted with DCM and filtrated over Celite® 545 (Sigma-Aldrich) and transferred to a separatory funnel. The organic phase was washed with saturated sat. aq. $NaHCO_3$, dried with $MgSO_4$ and concentrated *in vacuo*. The crude rhamnal was dissolved in DCM (40 mL) and AcOH (15.8 mL, 276 mmol, 10 eq.), Ac_2O (22.2 mL, 233 mmol, 8.5 eq.) were added at 0 °C. After 15 min stirring, HBr (33 wt% in AcOH, 1.5 mL, 9.1 mmol, 0.3 eq.) was dropwise added at 0 °C and the reaction was stirred for an additional 5 h. After reaction completion the mixture was diluted with ice-cold water and extracted DCM (3x). The combined organic layers were washed with sat. aq. $NaHCO_3$, dried with $MgSO_4$ and concentrated *in vacuo*. Column chromatography (95:5 → 85:15, pentane:EtOAc) gave the title compound **S18** (4.5 g, 16.4 mmol, 60% over 4 steps, average of 88% per step, white solid). TLC: R_f 0.26 (pentane:EtOAc, 8:2, v:v); IR (neat, cm^{-1}): 922, 1037, 1134, 1157, 1369, 1732, 2994; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 6.19 (dd, *J* = 3.8, 1.4 Hz, 1H, H-1), 5.27 (ddd, *J* = 11.6, 9.5, 5.3 Hz, 1H, H-3), 4.80 (t, *J* = 9.7 Hz, 1H, H-4), 3.94 (dq, *J* = 9.8, 6.2 Hz, 1H, H-5), 2.26 (ddd, *J* = 13.5, 5.3, 1.5 Hz, 1H, H-2), 2.12 (s, 3H, CH_3 Ac), 2.07 (s, 3H, CH_3 Ac), 2.03 (s, 3H, CH_3 Ac), 1.92 (ddd, *J* = 13.5, 11.7, 3.7 Hz, 1H, H-2), 1.19 (d, *J* = 6.3 Hz, 3H, CH_3); ^{13}C NMR (126 MH, $CDCl_3$, HSQC): δ 170.4, 170.1, 169.3 (C=O, Ac), 90.9 (C-1), 74.2 (C-4), 68.5 (C-3), 68.3 (C-5), 34.3 (C-2), 21.2 (CH_3 Ac), 21.1 (CH_3 Ac), 20.9 (CH_3 Ac), 17.7 (CH_3); HRMS: $[M+Na]^+$ calcd for $C_{12}H_{18}NaO_7$ 297.0950, found 297.0951.



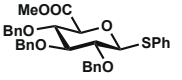
Phenyl 2-deoxy-3,4-di-*O*-acetyl-1-thio-L-rhamnopyranoside (S19). Compound **S18** (400 mg, 1.46 mmol) was dissolved in DCM (10 mL, 0.15M), and thiophenol (0.20 mL, 1.90 mmol, 1.3 eq.) was added, followed by the dropwise addition of $BF_3{\cdot}OEt_2$ (0.21 mL, 1.63 mmol, 1.1 eq.) at −80 °C. The reaction mixture was allowed to warm to room temperature in approximately 4 h. After 4 h, the reaction mixture quenched with sat. aq. $NaHCO_3$. The water layer was extracted with DCM (2x). The combined organic layer layers were washed with sat. aq. $NaHCO_3$ and dried with $MgSO_4$ and concentrated *in vacuo*. Column chromatography (95:5 → 85:15, pentane:EtOAc) gave the title compound **S19** (460 mg, 1.42 mmol, 97%, colorless oil, 1,3-*cis*:1,3-*trans*; 36:64). TLC: R_f 0.52 (pentane:EtOAc, 8:2, v:v); IR (thin film, cm^{-1}): 741, 910, 1049, 1219, 1366, 1740, 2982; Data of the major stereoisomer (1,3-*trans* product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.56 – 7.20 (m, 5H, CH_{arom} SPh), 5.60 (d, *J* = 5.6 Hz, 1H, H-1), 5.26 (ddd, *J* = 11.8, 9.3, 5.2 Hz, 1H, H-3), 4.83 – 4.71 (m, 1H, H-4), 4.37 (dq, *J* = 9.6, 6.2 Hz, 1H, H-5), 2.45 (ddd, *J* = 13.4, 5.2, 1.2 Hz, 1H, H-2_{eq}), 2.20 (ddd, *J* = 13.4, 11.8, 5.9 Hz, 1H, H-2_{ax}), 2.08 (s, 3H, Ac CH_3), 2.03 (s, 3H, Ac CH_3), 1.19 (d, *J* = 6.2 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 170.35, 170.31 (C=O, Ac), 134.67 ($C_{q\text{-}arom}$), 133.02, 132.41, 131.34, 129.14, 129.07, 127.41 (CH_{arom}), 83.14 (C-1), 74.91 (C-4), 69.45 (C-3), 66.90 (C-5), 36.01 (CH_3 Ac), 21.15 (CH_3 Ac), 21.01 (CH_3 Ac), 17.57 (CH_3); Data of the minor stereoisomer (1,3-*cis* product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.98 (ddd, *J* = 11.4, 9.5, 5.4 Hz, 1H, H-3), 3.52 (dq, *J* = 9.6, 6.2 Hz, 1H, H-4), 2.05 (s, 3H, Ac CH_3), 2.01 (s, 3H, Ac CH_3), 1.83 (dt, *J* = 12.7, 11.6 Hz, 1H, Ac CH_3), 1.26 (d, *J* = 6.2 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 170.50, 170.21 (C=O, Ac), 81.69 (C-1), 74.46 (C-5), 73.89 (C-4), 71.88 (C-3), 36.69 (CH_3 Ac), 21.10 (CH_3 Ac), 20.98 (CH_3 Ac), 18.05 (CH_3); HRMS: $[M+Na]^+$ calcd for $C_{16}H_{20}NaO_5S$ 347.0929, found 347.0928.



Phenyl 2-deoxy-3,4-di-*O*-benzyl-1-thio-L-rhamnopyranoside (S20). Compound **S19** (400 mg, 1.2 mmol) was dissolved in MeOH (6 mL, 0.2 M), and NaOMe (7 mg, 120 µmol, 0.1 eq.) was added. The reaction mixture was stirred for 4 h, and subsequently quenched with Amberlite IR120 H^+ and filtrated. The resulting filtrate was concentrated *in vacuo*. The crude product was dissolved in DMF (6 mL, 0.2 M) and cooled to 0 ^{0}C, and NaH (60% dispersion in mineral oil, 109 mg, 2.7 mmol, 2.2 eq.). The resulting suspension was stirred for 15 min, and benzyl bromide (323 µL, 2.7 mmol, 2.2 eq.) was dropwise added. The reaction mixture was allowed to warm up to room temperature and stirred for an additional 16 h. The reaction was quenched with MeOH and diluted with H_2O. The resulting reaction mixture was extracted with Et_2O (3x), and the combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. Column chromatography (95:5 → 85:15, pentane:Et_2O) gave the title compound **S20** (495 mg, 1.18 mmol, 95%, white solid, 1,3-*cis*:1,3-*trans*; 35:65). TLC: R_f 0.46 and 0.59 (pentane:Et_2O, 9:1, v:v); IR (thin film, cm^{-1}): 694, 737, 995, 1072, 2866; Data of the major stereoisomer (1,3-*trans* product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.54 – 7.14 (m, 15H, CH_{arom}), 5.58 (dd, *J* = 5.8, 1.3 Hz, 1H, H-1), 4.96 (d, *J* = 10.9 Hz, 1H, C*H*H Bn), 4.70 – 4.64 (m, 4H, CH*H* Bn, CH_2 Bn), 4.23 (dq, *J* = 9.4, 6.2 Hz, 1H, H-5), 3.94 (ddd, *J* = 11.5, 8.6, 4.8 Hz, 1H, H-3), 3.17 (t, *J* = 9.0 Hz, 1H, H-4), 2.47 (ddd, *J* = 13.2, 4.7, 1.3 Hz, 1H, H-2_{eq}), 2.09 (ddd, *J* = 13.4, 11.6, 5.7 Hz, 1H, H-2_{ax}), 1.29 (d, *J* = 6.2 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 138.6, 138.5 ($C_{q\text{-}arom}$), 131.3, 129.0, 128.6, 128.5, 128.1, 127.9, 127.2 (CH_{arom}), 84.5 (C-4), 83.9 (C-1), 77.8 (C-3), 75.4 (CH_2 Bn), 72.0 (CH_2 Bn), 68.5 (C-5), 36.7 (C-2), 18.2 (CH_3); Data of the minor stereoisomer (1,3-*cis* product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.94 (d, *J* = 10.9 Hz, 1H, C*H*H Bn), 4.73 (dd, *J* = 11.9, 2.0 Hz, 1H, H-1), 4.61 (d, *J* = 11.6 Hz, 1H, CH*H* Bn), 3.65 (ddd, *J* = 11.1, 8.7, 5.2 Hz, 1H, H-3), 3.39 (dq, *J* = 9.3, 6.1 Hz, 1H, H-5), 3.15 (t, *J* = 9.0 Hz, 1H, H-4), 1.79 (dt, *J* = 12.8, 11.6 Hz, 1H, H-2_{ax}), 1.36 (d, *J* = 6.2 Hz, 1H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 138.5, 138.3 ($C_{q\text{-}arom}$), 134.2, 131.4, 129.0, 128.2, 127.9, 127.5 (CH_{arom}), 83.5 (C-4), 82.0 (C-1), 80.6 (C-3), 75.8 (C-5), 75.5 (CH_2 Bn), 71.8 (CH_2 Bn), 37.3 (C-2), 18.6 (CH_3); HRMS: $[M+Na]^+$ calcd for $C_{26}H_{28}NaO_3S$ 443.1657, found 443.1651.

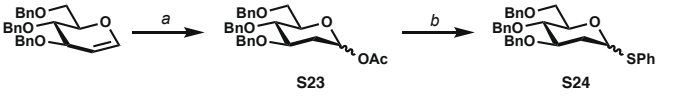


Phenyl 2,3,4,6-tetra-*O*-benzyl-1-thio-β-D-glucopyranoside (S21). Compound **S21** was obtained from D-glucose, according to a literature procedure.[66] TLC: R_f 0.73 (pentane:EtOAc, 9:1, v:v); $[\alpha]_D^{20}$ = 15.2° (*c* 1, DCM); IR (thin film, cm^{-1}): 714, 781, 1063, 1359, 1453, 2858, 2922; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.68 – 7.09 (m, 25H, CH_{arom}), 4.90 (d, *J* = 10.9 Hz, 1H, C*H*H Bn), 4.89 (d, *J* = 10.3 Hz, 1H, C*H*H Bn), 4.84 (d, *J* = 10.9 Hz, 1H, CH*H* Bn), 4.82 (d, *J* = 10.9 Hz, 1H, C*H*H Bn), 4.73 (d, *J* = 10.3 Hz, 1H CH*H* Bn), 4.67 (dd, *J* = 9.8, 0.9 Hz, 1H, H-1), 4.61 (d, *J* = 12.0 Hz, 1H C*H*H Bn), 4.59 (d, *J* = 10.8 Hz, 1H, CH*H* Bn), 4.54 (d, *J* = 12.0 Hz, 1H, CH*H* Bn), 3.79 (dd, *J* = 10.9, 1.9 Hz, 1H, H-6), 3.75 – 3.61 (m, 3H, H-3, H-4, H-6), 3.55 – 3.47 (m, 2H, H-2, H-5); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 138.5, 138.4, 138.2, 134.0 ($C_{q\text{-}arom}$), 132.1, 129.0, 128.6, 128.4, 128.1, 128.0, 127.9, 127.8, 127.8, 127.7, 127.6 (CH_{arom}), 87.6 (C-1), 86.9 (C-3), 81.0 (C-5), 79.2 (C-2), 78.0 (C-4), 76.0, 75.6, 75.2, 73.6 (CH_2 Bn), 69.2 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{40}H_{40}NaO_5S$ 655.2494, found 655.2496.



Methyl (phenyl 2,3,4-tri-*O*-benzyl-1-thio-β-D-glucopyranosyl uronate) (S22). Compound **S22** was obtained from D-glucose, according to a literature procedure.[66] TLC: R_f 0.56 (pentane:EtOAc, 9:1, v:v); IR (thin film, cm^{-1}): 697, 738, 1026, 1073, 1209, 1439, 1453, 1750, 2856, 2924; ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.71 – 7.08 (m, 20H, CH_{arom}), 4.88 (d, *J* = 10.3 Hz, 1H, C*H*H Bn), 4.88 (d, *J* = 10.9 Hz, 1H, C*H*H Bn), 4.84 (d, *J* = 10.9 Hz, 1H, CH*H* Bn), 4.78 (d, *J* = 10.8 Hz, 1H, C*H*H Bn), 4.73 (d, *J* = 10.2 Hz, 1H, CH*H* Bn), 4.68 (d, *J* = 9.8 Hz, 1H, H-1), 4.61 (d, *J* = 10.8 Hz, 1H, CH*H* Bn), 3.92 (d, *J* = 9.7 Hz, 1H, H-5), 3.84 (t, *J* = 9.4 Hz, 1H, H-4), 3.73 (s, 3H, CH_3 COOMe), 3.71 (t, *J* = 8.9 Hz, 1H, H-3), 3.52 (dd, *J* = 9.8, 8.7 Hz, 1H, H-2); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 168.8 (C=O), 138.2, 137.9, 137.8, 133.3 ($C_{q\text{-}arom}$), 132.3, 129.1, 128.6, 128.5, 128.5, 128.3, 128.1, 128.0, 128.0, 127.9 (CH_{arom}), 88.4 (C-1), 86.0 (C-3), 80.4 (C-2), 79.3 (C-4), 78.1 (C-5), 76.0, 75.6, 75.2 (CH_2 Bn), 52.6 (CH_3 COOMe); HRMS: $[M+Na]^+$ calcd for $C_{34}H_{34}NaO_6S$ 593.1968, found 593.1977.

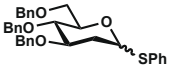
Preparation of donor S24



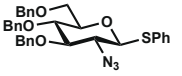
S23 S24

Scheme S4. Donor **S24** synthesis. *Reagents and conditions:* a) HBr·PPh_3, AcOH, **S23**: 83%; b) PhSH, *p*TsOH, DCM, **S24**: 91%.

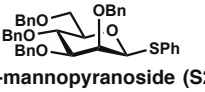
Phenyl 2-deoxy-3,4,6-tri-*O*-benzyl-1-thio-D-glucopyranoside (S23). Compound **S23** was obtained from 2-deoxy-tri-*O*-benzyl-D-glucal, according to a literature procedure as a mixture of stereoisomers (1,3-*cis*:1,3-*trans*; 10:90).[22] TLC: R_f 0.30 (pentane:EtOAc, 9:1, v:v); IR (thin film, cm^{-1}): 694, 734, 1026, 1078, 1362, 1454, 2863; Data of the major stereoisomer (1,3-*trans* product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.47 – 7.06 (m, 15H, CH_{arom}), 6.25 (dd, *J* = 3.5, 1.5 Hz, 1H, H-1), 4.90 (d, *J* = 10.6 Hz, 1H, C*H*H Bn), 4.68 – 4.60 (m, 2H, C*H*H Bn, CH*H* Bn), 4.54 (d, *J* = 10.7 Hz, 1H, C*H*H Bn), 4.51 (d, *J* = 12.1 Hz, 1H, CH*H* Bn), 4.00 – 3.92 (m, 1H, CH*H* Bn), 3.96 (ddd, *J* = 11.4, 8.8, 4.9 Hz, 1H, H-3), 3.84 (dq, *J* = 9.9, 1.9 Hz, 1H, H-5), 3.78 (dd, *J* = 10.7, 3.5 Hz, 1H, H-6) 3.71 (dd, *J* = 9.8, 8.9 Hz, 1H, H-4), 3.66 (dd, *J* = 10.7, 1.9 Hz, 1H, H-6), 2.28 (ddd, *J* = 13.6, 5.0, 1.7 Hz, 1H, H-2_{eq}), 2.04 (s, 3H, CH_3 Ac), 1.84 (ddd, *J* = 13.6, 11.5, 3.5 Hz, 1H, H-2_{ax}); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 169.4 (C=O), 138.4, 138.3, 138.1 ($C_{q\text{-}arom}$), 128.5, 128.5, 128.1, 128.0, 127.8, 127.8, 127.8, 127.7 (CH_{arom}), 92.3 (C-1), 77.6 (C-4), 76.9 (C-3), 75.3 (CH_2 Bn), 73.6 (CH_2 Bn), 73.5 (C-5), 71.9 (CH_2 Bn), 68.5 (C-6), 34.3 (C-2), 21.2 (CH_3 Ac); Data of the minor stereoisomer (1,3-*cis* product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.67 (dd, *J* = 10.0, 2.2 Hz, 1H, H-1), 2.36 (ddd, *J* = 12.5, 4.9, 2.2 Hz, 1H, H-2_{eq}), 2.10 (s, 3H, CH_3 Ac). ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 169.4 (C=O), 92.9 (C-1), 75.1 (CH_2 Bn), 73.6 (CH_2 Bn), 71.8 (CH_2 Bn), 35.5 (C-2); HRMS: $[M+Na]^+$ calcd for $C_{29}H_{32}NaO_6$ 499.2091, found 499.2096.



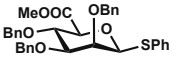
Phenyl 2-deoxy-3,4,6-tri-*O*-benzyl-1-thio-D-glucopyranoside (S24). Compound **S23** (0.7 g, 1.5 mmol) was dissolved in DCM (14 mL, 0.1 M), followed by the addition of thiophenol (0.3 mL, 3.0 mmol, 2 eq.) and *p*TsOH (0.56 g, 3.0 mmol, 2 eq.). After 16 h of stirring the reaction was quenched with sat. aq. $NaHCO_3$ and extracted with DCM (3x). The combined organic layers were washed with brine and dried over $MgSO_4$. Column chromatography (95:5 → 80:20, pentane:Et_2O) gave the title compound **S24** (702 mg, 1.33 mmol, 91%, colorless oil, 1,3-*cis*:1,3-*trans*; 40:60). TLC: R_f 0.60 (pentane:EtOAc, 9:1, v:v); IR (thin film, cm^{-1}): 694, 734, 1026, 1078, 1362, 1454, 2863; Data of the major stereoisomer (1,3-*trans* product): ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.70 – 6.94 (m, 20H, CH_{arom}), 5.69 (dd, *J* = 5.6, 1.2 Hz, 1H, H-1), 4.90 (d, *J* = 10.9 Hz, 1H, C*H*H Bn), 4.74 – 4.51 (m, 4H, CH_2 Bn, CH_2 Bn, CH_2 Bn, CH_2 Bn), 4.46 (d, *J* = 12.0 Hz, 1H, CH*H* Bn), 4.30 (ddd, *J* = 9.8, 4.1, 2.0 Hz, 1H, H-5), 3.97 (ddd, *J* = 11.6, 8.7, 4.9 Hz, 1H, H-3), 3.90 – 3.76 (m, 1H, H-6), 3.73 (dd, *J* = 10.8, 4.6 Hz, 1H, H-5), 3.66 (ddd, *J* = 8.8, 5.0, 2.9 Hz, 1H, H-4), 2.49 – 2.41 (m, 1H, H-2_{eq}), 2.13 (ddd, *J* = 13.4, 11.7, 5.7 Hz, 1H, H-2_{ax}); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 138.5, 138.5, 138.2 ($C_{q\text{-}arom}$), 131.3, 129.0, 129.0, 128.6, 128.5, 128.5, 128.1, 128.0, 127.9, 127.8, 127.8 (CH_{arom}), 84.2 (C-1), 78.1 (C-4), 78.0 (C-3), 75.2, 73.5, 72.0 (CH_2 Bn), 71.8 (C-5), 68.9 (C-6), 36.4 (C-2). Data of the minor stereoisomer (1,3-*cis* product): ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.75 (dd, *J* = 11.9, 1.9 Hz, 1H, H-1), 1.88 – 1.74 (m, 1H, H-2). ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 82.2 (C-1), 37.0 (C-2); HRMS: $[M+Na]^+$ calcd for $C_{33}H_{34}NaO_4S$ 549.2070, found 549.2081.



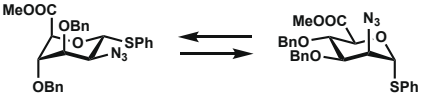
Phenyl 2-azido-2-deoxy-3,4,6-tetra-*O*-benzyl-1-thio-β-D-glucopyranoside (S25). Compound **S25** was obtained from D-glucosamine, according to a literature procedure.[67] TLC: R_f 0.61 (pentane:EtOAc, 9:1, v:v); IR (thin film, cm^{-1}): 697, 1101, 1105, 1146, 1276, 1453, 2109, 2856, 2919; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.60 (m, 2H, CH_{arom}), 7.35- 7.19 (m, 18H, CH_{arom}), 4.86 (d, *J* = 10.5 Hz, 1H, C*H*H Bn), 4.83 (d, *J* = 10.5 Hz, 1H, CH*H* Bn), 4.79 (d, *J* = 11.0 Hz, 1H, CH*H* Bn), 4.62 (d, *J* = 12.0 Hz, 1H, C*H*H Bn), 4.58 (d, *J* = 10.5 Hz, 1H, CH*H* Bn), 4.54 (d, *J* = 12.0 Hz, 1H, C*H*H Bn), 4.41 (d, *J* = 10.0 Hz, 1H, H-1), 3.80 – 3.71 (m, 2H, H-6), 3.61 (t, *J* = 9.5 Hz, 1H, H-4), 3.51 (t, *J* = 9.5 Hz, 1H, H-3), 3.47 (ddd, *J* = 2.0, 4.0, 9.5 Hz, 1H, H-5), 3.34 (t, *J* = 9.5 Hz, 1H, H-2); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 138.2, 137.8, 137.6 ($C_{q\text{-}arom}$), 133.6, 131.1, 129.0, 128.5, 128.4, 128.3, 128.2, 128.0, 127.9, 127.8, 127.6, 127.5 (CH_{arom}), 85.9 (C-1), 85.0 (C-3), 79.3 (C-5), 77.5 (C-4), 75.9, 75.0, 73.4 (CH_2 Bn), 68.7 (C-6), 65.0 (C-2); HRMS: $[M+Na]^+$ calcd for $C_{33}H_{33}N_3NaO_4S$ 590.2084, found 590.2094.



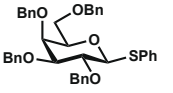
Phenyl 2,3,4,6-tetra-*O*-benzyl-1-thio-β-D-mannopyranoside (S26). Compound **S26** was obtained from D-mannose, according to a literature procedure.[19] TLC: R_f 0.81 (pentane:EtOAc, 9:1, v:v); IR (thin film, cm^{-1}): 694, 731, 1026, 1064, 1362, 1454, 2863, 3029; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.53 – 7.17 (m, 25H, CH_{arom}), 5.05 (d, *J* = 11.5 Hz, 1H, C*H*H Bn), 4.89 (d, *J* = 10.9 Hz, 1H, C*H*H Bn), 4.87 (d, *J* = 11.4 Hz, 1H, CH*H* Bn), 4.77 (d, *J* = 0.9 Hz, 1H, H-1), 4.73 (d, *J* = 11.8 Hz, 1H, CH*H* Bn), 4.69 (d, *J* = 11.8 Hz, 1H, C*H*H Bn), 4.60 (m, 2H, CH*H* Bn, C*H*H Bn), 4.55 (d, *J* = 11.8 Hz, 1H, CH*H* Bn), 4.15 (d, *J* = 2.2 Hz, 1H, H-2), 3.94 (t, *J* = 9.5 Hz, 1H, H-4), 3.84 (dd, *J* = 10.9, 1.8 Hz, 1H, H-6), 3.74 (dd, *J* = 10.9, 6.5 Hz, 1H, H-6), 3.63 (dd, *J* = 9.4, 2.9 Hz, 1H, H-3), 3.54 (ddd, *J* = 9.5, 6.5, 1.8 Hz, 1H, H-5); ^{13}C NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.7, 138.4, 138.3, 138.2, 135.8 ($C_{q\text{-}arom}$), 130.7, 129.0, 128.6, 128.5, 128.4, 128.4, 128.3, 128.2, 127.9, 127.9, 127.8, 127.7, 127.5, 127.1 (CH_{arom}), 87.8 (C-1), 84.5 (C-3), 80.3 (C-5), 77.7 (C-2), 75.3 (CH_2 Bn), 75.2 (CH_2 Bn), 75.1 (C-4), 73.6 (CH_2 Bn), 72.7 (CH_2 Bn), 70.0 (C-6); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 87.8 ($J_{C1,H1}$ = 154 Hz, C-1 β); HRMS: $[M+NH_4]^+$ calcd for $C_{40}H_{44}NO_5S$ 650.29347, found 650.29381.



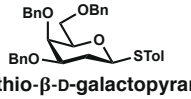
Methyl (phenyl 2,3,4-tri-*O*-benzyl-1-thio-β-D-mannopyranosyl uronate) (S27). Compound **S27** was obtained from D-mannose, according to a literature procedure.[66] TLC: R_f 0.40 (pentane:EtOAc, 9:1, v:v); IR (thin film, cm^{-1}): 695, 734, 1025, 1067, 1131, 1200, 1286, 1438, 1453, 1747, 2850; ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.53 – 7.24 (m, 20H, CH_{arom}), 5.05 (d, *J* = 11.4 Hz, 1H, C*H*H Bn), 4.87 (d, *J* = 11.4 Hz, 1H, CH*H* Bn), 4.86 (d, *J* = 10.8 Hz, 1H, C*H*H Bn), 4.78 (d, *J* = 1.2 Hz, 1H, H-1), 4.74 – 4.67 (m, 3H, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.31 (t, *J* = 9.5 Hz, 1H, H-4), 4.14 (dd, *J* = 2.9, 1.2 Hz, 1H, H-2), 3.87 (d, *J* = 9.5 Hz, 1H, H-5), 3.72 (s, 3H, CH_3 COOMe), 3.62 (dd, *J* = 9.5, 2.9 Hz, 1H, H-3); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 168.4 (C=O), 138.2, 138.0, 135.2 ($C_{q\text{-}arom}$), 131.0, 129.1, 128.6, 128.5, 128.4, 128.3, 128.2, 128.0, 127.9, 127.8, 127.7, 127.5 (CH_{arom}), 89.0 (C-1), 83.5 (C-3), 78.9 (C-5), 77.4 (C-2), 75.7 (C-4), 75.4, 75.3, 72.9 (CH_2 Bn), 52.5 (C-5); HRMS: $[M+Na]^+$ calcd for $C_{34}H_{34}NaO_6S$ 593.1968, found 593.1981.



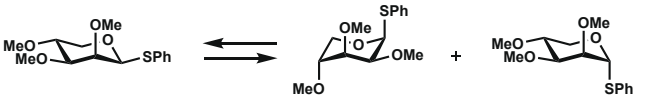
Methyl (phenyl 2-azido-2-deoxy-3,4-tri-*O*-benzyl-1-thio-α-D-mannopyranosyl uronate) (S28). Compound **S28** was obtained from D-mannosamine, according to a literature procedure. TLC: R_f 0.45 (pentane:EtOAc, 9:1, v:v); IR (thin film, cm^{-1}): 695, 736, 1025, 1119, 1206, 1439, 1453, 1750, 2102; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.65 – 7.26 (m, 15H, CH_{arom}), 5.61 (d, *J* = 7.6 Hz, 1H, H-1), 4.68 (d, *J* = 11.4 Hz, 1H, C*H*H Bn), 4.63 (d, *J* = 4.4 Hz, 1H, H-5), 4.59 (s, 2H, CH_2 Bn, CH_2 Bn), 4.21 (dd, *J* = 5.7, 4.4 Hz, 1H, H-4), 3.93 (dd, *J* = 5.7, 3.0 Hz, 1H, H-3), 3.72 (dd, *J* = 9.4, 3.5 Hz, 1H, H-2), 3.54 (s, 3H, CH_3 COOMe); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 169.5 (C=O), 137.5, 137.0 ($C_{q\text{-}arom}$), 132.6 (CH_{arom}), 132.2 ($C_{q\text{-}arom}$), 129.1, 128.6, 128.6, 128.3, 128.2, 128.2, 128.0, 127.9 (CH_{arom}), 82.3 (C-1), 77.2 (C-3), 74.9 (C-4), 73.2 (CH_2 Bn), 73.1 (C-5), 58.9 (C-2), 52.4 (CH_3 COOMe); HRMS: $[M+Na]^+$ calcd for $C_{27}H_{27}N_3NaO_5S$ 528.1564, found 528.1574.



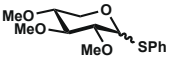
Phenyl 2,3,4,6-tetra-*O*-benzyl-1-thio-β-D-galactopyranoside (S29). Compound **S29** was obtained from D-galactose, according to a literature procedure.[68] TLC: R_f 0.75 (pentane:EtOAc, 9:1, v:v); IR (thin film, cm^{-1}): 714, 782, 1060, 1360, 1452, 2855, 2927; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC) δ 7.63 – 7.11 (m, 30H, CH_{arom}), 4.97 (d, *J* = 11.5 Hz, 1H, C*H*H Bn), 4.78 (d, *J* = 10.2 Hz, 1H, C*H*H Bn), 4.76 – 4.70 (m, 3H, CH*H* Bn, CH*H* Bn, C*H*H Bn), 4.64 (d, *J* = 9.7 Hz, 1H, H-1), 4.60 (d, *J* = 11.6 Hz, 1H, CH*H* Bn), 4.47 (d, *J* = 11.7 Hz, 1H, C*H*H Bn), 4.41 (d, *J* = 11.7 Hz, 1H, CH*H* Bn), 3.98 (dd, *J* = 2.8, 0.8 Hz, 1H, H-4), 3.93 (t, *J* = 9.4 Hz, 1H, H-2), 3.68 – 3.58 (m, 4H, H-3, H-5, H-6, H-6); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 138.9, 138.5, 138.4, 138.0, 134.3 ($C_{q\text{-}arom}$), 131.7, 128.9, 128.6, 128.5, 128.4, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 127.2 (CH_{arom}), 87.9 (C-1), 84.3 (C-3), 76.9 (C-5), 76.8 (C-2), 75.8, 74.6 (CH_2 Bn), 73.7 (C-4), 72.9 (CH_2 Bn), 68.9 (C-6); HRMS: $[M+NH_4]^+$ calcd for $C_{40}H_{44}NO_5S$ 650.29347, found 650.29380.



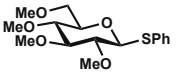
***p*-Tolyl 2-deoxy-3,4,6-tetra-*O*-benzyl-1-thio-β-D-galactopyranoside (S30).** Compound **S30** was obtained from D-galactose, according to a literature procedure.[70] TLC: R_f 0.65 (pentane:EtOAc, 9:1, v:v); IR (thin film, cm^{-1}): 656, 733, 808, 1027, 1061, 1093, 1360, 1454, 1493, 2862, 3029; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.45 – 6.99 (m, 20H, CH_{arom}), 4.93 (d, *J* = 11.7 Hz, 1H, C*H*H Bn), 4.68 (dd, *J* = 11.8, 2.2 Hz, 1H, H-1), 4.62 (d, *J* = 11.7 Hz, 1H, C*H*H Bn), 4.60 – 4.54 (m, 2H, CH*H* Bn, CH*H* Bn), 4.46 (d, *J* = 11.6 Hz, 1H, C*H*H Bn), 4.41 (d, *J* = 11.7 Hz, 1H, CH*H* Bn), 3.85 (s, 1H, H-4), 3.65 (m, 2H, H-6), 3.58 (ddd, *J* = 11.6, 4.5, 2.4 Hz, 1H, H-3), 3.53 (t, *J* = 6.1 Hz, 1H, H-5), 2.27 (q, *J* = 11.9 Hz, 1H, $H\text{-}2_{ax}$), 2.15 (dt, *J* = 12.9, 2.9 Hz, 1H, $H\text{-}2_{eq}$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 139.1, 138.3, 138.2 ($C_{q\text{-}arom}$), 137.4 (CH_{arom}), 132.0 ($C_{q\text{-}arom}$), 130.6, 129.6, 128.6, 128.5, 128.3, 128.1, 128.0, 127.8, 127.8, 127.5, 127.5 (CH_{arom}), 83.4 (C-1), 78.5 (C-3), 78.1 (C-5), 74.2, 73.7 (CH_2 Bn), 71.9 (C-4), 70.3 (CH_2 Bn), 69.6, (C-6) 32.6 (C-2); HRMS: $[M+Na]^+$ calcd for $C_{27}H_{29}NaO_4$ 440.1958, found 440.1960.



Phenyl 2,3,4-tri-*O*-methyl-1-thio-D-lyxopyranoside (S31). The title compound was prepared according to general procedure V from D-lyxose. Column chromatography (95:5 → 85:15, pentane:EtOAc) yielded compound **S31** (334 mg, 1.17 mmol, 27% over 5 steps, average of 77% per step, colorless oil, 1,2-*cis*:1,2-*trans*; 72:28). TLC: R_f 0.21 (pentane:EtOAc, 8:2, v:v); IR (thin film, cm^{-1}): 692, 743, 934, 1045, 1069, 1196, 1439, 1584, 2825, 2927; Data of the major stereoisomer (1,2-*cis* isomer product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC, HH-NOESY, HMBC-Gated): δ 7.53 – 7.16 (m, 5H, CH_{arom} SPh), 5.29 (d, *J* = 4.1 Hz, 1H, H-1), 4.26 (dd, *J* = 9.8, 3.9 Hz, 1H, H-5), 3.88 (dd, *J* = 4.3, 2.5 Hz, 1H, H-2), 3.56 – 3.47 (m, 9H, H-3, H-4, H-5, CH_3 Me, CH_3 Me), 3.42 (d, *J* = 0.9 Hz, 3H, CH_3 Me); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC, HMBC-Gated): δ 136.9 ($C_{q\text{-}arom}$ SPh), 130.2, 128.5, 126.4 (CH_{arom} SPh), 87.2 (C-1), 78.7 (C-3), 76.8 (C-2), 75.9 (C-4), 60.4 (C-5), 58.7, 57.9, 57.1 (CH_3 Me); ^{13}C-GATED NMR (126 MHz, $CDCl_3$): δ 87.2 ($J_{C1\text{-}H1}$= 158 Hz, 1,2-*cis*); Data of the minor stereoisomer (1,2-*trans* isomer product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC, HH-NOESY, HMBC-Gated): δ 7.53 – 7.16 (m, 5H, CH_{arom} SPh), 5.47 (d, *J* = 3.4 Hz, 1H, H-1), 3.92 – 3.80 (m, 2H, H-5_{ax}, H-5_{eq}), 3.76 (t, *J* = 3.3 Hz, 1H, H-2), 3.62 (td, *J* = 8.4, 4.8 Hz, 1H, H-4), 3.56 – 3.47 (m, 4H, H-3, CH_3 Me), 3.46 (s, 3H, CH_3 Me), 3.45 (s, 3H, CH_3 Me); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC, HMBC-Gated): δ 134.1 ($C_{q\text{-}arom}$ SPh), 130.9, 128.7, 127.0 (CH_{arom} SPh), 84.8 (C-1), 79.4 (C-3), 78.1 (C-2), 75.8 (C-4), 61.7 (C-5), 58.4, 58.2, 57.8 (CH_3 Me); ^{13}C-GATED NMR (126 MHz, $CDCl_3$): δ 84.8 ($J_{C1\text{-}H1}$= 164 Hz, 1,2-*trans*); HRMS: $[M+Na]^+$ calcd for $C_{14}H_{20}NaO_4S$ 307.09745, found 307.09752.

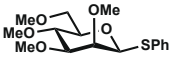


Phenyl 2,3,4-tri-*O*-methyl-1-thio-D-xylopyranoside (S32). The title compound was prepared according to general procedure V from D-xylose. Column chromatography (95:5 → 85:15, pentane:EtOAc) yielded compound **S32** (1.24 g, 4.35 mmol, 79%, colorless oil, 1,2-*cis*:1,2-*trans*; 18:82). TLC: R_f 0.29 (pentane:EtOAc, 8.5:1.5, v:v); IR (thin film, cm^{-1}): 692, 745, 1051, 1094, 1130, 1157, 1439, 1462, 2831, 2899, 2931; Data of the major stereoisomer (1,2-*trans* isomer product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC): δ 7.54 – 7.23 (m, 5H, CH_{arom} SPh), 4.59 (d, *J* = 8.9 Hz, 1H, H-1), 4.11 (dd, *J* = 11.3, 4.6 Hz, 1H, H-5_{eq}), 3.62 (s, 3H, CH_3 Me), 3.59 (s, 3H, CH_3 Me), 3.46 (s, 3H, CH_3 Me), 3.26 (ddd, *J* = 9.2, 8.2, 4.6 Hz, 1H, H-4), 3.23– 3.15 (m, 2H, H-3, H-5_{ax}), 3.07 (dd, *J* = 8.9, 7.9 Hz, 1H, H-2); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC): δ 133.9 ($C_{q\text{-}arom}$), 131.9, 129.0, 127.5 (CH_{arom}), 87.8 (C-1), 86.5 (C-3), 82.0 (C-2), 79.1 (C-4), 66.4 (C-5), 60.7 (CH_3 Me, CH_3 Me), 58.7 (CH_3 Me); Data of the minor stereoisomer (1,2-*cis* isomer product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC): δ 5.65 (d, *J* = 5.3 Hz, 1H, H-1), 4.03 – 3.94 (m, 1H, H-5), 3.79 (dd, *J* = 11.5, 5.5 Hz, 1H, H-5), 3.64 (s, 3H, CH_3 Me), 3.52 (s, 3H, CH_3 Me), 3.50 (s, 3H, CH_3 Me), 3.35 (t, *J* = 9.0 Hz, 1H, H-3); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC): δ 134.6 ($C_{q\text{-}arom}$), 131.6, 129.1, 127.3 (CH_{arom}), 87.0 (C-1), 82.9 (C-3), 61.1 (CH_3 Me), 60.7 (C-5), 59.1, 58.4 (CH_3 Me); HRMS: $[M+Na]^+$ calcd for $C_{14}H_{20}NaO_4S$ 307.09745, found 307.09757.

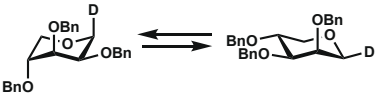


Phenyl 2,3,4,6-tetra-*O*-methyl-1-thio-β-D-glucopyranoside (S33). Phenyl 1-thio-β-D-glucose (1.36 g, 5.0 mmol)[19] was dissolved in DMF (25 mL, 0.25 M) and cooled to 0 °C. NaH (60% dispersion in mineral oil, 0.96 g, 24.0 mmol, 4.8 eq.) was added, and the resulting mixture was stirred for 10 min. Subsequently, methyl iodide (1.5 mL, 24.0 mmol, 4.8 eq.) was added, and the reaction mixture was allowed to warm up to room temperature and stirred for an additional 16 h. The reaction was quenched with MeOH and diluted with H_2O, after which the resulting mixture was extracted with Et_2O (3x). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. Column chromatography (75:15 → 80:20, pentane:EtOAc) yielded compound **S33** (1.05 g, 3.2 mmol, 64%, colorless solid). TLC: R_f 0.33 (pentane:EtOAc, 8:2, v:v); IR (thin film, cm^{-1}): 2932, 2833, 1097; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.64 – 7.21 (m, 5H, CH_{arom}), 4.52 (d, *J* = 9.8 Hz, 1H, H-1), 3.71 – 3.63 (m, 4H, CH_3, H-6), 3.63 (s, 3H, CH_3), 3.59 (dd, *J* = 10.8, 4.7 Hz, 1H, H-6), 3.56 (s, 3H, CH_3), 3.42 (s, 3H, CH_3), 3.32 (ddd, *J* = 9.4, 4.7, 2.0 Hz, 1H, H-5), 3.24 (t, *J* = 8.6 Hz, 1H, H-3), 3.19 (t, *J* = 9.3 Hz, 1H, H-4), 3.08 (dd, *J* = 9.8, 8.3 Hz, 1H, H-2); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 134.1 ($C_{q\text{-}arom}$), 131.8, 128.9, 127.4 (CH_{arom}),

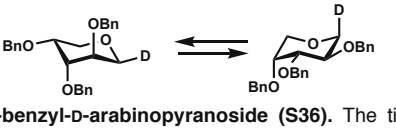
88.8 (C-4), 87.5 (C-1), 82.7 (C-2), 79.4 (C-3), 78.9 (C-5), 71.5 (C-6), 61.1, 61.0, 60.6, 59.5 (CH_3 Me); HRMS: $[M+Na]^+$ calcd for $C_{16}H_{24}NaO_5S$ 351.1237, found 351.1239.



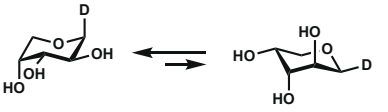
Phenyl 2,3,4,6-tetra-*O*-methyl-1-thio-β-D-mannopyranoside (S34). Phenyl 1-thio-β-D-mannose (0.5 g, 1.8 mmol)[19] was dissolved in DMF (9.2 mL, 0.2 M) and cooled to 0 °C. NaH (60% dispersion in mineral oil, 0.35 g, 8.8 mmol, 4.8 eq.) was added, and the resulting mixture was stirred for 10 min. Subsequently, methyl iodide (0.55 mL, 8.8 mmol, 4.8 eq.) was added, and the reaction mixture was allowed to warm up to room temperature and stirred for an additional 16 h. The reaction was quenched with MeOH and diluted with H_2O, after which the resulting mixture was extracted with Et_2O (3x). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. Column chromatography (75:15 → 80:20, pentane:EtOAc) yielded compound **S34** (0.5 g, 1.5 mmol, 83%, colorless solid). TLC: R_f 0.30 (pentane:EtOAc, 8:2, v:v); IR (thin film, cm^{-1}): 2982, 2907, 1069, 737; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.74 – 7.04 (m, 5H, CH_{arom} SPh), 4.71 (d, *J* = 1.0 Hz, 1H, H-1), 3.89 (dd, *J* = 3.2, 1.0 Hz, 1H, H-2), 3.74 – 3.58 (m, 5H, CH_3, H-6), 3.53 (s, 6H, CH_3, CH_3), 3.45 (t, *J* = 9.5 Hz, 1H, H-4), 3.39 (s, 3H, CH_3), 3.31 (ddd, *J* = 9.7, 5.9, 1.9 Hz, 1H, H-5), 3.24 (dd, *J* = 9.3, 3.1 Hz, 1H, H-3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 135.5 ($C_{q\text{-}arom}$), 130.7, 128.9, 127.1 (CH_{arom}), 87.5 (C-1), 86.1 (C-3), 79.7 (C-5), 79.1 (C-2), 76.4 (C-4), 71.9 (C-6), 62.1, 60.9, 59.4, 58.1 (CH_3 Me); HRMS: $[M+Na]^+$ calcd for $C_{16}H_{24}NaO_5S$ 351.1237, found 351.1240.



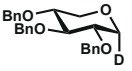
1-Deutero-1-deoxy-2,3,4-tri-*O*-benzyl-D-lyxopyranoside (S35). The title compound was prepared according to general procedure VI yielding compound **S35** (33 mg, 81 µmol, 81%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). TLC: R_f 0.57 (pentane:EtOAc, 9:1, v:v); $[\alpha]_D^{20}$ –30.2° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 731, 1026, 1096, 1350, 1452, 2875, 2916; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, NOESY): δ 7.38 – 7.26 (m, 15H, CH_{arom}), 4.71 (d, *J* = 12.1 Hz, 1H, C*H*H Bn), 4.65 – 4.58 (m, 5H, CH*H* Bn, CH_2 Bn, CH_2 Bn), 3.88 (dd, *J* = 11.8, 3.5 Hz, 1H, H-5), 3.82 (t, *J* = 3.0 Hz, 1H, H-2), 3.78 (td, *J* = 6.4, 3.5 Hz, 1H, H-4), 3.68 (dd, *J* = 6.7, 3.0 Hz, 1H, H-3), 3.47 (d, *J* = 2.8 Hz, 1H, H-1), 3.41 (dd, *J* = 11.7, 6.1 Hz, 1H, H-5); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 138.7, 138.4, 138.4 ($C_{q\text{-}arom}$), 128.5, 128.5, 128.5, 127.9, 127.9, 127.8, 127.8, 127.7 (CH_{arom}), 77.9 (C-3), 75.2 (C-4), 73.2 (C-2), 72.6, 71.6 (CH_2 Bn), 67.3 (C-5), 66.2 (t, *J* = 23.0 Hz, C-1); ^2H NMR (77 MHz, $CHCl_3$) δ 3.86 (D-1); HRMS: $[M+NH_4]^+$ calcd for $C_{26}H_{31}DNO_4$ 423.23941, found 423.23876.



1-Deutero-1-deoxy-2,3,4-tri-*O*-benzyl-D-arabinopyranoside (S36). The title compound was prepared according to general procedure VI yielding compound **S36** (35 mg, 86 µmol, 86%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). TLC: R_f 0.52 (pentane:EtOAc, 9:1, v:v); ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, NOESY): δ 7.38 – 7.26 (m, 15H, CH_{arom}), 4.71 (d, *J* = 12.2 Hz, 1H, C*H*H Bn), 4.68 – 4.57 (m, 5H, CH*H* Bn, CH_2 Bn, CH_2 Bn), 3.89 – 3.79 (m, 3H, H-1, H-2, H-5), 3.76 (dd, *J* = 6.6, 3.4 Hz, 1H, H-3), 3.68 (dd, *J* = 6.6, 2.4 Hz, 1H, H-4), 3.51 (t, *J* = 7.9 Hz, 1H, H-5); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 138.7, 138.4 ($C_{q\text{-}arom}$), 128.5, 128.5, 128.5, 127.9, 127.8, 127.8, 127.8, 127.7 (CH_{arom}), 77.7 (C-4), 75.1 (C-3), 73.3 (C-2), 72.6, 72.5, 71.5 (CH_2 Bn), 66.8 (t, *J* = 23.4 Hz, C-1), 66.4 (C-5); ^2H NMR (77 MHz, $CHCl_3$): δ 3.44 (D-1); HRMS: $[M+NH_4]^+$ calcd for $C_{26}H_{31}DNO_4$ 423.23941, found 423.23876.

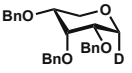


1-Deutero-1-deoxy-D-arabinopyranoside (S37). The title compound was prepared according to general procedure VII yielding compound **S37** (12 mg, 89 µmol, 89%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). TLC: R_f 0.53 (DCM:MeOH, 8:2, v:v); $[\alpha]_D^{20}$ –6.1° (*c* 0.25, MeOH); IR (thin film, cm^{-1}): 1014, 1410, 1449, 1647, 2951, 3294; ^{1}H NMR (400 MHz, Methanol-d_4, HH-COSY, HSQC, NOESY): δ 3.87 (dt, *J* = 5.8, 2.9 Hz, 1H, H-4), 3.79 (d, *J* = 3.8 Hz, 1H, H-1), 3.74 (dd, *J* = 7.4, 4.1 Hz, 1H, H-2), 3.72 (dd, *J* = 11.7, 5.2 Hz, 1H, H-5), 3.56 (dd, *J* = 7.4, 3.4 Hz, 1H, H-3), 3.50 (dd, *J* = 11.7, 2.6 Hz, 1H, H-5); ^{13}C NMR (101 MHz, MeOD, HSQC): δ 74.2 (C-3), 70.4 (C-5), 70.0 (t, *J* = 21.9 Hz, C-1), 69.3 (C-2), 69.0 (C-4); ^{2}H NMR (77 MHz, MeOH): δ 3.15 (D-1); HRMS: $[M+H]^+$ calcd for $C_5H_{10}DO_4$ 136.07201, found 136.07146.

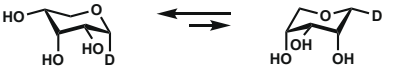


1-Deutero-1-deoxy-2,3,4-tri-*O*-benzyl-D-xylopyranoside (S38). The title compound was prepared according to general procedure VI yielding compound **S38** (35 mg, 86 µmol, 86%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). TLC: R_f 0.44 (pentane:EtOAc, 9:1, v:v); $[\alpha]_D^{20}$ –121.8° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 733, 1026, 1070, 1454, 1497, 2851, 2916; ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, NOESY): δ 7.45 – 7.18 (m, 15H, CH_{arom}), 4.89 (s, 2H, CH_2 Bn), 4.73 (d, *J* = 11.6 Hz, 2H, CH_2 Bn), 4.63 (d, *J* = 11.6 Hz, 2H, CH_2 Bn), 3.96 – 3.90 (m, 2H, H-1, H-5_{eq}), 3.60 – 3.47 (m, 3H, H-2, H-3, H-4), 3.14 (dd, *J* = 11.1, 9.9 Hz, 1H, H-5_{ax}); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 138.9, 138.4 ($C_{q\text{-}arom}$), 128.6, 128.5, 128.1, 127.9, 127.7 (CH_{arom}), 85.3 (C-3), 78.1, 78.1 (C-2/C-4), 75.6, 73.5, 73.5 (CH_2 Bn), 68.9 (C-5), 68.7, (t, *J* = 22.5 Hz, C-1); ^{2}H NMR (77 MHz, $CHCl_3$) δ 3.16 (D-1); HRMS: $[M+NH_4]^+$ calcd for $C_{26}H_{31}DNO_4$ 423.23941, found 423.23871.

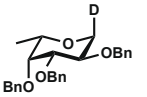
1-Deutero-1,2-di-deoxy-3,4-di-*O*-benzyl-D-xylopyranoside (S39). The title compound was prepared according to general procedure VI yielding compound **S39** (22 mg, 74 µmol, 74%, colorless oil, 1,3-*cis*:1,3-*trans*; >98:2). TLC: R_f 0.63 (pentane:EtOAc, 8:2, v:v); $[\alpha]_D^{25}$ –16.2° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 730, 1020, 1077, 1456, 1496, 2850, 2910; ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, NOESY): δ 7.65 – 6.57 (m, 10H, CH_{arom}), 4.74 (d, *J* = 11.8 Hz, 1H, C*H*H Bn), 4.71 – 4.63 (m, 3H, CH*H* Bn, C*H*H Bn, CH*H* Bn), 3.95 (dd, *J* = 11.5, 4.3 Hz, 1H, H-5), 3.58 (ddd, *J* = 9.1, 7.3, 4.5 Hz, 1H, H-3), 3.47 (ddd, *J* = 8.1, 7.3, 4.3 Hz, 1H, H-4), 3.39 (dd, *J* = 9.9, 2.8 Hz, 1H, H-1), 3.29 (dd, *J* = 11.5, 8.2 Hz, 1H, H-5), 2.06 (ddd, *J* = 13.4, 4.5, 2.9 Hz, 1H, H-2_{eq}), 1.64 (ddd, *J* = 13.4, 9.9, 9.2 Hz, 1H, H-2_{ax}); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 138.8, 138.6 ($C_{q\text{-}arom}$), 128.5, 128.5, 127.9, 127.8, 127.7, 127.7 (CH_{arom}), 78.0 (C-3), 77.3 (C-4), 72.8, 71.7 (CH_2 Bn), 68.2 (C-5), 65.24 (t, *J* = 22.3 Hz, C-1), 30.3 (C-2); ^{2}H NMR (77 MHz, $CHCl_3$): δ 3.89 (D-1); HRMS: $[M+Na]^+$ calcd for $C_{19}H_{21}NaDO_3$ 322.1524, found 322.1526.



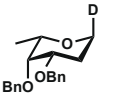
1-Deutero-1-deoxy-2,3,4-tri-*O*-benzyl-D-ribopyranoside (S40). The title compound was prepared according to general procedure VI yielding compound **S40** (28 mg, 69 µmol, 69%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). TLC: R_f 0.62 (pentane:EtOAc, 9:1, v:v); ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, NOESY): δ 7.56 – 7.17 (m, 15H, CH_{arom}), 4.88 (s, 2H, CH_2 Bn), 4.56 (d, *J* = 12.1 Hz, 2H, CH_2 Bn), 4.52 (d, *J* = 12.1 Hz, 2H, CH_2 Bn), 4.21 (t, *J* = 2.1 Hz, 1H, H-3), 3.74 – 3.68 (m, 3H, H-1, H-5, H-5), 3.48 – 3.43 (m, 3H, H-2, H-4); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 139.4, 138.3 ($C_{q\text{-}arom}$), 128.6, 128.3, 127.9, 127.8, 127.6, 127.4 (CH_{arom}), 75.8, 75.7 (C-2/C-4), 74.0 (C-3), 73.8, 71.2, 71.2 (CH_2 Bn), 64.5 (C-5), 64.2 (t, *J* = 22.7 Hz, C-1); ^{2}H NMR (77 MHz, $CHCl_3$): δ 3.71 (D-1); HRMS: $[M+NH_4]^+$ calcd for $C_{26}H_{31}DNO_4$ 423.23941, found 423.23877.



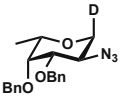
1-Deutero-1-deoxy-D-ribopyranoside (S41). The title compound was prepared according to general procedure VII yielding compound **S41** (12 mg, 89 µmol, 89%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). TLC: R_f 0.50 (DCM:MeOH, 8:2, v:v); $[\alpha]_D^{20}$ 10.5° (*c* 1, MeOH); IR (thin film, cm^{-1}): 1013, 1043, 1105, 1412, 1448, 1645, 2920, 3368; ^{1}H NMR (500 MHz, Methanol-d_4, HH-COSY, HSQC, NOESY): δ 3.86 (t, *J* = 2.9 Hz, 1H, H-3), 3.70 – 3.65 (m, 2H, H-2, H-4), 3.62 (dd, *J* = 11.0, 7.3 Hz, 1H, H-5), 3.54 – 3.48 (m, 2H, H-1, H-5); ^{13}C NMR (126 MHz, MeOD, HSQC): δ 68.9 (C-3), 67.9 (C-2), 67.9 (C-4), 67.8 (C-5), 66.6 (t, *J* = 21.5 Hz, C-1); ^{2}H NMR (77 MHz, MeOH): δ 3.57 (D-1); HRMS: $[M+H]^+$ calcd for $C_5H_{10}DO_4$ 136.07201, found 136.07141.



1-Deutero-1-deoxy-2,3,4-tri-*O*-benzyl-α-L-fucopyranoside (S42). The title compound was prepared according to general procedure VI yielding compound **S42** (31 mg, 74 µmol, 74%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). The title compound was also prepared according to general procedure VIII yielding compound **S42** (40 mg, 95 µmol, 95%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2) in Et_2O or yielding compound **S42** (23 mg, 55 µmol, 55%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2) in MeCN. The title compound was also prepared according to general procedure IX yielding compound **S42** (38 mg, 91 µmol, 91%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). TLC: R_f 0.54 (pentane:EtOAc, 9:1, v:v); $[\alpha]_D^{20}$ –35.0° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 694, 733, 1026, 1070, 1088, 1360, 1454, 1497, 2851, 2916; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, NOESY): δ 7.42 – 7.24 (m, 15H, CH_{arom}), 4.99 (d, *J* = 11.6 Hz, 1H, C*H*H Bn), 4.86 – 4.75 (m, 3H, CH*H* Bn, CH_2 Bn), 4.71 – 4.63 (m, 2H, CH_2 Bn), 4.06 – 4.00 (m, 2H, H-1, H-2), 3.64 (dd, *J* = 2.9, 1.1 Hz, 1H, H-4), 3.54 (dd, *J* = 8.7, 2.9 Hz, 1H, H-3), 3.40 (qd, *J* = 6.4, 1.1 Hz, 1H, H-5), 1.14 (d, *J* = 6.4 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 138.8, 138.6 ($C_{q\text{-}arom}$), 128.6, 128.5, 128.5, 128.3, 127.9, 127.8, 127.7, 127.7, 127.6 (CH_{arom}), 84.2 (C-3), 77.1 (C-4), 75.2 (C-5), 75.1 (CH_2 Bn), 74.9 (C-2), 73.6, 72.9 (CH_2 Bn), 66.8 (t, *J* = 23.5 Hz, C-1), 17.3 (CH_3); ^{2}H NMR (77 MHz, $CHCl_3$): δ 3.17 (D-1); HRMS: $[M+NH_4]^+$ calcd for $C_{27}H_{33}DNO_4$ 437.25506, found 437.25445.

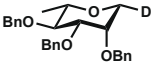


1-Deutero-1,2-di-deoxy-3,4-di-*O*-benzyl-α-L-fucopyranoside (S43). The title compound was prepared according to general procedure VI yielding compound **S43** (26 mg, 83 µmol, 83%, colorless oil, 1,3-*cis*:1,3-*trans*; <2:98). TLC: R_f 0.21 (pentane:EtOAc, 9:1, v:v); IR (thin film, cm^{-1}): 696, 733, 1028, 1063, 1082, 1105, 1175, 1364, 1454, 2855, 2927, 2949; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.54 – 7.18 (m, 10H, CH_{arom}), 4.98 (d, *J* = 11.7 Hz, 1H, C*H*H Bn), 4.71 (d, *J* = 11.7 Hz, 1H, CH*H* Bn), 4.65 (d, *J* = 12.1 Hz, 1H, C*H*H Bn), 4.60 (d, *J* = 12.2 Hz, 1H, CH*H* Bn), 4.01 (dd, *J* = 5.0, 1.7 Hz, 1H, H-1), 3.58 (dt, *J* = 2.5, 1.2 Hz, 1H, H-4), 3.55 (ddd, *J* = 11.7, 4.5, 2.5 Hz, 1H, H-3), 3.34 (qd, *J* = 6.4, 1.1 Hz, 1H, H-5), 2.16 (td, *J* = 12.2, 4.9 Hz, 1H, H-2_{ax}), 1.76 (ddt, *J* = 12.6, 4.5, 1.6 Hz, 1H, H-2_{eq}), 1.17 (d, *J* = 6.4 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 139.0, 138.7 ($C_{q\text{-}arom}$), 128.6, 128.6, 128.3, 127.7, 127.6, 127.4 (CH_{arom}), 79.2 (C-3), 76.0 (C-4), 75.1 (C-5), 74.6 (CH_2 Bn), 70.1 (CH_2 Bn), 65.8 (t, *J* = 21.2 Hz, C-1), 26.9 (C-2), 18.0 (CH_3); ^{2}H NMR (77 MHz, $CHCl_3$): δ 3.40 (D-1); HRMS: $[M+NH_4]^+$ calcd for $C_{20}H_{27}DNO_3$ 331.21320, found 331.21289.

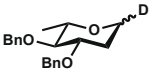


1-Deutero-2-azido-2-deoxy-3,4-di-*O*-benzyl-α-L-fucopyranoside (S44). The title compound was prepared according to general procedure VI yielding compound **S44** (23 mg, 65 µmol, 65%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). TLC: R_f 0.35 (pentane:EtOAc, 9:1, v:v); $[\alpha]_D^{20}$ –2.1° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 1123, 1265, 1724, 2106; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, NOESY): δ 7.47 – 7.27 (m, 10H, CH_{arom}), 4.95 (d, *J* = 11.5 Hz, 1H, C*H*H Bn), 4.76 (d, *J* = 11.6 Hz, 1H, C*H*H Bn), 4.71 (d, *J* = 11.6 Hz, 1H,

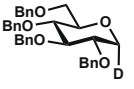
CH*H* Bn), 4.64 (d, *J* = 11.5 Hz, 1H, CH*H* Bn), 4.02 (dd, *J* = 9.6, 5.5 Hz, 1H, H-2), 3.97 (d, *J* = 5.5 Hz, 1H, H-1), 3.65 (d, *J* = 2.7 Hz, 1H, H-4), 3.43 (dd, *J* = 9.6, 2.7 Hz, 1H, H-3), 3.38 (q, *J* = 6.5 Hz, 1H, H-5), 1.17 (d, *J* = 6.3 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 138.3, 137.7 ($C_{q\text{-}arom}$), 128.7, 128.5, 128.4, 128.1, 128.0, 127.9 (CH_{arom}), 83.3 (C-3), 75.5 (C-2), 75.2 (C-5), 75.0, 72.2 (CH_2 Bn), 68.2 (t, *J* = 21.2 Hz, C-1), 58.3 (C-4), 17.5 (CH_3); ^2H NMR (77 MHz, $CHCl_3$): δ 3.08 (D-1); HRMS: $[M\text{-}N_2\text{+}H]^+$ calcd for $C_{20}H_{23}DNO_3$ 327.18135, found 327.18146.



1-Deutero-1-deoxy-2,3,4-tri-*O*-benzyl-β-L-rhamnopyranoside (S45). The title compound was prepared according to general procedure VI yielding compound **S45** (33 mg, 79 µmol, 79%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). The title compound was also prepared according to general procedure VIII yielding compound **S45** (36 mg, 86 µmol, 86%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2) in Et_2O or yielding compound **S45** (25 mg, 60 µmol, 60%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2) in MeCN. The title compound was also prepared according to general procedure IX yielding compound **S45** (39 mg, 93 µmol, 93%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). TLC: R_f 0.38 (pentane:EtOAc, 9:1, v:v); $[\alpha]_D^{20}$ 26.1° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 694, 733, 1026, 1092, 1113, 1354, 1452, 1497, 2860; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, NOESY): δ 7.46 – 7.26 (m, 15H, CH_{arom}), 4.99 (d, *J* = 10.8 Hz, 1H, C*H*H Bn), 4.81 (d, *J* = 12.7 Hz, 1H, CH*H* Bn), 4.72 – 4.61 (m, 3H, CH_2 Bn, C*H*H Bn), 4.57 (d, *J* = 11.9 Hz, 1H, CH*H* Bn), 3.75 (dd, *J* = 3.3, 1.0 Hz, 1H, H-2), 3.62 (t, *J* = 9.2 Hz, 1H, H-4), 3.53 (dd, *J* = 9.3, 3.2 Hz, 1H, H-3), 3.28 (dq, *J* = 9.0, 6.0 Hz, 1H, H-5), 3.24 (s, 1H, H-1), 1.36 (d, *J* = 6.2 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 138.7, 138.5, 138.4 ($C_{q\text{-}arom}$), 128.5, 128.2, 127.8, 127.7 (CH_{arom}), 82.8 (C-4), 80.8 (C-3), 76.5 (C-5), 75.7 (CH_2 Bn), 72.6 (C-2), 71.7, 71.3 (CH_2 Bn), 66.8 (t, *J* = 23.5 Hz, C-1), 18.4 (CH_3); ^2H NMR (77 MHz, $CHCl_3$): δ 4.03 (D-1); HRMS: $[M\text{+}NH_4]^+$ calcd for $C_{27}H_{33}DNO_4$ 437.25506, found 437.25446.

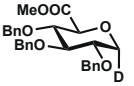


1-Deutero-1,2-di-deoxy-3,4-di-*O*-benzyl-L-rhamnopyranoside (S46). The title compound was prepared according to general procedure VI yielding compound **S46** (27 mg, 86 µmol, 86%, colorless oil, 1,3-*cis*:1,3-*trans*; 66:34). TLC: R_f 0.24 (pentane:Et_2O, 8:2, v:v); IR (thin film, cm^{-1}): 696, 735, 1089, 1107, 1360, 1454, 2855, 2924. Data of the major stereoisomer (1,3-*cis* product): ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.38 – 7.21 (m, 10H, CH_{arom}), 4.96 (d, *J* = 10.9 Hz, 1H, C*H*H Bn), 4.70 (d, *J* = 11.7 Hz, 1H, CH*H* Bn), 4.66 (d, *J* = 10.9 Hz, 1H, C*H*H Bn), 4.63 (d, *J* = 11.7 Hz, 1H, CH*H* Bn), 3.59 (ddd, *J* = 11.4, 8.6, 5.1 Hz, 1H, H-3), 3.33 (dd, *J* = 12.8, 2.0 Hz, 0. 66H, H-1), 3.27 (dq, *J* = 9.2, 6.1 Hz, 1H, H-5), 3.10 (t, *J* = 8.9 Hz, 1H, H-4), 2.08 (ddd, *J* = 13.0, 5.1, 2.0 Hz, 1H, $H\text{-}2_{eq}$), 1.67 (td, *J* = 12.9, 11.3 Hz, 1H, $H\text{-}2_{ax}$), 1.30 (d, *J* = 6.1 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CHCl_3$, HSQC): δ 138.7 ($C_{q\text{-}arom}$), 128.5, 128.5, 128.2, 127.8, 127.7 (CH_{arom}), 84.5 (C-4), 81.1 (H-3), 76.1 C-5), 75.5 (CH_2 Bn), 71.5 (CH_2 Bn), 65.2 (t, *J* = 22.4 Hz, C-1), 31.8 (C-2), 18.7 (CH_3); ^2H NMR (77 MHz, $CHCl_3$): δ 3.91 (D-1); Data of the minor stereoisomer (1,3-*trans* product): ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): 3.88 (dd, *J* = 5.0, 1.7 Hz, 0.34 H, H-1'); ^2H NMR (77 MHz, $CHCl_3$): δ 3.36 (D-1'); HRMS: $[M\text{+}NH_4]^+$ calcd for $C_{20}H_{27}DNO_3$ 331.21320, found 331.21269.

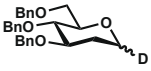


1-Deutero-1-deoxy-2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside (S47). The title compound was prepared according to general procedure VI yielding compound **S47** (37 mg, 70 µmol, 70%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). The title compound was prepared according to general procedure IX yielding compound **S47** (48 mg, 91 µmol, 91%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). TLC: R_f 0.69 (pentane:EtOAc, 8:2, v:v); $[\alpha]_D^{20}$ 5.3° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 698, 731, 1024, 1093, 1123, 1353, 1451, 1499, 2867; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.61 – 6.96 (m, 20H, CH_{arom}), 4.97 (d, *J* = 11.0 Hz, 1H, C*H*H Bn), 4.84 (d, *J* = 11.0 Hz, 1H, CH*H* Bn), 4.83 (d, *J* = 10.7 Hz, 1H, C*H*H Bn), 4.71 (d, *J* = 11.6 Hz, 1H, C*H*H Bn), 4.63 (d, *J* = 11.6 Hz, 1H, CH*H* Bn), 4.59 (d, *J* = 12.2 Hz, 1H, C*H*H Bn), 4.50 (d, *J* = 12.2 Hz, 1H, CH*H* Bn), 4.48 (d, *J* = 10.7 Hz, 1H, CH*H* Bn), 4.01 (d, *J* = 4.5 Hz, 1H, H-1), 3.74 – 3.59 (m, 4H, H-2, H-6, H-6, H-5), 3.56 (ddd, *J* = 9.2, 5.7, 3.5 Hz, 1H, H-4), 3.37 (ddd, *J* = 9.5, 4.3, 2.1 Hz, 1H, H-3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 138.8, 138.3, 138.2, 138.0 ($C_{q\text{-}arom}$), 128.6, 128.5, 128.5, 128.1, 128.1, 128.1, 128.0,

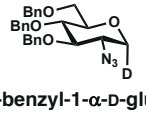
128.0, 127.9, 127.8, 127.7 (CH_{arom}), 86.5 (C-2/C-5), 79.3 (C-3), 78.5 (C-5/C-2), 77.9 (C-4), 75.7 (CH_2 Bn), 75.3 (CH_2 Bn), 73.7 (CH_2 Bn), 73.4 (CH_2 Bn), 69.1 (C-6), 67.9 (t, J = 21.5 Hz, C-1); HRMS: $[M+Na]^+$ calcd for $C_{34}H_{35}NaDO_5$ 548.2518, found 548.2521.



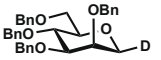
Methyl (2,3,4-tri-*O*-benzyl-1-deoxy-α-deuterio-D-glucopyranosyl uronate) (S48). The title compound was prepared according to general procedure VI yielding compound **S48** (20 mg, 43 µmol, 43%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). TLC: R_f 0.73 (pentane:EtOAc, 8:2, v:v); $[\alpha]_D^{25}$ 54.5° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 695, 734, 1027, 1070, 1211, 1438, 1454, 1747, 2950; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 – 7.13 (m, 20H, CH_{arom}), 4.93 (d, J = 11.0 Hz, 1H, C*H*H Bn), 4.84 (d, J = 11.0 Hz, 1H, CH*H* Bn), 4.79 (d, J = 10.8 Hz, 1H, C*H*H Bn), 4.72 (d, J = 11.6 Hz, 1H, C*H*H Bn), 4.62 (d, J = 11.6 Hz, 1H, CH*H* Bn), 4.57 (d, J = 10.8 Hz, 1H, CH*H* Bn), 4.02 (d, J = 4.4 Hz, 1H, H-1), 3.84 (d, J = 9.4 Hz, 1H, H-5), 3.70 (s, 3H, CH_3 COOMe), 3.75 – 3.64 (m, 3H, H-2, H-3, H-4); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 169.8 (C=O), 138.6, 138.1, 137.9 ($C_{q\text{-}arom}$), 128.7, 128.6, 128.5, 128.1, 128.1, 128.0, 128.0, 128.0, 127.9 (CH_{arom}), 85.3 (C-3), 79.5 (C-4), 78.7 (C-5), 77.7 (C-2), 75.7, 75.3, 73.6 (CH_2 Bn), 68.0 (t, J = 21.1 Hz, C-1), 52.6 (CH_3 COOMe); ^{2}H NMR (77 MHz, $CHCl_3$): δ 3.26 (D-1); HRMS: $[M+Na]^+$ calcd for $C_{28}H_{29}DO_6Na$ 486.1997, found 486.2004.



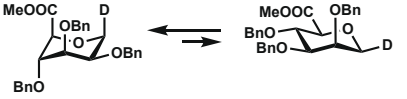
1-Deutero-1,2-di-deoxy-3,4,6-tri-*O*-benzyl-D-glucopyranoside (S49). The title compound was prepared according to general procedure VI yielding compound **S49** (32 mg, 76 µmol, 76%, colorless oil, 1,3-*cis*:1,3-*trans*; 52:48). TLC: R_f 0.62 (pentane:EtOAc, 8:2, v:v); IR (thin film, cm^{-1}): 734, 1027, 1086, 1360, 1452, 2862, 2922; Data of the major stereoisomer (1,3-*cis* product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.40 – 7.11 (m, 15H, CH_{arom}), 4.90 (d, J = 10.8 Hz, 1H, C*H*H Bn), 4.70 (d, J = 11.7 Hz, 1H, C*H*H Bn), 4.63 (d, J = 10.3 Hz, 1H, CH*H* Bn), 4.60 (d, J = 10.8 Hz, 1H, C*H*H Bn), 4.53 (d, J = 12.2 Hz, 1H, CH*H* Bn), 4.52 (d, J = 10.8 Hz, 1H, CH*H* Bn), , 3.72 – 3.59 (m, 3H, H-3, H-6, H-6), 3.49 (t, J = 9.1 Hz, 1H, H-4), 3.39 – 3.31 (m, 1.52H, H-1, H-5), 2.07 (ddd, J = 13.0, 5.0, 1.9 Hz, 1H, H-2_{eq}), 1.70 (dddd, J = 16.3, 12.9, 9.5, 3.9 Hz, 1H, H-2_{ax}); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 138.7, 138.6, 138.2 ($C_{q\text{-}arom}$), 128.5, 128.5, 128.5, 128.1, 128.1, 127.8, 127.7, 127.7 (CH_{arom}), 81.3 (C-3), 79.4 (C-5), 78.6 (C-4), 75.2, 73.7, 71.5 (CH_2 Bn), 69.6 (C-6), 65.5 (t, J = 22.5 Hz, C-1), 31.5 (C-2); ^{2}H NMR (77 MHz, $CHCl_3$): δ 4.05 (D-1); Data of the minor stereoisomer (1,3-*trans* product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): 3.98 (dd, J = 5.0, 1.7 Hz, 0.48 H, H-1'); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 65.5 (t, J = 22.5 Hz, C-1); ^{2}H NMR (77 MHz, $CHCl_3$): δ 3.36 (D-1'); HRMS: $[M+Na]^+$ calcd for $C_{27}H_{29}DO_4Na$ 442.2099, found 442.2103.



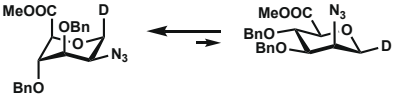
1-Deutero-2-azido-1,2-di-deoxy-3,4,6-tri-*O*-benzyl-1-α-D-glucopyranoside (S50). The title compound was prepared according to general procedure VI yielding compound **S50** (24 mg, 52 µmol, 52%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). TLC: R_f 0.77 (pentane:EtOAc, 8:2, v:v); $[\alpha]_D^{25}$ −9.2° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 697, 735, 1027, 1059, 1109, 1137, 1261, 1362, 1454, 1497, 2104, 2866; ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.51 – 6.88 (m, 15H, CH_{arom}), 4.88 (s, 2H, CH_2 Bn), 4.80 (d, J = 10.8 Hz, 1H, C*H*H Bn), 4.60 (d, J = 12.1 Hz, 1H, C*H*H Bn), 4.52 (d, J = 10.8 Hz, 1H, CH*H* Bn), 4.51 (d, J = 12.1 Hz, 1H, CH*H* Bn), 4.01 (d, J = 5.4 Hz, 1H, H-1), 3.71 – 3.57 (m, 4H, H-2, H-4, H-6, H-6), 3.51 (dd, J = 9.5, 8.9 Hz, 1H, H-3), 3.36 (ddd, J = 9.7, 4.1, 2.3 Hz, 1H, H-5); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 138.0, 137.9, 137.9 ($C_{q\text{-}arom}$), 128.6, 128.6, 128.6, 128.3, 128.1, 128.1, 128.0, 128.0, 127.9 (CH_{arom}), 85.5 (C-3), 79.7 (C-5), 78.3 (C-4), 75.7, 75.2, 73.7 (CH_2 Bn), 68.8 (C-6), 68.0 (t, J = 21.5 Hz, C-1), 61.9 (C-2); HRMS: $[M+Na]^+$ calcd for $C_{27}H_{28}DN_3NaO_4$ 483.2113, found 483.2118.



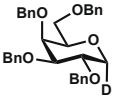
1-Deutero-1-deoxy-2,3,4,6-tetra-*O*-benzyl-β-D-mannopyranoside (S51). The title compound was prepared according to general procedure VI yielding compound **S51** (49 mg, 93 µmol, 93%, colorless oil, 1,2-*cis*:1,2-*trans*; 97:3). TLC: R_f 0.60 (pentane:EtOAc, 8:2, v:v); $[\alpha]_D^{20}$ –28.3° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 699, 723, 1020, 1090, 1128, 1356, 1454, 1498, 2860; Data of the major stereoisomer (1,2-*cis* product): ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.66 – 7.03 (m, 20H, CH_{arom}), 4.92 (d, *J* = 10.8 Hz, 1H, C*H*H Bn), 4.80 (d, *J* = 12.6 Hz, 1H, C*H*H Bn), 4.65 (d, *J* = 12.4 Hz, 1H, C*H*H Bn), 4.63 – 4.54 (m, 4H, C*H*H Bn, CH*H* Bn, CH*H* Bn, CH*H* Bn), 4.52 (d, *J* = 10.8 Hz, 1H, CH*H* Bn), 3.89 (t, *J* = 9.4 Hz, 1H, H-4), 3.79 – 3.64 (m, 3H, H-2, H-6, H-6), 3.57 (dd, *J* = 9.3, 3.3 Hz, 1H, H-3), 3.42 (ddd, *J* = 9.6, 5.9, 2.1 Hz, 1H, H-5), 3.27 (s, 0.95H, H-1); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 138.5, 138.4, 138.3, 138.3 ($C_{q\text{-}arom}$), 129.4, 128.5, 128.5, 128.4, 128.4, 128.1, 128.1, 128.0, 127.8, 127.7, 127.7 (CH_{arom}), 82.9 (C-3), 79.8 (C-5), 75.4 (CH_2 Bn), 75.3 (C-4), 73.6 (CH_2 Bn), 72.3 (C-2), 71.6, 71.0 (CH_2 Bn), 69.8 (C-6), 66.5 (t, *J* = 22.2 Hz, C-1); Data of the minor stereoisomer (1,2-*trans* product): ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.11 (d, *J* = 2.3 Hz, 0.05 H); HRMS: $[M+Na]^+$ calcd for $C_{34}H_{35}NaDO_5$ 548.2518, found 548.2521.



Methyl (2,3,4-tri-*O*-benzyl-1-deoxy-β-deuterio-D-mannopyranosyl uronate) (S52). The title compound was prepared according to general procedure VI yielding compound **S52** (35 mg, 76 µmol, 76%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). TLC: R_f 0.72 (pentane:EtOAc, 8:2, v:v); $[\alpha]_D^{25}$ –8.3° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 696, 735, 1027, 1091, 1104, 1205, 1454, 1750, 2869; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.80 – 7.15 (m, 15H, CH_{arom}), 4.66 (s, 2H, CH_2 Bn), 4.62 (d, *J* = 12.2 Hz, 1H. C*H*H Bn), 4.60 – 4.52 (m, 3H, C*H*H Bn, CH*H* Bn, CH*H* Bn), 4.26 (dd, *J* = 6.3, 4.9 Hz, 1H, H-4), 4.13 (d, *J* = 4.8 Hz, 1H, H-5), 3.88 (t, *J* = 3.2 Hz, 1H, H-2), 3.74 (dd, *J* = 6.1, 2.9 Hz, 1H, H-3), 3.63 (s, 3H, CH_3 COOMe), 3.58 (d, *J* = 3.5 Hz, 1H, H-1); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 170.0 (C=O), 138.3, 138.2, 138.0 ($C_{q\text{-}arom}$), 131.2, 128.6, 128.5, 128.4, 128.0, 128.0, 127.9, 127.8, 127.8, 127.8, 124.9 (CH_{arom}), 76.7 (C-3), 76.2 (C-4), 75.4 (C-5), 73.6, 72.2 (CH_2 Bn), 71.9 (C-2), 71.4 (CH_2 Bn), 63.7 (td, *J* = 21.5 Hz, C-1), 52.3 (CH_3 COOMe); ^2H NMR (77 MHz, $CHCl_3$): δ 4.21 (D-1); HRMS: $[M+Na]^+$ calcd for $C_{28}H_{29}DO_6Na$ 486.1997, found 486.1998.

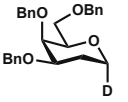


Methyl (2-azido-3,4-di-*O*-benzyl-1,2-dideoxy-β-deuterio-D-glucopyranosyl uronate) (S53). The title compound was prepared according to general procedure VI yielding compound **S53** (21 mg, 53 µmol, 53%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). TLC: R_f 0.56 (pentane:EtOAc, 8:2, v:v); $[\alpha]_D^{25}$ –4.1° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 698, 738, 1026, 1100, 1133, 1278, 1454, 1750, 2102, 2880; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.38 – 7.24 (m, 10H, CH_{arom}), 4.68 (s, 2H, CH_2 Bn), 4.61 (s, 2H, CH_2 Bn), 4.20 (dd, *J* = 6.0, 5.0 Hz, 1H, H-4), 4.13 (d, *J* = 5.0 Hz, 1H, H-5), 3.84 – 3.76 (m, 2H, H-2, H-3), 3.65 (d, *J* = 1.5 Hz, 1H, H-1), 3.59 (s, 3H, CH_3 COOMe); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 169.5 (C=O), 137.6, 137.2 ($C_{q\text{-}arom}$), 128.7, 128.6, 128.2, 128.2, 128.1, 128.0 (CH_{arom}), 77.7 (C-3), 75.1 (C-4/C-5), 75.1 (C-5/C-4), 73.7, 72.6 (CH_2 Bn), 63.7 (bs, C-1), 56.2 (C-2), 52.4 (CH_3 COOMe); HRMS: $[M+Na]^+$ calcd for $C_{21}H_{22}DN_3NaO_5$ 421.1593, found 421.1591.

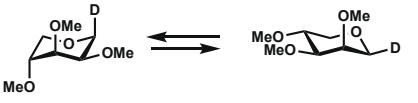


1-Deutero-1-deoxy-2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranoside (S54). The title compound was prepared according to general procedure VI yielding compound **S54** (45 mg, 86 µmol, 86%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). TLC: R_f 0.65 (pentane:EtOAc, 8:2, v:v); $[\alpha]_D^{20}$ 1.2° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 690, 730, 1029, 1092, 1129, 1350, 1449, 1493, 2867; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.43 – 7.21 (m, 20H, CH_{arom}), 4.94 (d, *J* = 11.5 Hz, 1H, C*H*H Bn), 4.81 – 4.73 (m, 3H, CH*H* Bn, C*H*H Bn,

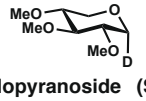
C*H*H Bn), 4.64 (d, *J* = 11.5 Hz, 1H, CH*H* Bn), 4.59 (d, *J* = 11.6 Hz, 1H, CH*H* Bn), 4.47 (d, *J* = 11.9 Hz, 1H, C*H*H Bn), 4.39 (d, *J* = 11.9 Hz, 1H, CH*H* Bn), 4.08 – 3.99 (m, 2H, H-1, H-3), 3.93 (dd, *J* = 2.9, 1.1 Hz, 1H, H-4), 3.59 – 3.50 (m, 2H, H-6, H-2), 3.49 (td, *J* = 6.0, 1.1 Hz, 1H, H-5), 3.43 (dd, *J* = 8.9, 6.1 Hz, 1H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 138.7, 138.7, 138.6, 138.0 ($C_{q\text{-arom}}$), 128.5, 128.5, 128.4, 128.4, 128.1, 127.9, 127.9, 127.8, 127.7, 127.7, 127.6 (CH_{arom}), 83.8 (C-2), 78.0 (C-5), 75.3 (C-3), 74.8 (CH_2 Bn), 74.5 (C-4), 73.7, 73.7, 72.8 (CH_2 Bn), 69.4 (C-6), 68.3 (t, *J* = 21.2 Hz, C-1); HRMS: $[M+Na]^+$ calcd for $C_{34}H_{35}NaDO_5$ 548.2518, found 548.2518.



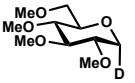
1-Deutero-1,2-di-deoxy-3,4,6-tri-*O*-benzyl-1-α-D-galactopyranoside (S55). The title compound was prepared according to general procedure VI yielding compound **S55** (38 mg, 91 µmol, 91%, colorless oil, 1,3-*cis*:1,3-*trans*; <2:98). TLC: R_f 0.52 (pentane:EtOAc, 8:2, v:v); IR (thin film, cm^{-1}): 730, 1025, 1080, 1368, 1450, 2863, 2920; ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 – 7.05 (m, 15H, CH_{arom}), 4.93 (d, *J* = 11.7 Hz, 1H, C*H*H Bn), 4.66 – 4.56 (m, 3H, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.49 (d, *J* = 11.9 Hz, 1H, C*H*H Bn), 4.41 (d, *J* = 11.9 Hz, 1H, CH*H* Bn), 4.04 (dd, *J* = 5.0, 1.8 Hz, 1H, H-1), 3.85 (dt, *J* = 2.4, 1.1 Hz, 1H, H-4), 3.63 – 3.56 (m, 1H, H-6), 3.54 (ddd, *J* = 11.7, 4.5, 2.5 Hz, 1H, H-3), 3.50 – 3.42 (m, 2H, H-5, H-6), 2.19 (td, *J* = 12.2, 4.9 Hz, 1H, H-2_{ax}), 1.77 (ddt, *J* = 12.6, 4.5, 1.6 Hz, 1H, H-2_{eq}); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 138.9, 138.6, 138.1 ($C_{q\text{-arom}}$), 128.5, 128.5, 128.4, 128.3, 128.0, 127.8, 127.7, 127.6, 127.4 (CH_{arom}), 78.6 (C-3), 78.1 (C-5), 74.4, 73.6 (CH_2 Bn), 73.4 (C-4), 70.2 (CH_2 Bn), 70.0 (C-6), 66.0 (t, *J* = 21.5 Hz, C-1), 27.3 (C-2); HRMS: $[M+Na]^+$ calcd for $C_{27}H_{29}NaDO_4$442.2099, found 442.2106.



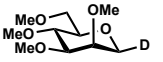
1-Deutero-1-deoxy-2,3,4-tri-*O*-methyl-D-lyxopyranoside (S56). The title compound was prepared according to general procedure VI yielding compound **S56** (16 mg, 90 µmol, 90%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). TLC: R_f 0.28 (pentane:EtOAc, 5:5, v:v); $[\alpha]_D^{20}$ −133.7° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 733, 953, 1072, 1096, 1357, 1462, 2824, 2897; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, NOESY): δ 3.88 (dd, *J* = 11.7, 3.7 Hz, 1H, H-5), 3.62 (t, *J* = 2.9 Hz, 1H, H-2), 3.54 (dt, *J* = 6.9, 3.4 Hz, 1H, H-4), 3.51 (s, 3H, CH_3), 3.47 (s, 3H, CH_3), 3.45 (m, 4H, H-1, CH_3), 3.42 (dd, *J* = 7.1, 3.2 Hz, 1H, H-3), 3.35 (dd, *J* = 11.8, 6.8 Hz, 1H, H-5); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 80.2 (C-3), 76.3 (C-4), 75.0 (C-2), 66.6 (C-5), 65.3 (t, *J* = 22.5 Hz, C-1), 58.3, 58.0, 57.4 (CH_3 Me); ^{2}H NMR (77 MHz, $CHCl_3$): δ 3.85 (D-1); HRMS: $[M+H]^+$ calcd for $C_8H_{16}DO_4$ 178.11896, found 178.11840.



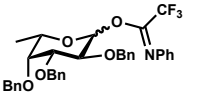
1-Deutero-1-deoxy-2,3,4-tri-*O*-methyl-D-xylopyranoside (S57). The title compound was prepared according to general procedure VI yielding compound **S57** (15 mg, 85 µmol, 85%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). TLC: R_f 0.62 (pentane:EtOAc, 5:5, v:v); $[\alpha]_D^{20}$ −1.8° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 841, 922, 1022, 1099, 1161, 1462, 2827, 2932; ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, NOESY): δ 4.00 (dd, *J* = 5.0, 1.2 Hz, 1H, H-5_{eq}), 3.97 (td, *J* = 4.9, 1.2 Hz, 1H, H-1), 3.63 (s, 3H, CH_3), 3.48 (s, 6H, CH_3, CH_3), 3.26 – 3.19 (m, 2H, H-2, H-4), 3.12 (t, *J* = 8.3 Hz, 1H, H-3), 3.09 (dd, *J* = 11.2, 9.9 Hz, 1H, H-5_{ax}); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 86.0 (C-3), 79.6, 79.5 (C-2/C-4), 68.2 (C-5), 67.9 (t, *J* = 21.5 Hz, C-1), 60.7 (CH_3 Me), 58.9 (CH_3 Me, CH_3 Me; ^{2}H NMR (77 MHz, $CHCl_3$): δ 3.08 (D-1); HRMS: $[M+H]^+$ calcd for $C_8H_{16}DO_4$ 178.11896, found 178.11847.



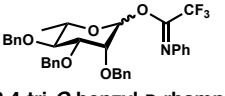
1-Deuterio-1-deoxy-2,3,4,6-tetra-*O*-methyl-α-D-glucopyranoside (S58). The title compound was prepared according to general procedure VI yielding compound **S58** (21 mg, 95 µmol, 95%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). TLC: R_f 0.69 (pentane:EtOAc, 5:5, v:v); $[\alpha]_D^{20}$ 4.2° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 830, 920, 1031, 1086, 1464, 2821, 2940; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, NOESY): δ 4.04 (d, *J* = 5.2 Hz, 1H, H-1), 3.64 (s, 3H, CH_3), 3.60 (dd, *J* = 10.4, 2.1 Hz, 1H, H-6), 3.54 (s, 4H, CH_3, H-6), 3.47 (s, 3H, CH_3), 3.40 (s, 3H, CH_3), 3.29 – 3.18 (m, 2H, H-2, H-5), 3.18 – 3.05 (m, 2H, H-3, H-4); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 87.9 (C-3), 80.0 (C-2), 79.7 (C-4), 79.1 (C-5), 71.8 (C-6), 67.4 (t, *J* = 21.7 Hz, C-1), 60.8, 60.6, 59.4, 58.9 (CH_3); HRMS: $[M+H]^+$ calcd for $C_{10}H_{19}NaDO_5$ 244.1256, found 244.1267.



1-Deuterio-1-deoxy-2,3,4,6-tetra-*O*-methyl-β-D-mannopyranoside (S59). The title compound was prepared according to general procedure VI yielding compound **S59** (22 mg, 99 µmol, 99%, colorless oil, 1,2-*cis*:1,2-*trans*; 97:3). TLC: R_f 0.71 (pentane:EtOAc, 5:5, v:v); $[\alpha]_D^{20}$ −16.1° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 833, 923, 1028, 1090, 1465, 2825, 2930; Data of the major stereoisomer (1,2-*cis* product): ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, NOESY): δ 3.65 (dd, *J* = 10.3, 2.0 Hz, 1H, H-6), 3.62 (dd, *J* = 3.4, 0.9 Hz, 1H, H-2), 3.56 (dd, *J* = 10.3, 6.4 Hz, 1H, H-6), 3.53 (s, 3H, CH_3), 3.50 (s, 3H, CH_3), 3.45 (s, 3H, CH_3), 3.41 (s, 3H, CH_3), 3.36 (t, *J* = 9.3 Hz, 1H, H-4), 3.31 – 3.23 (m, 2.96H, H-1, H-3, H-5); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 84.6 (C-3), 79.5 (C-5), 77.0 (C-4), 75.2 (C-2), 72.4 (C-6), 65.5 (t, *J* = 22.7 Hz, C-1), 61.0, 59.4, 57.4, 57.3 (CH_3); Data of the minor stereoisomer (1,2-*trans* product): ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, NOESY): 4.17 (d, *J* = 1.5 Hz, 0.04H); HRMS: $[M+H]^+$ calcd for $C_{10}H_{19}NaDO_5$ 244.1256, found 244.1269.

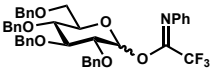


2,2,2-trifluoro-*N*-phenylacetimidoyl 2,3,4-tri-*O*-benzyl-D-fucopyranoside (S60). 2,3,4-tri-*O*-benzyl-α/β-D-fucopyranoside (87 mg, 0.2 mmol) was dissolved in acetone (2 mL, 0.1 M) and water (0.2 mL, 50 eq.) and cooled on ice. Subsequently, $CsCO_3$ (130 mg, 0.4 mmol, 1.8 eq.) and 2,2,2-trifluoro-*N*-phenylacetimidoyl chloride (83 mg, 0.4 mmol, 1.8 mmol) was added and the solution was allowed to attain room temperature After stirring for 18 h, the solution was diluted with H_2O and EtOAc. The aqueous layer was extracted (3x) with EtOAc followed by washing the combined organic layer with H_2O, sat. aq. $NaHCO_3$ and brine respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo* to yield the crude product as a colorless oil. Flash column chromatography (95:5 → 80:20; pentane:Et_2O) yielded the title compound **S60** (102 mg, 0.17 mmol, 76%, α:β; 33:67) as a colorless oil. Spectroscopic data was in accordance with literature.[69] TLC: R_f 0.4 (pentane: Et_2O, 9:1, v:v); Data for the anomeric mixture: (500 MHz, Toluene-d_8, *T* = 333 K, HH-COSY, HSQC): δ 7.64 – 6.60 (m, 30H, CH_{arom}), 6.38 (s, 0.5H, H-1α), 5.54 (s, 1H, H-1β), 5.06 – 4.61 (m, 9H, CH_2 Bnα, CH_2 Bnα, CH_2 Bnα, CH_2 Bnβ, CH_2 Bnβ, CH_2 Bnβ), 4.16 (dd, *J* = 10.1, 3.5 Hz, 0.5H, H-2α), 4.08 – 3.98 (m, 1.5H, H-2β, H-5α), 3.96 (dd, *J* = 10.1, 2.8 Hz, 0.5H, H-3α), 3.67 (dd, *J* = 2.8, 1.3 Hz, 0.5H, H-4α), 3.63 – 3.47 (m, 2H, H-3β, H-4β), 3.41 (s, 1H, H-5β), 1.18 (m, 4.5H, $CH_{3α}$, $CH_{3β}$); ^{13}C NMR (101 MHz, Toluene-d_8, *T* = 333 K, HSQC): δ 144.1, 144.0, 138.9, 138.7, 138.7, 138.6, 138.5, 135.4 ($C_{q\text{-}arom}$), 129.5, 128.8, 128.7, 128.6, 128.5, 128.5, 128.5, 128.4, 128.3, 127.9, 127.8, 127.8, 127.8, 127.7, 126.6, 124.3, 124.2, 120.8, 119.8, 119.6 (CH_{arom}), 98.0 (C-1β), 95.4 (bs, C-1α), 82.8 (C-3β), 78.9 (C-3α), 78.4 (C-2β), 78.0 (C-4α), 76.7 (C-4β), 76.0 (C-2α), 75.5, 75.2, 75.1, 73.6, 73.6, 73.5 (CH_2 Bn), 71.9 (C-5β), 69.9 (C-5α), 16.8 ($CH_{3β}$), 16.8 ($CH_{3α}$).



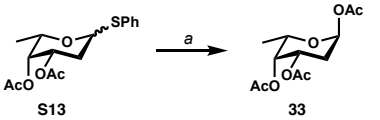
2,2,2-trifluoro-*N*-phenylacetimidoyl 2,3,4-tri-*O*-benzyl-D-rhamnopyranoside (S61). 2,3,4-tri-*O*-benzyl-α/β-D-rhamnopyranoside (87 mg, 0.2 mmol) was dissolved in acetone (2 mL, 0.1 M) and water (0.2 mL, 50

eq.) and cooled on ice. Subsequently, $CsCO_3$ (130 mg, 0.4 mmol, 1.8 eq.) and 2,2,2-trifluoro-*N*-phenylacetimidoyl chloride (83 mg, 0.4 mmol, 1.8 mmol) was added and the solution was allowed to attain room temperature After stirring for 18 h, the solution was diluted with H_2O and EtOAc. The aqueous layer was extracted (3x) with EtOAc followed by washing the combined organic layer with H_2O, sat. aq. $NaHCO_3$ and brine respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo* to yield the crude product as a colorless oil. Flash column chromatography (95:5 → 80:20; pentane:Et_2O) yielded the title compound **S60** (109 mg, 0.18 mmol, 81%, α:β; 71:29) as a colorless oil. Spectroscopic data was in accordance with literature.[69] TLC: R_f 0.4 (pentane: Et_2O, 9:1, v:v); Data for the anomeric mixture: (500 MHz, Toluene-d_8, T = 333 K, HH-COSY, HSQC): δ 7.74 – 6.66 (m, 28H, CH_{arom}), 6.09 (bs, 1H, H-1$_\alpha$), 5.52 (bs, 0.4H, H-1$_\beta$), 4.96 – 4.46 (m, 8.4H, CH_2 Bn$_\alpha$, CH_2 Bn$_\alpha$, CH_2 Bn$_\alpha$, CH_2 Bn$_\beta$, CH_2 Bn$_\beta$, CH_2 Bn$_\beta$), 4.05 (d, J = 2.9 Hz, 0.4H, H-3$_\beta$), 3.91 – 3.72 (m, 3H, H-2$_\alpha$, H-3$_\alpha$, H-5$_\alpha$), 3.74 – 3.58 (m, 1.4H, H-2$_\beta$, H-4$_\alpha$), 3.48 (d, J = 9.1 Hz, 0.4H, H-4$_\beta$), 3.25 (bs, 0.4H, H-5$_\beta$), 1.34 (m, 4.2H, $CH_{3\alpha}$, $CH_{3\beta}$); ^{13}C NMR (101 MHz, Toluene-d_8, T = 333 K, HSQC): δ 143.9, 138.7, 138.5, 138.1 ($C_{q\text{-}arom}$), 129.6, 128.9, 128.9, 128.6, 128.5, 128.5, 128.4, 128.4, 128.2, 128.2, 128.1, 128.0, 127.9, 127.9, 127.8, 127.8, 126.6, 124.5, 120.8, 119.7, 119.6 (CH_{arom}), 96.5 (C-1$_\beta$), 96.2 (C-1$_\alpha$), 82.4 (C-4$_\beta$), 80.1 (C-4$_\alpha$), 79.9 (C-2$_\beta$), 79.3 (C-2$_\alpha$), 75.6, 75.5, 74.4 (CH_2 Bn), 74.2 (C-3$_\alpha$), 73.7 (C-3$_\beta$), 73.2 (C-5$_\beta$), 73.1, 72.9, 72.4 (CH_2 Bn), 71.3 (C-5$_\alpha$), 18.2 ($CH_{3\alpha}$), 18.1 ($CH_{3\beta}$).



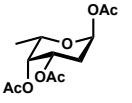
2,2,2-trifluoro-*N*-phenylacetimidoyl 2,3,4-tri-*O*-benzyl-D-rhamnopyranoside (S62). 2,3,4-tri-*O*-benzyl-α/β-D-rhamnopyranoside (108 mg, 0.2 mmol) was dissolved in acetone (2 mL, 0.1 M) and water (0.2 mL, 50 eq.) and cooled on ice. Subsequently, $CsCO_3$ (130 mg, 0.4 mmol, 1.8 eq.) and 2,2,2-trifluoro-*N*-phenylacetimidoyl chloride (83 mg, 0.4 mmol, 1.8 mmol) was added and the solution was allowed to attain room temperature After stirring for 18 h, the solution was diluted with H_2O and EtOAc. The aqueous layer was extracted (3x) with EtOAc followed by washing the combined organic layer with H_2O, sat. aq. $NaHCO_3$ and brine respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo* to yield the crude product as a colorless oil. Flash column chromatography (95:5 → 80:20; pentane:Et_2O) yielded the title compound **S60** (142 mg, 197 µmol, 98%, α:β; 50:50) as a colorless syrup. Spectroscopic data was in accordance with literature.[70] TLC: R_f 0.4 (pentane: Et_2O, 9:1, v:v); Data for the anomeric mixture: (500 MHz, Toluene-d_8, T = 333 K, HH-COSY, HSQC) δ 7.78 – 6.70 (m, 50H, CH_{arom}), 6.44 (bs, 1H, H-1$_\alpha$), 5.59 (bs, 1H, H-1$_\beta$), 4.99 – 4.49 (m, 16H, CH_2 Bn$_\alpha$, CH_2 Bn$_\alpha$, CH_2 Bn$_\alpha$, CH_2 Bn$_\alpha$, CH_2 Bn$_\beta$, CH_2 Bn$_\beta$, CH_2 Bn$_\beta$, CH_2 Bn$_\beta$), 4.06 (t, J = 9.3 Hz, 1H, H-4$_\alpha$), 3.99 (m, 1H, H-6$_\alpha$), 3.80 – 3.32 (m, 10H, H-2$_\alpha$, H-3$_\alpha$, H-5$_\alpha$, H-6$_\alpha$, H-2$_\beta$, H-3$_\beta$, H-4$_\beta$, H-5$_\beta$, H-6$_\beta$, H-6$_\beta$); ^{13}C NMR (101 MHz, Toluene-d_8, T = 333 K, HSQC): δ 143.9, 143.7, 143.4, 138.9, 138.7, 138.3, 138.2, 138.1, 138.1, 135.9, 135.8, 133.5, 133.5, 133.2, 133.2 ($C_{q\text{-}arom}$), 129.4, 128.8, 128.5, 128.5, 128.4, 128.4, 128.2, 128.1, 128.0, 128.0, 127.9, 127.9, 127.9, 127.8, 127.9, 127.90, 127.80, 127.7, 127.7, 127.6, 126.7, 126.7, 126.4, 126.1, 126.0, 126.0, 124.4, 124.3, 120.7, 119.6, 119.6 (CH_{arom}), 97.6 (C-1$_\beta$), 93.9 (C-1$_\alpha$), 84.7, 81.7, 81.2, 79.7, 77.6, 77.6, 76.0, 75.7, 75.6, 75.3, 75.0, 75.0, 73.7, 73.6, 73.5, 73.5, 68.6.

Preparation of Donor 33



S13 **33**

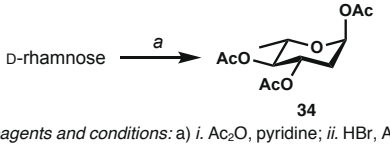
Scheme S5. Donor **33** synthesis. *Reagents and conditions:* a) NIS, AcOH, Et_2O, 1,2-dichloroethane, **33**: 67%.



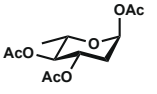
Acetyl 3,4-di-*O*-acetyl-2-deoxy-α-L-fucopyranoside (33). Glacial acetic acid (11.9 mL, 208 mmol, 100 eq.) was added to a mixture of NIS (0.52 g, 2.29 mmol, 1.1 eq.) in Et_2O (10.4 mL) and 1,2-dichloroethane (10.4 mL). The formed solution was added to compound **S13** (0.69 g, 2.1 mmol). After 45 min of stirring,

the reaction was quenched with sat. aq. NaS_2O_3. The aqueous mixture was extracted with DCM (3x), dried over $MgSO_4$ and concentrated *in vacuo*. Column chromatography (pentane:EtOAc, 10:90 → 70:30) was performed to yield title compound **33** as an 1:4 1,3-*cis*/1,3-*trans* mixture (0.49 g, 1.8 mmol, 86%, colorless oil). Additional purification by column made it possible to solely isolate the 1,3-*trans* product (0.38 g, 1.4 mmol, 67%, colorless solid). TLC: R_f 0.45 (pentane:EtOAc, 3:7, v:v); IR (neat, cm^{-1}): 802, 927, 987, 1011, 1038, 1194, 1222, 1368, 1441, 1739; Data for the major stereoisomer (1,3-*trans* product): ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 6.32 (d, *J* = 2.7 Hz, 1H, H-1), 5.32 (ddd, *J* = 12.5, 5.1, 3.0 Hz, 1H, H-3), 5.28 – 5.22 (m, 1H, H-4), 4.20 (q, *J* = 6.5 Hz, 1H, H-5), 2.21 (td, *J* = 13.0, 3.6 Hz, 1H, H-2), 2.20 (s, 3H, CH_3 Ac), 2.14 (s, 3H, CH_3 Ac), 2.04 (s, 3H, CH_3 Ac), 1.91 (ddt, *J* = 13.4, 5.1, 1.2 Hz, 1H, H2), 1.18 (d, *J* = 6.5 Hz, 3H, H-6, H-6, H-6); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 170.8, 170.3, 169.5 (C=O Ac), 92.1 (C-1), 69.4 (C-4), 67.5 (C-5), 66.4 (C-3), 28.9 (C-2), 21.3, 21.1, 20.9 (CH_3 Ac), 16.7 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{12}H_{18}NaO_7$ 297.09447, found 297.09439.

Preparation of donor 34



Scheme S6. Donor **34** synthesis. *Reagents and conditions:* a) *i.* Ac_2O, pyridine; *ii.* HBr, AcOH, DCM; *iii.* $CuSO_4{\cdot}5H_2O$, Ac_2O, NaOAc, AcOH, Zn; *iv.* Ac_2O, HBr, AcOH, **34**: 60%.



2-deoxy-1,3,4-tri-*O*-acetyl-α-L-rhamnopyranoside (34). To suspension of L-rhamnose (4.5 g, 27.5 mmol) in pyridine (25 mL), Ac_2O (32 mL, 340 mmol, 12 eq.) at 0 °C. After stirring for an additional 16 h at room temperature. The mixture was concentrated *in vacuo* and co-evaporated three times with heptane. The resulting colorless oil was used in the next step without further purification. The crude product was dissolved in DCM (18 mL), followed by the addition of Ac_2O (1 mL, 10.6 mmol, 0.4 eq.). To the solution HBr (33 wt% in AcOH, 8.5 mL, 55.0 mmol, 2.0 eq.) was added dropwise at 0 °C and stirred for an additional 4 h at room temperature. The mixture was then concentrated under reduced pressure and the yellow oil was used as a crude product in the next step. $CuSO_4{\cdot}5H_2O$ (0.88 g), Ac_2O (3.6 mL, 38 mmol, 1.4 eq.), sodium acetate (4.5 g, 55 mmol, 2 eq.), AcOH (3.2 mL) were suspended in acetonitrile (12 mL), and subsequently Zn (dust, 3.6 g, 55 mmol, 2 eq.) was added. After 45 min of stirring the rhamnosyl bromide was added in 60 mL acetonitrile via a dropping funnel over 40 min. The reaction was allowed to stir for an additional 2 h. After reaction completion the mixture was diluted with DCM and filtrated over Celite® 545 (Sigma-Aldrich) and transferred to a separatory funnel. The organic phase was washed with saturated sat. aq. $NaHCO_3$, dried with $MgSO_4$ and concentrated *in vacuo*. The crude rhamnal was dissolved in DCM (40 mL) and AcOH (15.8 mL, 276 mmol, 10 eq.), Ac_2O (22.2 mL, 233 mmol, 8.5 eq.) were added at 0 °C. After 15 min stirring, HBr (33 wt% in AcOH, 1.5 mL, 9.1 mmol, 0.3 eq.) was dropwise added at 0 °C and the reaction was stirred for an additional 5 h. After reaction completion the mixture was quenched with ice-cold water and extracted DCM (3x). The combined organic layers were washed with sat. aq. $NaHCO_3$, dried with $MgSO_4$ and concentrated *in vacuo*. Column chromatography (95:5 → 85:15, pentane:EtOAc) gave the title compound **34** (4.5 g, 16.4 mmol, 60% over 4 steps, average of 88% per step, white solid). TLC: R_f 0.26 (pentane:EtOAc, 8:2, v:v). IR (neat, cm^{-1}): 922, 1037, 1134, 1157, 1369, 1732, 2994; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 6.19 (dd, *J* = 3.8, 1.4 Hz, 1H, H-1), 5.27 (ddd, *J* = 11.6, 9.5, 5.3 Hz, 1H, H-3), 4.80 (t, *J* = 9.7 Hz, 1H, H-4), 3.94 (dq, *J* = 9.8, 6.2 Hz, 1H, H-5), 2.26 (ddd, *J* = 13.5, 5.3, 1.5 Hz, 1H, H-2), 2.12 (s, 3H, CH_3 Ac), 2.07 (s, 3H, CH_3 Ac), 2.03 (s, 3H, CH_3 Ac), 1.92 (ddd, *J* = 13.5, 11.7, 3.7 Hz, 1H, H-2), 1.19 (d, *J* = 6.3 Hz, 3H, CH_3); ^{13}C NMR (126 MH, $CDCl_3$, HSQC): δ 170.4, 170.1, 169.3 (C=O, Ac), 90.9 (C-1), 74.2 (C-4), 68.5 (C-3), 68.3 (C-5), 34.3 (C-2), 21.2, 21.1, 20.9 (CH_3 Ac), 17.7 (CH_3); HRMS: $[M+Na]^+$ calcd for $C_{12}H_{18}NaO_7$ 297.0950, found 297.0951.

References and notes

(1) Zhu, X.; Schmidt, R. R. New Principles for Glycoside-Bond Formation. *Angew. Chem. Int. Ed.* **2009**, *48* (11), 1900–1934.

(2) Seeberger, P. H. The Logic of Automated Glycan Assembly. *Acc. Chem. Res.* **2015**, *48* (5), 1450–1463.

(3) Wang, C. C.; Lee, J. C.; Luo, S. Y.; Kulkarni, S. S.; Huang, Y. W.; Lee, C. C.; Chang, K. L.; Hung, S. C. Regioselective One-Pot Protection of Carbohydrates. *Nature* **2007**, *446* (7138), 896–899.

(4) Leng, W.; Yao, H.; He, J.; Liu, X. Venturing beyond Donor-Controlled Glycosylation: New Perspectives toward Anomeric Selectivity. *Acc. Chem. Res.* **2018**, *51* (3), 628–639.

(5) Nigudkar, S. S.; Demchenko, A. V. Stereocontrolled 1,2-*Cis* Glycosylation as the Driving Force of Progress in Synthetic Carbohydrate Chemistry. *Chem. Sci.* **2015**, *6* (5), 2687–2704.

(6) A. V. Demchenko. *Handbook of Chemical Glycosylation: Advances in Stereoselectivity and Therapeutic Relevance*; Wiley, **2008**.

(7) Bennett, C. S. Selective Glycosylations with Deoxy Sugars. In *Selective Glycosylations: Synthetic Methods and Catalysts*; Bennett, C. S., Ed.; Wiley-VCH Verlag GmbH & Co. KGaA, **2017**; pp 277–295.

(8) Bohé, L.; Crich, D. A Propos of Glycosyl Cations and the Mechanism of Chemical Glycosylation. *Comptes Rendus Chimie* **2011**, *14* (1), 3–16.

(9) Crich, D. Mechanism of a Chemical Glycosylation Reaction. *Acc. Chem. Res.* **2010**, *43* (8), 1144–1153.

(10) Adero, P. O.; Amarasekara, H.; Wen, P.; Bohé, L.; Crich, D. The Experimental Evidence in Support of Glycosylation Mechanisms at the S_N1–S_N2 Interface. *Chem. Rev.* **2018**, *118* (17), 8242–8284.

(11) van der Vorm, S.; Overkleeft, H. S.; van der Marel, G. A.; Codée, J. D. C. Stereoselectivity of Conformationally Restricted Glucosazide Donors. *J. Org. Chem.* **2017**, *82* (9), 4793–4811.

(12) Frihed, T. G.; Bols, M.; Pedersen, C. M. Mechanisms of Glycosylation Reactions Studied by Low-Temperature Nuclear Magnetic Resonance. *Chem. Rev.* **2015**, *115* (11), 4963–5013.

(13) Frihed, T. G.; Walvoort, M. T. C.; Codée, J. D. C.; van der Marel, G. A.; Bols, M.; Pedersen, C. M. Influence of O6 in Mannosylations Using Benzylidene Protected Donors: Stereoelectronic or Conformational Effects? *J. Org. Chem.* **2013**, *78* (6), 2191–2205.

(14) Kaeothip, S.; Yasomanee, J. P.; Demchenko, A. V. Glycosidation of Thioglycosides in the Presence of Bromine: Mechanism, Reactivity, and Stereoselectivity. *J. Org. Chem.* **2012**, *77* (1), 291–299.

(15) Walvoort, M. T. C.; Lodder, G.; Mazurek, J.; Overkleeft, H. S.; Codée, J. D. C.; van der Marel, G. A. Equatorial Anomeric Triflates from Mannuronic Acid Esters. *J. Am. Chem. Soc.* **2009**, *131* (34), 12080–12081.

(16) Liu, J.; Gin, D. Y. C2-Amidoglycosylation. Scope and Mechanism of Nitrogen Transfer. *J. Am. Chem. Soc.* **2002**, *124* (33), 9789–9797.

(17) Garcia, B. A.; Gin, D. Y. Dehydrative Glycosylation with Activated Diphenyl Sulfonium Reagents. Scope, Mode of C(1)-Hemiacetal Activation, and Detection of Reactive Glycosyl Intermediates. *J. Am. Chem. Soc.* **2000**, *122* (18), 4269–4279.

(18) Crich, D.; Sun, S. Are Glycosyl Triflates Intermediates in the Sulfoxide Glycosylation Method? A Chemical and ^{1}H, ^{13}C, and ^{19}F NMR Spectroscopic Investigation. *J. Am. Chem. Soc.* **1997**, *119* (46), 11217–11223.

(19) Vorm, S. van der; Hansen, T.; Overkleeft, H. S.; Marel, G. A. van der; Codée, J. D. C. The Influence of Acceptor Nucleophilicity on the Glycosylation Reaction Mechanism. *Chem. Sci.* **2017**, *8* (3), 1867–1875.

(20) Moumé-Pymbock, M.; Crich, D. Stereoselective *C*-Glycoside Formation with 2-*O*-Benzyl-4,6-*O*-Benzylidene Protected 3-Deoxy Gluco- and Mannopyranoside Donors: Comparison with *O*-Glycoside Formation. *J. Org. Chem.* **2012**, *77* (20), 8905–8912.

(21) Codée, J. D. C.; Walvoort, M. T. C.; Jong, A. R. de; Lodder, G.; Overkleeft, H. S.; Marel, G. A. van der. Mannuronic Acids: Reactivity and Selectivity. *J. Carbohydr. Chem.* **2011**, *30* (7–9), 438–457.

(22) Beaver, M. G.; Woerpel, K. A. Erosion of Stereochemical Control with Increasing Nucleophilicity: *O*-Glycosylation at the Diffusion Limit. *J. Org. Chem.* **2010**, *75* (4), 1107–1118.

(23) Walvoort, M. T. C.; Dinkelaar, J.; van den Bos, L. J.; Lodder, G.; Overkleeft, H. S.; Codée, J. D. C.; van der Marel, G. A. The Impact of Oxacarbenium Ion Conformers on the Stereochemical Outcome of Glycosylations. *Carbohydr. Res.* **2010**, *345* (10), 1252–1263.

(24) Lucero, C. G.; Woerpel, K. A. Stereoselective *C*-Glycosylation Reactions of Pyranoses: The Conformational Preference and Reactions of the Mannosyl Cation. *J. Org. Chem.* **2006**, *71* (7), 2641–2647.

(25) Crich, D.; Vinogradova, O. On the Influence of the C2–O2 and C3–O3 Bonds in 4,6-*O*-Benzylidene-Directed β-Mannopyranosylation and α-Glucopyranosylation. *J. Org. Chem.* **2006**, *71* (22), 8473–8480.

(26) Krumper, J. R.; Salamant, W. A.; Woerpel, K. A. Continuum of Mechanisms for Nucleophilic Substitutions of Cyclic Acetals. *Org. Lett.* **2008**, *10* (21), 4907–4910.

(27) Zhu, X.; Kawatkar, S.; Rao, Y.; Boons, G. J. Practical Approach for the Stereoselective Introduction of β-Arabinofuranosides. *J. Am. Chem. Soc.* **2006**, *128* (36), 11948–11957.

(28) Ishiwata, A.; Akao, H.; Ito, Y. Stereoselective Synthesis of a Fragment of Mycobacterial Arabinan. *Org. Lett.* **2006**, *8* (24), 5525–5528.

(29) Nukada, T.; Bérces, A.; Wang, L.; Zgierski, M. Z.; Whitfield, D. M. The Two-Conformer Hypothesis: 2,3,4,6-Tetra-*O*-Methyl-Mannopyranosyl and -Glucopyranosyl Oxacarbenium Ions. *Carbohydr. Res.* **2005**, *340* (5), 841–852.

(30) Larsen, C. H.; Ridgway, B. H.; Shaw, J. T.; Smith, D. M.; Woerpel, K. A. Stereoselective *C*-Glycosylation Reactions of Ribose Derivatives: Electronic Effects of Five-Membered Ring Oxocarbenium Ions. *J. Am. Chem. Soc.* **2005**, *127* (31), 10879–10884.

(31) Ayala, L.; Lucero, C. G.; Romero, J. A. C.; Tabacco, S. A.; Woerpel, K. A. Stereochemistry of Nucleophilic Substitution Reactions Depending upon Substituent: Evidence for Electrostatic Stabilization of Pseudoaxial Conformers of Oxocarbenium Ions by Heteroatom Substituents. *J. Am. Chem. Soc.* **2003**, *125* (50), 15521–15528.

(32) Romero, J. A. C.; Tabacco, S. A.; Woerpel, K. A. Stereochemical Reversal of Nucleophilic Substitution Reactions Depending upon Substituent: Reactions of Heteroatom-Substituted Six-Membered-Ring Oxocarbenium Ions through Pseudoaxial Conformers. *J. Am. Chem. Soc.* **2000**, *122* (1), 168–169.

(33) Parent, J. F.; Deslongchamps, P. Bent Bonds (τ) and the Antiperiplanar Hypothesis, and the Reactivity at the Anomeric Center in Pyranosides. *Org. Biomol. Chem.* **2016**, *14* (47), 11183–11198.

(34) Ardèvol, A.; Rovira, C. The Molecular Mechanism of Enzymatic Glycosyl Transfer with Retention of Configuration: Evidence for a Short-Lived Oxocarbenium-Like Species. *Angew. Chem. Int. Ed.* **2011**, *50* (46), 10897–10901.

(35) Iglesias-Fernández, J.; Hancock, S. M.; Lee, S. S.; Khan, M.; Kirkpatrick, J.; Oldham, N. J.; McAuley, K.; Fordham-Skelton, A.; Rovira, C.; Davis, B. G. A Front-Face "S_Ni Synthase" Engineered from a Retaining "Double-S_N2" Hydrolase. *Nat. Chem. Biol.* **2017**, *13* (8), 874–881.

(36) Beenakker, T. J. M.; Wander, D. P. A.; Offen, W. A.; Artola, M.; Raich, L.; Ferraz, M. J.; Li, K.-Y.; Houben, J. H. P. M.; van Rijssel, E. R.; Hansen, T.; *et al.* Carba-Cyclophellitols Are Neutral Retaining-Glucosidase Inhibitors. *J. Am. Chem. Soc.* **2017**, *139* (19), 6534–6537.

(37) Martin, A.; Arda, A.; Désiré, J.; Martin-Mingot, A.; Probst, N.; Sinaÿ, P.; Jiménez-Barbero, J.; Thibaudeau, S.; Blériot, Y. Catching Elusive Glycosyl Cations in a Condensed Phase with HF/SbF_5 Superacid. *Nat. Chem.* **2016**, *8* (2), 186–191.

(38) Elferink, H.; Severijnen, M. E.; Martens, J.; Mensink, R. A.; Berden, G.; Oomens, J.; Rutjes, F. P. J. T.; Rijs, A. M.; Boltje, T. J. Direct Experimental Characterization of Glycosyl Cations by Infrared Ion Spectroscopy. *J. Am. Chem. Soc.* **2018**, *140* (19), 6034–6038.

(39) Mucha, E.; Marianski, M.; Xu, F. F.; Thomas, D. A.; Meijer, G.; Helden, G. von; Seeberger, P. H.; Pagel, K. Unravelling the Structure of Glycosyl Cations via Cold-Ion Infrared Spectroscopy. *Nat. Commun.* **2018**, *9* (1), 4174.

(40) Novel corrections and functionals, including B3LYP-D3 and ωB97XD were also used, and showed comparable results (see SI for full details).

(41) The effect of the solvent on the outcome of the addition reactions to the fuco- and rhamno-configured oxocarbenium ions **19** and **22**, respectively, has been investigated by performing the reactions in Et_2O and MeCN. The outcome of these reactions was similar to the outcome of the reactions in DCM, with the 1,2-*cis*-addition products being formed as the sole anomer. These results are in line with the structures of the intermediate oxocarbenium ions as revealed by the CEL maps of these ions in the respective solvents (see SI for full details).

(42) For ease of visualization, the Cremer-Pople globe is turned 180° with respect to its common representation and both poles (the $^4C_1$ and $^1C_4$ structures) are omitted as these conformations are very high in energy.

(43) Pierre Deslongchamps; Yves L. Dory; Shigui Li. 1994 R.U. Lemieux Award Lecture Hydrolysis of Acetals and Ketals. Position of Transition States along the Reaction Coordinates, and Stereoelectronic Effects. *Can. J. Chem.* **1994**, *10* (72), 2021–2027.

(44) van Rijssel, E. R.; van Delft, P.; Lodder, G.; Overkleeft, H. S.; van der Marel, G. A.; Filippov, D. V.; Codée, J. D. C. Furanosyl Oxocarbenium Ion Stability and Stereoselectivity. *Angew. Chem. Int. Ed.* **2014**, *53* (39), 10381–10385.

(45) van Rijssel, E. R.; van Delft, P.; van Marle, D. V.; Bijvoets, S. M.; Lodder, G.; Overkleeft, H. S.; van der Marel, G. A.; Filippov, D. V.; Codée, J. D. C. Stereoselectivity in the Lewis Acid Mediated Reduction of Ketofuranoses. *J. Org. Chem.* **2015**, *80* (9), 4553–4565.

(46) Madern, J. M.; Hansen, T.; van Rijssel, E. R.; Kistemaker, H. A. V.; van der Vorm, S.; Overkleeft, H. S.; van der Marel, G. A.; Filippov, D. V.; Codée, J. D. C. Synthesis, Reactivity, and Stereoselectivity of 4-Thiofuranosides. *J. Org. Chem.* **2019**, *84* (3), 1218–1227.

(47) Jensen, H. H.; Lyngbye, L.; Jensen, A.; Bols, M. Stereoelectronic Substituent Effects in Polyhydroxylated Piperidines and Hexahydropyridazines. *Chem. Eur. J.* **2002**, *8* (5), 1218–1226.

(48) Jensen, H. H.; Bols, M. Stereoelectronic Substituent Effects. *Acc. Chem. Res.* **2006**, *39* (4), 259–265.

(49) Bucher, C.; Gilmour, R. Fluorine-Directed Glycosylation. *Angew. Chem. Int. Ed.* **2010**, *49* (46), 8724–8728.

(50) Beaver, M. G.; Billings, S. B.; Woerpel, K. A. *C*-Glycosylation Reactions of Sulfur-Substituted Glycosyl Donors: Evidence against the Role of Neighboring-Group Participation. *J. Am. Chem. Soc.* **2008**, *130* (6), 2082–2086.

(51) Codée, J. D. C.; Litjens, R. E. J. N.; den Heeten, R.; Overkleeft, H. S.; van Boom, J. H.; van der Marel, G. A. Ph_2SO/Tf_2O: A Powerful Promotor System in Chemoselective Glycosylations Using Thioglycosides. *Org. Lett.* **2003**, *5* (9), 1519–1522.

(52) Addition reactions, in which L-fucose, L-rhamnose and D-glucose *N*-phenyl trifluoroacetimidate donors were used in conjunction with a catalytic amount of TMSOTf (0.1 equiv.) and TES-*d*, proceeded with a similar stereochemical outcome (see SI for full details).

(53) Hagen, B.; Ali, S.; Overkleeft, H. S.; van der Marel, G. A.; Codée, J. D. C. Mapping the Reactivity and Selectivity of 2-Azidofucosyl Donors for the Assembly of *N*-Acetylfucosamine-Containing Bacterial Oligosaccharides. *J. Org. Chem.* **2017**, *82* (2), 848–868.

(54) Guillemineau, M.; Auzanneau, F. I. Challenging Deprotection Steps During the Synthesis of Tetra- and Pentasaccharide Fragments of the LeaLex Tumor-Associated Hexasaccharide Antigen. *J. Org. Chem.* **2012**, *77* (20), 8864–8878.

(55) Mong, K. K. T.; Wong, C. H. Reactivity-Based One-Pot Synthesis of a Lewis Y Carbohydrate Hapten: A Colon–Rectal Cancer Antigen Determinant. *Angew. Chem.* **2002**, *114* (21), 4261–4264.

(56) The experimental data of the model glycosylations of the mono-substituted pyranosyl donors were obtained from the work of Woerpel and co-workers (Experimental conditions: allyltrimethylsilane (4.0 eq.), Lewis acid ($BF_3{\cdot}OEt_2$ or $SnBr_4$; 1.0 eq.), pyranosyl-1-*O*-acetyl donor in DCM (0.15 M), −78 °C to room temperature.). The model glycosylations of the multi-substituted pyranosyl donors were done with pre-activation conditions (Experimental conditions: pre-activation conditions; TES-*d* (2 eq.), Tf_2O (1.3 eq.), Ph_2SO (1.3 eq.), TTBP (2.5 eq.), pyranosyl-1-*S*-thiophenyl donors, DCM (0.05 M), −80 °C to −60 °C, 96 h.).

(57) To keep the calculation time manageable, large protection groups (BnO–) were substituted with electronic comparable smaller groups (MeO–) (see SI for full details).

(58) Olah, G. A.; Parker, D. G.; Yoneda, N.; Pelizza, F. Oxyfunctionalization of Hydrocarbons. 1. Protolytic Cleavage-Rearrangement Reactions of Tertiary Alkyl Hydroperoxides with Magic Acid. *J. Am. Chem. Soc.* **1976**, *98* (8), 2245–2250.

(59) van der Vorm, S.; van Hengst, J. M. A.; Bakker, M.; Overkleeft, H. S.; van der Marel, G. A.; Codée, J. D. C. Mapping the Relationship between Glycosyl Acceptor Reactivity and Glycosylation Stereoselectivity. *Angew. Chem. Int. Ed.* **2018**, *57* (27), 8240–8244.

(60) van Rijssel, E. R.; van Delft, P.; Lodder, G.; Overkleeft, H. S.; van der Marel, G. A.; Filippov, D. V.; Codée, J. D. C. Furanosyl Oxocarbenium Ion Stability and Stereoselectivity. *Angew. Chem. Int. Ed.* **2014**, 53 (39), 10381–10385.

(61) Ribeiro, R. F.; Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. Use of Solution-Phase Vibrational Frequencies in Continuum Models for the Free Energy of Solvation. *J. Phys. Chem. B* **2011**, 115 (49), 14556–14562.

(62) Bally, T.; Rablen, P. R. Quantum-Chemical Simulation of ^{1}H NMR Spectra. 2. Comparison of DFT-Based Procedures for Computing Proton–Proton Coupling Constants in Organic Molecules. *J. Org. Chem.* **2011**, 76 (12), 4818–4830.

(63) Chervin, S. M.; Lowe, J. B.; Koreeda, M. Synthesis and Biological Evaluation of a New Sialyl Lewis X Mimetic Derived from Lactose. *J. Org. Chem.* **2002**, 67 (16), 5654–5662.

(64) Hagen, B.; Ali, S.; Overkleeft, H. S.; van der Marel, G. A.; Codée, J. D. C. Mapping the Reactivity and Selectivity of 2-Azidofucosyl Donors for the Assembly of *N*-Acetylfucosamine-Containing Bacterial Oligosaccharides. *J. Org. Chem.* **2017**, 82 (2), 848–868.

(65) Tanikawa, T.; Fridman, M.; Zhu, W.; Faulk, B.; Joseph, I. C.; Kahne, D.; Wagner, B. K.; Clemons, P. A. Using Biological Performance Similarity to Inform Disaccharide Library Design. *J. Am. Chem. Soc.* **2009**, 131 (14), 5075–5083.

(66) Dinkelaar, J.; de Jong, A. R.; van Meer, R.; Somers, M.; Lodder, G.; Overkleeft, H. S.; Codée, J. D. C.; van der Marel, G. A. Stereodirecting Effect of the Pyranosyl C-5 Substituent in Glycosylation Reactions. *J. Org. Chem.* **2009**, 74 (14), 4982–4991.

(67) Greenberg, W. A.; Priestley, E. S.; Sears, P. S.; Alper, P. B.; Rosenbohm, C.; Hendrix, M.; Hung, S.-C.; Wong, C.-H. Design and Synthesis of New Aminoglycoside Antibiotics Containing Neamine as an Optimal Core Structure: Correlation of Antibiotic Activity with *in Vitro* Inhibition of Translation. *J. Am. Chem. Soc.* **1999**, 121 (28), 6527–6541.

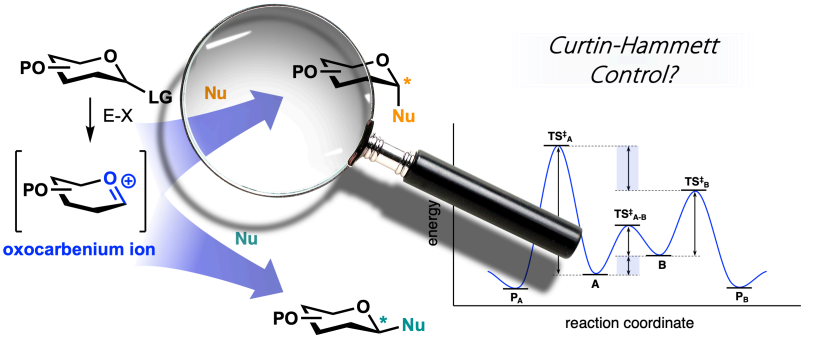
(68) Podilapu, A. R.; Kulkarni, S. S. First Synthesis of Bacillus Cereus Ch HF-PS Cell Wall Trisaccharide Repeating Unit. *Org. Lett.* **2014**, 16 (16), 4336–4339.

(69) Adinolfi, M.; Barone, G.; Iadonisi, A.; Schiattarella, M. Activation of Glycoyl Trihaloacetimidates with Acid-Washed Molecular Sieves in the Glycosidation Reaction. *Org. Lett.* **2003**, 5 (7), 987–989.

(70) Wang, L.; Overkleeft, H. S.; van der Marel, G. A.; Codée, J. D. C. Reagent Controlled Stereoselective Synthesis of α-Glucans. *J. Am. Chem. Soc.* **2018**, 140 (13), 4632–4638.

Chapter 3

Dissecting Curtin-Hammett Scenarios for Addition Reactions to Glycosyl Oxocarbenium Ions



Abstract | Glycosyl cations play an all-important role in glycosylation reactions, determining the reactivity of glycosylating agents and shaping the stereoselectivity. Notwithstanding the high reactivity of these species, they can be at the basis of highly stereoselective addition reactions. The nature of the incoming nucleophile also plays an important role, and it has been difficult to delineate clear structure-reactivity-stereoselectivity relationships for addition reactions to glycosyl oxocarbenium ions, hampering the development of stereoselective glycosylation methodologies. We show in this chapter how the nature of typical S_N1-nucleophiles, *i.e.*, triethyl deuteriosilane (TES-*d*) and allyltrimethylsilane (allyl-TMS) affects the stereochemical outcome of addition reactions to glycosyl cations. TES-*d* adds to oxocarbenium ions following a barrierless reaction pathway, and the stereoselectivity of these reactions can be reliably predicted and understood from the distribution of the cation conformers, the stability of which is dictated by the nature and orientation of the ring substituents. The stereoselectivity of the addition reactions of allyl-TMS, however, often does not mirror the mixture of glycosyl cation conformers. For these reactions we have computationally dissected Curtin-Hammett kinetic scenarios to accurately show how the outcome of these addition reactions is influenced by the reactivity of the different glycosyl oxocarbenium ion conformers and the incoming nucleophile. By performing activation strain and Kohn-Sham molecular orbital analyses, it was found that the disparate stereoselectivity originates from (i) the stability of the different glycosyl cation conformers; (ii) the position of the transition state along the reaction coordinate; and (iii) the (steric) Pauli repulsion between the nucleophile and the glycosyl cation. The offered quantitative mechanistic insights will serve as a guide for the interpretation of glycosylation results and as the basis to further explore addition reaction mechanisms to cyclic carbocations.

Introduction

Six-membered oxocarbenium ions are important reactive intermediates in organic synthesis. The stability of glycosyl oxocarbenium ions determines the reactivity of glycosyl donors and plays a paramount role in the stereochemical outcome of glycosylation reactions.[1–13] The intrinsic high reactivity and fleeting nature of glycosyl oxocarbenium ions represents a major challenge in studying these species and determining clear structure−reactivity-stereoselectivity principles. Due to the extremely short lifetime of these intermediates,[14,15] there is currently no (spectroscopic) technique available in conventional reaction media to study these species in a direct manner and assess their behavior, leaving a major gap in our understanding of reactions involving these ions.[16–24] Therefore, computational techniques have been used to gain insight into their structure and reactivity.

Chapter 2 reported on a strategy to map the complete conformational space an oxocarbenium ion can adopt to establish the conformational preference of these species. The shape of the cations, preferentially adopting flattened structures to allow stabilization of the cationic sp^2-hybridized carbon by delocalization of electron density from the adjacent oxygen, is influenced by the substituents on the ring.[18,25–28] Electron-rich substituents (*e.g.*, *O*-, *N*-, *F*-moieties) at the C3- and C4-position prefer to adopt an axial position, while at the C2-position these groups have a preference for a *pseudo*-equatorial position. Various experimental studies have shown that the conformation of a glycosyl cation can have a significant impact on the stereoselectivity of reactions, in which these ions can form.[1,16,18,29–32] In Chapter 2 it was shown that oxocarbenium ions can be trapped using triethylsilane-*d* (TES-*d*) to reveal the conformational preference of the cations. Highly stereoselective addition reactions were observed for oxocarbenium ions, that preferentially take up a single structure (or family of closely related structures). Diastereomeric mixtures were obtained when oxocarbenium ions were formed that could adopt different low energy conformations. Notably, some addition reactions described in Chapter 2, proceeded with a markedly different stereochemical outcome than analogous reactions reported in literature using different typical S_N1-nucleophiles. As shown in Figure 1A, the addition of TES-*d* to a mannosyl oxocarbenium ion, that preferentially adopts a $^3H_4$-half chair conformation, takes place from the top side of the cation to provide the β-linked product with excellent diastereoselectivity (97:3). In contrast, the addition of allyl-trimethylsilane (allyl-TMS) provides a mixture of anomers (34:66), in which the opposite anomer (*i.e.*, the α-linked product) prevails.[18,33]

The difference in stereochemical outcome may be explained by invoking different kinetic scenarios for the addition of the nucleophile to the oxocarbenium ion conformers. Figure 1B-D shows three relevant Curtin-Hammett scenarios[34,35] for the addition of a nucleophile to an oxocarbenium ion, that can adopt two relatively stable conformers **A** and

B. These scenarios can be divided into two classes: in the first class (class I, Figure 1B), the barrier for interconversion of the oxocarbenium ion conformers **A** and **B** is higher than the barrier of the addition reactions to both, while in the second class (class II-a and II-b, Figure 1C-D) the barrier for the addition is higher than the barrier for interconversion. For class I, the outcome is determined by the difference in energy between oxocarbenium ion conformers **A** and **B** ($\Delta\Delta G°$). While for class II the difference in activation energies of the transition states (TSs, $\Delta\Delta G^{‡}$) leading from the oxocarbenium ions conformers **A** and **B** to the products, dictates the product distribution. If the transition state from the higher energy intermediate is lower than the transition state from the lower energy intermediates, the higher energy intermediate is responsible for product formation (this is typically referred to as the Curtin-Hammett scenario). Although the latter scenario is often invoked to account for a particular (stereochemical) outcome, there is often little quantitative evidence to explain this kinetic pathway, and it is exceedingly difficult to predict such a Curtin-Hammett pathway beforehand. This presents an enormous challenge in the development of stereoselective glycosylation methodologies.

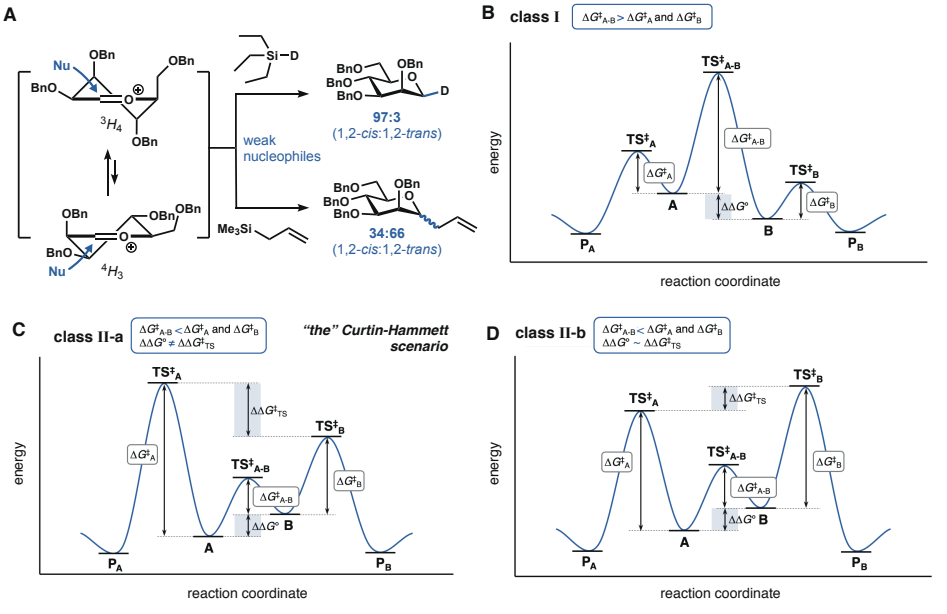


Figure 1. Curtin-Hammett scenarios for the addition of the nucleophile to the glycosyl oxocarbenium ion. (A) Experimentally found Curtin-Hammett scenario, in which two typical S_N1-like nucleophiles, including, allyltrimethylsilane and triethylsilane-*d*, give contrasting stereoselectivities; (B) Curtin-Hammett scenario class I, in which the barrier for interconversion between the reactive species is higher compared to the barrier of addition; (C) and (D) Curtin-Hammett scenario class II-a and II-b, in which the barrier for the addition is higher compared to the interconversion.

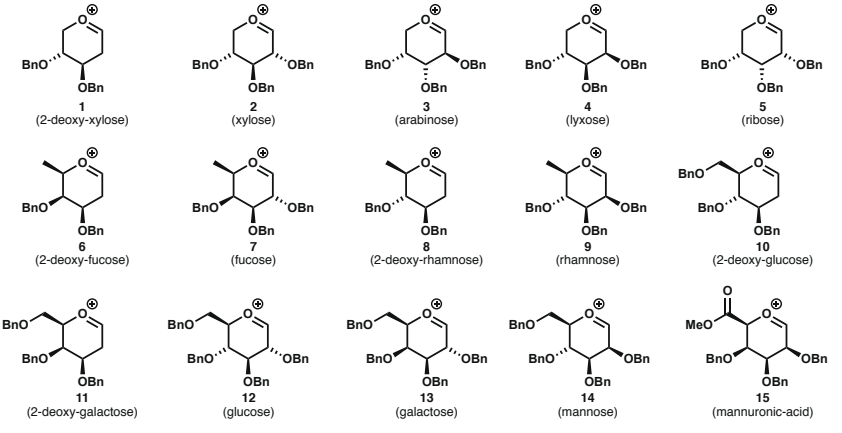
This chapter reports on a study to dissect the Curtin-Hammett scenarios at play during addition reactions to glycosyl cations. It is shown that many of the reactions reported in Chapter 2 proceed via an addition reaction following a barrierless pathway from the intermediate oxocarbenium ions (*i.e.*, class I, Figure 1B). For a selection of reactions, addition reaction barriers were found. In these cases, the relative stability of the oxocarbenium ion conformers cannot account for the stereochemical outcome of the addition reactions, and in-depth transition state analyses revealed the factors that determine the relative energies of the reaction barriers involved. By the use of the activation strain model (ASM) of reactivity and Kohn-Sham molecular orbital (KS-MO) theory, in combination with the matching energy decomposition analysis (EDA), a quantitative description of the various physical factors that control, and distinguish, the addition reactions, is provided. These analyses have revealed the origin of the stereoselectivity of reactions taking place following Curtin-Hammett scenarios of class II (Figure 1C and 1D).

Results and discussion

To investigate the addition reaction to glycosyl cations, a panel of 15 popular glycosyl donors, systematically differing in the number of substituents and their stereochemistry, were subjected to a series of glycosylation reactions with two typical S_N1 nucleophiles: triethylsilane-*d* (TES-*d*)[18,36,37] and allyltrimethylsilane (allyl-TMS). Table 1 summarizes the observed stereoselectivity of the experimental reactions of the thioglycoside donors, obtained by pre-activation of the donors using the diphenyl sulfoxide (Ph_2SO)/triflic anhydride (Tf_2O) activator.[38] Table 1 also reports the theoretical stereochemical preference of the corresponding glycosyl cation based on their conformational preference, established as described in Chapter 2.

As can be seen from Table 1, the majority of the reactions (Table 1, Entry 1-7, 11-13 and 15) proceeds with a similar stereoselectivity for both nucleophiles. In all these cases, the theoretical stereochemical outcome, determined from the population of the different oxocarbenium ion conformational states, matches the stereochemical outcome of the addition reactions. The stereochemical outcome of the addition reactions to oxocarbenium ions **8**-**10** and **14** (Table 1, Entry 8-10 and 14; marked blue) differs for the two nucleophiles (*i.e.*, TES-*d* and allyl-TMS). Of note, all these cations share the same stereochemistry at C3-, C4- and C5-position and can be regarded as belonging to the mannosyl-like series, showing a preference for the formation of *trans*-products when allyl-TMS is used, and a preference for *cis*-products when TES-*d* is used.

Table 1. Computed and experimentally found stereoselectivity for *d*- and *C*-glycosylation reactions on glycosyl cations. For the 2-deoxy-glycosides (Entry 1, 6, 8, 10 and 11) the *cis*:*trans* ratio is expressed as the relationship between the substituent on the C3-position and the coupled nucleophile; for the other glycopyranosides (Entry 2-5, 7, 9 and 12-15) the *cis*:*trans* ratio is expressed as the relationship between the substituent on the C2-position and the coupled nucleophile. For the computational studies, per-*O*-methylated oxocarbenium ions were used, where the experimental glycosylation used per-*O*-benzylated substrates. The generation of all computed data is described in Chapter 2 and based on the CEL map calculations. In cases where the allyl-TMS and TES-*d* results do not match, the entry is marked blue. All glycosyl cations are depicted as their D-analogue for ease of comparison, but cations **6-9** were used as L-sugars.



Entry	glycosyl cation	*experimental* allyltrimethylsilane (allyl-TMS)	*experimental* triethylsilane-*d* (TES-*d*)	*computed* glycosyl cation
1	**1**	>98:2	>98:2	>98:2
2	**2**	>98:2	>98:2	>98:2
3	**3**	>98:2	>98:2	>98:2
4	**4**	>98:2	>98:2	>98:2
5	**5**	>98:2	>98:2	>98:2
6	**6**	<2:98	<2:98	<2:98
7	**7**	>98:2	>98:2	>98:2
8	**8**	9:91	66:34	71:29
9	**9**	23:77	>98:2	>98:2
10	**10**	<2:98	52:48	52:48
11	**11**	<2:98	<2:98	<2:98
12	**12**	>98:2	>98:2	>98:2
13	**13**	>98:2	>98:2	>98:2
14	**14**	34:66	97:3	97:3
15	**15**	>98:2	>98:2	>98:2

While for TES-*d* the stereoselectivity matches well with the computed selectivities, the observed stereoselectivity for the allyl-TMS additions cannot simply be rationalized based on the relative ground state energy of the different oxocarbenium ion conformers.

Thus, to understand the differences in stereochemical outcome, a series of DFT computations were performed to study the transition states of the addition reactions to the oxocarbenium ions, following the approach graphically depicted in Figure 2. All computations were performed by utilizing the B3LYP exchange-correlation (XC) functional[39,40] with a 6-311G(d,p) basis set. Solvation effects of CH_2Cl_2 were taken into account using a polarizable continuum model (For more information see Supplementary Information).[41]

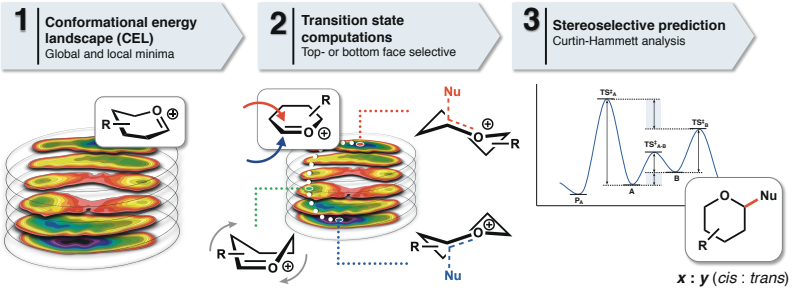


Figure 2. Overview of the workflow to map the stereoselective preference of six-membered ring oxocarbenium ions. (1) The complete conformational space of a six membered ring was scanned by computing 729 pre-fixed structures. The associated energies were graphed on slices dividing the Cremer-Pople sphere; (2) Low energy top- and bottom face selective conformers are selected as initial structure to search for relevant transition states, and relevant conformational transition states were selected which connect the top the bottom of the CEL map; (3) Based on the Curtin-Hammett analysis, the stereochemical outcome of addition reactions to oxocarbenium ions can be computed.

Based on the conformational energy landscape (CEL) maps, generation of which is outlined in Chapter 2 (Figure 2-1), the relevant low-energy conformations of the glycosyl cations were selected for further transition state analysis.[18] Chapter 2 revealed two families of structures to be most relevant: the continuum of (^3E, $^3H_4$, E_4, and $B_{2,5}$)-like structures that are preferentially attacked from the top face, and the 'opposite' family of structures, composed of the (^4E, $^4H_3$, E_3, and $^{2,5}B$)-like conformers, which are likely to be approached by an incoming nucleophile from the bottom face. To find relevant transition states, the two lowest energy structures were selected for each cation, including a conformer from the top face selective family, and a conformer from the bottom face selective family (Figure 2-2). Computationally, the nucleophile was brought closer to the cation in a step-wise manner to find a saddle point on the generated potential energy surface, which was used as a starting point for the TS search. This scan was only performed for the reaction pathways leading to a chair-like TS, since this is the most relevant reaction path (see SI for a detailed study on the diastereotopic selectivity of both allyl-TMS and TES-H additions leading to chair-like

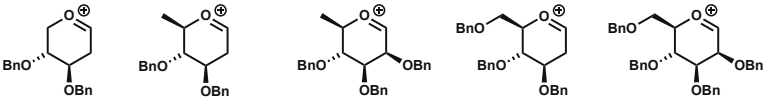
and skew boat TSs; Figure S2-S4). The transition state for the conformational change from the top face selective-structure to the bottom face selective structure was also computed. For these transition state structures, the initial structure for optimization, was provided by the CEL maps, by selecting the saddle point along the conformer interconversion itinerary from the top to the bottom part of the CEL map. These initial TS structures were optimized to find a stationary point, which is verified by performing a vibrational analysis. The character of the normal mode associated with the imaginary frequency of the transition state was analyzed to ensure that it is associated with the reaction of interest. Based on the obtained transition states, the respective reaction profiles were constructed and used to perform a Curtin-Hammett analysis to understand the stereochemical outcome of the addition reactions.

To put this workflow to practice, the addition reaction of TES-H to the 15 glycosyl cations (Table 1) was computed. For the majority of the glycosyl cations, including cations **2-7, 9**, and **12-15**, it was found that the addition of the nucleophile followed a barrierless pathway forming the product complex. These barrierless reactions can be attributed to the very high reactivity of these reactive intermediates. For these cations, formation of the oxocarbenium ions thus represents the reaction's TS and the relative energy levels of these ions is predictive for the stereochemical outcome of the reactions, involving these cations. A Curtin-Hammett class I scenario applies to these ions and the oxocarbenium ion CEL maps generated can be used to rationalize the stereochemical outcome of the triethylsilane additions to these ions.

For cations **1**, **8**, **10** and **11** a TS for the addition was found, which was higher than the interconversion barrier between the top and bottom face selective conformers (see SI for all TS structures; Figure S1). For oxocarbenium ions **1**, **8**, and **10**, the energy levels for the ground state oxocarbenium ion conformers, the barrier for their interconversion ($\Delta G^{\ddagger}_{conf}$), and the computed energy levels of the TS for the top and bottom face additions are summarized in Table 2 (for the analysis of cation **11** see SI; Table S2; not included in the main-text to keep the analysis concise). No significant deviation was found from the "intrinsic" preference of the cations for the addition reaction of TES-H in terms of stereoselectivity, which is completely in line with the experimental results. For 2-deoxy xylosyl cation **1**, the $^{3}H_{4}$ conformer is the most stable oxocarbenium ion because the *O*-substituents on the C3- and C4-position are placed in an axial position, which stabilizes the glycosyl cation through electrostatic interaction.[1,18,29,30] This conformation is 3.2 kcal mol^{-1} more stable than the 'opposite' $^{4}H_{3}$ structure, and the interconversion barrier for the cation is 7.0 kcal mol^{-1}. The TS leading to the addition products from both conformers are found at 9.9 kcal mol^{-1} (top face; $^{3}H_{4}$) and 13.4 kcal mol^{-1} (bottom face; $^{4}H_{3}$). The large difference in energy of these addition TSs ($\Delta\Delta G^{\ddagger}_{addition}$ = –3.5 kcal mol^{-1}) accounts for the stereoselectivity found in the addition reaction (*cis*:*trans* = >98:2), and in this case a Curtin-

Hammett scenario of class II-b applies. A similar analysis holds for oxocarbenium ion **8** and **10**. The difference in kinetic scenarios for the reactions of **8** and **10** and their C2-alkoxy counterparts **9** and **14**, that react with TES-H following a barrierless reaction path, can be explained by the electron withdrawing effect of the C2-alkoxy groups, which destabilize cations **9** and **10**, and which are therefore more reactive than **8** and **10**.

Table 2. Computed and experimentally found stereoselectivity for *d*- and *C*-glycosylation reactions on glycosyl cations. For the 2-deoxy-glycosides the *cis*:*trans* ratio is expressed as the relationship between the substituent on C3-position and the coupled nucleophile; for the other glycopyranoside the *cis*:*trans* ratio is expressed as the relationship between the substituent on C2-position and the coupled nucleophile. For the computational studies, per-*O*-methylated oxocarbenium ions were used, where the experimental glycosylation used per-*O*-benzylated substrates. All data computed at PCM(CH_2Cl_2)-B3LYP/6-311G(d,p). All relative energies ($\Delta\Delta G$) are reported with respect to the conversion of $^4H_3 \rightarrow {}^3H_4$, therefore $\Delta\Delta G°$ is expressed as $\Delta\Delta G° = \Delta G°_{^3H_4} - \Delta G°_{^4H_3}$, the $\Delta\Delta G^‡_{addition}$ is expressed as $\Delta\Delta G^‡_{addition} = \Delta G^‡_{top} - \Delta G^‡_{bottom}$. Both $\Delta G^‡_{top}$ and $\Delta G^‡_{bottom}$ are relative to the lowest-energy conformer.[42,43] All glycosyl cations are depicted as their D-analogue for ease of comparison, but cation **8** and **9** were used as L-sugars. [a] Nonexistent: encounter of reactants induces addition reaction without barrier; [b] Barrierless addition was found, therefore the computed stereoselectivity is based on the conformational preference of the cation (*i.e.*, CEL map).



	3	8	9	10	14
Glycosyl cation					
$\Delta G°_{^3H_4}$	0.0	0.0	0.0	0.0	0.0
$\Delta G°_{^4H_3}$	3.2	0.6	3.1	0.2	1.9
$\Delta\Delta G°$	−3.2	−0.6	−3.1	−0.2	−1.9
$\Delta G^‡_{conf}$	7.0	2.9	3.6	2.7	2.6
triethylsilane (TES-d/H) addition					
exp.	**>98:2**	**66:34**	**>98:2**	**52:48**	**97:3**
$\Delta G^‡_{top}$	9.9	11.1	[a]	10.9	[a]
$\Delta G^‡_{bottom}$	13.4	11.5	[a]	10.6	[a]
$\Delta\Delta G^‡_{addition}$	−3.5	−0.4	[a]	0.3	[a]
comp.	**>98:2**	**72:28**	**>98:2**[b]	**33:67**	**>98:2**[b]
allyltrimethylsilane (allyl-TMS) addition					
exp.	**>98:2**	**9:91**	**23:77**	**<2:98**	**34:66**
$\Delta G^‡_{top}$	10.4	12.9	7.5	11.9	9.6
$\Delta G^‡_{bottom}$	12.8	11.8	6.9	10.7	9.4
$\Delta\Delta G^‡$	−2.4	1.1	0.6	1.2	0.2
comp.	**>98:2**	**7:93**	**20:80**	**5:95**	**38:62**

For the reactions with allyl-TMS, a weaker nucleophile (Mayr's reactivity parameters: $N_{TES\text{-}H} = 3.58$; $N_{allyl\text{-}TMS} = 1.68$)[44] than triethylsilane, barrierless addition reactions were found for oxocarbenium ions **2-7**, **12**, **13** and **15**, proceeding via a Curtin-Hammett scenario of class I. For the other cations (**1**, **8-11** and **14**), TSs were found for the addition reactions that were higher than the barrier for interconversion of the oxocarbenium ion conformers (see Table 2; Figure 3B and 3C shows reaction profiles of representative examples). The addition TSs were slightly higher in terms of energy compared to those that were found for triethylsilane. Notably, again all these cations, barred one (*i.e.*, cation **11**), have the *manno*-like stereochemistry and clear structure-reactivity-selectivity principles can be derived from this series. The substituents at the C3 and C4-position in *manno*-configured oxocarbenium ions can adopt an axial orientation when the ion takes up a $^3H_4$-half chair conformation (here the mannopyranose structures in the D-series will be used; Figure 3A). As discussed above, the electrostatic stabilization by the substituents on the cation overrides the steric preference of the substituents, however with an increasing number of substituents and a weaker nucleophile (*i.e.*, late TS), one can imagine that steric interactions become important and counterbalance the "intrinsic" preference of the cations (Figure 3A). In almost all cases deviation was found from the "intrinsic" preference of the cations (except cation **1**) for the addition reaction of Allyl-TMS in terms of stereoselectivity, which is completely in line with the experimental results.

For 2-deoxy-xylosyl cation **1**, the addition of allyl-TMS preferentially occurs from the top face on the $^3H_4$-ion, in line with triethylsilane, via a TS structure corresponding to a barrier height of 10.4 kcal mol^{-1}. The TS for attack on the other side (bottom face; $^4H_3$-cation), however, requires more energy ($\Delta G^{\ddagger}_{bottom}$ = 12.8 kcal mol^{-1}), which expresses itself in the observed stereoselectivity of this addition reaction.

For 2-deoxy rhamnosyl ion **8**, the addition of allyl-TMS results in a 1,3-*trans* selectivity (7:93), in contrast to triethylsilane (72:28; *vide supra*). This can be attributed to the found TSs, which are 12.9 kcal mol^{-1} (top face; $^3H_4$) and 11.8 kcal mol^{-1} (bottom face; $^4H_3$). To understand the shift to more *trans*-product than expected on the basis of the preference of the cation, one can analyze both approaches and can imagine that the top face addition follows a more sterically crowed path (*i.e.*, the more hindered face) as a result of the axial groups in the $^3H_4$ conformation (*i.e.*, C3- and C5-position). This leads to a higher barrier for the late TS of allyl-TMS, and therefore follows a Curtin-Hammett class II-a type scenario. Cation **10** (Figure 3B and 3D) closely resembles 2-deoxy rhamnosyl cation **8**, and thus addition reactions to **10** proceed via a similar kinetic scenario. The difference in stereochemical outcome of the reactions involving triethylsilane and allyl-TMS, and ions **8** and **10** are well accounted for by their differences in $\Delta\Delta G^{\ddagger}_{addition}$. Additionally, the allyl-TMS addition reactions to rhamnosyl cation **9** and mannosyl cation **14** (Figure 3C and 3E), provide more of the β-products (**9** α:β = 77:23; **14** α:β = 66:34) than the addition reactions

to the 2-deoxy cations **8** (α:β = 91:9) and **10** (α:β = <98:2). From Table 2 it becomes apparent that this difference (**9** *vs* **14** and **8** *vs* **10**) can be related to the larger difference in ground state energy of the $^{3}H_{4}$- *vs* the $^{4}H_{3}$-half chair conformers for the C2-alkoxy cations, favoring the former conformation. The more reactive cations **9** and **14**, with respect to ions **8** and **10**, lead to lower activation barriers for the former ions. In line with the kinetic scenarios for the allyl-TMS addition reactions to **8** and **10**, the reactions of **9** and **14** with allyl-TMS can be described by a Curtin-Hammett II-a scenario.

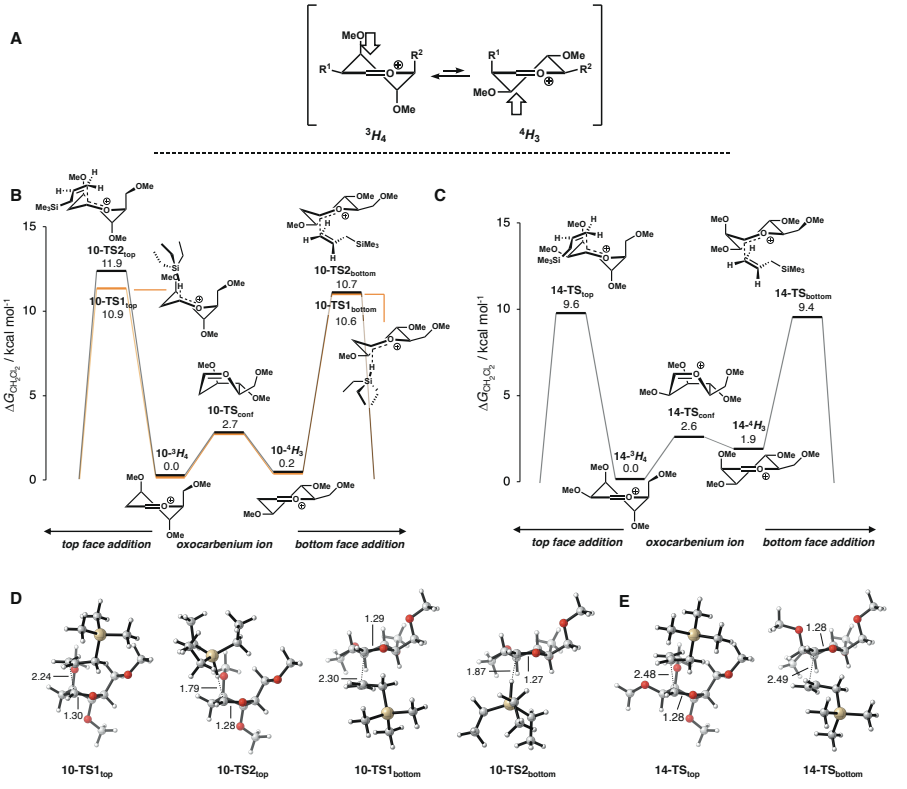


Figure 3. Selected reaction profiles for addition reactions to glycosyl cations. (A) Simplified conformational equilibrium of *manno*-like configured glycosyl cations, and the direction of the incoming nucleophile; R^1 = H or OMe/OBn and R^2 = H or CH_2OMe/CH_2OBn; Reaction profiles for the allyl-TMS (black) and TES-H (orange) addition at cation **10** (B) and **14** (C); Transition state structures with key bond lengths (in Å) for cation **10** (D) and **14** (E). Computed at PCM(CH_2Cl_2)-B3LYP/6-311G(d,p).

Overall, the computed activation barriers excellently explain the differences in stereochemistry of the triethylsilane and allyl-TMS additions. The computational analysis of the stability and conformational behavior of the oxocarbenium ion conformers, using the CEL mapping method, combined with the quantitative analyses of the activation barriers for the addition reactions to the cations, provides an accurate description of the

different Curtin-Hammett type kinetic scenarios that operate during addition reactions to substituted pyranosyl oxocarbenium ions.

To understand why the addition reactions with allyl-TMS deviate from the "intrinsic" preference imposed by the stability of the cations and follow Curtin-Hammett type kinetic scenarios, the activation strain model (ASM)[45–50] of reactivity was applied in the gas-phase (see SI for computational method). First, the addition reaction of allyl-TMS to **1**, **8**, **10** and **14** was studied. The ASM allows one to decompose the solution-phase potential energy surface, *i.e.*, total energy of the reacting components ($\Delta E(\zeta)$) along the reaction pathway, into the total strain and interaction energy, $\Delta E_{\text{strain}}(\zeta)$ and $\Delta E_{\text{int}}(\zeta)$, respectively. Herein, the total strain energy, $\Delta E_{\text{strain}}(\zeta)$, is the penalty that needs to be paid in order to deform the individual reactants from their equilibrium structure to the geometry they adopt during the reaction at point ζ along the reaction coordinate. The interaction energy, $\Delta E_{\text{int}}(\zeta)$, accounts for all the mutual interactions that occur between these two deformed reactants. In this study, the energy terms are projected on the stretch of the C=O$^+$ (C1–O5) bond, which lengthens as the reactions progresses. This critical reaction coordinate undergoes a well-defined change during the addition reaction from the reactants via the transition state to the product.[51–53]

The interaction energy can be further decomposed using the energy decomposition analysis (EDA)[54–56] scheme, which dissects the $\Delta E_{\text{int}}(\zeta)$ into three physically meaningful energy terms, namely, (i) the electrostatic interactions between the unperturbed charge distribution of the deformed reactants: $\Delta V_{\text{elstat}}(\zeta)$; (ii) the destabilizing Pauli repulsion between the overlapping occupied-occupied closed-shell orbitals of both fragments due to the Pauli principle (*i.e.*, steric interactions), $\Delta E_{\text{Pauli}}(\zeta)$; and (iii) the stabilizing orbital interactions, which account for polarization and charge transfer between the fragments, such as HOMO–LUMO interactions, $\Delta E_{\text{oi}}(\zeta)$. Thus, the combined ASM/EDA approach allows the quantitative assessment of all physical factors that influence the total energy of a reaction path and its transition state, and hence can be used to quantify the intrinsic differences between chemical reactions.

Figure 4 displays the ASM/EDA analyses for the addition of allyl-TMS to both the $^3H_4$ and $^4H_3$-conformer of **1**, **8**, **10** and **14**. Figure 4A (left panel) shows the ASM results of the 2-deoxy-xylosyl cation **1**, in which the lower activation barrier for the top face attack (black line) compared to the bottom face attack (red line) exclusively originates from a less destabilizing strain energy (lower ΔE_{strain} curve at the same ζ). By decomposing the total strain energy term into the strain energy of the individual reactants (SI Figure S5), it was found that the less destabilizing strain energy of the top face attack can mainly be attributed to the "intrinsic" stability of the $^3H_4$-cation **1**, which is 3.2 kcal mol^{-1} more stable than its $^4H_3$-counterpart (see Table 2).

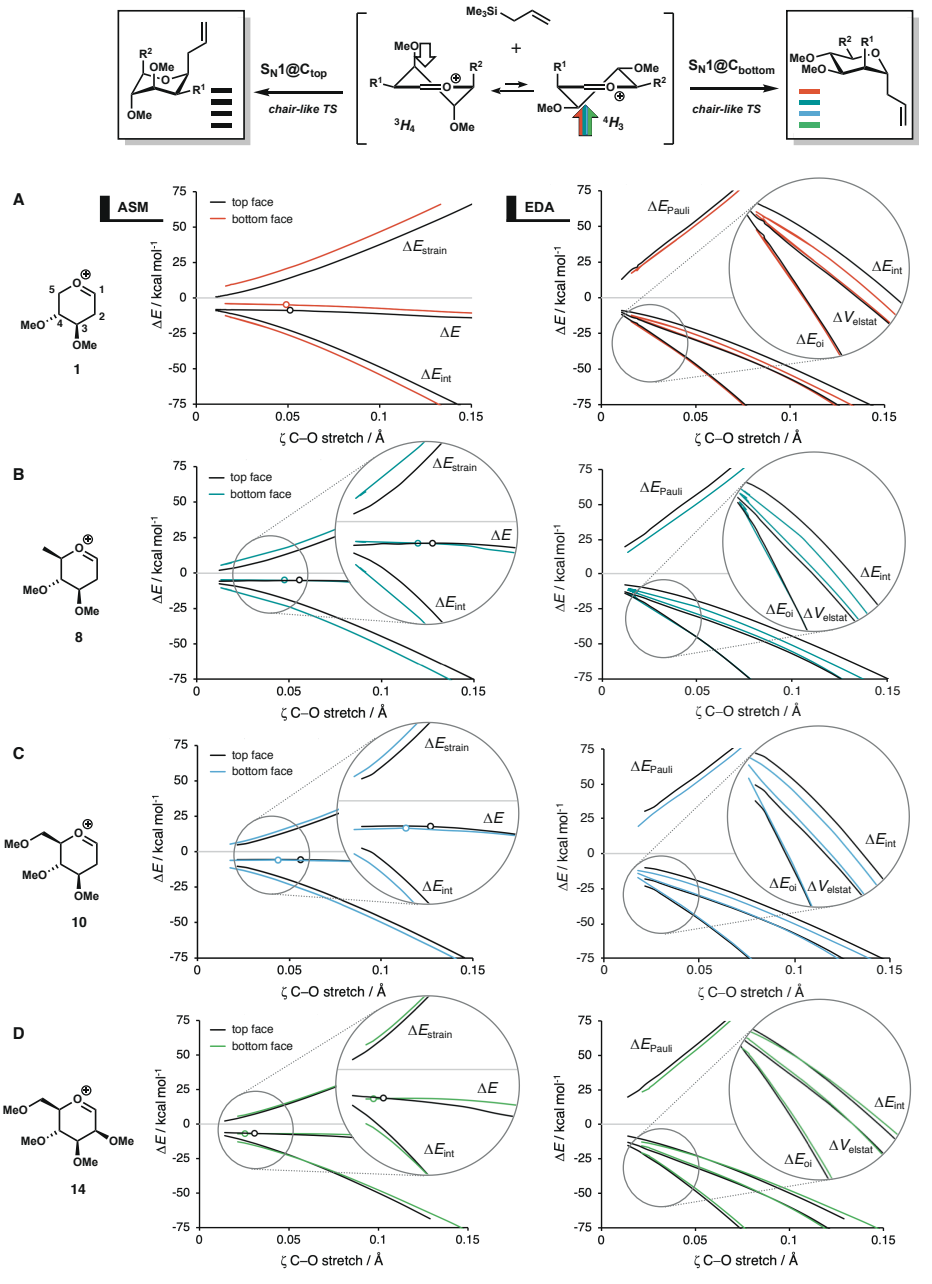


Figure 4. Activation strain analysis (left) and energy decomposition analysis (right) of the allyl-TMS addition reaction of cation **1**, **8**, **10** and **14** (top face = black; bottom face = red/purple/blue/green), where the energy values are projected on the C–O stretch. R^1 = H or OMe and R^2 = H, Me or CH_2OMe. TSs are indicated by dots; Computed in the gas-phase at ZORA-B3LYP/TZ2P//PCM(CH_2Cl_2)-B3LYP/6-311G(d,p).

The addition at both faces (top and bottom face) follows a similar reaction path, through a chair-like transition state, which is reflected in a similar strain energy path, only the offset is different as a result of the intrinsic stability of the conformation of the cations. This behavior can be found for all computed cations, thus the strain is always less destabilizing for the more stable conformer, *i.e.*, the conformer with more axial electron-rich substituents at distal positions ($^3H_4$ conformer). As discussed above, the axial orientated substituents at the C3- and C4-position are able to stabilize the cation by electrostatic interactions (see Table S5 and Figure S11).[1,18,29,30]

In contrast, for cations **8**, **10** and **14** (Figure 4B-D), the bottom face attack is favored, which originates solely from a more stabilizing interaction energy. For these cations, the strain energy is, as above described, less destabilizing for the top face attack, however, the difference with the bottom face attack is significantly less compared to cation **1**, and therefore the interaction energy controls the face selectivity. This can be traced back to the relatively small energy difference between the $^3H_4$- and $^4H_3$-conformer for these cations (see Table 2). For all cations (**1**, **8**, **10** and **14**), the interaction energy is always more stabilizing for the conformer with lowest number of axial electron-rich substituents at distal positions (*i.e.*, $^4H_3$ conformer).

In order to understand the origin of the more stabilizing interaction energy for the bottom face attack, an EDA was performed, and the results are depicted in Figure 4B-D (right panel). In all cases the difference in interaction energy can be traced to the Pauli repulsion, with the other terms (*i.e.*, ΔE_{oi} and ΔV_{elstat}) being almost equal for the top and bottom face attack. The more destabilizing Pauli repulsion for the top face attack can be directly traced back to the axial groups (C3- and C5-position) present in the $^3H_4$ conformation, which cause steric interactions with the incoming allyl-TMS (Figure 5; see SI for Kohn-Sham molecular orbital analysis and double consistent geometries).

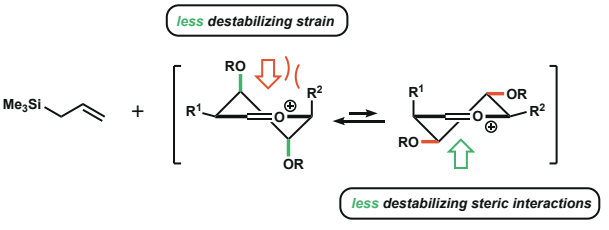


Figure 5. Schematic representation of the controlling factors (green = stabilizing; red = destabilizing factors) of the stereoselectivity of *C*-glycosylation reactions, in which the strain is always less destabilizing for the more stable conformer (*i.e.*,$^3H_4$), while the Pauli repulsion is also always more destabilizing for this conformation; R^1 = H or OBn and R^2 = H, Me or CH_2OBn.

From the activation strain and energy decomposition analysis, it can be concluded for *C*-glycosylations that the strain is always less destabilizing for the more stable conformer, while the Pauli repulsion is also always more destabilizing for this conformation (Figure 5), and the magnitude of both effects will ultimately determine the face selectivity: (i) for the "stripped" model glycosyl cation **1**, a regime of strong "intrinsic" conformational preference can be found, in which the strain determines the face selectivity, and this is more favored for the conformer with the most axial electron-rich substituents at distal positions; (ii) for the more decorated cations **8**, **10** and **14**, a regime of weak "intrinsic" preference of the cation can be found, in which the interaction energy determines the face selectivity, and this results in an addition at the least hindered face as a result of a less destabilizing (steric) Pauli repulsion with allyl-TMS.

To understand the contrasting behavior between allyl-TMS and TES-*d*, in which TES-*d* does follow the "intrinsic" preference of the cations, a similar analysis for the addition reactions of TES-H to cation **1** and **10** (see SI for the analysis; Figure S9 and S10) was performed. The addition of TES-H proceeds following a reaction path having a significantly earlier TS (*i.e.*, less C–O bond stretch), because of the higher nucleophilicity of triethylsilane.[33] These early TSs resemble more closely the reactants (*i.e.*, the glycosyl cation), in which steric interactions play a minor role. Indeed, the difference in Pauli repulsion for both faces in an early TS (*i.e.*, Nuc is relatively far away from the electrophile) is smaller, which cause the strain to take full control (*i.e.*, "intrinsic" preference of the cation).

Overall, the ASM-EDA analyses provide a quantitative description of the various physical factors that control the addition reactions on the different oxocarbenium ion conformers, allowing for an accurate and well substantiated description of Curtin-Hammett kinetic scenarios at play.

Conclusion

In conclusion, in this chapter different kinetic scenarios were mapped through which S_N1-type addition reactions of six-membered ring glycosyl oxocarbenium ions can proceed. A combined computational and experimental approach has unraveled how the reactivity of oxocarbenium ions, governed by the substitution pattern on the carbohydrate ring, in combination with the reactivity of the incoming nucleophile, determines the stereochemical outcome of the S_N1-type addition reactions. Using the conformational energy landscape (CEL) maps different low energy oxocarbenium ion conformers were selected, which were used as a starting point to find transition states for addition reactions taking place by a top or bottom face attack of the nucleophile. Using the stability of the

different oxocarbenium ion conformers, the barrier for their interconversion and addition, possible Curtin-Hammett kinetic scenarios have been dissected.

It has been shown that many addition reactions with triethylsilane proceed with a barrierless pathway, from the high energy – but relatively stable – oxocarbenium ion conformers to the products. For these cations the population of conformational families with a preference for top or bottom face attack provides an adequate explanation for the stereochemistry observed in reactions of these cations. Reactions of the weaker nucleophile, allyl-TMS, with relatively stable oxocarbenium ions, such as those having the *manno*-configuration, a Curtin-Hammett kinetic scenario takes effect. A reaction path with a barrier is followed and for these reactions the relative energy level of transition states of the top and bottom face addition is decisive in determining the stereochemical outcome.

By using the activation strain analysis, a quantitative description of the factors influencing the stereoselectivity could be provided, and revealed how the interplay between the oxocarbenium ion stability, and the build-up of (steric) Pauli repulsion along the reaction, and the position of the transition state along the reaction coordinate, dictate the height of the reaction barrier for these addition reactions. For *C*-glycosylations, general guidelines emerged to understand the selectivity: (i) for "stripped" glycosyl cations, a regime of strong "intrinsic" conformational preference can be found, in which the strain determines the face selectivity, and this is more favored for the conformer with the most axial electron-rich substituents at distal positions; (ii) for the more decorated cations, a regime of weak "intrinsic" preference of the cation can be found, in which the interaction energy determines the face selectivity, and this results in an addition at the least hindered face as a result of a less destabilizing (steric) Pauli repulsion with allyl-TMS.

The mechanistic insight offered here will be instrumental in the interpretation of the outcome of glycosylation reactions in the future and serve as the basis to further explore oxocarbenium ions as reactive intermediates and map the effect of various protecting and functional group patterns.

Supporting information

Computation method

Computational details • The density functional theory (DFT) computations were performed using Gaussian 09 rev D.01.[57] For all computation, the hybrid functional B3LYP and the 6-311G(d,p) basis set were used. The geometry convergence criteria were set to tight (opt=tight; max. force=$1.5 \cdot 10^{-7}$, max. displacement=$6.0 \cdot 10^{-7}$), and an internally defined super-fine grid size was used (SCF=tight, int=veryfinegrid), which is a pruned 175,974 grid for first-row atoms and a 250,974 grid for all other atoms. These parameters were chosen as a recent paper indicated a significant dependence of the computed frequencies on the molecule orientation when a smaller grid size is used.[58] Geometries were optimized without symmetry constraints. All calculated stationary points have been verified by performing a vibrational analysis, to be energy minima (no imaginary frequencies) or transition states (only one imaginary frequency). The character of the normal mode associated with the imaginary frequency of the transition state has been analyzed to ensure that it is associated with the reaction of interest. Solvation in CH_2Cl_2 was taken into account in the computations using the PCM implicit solvation model. Solvent effects were explicitly used in the solving of the SCF equations and during the optimization of the geometry and the vibrational analysis. The potential energy surfaces of the studied addition reactions were obtained by performing intrinsic reaction coordinate (IRC) calculations, which, in turn, were analyzed using the PyFrag program (*vide infra*).[59] The optimized structures were illustrated using CYLview.[60]

The denoted free Gibbs energy was calculated using Equation S1, in which ΔE_{gas} is the gas-phase energy (electronic energy), $\Delta G^{T}_{gas,QH}$ (T = 213.15 K, p = 1 atm., C = 1 M) is the sum of corrections from the electronic energy to the free Gibbs energy in the quasi-harmonic oscillator approximation, including zero-point-vibrational energy, and ΔG_{solv} is their corresponding free solvation Gibbs energy. The $\Delta G^{T}_{gas,QH}$ was computed using the quasi-harmonic approximation in the gas phase according to the work of Truhlar. The quasi-harmonic approximation is the same as the harmonic oscillator approximation except that vibrational frequencies lower than 100 cm^{-1} were raised to 100 cm^{-1} as a way to correct for the breakdown of the harmonic oscillator model for the free energies of low-frequency vibrational modes.[61]

$$\Delta G^{T}_{CH_2Cl_2} = \Delta E_{gas} + \Delta G^{T}_{gas,QH} + \Delta G_{solv} = \Delta G^{T}_{gas} + \Delta G_{solv} \quad \text{(Eq. S1)}$$

Activation strain and energy decomposition analysis • The activation strain model (ASM) analysis and energy decomposition analysis (EDA) were performed using the Amsterdam Density Functional (ADF2017.103)[62–64] software package based on the solution-phase structures obtained by Gaussian 09. For all computations, the B3LYP functional was used. The basis set used, denoted TZ2P, is of triple-ζ quality for all atoms and has been improved by two sets of polarization functions.[65] The accuracies of the fit scheme (Zlm fit) and the integration grid (Becke grid) were, for all calculations, set to VERYGOOD.[66,67] Relativistic effects were accounted for by using the zeroth-order regular approximation (ZORA).[68,69] All computations were performed in the gas-phase on the obtained solution-phase structures (*vide infra*).

The activation strain model (ASM) of chemical reactivity[45–48], also known as the distortion/interaction model[49,50], is a fragment-based approach in which the energy corresponding to a chemical reaction, *i.e.*, potential energy surface, can be described with respect to, and understood in terms of the characteristics of, the reactants. It considers the rigidity of the reactants as well as to which extent they need to deform during the reaction plus their capability to interact with each other as the reaction proceeds. In this model, the total energy, $\Delta E(\zeta)$, is decomposed into the respective total strain and interaction energy, $\Delta E_{strain}(\zeta)$ and $\Delta E_{int}(\zeta)$, and project these values onto the reaction coordinate ζ (Eq. S2).

$$\Delta E(\zeta) = \Delta E_{strain}(\zeta) + \Delta E_{int}(\zeta) \quad \text{(Eq. S2)}$$

In this equation, the total strain energy, $\Delta E_{strain}(\zeta)$, is the penalty that needs to be paid to deform the reactants from their equilibrium structure to the geometry they adopt during the reaction at point ζ of the reaction coordinate. On the other hand, the interaction energy, $\Delta E_{int}(\zeta)$, accounts for all the chemical interactions that occur between these two deformed reactants along the reaction coordinate. The total strain energy can, in turn, be further decomposed into the strain energies corresponding to the deformation of the glycosyl cation, $\Delta E_{strain,cation}(\zeta)$, as well as from the nucleophile, $\Delta E_{strain,nuc}(\zeta)$ (Eq. S3).

$$\Delta E_{strain}(\zeta) = \Delta E_{strain,cation}(\zeta) + \Delta E_{strain,nuc}(\zeta) \quad \text{(Eq. S3)}$$

In this study, the solution-phase potential energy surface, $\Delta E_{solution}(\zeta)$, was decomposed into the $\Delta E_{solvation}(\zeta)$, which accounts for the interaction between the solute and solvent, and the $\Delta E_{solute}(\zeta)$, which is the reaction system in vacuum with the solution-phase geometry (Eq. S4).[70,71]

$$\Delta E_{solution}(\zeta) = \Delta E_{solvation}(\zeta) + \Delta E_{solute}(\zeta) \quad \text{(Eq. S4)}$$

The solute term, $\Delta E_{solute}(\zeta)$, is subsequently decomposed into the solvent-free strain, $\Delta E_{solute\text{-}train}(\zeta)$, and interaction energy, $\Delta E_{solute\text{-}int}(\zeta)$, which are referred to as solute strain and solute interaction, respectively, to distinguish between the two solution-phase activation strain schemes (Eq. S5).

$$\Delta E_{solution}(\zeta) = \Delta E_{solvation}(\zeta) + \Delta E_{solute\text{-}strain}(\zeta) + \Delta E_{solute\text{-}int}(\zeta) \quad \text{(Eq. S5)}$$

For clarity reasons, ΔE_{solute}, $\Delta E_{solute\text{-}strain}$ and $\Delta E_{solute\text{-}int}$ are denoted as ΔE, ΔE_{strain} and ΔE_{int} in all the result and discussion sections of the main-text and SI.

The interaction energy between the deformed reactants can be further analyzed in terms of quantitative Kohn-Sham molecular orbital theory (KS-MO) together with a canonical energy decomposition analysis (EDA).[54–56] The EDA decomposes the $\Delta E_{solute\text{-}int}(\zeta)$ into the following three physically meaningful energy terms (Eq. S6):

$$\Delta E_{solute\text{-}int}(\zeta) = \Delta V_{elstat}(\zeta) + \Delta E_{Pauli}(\zeta) + \Delta E_{oi}(\zeta) \quad \text{(Eq. S6)}$$

Herein, $\Delta V_{elstat}(\zeta)$ is the classical electrostatic interaction between the unperturbed charge distributions of the (deformed) reactants and is usually attractive. The Pauli repulsion, $\Delta E_{Pauli}(\zeta)$, comprises the destabilizing interaction between occupied closed-shell orbitals of both fragments due to the Pauli principle. The orbital interaction energy, $\Delta E_{oi}(\zeta)$, accounts for polarization and charge transfer between the fragments, such as HOMO–LUMO interactions.

In this study, in both the activation strain diagrams and accompanied energy decomposition plots, the energy terms are projected onto the C–O stretch, unless otherwise stated. This critical reaction coordinate undergoes a well-defined change during the reaction from the reactant via the transition state to the product.[51,52]

Transition state structures

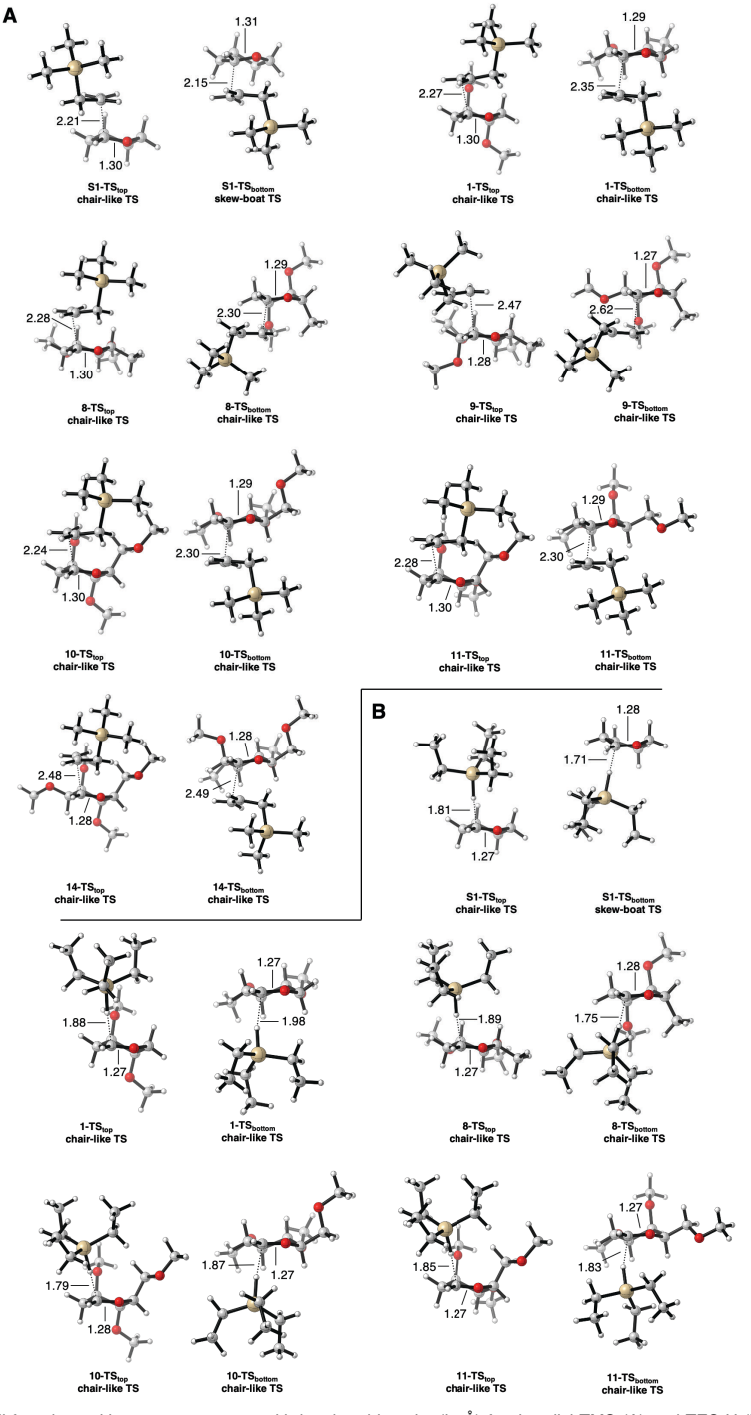


Figure S1. All found transition state structures with key bond lengths (in Å) for the allyl-TMS (A) and TES-H (B) addition reactions for a panel of 15 glycosyl cations. Computed at PCM(CH_2Cl_2)-B3LYP/6-311G(d,p).

Stereotopic face-selectivity • The face selectivity of the addition reaction of both allyl-TMS and triethylsilane at the half-chair conformation of "stripped" model oxocarbenium ion **S1** was computationally studied. The transition state structures of the S_N1-addition reactions with allyl-TMS for the top and bottom face attack at **S1**, as well as their corresponding reactant complex (ΔE_{RC}), electronic activation barriers ($\Delta E^{\ddagger}$), and reaction energies ($\Delta E_{rxn\text{-}int}$) are shown in Figure S2B. The top face addition resulted in a chair-like TS structure (Figure S2C; left structure), while the bottom face addition proceeds through a skew-boat TS (Figure S2C; right structure). As expected, based on the experimental model devised by the group of Woerpel[1,30], it was found that the nucleophilic attack from the top face is favored by more than 3 kcal mol^{-1}.

To gain quantitative insight into the physical factors leading to this face-selectivity, activation strain model (ASM) analysis was performed. By applying the ASM, it was found that the preferred nucleophilic attack at the top face of **S1** originates from a synergetic effect of a more stabilizing interaction energy and a less destabilizing strain energy (Figure S2D). To understand the origin of the less destabilizing strain energy, the total strain energy was decomposed into the strain energies of the separate reactants, according to Equation S3 (Figure S2E). The more stabilizing strain energy of the attack at the top face is exclusively caused by the deformation of glycosyl cation **S1**. When comparing the geometries of the glycosyl cation at consistent geometries with a C–O distance of 0.052 Å stretch (close to the TS for both additions) for the attack at the top and bottom face, it was found that the deformation of the most crucial dihedral angle, $\angle_{C2\text{-}C1\text{-}O5\text{-}C5}$, did not match the observed trend (Figure S2F). Instead, the remaining ring dihedral angles could be attributed to the trend, in which the top face attack (chair-like TS) showed significant less deformation.

To dissect the more stabilizing interaction energy for the top face attack, a canonical energy decomposition analysis (EDA) was performed (Figure S2G). It was established that the trend in ΔE_{int} is predominantly determined by the ΔE_{oi} and ΔV_{elstat}, in which the top face attack has more stabilizing orbital and electrostatic interactions. One might be tempted to conclude that the face-selectivity is determined instead by the less destabilizing Pauli interactions. However, it should be noted that the EDA terms are highly dependent on the Nuc•••C distance (*vide infra*), which is 0.06 Å longer for top face attack compared to bottom face (2.21 Å for top face and 2.15 Å for bottom face) at a C–O bond stretch of 0.052 Å. To remedy this and account for the effect of the different nucleophile–substrate bond distances on the EDA terms, the same consistent geometries were taken, but now the Nuc•••C bond of the top face addition was artificially shortened to the same length as the bottom face attack (see Table S1). This resulted in a more stabilizing ΔE_{oi} and ΔV_{elstat} interaction for the top face attack compared to the bottom face attack (top face: ΔE_{oi} = –56.1 and ΔV_{elstat} = –35.9 kcal mol^{-1}, and bottom face: ΔE_{oi} = –54.5 and ΔV_{elstat} = –33.6 kcal mol^{-1}). Projecting the ASM and EDA on the Nuc•••C distance (see Figure S3C and S3D) supports this, showing significantly more stabilizing ΔE_{oi} and ΔV_{elstat} for the top face addition during the whole reaction path, while the ΔE_{Pauli} is virtually the same.

The same analysis was performed for triethylsilane as the nucleophile, which results in similar trends (Figure S4). The strong face selectivity is maintained, and it again originates from a cooperative effect of a more stabilizing interaction energy and less destabilizing strain (Figure S4D). Importantly, TES-H is a stronger nucleophile compared to allyl-TMS, which results in an earlier transition state (*i.e.*, less C–O stretch at the TS; Figure S4C). This leads to lower overall reaction barriers and TS structures which include significant less deformation of the key dihedral angle, $\angle_{C2\text{-}C1\text{-}O5\text{-}C5}$, compared to the allyl-TMS system. The computational results support that for both nucleophiles the chair-like TS is the most relevant face of attack, and only this approach will be considered in the remaining analysis.

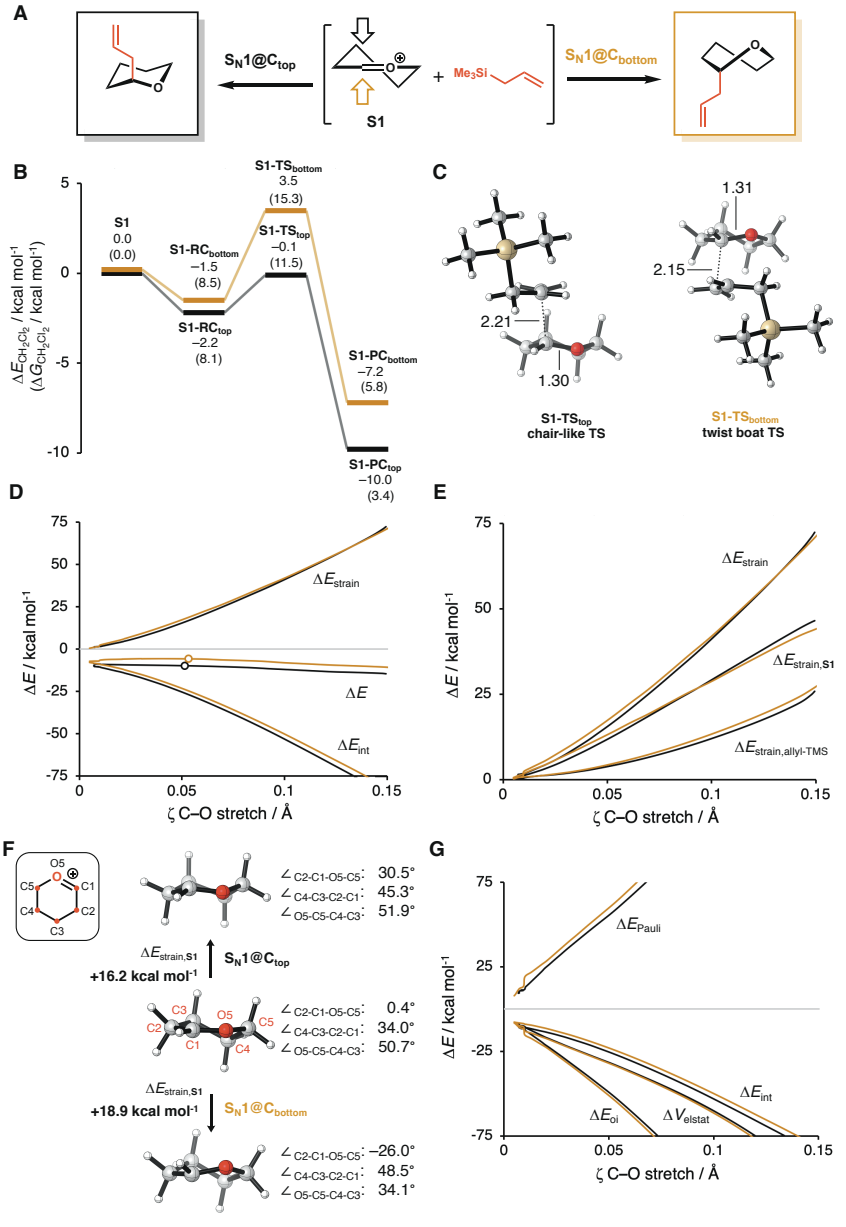


Figure S2. (A) Computationally analyzed allyl-TMS addition reactions of model glycosyl cation **S1**; (B) Reaction profiles for the top and bottom face addition reactions computed at PCM(CH_2Cl_2)-B3LYP/6-311G(d,p) and expressed as $\Delta E_{CH_2Cl_2}$ and $\Delta G_{CH_2Cl_2}$ values in kcal mol^{-1}; (C) The transition state structures with key bond lengths (in Å); (D) Activation strain analysis; (E) Strain decomposition analysis; (F) Deformation of the glycosyl cation upon the attack from the top face and bottom face at consistent geometries with the C–O bond stretch of 0.052 Å; and (G) Energy decomposition analysis of the addition reaction of model glycosyl cation **S1**, where the energy values are projected on the C–O bond stretch; TSs are indicated by dots; Computed in the gas-phase at ZORA-B3LYP/TZ2P//PCM(CH_2Cl_2)-B3LYP/6-311G(d,p).

Table S1. Activation strain and energy decomposition analyses (in kcal mol^{-1}) for the addition reaction at **S1**. Analyses at consistent geometries with a C–O bond stretch of 0.052 Å and a Nuc•••C bond distance of 2.15 Å. Computed at ZORA-B3LYP/TZ2P.

	$\Delta E^{\ddagger}$	ΔE_{strain}	ΔE_{int}	ΔV_{elstat}	ΔE_{Pauli}	ΔE_{oi}
S1$_{top}$	–9.8	16.2	–26.0	–35.9	66.0	–56.1
S1$_{bottom}$	–5.8	18.9	–24.6	–33.6	63.5	–54.5

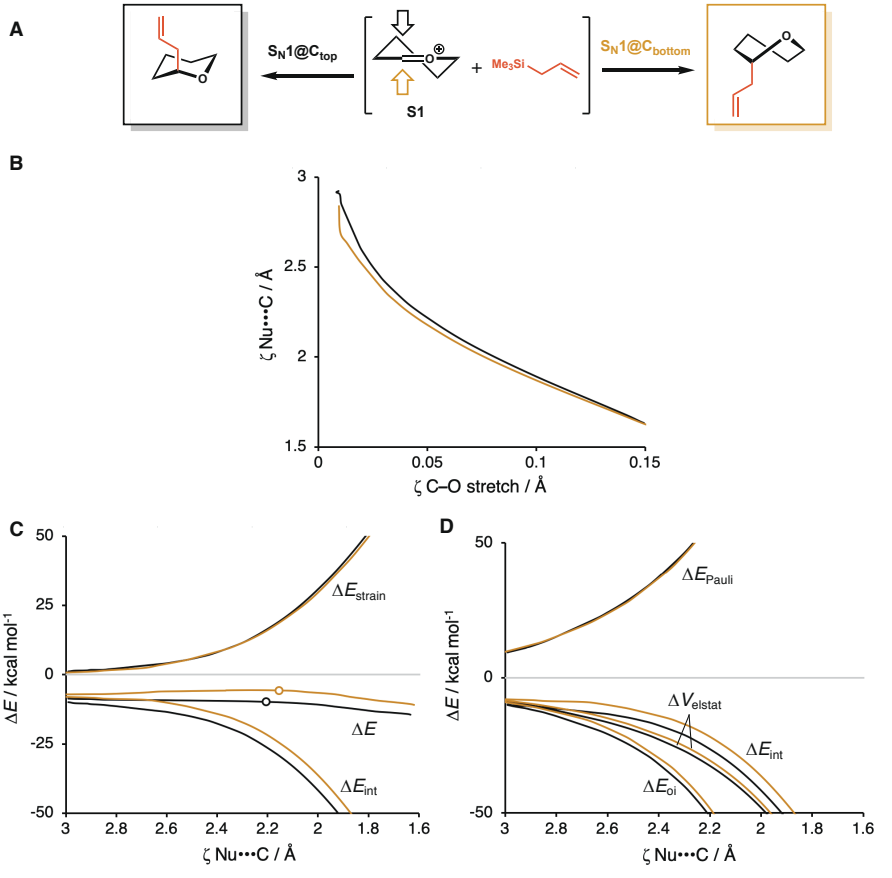


Figure S3. (A) Computationally analyzed allyl-TMS addition reactions of model glycosyl cation **S1**; (B) Nuc•••C distance projected on the C–O bond stretch; (C) Activation strain analysis; and (D) Energy decomposition analysis of the addition reaction of model glycosyl cation **S1**, where the energy values are projected on the Nuc•••C distance; TSs are indicated by dots; Computed in the gas-phase at ZORA-B3LYP/TZ2P//PCM(CH_2Cl_2)-B3LYP/6-311G(d,p).

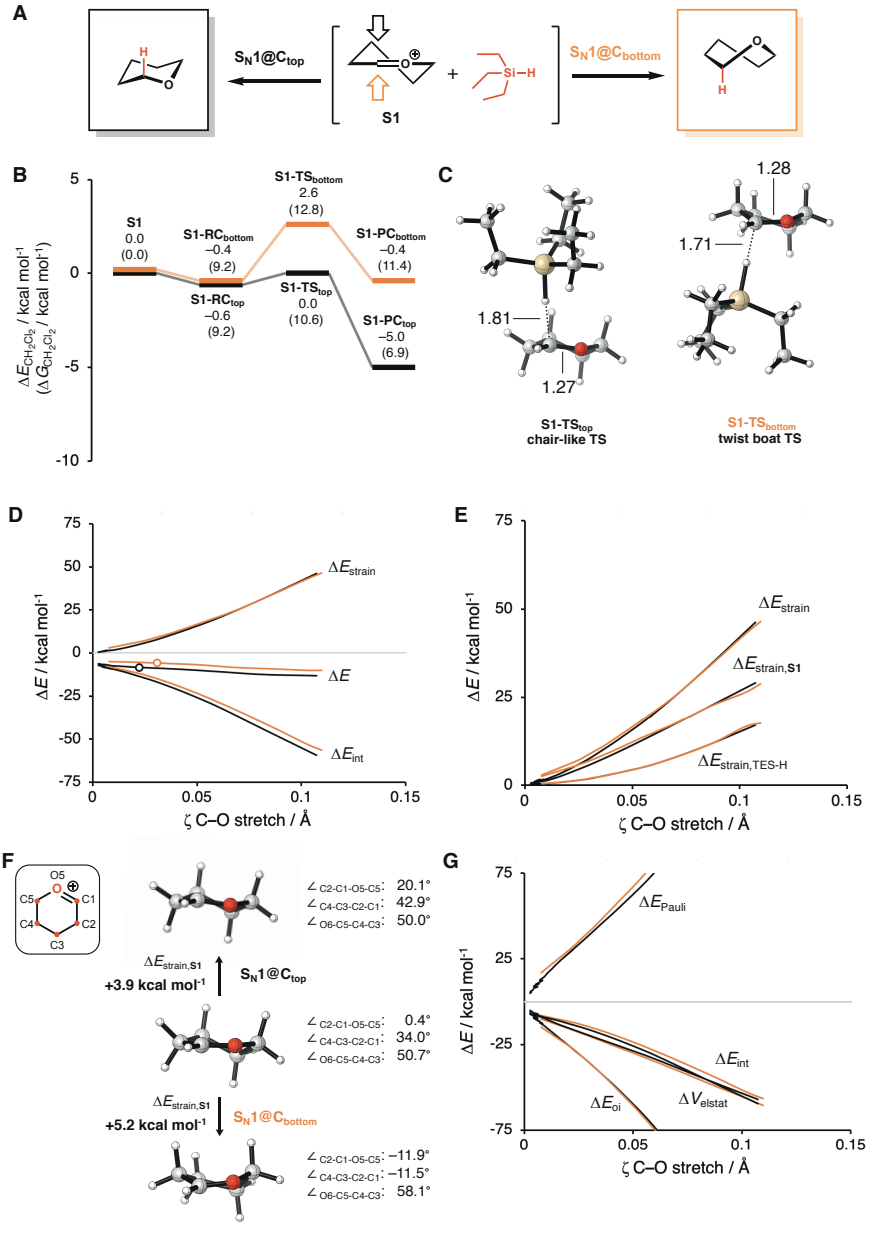
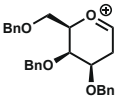


Figure S4. (A) Computationally analyzed triethylsilane addition reactions of model glycosyl cation **S1**; (B) Reaction profiles for the top and bottom face addition reactions computed at PCM(CH_2Cl_2)-B3LYP/6-311G(d,p) and expressed as $\Delta E_{CH_2Cl_2}$ and $\Delta G_{CH_2Cl_2}$ values in kcal mol^{-1}; (C) The transition state structures with key bond lengths (in Å); (D) Activation strain analysis; and (E) Strain decomposition analysis; (F) Deformation of the glycosyl cation upon the attack from the top face and bottom face at consistent geometries with a C–O bond stretch of 0.022 Å; and (G) Energy decomposition analysis of the addition reaction of model glycosyl cation **S1**, where the energy values are projected on the C–O bond stretch; TSs are indicated by dots; Computed in the gas-phase at ZORA-B3LYP/TZ2P//PCM(CH_2Cl_2)-B3LYP/6-311G(d,p).

DFT analysis of 11

Table S2. Computed and experimentally found stereoselectivity for *d*- and *C*-glycosylation reactions on glycosyl cations. The *cis*:*trans* ratio is expressed as the relationship between the substituent on C3-position and the coupled nucleophile; For the computational studies, per-*O*-methylated oxocarbenium ions were used, where the experimental glycosylation used per-*O*-benzylated substrates. All data computed at PCM(CH_2Cl_2)-B3LYP/6-311G(d,p). $\Delta\Delta G^\circ$ is expressed as $\Delta\Delta G^\circ = \Delta G^\circ{}_{^3H_4} - \Delta G^\circ{}_{^4H_3}$. The $\Delta\Delta G^\ddagger_{addition}$ is expressed as $\Delta\Delta G^\ddagger_{addition} = \Delta G^\ddagger_{top} - \Delta G^\ddagger_{bottom}$, and both $\Delta G^\ddagger_{top}$ and $\Delta G^\ddagger_{bottom}$ are relative to the lowest-energy conformer.[42,43]



11

Glycosyl cation	
$\Delta G^\circ{}_{^3H_4}$	0.0
$\Delta G^\circ{}_{^4H_3}$	3.2
$\Delta\Delta G^\circ$	–3.2
$\Delta G^\ddagger_{conf}$	7.0
triethylsilane (TES-d/H) addition	
exp.	**>98:2**
$\Delta G^\ddagger_{top}$	9.9
$\Delta G^\ddagger_{bottom}$	13.4
$\Delta\Delta G^\ddagger_{addition}$	–3.5
comp.	**>98:2**
allyltrimethylsilane (allyl-TMS) addition	
exp.	**>98:2**
$\Delta G^\ddagger_{top}$	10.4
$\Delta G^\ddagger_{bottom}$	12.8
$\Delta\Delta G^\ddagger$	–2.4
comp.	**>98:2**

Strain decomposition analysis of cation 1, 8, 10 and 14

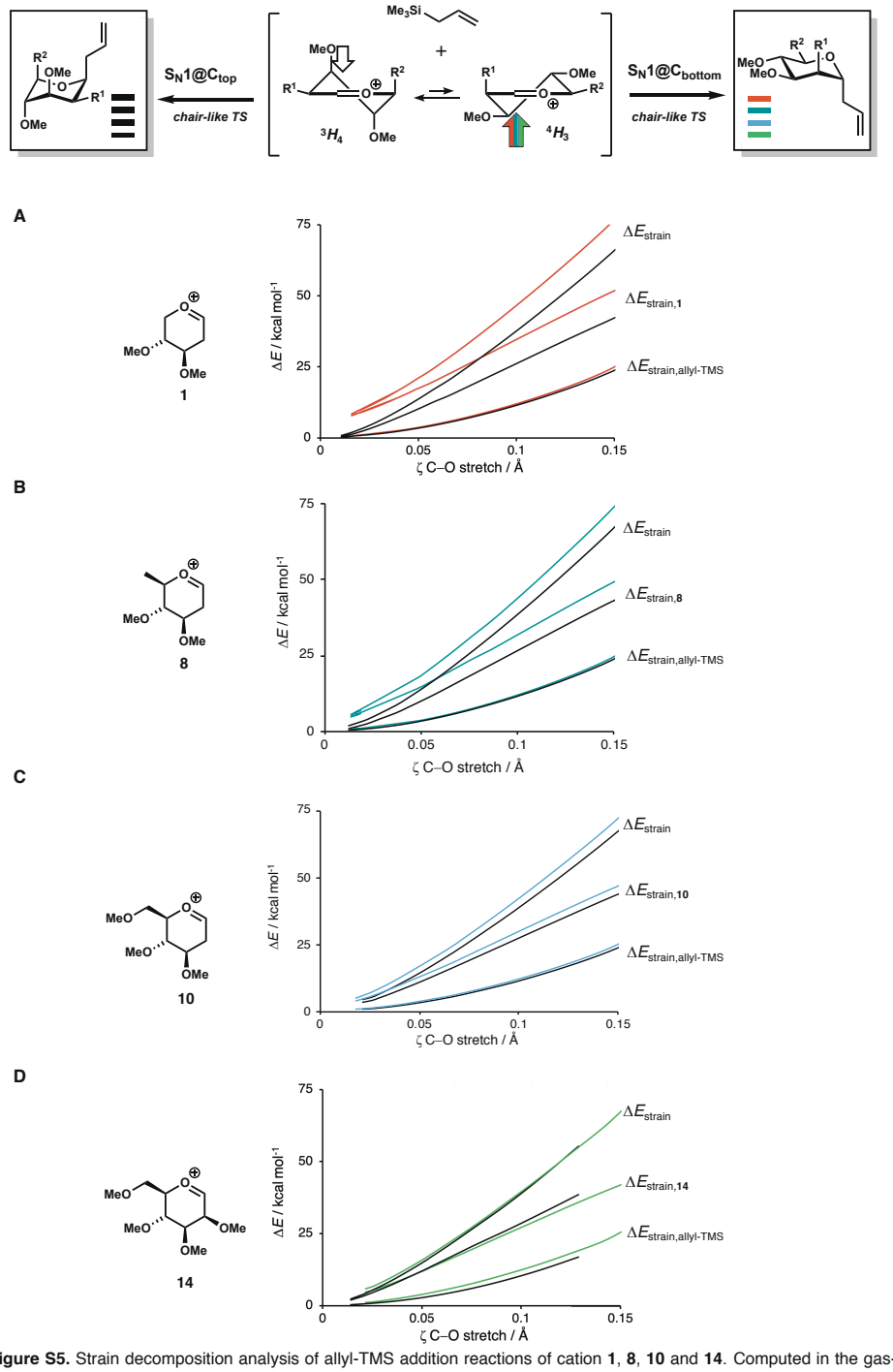


Figure S5. Strain decomposition analysis of allyl-TMS addition reactions of cation **1**, **8**, **10** and **14**. Computed in the gas-phase at ZORA-B3LYP/TZ2P//PCM(CH_2Cl_2)-B3LYP/6-311G(d,p).

Numerical experiment consistent C–O bond stretch and Nuc···C bond distance of 1, 8, 10 and 14

Table S3. Numerical experiment with a consistent C–O bond stretch and Nuc···C bond distance of **1**, **8**, **10** and **14**. Activation strain and energy decomposition analyses (in kcal mol^{-1}) for the allyl-TMS addition reaction at cation **1**, **8**, **10** and **14**. Analyses at consistent geometries with a C–O bond stretch of 0.03 Å and a Nuc···C bond distance of 2.45 Å. Computed at ZORA-B3LYP/TZ2P//PCM(CH_2Cl_2)-B3LYP/6-311G(d,p).

	ΔE^*	ΔE_{strain}	ΔE_{int}	ΔV_{elstat}	ΔE_{Pauli}	ΔE_{oi}
1$_{top\ face}$	–8.6	6.5	–15.1	–19.9	32.4	–27.6
1$_{bottom\ face}$	–4.3	13.5	–17.8	–20.5	32.6	–29.8
8$_{top\ face}$	–5.3	6.6	–12.0	–19.3	34.3	–27.0
8$_{bottom\ face}$	–7.3	8.8	–16.2	–19.5	32.6	–29.3
10$_{top\ face}$	–5.5	6.6	–12.1	–21.0	36.1	–27.2
10$_{bottom\ face}$	–6.1	8.9	–15.0	–20.0	32.5	–27.6
14$_{top\ face}$	–6.7	7.3	–14.1	–22.5	38.8	–30.4
14$_{bottom\ face}$	–6.9	8.8	–15.6	–19.9	32.5	–28.2

Numerical experiment consistent C–O bond stretch and Nuc···C bond distance of 1

Table S4. Numerical experiment with a consistent C–O bond stretch and Nuc···C bond distance of **10**. Activation strain and energy decomposition analyses (in kcal mol^{-1}) for allyl-TMS and triethylsilane addition reactions at cation **10**. Analyses at consistent geometries with a C–O bond stretch of 0.03 Å and a Nuc···C bond stretch of 0.95 Å (measured from the product). Computed at ZORA-B3LYP/TZ2P//PCM(CH_2Cl_2)-B3LYP/6-311G(d,p). All relative energies ($\Delta\Delta E$) are reported with respect to the conversion of $^4H_3 \rightarrow {}^3H_4$, (*e.g.*, $\Delta\Delta E$ is expressed as $\Delta\Delta E = \Delta E_{^3H_4} - \Delta E_{^4H_3}$).

	$\Delta\Delta E^*$	$\Delta\Delta E_{strain}$	$\Delta\Delta E_{int}$	$\Delta\Delta V_{elstat}$	$\Delta\Delta E_{Pauli}$	$\Delta\Delta E_{oi}$
10$_{allyl\text{-}TMS}$	0.6	–2.3	2.9	–1.1	3.6	0.3
10$_{TESH}$	0.2	–2.6	2.8	0.2	1.8	0.8

Orbital analysis: Pauli repulsion

Cation 10

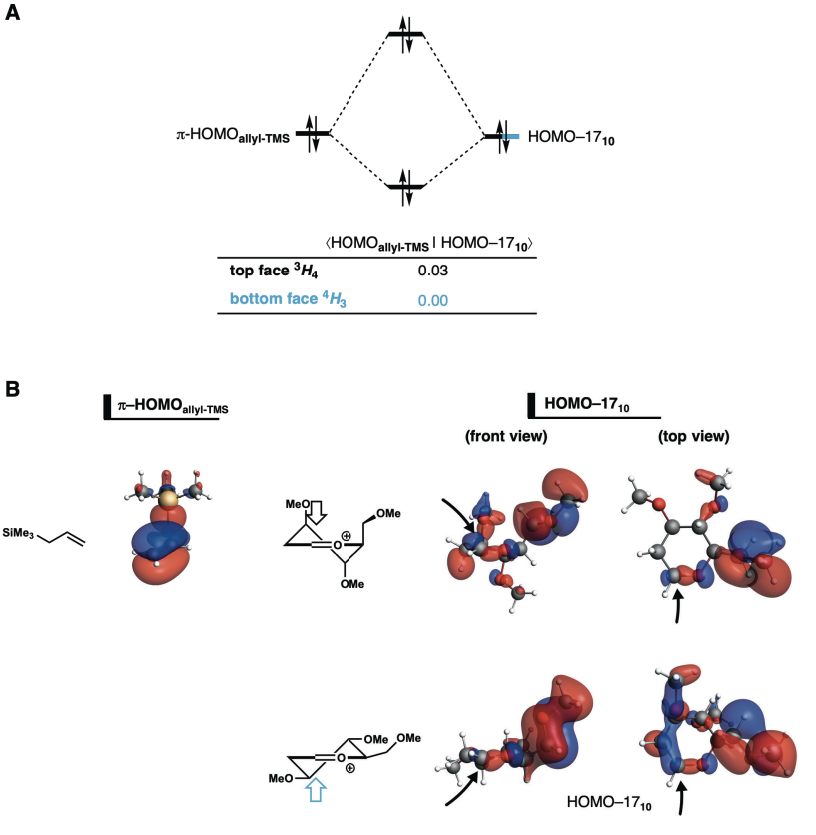
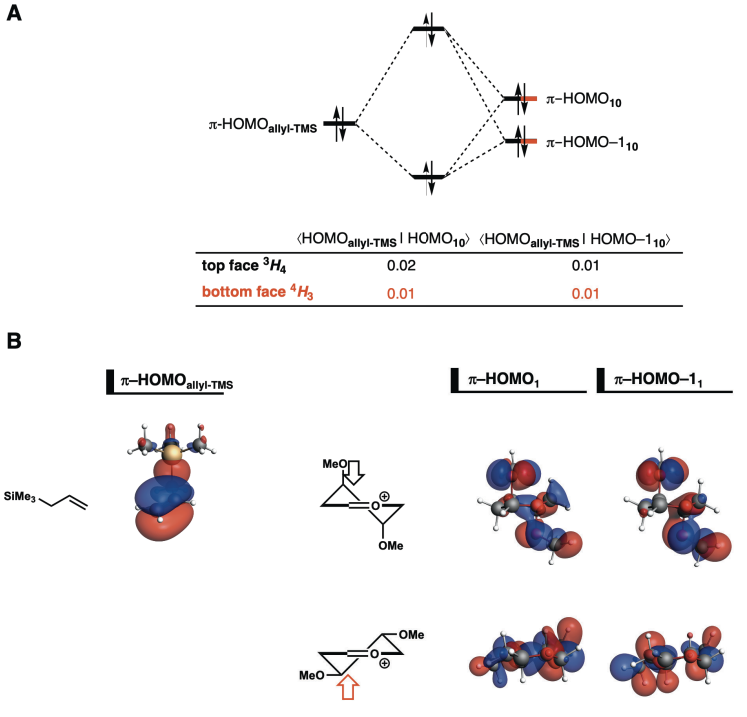


Figure S6. (A) Molecular orbital diagram of the most important occupied–occupied orbital overlap of the addition reaction of **10**; and (B) key occupied orbitals (isovalue = 0.03 Bohr$^{-3/2}$) computed at consistent geometries with a C–O bond stretch of 0.03 Å and a Nuc···C bond distance of 2.45 Å. Computed in the gas-phase at ZORA-B3LYP/TZ2P//PCM(CH_2Cl_2)-B3LYP/6-311G(d,p).

Cation 1 (focus on π–HOMOs on the substituents of the cation)

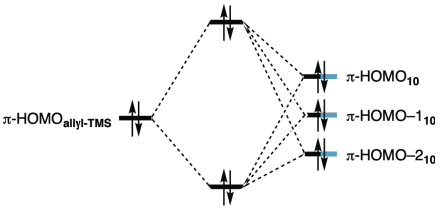


	⟨HOMO$_{allyl-TMS}$ I HOMO$_{10}$⟩	⟨HOMO$_{allyl-TMS}$ I HOMO–1$_{10}$⟩
top face $^3H_4$	0.02	0.01
bottom face $^4H_3$	0.01	0.01

Figure S7. (A) Molecular orbital diagram of the occupied–occupied orbital overlap of the addition reaction of **1**; and (B) occupied orbitals (isovalue = 0.03 Bohr$^{-3/2}$) computed at consistent geometries with a C–O bond stretch of 0.03 Å and a Nuc···C bond distance of 2.45 Å. Computed in the gas-phase at ZORA-B3LYP/TZ2P//PCM(CH_2Cl_2)-B3LYP/6-311G(d,p).

Cation 10 (focus on π–HOMOs on the substituents of the cation)

A



	⟨HOMO$_{allyl-TMS}$ I HOMO$_{10}$⟩	⟨HOMO$_{allyl-TMS}$ I HOMO–1$_{10}$⟩	⟨HOMO$_{allyl-TMS}$ I HOMO–2$_{10}$⟩
top face $^3H_4$	0.01	0.01	0.00
bottom face $^4H_3$	0.01	0.00	0.00

B

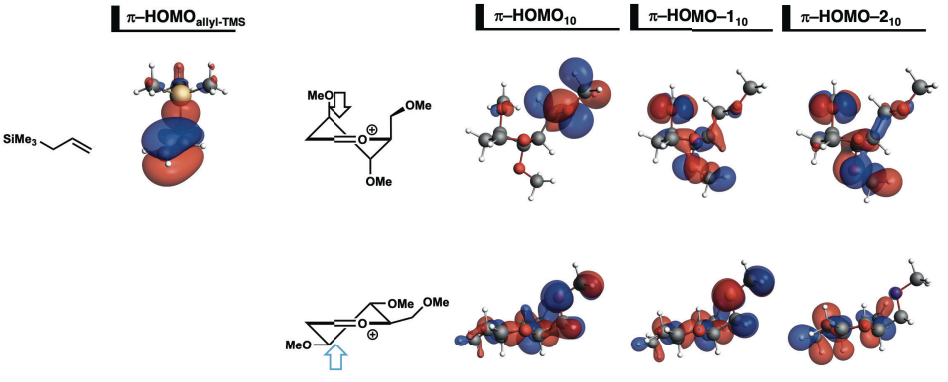


Figure S8. (A) Molecular orbital diagram of the occupied–occupied orbital overlap of the addition reaction of **10**; and (B) occupied orbitals (isovalue = 0.03 Bohr$^{-3/2}$) computed at consistent geometries with a C–O bond stretch of 0.03 Å and a Nuc···C bond distance of 2.45 Å. Computed in the gas-phase at ZORA-B3LYP/TZ2P//PCM(CH_2Cl_2)-B3LYP/6-311G(d,p).

ASM and EDA analysis of cation 1 with TES-H

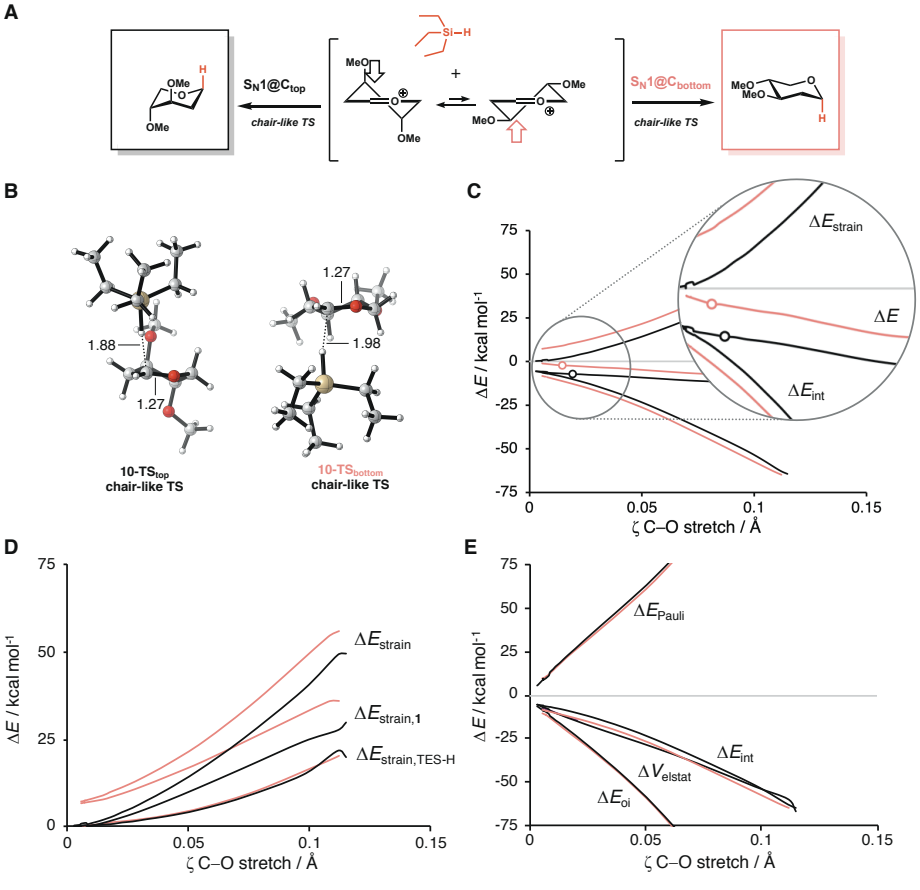


Figure S9. (A) Computationally analyzed TES-H addition reactions of glycosyl cation **1**; (B) The transition state structures with key bond lengths (in Å); (C) Activation strain analysis; (D) Strain decomposition analysis and (E) Energy decomposition analysis of the addition reaction of **1**, where the energy values are projected on the C–O stretch; TSs are indicated by dots; Computed in the gas-phase at ZORA-B3LYP/TZ2P//PCM(CH_2Cl_2)-B3LYP/6-311G(d,p).

ASM and EDA analysis of cation 10 with TES-H

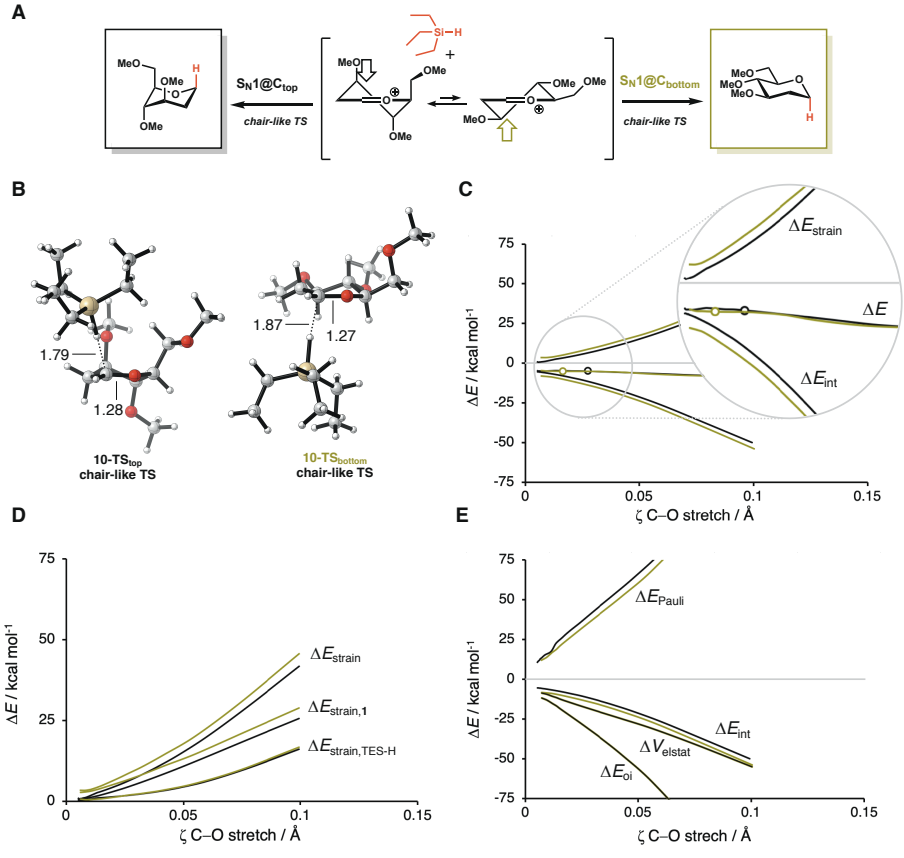


Figure S10. (A) Computationally analyzed TES-H addition reactions of glycosyl cation **10**; (B) The transition state structures with key bond lengths (in Å); (C) Activation strain analysis; (D) Strain decomposition analysis and (E) Energy decomposition analysis of the addition reaction of **10**, where the energy values are projected on the C–O stretch; TSs are indicated by dots; Computed in the gas-phase at ZORA-B3LYP/TZ2P//PCM(CH_2Cl_2)-B3LYP/6-311G(d,p).

Homolytic cleavage (spin-unrestricted fragmentation): ASM and EDA analysis of S2

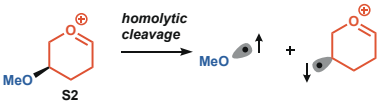
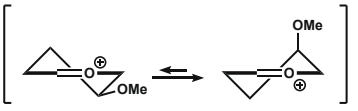


Figure S11. Activation strain and energy decomposition analysis of cation **S2**. All energies are computed at ZORA-B3LYP/TZ2P//PCM(CH_2Cl_2)-B3LYP/6-311G(d,p). All energies are reported with respect to the $^3H_4 \rightarrow {}^4H_3$ conversion and are expressed in kcal mol^{-1}.

$$\Delta\Delta E = \Delta E^{4H3} - \Delta E^{3H4} \qquad \text{(Eq. S7)}$$

Table S5. Activation strain and energy decomposition analysis of cation **S2**. All energies are computed at ZORA-B3LYP/TZ2P//PCM(CH_2Cl_2)-B3LYP/6-311G(d,p). All energies are reported with respect to the $^3H_4 \rightarrow {}^4H_3$ conversion and are expressed in kcal mol^{-1}.



	Pref. geom.	$\Delta\Delta E$	$\Delta\Delta E^{cation}_{strain}$	$\Delta\Delta E^{subs}_{strain}$	$\Delta\Delta E_{int}$	$\Delta\Delta V_{elstat}$	$\Delta\Delta E_{Pauli}$	$\Delta\Delta E_{oi}$
S2	$^4H_3$	–14.2	–8.4	–0.5	–5.3	–31.6	39.7	–13.4

Organic synthesis

General experimental procedures

All chemicals (Acros, Fluka, Merck, and Sigma-Aldrich) were used as received unless stated otherwise. Dichloromethane was stored over activated 4 Å molecular sieves (beads, 8-12 mesh, Sigma-Aldrich). Before use traces of water present in the donor, diphenyl sulfoxide (Ph_2SO) and tri-*tert*-butylpyrimidine (TTBP) were removed by co-evaporation with dry toluene. The acceptor, allyltrimethylsilane, was stored in stock solutions (DCM, 0.5 M) over activated 4 Å molecular sieves. Trifluoromethanesulfonic anhydride (Tf_2O) was distilled over P_2O_5 and stored at –20 °C under a nitrogen atmosphere. Overnight temperature control was achieved by an FT902 Immersion Cooler (Julabo). Column chromatography was performed on silica gel 60 Å (0.04 – 0.063 mm, Screening Devices B.V.). Size exclusion chromatography was carried out on Sephadex^{TM} (LH-20, GE Healthcare Life Sciences) by isocratic elution with DCM:MeOH (1:1, v:v). TLC-analysis was conducted on TLC Silica gel 60 (Kieselgel 60 F_{254}, Merck) with UV detection by (254 nm) and by spraying with 20% sulfuric acid in ethanol followed by charring at ± 150 °C or by spraying with a solution of $(NH_4)_6Mo_7O_{24}{\cdot}H_2O$ (25 g/l) and $(NH_4)_4Ce(SO_4)_4{\cdot}2H_2O$ (10 g/l) in 10% sulfuric acid in water followed by charring at ± 260 °C. High-resolution mass spectra were recorded on a Thermo Finnigan LTQ Orbitrap mass spectrometer equipped with an electrospray ion source in positive mode (source voltage 3.5 kV, sheath gas flow 10, capillary temperature 275 °C) with resolution R=60.000 at m/z=400 (mass range = 150-4000). ^{1}H, ^{2}H and ^{13}C NMR spectra were recorded on a Bruker AV-400 NMR instrument (400, 61 and 101 MHz respectively), a Bruker AV-500 NMR instrument (500, 75 and 126 MHz respectively), or a Bruker AV-600 NMR instrument (600, 92 and 150 MHz respectively). For samples measured in $CDCl_3$ chemical shifts (δ) are given in ppm relative to tetramethylsilane as an internal standard or the residual signal of the deuterated solvent. Coupling constants (J) are given in Hz. To get better resolution of signals with small coupling constants or overlapping signals a gaussian window function (LB = ± –1 and GB = ± 0.5) was used on the ^{1}H NMR spectrum. All given ^{13}C APT spectra are proton decoupled. NMR peak assignment was made using COSY, HSQC. If necessary additional NOESY, HMBC and HMBC-GATED experiments were used to elucidate the structure. The anomeric product ratios were based on the integration of ^{1}H NMR. If the stereochemistry of the coupled product could not be confirmed a deprotection step was performed to verify the stereochemistry. IR spectra were recorded on a Shimadzu FTIR-8300 IR spectrometer with a resolution of 4 cm^{-1} and are reported in cm^{-1}. Specific rotations were measured on an MCP 100 Anton Paar polarimeter in $CHCl_3$ (10 mg/mL) at 589 nm unless stated otherwise.

General procedure I: pre-activation Tf_2O/Ph_2SO based *C*-glycosylation

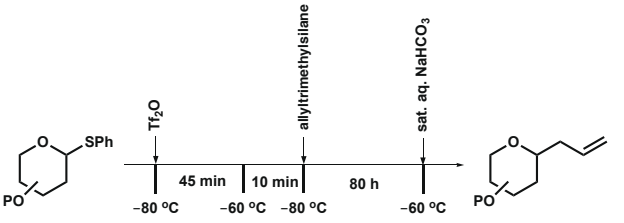
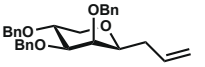
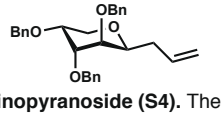


Figure S11. Schematic representation of the reaction procedure during pre-activation Ph_2SO/Tf_2O mediated glycosylation.[18]

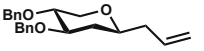
A solution of the donor (100 µmol), Ph_2SO (26 mg, 130 µmol, 1.3 eq.) and TTBP (62 mg, 250 µmol, 2.5 eq.) in DCM (2 mL, 0.05 M) was stirred over activated 3 Å molecular sieves (rods, size 1/16 in., Sigma-Aldrich) for 30 min under an atmosphere of N_2. The solution was cooled to −80 °C and Tf_2O (22 µl, 130 µmol, 1.3 eq.) was slowly added to the reaction mixture. The reaction mixture was allowed to warm to −60 °C in approximately 45 min, followed by cooling to −80 °C and the addition of the acceptor (200 µmol, 2 eq.) in DCM (0.4 mL, 0.5 M). The reaction was allowed to warm up to −60 °C and stirred for an additional 80 h at this temperature to ensure reaction completion. The reaction was quenched with sat. aq. $NaHCO_3$ at −60 °C and diluted with DCM (5 mL). The resulting solution was washed with H_2O and brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification by column chromatography yielded the corresponding *C*-coupled glycoside.



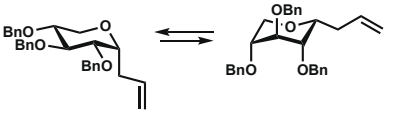
Allyl 2,3,4-tri-*O*-benzyl-1-deoxy-D-lyxopyranoside (S3). The title compound was prepared according to general procedure I. Column chromatography (95:5 → 80:20, pentane:Et_2O) yielded the title compound (36 mg, 81 µmol, 81%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). Spectroscopic data was in accordance with literature.[72] TLC: R_f 0.30 (pentane:Et_2O, 9:1, v:v); $[\alpha]_D^{25}$ 5.2°; IR (thin film, cm^{-1}): 695, 1091, 1361, 1450, 1480, 2855, 3012; ^1H NMR (500 MHz, Chloroform-*d,* HH-COSY, HSQC, HMBC, HH-NOESY): δ 7.85 – 6.84 (m, 15H, CH_{arom}), 5.77 – 5.55 (m, 1H, C*H* allyl), 5.05 – 4.95 (m, 3H, CH_2 allyl, C*H*H Bn), 4.89 – 4.73 (m, 3H, C*H*H Bn, C*H*H Bn, CH*H* Bn), 4.65 (m, 2H, CH*H* Bn, CH*H* Bn), 4.14 – 3.99 (m, 2H, H-4, H-5_{eq}), 3.76 (dd, *J* = 2.9, 1.1 Hz, 1H, H-2), 3.53 (dd, *J* = 8.8, 2.8 Hz, 1H, H-3), 3.26 (ddd, *J* = 7.4, 6.3, 1.1 Hz, 1H, H-1), 3.15 (dd, *J* = 12.8, 11.9 Hz, 1H, H-5_{ax}), 2.43 (dddt, *J* = 14.0, 7.9, 6.7, 1.4 Hz, 1H, C*H*H allylic), 2.25 – 2.17 (m, 1H, CH*H* allylic); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 138.8, 138.7, 138.7 ($C_{q\text{-}arom}$), 134.8 (*C*H allyl), 128.9, 128.6, 128.5, 128.5, 128.5, 128.4, 128.1, 127.8, 127.8, 127.7, 127.6 (CH_{arom}), 117.0 (*C*H_2 allyl), 83.7 (C-3), 79.1 (C-1), 75.6 (C-2), 75.4 (C-4), 74.8, 73.7, 73.0 (CH_2 Bn), 68.9 (C-5), 36.9 (*C*H_2 allylic); HRMS: $[M+Na]^+$ calcd for $C_{29}H_{32}NaO_4$ 467.2192, found 467.2190.



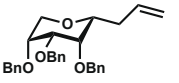
Allyl 2,3,4-tri-*O*-benzyl-1-deoxy-D-arabinopyranoside (S4). The title compound was prepared according to general procedure I. Column chromatography (95:5 → 80:20, pentane:Et_2O) yielded the title compound (30 mg, 68 µmol, 68%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). Spectroscopic data was in accordance with literature.[72] TLC: R_f 0.35 (pentane:Et_2O, 9:1, v:v); $[\alpha]_D^{25}$ −7.8°; IR (thin film, cm^{-1}): 1056, 1360, 1451, 1455, 2857, 3015; ^1H NMR (500 MHz, Chloroform-*d,* HH-COSY, HSQC, HMBC, HH-NOESY): δ 7.53 – 7.19 (m, 15H, CH_{arom}), 5.69 (dddd, *J* = 16.9, 10.2, 7.5, 6.5 Hz, 1H, C*H* allyl), 5.09 – 4.94 (m, 2H, CH_2 allyl), 4.75 (d, *J* = 12.2 Hz, 1H, C*H*H Bn), 4.60 – 4.45 (m, 3H, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.43 (d, *J* = 11.9 Hz, 1H, C*H*H Bn), 4.39 (d, *J* = 11.9 Hz, 1H, CH*H* Bn), 3.90 – 3.79 (m, 3H, H-3, H-4, H-5), 3.76 – 3.69 (m, 1H, H-1), 3.72 (t, *J* = 10.6 Hz, 1H, H-5), 3.34 (dd, *J* = 3.9, 1.5 Hz, 1H, H-2), 2.38 (dddt, *J* = 14.2, 7.9, 6.5, 1.5 Hz, 1H, C*H*H allylic), 2.17 (dddt, *J* = 14.1, 7.6, 6.5, 1.3 Hz, 1H, CH*H* allylic); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 138.8, 138.5, 138.1 ($C_{q\text{-}arom}$), 135.1 (*C*H allyl), 128.5, 128.5, 128.5, 128.3, 128.2, 128.1, 127.9, 127.8, 127.8, 127.8 (CH_{arom}), 117.1 (*C*H_2 allyl), 76.4 (C-2), 74.4 (C-1), 73.2 (CH_2 Bn), 73.1 (C-4), 72.9 (CH_2 Bn), 72.6 (C-3), 71.5 (CH_2 Bn), 64.7 (C-5), 35.3 (*C*H_2 allylic); HRMS: $[M+Na]^+$ calcd for $C_{29}H_{32}NaO_4$ 467.2192, found 467.2196.



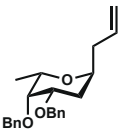
Allyl 3,4-di-*O*-benzyl-1,2-di-deoxy-D-xylopyranoside (S5). The title compound was prepared according to general procedure I. Column chromatography (95:5 → 80:20, pentane:Et_2O) yielded the title compound (20 mg, 59 µmol, 59%, colorless oil, 1,3-*cis*:1,3-*trans*; >98:2). TLC: R_f 0.37 (pentane:Et_2O, 9:1, v:v); $[\alpha]_D^{25}$ 2.2°; IR (thin film, cm^{-1}): 691, 1109, 1387, 1443, 1455, 2876; ^1H NMR (500 MHz, Chloroform-*d,* HH-COSY, HSQC, HMBC, HH-NOESY): δ 7.36 – 7.18 (m, 10H, CH_{arom}), 5.79 (ddt, *J* = 17.2, 10.2, 7.0 Hz, 1H, C*H* allyl), 5.15 – 4.99 (m, 2H, CH_2 allyl), 4.79 (d, *J* = 11.7 Hz, 1H, *C*HH Bn), 4.71 (s, 2H, CH_2 Bn), 4.66 (d, *J* = 11.7 Hz, 1H, CH*H* Bn), 4.02 (dd, *J* = 11.3, 5.1 Hz, 1H, H-5_{eq}), 3.60 – 3.43 (m, 2H, H-3, H-4), 3.42 – 3.26 (m, 1H, H-1), 3.14 (dd, *J* = 11.3, 10.1 Hz, 1H, H-5_{ax}), 2.36 – 2.25 (m, 1H, C*H*H allylic), 2.25 – 2.15 (m, 1H, CH*H* allylic), 2.11 (ddd, *J* = 13.1, 4.9, 2.0 Hz, 1H, H-2_{eq}), 1.36 (dt, *J* = 13.0, 11.2 Hz, 1H, H-2_{ax}); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 139.0, 138.5 ($C_{q\text{-}arom}$), 135.5 (*C*H allyl), 128.5, 128.5, 127.9, 127.8, 127.7, 127.7 (CH_{arom}), 117.4 (*C*H_2 allyl), 79.9 (C-3), 78.7 (C-4), 75.9 (C-1), 73.4, 72.0 (CH_2 Bn), 68.5 (C-5), 39.7 (*C*H_2 allylic), 37.4 (C-2); HRMS: $[M+Na]^+$ calcd for $C_{22}H_{26}NaO_3$ 361.1774, found 361.1770.



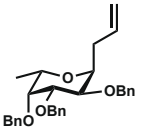
Allyl 2,3,4-tri-*O*-benzyl-1-deoxy-D-xylopyranoside (S6). The title compound was prepared according to general procedure I. Column chromatography (95:5 → 80:20, pentane:Et_2O) yielded the title compound (32 mg, 72 µmol, 72%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). Spectroscopic data was in accordance with literature.[72] TLC: R_f 0.25 (pentane:Et_2O, 9:1, v:v); $[\alpha]_D^{25}$ 8.9°; IR (thin film, cm^{-1}): 1101, 1360, 1451, 1489, 2869, 3001; ^1H NMR (500 MHz, Chloroform-*d,* HH-COSY, HSQC, HMBC, HH-NOESY): δ 7.38 – 7.26 (m, 15H, CH_{arom}), 5.77 (ddt, *J* = 17.1, 10.2, 7.0 Hz, 1H, C*H* allyl), 5.13 – 5.01 (m, 2H, CH_2 allyl), 4.65 (d, *J* = 11.8 Hz, 1H, C*H*H Bn), 4.62 – 4.56 (m, 4H, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.51 (d, *J* = 11.8 Hz, 1H, CH*H* Bn), 3.79 (ddd, *J* = 7.2, 5.2, 3.4 Hz, 1H, H-1), 3.77 – 3.70 (m, 2H, H-3, H-5), 3.46 – 3.37 (m, 1H, H-4) 3.42 (dd, *J* = 5.3, 3.7 Hz, 1H, H-2), 2.59 – 2.49 (m, 1H, C*H*H allylic), 2.36 (dddd, *J* = 13.4, 8.3, 4.1, 2.6 Hz, 1H, CH*H* allylic); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): 138.5, 138.4 ($C_{q\text{-}arom}$), 135.1 (*C*H allyl), 128.6, 128.5, 128.5, 128.3, 128.0, 127.9, 127.9, 127.8 (CH_{arom}), 117.1 (*C*H_2 allyl), 76.5, (C-2) 75.3 (C-1), 75.0 (C-3), 74.9 (C-4), 73.6, 72.8, 72.3 (CH_2 Bn), 64.7 (C-5), 33.1 (*C*H_2 allylic); HRMS: $[M+Na]^+$ calcd for $C_{29}H_{32}NaO_4$ 467.2192, found 467.2189.



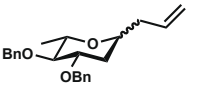
Allyl 2,3,4-tri-*O*-benzyl-1-deoxy-D-ribopyranoside (S7). The title compound was prepared according to general procedure I. Column chromatography (95:5 → 80:20, pentane:Et_2O) yielded the title compound (28 mg, 63 µmol, 63%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). Spectroscopic data was in accordance with literature.[72] TLC: R_f 0.12 (pentane:Et_2O, 9:1, v:v); $[\alpha]_D^{25}$ 4.4°; IR (thin film, cm^{-1}): 1098, 1369, 1420, 1476, 2850, 3062; ^1H NMR (500 MHz, Chloroform-*d,* HH-COSY, HSQC, HMBC, HH-NOESY): δ 7.44 – 7.22 (m, 15H, CH_{arom}), 5.77 (ddt, *J* = 17.2, 10.1, 7.1 Hz, 1H, C*H* allyl), 5.12 – 5.00 (m, 2H, CH_2 allyl), 4.94 (d, *J* = 11.8 Hz, 1H, C*H*H Bn), 4.80 (d, *J* = 12.5 Hz, 1H, C*H*H Bn), 4.73 (d, *J* = 11.8 Hz, 1H, CH*H* Bn), 4.69 – 4.57 (m, 3H, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.10 (dd, *J* = 12.2, 4.3 Hz, 1H, H-5), 3.91 – 3.67 (m, 3H, H-2, H-3, H-4), 3.46 (bs, 1H, H-1), 3.43 (dd, *J* = 12.2, 2.5 Hz, 1H, H-5), 2.73 (dt, *J* = 15.3, 7.8 Hz, 1H, C*H*H allylic), 2.41 (dddd, *J* = 13.4, 7.0, 4.0, 1.3 Hz, 1H, CH*H* allylic); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 139.0, 138.8, 138.6 ($C_{q\text{-}arom}$), 135.6 (*C*H allyl), 128.5, 128.4, 128.3, 128.2, 128.0, 127.6, 127.5, 127.5, 127.4 (CH_{arom}), 117.0 (*C*H_2 allyl), 78.8 (C-3), 78.2 (C-1), 74.6 (C-2), 73.2 (CH_2 Bn), 73.1 (C-4), 71.9, 71.6 (CH_2 Bn), 66.0 (C-5), 34.6 (*C*H_2 allyl); HRMS: $[M+Na]^+$ calcd for $C_{29}H_{32}NaO_4$ 467.2192, found 467.2191.



Allyl 2,3,4-tri-*O*-benzyl-1,2-dideoxy-D-fucopyranoside (S8). The title compound was prepared according to general procedure I. Column chromatography (95:5 → 80:20, pentane:Et_2O) yielded the title compound (34 mg, 96 µmol, 96%, colorless oil, 1,3-*cis*:1,3-*trans*; <2:98). TLC: R_f 0.30 (pentane:Et_2O, 9:1, v:v); $[\alpha]_D^{25}$ –32.9°; IR (thin film, cm^{-1}): 1100, 1390, 1410, 1490, 2860; ^{1}H NMR (500 MHz, Chloroform-*d,* HH-COSY, HSQC, HMBC, HH-NOESY): δ 7.53 – 7.03 (m, 10H), 5.83 – 5.71 (m, 1H, C*H* allyl), 5.08 – 4.99 (m, 2H, CH_2 allyl), 4.77 (d, *J* = 12.0 Hz, 1H, C*H*H Bn), 4.70 – 4.58 (m, 3H, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.06 (qd, *J* = 6.7, 4.1 Hz, 1H, H-1), 3.91 (qd, *J* = 6.7, 3.6 Hz, 1H, H-5), 3.85 (dt, *J* = 7.9, 3.2 Hz, 1H, H-3), 3.57 (t, *J* = 3.3 Hz, 1H, H-4), 2.37 – 2.28 (m, 1H, C*H*H allylic), 2.22 – 2.12 (m, 1H, CH*H* allylic), 2.08 (ddd, *J* = 13.3, 8.0, 4.1 Hz, 1H, H-2_{ax}), 1.56 (ddd, *J* = 13.3, 6.6, 3.8 Hz, 1H, H-2_{eq}), 1.33 (d, *J* = 6.6 Hz, 3H, CH_3); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 139.0, 138.9 ($C_{q\text{-}arom}$), 134.5 (*C*H allyl), 128.5, 128.4, 128.0, 127.6, 127.6, 127.4 (CH_{arom}), 116.9 (*C*H_2 allyl), 76.6 (C-4), 73.9 (C-3), 72.6, 71.3 (CH_2 Bn), 69.5 (C-5), 68.0 (C-1), 38.0 (*C*H_2 allylic), 31.7 (C-2), 16.6 (CH_3); HRMS: $[M+Na]^+$ calcd for $C_{23}H_{28}NO_3$ 375.1930, found 375.1926.

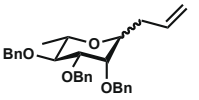


Allyl 2,3,4-tri-*O*-benzyl-1-deoxy-D-fucosepyranoside (S9). The title compound was prepared according to general procedure I. Column chromatography (95:5 → 80:20, pentane:Et_2O) yielded the title compound (35 mg, 76 µmol, 76%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). Spectroscopic data was in accordance with literature.[73] TLC: R_f 0.43 (pentane:Et_2O, 9:1, v:v); $[\alpha]_D^{25}$ –36.7°; IR (thin film, cm^{-1}): 699, 1160, 1350, 1440, 1431, 2880, 2910; ^{1}H NMR (500 MHz, Chloroform-*d,* HH-COSY, HSQC, HMBC, HH-NOESY): δ 8.06 – 6.84 (m, 15H, CH_{arom}), 5.76 (ddt, *J* = 17.1, 10.2, 6.9 Hz, 1H, C*H* allyl), 5.14 – 4.93 (m, 2H, CH_2 allyl), 4.80 – 4.53 (m, 5H, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn), 4.52 (d, *J* = 11.8 Hz, 1H, CH*H* Bn), 4.06 (ddd, *J* = 8.5, 5.2, 2.4 Hz, 1H, H-1), 3.95 (dd, *J* = 6.7, 3.8 Hz, 1H, H-5), 3.82 – 3.70 (m, 3H, H-2, H-3, H-4), 2.40 (dddt, *J* = 14.7, 9.4, 6.8, 1.4 Hz, 1H, C*H*H allylic), 2.31 (dddd, *J* = 13.4, 6.9, 4.1, 1.4 Hz, 1H, CH*H* allylic), 1.29 (d, *J* = 6.7 Hz, 3H, CH_3); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 139.0, 138.7, 138.5 ($C_{q\text{-}arom}$), 135.5 (*C*H allyl), 128.5, 128.4, 128.3, 128.1, 127.9, 127.7, 127.7, 127.7, 127.6 (CH_{arom}), 117.9 (*C*H_2 allyl), 76.9 (C-3), 76.7 (C-4), 76.0 (C-2), 73.2, 73.1, 73.1(CH_2 Bn), 70.3, (C-1), 68.8 (C-5), 31.2 (*C*H_2 allylic), 14.5 (CH_3); HRMS: $[M+Na]^+$ calcd for $C_{30}H_{34}NaO_4$ 481.2349, found 481.2347.

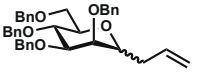


Allyl 2,3,4-tri-*O*-benzyl-1,2-dideoxy-D-rhamnopyranoside (S10). The title compound was prepared according to general procedure I. Column chromatography (95:5 → 80:20, pentane:Et_2O) yielded the title compound (25 mg, 71 µmol, 71%, colorless oil, 1,3-*cis*:1,3-*trans*; 9:91). TLC: R_f 0.32 (1,3-*trans*) and 0.40 (1,3-*cis*) (pentane:Et_2O, 9:1, v:v); IR (thin film, cm^{-1}): 1101, 1384, 1430, 1470, 2841; data of the *trans*-anomer: ^{1}H NMR (500 MHz, Chloroform-*d,* HH-COSY, HSQC, HMBC, HH-NOESY): δ 7.53 – 7.10 (m, 10H, CH_{arom}), 5.75 (ddt, *J* = 16.0, 11.1, 7.0 Hz, 1H, C*H* allyl), 5.12 – 4.99 (m, 2H, CH_2 allyl), 4.86 (d, *J* = 11.1 Hz, 1H, C*H*H Bn), 4.73 – 4.55 (m, 3H, CH*H* Bn, C*H*H Bn, CH*H* Bn), 3.99 (tt, *J* = 8.1, 4.4 Hz, 1H, H-1), 3.77 (ddd, *J* = 9.8, 7.5, 4.5 Hz, 1H, H-3), 3.69 (dq, *J* = 7.8, 6.3 Hz, 1H, H-5), 3.13 (t, *J* = 7.7 Hz, 1H, H-4), 2.45 (dddt, *J* = 14.4, 8.1, 6.7, 1.4 Hz, 1H, C*H*H allylic), 2.21 (dtt, *J* = 14.2, 7.1, 1.2 Hz, 1H, CH*H* allylic), 2.01 (ddd, *J* = 13.3, 4.6, 3.5 Hz, 1H, H-2_{eq}), 1.75 (ddd, *J* = 13.3, 9.9, 5.2 Hz, 1H, H-2_{ax}), 1.29 (d, *J* = 6.2 Hz, 3H, CH_3); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 138.7, 138.6 ($C_{q\text{-}arom}$), 134.9 (*C*H allyl), 128.5, 128.5, 128.1, 127.8, 127.8, 127.8 (CH_{arom}), 117.1 (*C*H_2 allyl), 83.0 (C-4), 76.8 (C-3), 74.7, 71.5 (CH_2 Bn), 70.6 (C-1), 69.6 (C-5), 36.8 (*C*H_2 allylic), 33.0 (C-2), 18.4 (CH_3); diagnostic signals of the *cis*-anomer: ^{1}H NMR (500 MHz, Chloroform-*d,* HH-COSY, HSQC, HMBC, HH-NOESY): δ 4.95 (d, *J* = 10.9 Hz, 1H, C*H*H Bn), 4.70 (d, *J* = 11.6 Hz, 2H, C*H*H Bn), 3.42 – 3.34 (m, 1H, H-1), 3.35 – 3.28 (m, 1H, H-3), 3.09 (t, *J* = 8.9 Hz, 1H, H-4), 2.40 – 2.25 (m,

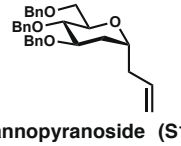
1H, C*H*H allylic); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 134.6 (*C*H allyl), 117.2 (*C*H_2 allyl), 84.5 (C-4), 75.4 (C-1), 75.4 (C-3), 74.8 (CH_2 Bn); HRMS: $[M+Na]^+$ calcd for $C_{23}H_{28}NO_3$ 375.1930, found 375.1932.



Allyl 2,3,4-tri-*O*-benzyl-1-deoxy-D-rhamnopyranoside (S11). The title compound was prepared according to general procedure I. Column chromatography (95:5 → 80:20, pentane:Et_2O) yielded the title compound (38 mg, 83 µmol, 83%, colorless oil, 1,2-*cis*:1,2-*trans*; 23:77). TLC: R_f 0.34 (1,2-*trans*) and 0.46 (1,2-*cis*) (pentane:Et_2O, 9:1, v:v); IR (thin film, cm^{-1}): 670, 1170, 1350, 1440, 1483, 2842, 2901; data of the *trans*-anomer: ^{1}H NMR (500 MHz, Chloroform-*d,* HH-COSY, HSQC, HMBC, HH-NOESY): δ 7.48 – 7.13 (m, 15H, CH_{arom}), 5.77 – 5.58 (m, 1H, C*H* allyl), 5.05 – 4.91 (m, 2H, C*H*$_2$ allyl), 4.84 (d, *J* = 11.1 Hz, 1H, C*H*H Bn), 4.81 – 4.55 (m, 5H, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.01 (ddd, *J* = 8.2, 6.6, 3.4 Hz, 1H, H-1), 3.74 (dd, *J* = 7.9, 3.1 Hz, 1H, H-3), 3.67 (dd, *J* = 7.7, 6.1 Hz, 1H, H-5), 3.66 – 3.59 (m, 1H, H-2), 3.58 (t, *J* = 7.8 Hz, 1H, H-4), 2.34 (tdd, *J* = 8.2, 6.5, 1.4 Hz, 1H, C*H*H allylic), 2.23 (dqd, *J* = 14.2, 6.9, 1.6 Hz, 1H, CH*H* allylic), 1.33 (d, *J* = 6.2 Hz, 3H, CH_3); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 138.9, 138.6, 138.4 ($C_{q\text{-}arom}$), 134.4 (*C*H allyl), 128.6, 128.6, 128.5, 128.5, 128.2, 128.2, 128.0, 127.9, 127.8, 127.8, 127.7, 127.6 (CH_{arom}), 117.9 (*C*H_2 allyl), 80.3 (C-4), 78.1 (C-3), 75.3 (C-2), 74.8 (CH_2 Bn), 73.2 (C-1), 72.1, 71.8 (CH_2 Bn), 69.8 (C-5), 34.1 (*C*H_2 allylic), 18.2 (CH_3); diagnostic signals of the *cis*-anomer: ^{1}H NMR (500 MHz, Chloroform-*d,* HH-COSY, HSQC, HMBC, HH-NOESY): δ 3.78 (dd, *J* = 2.7, 1.0 Hz, 1H, H-2), 3.36 – 3.28 (m, 2H, H-1, H-5), 2.50 – 2.39 (m, 1H, C*H*H allylic); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 134.9 (*C*H allyl), 117.3 (*C*H_2 allyl), 78.3 (C-1), 76.1 (C-5), 74.9 (C-2), 35.9 (*C*H_2 allylic), 19.6 (CH_3); HRMS: $[M+Na]^+$ calcd for $C_{30}H_{34}NaO_4$ 481.2349, found 481.2355.

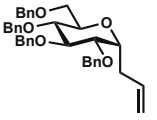


Allyl 2,3,4-tri-*O*-benzyl-1-deoxy-D-mannopyranoside (S12). The title compound was prepared according to general procedure I. Column chromatography (95:5 → 80:20, pentane:Et_2O) yielded the title compound (45 mg, 80 µmol, 80%, colorless oil, 1,2-*cis*:1,2-*trans*; 34:66). Spectroscopic data was in accordance with literature.[74] TLC: R_f 0.23 (1,2-*trans*) and 0.30 (1,2-*cis*) (pentane:Et_2O, 9:1, v:v); IR (thin film, cm^{-1}): 691, 1130, 1389, 1440, 1467, 2830, 2901; data of the *trans*-anomer: ^{1}H NMR (500 MHz, Chloroform-*d,* HH-COSY, HSQC, HMBC, HH-NOESY): δ 7.41 – 7.23 (m, 20H, CH_{arom}), 5.81 – 5.69 (m, 1H, C*H* allyl), 5.06 – 4.98 (m, 2H C*H*$_2$ allyl), 4.74 – 4.65 (m, 2H, C*H*H Bn, CH*H* Bn), 4.61 – 4.48 (m, 6H, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.04 (ddd, *J* = 7.8, 6.1, 4.7 Hz, 1H, H-1), 3.88 – 3.81 (m, 2H, H-4, H-5), 3.80 – 3.74 (m, 2H, H-3, H-6), 3.71 (dd, *J* = 10.3, 3.5 Hz, 1H, H-6), 3.62 (dd, *J* = 4.9, 2.9 Hz, 1H, H-2), 2.39 – 2.27 (m, 2H, C*H*H allylic, CH*H* allylic); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 138.6, 138.4, 138.4, 138.3 ($C_{q\text{-}arom}$), 134.0 (*C*H allyl), 128.5, 128.4, 128.4, 128.4, 128.3, 128.2, 128.2, 128.1, 128.1, 128.1, 128.0, 127.8, 127.7, 127.7, 127.6 (CH_{arom}), 117.3 (*C*H_2 allyl), 77.0 (C-3), 75.3 (C-2), 75.0, 74.0 (CH_2 Bn), 73.9 (C-5), 73.4 (CH_2 Bn), 72.5 (C-1), 72.2, 71.7 (CH_2 Bn), 69.3 (C-6), 33.9 (*C*H_2 allylic); diagnostic signals of the *cis*-anomer: ^{1}H NMR (500 MHz, Chloroform-*d,* HH-COSY, HSQC, HMBC, HH-NOESY): δ 4.87 (d, *J* = 10.8 Hz, 1H, C*H*H Bn), 4.78 (d, *J* = 11.7 Hz, 1H, C*H*H Bn), 3.46 (ddd, *J* = 9.7, 5.8, 1.8 Hz, 1H, H-5), 3.36 – 3.30 (m, 1H, H-1), 2.50 (dtt, *J* = 12.7, 6.4, 1.6 Hz, 1H, C*H*H allylic); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 134.8 (*C*H allyl), 117.4 (*C*H_2 allyl), 80.0 (C-5), 78.4 (C-1), 75.4, 74.5, 73.6, 72.6 (CH_2 Bn), 69.9 (C-6). HRMS: $[M+Na]^+$ calcd for $C_{37}H_{40}NaO_5$ 587.2768, found 587.2781.

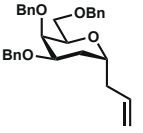


Allyl 2,3,4-tri-*O*-benzyl-1,2-dideoxy-D-mannopyranoside (S13). The title compound was prepared according to general procedure I. Column chromatography (95:5 → 80:20, pentane:Et_2O) yielded the title compound (42 mg, 92 µmol, 92%, colorless oil, 1,3-*cis*:1,3-*trans*; <2:98). TLC: R_f 0.14 (pentane:Et_2O, 9:1, v:v); $[\alpha]_D^{25}$ 48.6°; IR (thin film, cm^{-1}): 1113, 1397, 1433, 1456, 2890; ^{1}H NMR (500 MHz, Chloroform-*d,* HH-COSY, HSQC, HMBC, HH-NOESY): δ 7.37 – 7.23 (m, 15H, CH_{arom}), 5.82 – 5.70 (m, 1H, C*H* allyl), 5.08 –

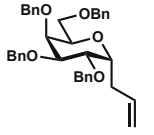
5.00 (m, 2H, C*H*$_2$ allyl), 4.78 (d, *J* = 11.1 Hz, 1H, C*H*H Bn), 4.63 – 4.47 (m, 5H, C*H*H Bn, CH*H* Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.04 (tt, *J* = 7.4, 4.5 Hz, 1H, H-1), 3.83 – 3.73 (m, 3H, H-3, H-5, H-6), 3.70 – 3.63 (m, 1H, H-6), 3.54 (t, *J* = 7.1 Hz, 1H, H-4), 2.45 (dddt, *J* = 14.3, 7.9, 6.6, 1.4 Hz, 1H, C*H*H allylic), 2.22 (dtt, *J* = 14.3, 7.3, 1.2 Hz, 1H, CH*H* allylic), 1.99 (dt, *J* = 13.4, 4.3 Hz, 1H, H-2$_{eq}$), 1.76 (ddd, *J* = 13.3, 9.4, 5.0 Hz, 1H, H-2$_{ax}$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 138.6, 138.5, 138.4 ($C_{q\text{-}arom}$), 134.8 (*C*H allyl), 128.5, 128.5, 128.5, 128.1, 128.0, 127.8, 127.8, 127.8, 127.7 (CH_{arom}), 117.2 (*C*H$_2$ allyl), 77.0 (C-4), 76.5 (C-3), 74.2, 73.5 (CH$_2$ Bn), 72.9 (C-5), 71.5 (CH$_2$ Bn), 70.6 (C-1), 69.2 (C-6), 36.9 (*C*H$_2$ allylic), 32.5 (C-2); HRMS: [M+Na]$^+$ calcd for $C_{30}H_{34}NaO_4$ 481.2349, found 481.2350.



Allyl 2,3,4-tri-*O*-benzyl-1-deoxy-D-glucopyranoside (S14). The title compound was prepared according to general procedure I. Column chromatography (95:5 → 80:20, pentane:Et$_2$O) yielded the title compound (40 mg, 71 µmol, 71%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). TLC: R$_f$ 0.23 (pentane:Et$_2$O, 9:1, v:v); $[\alpha]_D^{25}$ 28.7°; IR (thin film, cm^{-1}): 696, 1108, 1367, 1441, 2870; ^{1}H NMR (500 MHz, Chloroform-*d,* HH-COSY, HSQC, HMBC, HH-NOESY): δ 7.38 – 7.13 (m, 20H, CH_{arom}), 5.81 (dddd, *J* = 16.6, 10.2, 7.4, 6.3 Hz, 1H, C*H* allyl), 5.17 – 4.98 (m, 2H, C*H*$_2$ allyl), 4.93 (d, *J* = 11.0 Hz, 1H, C*H*H Bn), 4.84 – 4.76 (m, 2H, C*H*H Bn, CH*H* Bn), 4.69 (d, *J* = 11.6 Hz, 1H, C*H*H Bn), 4.67 – 4.58 (m, 2H, CH*H* Bn, C*H*H Bn), 4.50 – 4.44 (m, 2H, CH*H* Bn, CH*H* Bn), 4.13 (dt, *J* = 10.4, 5.0 Hz, 1H, H-1), 3.80 (dd, *J* = 9.5, 7.5 Hz, 1H, H-3), 3.76 (dd, *J* = 9.4, 5.5 Hz, 1H, H-2), 3.70 (dd, *J* = 10.6, 3.4 Hz, 1H, H-5), 3.67 – 3.59 (m, 3H, H-4, H-5, H-6), 2.56 – 2.44 (m, 2H, C*H*H allylic, CH*H* allylic); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 138.9, 138.4, 138.3, 138.2 ($C_{q\text{-}arom}$), 134.9 (*C*H allyl), 128.6, 128.5, 128.5, 128.1, 128.1, 128.0, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7 (CH_{arom}), 117.6 (*C*H$_2$ allyl), 82.6 (C-3), 79.8 (C-2), 78.2 (C-4), 75.6, 75.2 (CH$_2$ Bn), 73.8 (C-1), 73.6, 73.2 (CH$_2$ Bn), 71.2 (C-5), 69.0 (C-6), 29.9 (*C*H$_2$ allylic); HRMS: [M+Na]$^+$ calcd for $C_{37}H_{40}NaO_5$ 587.2768, found 587.2770.



Allyl 2,3,4-tri-*O*-benzyl-1,2-dideoxy-D-galactopyranoside (S15). The title compound was prepared according to general procedure I. Column chromatography (95:5 → 80:20, pentane:Et$_2$O) yielded the title compound (36 mg, 79 µmol, 79%, colorless oil, 1,3-*cis*:1,3-*trans*; <2:98). TLC: R$_f$ 0.218 (pentane:Et$_2$O, 9:1, v:v); $[\alpha]_D^{25}$ 17.7°; IR (thin film, cm^{-1}): 1089, 1389, 1447, 1458, 2867; ^{1}H NMR (500 MHz, Chloroform-*d,* HH-COSY, HSQC, HMBC, HH-NOESY): δ 7.47 – 7.20 (m, 15H, CH_{arom}), 5.77 (dddd, *J* = 17.0, 10.4, 7.5, 6.5 Hz, 1H, C*H* allyl), 5.12 – 4.97 (m, 2H, C*H*$_2$ allyl), 4.72 (d, *J* = 11.9 Hz, 1H, C*H*H Bn), 4.67 – 4.49 (m, 5H, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn,), 4.05 (dt, *J* = 7.9, 4.1 Hz, 1H, H-5), 3.99 (dt, *J* = 7.1, 3.6 Hz, 1H, H-1), 3.90 (dd, *J* = 10.6, 7.5 Hz, 1H, H-6), 3.81 (dt, *J* = 7.7, 3.2 Hz, 1H, H-3), 3.78 – 3.76 (m, 1H, H-4), 3.70 (dd, *J* = 10.6, 4.3 Hz, 1H, H-6), 2.36 (dddd, *J* = 13.9, 8.3, 6.8, 1.4 Hz, 1H, C*H*H allylic), 2.22 – 2.12 (m, 1H, CH*H* allylic), 2.06 (ddd, *J* = 13.3, 7.7, 4.1 Hz, 1H, H-2), 1.56 – 1.51 (m, 1H, H-2); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 138.8, 138.7, 138.7 ($C_{q\text{-}arom}$), 135.0 (*C*H allyl), 128.5, 128.5, 128.4, 127.9, 127.7, 127.7, 127.6, 127.5, 127.4 (CH_{arom}), 117.1 (*C*H$_2$ allyl), 75.1 (C-4), 73.7 (C-3), 73.5 (C-5), 73.4, 72.6, 71.3 (CH$_2$ Bn), 68.0 (C-1), 68.0 (C-6), 38.0 (*C*H$_2$ allylic); HRMS: [M+Na]$^+$ calcd for $C_{30}H_{34}NaO_4$ 481.2349, found 481.2355.



Allyl 2,3,4-tri-*O*-benzyl-1-deoxy-D-galactopyranoside (S16). The title compound was prepared according to general procedure I. Column chromatography (95:5 → 80:20, pentane:Et$_2$O) yielded the title compound (56 mg, 80 µmol, 80%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). TLC: R$_f$ 0.22 (pentane:Et$_2$O, 9:1, v:v); $[\alpha]_D^{25}$ 18.3°; IR (thin film, cm^{-1}): 680, 1160, 1370, 1441, 1459, 2879; 743; ^{1}H NMR (500 MHz,

Chloroform-*d*, HH-COSY, HSQC, HMBC, HH-NOESY): δ 7.91 – 6.50 (m, 20H, CH_{arom}), 5.75 (ddt, *J* = 17.1, 10.2, 6.9 Hz, 1H, C*H* allyl), 5.13 – 4.98 (m, 2H, CH_2 allyl), 4.80 – 4.63 (m, 2H, C*H*H Bn, C*H*H Bn), 4.65 – 4.39 (m, 6H, CH*H* Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn,), 4.05 (bs, 1H, H-5), 4.03 – 3.97 (m, 1H, H-3), 4.00 (dd, *J* = 4.0, 2.6 Hz, 2H, H-1), 3.88 – 3.81 (m, 1H, H-6), 3.75 (s, 1H, H-4), 3.72 (dd, *J* = 6.9, 2.8 Hz, 1H, H-2), 3.66 (dd, *J* = 10.6, 4.7 Hz, 1H, H-6), 2.47 – 2.38 (m, 1H, C*H*H allylic), 2.38 – 2.29 (m, 1H, CH*H* allylic); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 138.8, 138.7, 138.7, 138.5 ($C_{q\text{-}arom}$), 135.4 (*C*H allyl), 128.6, 128.6, 128.6, 128.5, 128.2, 128.1, 128.0, 128.0, 127.8, 127.8, 127.7 (CH_{arom}), 117.0 (CH_2 allyl), 76.7 (C-2), 76.7 (C-4), 74.5 (C-3), 73.4, 73.3, 73.3, 73.2 (CH_2 Bn), 73.0 (C-5), 70.8 (C-1), 67.5 (C-6), 33.9 (CH_2 allylic); HRMS: $[M+Na]^+$ calcd for $C_{37}H_{40}NaO_5$ 587.2768, found 587.2776.

References and notes

(1) Ayala, L.; Lucero, C. G.; Romero, J. A. C.; Tabacco, S. A.; Woerpel, K. A. Stereochemistry of Nucleophilic Substitution Reactions Depending upon Substituent: Evidence for Electrostatic Stabilization of Pseudoaxial Conformers of Oxocarbenium Ions by Heteroatom Substituents. *J. Am. Chem. Soc.* **2003**, *125* (50), 15521–15528.

(2) Walvoort, M. T. C.; Dinkelaar, J.; van den Bos, L. J.; Lodder, G.; Overkleeft, H. S.; Codée, J. D. C.; van der Marel, G. A. The Impact of Oxacarbenium Ion Conformers on the Stereochemical Outcome of Glycosylations. *Carbohydr. Res.* **2010**, *345* (10), 1252–1263.

(3) Crich, D. Mechanism of a Chemical Glycosylation Reaction. *Acc. Chem. Res.* **2010**, *43* (8), 1144–1153.

(4) Adero, P. O.; Amarasekara, H.; Wen, P.; Bohé, L.; Crich, D. The Experimental Evidence in Support of Glycosylation Mechanisms at the S_N1–S_N2 Interface. *Chem. Rev.* **2018**, *118* (17), 8242–8284.

(5) A. V. Demchenko. *Handbook of Chemical Glycosylation: Advances in Stereoselectivity and Therapeutic Relevance*; Wiley, **2008**.

(6) Bohé, L.; Crich, D. A Propos of Glycosyl Cations and the Mechanism of Chemical Glycosylation; the Current State of the Art. *Carbohydr. Res.* **2015**, *403*, 48–59.

(7) Bohé, L.; Crich, D. A Propos of Glycosyl Cations and the Mechanism of Chemical Glycosylation. *Comptes Rendus Chimie* **2011**, *14* (1), 3–16.

(8) Mydock, L. K.; Demchenko, A. V. Mechanism of Chemical *O*-Glycosylation: From Early Studies to Recent Discoveries. *Org. Biomol. Chem.* **2010**, *8* (3), 497–510.

(9) Nigudkar, S. S.; Demchenko, A. V. Stereocontrolled 1,2-*Cis* Glycosylation as the Driving Force of Progress in Synthetic Carbohydrate Chemistry. *Chem. Sci.* **2015**, *6* (5), 2687–2704.

(10) Hsu, C.-H.; Hung, S.-C.; Wu, C.-Y.; Wong, C.-H. Toward Automated Oligosaccharide Synthesis. *Angew. Chem. Int. Ed.* **2011**, *50* (50), 11872–11923.

(11) Lee, J.-C.; Greenberg, W. A.; Wong, C.-H. Programmable Reactivity-Based One-Pot Oligosaccharide Synthesis. *Nat. Protocols* **2007**, *1* (6), 3143–3152.

(12) Chen, J.; Hansen, T.; Zhang, Q.-J.; Liu, D.-Y.; Sun, Y.; Yan, H.; Codée, J. D. C.; Schmidt, R. R.; Sun, J.-S. 1-Picolinyl-5-Azido Thiosialosides: Versatile Donors for the Stereoselective Construction of Sialyl Linkages. *Angew. Chem. Int. Ed.* **2019**, *58* (47), 17000–17008.

(13) Hansen, T.; Ofman, T. P.; Vlaming, J. G. C.; Gagarinov, I. A.; Beek, J. van; Goté, T. A.; Tichem, J. M.; Ruijgrok, G.; Overkleeft, H. S.; Filippov, D. V.; van der Marel, G. A.; Codée, J. D. C. Reactivity-Stereoselectivity Mapping for the Assembly of Mycobacterium Marinum Lipooligosaccharides. *Angew. Chem. Int. Ed.* **2020**, *accepted*.

(14) Amyes, T. L.; Jencks, W. P. Lifetimes of Oxocarbenium Ions in Aqueous Solution from Common Ion Inhibition of the Solvolysis of .Alpha.-Azido Ethers by Added Azide Ion. *J. Am. Chem. Soc.* **1989**, *111* (20), 7888–7900.

(15) Chiappe, C.; Moro, G. L.; Munforte, P. Lifetime of the Glucosyl Oxocarbenium Ion and Stereoselectivity in the Glycosidation of Phenols with 1,2-Anhydro-3,4,6-Tri-*O*-Methyl-α-D-Glucopyranose. *Tetrahedron* **1997**, *53* (30), 10471–10478.

(16) Martin, A.; Arda, A.; Désiré, J.; Martin-Mingot, A.; Probst, N.; Sinaÿ, P.; Jiménez-Barbero, J.; Thibaudeau, S.; Blériot, Y. Catching Elusive Glycosyl Cations in a Condensed Phase with HF/SbF_5 Superacid. *Nat. Chem.* **2016**, *8* (2), 186–191.

(17) Elferink, H.; Severijnen, M. E.; Martens, J.; Mensink, R. A.; Berden, G.; Oomens, J.; Rutjes, F. P. J. T.; Rijs, A. M.; Boltje, T. J. Direct Experimental Characterization of Glycosyl Cations by Infrared Ion Spectroscopy. *J. Am. Chem. Soc.* **2018**, *140* (19), 6034–6038.

(18) Hansen, T.; Lebedel, L.; Remmerswaal, W. A.; van der Vorm, S.; Wander, D. P. A.; Somers, M.; Overkleeft, H. S.; Filippov, D. V.; Désiré, J.; Mingot, A.; Bleriot, Y.; van der Marel, G. A.; Thibaudeau, S.; Codée, J. D.

C. Defining the S_N1 Side of Glycosylation Reactions: Stereoselectivity of Glycopyranosyl Cations. *ACS Cent. Sci.* **2019**, *5* (5), 781–788.

(19) Hansen, T.; Elferink, H.; van Hengst, J. M. A.; Houthuijs, K. J.; Remmerswaal, W. A.; Kromm, A.; Berden, G.; van der Vorm, S.; Rijs, A. M.; Overkleeft, H. S.; Filippov, D. V.; Rutjes, F. P. J. T.; van der Marel, G. A.; Martens, J.; Oomens, J.; Codée, J. D. C.; Boltje, T. J. Characterization of Glycosyl Dioxolenium Ions and Their Role in Glycosylation Reactions. *Nat. Commun.* **2020**, *11* (1), 2664.

(20) Saito, K.; Ueoka, K.; Matsumoto, K.; Suga, S.; Nokami, T.; Yoshida, J. Indirect Cation-Flow Method: Flash Generation of Alkoxycarbenium Ions and Studies on the Stability of Glycosyl Cations. *Angew. Chem. Int. Ed.* **2011**, *50* (22), 5153–5156.

(21) Lebedel, L.; Ardá, A.; Martin, A.; Désiré, J.; Mingot, A.; Aufiero, M.; Aiguabella Font, N.; Gilmour, R.; Jiménez-Barbero, J.; Blériot, Y.; Thibaudeau, S. Structural and Computational Analysis of 2-Halogeno-Glycosyl Cations in the Presence of a Superacid: An Expansive Platform. *Angew. Chem. Int. Ed.* **2019**, *58* (39), 13758–13762.

(22) Elferink, H.; Mensink, R. A.; Castelijns, W. W. A.; Jansen, O.; Bruekers, J. P. J.; Martens, J.; Oomens, J.; Rijs, A. M.; Boltje, T. J. The Glycosylation Mechanisms of 6,3-Uronic Acid Lactones. *Angew. Chem. Int. Ed.* **2019**, *58* (26), 8746–8751.

(23) Marianski, M.; Mucha, E.; Greis, K.; Moon, S.; Pardo, A.; Kirschbaum, C.; Thomas, D. A.; Meijer, G.; Helden, G. von; Gilmore, K.; Seeberger, P. H.; Pagel, K. Remote Participation during Glycosylation Reactions of Galactose Building Blocks: Direct Evidence from Cryogenic Vibrational Spectroscopy. *Angew. Chem. Int. Ed.* **2020**, *59* (15), 6166–6171.

(24) Mucha, E.; Marianski, M.; Xu, F.-F.; Thomas, D. A.; Meijer, G.; von Helden, G.; Seeberger, P. H.; Pagel, K. Unravelling the Structure of Glycosyl Cations via Cold-Ion Infrared Spectroscopy. *Nature Communications* **2018**, *9* (1), 1–5.

(25) Hosoya, T.; Takano, T.; Kosma, P.; Rosenau, T. Theoretical Foundation for the Presence of Oxacarbenium Ions in Chemical Glycoside Synthesis. *J. Org. Chem.* **2014**, *79* (17), 7889–7894.

(26) Hosoya, T.; Kosma, P.; Rosenau, T. Contact Ion Pairs and Solvent-Separated Ion Pairs from D-Mannopyranosyl and D-Glucopyranosyl Triflates. *Carbohydr. Res.* **2015**, *401*, 127–131.

(27) Huang, M.; Garrett, G. E.; Birlirakis, N.; Bohé, L.; Pratt, D. A.; Crich, D. Dissecting the Mechanisms of a Class of Chemical Glycosylation Using Primary ^{13}C Kinetic Isotope Effects. *Nat. Chem.* **2012**, *4* (8), 663–667.

(28) Pierre Deslongchamps; Yves L. Dory; Shigui Li. R.U. Lemieux Award Lecture Hydrolysis of Acetals and Ketals. Position of Transition States along the Reaction Coordinates, and Stereoelectronic Effects. *Can. J. Chem.* **1994**, *10* (72), 2021–2027.

(29) Chamberland, S.; Ziller, J. W.; Woerpel, K. A. Structural Evidence That Alkoxy Substituents Adopt Electronically Preferred Pseudoaxial Orientations in Six-Membered Ring Dioxocarbenium Ions. *J. Am. Chem. Soc.* **2005**, *127* (15), 5322–5323.

(30) Romero, J. A. C.; Tabacco, S. A.; Woerpel, K. A. Stereochemical Reversal of Nucleophilic Substitution Reactions Depending upon Substituent: Reactions of Heteroatom-Substituted Six-Membered-Ring Oxocarbenium Ions through Pseudoaxial Conformers. *J. Am. Chem. Soc.* **2000**, *122* (1), 168–169.

(31) Vorm, S. van der; Hansen, T.; Overkleeft, H. S.; Marel, G. A. van der; Codée, J. D. C. The Influence of Acceptor Nucleophilicity on the Glycosylation Reaction Mechanism. *Chem. Sci.* **2017**, *8* (3), 1867–1875.

(32) Parent, J.-F.; Deslongchamps, G.; Deslongchamps, P. Bent Bond/Antiperiplanar Hypothesis: Modulating the Reactivity and the Selectivity in the Glycosylation of Bicyclic Pyranoside Models. *J. Org. Chem.* **2020**, *85* (6), 4220–4236.

(33) Crich, D.; Sharma, I. Is Donor–Acceptor Hydrogen Bonding Necessary for 4,6-*O*-Benzylidene-Directed β-Mannopyranosylation? Stereoselective Synthesis of β-*C*-Mannopyranosides and α-*C*-Glucopyranosides. *Org. Lett.* **2008**, *10* (21), 4731–4734.

(34) Seeman, J. I. The Curtin-Hammett Principle and the Winstein-Holness Equation: New Definition and Recent Extensions to Classical Concepts. *J. Chem. Educ.* **1986**, *63* (1), 42.

(35) Seeman, J. I. Effect of Conformational Change on Reactivity in Organic Chemistry. Evaluations, Applications, and Extensions of Curtin-Hammett Winstein-Holness Kinetics. *Chem. Rev.* **1983**, *83* (2), 83–134.

(36) van der Vorm, S.; Hansen, T.; van Rijssel, E. R.; Dekkers, R.; Madern, J. M.; Overkleeft, H. S.; Filippov, D. V.; van der Marel, G. A.; Codée, J. D. C. Furanosyl Oxocarbenium Ion Conformational Energy Landscape Maps as a Tool to Study the Glycosylation Stereoselectivity of 2-Azidofuranoses, 2-Fluorofuranoses and Methyl Furanosyl Uronates. *Chem. Eur. J.* **2019**, *25* (29), 7149–7157.

(37) van Rijssel, E. R.; van Delft, P.; Lodder, G.; Overkleeft, H. S.; Marel, G. A. van der; Filippov, D. V.; Codée, J. D. C. Furanosyl Oxocarbenium Ion Stability and Stereoselectivity. *Angew. Chem. Int. Ed.* **2014**, *53* (39), 10381–10385.

(38) Codée, J. D. C.; Litjens, R. E. J. N.; den Heeten, R.; Overkleeft, H. S.; van Boom, J. H.; van der Marel, G. A. Ph_2SO/Tf_2O: A Powerful Promotor System in Chemoselective Glycosylations Using Thioglycosides. *Org. Lett.* **2003**, *5* (9), 1519–1522.

(39) Becke, A. D. A New Mixing of Hartree–Fock and Local Density-functional Theories. *J. Chem. Phys.* **1993**, *98* (2), 1372–1377.

(40) Lee, C.; Yang, W.; Parr, R. G. Development of the Colle-Salvetti Correlation-Energy Formula into a Functional of the Electron Density. *Phys. Rev. B* **1988**, *37* (2), 785–789.

(41) Tomasi, J.; Mennucci, B.; Cammi, R. Quantum Mechanical Continuum Solvation Models. *Chem. Rev.* **2005**, *105* (8), 2999–3094.

(42) Peng, Q.; Duarte, F.; Paton, R. S. Computing Organic Stereoselectivity – from Concepts to Quantitative Calculations and Predictions. *Chem. Soc. Rev.* **2016**, *45* (22), 6093–6107.

(43) If $\Delta G^{\circ}{}^{3}{}_{H4} < \Delta G^{\circ}{}^{4}{}_{H3}$ then $\Delta\Delta G^{\ddagger}_{\text{addition}} = \Delta G^{\ddagger}_{\text{top}} - (\Delta G^{\ddagger}_{\text{bottom}} + \Delta\Delta G^{\circ})$, while if $\Delta G^{\circ}{}^{3}{}_{H4} > \Delta G^{\circ}{}^{4}{}_{H3}$ then $\Delta\Delta G^{\ddagger}_{\text{addition}} = (\Delta G^{\ddagger}_{\text{top}} + \Delta\Delta G^{\circ}) - \Delta G^{\ddagger}_{\text{bottom}}$ according to the work of the group Paton, see ref 33.

(44) Ammer, J.; Nolte, C.; Mayr, H. Free Energy Relationships for Reactions of Substituted Benzhydrylium Ions: From Enthalpy over Entropy to Diffusion Control. *J. Am. Chem. Soc.* **2012**, *134* (33), 13902–13911.

(45) Bickelhaupt, F. M.; Houk, K. N. Analyzing Reaction Rates with the Distortion/Interaction-Activation Strain Model. *Angew. Chem. Int. Ed.* **2018**, 10070–10086.

(46) Vermeeren, P.; van der Lubbe, S. C. C.; Fonseca Guerra, C.; Bickelhaupt, F. M.; Hamlin, T. A. Understanding Chemical Reactivity Using the Activation Strain Model. *Nat. Protocols* **2020**, *15* (2), 649–667.

(47) Zeist, W.-J. van; Bickelhaupt, F. M. The Activation Strain Model of Chemical Reactivity. *Org. Biomol. Chem.* **2010**, *8* (14), 3118–3127.

(48) Fernández, I.; Bickelhaupt, F. M. The Activation Strain Model and Molecular Orbital Theory: Understanding and Designing Chemical Reactions. *Chem. Soc. Rev.* **2014**, *43* (14), 4953–4967.

(49) Ess, D. H.; Houk, K. N. Distortion/Interaction Energy Control of 1,3-Dipolar Cycloaddition Reactivity. *J. Am. Chem. Soc.* **2007**, *129* (35), 10646–10647.

(50) Ess, D. H.; Houk, K. N. Theory of 1,3-Dipolar Cycloadditions: Distortion/Interaction and Frontier Molecular Orbital Models. *J. Am. Chem. Soc.* **2008**, *130* (31), 10187–10198.

(51) Galabov, B.; Koleva, G.; Schaefer III, H. F.; Allen, W. D. Nucleophilic Influences and Origin of the SN2 Allylic Effect. *Chem. Eur. J.* **2018**, *24* (45), 11637–11648.

(52) Vermeeren, P.; Hansen, T.; Jansen, P.; Swart, M.; Hamlin, T. A.; Bickelhaupt, F. M. A Unified Framework for Understanding Nucleophilicity and Protophilicity in the S_N2/E2 Competition. *Chem. Eur. J.* **2020**, *accepted*.

(53) Hansen, T.; Vermeeren, P.; Haim, A.; van Dorp, M. J. H.; Codée, J. D. C.; Bickelhaupt, F. M.; Hamlin, T. A. Regioselectivity of Epoxide Ring-Openings via S_N2 Reactions Under Basic and Acidic Conditions. *Eur. J. Org. Chem.* **2020**, *2020* (25), 3822–3828.

(54) Bickelhaupt, F. M.; Baerends, E. J. Kohn-Sham Density Functional Theory: Predicting and Understanding Chemistry. *Rev. Comp. Chem.* John Wiley & Sons, Ltd, **2007**; pp 1–86.

(55) Zhao, L.; Hopffgarten, M. von; Andrada, D. M.; Frenking, G. Energy Decomposition Analysis. *WIREs Comp. Mol. Sci.* **2018**, *8* (3).

(56) van Meer, R.; Gritsenko, O. V.; Baerends, E. J. Physical Meaning of Virtual Kohn–Sham Orbitals and Orbital Energies: An Ideal Basis for the Description of Molecular Excitations. *J. Chem. Theory Comput.* **2014**, *10* (10), 4432–4441.

(57) Gaussian 09, Revision D.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, Gaussian, Inc., Wallingford CT, **2013**.

(58) Bootsma, A. N.; Wheeler, S. Popular Integration Grids Can Result in Large Errors in DFT-Computed Free Energies. **2019**..

(59) Sun, X.; Soini, T. M.; Poater, J.; Hamlin, T. A.; Bickelhaupt, F. M. PyFrag 2019—Automating the Exploration and Analysis of Reaction Mechanisms. *J. Comp. Chem.* **2019**, *40* (25), 2227–2233.

(60) Legault, C.Y.; CYLview, 1.0b, Université de Sherbrooke, **2009** (cylview.org).

(61) Ribeiro, R. F.; Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. Use of Solution-Phase Vibrational Frequencies in Continuum Models for the Free Energy of Solvation. *J. Phys. Chem. B* **2011**, *115* (49), 14556–14562.

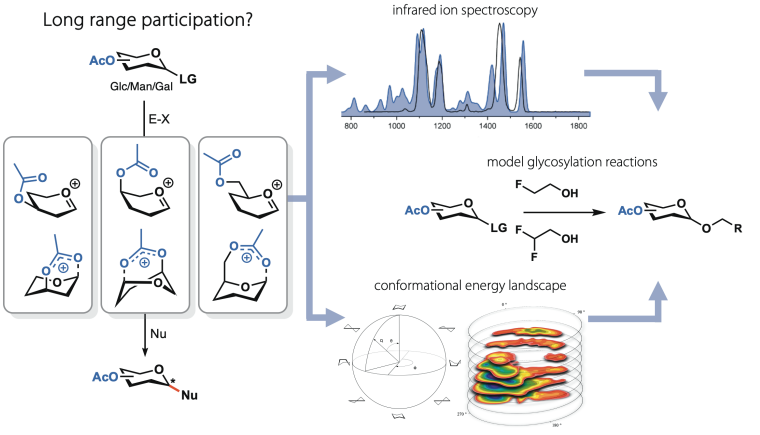
(62) ADF2017, SCM, Theoretical Chemistry, Vrije Universiteit, Amsterdam (The Netherlands), **2017**.

(63) Velde, G. te; Bickelhaupt, F. M.; Baerends, E. J.; Guerra, C. F.; Gisbergen, S. J. A. van; Snijders, J. G.; Ziegler, T. Chemistry with ADF. *J. Comp. Chem.* **2001**, *22* (9), 931–967.

(64) Fonseca Guerra, C.; Snijders, J. G.; te Velde, G.; Baerends, E. J. Towards an Order-*N* DFT Method. *Theor Chem Acc* **1998**, *99* (6), 391–403.
(65) Van Lenthe, E.; Baerends, E. J. Optimized Slater-Type Basis Sets for the Elements 1-118. *J Comput Chem* **2003**, *24* (9), 1142–1156.
(66) Franchini, M.; Philipsen, P. H. T.; Visscher, L. The Becke Fuzzy Cells Integration Scheme in the Amsterdam Density Functional Program Suite. *J. Comp. Chem.* **2013**, *34* (21), 1819–1827.
(67) Franchini, M.; Philipsen, P. H. T.; van Lenthe, E.; Visscher, L. Accurate Coulomb Potentials for Periodic and Molecular Systems through Density Fitting. *J. Chem. Theory Comput.* **2014**, *10* (5), 1994–2004.
(68) van Lenthe, E.; Baerends, E. J.; Snijders, J. G. Construction of the Foldy–Wouthuysen Transformation and Solution of the Dirac Equation Using Large Components Only. *J. Chem. Phys.* **1996**, *105* (6), 2373–2377.
(69) van Lenthe, E.; Baerends, E. J.; Snijders, J. G. Relativistic Total Energy Using Regular Approximations. *J. Chem. Phys.* **1994**, *101* (11), 9783–9792.
(70) Hamlin, T. A.; van Beek, B.; Wolters, L. P.; Bickelhaupt, F. M. Nucleophilic Substitution in Solution: Activation Strain Analysis of Weak and Strong Solvent Effects. *Chem. Eur. J.* **2018**, *24* (22), 5927–5938.
(71) Beek, B. van; Bochove, M. A. van; Hamlin, T. A.; Bickelhaupt, F. M. Nucleophilic Substitution at Di- and Triphosphates: Leaving Group Ability of Phosphate versus Diphosphate. *Electron. Struct.* **2019**, *1* (2).
(72) Lucero, C. G.; Woerpel, K. A. Stereoselective *C*-Glycosylation Reactions of Pyranoses: The Conformational Preference and Reactions of the Mannosyl Cation. *J. Org. Chem.* **2006**, *71* (7), 2641–2647.
(73) Uchiyama, T.; Woltering, T. J.; Wong, W.; Lin, C.-C.; Kajimoto, T.; Takebayashi, M.; Wéitz-Schmidt, G.; Asakura, T.; Noda, M.; Wong, C.-H. Design and Synthesis of *C*-Linked Fucosides as Inhibitors of E-Selectin. *Bio. Med. Chem.* **1996**, *4* (7), 1149–1165.
(74) Bertozzi, C.; Bednarski, M. *C*-Glycosyl Compounds Bind to Receptors on the Surface of Escherichia Coli and Can Target Proteins to the Organism. *Carbohydr. Res.* **1992**, *223*, 243–253.

Chapter 4

Characterization of Glycosyl Dioxolenium Ions and Their Role in Glycosylation Reactions



Abstract | Controlling the stereoselectivity of a chemical glycosylation reaction remains the major challenge in the synthesis of oligosaccharides. Though 1,2-*trans* glycosidic linkages can be installed using neighboring group participation, the construction of 1,2-*cis* linkages is difficult and has no general solution. Long-range participation (LRP) by distal acyl groups may steer the stereoselectivity, but contradictory results have been reported on the role and strength of this stereoelectronic effect. It has been exceedingly difficult to study the bridging dioxolenium ion intermediates because of their high reactivity and fleeting nature. In this chapter an integrated approach is reported, using infrared ion spectroscopy, DFT calculations and a systematic series of glycosylation reactions to probe these ions in detail. This chapter reveals how distal acyl groups can play a decisive role in shaping the stereochemical outcome of a glycosylation reaction and opens new avenues to exploit these species in the assembly of oligosaccharides and glycoconjugates to fuel biological research.

Published | Hansen, T.[‡]; Elferink, H.[‡]; Hengst, J. M. A. van; Houthuijs, K.; Remmerswaal, W. A.; Kromm, A.; Berden, G.; Vorm, S. van der; Rijs, A.; Overkleeft, H. S.; Filippov, D. V.; Rutjes, F. P. J. T.; van der Marel, G. A.; Martens J.; Oomens, J.; Codée, J. D. C.; Boltje, T. J. *Nature Communications.*, **2020**, 11 (1), 2664.

Preprint | *ChemRxiv*, **2019**.

Introduction

The principle challenge in chemical oligosaccharide synthesis is the stereoselective installation of glycosidic bonds.[1–4] Glycosidic bonds connecting monosaccharides can either exist as 1,2-*trans* or 1,2-*cis* diastereomers and the nature of the linkage has a profound influence on the structure and function of glycans. The most common approach to chemically create glycosidic bonds is a nucleophilic substitution reaction between a glycosyl donor carrying an anomeric leaving group, and a glycosyl acceptor containing a nucleophilic alcohol. The stereochemical outcome of glycosylation reactions can be controlled using neighboring group participation (NGP).[5,6] Acyl groups at the C-2 position of glycosyl donors can engage in NGP affording bicyclic C-1,C-2 dioxolenium ion intermediates that react in a stereospecific manner with glycosyl acceptors to afford 1,2-*trans* products (Figure 1A).[7] NGP of an *O*- or *N*-acyl functionality at C-2 is applicable to a wide variety of monosaccharides, and has enabled the stereoselective synthesis of numerous oligosaccharides both in solution and on solid support. For these reasons, NGP is one of the pillars upon which chemical oligosaccharide synthesis stands.[8,9]

By definition, NGP by a C-2 acyl group only allows access to 1,2-*trans* glycosides, and because of this it cannot be applied to the synthesis of C-2-deoxy or 1,2-*cis* glycosides. Long-range participation (LRP) of acyl functionalities farther away from the anomeric center, *i.e.* placed on the C-3, C-4 or C-6 hydroxyl groups, has also been suggested to direct the stereoselectivity of glycosylation reactions (Figure 1). Importantly, LRP potentially allows for the utilization of the relative stereochemistry of C-3, C-4, or C-6 groups to control the facial selectivity in glycosylation reactions thereby enabling the stereoselective synthesis of C-2-deoxy and 1,2-*cis* glycosides. However, contradictory results have been reported and there is an ongoing debate as to the role and strength of this stereoelectronic effect.[10–24] Indirect proof for LRP has been derived from the stereochemical outcome of glycosylation reactions and studies using model systems.[24] The ability of acyl substituents positioned at C-3, C-4 or C-6 to engage in LRP likely depends on their distance and stereochemical orientation with respect to the cationic center. In addition, the relative configuration of the neighboring substituents may influence LRP by steric and electronic effects.

Due to the instability of the intermediate dioxolenium ions and their short life time in solution, they are exceedingly difficult to detect. Direct characterization has only been reported with respect to NGP.[25,26] Although glycosyl cations have been characterized in super acid solution by NMR, protonation of the acetyl groups under these conditions prevents the assessment of their ability to engage in LRP.[27,28] This hampers the fundamental understanding of LRP and prevents its systematic development to advance stereoselective oligosaccharide synthesis.[27–30]

This chapter describes the use of infrared ion spectroscopy (IRIS) to characterize glucosyl, mannosyl and galactosyl dioxolenium ions formed *via* LRP and shows how the stability and reactivity of these species depend on the position and configuration of the acyl group. Using DFT calculations, the conformational energy landscape (CEL) of these

glycosyl cations was systematically mapped in gas and solution phase. Finally, through a series of glycosylation reactions, employing a set of model nucleophiles of gradually decreasing nucleophilicity, the importance of the remote dioxolenium ions in glycosylation reactions could be mapped. The combination of these techniques established the strength of LRP as: 3-Ac-Man >> 4-Ac-Gal > 3-Ac-Glc ~ 3-Ac-Gal > 4-Ac-Glc > 4-Ac-Man ~ 6-Ac-Glc/Gal/Man. The establishment of dioxolenium ion intermediates as possible reactive intermediates in glycosylation reactions opens up avenues to exploit these species for more stereoselective glycosylations.

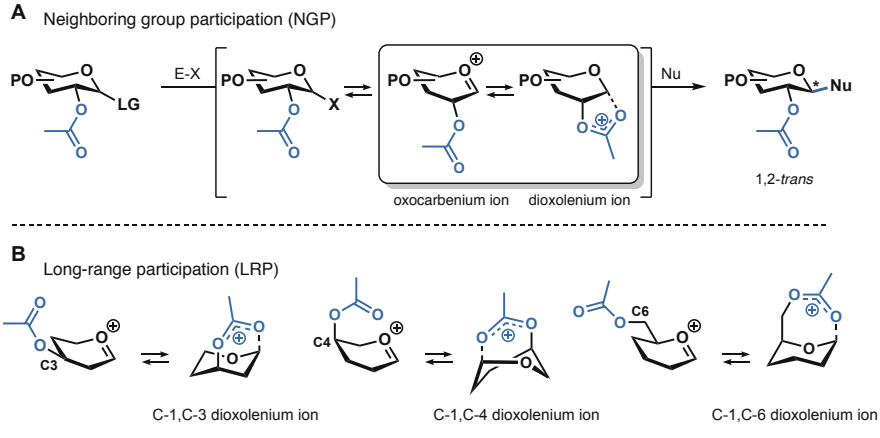


Figure 1. NGP (A) and LRP (B) in glycosylation reactions offers an opportunity to control the stereoselectivity of glycosylations. P = protection group; E-X = promoter system; and Nu = nucleophile.

Results and discussion

Recently, the group of Boltje and others have employed IRIS to characterize both glycosyl oxocarbenium and dioxolenium ions in the gas-phase.[31–34] In this method, glycosyl donors are introduced into the mass spectrometer *via* electrospray ionization (ESI) and, in a tandem-mass spectrometric (MS^2) scheme, glycosyl cations are formed from the isolated donors by collision induced dissociation (CID). This allowed the generation of "naked" glycosyl cations in the absence of a counter ion and solvent molecules, and characterization using multi photon infrared ion spectroscopy.[32,33] The IR spectra showed diagnostic vibrational bands and were used to characterize both C-1,C-2 dioxolenium ions and oxocarbenium ions.[32] In addition, the group of Boltje provided the first example of dioxolenium ions formed by LRP in uronic acid derivatives.[33] To systematically investigate whether LRP plays a role in glycosylation reactions, two sets of glycosyl donors were assembled, derived from the most commonly used pyranosides, D-glucose, D-mannose and D-galactose donors. They were equipped with an acyl group at either the C-3, C-4 or C-6 hydroxyl group (see Figure 2). The first set comprises *S*-phenyl donors equipped with

methyl ethers and acetyl esters (**1**-**9**) used for the IRIS studies and computational studies to minimize computing costs. The second set features benzyl ethers and benzoate esters (**10**-**18**) used in a matrix of model glycosylation reactions, as these represent the most commonly used protecting groups in synthetic carbohydrate chemistry. The benzyl ether and benzoate esters are structurally very similar, while differing significantly in electronic properties and their ability to stabilize an oxocarbenium ion.[35,36]

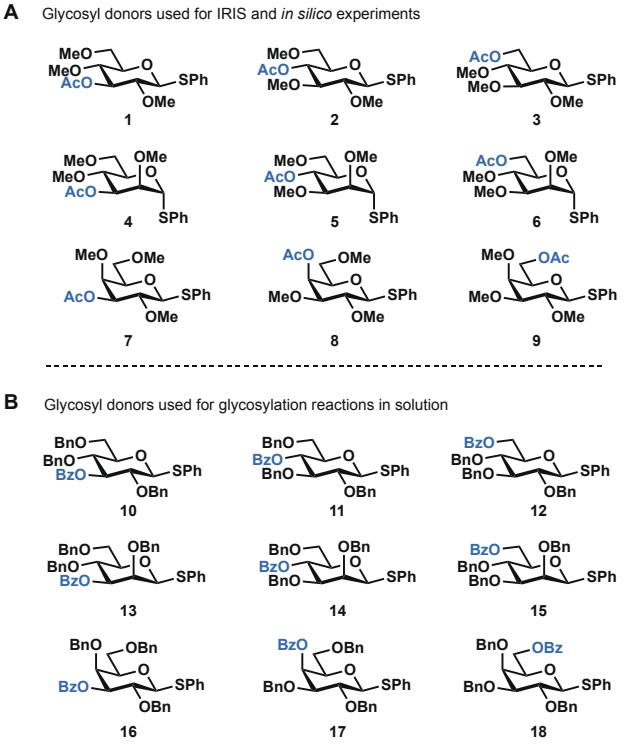


Figure 2. *S*-phenyl donors equipped with ester protection groups on systematically varied positions on the ring. (A). Glycosyl donors used for IRIS experiments and DFT computations. Donors **3**-**9** and **13**-**15** were converted into their corresponding sulfoxides prior for the IRIS experiments to improve the yield of the glycosyl cation generation;[33] (B) Glycosyl donors used for chemical glycosylation reaction in solution.

Glycosyl cations derived from **1**-**9** were formed from precursor ions using tandem-MS (see SI Figure S2-S10). IRIS of the glycosyl cations was carried out using the FELIX infrared free electron laser (IR-FEL) operating in the 700-1850 cm^{-1} frequency range which is well suited to detect the characteristic bands of oxocarbenium and dioxolenium ion structures (Figure 3A).[37] For example, oxocarbenium ions derived from **1**-**9** can be assigned on the basis of their characteristic $C_1{=}O_5^+$ stretch (~1600 cm^{-1}) and preservation of the acetyl C=O stretch near 1800 cm^{-1}. Conversely, the formation of a dioxolenium ion is signified by the absence of the acetyl C=O stretch and the $C_1{=}O_5^+$ stretch and appearance of a dioxolenium ion O-C=O^+ stretch- (~1550 cm^{-1}) and bending mode (~1500 cm^{-1}). Accurate spectral

assignments were made by comparing the experimental IR spectra with computed IR spectra obtained by high-level density functional theory (DFT) calculations (B3LYP/6-31++G(d,p)).[38] The experimental IR spectra of **1**-**9** are presented in Figure 3B-D (black line) together with the best matching calculated spectra (blue filled).

The IR spectra of the gluco-, manno- and galacto-C-3 acetyl derivatives **1**, **4** and **7** all confirm LRP of the C-3 acetyl group (Figure 3B), as indicated by a characteristic dioxolenium O-C=O$^+$ stretch (~1550 cm^{-1}) and the absence of an oxocarbenium C_1=O_5^+ or acetyl C=O stretch. The DFT calculated IR spectra of the formed dioxolenium ions matched well with the experimentally obtained spectra, while the computational spectra of the possible oxocarbenium ions derived from **1**, **4** and **7** did not (see SI Figure S2, S5, and S8).

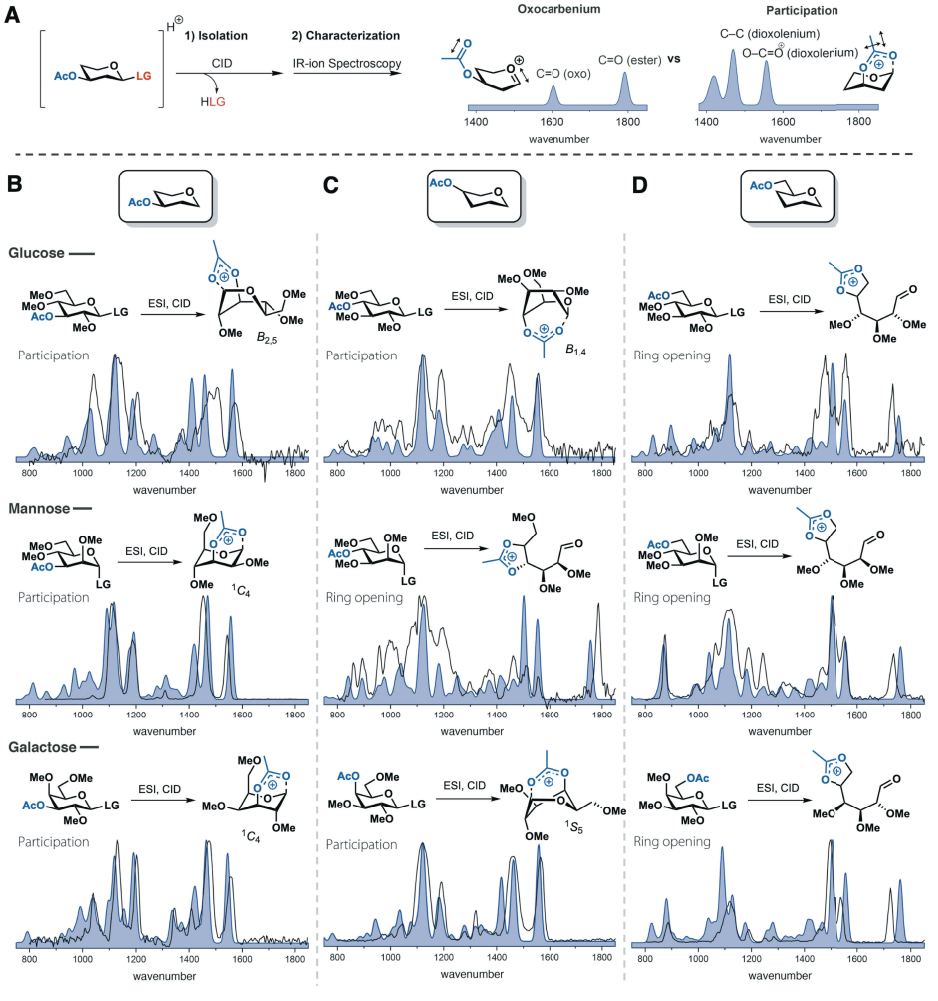


Figure 3. Comparison of the computed IR-ion spectra (filled) and the measured IR-ion spectra (black line) of the glycosyl cations derived from 3-Ac (A), 4-Ac (B) and 6-Ac (C) glucosyl, mannosyl and galactosyl donors **1**-**9**. Ring-opening of donors **3**, **5**, **6** and **9** have been presented as accessible structures, their exact conformation is presented in supporting information S4, S6, S7 and S10.

The calculated energy difference between the dioxolenium ions and the corresponding oxocarbenium ions also indicate LRP to be favorable for the C-3-acyl glycosides as all C-1,C-3 dioxolenium ions are lower in energy than their oxocarbenium ion counterparts (*vide infra*). From these experiments, it is clear that LRP of the equatorial C3-acetyl group of gluco-, manno- and galactopyranosides is favorable.

IRIS of C-4 acetyl derivatives **2**, **5** and **8** also produced characteristic IR spectra (Figure 3C, black line). The IRIS spectra of glucoside **2** and galactoside **8** showed the absence of a C=O ester stretch and instead showed diagnostic dioxolenium ion signals. In these cases, agreement between the experimental and calculated IR spectra provide clear evidence for LRP. Alternative structures lacking LRP were calculated but did not match the experimental spectrum (see SI, Figure S3 and S9). The IRIS spectrum of the ion resulting from C-4 acetyl mannose donor **5** showed distinctive dioxolenium absorptions at 1550 and 1500 cm^{-1} and a significant band at 1790 cm^{-1} suggesting the presence of a carbonyl functionality. A mixture of dioxolenium ions formed by LRP and oxocarbenium ions could explain this observation. However, comparing and mixing the DFT calculated spectra of these ions did not lead to a good match with the experimental spectrum (see SI, Figure S6). The only structure that was in good agreement with the experimental spectrum is the dioxolenium ion, formed by attack of the C-4 acetyl on the C-5 of the initially formed oxocarbenium ion (see Figure 3C, middle panel). This leads to ring opening and the formation of the C-4,C-5 dioxolenium ion with an aldehyde functionality at C-1. To the best of my knowledge, this type of rearrangement has not been reported before and the used gas-phase experimental conditions likely promote the formation of this species. Hence, the C-4 acetyl in mannose does not directly engage in LRP at the anomeric center. Taken together, these results show that the axial and equatorial C-4 esters in the glucose and galactose ions can engage in LRP, while the mannose ion provides a C-4,C-5 dioxolenium ion.

Finally, the cations of C-6 acetyl glycosides **3**, **6** and **9** were investigated. In all cases, a strong absorption near 1730 cm^{-1} was observed indicating the presence of a carbonyl functionality. However, a clear dioxolenium ion signature (~1550 cm^{-1}) was also observed. Again, neither the DFT calculated IR spectra of the oxocarbenium ion or LRP dioxolenium ion nor a mixture of the two matched with the experimental spectrum (see SI Figure S4, S7, and S10 respectively). Similar to the C-4 acetyl mannose donor **5**, the experimental spectrum was matched best with calculated spectra corresponding to the ring-opened structures featuring a C-5,C-6 dioxolenium ion, producing both the aldehyde C=O and the dioxolenium O-C=O^+ stretching bands. This suggests that C-6 acetyls are unlikely to provide LRP.

To verify that the methyl ether/acetyl ester protected set of glycosyl donors behave similar to their benzyl ether/benzoyl ester counterparts, IRIS experiments are performed with the mannosyl set **13**-**15** (see SI Figure S11-S13) and compared their spectra to those of

4-**6** (see SI Figure S5-S7). These experiments confirmed that the LRP behavior of these two sets of glycosyl donors is the same in the IRIS experiments.

To understand why some acetyl esters engage in LRP and lead to the formation of bicyclic dioxolenium ions from the parent oxocarbenium ions, while others do not, a computational method can be employed to investigate their relative stability. Chapter 2 describes the development of a DFT protocol to compute the relative energy of a large ensemble of oxocarbenium ion conformers, filling the complete conformational space these cations can occupy and plotted their relative energy to afford conformational energy landscape (CEL) maps.[29,39–41] Employing this method, one is able to find low energy conformers and relevant (conformational) pathways which connect these on the CEL. In the present chapter, the DFT method is adopted (see workflow in Figure 4) to evaluate the relative stability of the oxocarbenium and dioxolenium ions derived from **1**-**9** (Figure 5). Two rotamers of the acetyl ester were taken into account and separately visualized as a CEL map: rotamer 1 (R1) in which the acetyl is pointing towards C-1 making LRP geometrically feasible (Figure 5, left CEL map); and rotamer 2 (R2) in which the acetyl points away from C-1 making the inspection of the oxocarbenium ion possible (Figure 5, right CEL map). The geometry of all the conformers was optimized by DFT using the hybrid functional B3LYP and the basis set 6-311G(d,p), which presents an practicable trade-off between computing time and accuracy (For more information see Supplementary Information). To probe the difference in glycosyl cation structure between the IRIS gas-phase experiments devoid of solvent and glycosylation experiments performed in solution (*vide infra*), CEL maps were generated for ions formed in the gas-phase at room temperature and in solvent (computationally evaluated using a polarizable continuum model, see SI) at −60 °C at which the experimental glycosylations take place, respectively. Figure 5A-C depict the maps for the solution-phase ions, while Figure 5D summarizes the relative energy of the structures found in the solution-phase and the gas-phase (all gas-phase CEL maps can be found in SI Figure S14).

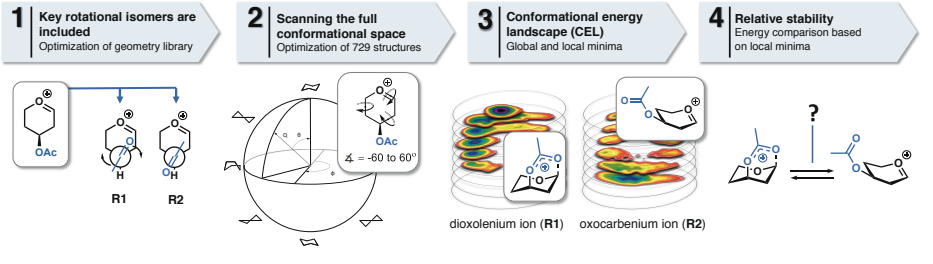
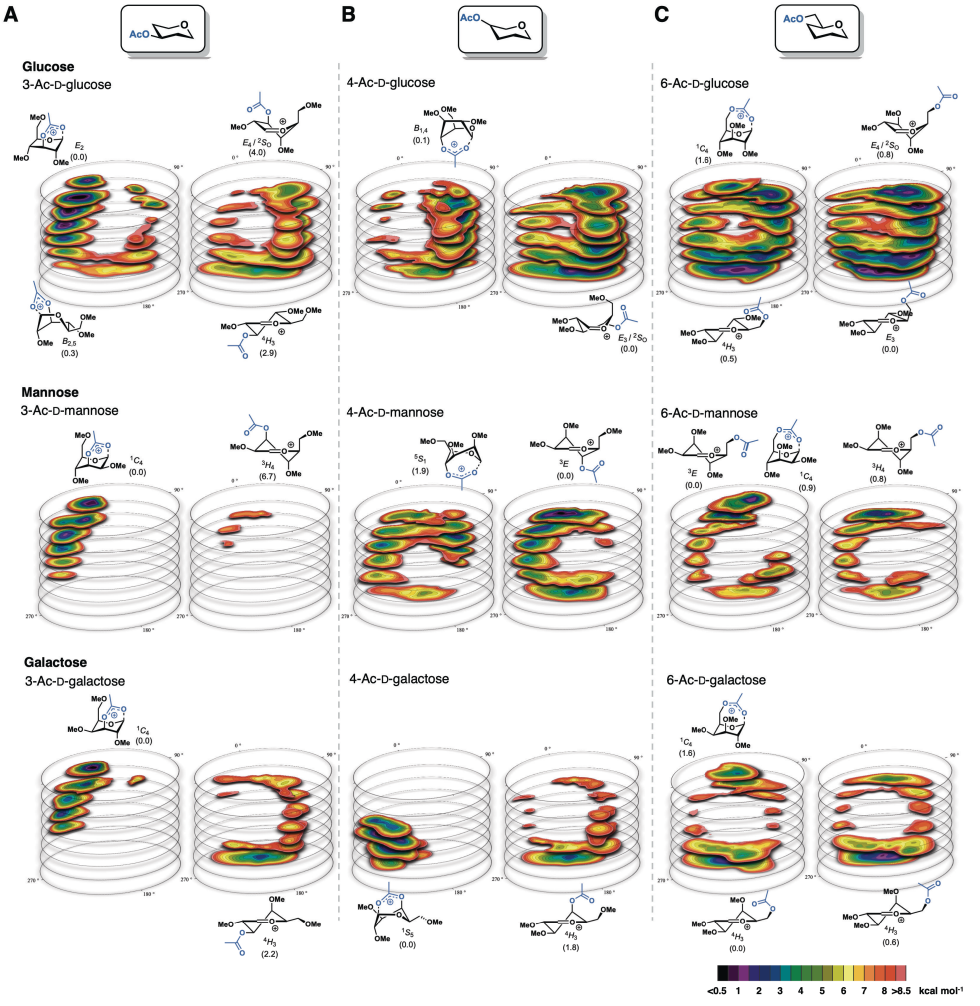


Figure 4. Overview of the workflow to map the relative stability of glycosyl dioxolenium- and oxocarbenium ions. (1) Two rotamers are used to probe long-range participation: R1 makes it geometrically feasible to form dioxolenium ions, where R2 generates the free oxocarbenium ion; (2) The complete conformational space of the six-membered rings was scanned by computing 729 pre-fixed structures per rotamer. A few canonical conformations (chair, half-chair, envelope, and boat) are depicted; (3) The associated energies were graphed on slices dividing the Cremer-Pople sphere. The CEL map of the R1 rotamer (left) and CEL map of the R2 rotamer (right); (4) Based on the CEL maps of R1 and R2 the relative stability of both intermediates can be evaluated.

Figure 5A shows the solution-phase CEL maps of the C-3 acetyl protected glucosyl, mannosyl, and galactosyl dioxolenium (R1) and oxocarbenium ions (R2). The computed local minima (in dark), show that formation of the dioxolenium ions (Figure 5A, left CEL-maps) is energetically favorable. For the gas-phase, the maps are similarly but with larger energy differences between the lowest energy dioxolenium and oxocarbenium ions (Figure 5D, final row). The comparison shows that the energy difference is largest for the C-3 acetyl mannose system, with the most favorable mannose C-1,C-3 dioxolenium ion adopting a $^{1}C_{4}$-conformation. The glucose and galactose ions benefit from LRP with the E_{2}-glucose and $^{1}C_{4}$-galactose C-1,C-3 dioxolenium ions being 2-3 kcal mol^{-1} more stable than the corresponding lowest energy $^{4}H_{3}$-oxocarbenium ions. In the mannose system the lowest energy oxocarbenium and dioxolenium ions are close in conformational space (*i.e.*, both conformations present in the top part of the CEL map), indicating that only a small conformational change is required for the formation of the dioxolenium ion from the oxocarbenium ion. In the glucose and galactose systems, the lowest energy oxocarbenium and dioxolenium ions are found in different regions of the conformational space. Hence, the conformational change required for the transition from the initially formed oxocarbenium ion to the more stable dioxolenium ion necessitates the crossing of a significant energy barrier. Overall the CEL maps suggest that participation of a C-3 acyl group is favorable for all three diastereoisomeric ions studied, which is corroborated by the IRIS experiments and is most beneficial in the mannose configured C-3 acetyl system.

A similar analysis of the C-4 acetyl systems (Figure 5B) reveals important differences between the glucose, mannose and galactose systems, again consistent with the IRIS experiments. The participation of the C-4 acetyl in the mannose ion is unfavorable, while the C-4 acetyl glucose and galactose systems benefit from LRP. The formation of the galactosyl C-1,C-4 dioxolenium ion, adopting a $^{1}S_{5}$-like structure, from the $^{4}H_{3}$-oxocarbenium ion requires only a minimal adjustment of the sugar ring conformation and is therefore facile. For the glucosyl C-4 acetyl case this requires significantly more structural rearrangement from the E_{3}-oxocarbenium ion to the lowest energy $B_{1,4}$-structure. Furthermore, the computations indicate that the glucose C-1,C-4 dioxolenium ion is more stable than the oxocarbenium ion in the gas-phase, while the relative energy of both ions is similar in solution. The relative instability of the mannosyl C-1,C-4 dioxolenium ion may be due to the *pseudo*-axial orientation of all substituents in the $^{5}S_{1}$-like structure, with the C-2 and C-3 substituents experiencing unfavorable eclipsing interactions that are not present in the glucose and galactose dioxolenium ions.

Finally, the C6-acetyl systems were probed. As can be seen from Figure 5C and 5D, the energy difference between the two acyl rotamers (R1 and R2) is small, indicating that LRP does not lead to significant stabilization of the ions.



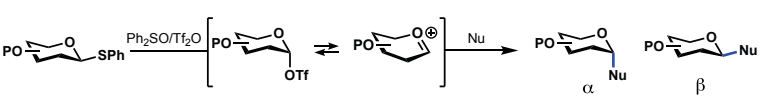
D

	dioxolenium ion		oxocarbenium ion			
	ΔG_{gas}	$\Delta G_{CH_2Cl_2}$	ΔG_{gas}	$\Delta G_{CH_2Cl_2}$	$\Delta\Delta G_{gas}$	$\Delta\Delta G_{CH_2Cl_2}$
3-Ac-glucose	E_2 (0.0) / $B_{2,5}$ (0.0)	E_2 (0.0)	E_4 / $^2S_0$ (5.5)	$^4H_3$ (2.9)	–5.5	–2.9
3-Ac-mannose	$^1C_4$ (0.0)	$^1C_4$ (0.0)	^3E (20.0)	$^3H_4$ (6.7)	–20.0	–6.7
3-Ac-galactose	$^1C_4$ (0.0)	$^1C_4$ (0.0)	$^4H_3$ (6.0)	$^4H_3$ (2.2)	–6.0	–2.2
4-Ac-glucose	$B_{1,4}$ (0.0)	$B_{1,4}$ (0.1)	^3E / $^2S_0$ (1.5)	^3E / $^2S_0$ (0.0)	–1.5	+0.1
4-Ac-mannose	$^5S_1$ (1.0)	$^5S_1$ (1.9)	^3E (0.0)	^3E (0.0)	+1.0	+1.9
4-Ac-galactose	$^1S_5$ (0.0)	$^1S_5$ (0.0)	$^4H_3$ (6.1)	$^4H_3$ (1.8)	–6.1	–1.8
6-Ac-glucose	$^1C_4$ (2.8)	$^1C_4$ (1.6)	E_4 / $^2S_0$ (0.0)	E_3 (0.0)	+2.8	+1.6
6-Ac-mannose	$^1C_4$ (0.4)	$^1C_4$ (0.9)	^3E (0.0)	^3E (0.0)	+0.4	+0.9
6-Ac-galactose	$^1C_4$ (0.6)	$^1C_4$ (1.6)	$^4H_3$ (0.0)	$^4H_3$ (0.0)	+0.6	+1.6

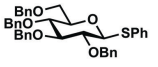
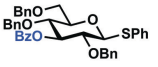
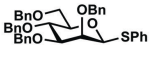
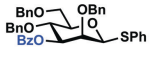
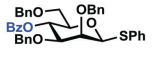
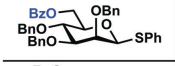
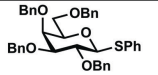
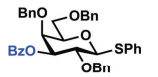
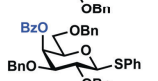
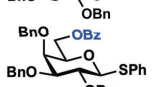
Figure 5. CEL maps of selected glycosyl cations in which the local minima identified are shown with their respective energy. Two acetyl ester rotamers (R1 = left and R2 = right) were considered for all computed glycosyl cations generating two sperate CEL maps. All energies are as computed at PCM(CH_2Cl_2)-B3LYP/6-311G(d,p) at T=213.15 K and expressed as solution-phase Gibbs free energy. A) CEL maps for the C3-acetyl pyranosyl ions; B) CEL maps for the C4-acetyl pyranosyl ions; C) CEL maps for the C6-acetyl pyranosyl ions; D) Table summarizing the relative energy of the dioxolenium and oxocarbenium ion conformers in the gas- and solution-phase.

Table 1. Experimentally found stereoselectivities for model glycosylation reactions. Experimental conditions: pre-activation based glycosylation conditions; nucleophile (2 eq.), Tf_2O (1.3 eq.), Ph_2SO (1.3 eq.), TTBP (2.5 eq.), DCM (0.05 M), –80 °C to –60 °C. The stereoselectivity of the reaction is expressed as α:β and based on ^{1}H-NMR of the purified compounds. In all cases, the NMR spectra for both the crude and purified compounds were compared to analyze whether the obtained stereoselectivity did not alter upon purification.

A



B

					
	>98:2 (41%)	75:25 (80%)	48:52 (58%)	36:64 (75%)	15:85 (70%)
	>98:2 (28%)	76:24 (91%)	58:42 (97%)	44:56 (95%)	40:60 (88%)
	>98:2 (19%)	79:21 (76%)	48:52 (70%)	34:66 (82%)	15:85 (76%)
	>98:2 (30%)	95:5 (82%)	77:23 (82%)	35:65 (83%)	17:83 (94%)
	>98:2 (39%)	>98:2 (84%)	80:20 (65%)	60:40 (75%)	33:67 (70%)
	>98:2 (61%)	>98:2 (79%)	>98:2 (87%)	>98:2 (87%)	>98:2 (94%)
	>98:2 (50%)	88:12 (77%)	71:29 (81%)	60:40 (83%)	31:69 (88%)
	>98:2 (64%)	>98:2 (56%)	78:22 (89%)	51:49 (99%)	35:65 (69%)
	>98:2 (33%)	87:13 (79%)	66:34 (69%)	31:69 (84%)	17:83 (73%)
	>98:2 (54%)	86:14 (77%)	66:34 (81%)	40:60 (82%)	41:59 (79%)
	>98:2 (55%)	97:3 (79%)	87:13 (65%)	63:37 (84%)	45:55 (86%)
	>98:2 (57%)	89:11 (74%)	61:39 (81%)	33:67 (83%)	15:85 (88%)

>90:10 >80:20 >60:40 >50:50 <50:50 <40:60 <20:80 <10:90 (α:β)

To correlate the IRIS and CEL map findings to solution-phase experiments, the influence of LRP in glycosylation reactions was probed using **10**-**18** (Table 1, Entry 2-4, 6-8 and 10-12 respectively). To this end, a matrix of glycosylation reactions was performed with a set of model alcohol nucleophiles of gradually increasing nucleophilicity.[42,43] The

trends observed relate to changes from an S_N2-type substitution reaction of the covalent intermediate (*e.g.*, a glycosyl triflate) for the most nucleophilic alcohols, to reactions involving more oxocarbenium character for the poorest nucleophiles (Table 1A). The glycosylation reactions were performed under pre-activation conditions using diphenyl sulfoxide (Ph_2SO)/triflic anhydride (Tf_2O) as an activator and the results compared to donors bearing solely benzyl ether protecting groups (Table 1, Entry 1, 5 and 9).[44]

The glycosylations of the C-3 benzoyl donors reveal a shift in stereoselectivity with respect to their C-3 benzyl counterparts towards the side of the α-products, formed on the S_N1-side of the reaction mechanism spectrum. The change in stereoselectivity between the benzoyl/benzyl donors can be explained as arising from the LRP of the C-3 acyl groups. This shift is most pronounced in the mannose series, where all glycosylations proceed to give solely the α-product (this is also observed in the glycosylation with the methyl/acetyl protected donor analog, supporting information, Table S1). These observations are in excellent agreement with the IRIS and the CEL maps results which indicate that C-1,C-3 dioxolenium ion formation is possible and most pronounced in the mannose system. For the glucose and galactose donors (Table 1, Entry 2 and 6), C-3 LRP provides less stabilization, which is reflected by the smaller impact on the α-selectivity in these cases.

In contrast, the stereoselectivity of the C-4 benzoate glucose and mannose donors is virtually identical to the selectivity of the C-4 benzyl glucose and mannose donors, revealing little influence of the group present at C-4 position. The IRIS experiments and CEL maps revealed that the formation of the mannosyl C-1,C-4 dioxolenium ion is not favorable. The C-4 acyl group in mannose thus has relatively little effect on the position of the mechanistic continuum at which the substitution reactions take place and LRP can be excluded. While IRIS and the CEL maps have shown that the formation of the glucosyl C-1,C-4 dioxolenium ion is favorable in the gas-phase, the glycosylation reactions of the glucosyl donor appear to be unaffected by the nature of the C-4 substituent. The solution-phase CEL maps have revealed the C-1,C-4 dioxolenium ion, and oxocarbenium ions to be of similar energy. This may account for the moderate effect of the C-4 acetyl group on the stereochemical outcome of the glucosylation reactions. In contrast to the C-4 acyl glucose and mannose series, the C-4 acyl group in the galactose donor is capable of LRP. Both IRIS and the CEL maps provide support for the formation of the bridged C-1,C-4 dioxolenium ion. The stability of this ion translates into the formation of more α-product in the glycosylations of the C-4 acyl galactosides.

Finally, the IRIS spectra of the C-6 acyl gluco-, manno,- and galactosyl donors provide no evidence for LRP of an acyl functionality on this position. This is corroborated by the CEL maps indicate that the formation of the dioxolenium ion bridging the C-1 and C-6 positions does not lead to significant stabilization of the ions. The matrix of glycosylation reactions indeed shows little influence of the C-6 acyl groups. Based on this combined dataset, LRP by C-6 acyl appears to have little influence on glycosylation reactions.

Conclusion

In conclusion, this chapter describes a systematic evaluation of LRP in glucosyl, mannosyl and galactosyl donors bearing an acyl protecting group at their C-3, C-4 or C-6 hydroxyl group functionality. A three-pronged approach consisting of IRIS, CEL computations, and glycosylation reactions was used to assess the effect of LRP in these glycosyl donors. These studies confirm that LRP can play a decisive role in shaping the stereochemical outcome of a glycosylation reaction. LRP plays a major role in glycosylations of C-3 acyl mannosides and to a somewhat lesser extent C-4 acyl galactosides. C-3 acyl groups in glucose and galactosyl donors can engage in LRP but this anchimeric assistance has relatively little influence on the stereochemical course of glycosylations of these donors. No important role for C-6 acyl LRP has been found. The strength of LRP thus follows the order: 3-Ac-Man >> 4-Ac-Gal > 3-Ac-Glc ~ 3-Ac-Gal > 4-Ac-Glc > 4-Ac-Man ~ 6-Ac-Glc/Gal/Man. The establishment of dioxolenium ion intermediates as possible reactive intermediates in glycosylation reactions opens up avenues to enhance and exploit this effect to gain stereocontrol.[14,45,46] These are expected to accelerate the assembly of glycoconjugates to fuel biological research.

Supporting information

Tandem-MS combined with IR ion spectroscopy

General procedure I: ion spectroscopy in a modified ion trap mass spectrometer • The experimental apparatus is based on a modified 3D quadrupole ion trap mass spectrometer (Bruker, AmaZon Speed ETD) that has been coupled to the beam line of the FELIX infrared free electron laser (IR-FEL).[37] Ammonium adducts of each thioether compound ($[M+NH_4]^+$) or protonated adducts from each thiosulfinyl compound ($[M+H]^+$) were generated by electrospray ionization from solutions of 10^{-6} M (in 50:50 acetonitrile:water) containing 2% ammonium acetate infused at 2 µl min^{-1}. The mass-isolated ions of interest were collisionally activated for 40 ms in order to generate the relevant oxonium products. These fragment ions were subsequently mass isolated and irradiated by the tunable mid-infrared beam. The FEL was operated to provide 5 µs optical pulses at 10 Hz having 60-120 mJ pulse energy over the entire IR frequency range (bandwidth ~0.4% of the center frequency). The actual pulse energy used for measurements was appropriately attenuated in order to avoid saturation of the signal. When a sufficient number of photons is absorbed, typically during a single macropulse, unimolecular dissociation occurs generating frequency-dependent fragment ion intensities in the mass spectrum. Relating the precursor ion intensity to the total fragmentation intensity in the observed mass spectrum (yield=ΣI(fragment ions)/ΣI(parent+fragment ions)) for each frequency position generates an infrared vibrational spectrum. The yield is obtained from several averaged mass spectra and is linearly corrected for laser power; the IR frequency is calibrated using a grating spectrometer. A frequency step size of 3 cm^{-1} was used in all spectra reported here.

General procedure II: simulation of IR spectra • For the calculation of gas-phase geometries and corresponding IR spectra we have used a workflow that has been reported previously.[47] The SMILES structure format of the oxocarbenium, dioxolenium and rearranged ions were used as input for the workflow using the cheminformatics toolbox RDKit.[48] A conformational search was performed using a distance geometry algorithm, yielding 500 random 3D-conformations, which were minimized using a classical forcefield.[49] A maximum of 40 conformations were selected by hierarchical on the root means squared distance between geometries.[50] These selected conformations were then submitted to Gaussian 16 for geometry optimization and frequency calculations using the semi-empirical PM6 level.[51] By comparing relative energies (electronic and thermal), unfavorable conformations were filtered by using an energy cut-off of 10 kcal/mol. When generating pyranosyl cations, this cut-off was increased to 20 kcal/mol, as the oxocarbenium ions would otherwise be filtered out because dioxolenium ions that were formed in the optimization were much lower in energy. Additionally, similar geometries were filtered based on (close to) identical calculated frequencies and corresponding intensities. After these filtering steps, the remaining structures were reoptimized using the B3LYP density functional and 6-31++G(d,p) basis set and thereafter a frequency calculation was performed. Harmonic vibrational frequencies were scaled by 0.975. To aid comparison to experimental spectra, Gaussian broadening (20 cm^{-1} at full width half maximum) was applied to the calculated vibrational lines. To obtain reliable energies the thermal energy of the frequency calculation was combined with the electronic energies calculated using second order Møller-Plesset perturbation theory and the 6-31++G(d,p) basis set.

DFT calculations

General procedure III: conformational energy landscape calculation of pyranosyl oxocarbenium ions • To keep the calculation time manageable, large protecting groups (*i.e.*, *O*-Bn) were substituted with electronic comparable smaller groups (*i.e.*, *O*-Me). The initial structure for the conformational energy landscape (CEL) mapping of the six-membered glycosyl cation was optimized by starting from a 'conformer distribution search' option included in the Spartan 10 program by utilizing DFT as the level of theory and B3LYP as hybrid functional in gas phase with 6-31G(d) as the basis set. All generated gas-phase geometries were re-optimized with Gaussian 09 rev. D.01 by using B3LYP/6-311G(d,p), after which a vibrational analysis was computed to obtain the thermodynamic properties. The gas-phase structures were then solvated by using the PCM implicit solvation model, with CH_2Cl_2 as solvent. Solvent effects were explicitly used in solving the SCF equations and during the optimization of the geometry. The geometry with

the lowest energy was selected as the starting point for the CEL. A complete survey of the possible conformational space was done by scanning three dihedral angles ranging from –60° to 60°, including the C1-C2-C3-C4 (D1), C3-C4-C5-O (D3) and C5-O-C1-C2 (D5). The resolution of this survey is determined by the step size which was set to 15° per puckering parameter, giving a total of 729 pre-fixed conformations per glycosyl cation spanning the entire conformational landscape. All other internal coordinates were unconstrained. Except when a C2-substituent was present on the oxocarbenium ring of interest, then the C2-H2 bond length was fixed based on the optimized structure to counteract rearrangements occurring for higher energy conformers. The 729 structures were computed with Gaussian 09 rev. D.01[52] again with a two-step procedure. First, the structures were optimized in the gas-phase with B3LYP/6-311G(d,p), after which a vibrational analysis was computed to obtain the thermodynamic properties. The gas-phase structures were then solvated by using the PCM implicit solvation model, with CH_2Cl_2 as solvent. For glycosyl cation bearing a C5-C6 substituent three separate staggered rotamers (*i.e.*, *gg*, *gt*, *tg*) of the O5-C5-C6-O6 dihedral angle (*i.e.*, –65°, 65°, 175°) were considered. Earlier work showed the importance of these rotamers and their crucial impact on the selectivity and reactivity of the ion.[41] The CEL maps were computed separately and the starting geometry was obtained from the method described above in which the lowest energy generated rotamers were used. For this specific study two extra rotamers were taken into account of the C-O bond rotamer of the ring carbon and the oxygen of one of the substituents which is protected by an acyl protecting group, bringing the total conformations for each glycosyl cation ion configuration to 4374 geometries. CEL maps were separately computed and visualized: rotamer 1 (R1) in which the acetyl is positioned in such a way that dioxolenium ion formation is geometrically feasible and rotamer 2 (R2) in which the acetyl points away and the free oxocarbenium ion can be found. The final denoted free Gibbs energy was calculated using Equation S1 in which ΔE_{gas} is the gas-phase energy (electronic energy), $\Delta G^{T}_{gas,QH}$ (T = reaction temperature, p = 1 atm. and C = 1 M) is the sum of corrections from the electronic energy to free Gibbs energy in the quasi-harmonic oscillator approximation also including ZPE, and ΔG_{solv} is their corresponding free solvation Gibbs energy. The $\Delta G^{T}_{gas,QH}$ were computed using the quasi-harmonic approximation in the gas phase according to the work of Truhlar.[53]

$$\Delta G^{T}_{CH_2Cl_2} = \Delta E_{gas} + \Delta G^{T}_{gas,QH} + \Delta G_{solv} \qquad \text{(Eq. S1)}$$
$$= \Delta G^{T}_{gas} + \Delta G_{solv}$$

The quasi-harmonic approximation is the same as the harmonic oscillator approximation except that vibrational frequencies lower than 100 cm^{-1} were raised to 100 cm^{-1} as a way to correct for the breakdown of the harmonic oscillator model for the free energies of low-frequency vibrational modes. All optimized structures were checked for the absence of imaginary frequencies. To visualize the energy levels of the conformers on the Cremer-Pople sphere, we have generated slices dissecting the sphere that combine closely associated conformers. The OriginPro software was employed to produce the energy heat maps, contoured at 0.5 kcal mol^{-1}. For ease of visualization, the Cremer-Pople globe is turned 180° with respect to its common representation. Visualization of conformations of interest was done with CYLview.[54]

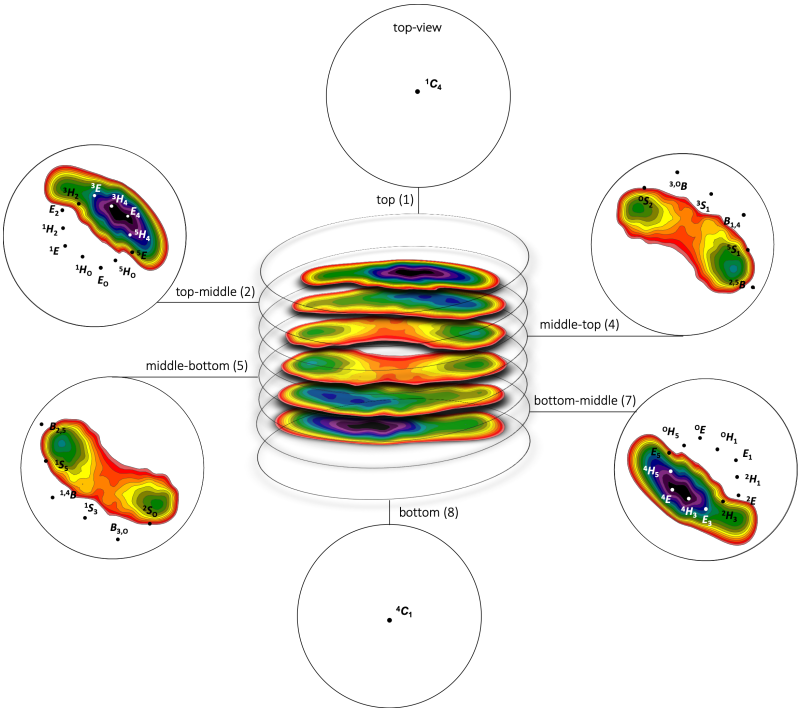


Figure S1. "Deconvolution" of the CEL map of the pyranosyl oxocarbenium ion showing a top view of the most important slices that have been combined to generate the complete CEL map.

IR-spectra • All IR-spectra that are described in this chapter are summarized in the following section. All relevant computed IR-spectra of low energy structures are compared with the measured IR-ion spectrum.

3-*O*-Acetyl-2,4,6-tri-*O*-methyl-gluco-D-pyranosyl cation

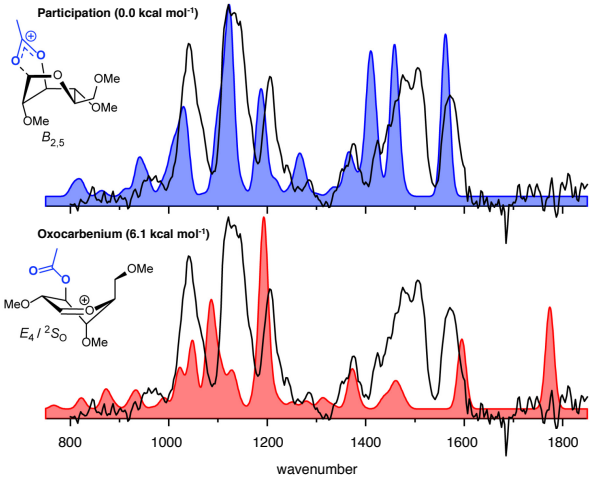


Figure S2. Comparison of the computed IR-spectra of low energy structures (filled) with the measured IR-ion spectrum (black line) of the m/z = 247 CID fragment of compound **1** (top structure). The computed IR-spectrum in blue was assigned as best match with the measured spectrum.

4-*O*-Acetyl-2,3,6-tri-*O*-methyl-gluco-D-pyranosyl cation

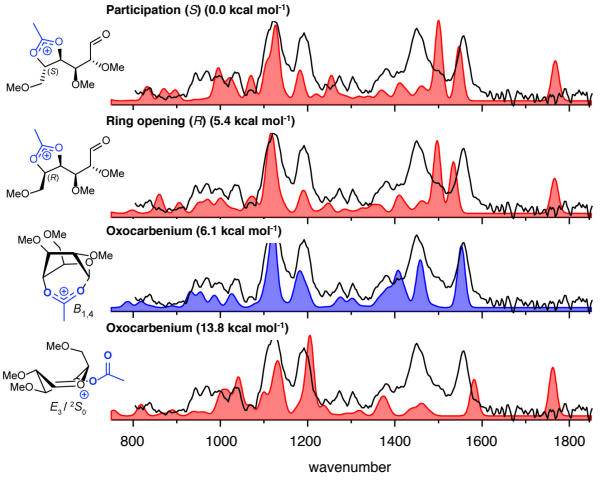


Figure S3. Comparison of the computed IR-spectra of low energy structures (filled) with the measured IR-ion spectrum (black line) of the m/z = 247 CID fragment of compound **2** (top structure). The computed IR-spectrum in blue was assigned as best match with the measured spectrum.

6-*O*-Acetyl-2,3,4-tri-*O*-methyl-gluco-D-pyranosyl cation

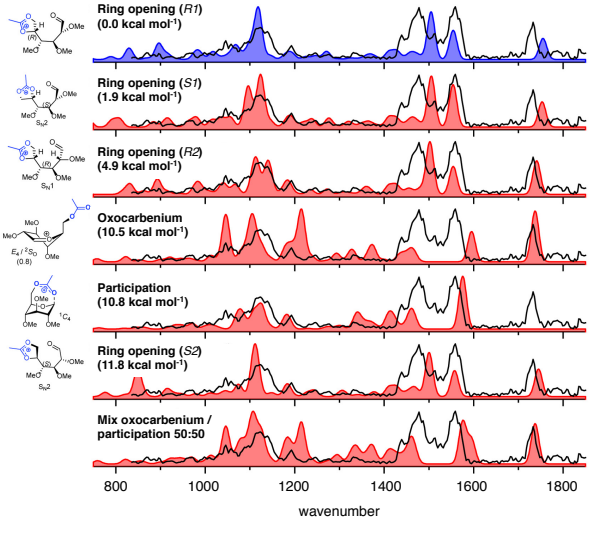


Figure S4. Comparison of the computed IR-spectra of low energy structures (filled) with the measured IR-ion spectrum (black line) of the m/z = 247 CID fragment of compound **3** (top structure). The computed IR-spectrum in blue was assigned as best match with the measured spectrum.

3-*O*-Acetyl-2,4,6-tri-*O*-methyl-manno-D-pyranosyl cation

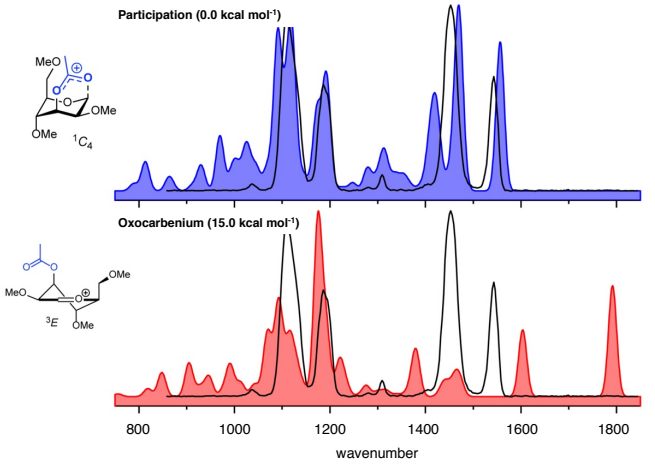


Figure S5. Comparison of the computed IR-spectra of low energy structures (filled) with the measured IR-ion spectrum (black line) of the m/z = 247 CID fragment of compound **4** (top structure). The computed IR-spectrum in blue was assigned as best match with the measured spectrum.

4-*O*-Acetyl-2,3,6-tri-*O*-methyl-manno-D-pyranosyl cation

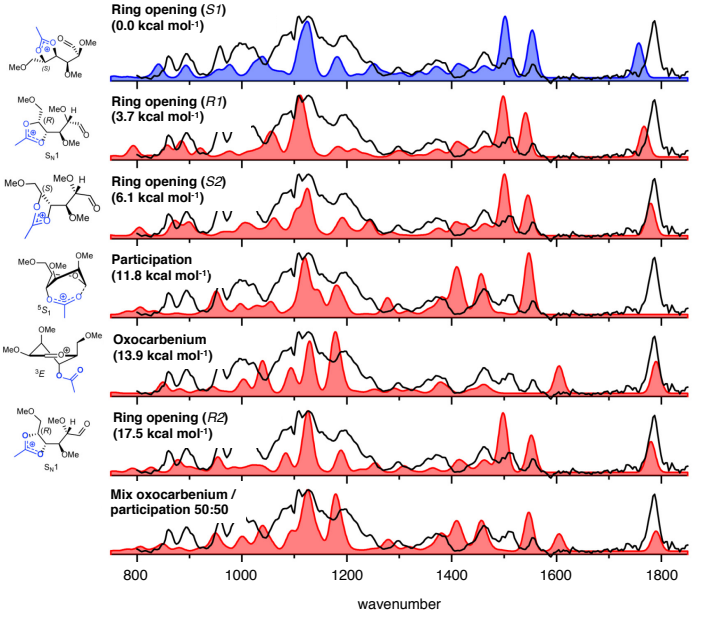


Figure S6. Comparison of the computed IR-spectra of low energy structures (filled) with the measured IR-ion spectrum (black line) of the m/z = 247 CID fragment of compound **5** (top structure). The computed IR-spectrum in blue was assigned as best match with the measured spectrum.

6-*O*-Acetyl-2,3,4-tri-*O*-methyl-manno-D-pyranosyl cation

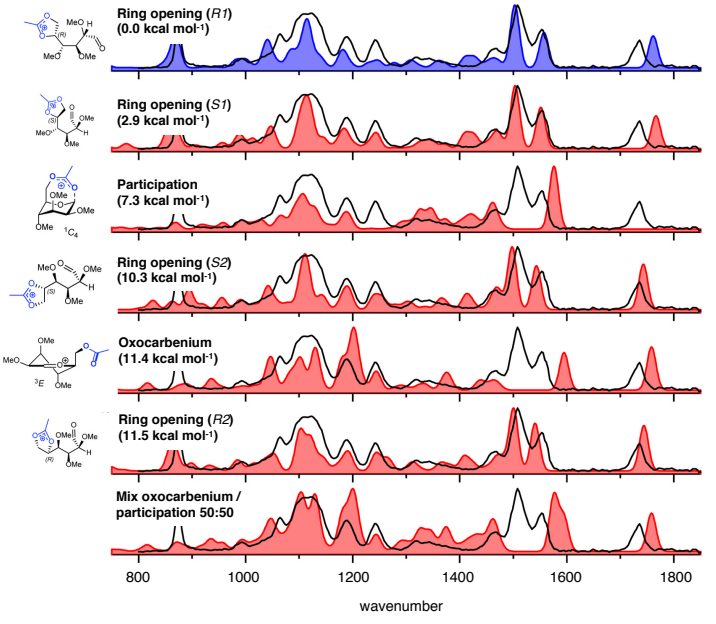


Figure S7. Comparison of the computed IR-spectra of low energy structures (filled) with the measured IR-ion spectrum (black line) of the m/z = 247 CID fragment of compound **6** (top structure). The computed IR-spectrum in blue was assigned as best match with the measured spectrum.

3-*O*-Acetyl-2,4,6-tri-*O*-methyl-galacto-D-pyranosyl cation

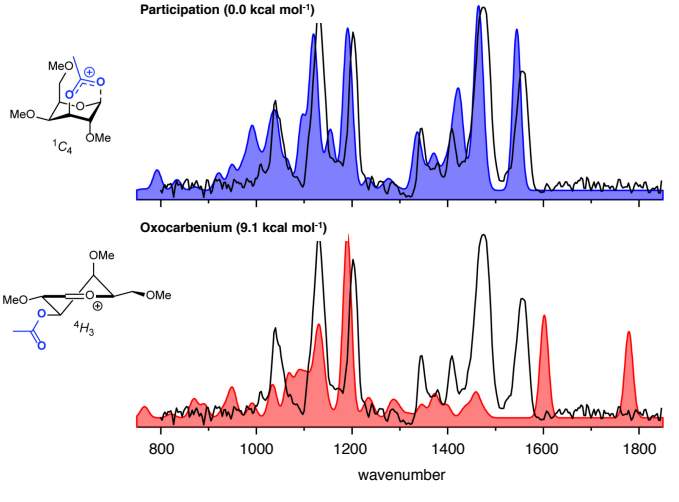


Figure S8. Comparison of the computed IR-spectra of low energy structures (filled) with the measured IR-ion spectrum (black line) of the m/z = 247 CID fragment of compound **7** (top structure). The computed IR-spectrum in blue was assigned as best match with the measured spectrum.

4-*O*-Acetyl-2,3,6-tri-*O*-methyl-galacto-D-pyranosyl cation

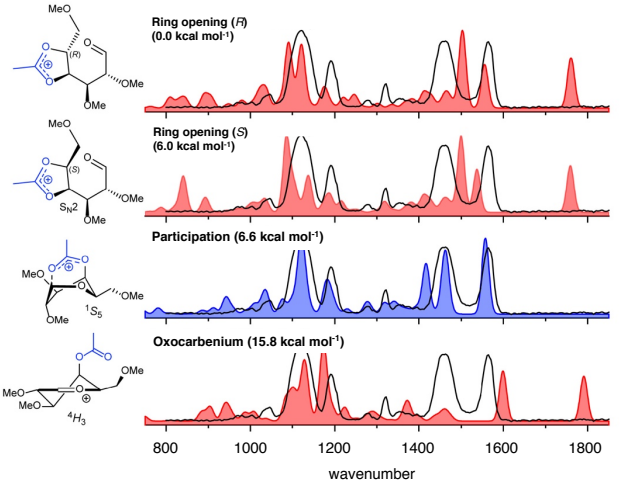


Figure S9. Comparison of the computed IR-spectra of low energy structures (filled) with the measured IR-ion spectrum (black line) of the m/z = 247 CID fragment of compound **8** (top structure). The computed IR-spectrum in blue was assigned as best match with the measured spectrum.

6-*O*-Acetyl-2,3,4-tri-*O*-methyl-galacto-D-pyranosyl cation

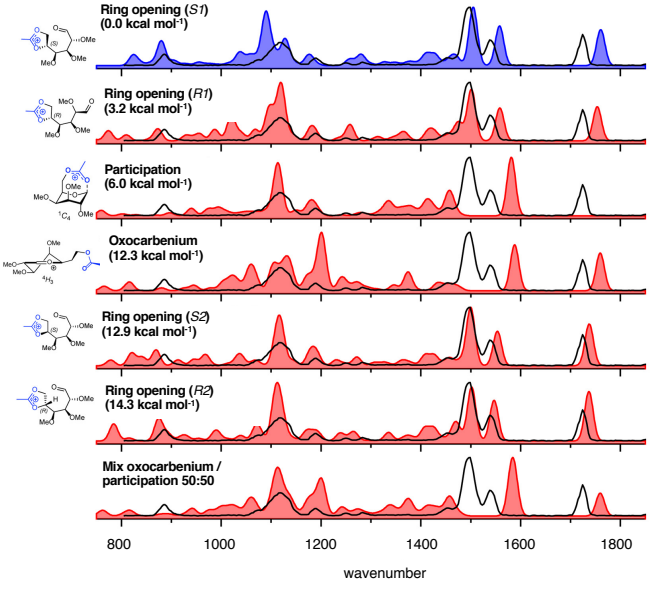


Figure S10. Comparison of the computed IR-spectra of low energy structures (filled) with the measured IR-ion spectrum (black line) of the m/z = 247 CID fragment of compound **9** (top structure). The computed IR-spectrum in blue was assigned as best match with the measured spectrum.

3-*O*-Benzoyl-2,4,6-tri-*O*-benzyl-manno-D-pyranosyl cation

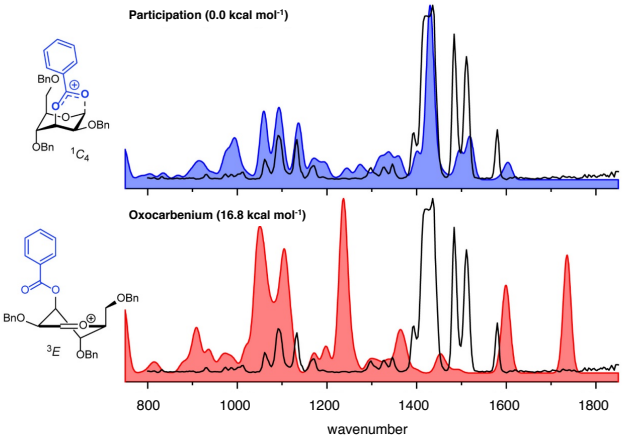


Figure S11. Comparison of the computed IR-spectra of low energy structures (filled) with the measured IR-ion spectrum (black line) of the m/z = 537 CID fragment of compound **13** (top structure). The computed IR-spectrum in blue was assigned as best match with the measured spectrum.

4-*O*-Benzoyl-2,3,6-tri-*O*-benzyl-manno-D-pyranosyl cation

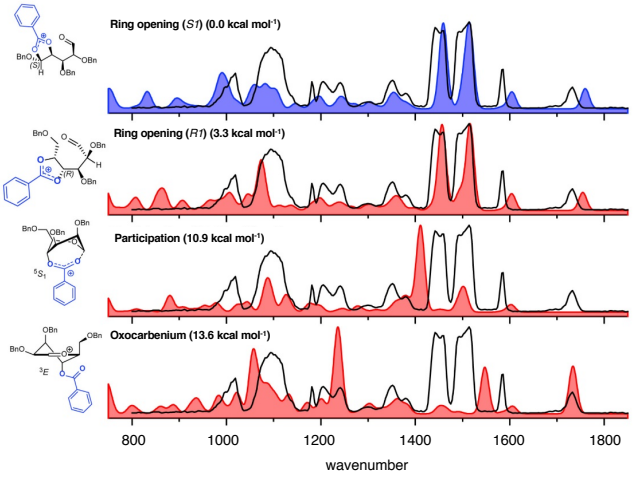


Figure S12. Comparison of the computed IR-spectra of low energy structures (filled) with the measured IR-ion spectrum (black line) of the m/z = 537 CID fragment of compound **14** (top structure). The computed IR-spectrum in blue was assigned as best match with the measured spectrum.

6-*O*-Benzoyl-2,3,4-tri-*O*-benzyl-manno-D-pyranosyl cation

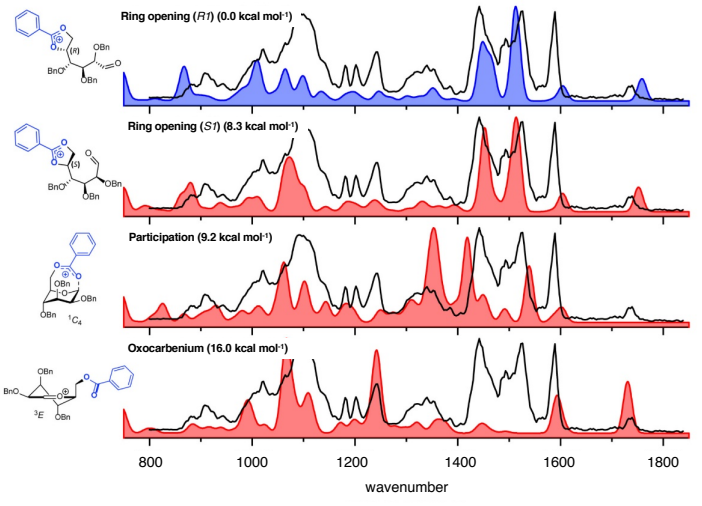


Figure S13. Comparison of the computed IR-spectra of low energy structures (filled) with the measured IR-ion spectrum (black line) of the m/z = 537 CID fragment of compound **15** (top structure). The computed IR-spectrum in blue was assigned as best match with the measured spectrum.

Organic synthesis

General experimental procedures • All chemicals (Merck, Sigma-Aldrich, Alfa Aesar, Honeywell, Boom and Merck KGaA) were of commercial grade and were used as received unless stated otherwise. Dichloromethane, tetrahydrofuran and toluene were stored over activated 4 Å molecular sieves (beads, 8-12 mesh, Sigma-Aldrich). Before use traces of water present in the donor, diphenyl sulfoxide (Ph2SO) and tri-*tert*-butylpyrimidine (TTBP) were removed by co-evaporation with dry toluene. The acceptors used in the model glycosylation reactions (ethanol, 2-fluoroethanol, 2,2-difluoroethanol and 2,2,2,-trifluoroethanol, 1,1,1,3,3,3-hexafluoro-2-propanol) were stored in stock solutions (DCM, 0.5 M) over activated 3 Å molecular rods (rods, size 1/16 in., Sigma Aldrich). Trifluoromethanesulfonic anhydride (Tf_2O) was distilled over P_2O_5 and stored at –20 °C under a nitrogen atmosphere. Deuterated chloroform was stored over activated 3 Å molecular rods (rods, size 1/16 in., Sigma Aldrich) and potassium carbonate. Flash column chromatography was performed on silica gel 60 Å (0.04 – 0.063 mm, Screening Devices B.V.). Size exclusion chromatography was performed on SephadexTM (LH-20, GE Healthcare Life Sciences) by isocratic elution with DCM:MeOH (1:1, v:v). TLC analysis was performed on TLC Silica gel 60 (Kieselgel 60 F254, Merck) with UV detection (254 nm) and by spraying with 20% H_2SO_4 in ethanol followed by charring at ± 260 °C or by spraying with a solution of $(NH_4)_6Mo_7O_{24}{\cdot}H_2O$ (25 g/L) and $(NH_4)_4Ce(SO_4)_4{\cdot}2H_2O$ (10 g/L) in 10% sulfuric acid in water followed by charring at ± 260 °C. TLC-MS analysis was performed on a Camag TLC-MS Interface coupled with an API165 (SCIEX) mass spectrometer (eluted with *tert*-butylmethylether/EtOAc/MeOH, 5/4/1, v/v/v +0.1% formic acid, flow rate 0.12 mL/min). High-resolution mass spectra (HRMS) were recorded on a Waters Synapt G2-Si (TOF) equipped with an electrospray ion source in positive mode (source voltage 3.5 kV) and an internal lock mass LeuEnk ($M+H^+$ = 556.2771) or on a Thermo Finnigan LTQ Orbitrap mass spectrometer equipped with an electrospray ion source in positive mode (source voltage 3.5 kV, sheath gas flow 10, capillary temperature 275 °C) with resolution R=60.000 at m/z=400 (mass range = 150-4000). Amberlite resin (Sigma Aldrich Amberlite IR120 H^+ form or Amberlite IRA-67 free base) was pre-washed with MeOH. ^1H and ^{13}C NMR spectra were recorded on a Bruker AV-400 NMR instrument (400 and 101 MHz respectively), a Bruker AV-500 NMR instrument (500 and 126 MHz respectively), a Bruker AV-600 NMR instrument (600 and 151 MHz respectively) or a Bruker AV-850 NMR instrument (850 and 214 MHz respectively. All samples were measured in $CDCl_3$, unless stated otherwise. Chemical shifts (δ) are given in ppm relative to tetramethylsilane as internal standard or the residual signal

of the deuterated solvent. Coupling constants (*J*) are given in Hz. To get better resolution of signals with small coupling constants or overlapping signals a gaussian window function (LB = ± –1 and GB = ± 0.5) was used on the ^{1}H NMR spectrum. All given ^{13}C APT spectra are proton decoupled. NMR peak assignment was accomplished using COSY, HSQC. If necessary, an additional NOESY, HMBC, and HMBC-gated experiment were used to further elucidate the structure. Stereochemical product ratios were based on integration of ^{1}H NMR (crude and purified). IR spectra were recorded on a Shimadzu FTIR-8300 IR spectrometer and are reported in cm^{-1}. Specific rotations were measured on an Anton Paar Polarimeter MCP 100 in $CHCl_3$ (10 mg/mL) at 589 nm, unless stated otherwise.

General procedure IV: acetylation procedure • To a solution of the glycoside in pyridine (0.10 M), Ac_2O (10 eq.) and cat. DMAP was added. The mixture was stirred to completion before being concentrated *in vacuo*. The resulting crude was dissolved in EtOAc and washed with 1 M aq. HCl solution, sat. aq. $NaHCO_3$ and brine. The organic layer was dried and the resulting solvent evaporated under reduced pressure to obtain the acetylated sugar.

General procedure V: methylation procedure • To a solution of the glycoside in DMF (0.20 M), NaH (60 wt% in mineral oil, 1.5 eq. per hydroxyl) and MeI (1.1 eq. per hydroxyl group) were added at room temperature under inert atmosphere. The mixture was allowed to stir to completion after which it was quenched by dropwise addition of methanol. The resulting suspension was taken up in diethyl ether and washed once with 5% aq. LiCl solution and brine. The resulting aqueous layer was extracted once with DCM. The combined organic layers were dried ($MgSO_4$), filtered and conc. *in vacuo*. The resulting residue was purified by crystallization or silica column chromatography.

General procedure VI: *S*-oxidation procedure • Based on the protocol by Gómez *et al.*[55], a solution of the thioglycoside in DCM (0.05 mM) was cooled to –78 °C under inert atmosphere and then *m*-CPBA (1.1 eq., 75 wt%) was added. The reaction was stirred for 3 h, diluted with DCM (30 mL) and washed with 10% aq. $Na_2S_2O_3$ solution, sat. aq. $NaHCO_3$ and brine. The organic layer was dried ($MgSO_4$), filtered, concentrated *in vacuo*. The resulting crude mixture was used directly for IRMPD experiments.

General procedure VII: pre-activation Tf_2O/Ph_2SO based *O*-glycosylation • A solution of the donor (100 µmol), Ph_2SO (26 mg, 130 µmol, 1.3 eq.) and TTBP (62 mg, 250 µmol, 2.5 eq.) in DCM (2 mL, 0.05 M) was stirred over activated 3 Å molecular sieves (rods, size 1/16 in., Sigma-Aldrich) for 30 min under an atmosphere of N_2. The solution was cooled to –80 °C and Tf_2O (22 µl, 130 µmol, 1.3 eq.) was slowly added to the reaction mixture. The reaction mixture was allowed to warm to –60 °C in approximately 45 min, followed by cooling to –80 °C and the addition of the acceptor (200 µmol, 2 eq.) in DCM (0.4 mL, 0.5 M). The reaction was allowed to warm up to –60 °C and stirred for an additional 4-18 h at this temperature till full reaction completion was observed. The reaction was quenched with sat. aq. $NaHCO_3$ at –60 °C and diluted with DCM (5 mL). The resulting solution was washed with H_2O and brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification by column chromatography yielded the corresponding *O*-coupled glycoside.

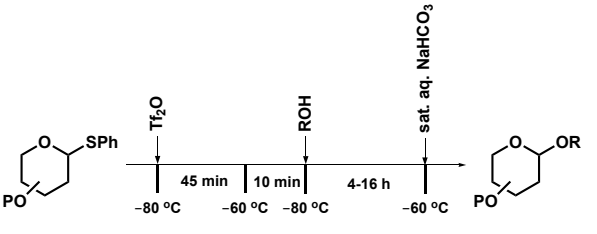
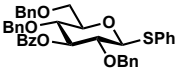
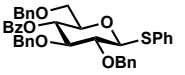


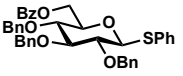
Figure S14. Schematic representation of the reaction procedure during pre-activation Ph_2SO/Tf_2O mediated glycosylation.



Phenyl 3-*O*-benzoyl-2,4,6-tri-*O*-benzyl-1-thio-β-D-glucopyranoside (10). The title compound was prepared according to literature procedure.[15] ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.00 – 7.91 (m, 2H, CH_{arom}), 7.62 – 7.57 (m, 2H, CH_{arom}), 7.57 – 7.52 (m, 1H, CH_{arom}), 7.44 – 7.24 (m, 10H, CH_{arom}), 7.14 – 7.07 (m, 8H, CH_{arom}), 7.02 (m, 2H, CH_{arom}), 5.58 (t, *J* = 9.2 Hz, 1H, H-3), 4.81 – 4.74 (m, 2H, H-1, C*H*H Bn), 4.64 (d, *J* = 12.0 Hz, 1H, C*H*H Bn), 4.58 – 4.51 (m, 2H, CH*H* Bn, CH*H* Bn), 4.51 – 4.45 (m, 2H, CH_2 Bn), 3.83 (t, *J* = 9.6 Hz, 1H, H-4), 3.80 – 3.73 (m, 2H, H-6, H-6), 3.64 – 3.58 (m, 2H, H-2, H-5); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 165.6 (C=O Bz), 138.2, 137.5, 137.4, 133.7 ($C_{q\text{-}arom}$), 133.2, 132.2, 129.9, 129.1, 128.5, 128.5, 128.4, 128.4, 128.3, 128.2, 127.9, 127.9, 127.8, 127.8, 127.7 (CH_{arom}), 87.6 (C-1), 79.0 (C-2/C-5), 78.7 (C-2/C-5), 78.1 (C-3), 75.9 (C-4), 74.9, 74.6, 73.6 (CH_2 Bn), 68.8 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{40}H_{38}NaO_6S$ 669.22813, found 669.22756.

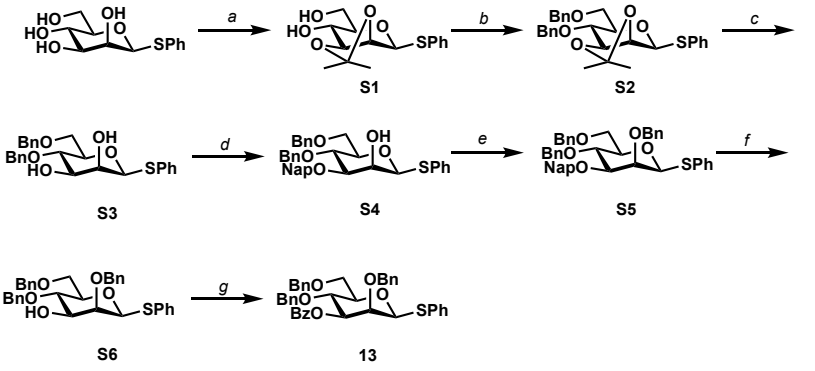


Phenyl 4-*O*-benzoyl-2,3,6-tri-*O*-benzyl-1-thio-β-D-glucopyranoside (11). The title compound was prepared according to literature procedure.[15] ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.23 – 8.18 (m, 1H, CH_{arom}), 8.03 – 7.95 (m, 2H, CH_{arom}), 7.76 – 7.70 (m, 1H, CH_{arom}), 7.67 – 7.63 (m, 2H, CH_{arom}), 7.62 – 7.55 (m, 2H, CH_{arom}), 7.47 (ddd, *J* = 8.1, 6.2, 1.6 Hz, 4H, CH_{arom}), 7.43 – 7.34 (m, 3H, CH_{arom}), 7.33 – 7.23 (m, 8H, CH_{arom}), 7.19 – 7.08 (m, 4H, CH_{arom}), 5.38 – 5.31 (m, 1H, H-4), 4.96 (d, *J* = 10.3 Hz, 1H, C*H*H Bn), 4.85 – 4.76 (m, 3H, H-1, C*H*H Bn, CH*H* Bn), 4.68 (d, *J* = 11.0 Hz, 1H, CH*H* Bn), 4.53 (s, 2H, CH_2 Bn), 3.88 (t, *J* = 9.0 Hz, 1H, H-3), 3.82 (dt, *J* = 10.1, 4.5 Hz, 1H, H-5), 3.72 – 3.61 (m, 3H, H-2, 2x H-6); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 165.5 (C=O Bz), 138.0, 138.0, 137.8 ($C_{q\text{-}arom}$), 134.7 (CH_{arom}), 133.7 ($C_{q\text{-}arom}$), 133.4, 132.0, 130.7, 129.9 (CH_{arom}), 129.7 ($C_{q\text{-}arom}$), 129.1, 129.0, 128.6, 128.6, 128.4, 128.4, 128.1, 128.1, 127.8, 127.7, 127.6 (CH_{arom}), 87.7 (C-1), 83.9 (C-3), 80.8 (C-2), 78.0 (C-5), 75.7, 75.6, 73.7 (CH_2 Bn), 71.4 (C-4), 69.9 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{40}H_{38}NaO_6S$ 669.22813, found 669.22815.

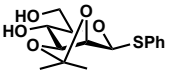


Phenyl 6-*O*-benzoyl-2,3,4-tri-*O*-benzyl-1-thio-β-D-glucopyranoside (12). The title compound was prepared according to literature procedure.[56] ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.07 – 8.00 (m, 2H, CH_{arom}), 7.65 – 7.56 (m, 1H, CH_{arom}), 7.58 – 7.51 (m, 2H, CH_{arom}), 7.51 – 7.42 (m, 2H, CH_{arom}), 7.45 – 7.38 (m, 2H, CH_{arom}), 7.40 – 7.22 (m, 13H, CH_{arom}), 7.25 – 7.16 (m, 1H, CH_{arom}), 7.16 – 7.10 (m, 2H, CH_{arom}), 4.97 – 4.83 (m, 4H, 2x C*H*H Bn, CH_2 Bn), 4.75 (d, *J* = 10.2 Hz, 1H, CH*H* Bn), 4.72 – 4.64 (m, 2H, H-1, H-6), 4.62 (d, *J* = 10.8 Hz, 1H, CH*H* Bn), 4.44 (dd, *J* = 11.9, 4.9 Hz, 1H, H-6), 3.77 (t, *J* = 8.6 Hz, 1H, H-3), 3.73 – 3.60 (m, 2H, H-4, H-5), 3.53 (dd, *J* = 9.8, 8.7 Hz, 1H, H-2); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 166.2 (C=O Bz), 138.2, 138.0, 137.6, 133.3 ($C_{q\text{-}arom}$), 133.3, 132.4 (CH_{arom}), 130.0 ($C_{q\text{-}arom}$), 129.9, 129.0, 128.7, 128.6, 128.5, 128.3, 128.2, 128.2, 128.1, 128.1, 128.0, 127.8 (CH_{arom}), 87.4 (C-1), 86.9 (C-3), 80.8 (C-2), 77.7 (C-4), 77.2 (C-5), 76.1, 75.6, 75.3 (CH_2 Bn), 63.7 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{40}H_{38}NaO_6S$ 669.22813, found 669.22788.

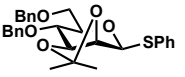
Preparation of donor 13



Scheme S1. Synthesis of donor **13**. *Reagents and conditions:* a) *i.* 2,2-dimethoxypropane, acetone, $Sc(OTf)_3$, *ii.* AcOH, MeOH, DCM, reflux, **S1**: 56%; b) BnBr, NaH, DMF, **S2**: 92%; c) *p*TsOH, MeOH, 50 °C, **S3**: 99%; d) *i.* di-*n*-butyltin(IV) oxide, toluene reflux, *ii.* NapBr, CsF, DMF, **S4**: 79%; e) BnBr, NaH, DMF, **S5**: 76%; f) DDQ, DCM, H_2O, **S6**: 62%; g) BzCl, pyridine, **13**: *quant.*

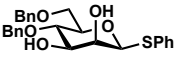


Phenyl 2,3-*O*-isopropylidene-1-thio-β-D-mannopyranoside (S1). According to a modified literature procedure.[57] Phenyl 1-thio-β-D-mannopyranoside[42] (4.6 g, 17.0 mmol) was suspended in 80 mL 2,2-dimethoxypropane and 25 mL acetone. 50 mg $Sc(OTf)_3$ was added, and the suspension was stirred until everything was dissolved. The solution was concentrated to 25% of the original volume, 50 mL acetone was added and the reaction was stirred for 1 h, before being quenched with 0.3 mL triethylamine and concentrated under reduced pressure. The residue was dissolved in DCM and washed with water. The organic phase was dried with $MgSO_4$ and concentrated to give the crude diisopropylidene as yellowish powder, which was used without further purification. The crude product was dissolved in 5:13:7 DCM/MeOH/AcOH and heated to a vigorous reflux until the title compound was the major product together with a few percent unreacted starting material. The reaction mixture was diluted with toluene, concentrated under reduced pressure and co-evaporated with toluene two more times. The residue was purified over silica (30% → 50% acetone in pentane) yielding the title compound (2.9 g, 9.5 mmol, 56%) as off-white powder. TLC: R_f 0.35 (pentane:acetone, 60:40, v:v); $[\alpha]_D^{25}$ –114.1° (*c* 0.27, $CHCl_3$); IR (thin film, cm^{-1}): 733, 1066, 1090, 1217, 1483, 3449; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.53 – 7.48 (m, 2H, CH_{arom}), 7.35 – 7.26 (m, 3H, CH_{arom}), 5.11 (d, *J* = 2.2 Hz, 1H, H-1), 4.45 (dd, *J* = 5.5, 2.2 Hz, 1H, H-2), 4.10 (dd, *J* = 7.2, 5.5 Hz, 1H, H-3), 3.96 – 3.89 (m, 1H, H-6), 3.86 – 3.78 (m, 2H, H-4, H-6), 3.32 (ddd, *J* = 9.7, 5.1, 3.6 Hz, 1H, H-5), 2.89 (d, *J* = 3.7 Hz, 1H, 4-OH), 2.31 (t, *J* = 6.6 Hz, 1H, 6-OH), 1.59 (s, 3H, CH_3 isoprop), 1.42 (s, 3H, CH_3 isopropylidene); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 134.7 ($C_{q\text{-}arom}$), 130.9, 129.3, 127.7 (CH_{arom}), 111.0 (C_q isoprop), 84.2 (C-1), 80.3 (C-3), 78.5 (C-5), 76.1 (C-2), 70.1 (C-4), 62.8 (C-6), 28.2, 26.5 (CH_3 isoprop); HRMS: $[M+Na]^+$ calcd for $C_{15}H_{20}NaO_5S$ 335.09237, found 335.09217.

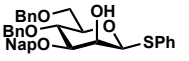


Phenyl 4,6-di-*O*-benzyl-2,3-*O*-isopropylidene-1-thio-β-D-mannopyranoside (S2). S1 (2.94 g, 9.41 mmol) was dissolved in DMF, and benzyl bromide (3.4 mL, 28.2 mmol, 3 eq.) and sodium hydride (60% dispersion in mineral oil, 1.1 g, 28.2 mmol, 3 eq) were added. When TLC shows full conversion, the reaction mixture was quenched with water and extracted twice with diethyl ether. Combined organic phases were dried with $MgSO_4$ and concentrated under reduced pressure. The residue was purified over silica (5% → 10% acetone in pentane) yielding the title compound (4.3 g, 8.6 mmol, 92%) as white powder. TLC: R_f 0.25 (pentane:acetone, 90:10, v:v); $[\alpha]_D^{25}$ –84.0° (*c* 0.43, $CHCl_3$); IR (thin film, cm^{-1}): 695, 736, 1059, 1216, 1380; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.58 – 7.53 (m, 2H, CH_{arom}), 7.35 – 7.18 (m, 13H, CH_{arom}), 5.07 (d, *J* = 2.1 Hz, 1H, H-1), 4.81 (d, *J* = 11.6 Hz, 1H, C*H*H Bn), 4.58 (d, *J* = 11.6 Hz, 1H, CH*H* Bn), 4.55

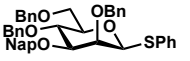
(s, 2H, CH_2 Bn), 4.46 (dd, *J* = 5.8, 2.1 Hz, 1H, H-2), 4.35 – 4.28 (m, 1H, H-3), 3.85 (dd, *J* = 10.2, 1.8 Hz, 1H, H-6), 3.70 – 3.63 (m, 1H, H-6), 3.63 – 3.56 (m, 2H, H-4, H-5), 1.57 (s, 3H, CH_3 isopropylidene), 1.42 (s, 3H, CH_3 isopropylidene); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 138.5, 138.0, 135.5 ($C_{q\text{-}arom}$), 130.5, 129.1, 128.5, 128.4, 128.1, 127.9, 127.8, 127.6, 127.2 (CH_{arom}), 110.7 ($C_{q\text{-}arom}$ isopropylidene), 84.4 (C-1), 79.8 (C-3), 78.5 (C-4), 76.1 (C-2), 75.4 (C-5), 73.6, 72.7 (CH_2 Bn), 70.4 (C-6), 27.9, 26.4 (CH_3 isopropylidene); HRMS: $[M+NH_4]^+$ calcd for $C_{29}H_{36}NO_5S$ 515.23087, found 515.23058.



Phenyl 4,6-di-*O*-benzyl-1-thio-β-D-mannopyranoside (S3). S2 (4.2 g, 8.5 mmol) and *p*TsOH (162 mg, 0.853 mmol, 0.1 eq) were dissolved in 75 mL methanol and heated to 50 °C. When the reaction was complete, the title compound was precipitated from the solution. Triethylamine (0.24 mL, 1.71 mmol, 0.2 eq.) was added and the mixture was cooled to –30 °C. The product was collected by filtration and washed with a few mL of very cold methanol, yielding the title compound (2.7 g, 6.0 mmol, 71%) as fluffy white solid (mp: 146 °C). The concentrated mother liquor contained ca. 1.1 g (28%) of slightly impure product of sufficient quality to use in subsequent reactions. TLC: R_f 0.15 (pentane:EtOAc, 60:40, v:v); $[\alpha]_D^{25}$ –114.1° (*c* 0.27, $CHCl_3$); IR (thin film, cm^{-1}): 733, 1066, 1217, 3449 ; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.61 – 7.46 (m, 2H, CH_{arom}), 7.38 – 7.16 (m, 13H, CH_{arom}), 4.84 (d, *J* = 1.1 Hz, 1H, H-1), 4.78 (d, *J* = 11.3 Hz, 1H, C*H*H Bn), 4.66 – 4.60 (m, 2H, C*H*H Bn, CH*H* Bn), 4.56 (d, *J* = 11.9 Hz, 1H, CH*H* Bn), 4.17 – 4.10 (m, 1H, H-2), 3.82 (dd, *J* = 10.9, 2.0 Hz, 1H, H-6), 3.75 (dd, *J* = 10.9, 5.1 Hz, 1H, H-6), 3.72 – 3.65 (m, 2H, H-3, H-4), 3.47 (dq, *J* = 7.4, 3.1, 2.5 Hz, 1H, H-5), 2.72 (d, *J* = 5.8 Hz, 1H, 2-OH), 2.61 – 2.53 (m, 1H, 3-OH); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 138.2, 138.2, 134.4 ($C_{q\text{-}arom}$), 131.3, 129.2, 128.7, 128.5, 128.2, 128.1, 128.0, 127.8, 127.6 (CH_{arom}), 87.1 (C-1), 79.6 (C-5), 75.8, 75.4 (C-3/C-4), 75.0, 73.7 (CH_2 Bn), 72.7 (C-2), 69.3 (C-5); HRMS: $[M+NH_4]^+$ calcd for $C_{26}H_{32}NO_5S$ 470.19957, found 470.19932.

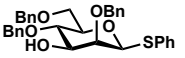


Phenyl 3-*O*-(2-naphthyl)methyl-4,6-di-*O*-benzyl-1-thio-β-D-mannopyranoside (S4). Diol **S3** (3.82 g, 8.44 mmol) and di-*n*-butyltin oxide (2.7 g, 11.0 mmol, 1.3 eq.) were refluxed in toluene for 2 h, while removing water using a Dean-Stark setup. The mixture was cooled to room temperature and concentrated under reduced pressure. The residue was dissolved in DMF, CsF (1.67 g, 11.0 mmol, 1.3 eq) and napthyl bromide (2.43 g, 11.0 mmol, 1.3 eq) were added. After overnight reaction, water and diethyl ether were added, causing the product to precipitate as white solid (3.36 g) Silica chromatography of the concentrated organic phase yielded an additional 590 mg product, bringing the total yield to 3.95 g (6.7 mmol, 79%). TLC: R_f 0.40 ($CHCl_3$:acetone, 90:10, v:v); $[\alpha]_D^{25}$ –32.2° (*c* 1.12, $CHCl_3$); IR (thin film, cm^{-1}):698, 738, 1027, 1074, 1089, 1120; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.85 – 7.72 (m, 4H, CH_{arom}), 7.55 – 7.43 (m, 5H, CH_{arom}), 7.35 – 7.18 (m, 13H, CH_{arom}), 4.93 – 4.87 (m, 2H, 2x C*H*H Bn/Nap), 4.82 (d, *J* = 11.8 Hz, 1H, CH*H* Bn/Nap), 4.79 – 4.78 (m, 1H, H-1), 4.62 – 4.57 (m, 2H, C*H*H Bn/Nap, CH*H* Bn/Nap), 4.54 (d, *J* = 11.9 Hz, 1H, CH*H* Bn/Nap), 4.30 (t, *J* = 2.9 Hz, 1H, H-2), 3.90 – 3.79 (m, 2H, H-4, H-6), 3.72 (dd, *J* = 10.9, 5.9 Hz, 1H, H-6), 3.66 (dd, *J* = 9.0, 3.3 Hz, 1H, H-3), 3.50 (ddd, *J* = 9.8, 5.9, 1.9 Hz, 1H, H-5), 2.72 (d, *J* = 3.0 Hz, 1H, OH); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 138.4, 138.2, 135.0, 135.0, 133.3, 133.2 ($C_{q\text{-}arom}$), 131.0, 129.1, 128.6, 128.5, 128.4, 128.1, 128.1, 127.9, 127.9, 127.9, 127.7, 127.4, 127.0, 126.4, 126.3, 125.9 (CH_{arom}), 86.8 (C-1), 82.6 (C-3), 79.8 (C-5), 75.4 (CH_2 Bn/Nap), 74.4 (C-4), 73.6, 72.1 (CH_2 Bn/Nap), 70.2 (C-4), 69.5 (C-6); HRMS: $[M+NH_4]^+$ calcd for $C_{37}H_{40}NO_5S$ 610.26217, found 610.26172.

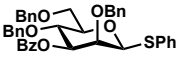


Phenyl 3-*O*-(2-naphthyl)methyl-2,4,6-tri-*O*-benzyl-1-thio-β-D-mannopyranoside (S5). S4 (3.30 g, 5.57 mmol) was dissolved in DMF at 0 °C. Benzyl bromide (0.99 mL, 8.35 mmol, 1.5 eq) and NaH (60% in mineral oil, 334 mg, 8.35 mmol, 1.5 eq) were added and the reaction mixture was allowed to warm to rt. When TLC showed full conversion, the reaction was quenched with water and extracted with diethyl ether. The organic phase was dried with $MgSO_4$ and concentrated under reduced pressure. The residue was purified over silica (15% diethyl ether in pentane) yielding the title compound (2.89 g, 4.2 mmol, 76%) as white solid. TLC: R_f 0.30 (pentane:Et_2O), 80:20, v:v); $[\alpha]_D^{25}$ –40.2° (*c* 0.59, $CHCl_3$); IR (thin film, cm^{-1}): 696, 738, 1026, 1072, 1122; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.85 – 7.76 (m, 3H, CH_{arom}), 7.73 – 7.67 (m, 1H, CH_{arom}), 7.54 – 7.41 (m, 8H, CH_{arom}), 7.38 – 7.15 (m, 17H, CH_{arom}), 5.09 (d, *J* = 11.5 Hz, 1H,

C*H*H Bn/Nap), 4.96 – 4.89 (m, 2H, C*H*H Bn/Nap, CH*H* Bn/Nap), 4.87 (d, *J* = 12.0 Hz, 1H, C*H*H Bn/Nap), 4.82 (d, *J* = 12.0 Hz, 1H, CH*H* Bn/Nap), 4.77 (d, *J* = 1.1 Hz, 1H, H-1), 4.64 – 4.58 (m, 2H, C*H*H Bn/Nap, CH*H* Bn/Nap), 4.55 (d, *J* = 11.7 Hz, 1H, CH*H* Bn/Nap), 4.17 (dd, *J* = 3.0, 1.1 Hz, 1H, H-2), 3.98 (t, *J* = 9.6 Hz, 1H, H-4), 3.86 (dd, *J* = 11.0, 1.9 Hz, 1H, H-6), 3.76 (dd, *J* = 10.9, 6.5 Hz, 1H, H-6), 3.68 (dd, *J* = 9.4, 2.9 Hz, 1H, H-3), 3.54 (ddd, *J* = 9.8, 6.5, 1.9 Hz, 1H, H-5); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 138.6, 138.4, 138.3, 135.8, 135.6, 133.3, 133.1 ($C_{q\text{-arom}}$), 130.6, 129.0, 128.5, 128.4, 128.4, 128.3, 128.1, 128.0, 127.9, 127.8, 127.7, 127.5, 127.1, 126.5, 126.3, 126.1, 125.7 (CH_{arom}), 87.7 (C-1), 84.3 (C-3), 80.2 (C-5), 77.7 (C-2), 75.3, 75.2 (CH_2 Bn/Nap), 75.1 (C-4), 73.6, 72.7 (CH_2 Bn/Nap), 69.9 (C-6); HRMS: $[M+NH_4]^+$ calcd for $C_{44}H_{46}NO_5S$ 700.30967, found 700.30861.

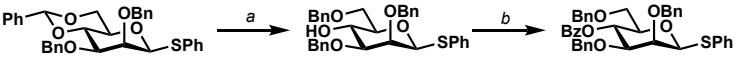


Phenyl 2,4,6-tri-*O*-benzyl-1-thio-β-D-mannopyranoside (S6). S5 (2.86 g, 4.19 mmol) was dissolved in 25mL 9:1 DCM/H_2O. DDQ (1.90 g, 8.38 mmol, 2 eq.) was added and the reaction was stirred at room temperature until TLC showed full conversion. The mixture was diluted with DCM and washed twice with sat. aq. $NaHCO_3$. The organic phase was dried with $MgSO_4$ and concentrated under reduced pressure. The residue was purified over silica (15% acetone in pentane), yielding the title compound (1.40 g, 2.58 mmol, 62%) as white solid. TLC: R_f 0.32 (pentane:acetone, 80:20, v:v); $[\alpha]_D^{25}$ –95.6° (*c* 0.95, $CHCl_3$); IR (thin film, cm^{-1}): 695, 732, 1027, 1062, 1073, 1089, 1452; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.57 – 7.51 (m, 2H, CH_{arom}), 7.48 – 7.44 (m, 2H, CH_{arom}), 7.41 – 7.20 (m, 16H, CH_{arom}), 5.03 (d, *J* = 11.5 Hz, 1H, C*H*H Bn), 4.82 (d, *J* = 1.1 Hz, 1H, H-1), 4.80 – 4.74 (m, 2H, C*H*H Bn, CH*H* Bn), 4.63 (d, *J* = 11.7 Hz, 1H, C*H*H Bn), 4.60 – 4.53 (m, 2H, 2x CH*H* Bn), 4.05 (dd, *J* = 3.5, 1.1 Hz, 1H, H-2), 3.86 (dd, *J* = 10.9, 2.0 Hz, 1H, H-6), 3.76 (dd, *J* = 11.0, 6.3 Hz, 1H, H-6), 3.73 – 3.69 (m, 1H, H-3), 3.65 (t, *J* = 9.3 Hz, 1H, H-4), 3.49 (ddd, *J* = 9.4, 6.1, 2.0 Hz, 1H, H-5), 2.18 (d, *J* = 7.8 Hz, 1H, OH); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 138.5, 138.2, 138.1, 135.4 ($C_{q\text{-arom}}$), 130.7, 129.1, 128.7, 128.6, 128.4, 128.4, 128.2, 128.2, 128.0, 128.0, 127.6, 127.3 (CH_{arom}), 87.8 (C-1), 80.7 (C-2), 79.8 (C-5), 76.5 (C-4), 76.3 (CH_2 Bn), 75.8 (C-3), 74.9, 73.6 (CH_2 Bn), 69.8 (C-6); HRMS: $[M+NH_4]^+$ calcd for $C_{33}H_{38}NO_5S$ 560.24652, found 560.24624.



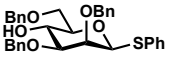
Phenyl 3-*O*-benzoyl-2,4,6-tri-*O*-benzyl-1-thio-β-D-mannopyranoside (13). S6 (1.4 g, 2.5 mmol) and benzoyl chloride (0.44 mL, 3.75 mmol, 1.5 eq) were dissolved in 5 mL pyridine. When TLC shows full conversion, the reaction mixture was diluted with ethyl acetate and washed twice with 1 M aq. HCl and once with sat. aq. $NaHCO_3$. The organic phase was dried with $MgSO_4$ and concentrated under reduced pressure. The residue was purified over silica (5% → 10% acetone in pentane), yielding the title compound in *quantitative* yield as colorless oil. TLC: R_f 0.28 (pentane:acetone, 90:10, v:v); $[\alpha]_D^{25}$ –74.7° (*c* 1.33, $CHCl_3$); IR (thin film, cm^{-1}): 695, 713, 733, 1025, 1062, 1089, 1266, 1452, 17165, 1718; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.03 – 7.97 (m, 2H, CH_{arom}), 7.61 – 7.52 (m, 3H, CH_{arom}), 7.46 – 7.41 (m, 2H, CH_{arom}), 7.35 (ddt, *J* = 8.0, 4.2, 2.3 Hz, 4H, CH_{arom}), 7.33 – 7.28 (m, 3H, CH_{arom}), 7.27 – 7.20 (m, 7H, CH_{arom}), 7.16 (dd, *J* = 5.0, 1.9 Hz, 3H, CH_{arom}), 7.10 – 7.05 (m, 2H, CH_{arom}), 5.26 (dd, *J* = 9.9, 3.2 Hz, 1H, H-3), 4.96 (d, *J* = 1.1 Hz, 1H, H-1), 4.82 (d, *J* = 11.4 Hz, 1H, C*H*H Bn), 4.74 (d, *J* = 11.4 Hz, 1H, CH*H* Bn), 4.71 – 4.64 (m, 2H, 2x C*H*H Bn), 4.60 – 4.54 (m, 2H, 2x CH*H* Bn), 4.37 (dd, *J* = 3.3, 1.1 Hz, 1H, H-2), 4.19 (t, *J* = 9.8 Hz, 1H, H-4), 3.89 – 3.78 (m, 2H, 2x H-6), 3.64 (ddd, *J* = 9.7, 5.4, 2.2 Hz, 1H, H-5); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 165.9 (C=O Bz), 138.5, 137.8, 137.7, 135.2 ($C_{q\text{-arom}}$), 133.5, 131.2, 129.9 (CH_{arom}), 129.6 ($C_{q\text{-arom}}$), 129.1, 128.7, 128.4, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.6, 127.4 (CH_{arom}), 87.8 (C-1), 80.1 (C-5), 78.6 (C-2), 77.9 (C-3), 75.9, 75.2, 73.7 (CH_2 Bn), 73.4 (C-4), 69.6 (C-6); HRMS: $[M+NH_4]^+$ calcd for $C_{40}H_{42}NO_6S$ 664.27274, found 669.27257.

Preparation of donor 14

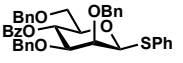


S7 **14**

Scheme S2. Synthesis of donor **14**. *Reagents and conditions:* a) TES-H, TFA, DCM, 0 °C, **S7**: 71%; b) BzCl, pyridine, **14**: 97%.

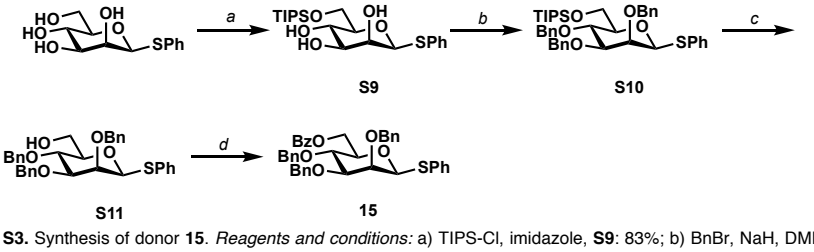


Phenyl 2,3,6-tri-*O*-benzyl-1-thio-β-D-mannopyranoside (S7). Phenyl 2,3-di-O-benzyl-4,6-O-benzylidene-1-thio-β-D-mannopyranoside[42] (2.00 g, 3.70 mmol) was dissolved in dichloromethane and cooled to 0 °C, after which TES-H (5.9 mL, 37.0 mmol, 10 eq) and TFA (2.8 mL, 37.0 mmol, 10 eq) were added. When TLC shows full conversion, the reaction is quenched with sat. aq. $NaHCO_3$ and diluted with DCM. Phases were separated and the aquatic phase was extracted with DCM. Combined organic phases were dried with $MgSO_4$ and concentrated under reduced pressure. The residue was purified over silica (15% acetone in pentane), yielding the title compound (1.42 g, 2.62 mmol, 71%) as waxy white solid. TLC: R_f 0.20 (pentane:EtOAc, 85:15, v:v); $[\alpha]_D^{25}$ –71.6° (*c* 0.83, $CHCl_3$); IR (thin film, cm^{-1}): 695, 732, 1026, 1064, 1128; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.53 – 7.44 (m, 4H, CH_{arom}), 7.38 – 7.25 (m, 13H, CH_{arom}), 7.25 – 7.18 (m, 3H, CH_{arom}), 4.98 (d, *J* = 11.4 Hz, 1H, C*H*H Bn), 4.86 (d, *J* = 11.4 Hz, 1H, CH*H* Bn), 4.80 (d, *J* = 1.1 Hz, 1H, H-1), 4.73 (d, *J* = 11.8 Hz, 1H, C*H*H Bn), 4.59 (d, *J* = 11.8 Hz, 1H, CH*H* Bn), 4.57 (s, 2H, CH_2 Bn), 4.15 (dd, *J* = 3.0, 1.1 Hz, 1H, H-2), 4.06 (td, *J* = 9.5, 1.9 Hz, 1H, H-4), 3.90 (dd, *J* = 10.4, 4.1 Hz, 1H, H-6), 3.80 (dd, *J* = 10.4, 6.4 Hz, 1H, H-6), 3.51 (ddd, *J* = 9.4, 6.3, 4.0 Hz, 1H, H-5), 3.44 (dd, *J* = 9.4, 3.0 Hz, 1H, H-3), 2.71 (d, *J* = 2.0 Hz, 1H, 4-OH); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 138.2, 137.9, 135.6 ($C_{q\text{-}arom}$), 130.8, 129.0, 128.7, 128.5, 128.5, 128.3, 128.1, 127.9, 127.9, 127.8, 127.7, 127.3 (CH_{arom}), 87.9 (C-1), 83.6 (C-3), 79.2 (C-5), 76.8 (C-2), 75.2, 73.8, 72.4 (CH_2 Bn), 71.2 (C-6), 68.7 (C-4); HRMS: $[M+NH_4]^+$ calcd for $C_{33}H_{38}NO_5S$ 560.24652, found 560.24596

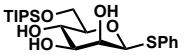


Phenyl 4-*O*-benzoyl-2,3,6-tri-*O*-benzyl-1-thio-β-D-mannopyranoside (14). S7 (1.40 g, 2.58 mmol) was dissolved in 5 mL pyridine with benzoyl chloride (0.45 mL, 3.87 mmol, 1.5 eq.) When TLC shows full conversion, the reaction mixture was diluted with ethyl acetate and washed with 1 M aq. HCl and sat. aq. $NaHCO_3$. The organic phase was dried and concentrated. The residue was purified over silica (10 → 15% EA in pentane) yielding the title compound (1.62 g, 2.51 mmol, 97%) as white amorphous solid. TLC: R_f 0.22 (pentane:EtOAc, 85:15, v:v); $[\alpha]_D^{25}$ –69.1° (*c* 1.01, $CHCl_3$); IR (thin film, cm^{-1}): 695, 711, 1027, 1068, 1109, 1266, 1452, 1724; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.00 – 7.91 (m, 2H, CH_{arom}), 7.61 – 7.47 (m, 6H, CH_{arom}), 7.43 (t, *J* = 7.8 Hz, 2H, CH_{arom}), 7.38 – 7.33 (m, 2H, CH_{arom}), 7.32 – 7.28 (m, 1H, CH_{arom}), 7.23 – 7.12 (m, 13H, CH_{arom}), 5.66 (t, *J* = 9.6 Hz, 1H, H-4), 5.08 (d, *J* = 11.5 Hz, 1H, C*H*H Bn), 4.87 (d, *J* = 11.6 Hz, 1H, CH*H* Bn), 4.84 (d, *J* = 1.1 Hz, 1H, H-1), 4.63 (d, *J* = 12.2 Hz, 1H, C*H*H Bn), 4.52 – 4.48 (m, 2H, C*H*H Bn, CH*H* Bn), 4.43 (d, *J* = 11.4 Hz, 1H, CH*H* Bn), 4.22 (dd, *J* = 3.0, 1.1 Hz, 1H, H-2), 3.83 – 3.75 (m, 2H, H-5, H-6), 3.74 – 3.66 (m, 2H, H-3, H-6); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 165.7 (C=O Bz), 138.3, 138.0, 137.5, 135.5 ($C_{q\text{-}arom}$), 133.3 , 130.8, 129.9 (CH_{arom}), 129.8 ($C_{q\text{-}arom}$), 129.0, 128.7, 128.5, 128.5, 128.4, 128.3, 128.0, 127.9, 127.9, 127.7, 127.5, 127.3 (CH_{arom}), 87.9 (C-1), 80.9 (C-3), 78.9 (C-5), 76.5 (C-2), 75.1, 73.7, 72.2 (CH_2 Bn), 70.6 (C-6), 69.5 (C-4); HRMS: $[M+NH_4]^+$ calcd for $C_{40}H_{42}NO_6S$ 664.27274, found 669.27235.

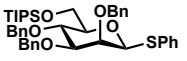
Preparation of donor 15



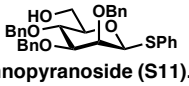
Scheme S3. Synthesis of donor **15**. *Reagents and conditions:* a) TIPS-Cl, imidazole, **S9**: 83%; b) BnBr, NaH, DMF, **S10**: 81%; c) TFA, THF, water, **S11**: 93%; d) BzCl, pyridine, **15**: 78%.



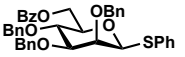
Phenyl 6-*O*-triisopropylsilyl-1-thio-β-D-mannopyranoside (S9). Phenyl 1-thio-β-D-mannopyranoside[42] (5.45 g, 20 mmol) was dissolved in DMF after which imidazole (3.4 g, 50 mmol, 2.5 eq) and triisopropylsilyl chloride (5.4 mL, 25 mmol, 1.25 eq) were added. After reacting overnight, excess reagent was destroyed by the addition of 7.5 mL methanol. After stirring for an additional 30 min, the reaction mixture was concentrated under reduced pressure, dissolved in diethyl ether and washed with water. The organic phase was dried with $MgSO_4$ and concentrated, the residue was purified over silica (20% acetone in pentane) yielding the title compound (6.3 g, 14.7 mmol, 73%) as colorless oil. TLC: R_f 0.40 (pentane:acetone, 60:40, v:v); $[\alpha]_D^{25}$ –83.6° (*c* 0.73, $CHCl_3$); IR (thin film, cm^{-1}): 688, 734, 882, 946, 1264, 2865; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.55 – 7.40 (m, 2H, CH_{arom}), 7.30 – 7.22 (m, 3H, CH_{arom}), 4.87 (d, *J* = 1.1 Hz, 1H, H-1), 4.21 (t, *J* = 4.3 Hz, 1H, H-2), 4.07 – 3.98 (m, 2H, 2x H-6), 3.96 (d, *J* = 2.0 Hz, 1H, 3-OH), 3.91 – 3.81 (m, 2H, H-4, 4-OH), 3.65 (ddd, *J* = 9.1, 5.5, 3.3 Hz, 1H, H-3), 3.45 – 3.35 (m, 2H, H-5, 2-OH), 1.15 – 1.02 (m, 21H, 3x CH TIPS, 6x CH_3 TIPS); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 134.8 ($C_{q\text{-}arom}$), 131.0, 129.1, 127.4 (CH_{arom}), 87.3 (C-1), 78.7 (C-5), 75.1 (C-3), 72.2 (C-2), 70.8 (C-4), 65.5 (C-6), 18.0 (CH_3 TIPS), 11.8 (CH TIPS); HRMS: $[M+Na]^+$ calcd for $C_{21}H_{36}NaO_5SSi$ 451.19449, found 451.19430.



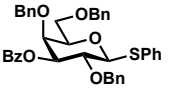
Phenyl 6-*O*-triisopropylsilyl-2,3,4-tri-*O*-benzyl-1-thio-β-D-mannopyranoside (S10). S9 (4.07 g, 9.50 mmol) was dissolved in DMF and cooled to 0 °C, after which benzyl bromide (4.2 mL, 35.6 mmol, 3.75 eq) and NaH (60% dispersion in mineral oil, 1.43 g, 35.6 mmol, 3.75 eq) were added after which the reaction mixture was slowly allowed to warm to RT. When TLC showed full conversion, the reaction was quenched with water. The aqueous phase was extracted twice with diethyl ether, combined organic phases were dried with sodium sulfate and concentrated under reduced pressure. The residue was purified over silica (10% diethyl ether in pentane) to yield the title compound (5.40 g, 7.7 mmol, 81%) as waxy white solid. TLC: R_f 0.40 (pentane:Et_2O, 85:15, v:v); $[\alpha]_D^{25}$ –30.8° (*c* 0.59, $CHCl_3$); IR (thin film, cm^{-1}): 695, 732, 1062, 1088, 1134, 1453; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.54 – 7.46 (m, 4H, CH_{arom}), 7.38 – 7.24 (m, 13H, CH_{arom}), 7.24 – 7.16 (m, 3H, CH_{arom}), 5.05 (d, *J* = 11.4 Hz, 1H, C*H*H Bn), 4.90 (d, *J* = 11.0 Hz, 1H, C*H*H Bn), 4.84 (d, *J* = 11.4 Hz, 1H, CH*H* Bn), 4.78 – 4.72 (m, 2H, H-1, C*H*H Bn), 4.69 (d, *J* = 11.8 Hz, 1H, CH*H* Bn), 4.65 (d, *J* = 11.0 Hz, 1H, CH*H* Bn), 4.13 (dd, *J* = 3.0, 1.1 Hz, 1H, H-2), 3.99 (dd, *J* = 10.9, 1.8 Hz, 1H, H-6), 3.92 (t, *J* = 8.2 Hz, 1H, H-4), 3.88 (dd, *J* = 9.6, 4.9 Hz, 1H, H-6), 3.63 (dd, *J* = 9.5, 3.0 Hz, 1H, H-3), 3.38 (ddd, *J* = 9.7, 6.2, 1.8 Hz, 1H, H-5), 1.44 – 0.80 (m, 21H, 6x CH_3 TIPS, 3x CH TIPS); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 138.6, 138.4, 138.3, 136.5 ($C_{q\text{-}arom}$), 130.4, 128.9, 128.6, 128.5, 128.5, 128.3, 128.2, 128.1, 127.9, 127.9, 127.7, 127.6, 126.9 (CH_{arom}), 87.9 (C-1), 84.4 (C-3), 81.8 (C-5), 78.0 (C-2), 75.4, 75.1 (CH_2 Bn), 74.9 (C-4), 72.7 (CH_2 Bn), 63.4 (C-6), 18.2, 18.1 (CH_3 TIPS), 12.1 (CH TIPS); HRMS: $[M+NH_4]^+$ calcd for $C_{42}H_{58}NO_5SSi$ 716.37995, found 716.37934.



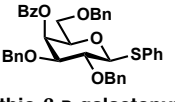
Phenyl 2,3,4-tri-*O*-benzyl-1-thio-β-D-mannopyranoside (S11). S10 (5.24 g, 7.50 mmol) was dissolved in 30 mL THF, to which 10 mL and 10 mL TFA were added. The reaction mixture was stirred at room temperature until TLC showed full conversion. The solution was diluted with water, neutralized with 20 g K_2CO_3, partially concentrated to remove organic solvents and extracted twice with ethyl acetate. Combined organic phases were dried and concentrated under reduced pressure. The residue was purified over silica (15% acetone in pentane), yielding the title compound (3.77 g, 7.0 mmol, 93%) as colorless oil. TLC: R_f 0.35 (pentane:acetone, 80:20, v:v); $[\alpha]_D^{25}$ –19.7° (*c* 0.67, $CHCl_3$); IR (thin film, cm^{-1}): 695, 732, 1026, 1072, 1452; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.50 – 7.23 (m, 20H, CH_{arom}), 5.05 (d, *J* = 11.3 Hz, 1H, C*H*H Bn), 4.91 (d, *J* = 10.9 Hz, 1H, C*H*H Bn), 4.83 (d, *J* = 11.3 Hz, 1H, CH*H* Bn), 4.80 (d, *J* = 1.1 Hz, 1H, H-1), 4.78 – 4.68 (m, 2H, CH_2 Bn), 4.66 (d, *J* = 10.9 Hz, 1H, CH*H* Bn), 4.14 (dd, *J* = 2.9, 1.2 Hz, 1H, H-2), 3.99 (t, *J* = 9.5 Hz, 1H, H-4), 3.87 (ddd, *J* = 12.0, 6.9, 2.9 Hz, 1H, H-6), 3.74 (ddd, *J* = 12.1, 7.0, 5.7 Hz, 1H, H-6), 3.65 (dd, *J* = 9.5, 2.9 Hz, 1H, H-3), 3.37 (ddd, *J* = 9.6, 5.7, 2.9 Hz, 1H, H-5), 2.22 (t, *J* = 6.9 Hz, 1H, OH); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 138.2, 138.1, 138.1, 135.2 ($C_{q\text{-}arom}$), 130.6, 129.1, 128.6, 128.5, 128.4, 128.3, 128.3, 128.0, 127.9, 127.8, 127.7, 127.4 (CH_{arom}), 87.8 (C-1), 84.2 (C-3), 80.1 (C-5), 77.7 (C-2), 75.4, 75.4 (CH_2 Bn), 74.8 (C-4), 72.7 (CH_2 Bn), 62.6 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{33}H_{34}NaO_5S$ 565.20192, found 565.20152.



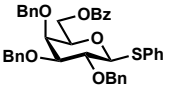
Phenyl 6-benzoyl-2,3,4-tri-O-benzyl-1-thio-β-D-mannopyranoside (15). S11 (2.98 g, 5.50 mmol) was dissolved in 10 mL pyridine, to which benzoyl chloride (0.96 mL, 8.25 mmol, 1.5 eq) was added. When TLC showed full conversion of the starting material, the reaction mixture was diluted with ethyl acetate and washed twice with 1 M aq. HCl and with sat. aq. $NaHCO_3$. The organic phase was dried and concentrated under reduced pressure. The residue was purified by recrystallization from ethyl acetate/pentane, obtaining the title compound (2.79 g, 4.3 mmol, 78%) as fluffy white solid (melting point: 137 ºC); TLC: R_f 0.20, (pentane:EtOAc, 90:10, v:v); $[\alpha]_D^{25}$ –44.1° (*c* 0.85, $CHCl_3$); IR (thin film, cm^{-1}): 697, 713, 1027, 1070, 1090, 1120, 1274, 1720; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.05 – 8.00 (m, 2H, CH_{arom}), 7.59 – 7.53 (m, 1H, CH_{arom}), 7.52 – 7.47 (m, 4H, CH_{arom}), 7.42 – 7.26 (m, 14H, CH_{arom}), 7.21 – 7.08 (m, 3H, CH_{arom}), 5.07 (d, *J* = 11.4 Hz, 1H, C*H*H Bn), 4.95 (d, *J* = 10.9 Hz, 1H, C*H*H Bn), 4.87 (d, *J* = 11.3 Hz, 1H, CH*H* Bn), 4.79 (d, *J* = 1.1 Hz, 1H, H-1), 4.77 (d, *J* = 12.0 Hz, 1H, C*H*H Bn), 4.75 – 4.69 (m, 2H, H-6, CH*H* Bn), 4.66 (d, *J* = 10.9 Hz, 1H, CH*H* Bn), 4.39 (dd, *J* = 11.7, 7.5 Hz, 1H, H-6), 4.19 (dd, *J* = 2.9, 1.1 Hz, 1H, H-2), 4.00 (t, *J* = 9.5 Hz, 1H, H-4), 3.74 – 3.67 (m, 2H, H-3, H-5); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 166.4 (C=O Bz), 138.3, 137.9, 137.9, 135.6 ($C_{q\text{-}arom}$), 133.1, 130.8 CH_{arom}), 130.2 ($C_{q\text{-}arom}$), 129.9, 128.9, 128.7, 128.6, 128.4, 128.4, 128.3, 128.1, 128.0, 127.8, 127.8, 127.2 (CH_{arom}), 87.8 (C-1), 84.3 (C-3), 77.9 (C-5), 77.6 (C-2), 75.5, 75.3 (CH_2 Bn), 74.8 (C-4), 72.7 (CH_2 Bn), 64.5 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{40}H_{38}NaO_6S$ 669.22813, found 669.22749.



Phenyl 3-*O*-benzoyl-2,4,6-tri-*O*-benzyl-1-thio-β-D-galactopyranoside (16). Compound was prepared according to literature procedure.[15] ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.99 – 7.92 (m, 2H, CH_{arom}), 7.62 – 7.57 (m, 2H, CH_{arom}), 7.57 – 7.53 (m, 1H, CH_{arom}), 7.43 – 7.38 (m, 2H, CH_{arom}), 7.34 – 7.19 (m, 13H, CH_{arom}), 7.16 – 7.13 (m, 5H, CH_{arom}), 5.28 (dd, *J* = 9.6, 3.0 Hz, 1H, H-3), 4.80 (d, *J* = 10.6 Hz, 1H, C*H*H Bn), 4.77 (d, *J* = 9.6 Hz, 1H, H-1), 4.67 (d, *J* = 11.5 Hz, 1H, C*H*H Bn), 4.59 (d, *J* = 10.5 Hz, 1H, CH*H* Bn), 4.54 – 4.46 (m, 2H, C*H*H Bn, CH*H* Bn), 4.43 (d, *J* = 11.7 Hz, 1H, CH*H* Bn), 4.16 (dd, *J* = 3.1, 1.0 Hz, 1H, H-4), 4.11 (t, *J* = 9.7 Hz, 1H, H-2), 3.84 (ddd, *J* = 7.0, 5.7, 1.0 Hz, 1H, H-5), 3.72 – 3.63 (m, 2H, 2x H-6); ^{13}C NMR (101 MHz, $CDCl_3$): δ 165.8 (C=O Bz), 138.2, 137.9, 137.8, 134.0 ($C_{q\text{-}arom}$), 133.4, 131.6, 129.9 (CH_{arom}), 129.7 ($C_{q\text{-}arom}$), 129.0, 128.6, 128.5, 128.3, 128.3, 128.3, 127.9, 127.9, 127.8, 127.7, 127.3 (CH_{arom}), 87.8 (C-1), 77.6 (C-3), 77.1 (C-5), 75.5 (C-2), 75.5 (CH_2 Bn), 75.0 (CH_2 Bn), 74.7 (C-4), 73.6 (CH_2 Bn), 68.4 (C-6); HRMS: $[M+NH_4]^+$ calcd for $C_{40}H_{42}NO_6S$ 664.27274, found 664.27236.

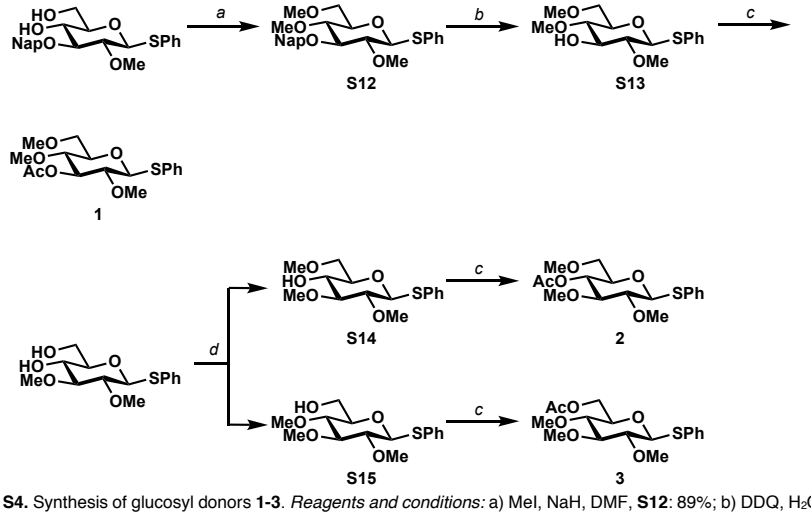


Phenyl 4-*O*-benzoyl-2,3,6-tri-*O*-benzyl-1-thio-β-D-galactopyranoside (17). The title compound was prepared according to literature procedure.[15] ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.02 – 7.96 (m, 2H, CH_{arom}), 7.66 – 7.63 (m, 2H, CH_{arom}), 7.62 – 7.56 (m, 1H, CH_{arom}), 7.49 – 7.42 (m, 2H, CH_{arom}), 7.41 – 7.25 (m, 15H, CH_{arom}), 7.23 – 7.20 (m, 4H, CH_{arom}), 5.89 (dd, *J* = 3.1, 1.0 Hz, 1H, H-4), 4.85 (d, *J* = 11.1 Hz, 1H, C*H*H Bn), 4.73 (s, 2H, CH_2 Bn), 4.70 (d, *J* = 9.4 Hz, 1H, H-1), 4.55 – 4.49 (m, 2H, C*H*H Bn, CH*H* Bn), 4.44 (d, *J* = 11.7 Hz, 1H, CH*H* Bn), 3.89 (td, *J* = 6.4, 5.9, 1.0 Hz, 1H, H-5), 3.76 (dd, *J* = 9.1, 3.1 Hz, 1H, H-3), 3.72 – 3.66 (m, 2H, H-2, H-6), 3.58 (dd, *J* = 9.6, 6.8 Hz, 1H, H-6); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 165.8 (C=O Bz), 138.4, 137.7 ($C_{q\text{-}arom}$), 133.3, 133.0 (CH_{arom}), 130.1 ($C_{q\text{-}arom}$), 129.9, 129.0, 128.5, 128.5, 128.5, 128.4, 128.3, 128.0, 127.9, 127.9, 127.8 (CH_{arom}), 87.3 (C-1), 81.6 (C-3), 76.6 (C-2), 76.4 (C-5), 75.8, 73.8, 71.9 (CH_2 Bn), 68.5 (C-6), 67.4 (C-4); HRMS: $[M+NH_4]^+$ calcd for $C_{40}H_{42}NO_6S$ 664.27274, found 664.27250.

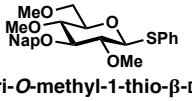


Phenyl 6-*O*-benzoyl-2,3,4-tri-*O*-benzyl-1-thio-β-D-galactopyranoside (18). Phenyl 2,3,4-tri-*O*-benzyl-1-thio-β-D-galactopyranoside[58] (1.45 g, 2.67 mmol) was dissolved in 10 mL pyridine after which benzoyl chloride (0.47 mL, 4.01 mmol, 1.5 eq) was added. When TLC shows full conversion, the reaction mixture was diluted with ethyl acetate and washed with 1M aq. HCl and sat. aq. $NaHCO_3$. The organic phase was dried and concentrated. The residue was purified over silica (10% ethyl acetate in pentane) yielding the title compound (1.28 g, 2.0 mmol, 74%) as white amorphous solid. TLC: R_f 0.30, (pentane:EtOAc, 90:10, v:v); $[\alpha]_D^{25}$ -18.1° (*c* 0.42, $CHCl_3$); IR (thin film, cm^{-1}): 698, 713, 736, 1026, 1070, 1271, 1452, 1718 ; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC) δ 8.00 – 7.92 (m, 2H, CH_{arom}), 7.56 (ddt, *J* = 6.7, 3.7, 1.7 Hz, 3H, CH_{arom}), 7.47 – 7.22 (m, 17H, CH_{arom}), 7.19 – 7.05 (m, 3H, CH_{arom}), 5.02 (d, *J* = 11.6 Hz, 1H, C*H*H Bn), 4.86 (d, *J* = 10.2 Hz, 1H, C*H*H Bn), 4.82 – 4.72 (m, 3H, C*H*H Bn, 2x CH*H* Bn), 4.71 – 4.63 (m, 2H, H-1, CH*H* Bn) 4.51 (dd, *J* = 11.3, 7.3 Hz, 1H, H-6), 4.37 (dd, *J* = 11.3, 5.2 Hz, 1H, H-6), 3.98 (t, *J* = 9.5 Hz, 1H, H-2), 3.90 (d, *J* = 2.8 Hz, 1H, H-4), 3.74 (dd, *J* = 7.2, 5.4 Hz, 1H, H-5), 3.63 (dd, *J* = 9.2, 2.8 Hz, 1H, H-3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC) δ 166.2 (C=O), 138.3, 138.2, 134.4 ($C_{q\text{-}arom}$), 133.2, 131.5 (CH_{arom}), 129.8 ($C_{q\text{-}arom}$), 128.8, 128.6, 128.5, 128.4, 128.4, 128.2, 127.9, 127.8, 127.7, 127.2 (CH_{arom}), 88.1 (C-1), 84.2 (C-3), 77.6 (C-2), 76.2 (C-5), 75.8, 74.5 (CH_2 Bn), 73.6 (C-4), 73.3 (CH_2 Bn), 64.0 (C-6); HRMS: $[M+NH_4]^+$ calcd for $C_{40}H_{42}NO_6S$ 664.27274, found 664.27231.

Preparation of donors 1-3

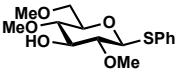


Scheme S4. Synthesis of glucosyl donors **1-3**. *Reagents and conditions:* a) MeI, NaH, DMF, **S12**: 89%; b) DDQ, H_2O/DCM, **S13**: 81%; c) Ac_2O, pyridine, **1**: 97%, **2**: 57%. **3**: 97%; d) MeI, NaH, DMF, **S14**: 21%, **S15**: 32%.

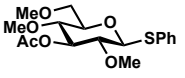


Phenyl 3-*O*-(2-methylnaphthyl)-2,4,6-tri-*O*-methyl-1-thio-β-D-glucopyranose (S12). *Via* general methylation protocol starting with phenyl 3-*O*-(2-methylnaphthyl)-2-*O*-methyl-1-thio-β-D-glucopyranose[33] (85 mg, 0.21 mmol). The residue was purified by crystallization in MeOH to afford the product **S12** (83 mg, 89%) as white solid; TLC: R_f = 0.23 (EtOAc:*n*-heptane, 20:80, v:v); 1H NMR (400 MHz, $CDCl_3$): δ 7.83 (dd, *J* = 6.0, 3.5 Hz, 4H, CH_{arom}), 7.65 – 7.38 (m, 5H, CH_{arom}), 7.36 – 7.15 (m, 3H, CH_{arom}), 5.03 (d, *J* = 11.2 Hz, 1H, C*H*H Nap), 4.99 (d, *J* = 11.2 Hz, 1H, C*H*H Nap), 4.53 (d, *J* = 9.8 Hz, 1H, H-1), 3.66 (dd, *J* = 10.9, 1.8 Hz, 1H, H-6), 3.63 (s, 3H, CH_3 Me), 3.62 – 3.50 (m, 5H, H-6, H-3, CH_3 Me), 3.40 (s, 3H, CH_3 Me), 3.37 – 3.26 (m, 2H, H-5, H-4), 3.18 (dd, *J* = 9.8, 8.8 Hz, 1H, H-2); ^{13}C NMR (101 MHz, $CDCl_3$): δ 136.2, 134.1, 133.5, 133.1, 131.9, 129.0, 128.2, 128.1, 127.8, 127.5, 126.7, 126.2, 126.2, 126.0, 87.7 (C-1), 86.8 (C-3),

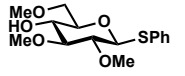
82.9 (C-2), 79.6 (C-4), 79.1 (C-5), 75.7, 71.5 (C-6), 61.2, 60.8, 59.5 (CH_3 Me); HRMS: $[M+Na]^+$ calcd for $C_{26}H_{30}O_5S$, 477.1712, found 477.1694.



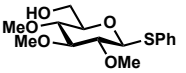
Phenyl 2,4,6-tri-*O*-methyl-1-thio-β-D-glucopyranose (S13) To a well stirred emulsion of **S12** (75 mg, 0.16 mmol) in DCM and H_2O (7/1, v/v, 1.6 mL) was added DDQ (56 mg, 0.25 mmol) and the suspension was protected from light and stirred at room temperature for 1.5 h. The mixture was diluted with DCM (20 mL) and washed (2 x 10 mL) with 10% $Na_2S_3O_3$ in H_2O w:w, to reduce the remaining DDQ. The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*. Silica gel column chromatography of the residue afforded **S13** as white solid (42 mg, 81%); TLC: R_f = 0.35 (EtOAc:*n*-heptane, 40:60, v:v); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.59 – 7.44 (m, 2H, CH_{arom}), 7.39 – 7.20 (m, 3H, CH_{arom}), 4.60 – 4.48 (m, 1H, H-1), 3.68 – 3.56 (m, 6H, H-6, H-6, CH_3 Me, H-3), 3.56 (s, 3H, CH_3 Me), 3.40 (s, 3H, CH_3 Me), 3.33 (ddd, *J* = 9.7, 4.5, 2.0 Hz, 1H, H-5), 3.26 – 3.20 (m, 1H, H-4), 3.08 (dd, *J* = 9.7, 8.8 Hz, 1H, H-2), 2.67 (s, 1H, 3-OH); ^{13}C NMR (126 MHz, $CDCl_3$): δ 134.1 ($C_{q\text{-}arom}$), 132.0, 131.8, 129.1, 129.0, 127.5 (CH_{arom}), 87.2 (C-1), 82.5 (C-2), 79.1 (C-4), 78.8 (C-5), 78.6 (C-3), 71.6 (C-6), 61.2, 60.7, 59.5 (CH_3 Me); HRMS: $[M+Na]^+$ calcd for $C_{15}H_{22}O_5S$, 337.1086, found 337.1086.



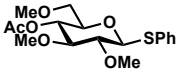
Phenyl 3-*O*-acetyl-2,4,6-tri-*O*-methyl-1-thio-β-D-glucopyranose (1). *Via* general acetylation protocol starting with **S13** (40 mg, 0.13 mmol). The product **1** (44 mg, 97%) was obtained as a pale oil; TLC: R_f = 0.49 (EtOAc:*n*-heptane, 40:60, v:v); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.60 – 7.47 (m, 2H, CH_{arom}), 7.38 – 7.20 (m, 4H, CH_{arom}), 5.13 (t, *J* = 9.0 Hz, 1H, H-3), 4.58 (d, *J* = 9.8 Hz, 1H, H-1), 3.67 – 3.57 (m, 3H, H-6, H-6), 3.50 (s, 3H, CH_3 Me), 3.42 (s, 3H, CH_3 Me), 3.40 (s, 3H, CH_3 Me), 3.38 (dd, *J* = 3.8, 1.8 Hz, 1H, H-5), 3.37 – 3.32 (m, 1H, H-4), 3.16 (t, *J* = 9.5 Hz, 1H, H-2), 2.14 (s, 3H, CH_3 Ac); ^{13}C NMR (126 MHz, $CDCl_3$): δ 170.1 (C=O), 133.7, 132.2, 129.0, 128.9, 127.7 (CH_{arom}), 87.4 (C-1), 80.6 (C-2), 78.7 (C-5), 77.5 (C-4), 77.5 (C-3), 71.2 (C-6), 60.3, 60.1, 59.5 (CH_3 Me), 21.2; (CH_3 Ac) HRMS: $[M+Na]^+$ calcd for $C_{17}H_{24}O_6S$, 379.1191, found 379.1205.



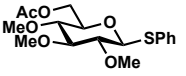
Phenyl 2,3,6-tri-*O*-methyl-1-thio-β-D-glucopyranoside (S14). To a solution of phenyl 2,3-di-*O*-methyl-1-thio-β-D-glucopyranoside[59] (100 mg, 0.33 mmol) in DMF (3.0 mL), NaH (33 mg, 0.83 mmol, 60 wt% in mineral oil) was added. The mixture was allowed to stir for 5 min before MeI (21 µL, 0.33 mmol) was added and was left at room temperature for 1 hour under argon. The reaction was quenched by addition of sat. aq. NH_4Cl (0.5 mL), diluted with EtOAc (15 mL) and washed once with water (10 mL) and once with brine. The organic layer was dried ($MgSO_4$), filtered and concentrated *in vacuo*. Silica column chromatography of the crude (30% EtOAc in *n*-heptane) afforded Phenyl 2,3,6-tri-*O*-methyl-1-thio-β-D-glucopyranoside **S14** (34 mg, 32%) as a clear oil. Phenyl 2,3,4-tri-*O*-methyl-1-thio-β-D-glucopyranoside (22 mg, 21%) was obtained as main by-product; TLC: R_f = 0.35 (EtOAc:*n*-heptane, 50:50, v:v); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 – 7.40 (m, 2H, CH_{arom}), 7.40 – 7.13 (m, 3H, CH_{arom}), 4.55 (d, *J* = 9.7 Hz, 1H, H-1), 3.66 (pd, *J* = 4.1 Hz, 5H, H-6, H-6, CH_3 Me), 3.61 (s, 3H, CH_3 Me), 3.57 – 3.49 (m, 1H, H-4), 3.48 – 3.34 (m, 4H, CH_3 Me, H-5), 3.18 (t, *J* = 8.8 Hz, 1H, H-3), 3.08 (dd, *J* = 9.7, 8.7 Hz, 1H, H-2), 2.83 (d, *J* = 2.1 Hz, 1H, 4-OH); ^{13}C NMR (101 MHz, $CDCl_3$): δ 133.9, 132.0, 129.0, 128.6 (CH_{arom}), 88.0 (C-3), 87.7 (C-1), 82.5 (C-2), 77.8 (C-5), 73.0 (C-6), 71.7 (C-4), 61.2, 60.8, 59.7 (CH_3 Me); HRMS: $[M+Na]^+$ calcd for $C_{15}H_{22}O_5S$, 337.1086, found 337.1084.



Phenyl 2,3,4-tri-*O*-methyl-1-thio-β-D-glucopyranoside (S15). Afforded as main by-product in the synthesis of phenyl 2,3,6-tri-*O*-methyl-1-thio-β-D-glucopyranoside. TLC: R_f = 0.44 (EtOAc:*n*-heptane, 50:50, v:v); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53 – 7.46 (m, 2H, CH_{arom}), 7.35 – 7.24 (m, 3H, CH_{arom}), 4.55 (d, *J* = 9.8 Hz, 1H, H-1), 3.92 – 3.78 (m, 1H, H-6), 3.74 – 3.64 (m, 4H, H-6, CH_3 Me), 3.62 (s, 3H, CH_3 Me), 3.55 (s, 3H, CH_3 Me), 3.29 – 3.20 (m, 2H, H-5, H-3), 3.17 – 3.08 (m, 1H, H-4), 3.03 (dd, *J* = 9.8, 8.6 Hz, 1H, H-4), 1.92 (t, *J* = 6.7 Hz, 1H, 6-OH); ^{13}C NMR (101 MHz, $CDCl_3$): δ 132.0, 129.1, 127.8 (CH_{arom}), 88.6 (C-3), 87.2 (C-1), 82.8 (C-2), 79.7 (C-4), 79.2 (C-5), 62.4 (C-6), 61.1, 61.0, 60.7 (CH_3 Me); HRMS: $[M+Na]^+$ calcd for $C_{15}H_{22}O_5S$, 337.1086, found 337.1083.

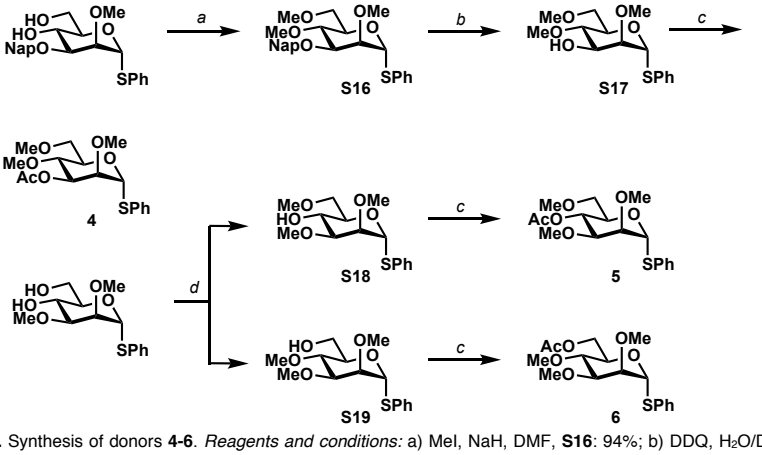


Phenyl 4-*O*-acetyl-2,3,6-tri-*O*-methyl-1-thio-β-D-glucopyranoside (2). *Via* general acetylation protocol starting with **S14** (20 mg, 0.064 mmol). **2** (13 mg, 57%) was obtained as a white amorphous solid. TLC: R_f = 0.49 (EtOAc:*n*-heptane, 40:60, v:v); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 – 7.47 (m, 1H), 7.41 – 7.19 (m, 2H, CH_{arom}), 4.85 (t, *J* = 9.6 Hz, 1H, H-4), 4.53 (d, *J* = 9.8 Hz, 1H, H-1), 3.59 (s, 3H, CH_3 Me), 3.54 (s, 3H, CH_3 Me), 3.50 (ddd, *J* = 9.8, 5.9, 3.2 Hz, 1H, H-5), 3.46 – 3.42 (m, 2H, H-6, H-6), 3.35 – 3.26 (m, 4H, H-3, CH_3 Me), 3.13 (dd, *J* = 9.8, 8.7 Hz, 1H, H-2), 2.09 (s, 1H, CH_3 Ac); ^{13}C NMR (101 MHz, $CDCl_3$): δ 170.0, 132.2, 129.0, 127.7 (CH_{arom}), 87.4 (C-1), 86.0 (C-3), 82.2 (C-2), 77.5 (C-5), 72.2 (C-6), 70.9 (C-4), 61.0, 60.9, 59.6 (CH_3 Me), 21.1 (CH_3 Ac); HRMS: $[M+Na]^+$ calcd for $C_{17}H_{24}O_6S$, 379.1191, found 379.1193.

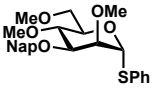


Phenyl 6-*O*-acetyl-2,3,4-tri-*O*-methyl-1-thio-β-D-glucopyranoside (3). *Via* general acetylation protocol starting with **S15** (33 mg, 0.10 mmol). **3** (36 mg, 96%) was obtained as a white amorphous solid. TLC: R_f = 0.50 (EtOAc:*n*-heptane, 40:60, v:v); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 – 7.50 (m, 2H, CH_{arom}), 7.41 – 7.20 (m, 3H, CH_{arom}), 4.49 (d, *J* = 9.8 Hz, 1H, H-1), 4.35 (dd, *J* = 11.8, 2.2 Hz, 1H, H-6), 4.20 (dd, *J* = 11.8, 6.2 Hz, 1H, H-6), 3.65 (s, 3H, CH_3 Me), 3.61 (s, 3H, CH_3 Me), 3.52 (s, 3H, CH_3 Me), 3.41 (ddd, *J* = 9.9, 6.2, 2.1 Hz, 1H, H-5), 3.24 (t, *J* = 8.8 Hz, 1H, H-3), 3.06 (pddd, *J* = 9.9, 8.8, 7.9 Hz, 2H, H-4, H-2), 2.08 (s, 3H, CH_3 Ac); ^{13}C NMR (101 MHz, $CDCl_3$): δ 170.9, 133.7, 132.1, 128.9, 127.7 (CH_{arom}), 88.7 (C-3), 87.2 (C-1), 82.7 (C-2), 79.9 (C-4), 76.9 (C-5), 63.7 (C-6), 61.2, 61.0, 60.8 (CH_3 Me), 21.0 (CH_3 Ac); HRMS: $[M+Na]^+$ calcd for $C_{17}H_{24}O_6S$, 379.1191, found 379.1198.

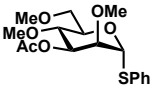
Preparation of donor 4-6



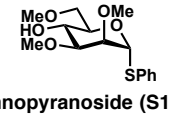
Scheme S5. Synthesis of donors **4-6**. *Reagents and conditions:* a) MeI, NaH, DMF, **S16**: 94%; b) DDQ, H_2O/DCM, **S17**: 86%; c) Ac_2O, pyridine, **4**: 98%, **5**: 97%, **6**: *quant.*; d) MeI, NaH, DMF, **S18**: 11%, **S19**: 43%.



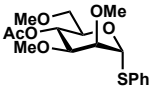
Phenyl 3-*O*-(2-methylnaphthyl)-2,4,6-tri-*O*-methyl-1-thio-α-D-mannoyranose (S16). *Via* general methylation protocol starting with phenyl 3-*O*-(2-methylnaphthyl)-2-*O*-methyl-1-thio-α-D-mannopyranose[33] (350 mg, 0.82 mmol). The residue was purified by silica column chromatography (20% EtOAc in toluene) to afford the product **S19** (352 mg, 94%) as a white amorphous solid. TLC: R_f = 0.19 (EtOAc:*n*-heptane, 20:80, v:v); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 – 7.78 (m, 4H, CH_{arom}), 7.63 – 7.38 (m, 5H, CH_{arom}), 7.35 – 7.12 (m, 3H, CH_{arom}), 5.59 (d, *J* = 1.5 Hz, 1H, H-1), 4.92 (d, *J* = 12.2 Hz, 1H, C*H*H Nap), 4.87 (d, *J* = 12.2 Hz, 1H, C*H*H Nap), 4.09 (ddd, *J* = 9.7, 4.6, 1.9 Hz, 1H, H-5), 3.80 (dd, *J* = 9.4, 3.1 Hz, 1H, H-3), 3.76 – 3.63 (m, 3H, H-2, H-4, H-6), 3.62 – 3.59 (m, 4H, CH_3 Me, H-6), 3.43 (s, 3H, CH_3 Me), 3.38 (s, 1H, CH_3 Me); ^{13}C NMR (101 MHz, $CDCl_3$): δ 135.9, 134.7, 133.5, 133.2, 131.2, 129.1, 128.3, 128.1, 127.9, 127.4, 126.7, 126.3, 126.1, 126.0 (CH_{arom}), 85.1 (C-1), 80.0 (C-3), 79.8 (C-2), 76.5 (C-4), 72.7, 72.6 (C-5), 71.5 (C-6), 61.0, 59.3, 58.6 (CH_3 Me); HRMS: $[M+Na]^+$ calcd for $C_{26}H_{30}O_5S$, 477.1712, found 477.1694.



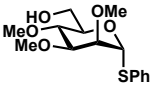
Phenyl 3-*O*-acetyl-2,4,6-tri-*O*-methyl-1-thio-α-D-mannopyranoside (4). To a well stirred emulsion of **S16** (330 mg, 0.73 mmol) in DCM and H_2O (7/1, v/v, 7.3 mL) was added DDQ (247 mg, 1.1 mmol) and the suspension was protected from light and stirred at room temperature for 1.5 h. The mixture was diluted with DCM (100 mL) and washed (2 x 20 mL) with 10% $Na_2S_3O_3$ in H_2O w/w, to reduce the remaining DDQ. The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*. Silica gel column chromatography (30% EtOAc in *n*-heptane) of the residue afforded **S17** as a clear oil (0.196 mg, 86%). TLC: (EtOAc:*n*-heptane, 40:60, v:v): R_f = 0.13; HRMS: $[M+Na]^+$ calcd for $C_{15}H_{22}O_5S$, 337.1086, found 337.1106. **S17** was directly acetylated *via* general acetylation protocol starting with **S17** (189 mg, 0.60 mmol). The product **4** (210 mg, 98%) was obtained as a pale oil. TLC: R_f = 0.67 (EtOAc:*n*-heptane, 50:50, v:v); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55 – 7.45 (m, 2H, CH_{arom}), 7.33 – 7.28 (m, 3H, CH_{arom}), 5.60 (d, *J* = 1.9 Hz, 1H, H-1), 5.11 (dd, *J* = 9.6, 3.3 Hz, 1H, H-3), 4.16 (ddd, *J* = 9.8, 4.3, 2.0 Hz, 1H, H-5), 3.88 (dd, *J* = 3.3, 1.9 Hz, 1H, H-2), 3.75 (t, *J* = 9.7 Hz, 1H, H-4), 3.67 (dd, *J* = 10.8, 4.2 Hz, 1H, H-6), 3.58 (dd, *J* = 10.7, 2.0 Hz, 1H, H-6), 3.49 (s, 3H, CH_3 Me), 3.42 (s, 3H, CH_3 Me), 3.39 (s, 3H, CH_3 Me), 2.16 (s, 3H, CH_3 Ac); ^{13}C NMR (126 MHz, $CDCl_3$): δ 170.5 (C=O), 134.6, 131.3, 129.2, 127.4 (CH_{arom}), 84.9 (C-1), 79.9 (C-2), 74.7 (C-4), 74.0 (C-3), 72.3 (C-5), 71.2 (C-6), 60.6, 59.4, 58.6 (CH_3 Me), 21.3 (CH_3 Ac); HRMS: $[M+Na]^+$ calcd for $C_{17}H_{24}O_6S$, 379.1191, found 379.1199.



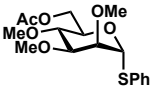
Phenyl 2,3,6-tri-*O*-methyl-1-thio-α-D-mannopyranoside (S18). To a solution of phenyl 2,3-di-*O*-methyl-1-thio-α-D-mannopyranoside[32] (196 mg, 0.653 mmol) in DMF (6.5 mL), NaH (78 mg, 1.96 mmol, 60 wt% in mineral oil) was added. The mixture was allowed to stir for 5 min before MeI (41 µL, 0.653 mmol) was added and was left at room temperature for 1 hour under argon. The reaction was quenched by addition of sat. aq. NH_4Cl (0.5 mL), diluted with EtOAc (15 mL) and washed once with water (10 mL) and once with brine. The organic layer was dried ($MgSO_4$), filtered and concentrated *in vacuo*. Silica column chromatography of the crude (40% Et_2O in toluene) afforded phenyl 2,3,6-tri-*O*-methyl-1-thio-α-D-mannopyranoside **S22** (88 mg, 43%) as a clear oil. Phenyl 2,3,4-tri-*O*-methyl-1-thio-β-D-glucopyranoside (22 mg, 11%) was obtained as by-product; TLC: R_f = 0.28 (Et_2O:toluene, 40:60, v:v); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.60 – 7.51 (m, 2H, CH_{arom}), 7.39 – 7.21 (m, 3H, CH_{arom}), 5.69 (d, *J* = 1.5 Hz, 1H, H-1), 4.24 (dt, *J* = 9.2, 4.3 Hz, 1H, H-5), 3.97 (t, *J* = 9.6 Hz, 1H, H-4), 3.91 (dd, *J* = 3.1, 1.6 Hz, 1H, H-2), 3.80 – 3.67 (m, 2H, H-6, H-6), 3.53 (s, 3H, CH_3 Me), 3.49 – 3.44 (m, 4H, CH_3 Me, H-3), 3.41 (s, 3H, CH_3 Me), 2.71 (s, 1H, 4-OH); ^{13}C NMR (126 MHz, $CDCl_3$): δ 134.6, 131.4, 129.2, 127.6 (CH_{arom}), 85.2 (C-1), 81.4 (C-3), 77.7 (C-2), 72.4 (C-5), 71.9 (C-6), 67.8 (C-4), 59.6, 58.3, 57.3 (CH_3 Me); HRMS: $[M+Na]^+$ calcd for $C_{15}H_{22}O_5S$, 337.1086, found 337.1090.



Phenyl 4-*O*-acetyl-2,3,6-tri-*O*-methyl-1-thio-α-D-mannopyranoside (5). *Via* general acetylation protocol starting with **S18** (80 mg, 0.25 mmoL). The title compound (88 mg, 97%) was obtained as a pale oil. TLC: R_f = 0.63 (EtOAc:*n*-heptane, 50:50, v:v); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.63 – 7.49 (m, 2H, CH_{arom}), 7.46 – 7.15 (m, 3H, CH_{arom}), 5.63 (d, *J* = 1.9 Hz, 1H, H-1), 5.26 (t, *J* = 9.7 Hz, 1H, H-4), 4.30 (dt, *J* = 9.5, 4.5 Hz, 1H, H-5), 3.89 (dd, *J* = 3.1, 1.9 Hz, 1H, H-2), 3.56 (dd, *J* = 9.5, 3.1 Hz, 1H, H-3), 3.52 – 3.46 (m, 5H, H-6, H-6, CH_3 Me), 3.45 (s, 3H, CH_3 Me), 3.33 (s, 3H, CH_3 Me), 2.10 (s, 3H, CH_3 Ac); ^{13}C NMR (126 MHz, $CDCl_3$): δ 170.0 (C=O), 134.3, 131.7, 129.2, 127.8 (CH_{arom}), 85.3 (C-1), 79.2 (C-3), 78.3 (C-2), 72.0 (C-6), 71.0 (C-5), 68.9 (C-4), 59.5, 58.5, 57.9 (CH_3 Me), 21.1 (CH_3 Ac); HRMS: $[M+Na]^+$ calcd for $C_{17}H_{24}O_6S$, 379.1191, found 379.1201.

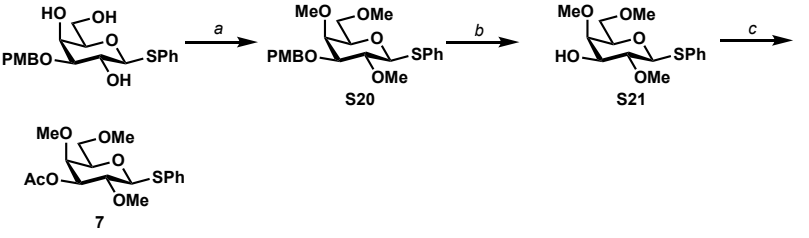


Phenyl 2,3,4-tri-*O*-methyl-1-thio-α-D-mannopyranoside (S19). Isolated as main by-product in the synthesis of Phenyl 2,4,6-tri-*O*-methyl-1-thio-α-D-mannopyranoside.[60] TLC: R_f = 0.25 (Et_2O:toluene, 40:60, v:v); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.51 – 7.40 (m, 2H, CH_{arom}), 7.40 – 7.16 (m, 3H, CH_{arom}), 5.61 (d, *J* = 1.8 Hz, 1H, H-1), 4.04 (ddd, *J* = 9.5, 4.7, 2.9 Hz, 1H, H-5), 3.88 – 3.73 (m, 3H, H-2, H-6, H-6), 3.57 (s, 3H, H-4, CH_3 Me), 3.55 – 3.49 (m, 4H, H-3, CH_3 Me), 3.48 (s, 3H, CH_3 Me), 1.98 (s, 1H, 6-OH); ^{13}C NMR (126 MHz, $CDCl_3$): δ 134.2, 131.8, 129.3, 127.8 (CH_{arom}), 85.0 (C-1), 81.7 (C-3), 78.8 (C-2), 76.6 (C-4), 73.1 (C-5), 62.3 (C-6), 61.0, 58.4, 57.9 (CH_3 Me).



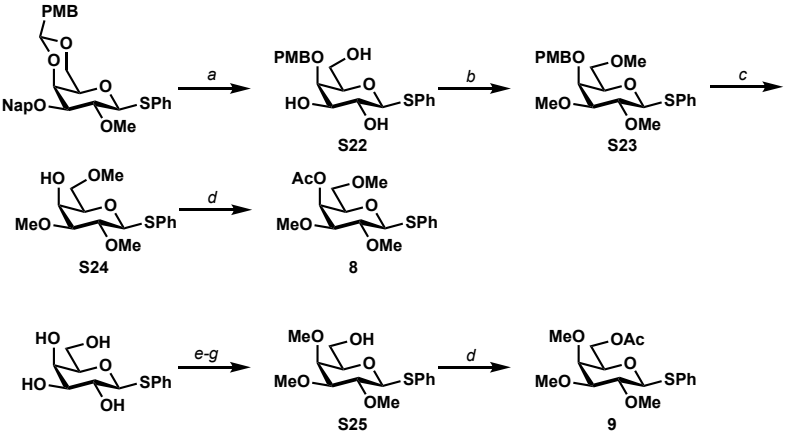
Phenyl 6-*O*-acetyl-2,3,4-tri-*O*-methyl-1-thio-α-D-mannopyranoside (6). *Via* general acetylation protocol starting with **S19** (22 mg, 70 µmol). Obtained **6** (25 mg, *quant.*) as a clear oil. TLC: R_f = 0.63 (EtOAc:*n*-heptane, 50:50, v:v); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.60 – 7.38 (m, 2H, CH_{arom}), 7.40 – 7.16 (m, 3H, CH_{arom}), 5.64 (d, *J* = 1.6 Hz, 1H, H-1), 4.37 – 4.28 (m, 2H, H-6, H-6), 4.23 (ddd, *J* = 8.5, 5.1, 3.1 Hz, 1H, H-5), 3.86 (dd, *J* = 3.0, 1.7 Hz, 1H, H-2), 3.54 (s, 3H, CH_3 Me), 3.53 – 3.49 (m, 4H, H-3, CH_3 Me), 3.47 (s, 4H, H-4, CH_3 Me), 2.06 (s, 3H, CH_3 Ac); ^{13}C NMR (126 MHz, $CDCl_3$): δ 170.9 (C=O), 134.2, 131.6, 129.2, 127.7 (CH_{arom}), 84.6 (C-1), 81.7 (C-3), 78.5 (C-2), 76.7 (C-4) 70.8 (C-5), 63.6 (C-6), 61.0, 58.2, 57.8 (CH_3 Me), 21.0 (CH_3 Ac); HRMS: $[M+Na]^+$ calcd for $C_{17}H_{24}O_6S$, 379.1191, found 379.1202.

Preparation of donors 7

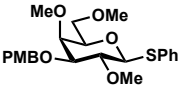


Scheme S6. Synthesis of donor **7**. *Reagents and conditions:* a) MeI, NaH, DMF, **S20**: 99%; b) *p*TsOH, MeOH, **S21**: 81%; c) Ac_2O, pyridine, **7**: *quant.*

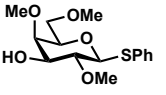
Preparation of donors 8 and 9



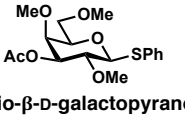
Scheme S7. Synthesis of donors **8** and **9**. *Reagents and conditions:* a) BH_3, TMSOTf, THF, **S22**: 75%; b) MeI, NaH, DMF, **S23**: 97%; c) *p*TsOH, MeOH, **S24**: 81%; d) Ac_2O, pyridine, **8**: *quant.*, **9**: *quant.*; e) TBS-Cl, imidazole, DMF; f) MeI, NaH, DMF; g) TBAF, THF, **S25**: 27% over three steps.



Phenyl 2,4,6-tri-*O*-methyl-3-*O*-*p*-methoxybenzyl-1-thio-β-D-galactopyranoside (S20). *Via* general methylation protocol starting with phenyl 3-*O*-*p*-methoxybenzyl-1-thio-β-D-galactopyranoside (327 mg, 0.833 mmol). The residue was purified by silica column chromatography (30% EtOAc in *n*-heptane) to obtain the product **S25** (359 mg, 99%) as a white amorphous solid. TLC: R_f = 0.31 (EtOAc:*n*-heptane, 30:70, v:v); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 – 7.46 (m, 2H, CH_{arom}), 7.40 – 7.13 (m, 5H, CH_{arom}), 6.97 – 6.81 (m, 2H, CH_{arom}), 4.70 – 4.63 (m, 2H, 2 x C*H*H PMB), 4.49 (d, *J* = 9.3 Hz, 1H, H-1), 3.81 (s, 3H, CH_3 Me), 3.62 – 3.58 (m, 4H, H-4, CH_3 Me), 3.58 – 3.55 (m, 4H, H-6, CH_3 Me), 3.55 – 3.45 (m, 4H, H-6, H-2, H-5), 3.42 (dd, *J* = 9.2, 2.9 Hz, 1H, H-3), 3.36 (s, 3H, CH_3 Me); ^{13}C NMR (101 MHz, $CDCl_3$): δ 134.3, 131.6, 130.4, 129.3, 128.7, 127.1, 113.9 (CH_{arom}), 87.9 (C-1), 83.2 (C-3), 79.4 (C-2), 77.0 (C-5), 76.0 (C-4), 72.3, 70.7 (C-6), 61.3, 61.3, 59.2 (CH_3 Me); HRMS: $[M+Na]^+$ calcd for $C_{23}H_{30}O_6S$, 457.1661, found 457.1658.

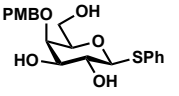


Phenyl 2,4,6-tri-*O*-methyl-1-thio-β-D-galactopyranoside (S21). S20 (359 mg, 0.826 mmol) was suspended in methanol (4.13 mL) and heated to 50 °C before *p*TsOH (157 mg, 0.826 mmol) was added. The suspension stirred for 18 h before being neutralized by addition of TEA. The mixture was concentrated in *vacuo*. Silica column chromatography (50% ethyl acetate in *n*-heptane) of the residue obtained the product **S21** (210 mg, 81%) as a clear oil; TLC: R_f = 0.23 (EtOAc:*n*-heptane, 50:50, v:v); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.59 – 7.47 (m, 1H, CH_{arom}), 7.37 – 7.14 (m, 3H, CH_{arom}), 4.50 (d, *J* = 9.6 Hz, 1H, H-1), 3.71 – 3.50 (m, 11H, 2 x CH_3 Me, H-3, H-4, H-5, H-6, H-6), 3.37 (s, 3H, CH_3 Me), 3.29 (ddd, *J* = 9.7, 7.2, 3.1 Hz, 1H, H-2), 2.47 (d, *J* = 6.9 Hz, 1H, 4-OH); ^{13}C NMR (126 MHz, $CDCl_3$): δ 134.3, 131.7, 128.9, 127.4 (CH_{arom}), 87.7 (C-1), 80.8 (C-2), 78.4 (C-5), 77.3 (C-3), 75.8 (C-4), 70.7 (C-6), 61.9, 61.5, 59.3 (CH_3 Me); HRMS: $[M+Na]^+$ calcd for $C_{15}H_{22}O_5S$, 337.1086, found 337.1104.

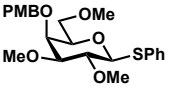


Phenyl 3-*O*-acetyl-2,4,6-tri-O-methyl-1-thio-β-D-galactopyranoside (7). *Via* general acetylation protocol starting with **S21** (150 mg, 0.477 mmol). **7** (170 mg, *quant.*) was obtained as a pale oil. TLC: R_f = 0.64

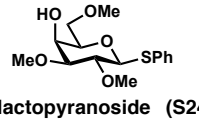
(EtOAc:*n*-heptane, 50:50, v:v); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 – 7.48 (m, 2H, CH_{arom}), 7.40 – 7.11 (m, 3H, CH_{arom}), 4.87 (dd, *J* = 9.7, 3.1 Hz, 1H, H-3), 4.57 (d, *J* = 9.8 Hz, 1H, H-1), 3.71 (dd, *J* = 3.2, 1.0 Hz, 1H, H-4), 3.68 – 3.45 (m, 10H, 2 x CH_3 Me, H-2, H-5, H-6, H-6), 3.34 (s, 3H, CH_3 Me), 2.15 (s, 3H, CH_3 Ac); ^{13}C NMR (101 MHz, $CDCl_3$): δ 170.4 (C=O), 134.0, 131.8, 128.9, 128.9, 127.4 (CH_{arom}), 87.9 (C-1), 77.4 (C-2), 77.3 (C-3), 76.7 (C-5), 76.6 (C-4), 70.5 (C-6), 61.4, 61.1, 59.3 (CH_3 Me), 21.2 (CH_3 Ac); HRMS: $[M+Na]^+$ calcd for $C_{17}H_{24}O_6S$, 379.1191, found 379.1211.



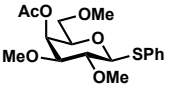
Phenyl 4-*O*-*p*-methoxybenzyl-1-thio-β-D-galactopyranoside (S22). Phenyl 4,6-*O*-*p*-methoxybenzylidene-1-thio-β-D-galactopyranoside (1.0 g, 2.56 mmol) was dissolved in DCM (26 mL) after which 1 M BH_3 in THF (18 mL, 18 mmol) was added at 0 °C. The mixture was allowed to warm up to room temperature in 20 min before TMSOTf (46 µL, 0.26 mmol) was added. After full conversion was observed after 3 h, the reaction was cooled to 0 °C and triethylamine (0.5 mL) was added. The mixture was quenched by careful addition of methanol and subsequently concentrated *in vacuo*. Silica column chromatography (70% ethyl acetate in *n*-heptane) of the residue gave the product **S22** (756 mg, 75%) as a white amorphous solid; TLC: R_f = 0.15 (EtOAc:*n*-heptane, 80:20, v:v); ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.71 – 7.46 (m, 2H, CH_{arom}), 7.40 – 7.10 (m, 5H, CH_{arom}), 7.01 – 6.81 (m, 2H, CH_{arom}), 4.89 (d, *J* = 11.0 Hz, 1H, C*H*H PMB), 4.70 – 4.46 (m, 2H, H-1, C*H*H PMB), 4.24 (dd, *J* = 4.5, 1.3 Hz, 1H, H-4), 4.11 – 4.04 (m, 1H, 2-OH), 3.92 (dd, *J* = 2.8, 0.8 Hz, 1H, 3-OH), 3.79 (s, 3H, CH_3 Me), 3.78 – 3.60 (m, 5H, H-2, H-3, H-5, H-6, H-6); ^{13}C NMR (101 MHz, Acetone-d_6) δ 160.1, 135.8, 132.5, 131.6, 131.6, 130.0, 129.5, 127.4, 114.3 (CH_{arom}), 89.0 (C-1), 89.0, 80.3, 80.3, 77.3, 77.2, 77.1, 77.0, 75.2, 71.0, 70.9, 70.9, 62.0, 61.8, 55.5, 55.0; HRMS: $[M+Na]^+$ calcd for $C_{20}H_{24}O_6S$, 415.1191, found 415.1187.



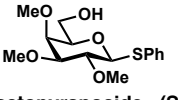
Phenyl 2,3,6-tri-*O*-methyl-4-*O*-*p*-methoxybenzyl-1-thio-β-D-galactopyranoside (S23). *Via* general methylation protocol starting with **S22** (316 mg, 0.81 mmol). Crystallization of the residue from methanol gave **S23** (340 mg, 97%) as a white solid. TLC: R_f = 0.60 (EtOAc:*n*-heptane, 50:50, v:v); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63 – 7.42 (m, 2H, CH_{arom}), 7.33 – 7.25 (m, 2H, CH_{arom}), 7.24 – 7.18 (m, 3H, CH_{arom}), 6.93 – 6.83 (m, 2H, CH_{arom}), 4.83 (d, *J* = 11.3 Hz, 1H, C*H*H PMB), 4.55 (d, *J* = 11.3 Hz, 1H, C*H*H PMB), 4.50 (d, *J* = 9.6 Hz, 1H, H-1), 3.91 (d, *J* = 2.8 Hz, 1H, H-4), 3.82 (s, 3H, CH_3 Me), 3.57 (s, 3H, CH_3 Me), 3.55 – 3.41 (m, 7H, CH_3 Me, H-6, H-6, H-2, H-5), 3.28 (s, 3H, CH_3 Me), 3.22 (dd, *J* = 9.2, 2.8 Hz, 1H, H-3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.3, 134.3, 131.7, 131.1, 129.6, 128.8, 127.1, 113.7 CH_{arom}), 87.7 (C-1), 86.6 (C-3), 79.0 (C-2), 77.3 (C-5), 74.1, 72.2 (C-4), 71.1 (C-6), 61.2, 59.3, 58.4 (CH_3 Me); HRMS: $[M+Na]^+$ calcd for $C_{23}H_{30}O_6S$, 457.1661, found 457.1661.



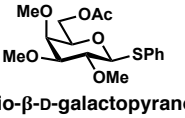
Phenyl 2,3,6-tri-*O*-methyl-1-thio-β-D-galactopyranoside (S24). S23 (315 mg, 0.725 mmol) was suspended in methanol (3.62 mL) and heated to 50 °C before *p*TsOH (138 mg, 0.725 mmol) was added. The suspension stirred for 18 h before being neutralized by addition of triethylamine. The mixture was concentrated in *vacuo*. Silica column chromatography (50% ethyl acetate in *n*-heptane) of the residue obtained the product **S24** (171 mg, 75%) as a clear oil. TLC: R_f = 0.31 (EtOAc:*n*-heptane, 50:50, v:v); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.65 – 7.41 (m, 2H, CH_{arom}), 7.38 – 7.13 (m, 3H, CH_{arom}), 4.51 (d, *J* = 9.7 Hz, 1H, H-1), 4.12 (s, 1H, H-4), 3.72 (dd, *J* = 10.0, 5.8 Hz, 1H, H-6), 3.64 (dd, *J* = 10.0, 5.6 Hz, 1H, H-6), 3.57 (s, 3H, CH_3 Me), 3.54 (t, *J* = 5.4 Hz, 1H, H-5), 3.51 (s, 3H, CH_3 Me), 3.39 (s, 3H, CH_3 Me), 3.35 (t, *J* = 9.3 Hz, 1H, H-2), 3.23 (dd, *J* = 8.9, 3.2 Hz, 1H, H-3), 2.61 – 2.39 (m, 1H, 4-OH); ^{13}C NMR (126 MHz, $CDCl_3$): δ 133.9, 132.0, 128.9, 127.5 (CH_{arom}), 87.6 (C-1), 84.8 (C-3), 78.6 (C-2), 76.9 (C-5), 71.9 (C-6), 66.2 (C-4), 61.3, 59.6, 57.7 (CH_3 Me); HRMS: $[M+Na]^+$ calcd for $C_{15}H_{22}O_5S$, 337.1086, found 337.1092.



Phenyl 4-*O*-acetyl-2,3,6-tri-O-methyl-1-thio-β-D-galactopyranoside (8). *Via* general acetylation protocol starting with **S24** (171 mg, 0.54 mmol). The product **8** (193 mg, *quant.*) was obtained as a pale oil. TLC: R_f = 0.50 (EtOAc:*n*-heptane, 50:50, v:v); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.57 (dt, *J* = 8.6, 2.1 Hz, 2H, CH_{arom}), 7.36 – 7.16 (m, 3H, CH_{arom}), 5.48 (d, *J* = 1.6 Hz, 1H, H-4), 4.64 – 4.48 (m, 1H, H-1), 3.70 – 3.64 (m, 1H, H-5), 3.57 (s, 3H, CH_3 Me), 3.50 (dd, *J* = 9.9, 6.1 Hz, 1H, H-6), 3.42 (s, 3H, CH_3 Me), 3.41 – 3.38 (m, 1H, H-6), 3.33 (s, 3H, CH_3 Me), 3.28 (dd, *J* = 5.5, 1.5 Hz, 2H, H-2, H-3), 2.13 (s, 3H, CH_3 Ac); ^{13}C NMR (126 MHz, $CDCl_3$): δ 170.4, 133.8, 132.0, 128.9, 127.6 (CH_{arom}), 87.6 (C-1), 83.6 (C-3), 78.5 (C-2), 76.1 (C-5), 71.1 (C-6), 66.6 (C-4), 61.4, 59.5, 57.9 (CH_3 Me), 21.0 (CH_3 Ac); HRMS: $[M+Na]^+$ calcd for $C_{17}H_{24}O_6S$, 379.1191, found 379.1201.



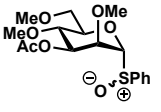
Phenyl 2,3,4-tri-*O*-methyl-1-thio-β-D-galactopyranoside (S25). To a mixture of phenyl 1-thio-β-galactopyranoside (1.00 g, 1 eq, 3.67 mmol) in DMF (18.4 mL) was added imidazole (375 mg, 5.51 mmol) and TBS-Cl (664 mg, 4.41 mmol). The reaction was stirred for 2 h before being quenched by the addition of 0.5 mL of MeOH. The mixture was partitioned between H_2O and Et_2O, and the aqueous layer was extracted. The combined organic phases were subsequently washed with aq. 1 M HCl, sat aq. $NaHCO_3$ and brine before being dried over $MgSO_4$, filtered, and conc. *in vacuo*. The crude product was dissolved in DMF (18.4 mL) and to this solution was added MeI (1.82 g, 804 µL, 3.5 eq, 12.9 mmol) and NaH (0.73 g, 18.4 mmol, 60 wt% in mineral oil) at 0 °C. The reaction stirred at ambient temperature for 18 h before being quenched by careful addition of MeOH (0.5 mL) at 0 °C. The residue was taken up in Et_2O and washed with 5% aq. LiCl and brine. The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was dissolved in 4 mL of THF and treated with 7.3 mL of 1.0 M TBAF (in THF, 2 eq, 7.3 mmol). The mixture was stirred for 3 h and subsequently taken up in EtOAc and H_2O. The water layer was further extracted with EtOAc, and the combined organic layers were dried (MgSO4), filtered and concentrated *in vacuo*. Purification of the residue by Silica column chromatography (50% ethyl acetate in *n*-heptane) afforded S25 (302 mg, 26%) as a white amorphous solid. In addition, the 4-OH regio-isomer (113 mg, 10 %) was obtained. TLC: R_f = 0.13 (EtOAc:*n*-heptane, 50:50, v:v). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52 (dt, *J* = 8.5, 2.0 Hz, 2H, CH_{arom}), 7.35 – 7.13 (m, 3H, CH_{arom}), 4.53 (d, *J* = 9.7 Hz, 1H, H-1), 3.92 (dd, *J* = 11.2, 7.6 Hz, 1H, H-6), 3.75 – 3.66 (m, 1H, H-6), 3.64 (d, *J* = 2.8 Hz, 1H, H-4), 3.60 (s, 3H, CH_3 Me), 3.55 (s, 3H, CH_3 Me), 3.54 (s, 3H, CH_3 Me), 3.48 – 3.35 (m, 2H, H-2, H-5), 3.22 (dd, *J* = 9.2, 3.0 Hz, 1H, H-3), 2.01 (d, *J* = 7.4 Hz, 1H, 6-OH); ^{13}C NMR (126 MHz, $CDCl_3$): δ 134.1, 131.8, 129.0, 127.4 (CH_{arom}), 87.7 (C-1), 86.2 (C-3), 79.4 (C-2), 79.0 (C-5), 76.0 (C-4), 62.5 (C-6), 61.4, 61.3, 58.5 (CH_3 Me); HRMS: $[M+Na]^+$ calcd for $C_{15}H_{22}O_5S$, 337.1086, found 337.1093.



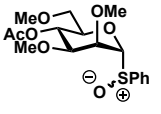
Phenyl 6-*O*-acetyl-2,3,4-tri-*O*-methyl-1-thio-β-D-galactopyranoside (9). *Via* general acetylation protocol starting with **S25** (205 mg, 0.65 mmol). Product **9** (233 mg, *quant.*) was obtained as a pale amorphous solid. TLC: R_f = 0.58 (EtOAc:*n*-heptane, 50:50, v:v). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.63 – 7.45 (m, 2H, CH_{arom}), 7.35 – 7.18 (m, 3H, CH_{arom}), 4.49 (d, *J* = 9.7 Hz, 1H, H-1), 4.31 (dd, *J* = 11.3, 7.2 Hz, 1H, H-6), 4.24 (dd, *J* = 11.3, 5.4 Hz, 1H, H-6), 3.61 (m, 1H, H-4), 3.60 (s, 3H, CH_3 Me), 3.59 – 3.56 (m, 1H, H-5), 3.56 (s, 3H, CH_3 Me), 3.54 (s, 3H), 3.46 – 3.39 (m, 1H, H-2), 3.21 (dd, *J* = 9.2, 3.0 Hz, 1H, H-3), 2.07 (s, 3H, CH_3 Ac); ^{13}C NMR (126 MHz, $CDCl_3$): δ 170.8, 134.3, 131.9, 128.8, 127.4 (CH_{arom}), 87.9 (C-1), 86.1 (C-3), 79.3 (C-2), 76.1 (C-5), 75.7 (C-4), 63.5 (C-6), 61.5, 61.3, 58.6 (CH_3 Me), 21.0 (CH_3 Ac); HRMS: $[M+Na]^+$ calcd for $C_{17}H_{24}O_6S$, 379.1191, found 379.1195.

Phenyl 3-*O*-acetyl-2,4,6-tri-*O*-methyl-1-thiosulfinyl-β-D-glucopyranoside (S26). *Via* general *S*-oxidation protocol starting with **1** (10 mg, 0.028 mmol). HRMS: $[M+Na]^+$ calcd for $C_{17}H_{17}O_7S$, 395.1140, found 395.1150.

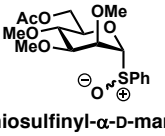
Phenyl 6-*O*-acetyl-2,3,4-tri-*O*-methyl-1-thiosulfinyl-β-D-glucopyranoside (S27). *Via* general *S*-oxidation protocol starting with **2** (10 mg, 0.028 mmol). HRMS: $[M+Na]^+$ calcd for $C_{17}H_{17}O_7S$, 395.1140, found 395.1153.



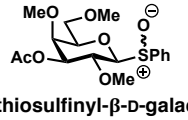
Phenyl 3-*O*-acetyl-2,4,6-tri-*O*-methyl-1-thiosulfinyl-α-D-mannopyranoside (S28). *Via* general *S*-oxidation protocol starting with **3** (17 mg, 0.048 mmol). HRMS: $[M+Na]^+$ calcd for $C_{17}H_{24}O_7S$, 395.1140, found 379.1151.



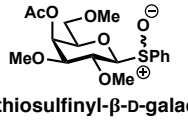
Phenyl 4-*O*-acetyl-2,3,6-tri-*O*-methyl-1-thiosulfinyl-α-D-mannopyranoside (S29). *Via* general *S*-oxidation protocol starting with **4** (10 mg, 0.028 mmol). HRMS: $[M+Na]^+$ calcd for $C_{17}H_{24}O_7S$, 395.1140, found 379.1150.



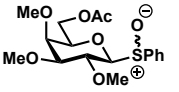
Phenyl 6-*O*-acetyl-2,3,4-tri-*O*-methyl-1-thiosulfinyl-α-D-mannopyranoside (S30). *Via* general *S*-oxidation protocol starting with **5** (25 mg, 0.070 mmol). HRMS: $[M+Na]^+$ calcd for $C_{17}H_{17}O_7S$, 395.1140, found 395.1146.



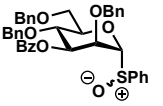
Phenyl 3-*O*-acetyl-2,4,6-tri-*O*-methyl-1-thiosulfinyl-β-D-galactopyranoside (S31). *Via* general *S*-oxidation protocol starting with **6** (10 mg, 0.028 mmol). HRMS: $[M+Na]^+$ calcd for $C_{17}H_{17}O_7S$, 395.1140, found 395.1147.



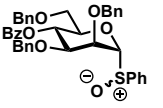
Phenyl 4-*O*-acetyl-2,3,6-tri-*O*-methyl-1-thiosulfinyl-β-D-galactopyranoside (S32). *Via* general *S*-oxidation protocol starting with **7** (13 mg, 0.035 mmol); HRMS: $[M+Na]^+$ calcd for $C_{17}H_{17}O_7S$, 395.1140, found 395.1153.



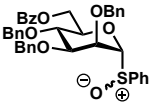
Phenyl 6-*O*-acetyl-2,3,4-tri-*O*-methyl-1-thiosulfinyl-β-D-galactopyranoside (S33). *Via* general *S*-oxidation protocol starting with **8** (12 mg, 0.033 mmol); HRMS: $[M+Na]^+$ calcd for $C_{17}H_{17}O_7S$, 395.1140, found 395.1151.



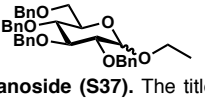
Phenyl 3-*O*-benzoyl-2,4,6-tri-*O*-benzyl-1-thiosulfinyl-β-D-mannopyranoside (S34). *Via* general *S*-oxidation protocol starting with **13** (20 mg, 0.031 mmol). HRMS: $[M+Na]^+$ calcd for $C_{40}H_{38}O_7S$, 685.2236, found 685.2208.



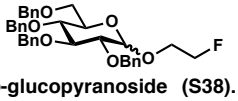
Phenyl 4-*O*-benzoyl-2,3,6-tri-*O*-benzyl-1-thiosulfinyl-β-D-mannopyranoside (S35). *Via* general *S*-oxidation protocol starting with **14** (20 mg, 0.031 mmol). HRMS: $[M+Na]^+$ calcd for $C_{40}H_{38}O_7S$, 685.2236, found 685.2206.



Phenyl 6-*O*-benzoyl-2,3,4-tri-*O*-benzyl-1-thiosulfinyl-β-D-mannopyranoside (S36). *Via* general *S*-oxidation protocol starting with **15** (20 mg, 0.031 mmol). HRMS: $[M+Na]^+$ calcd for $C_{40}H_{38}O_7S$, 685.2236, found 685.2208.

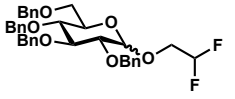


Ethyl 2,3,4,6-tetra-*O*-benzyl-D-glucopyranoside (S37). The title compound was prepared according to general procedure VII. Column chromatography (100:0 → 90:10, pentane:EtOAc) yielded the title compound (40 mg, 58 µmol, 70%, colorless oil, α:β; 15:85). TLC: R_f 0.50 (pentane:EtOAc, 90:10, v:v); IR (thin film, cm^{-1}): 733, 1026, 1065, 1358, 1452, 1497, 2864, 2901; Data of the major stereoisomer (β product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.39 – 7.08 (m, 20H, CH_{arom}), 5.00 – 4.89 (m, 2H, C*H*H Bn, C*H*H Bn), 4.82 (d, *J* = 10.9 Hz, 1H, C*H*H Bn), 4.79 (d, *J* = 11.0 Hz, 1H, CH*H* Bn), 4.72 (d, *J* = 10.9 Hz, 1H, CH*H* Bn), 4.64 – 4.55 (m, 2H, C*H*H Bn), 4.52 (d, *J* = 10.6 Hz, 1H, CH*H* Bn), 4.40 (d, *J* = 7.8 Hz, 1H, H-1), 4.01 (dq, *J* = 9.5, 7.1 Hz, 1H, C*H*HCH$_3$ Et), 3.68 (t, *J* = 5.5 Hz, 1H, H-6), 3.63 (t, *J* = 8.7 Hz, 1H, H-3), 3.72 – 3.54 (m, 1H, CH*H*CH$_3$ Et) 3.57 (t, *J* = 9.2 Hz, 1H, H-4), 3.45 (dd, *J* = 8.9, 7.8 Hz, 1H, H-2), 3.50 – 3.41 (m, 1H, H-5), 1.29 (t, *J* = 7.1 Hz, 3H, CH_3 Et); ^{13}C NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.8, 138.7, 138.3, 138.2 ($C_{q\text{-}arom}$), 128.5, 128.5, 128.5, 128.5, 128.3, 128.2, 128.1, 128.1, 128.0, 127.9, 127.9, 127.8, 127.7, 127.7 (CH_{arom}), 103.6 (C-1), 84.8 (C-3), 82.4 (C-2), 78.1 (C-4), 75.8 (CH_2 Bn), 75.1 (CH_2 Bn), 75.0 (C-5), 74.9 (CH_2 Bn), 73.6 (CH_2 Bn), 69.2 (C-6), 65.7 (*C*H$_2$CH$_3$ Et), 15.5 (CH_3 Et); Data of the minor stereoisomer (α product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.00 (d, *J* = 10.9 Hz, 1H, C*H*H Bn), 4.76 (d, *J* = 3.7 Hz, 1H, H-1), 4.46 (d, *J* = 11.7 Hz, 1H, CH*H* Bn); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 96.7 (C-1); HRMS: $[M+Na]^+$ calcd for $C_{36}H_{40}O_6$ 591.27171, found 591.27077.

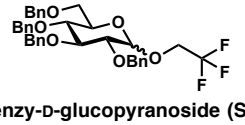


2-Fluoroethyl 2,3,4,6-tetra-*O*-benzy-D-glucopyranoside (S38). The title compound was prepared according to general procedure VII. Column chromatography (97:3 → 90:10, pentane:EtOAc) yielded the

title compound (44 mg, 75 µmol, 75%, colorless oil, α:β; 36:64). TLC: R_f 0.34, 0.46 (pentane:EtOAc, 85:15, v:v); IR (thin film, cm^{-1}): 695, 734, 1027, 1065, 1360, 1453, 1497, 2901; Data of the major stereoisomer (β product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.41 – 7.08 (m, 20H, CH_{arom}), 5.01 – 4.90 (m, 2H, C*H*H Bn, CH*H* Bn), 4.87 – 4.42 (m, 9H, H-1, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, CH_2CHHF, CH_2CHHF), 4.12 (dddd, *J* = 33.2, 12.1, 4.5, 2.5 Hz, 1H, C*H*HCH_2F), 3.94 – 3.54 (m, 5H, H-3, H-4, H-6, H-6, CH*H*CH_2F), 3.49 (dd, *J* = 8.9, 7.8 Hz, 1H, H-2) 3.52 – 3.43 (m, 1H, H-5); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): ^{13}C NMR (101 MHz, $CDCl_3$): δ 138.9, 138.7, 138.5, 138.3, 138.2, 138.1, 138.0 ($C_{q\text{-}arom}$), 128.6, 128.5, 128.3, 128.1, 128.1, 128.0, 128.0, 128.0, 127.9, 127.8, 127.8, 127.8, 127.8, 127.7 (CH_{arom}), 103.9 (C-1), 84.7 (C-3), 82.7 (d, *J* = 169.8 Hz, CH_2F), 82.2 (C-2), 77.8 (C-4), 75.8 (C-5), 75.2 (CH_2 Bn), 75.0 (CH_2 Bn), 74.9 (CH_2 Bn), 73.6 (CH_2 Bn), 69.0 (d, *J* = 20.0 Hz, *C*H_2CH_2F), 68.9 (C-6); Data of the minor stereoisomer (α product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.79 (d, *J* = 3.7 Hz, 1H, H-1), 4.01 (t, *J* = 9.3 Hz, 1H, H-3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 97.5 (C-1), 82.6 (d, *J* = 169.9 Hz, CH_2F), 67.1 (d, *J* = 20.2 Hz, *C*H_2CH_2F); HRMS: $[M+Na]^+$ calcd for $C_{36}H_{39}FO_6$ 609.2628, found 609.2638.

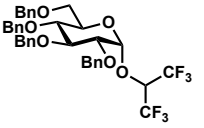


2,2-Difluoroethyl 2,3,4,6-tetra-*O*-benzy-D-glucopyranoside (S39). The title compound was prepared according to general procedure VII. Column chromatography (97:3 → 90:10, pentane:EtOAc) yielded the title compound (35 mg, 58 µmol, 58%, colorless oil, α:β; 48:52). TLC: R_f 0.31 (pentane:EtOAc, 90:10, v:v); IR (thin film, cm-1): 695, 733, 1027, 1066, 1360, 1453, 1497, 2865; Data of the major stereoisomer (β product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.42 – 7.09 (m, 20H, CH_{arom}), 5.96 (tt, *J* = 55.1, 4.2 Hz, 1H, CHF_2), 4.93 (d, *J* = 10.9 Hz, 1H, C*H*H Bn), 4.90 (d, *J* = 11.0 Hz, 1H, C*H*H Bn), 4.84 – 4.74 (m, 2H, C*H*H Bn, CH*H* Bn), 4.70 (d, *J* = 10.8 Hz, 1H, C*H*H Bn), 4.63 (d, *J* = 12.1 Hz, 1H, C*H*H Bn), 4.60 (d, *J* = 11.1 Hz, 1H, CH*H* Bn), 4.53 (d, *J* = 12.2 Hz, 1H, CH*H* Bn), 4.43 (d, *J* = 7.6 Hz, 1H, H-1), 4.03 (dddd, *J* = 19.8, 11.8, 10.8, 3.4 Hz, 1H, CH*H*CHF_2), 3.86 – 3.55 (m, 5H, H-3, H-4, H-6, H-6, C*H*HCHF_2), 3.48 (dd, *J* = 9.0, 7.7 Hz, 1H, H-2) 3.48 – 3.44 (m, 1H, H-5); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ ^{13}C NMR (101 MHz, $CDCl_3$): δ 138.8, 138.6, 138.3, 138.1 ($C_{q\text{-}arom}$), 128.6, 128.5, 128.5, 128.2, 128.1, 128.0, 127.9, 127.9 (CH_{arom}), 114.2 (t, *J* = 241.3 Hz, CHF_2), 104.1 (C-1), 84.5 (C-3), 82.0 (C-2), 77.6 (C-4), 76.8 (CH_2 Bn), 75.9 (CH_2 Bn), 75.1 (CH_2 Bn), 75.0 (C-5), 73.6 (CH_2 Bn), 70.7, 68.8 (C-6), 67.3 (t, *J* = 28.8 Hz, *C*H_2CHF_2); Data of the minor stereoisomer (α product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.75 (d, *J* = 3.6 Hz, 1H, H-1), 3.96 (t, *J* = 9.0 Hz, 1H, H-3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 98.0 (C-1), 73.6 (CH_2 Bn), 68.8 (t, *J* = 28.9 Hz, *C*H_2CHF_2) 68.3 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{36}H_{38}F_2O_6$ 627.2534, found 627.2538.

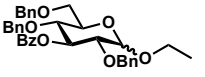


2,2,2-Trifluoroethyl 2,3,4,6-tetra-*O*-benzy-D-glucopyranoside (S40). The title compound was prepared according to general procedure VII. Column chromatography (97:3 → 90:10, pentane:EtOAc) yielded the title compound (50 mg, 80 µmol, 80%, colorless oil, α:β; 72:28). TLC: R_f 0.36 (pentane:EtOAc, 90:10, v:v); IR (thin film, cm^{-1}): 695, 734, 1027, 1047, 1070, 1154, 1277, 1361, 1453, 1497, 2899; Data of the major stereoisomer (α product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.61 – 6.74 (m, 20H, CH_{arom}), 4.98 (d, *J* = 12.0 Hz, 1H, C*H*H Bn), 4.83 (d, *J* = 11.9 Hz, 1H, C*H*H Bn), 4.82 – 4.76 (m, 2H, C*H*H Bn, CH*H* Bn), 4.80 (d, *J* = 2.2 Hz, 1H, H-1), 4.63 (d, *J* = 12.0 Hz, 1H, CH*H* Bn), 4.59 (d, *J* = 12.1 Hz, 1H C*H*H Bn), 4.47 (d, *J* = 11.7 Hz, 1H, CH*H* Bn), 4.46 (d, *J* = 12.1 Hz, 1H, CH*H* Bn), 3.98 (dd, *J* = 9.7, 8.9 Hz, 1H, H-3), 3.88 (q, *J* = 8.7 Hz, 2H, C*H*$_2CF_3$), 3.81 – 3.61 (m, 3H, H-4, H-6, H-6), 3.59 (dd, *J* = 9.6, 3.6 Hz, 1H, H-2); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 138.8, 138.6, 138.2, 138.1, 138.0, 137.8 ($C_{q\text{-}arom}$), 128.6, 128.6, 128.6, 128.5, 128.2, 128.1, 128.1, 128.0, 127.9, 127.9, 127.8, 127.8 (CH_{arom}), 128.2 (q, *J* = 279.5 Hz, CH_2*C*F_3), 97.9 (C-1), 81.7 (C-3), 79.8 (C-2), 77.3 (C-4), 75.9 (CH_2 Bn), 75.3 (CH_2 Bn), 73.6 (CH_2 Bn), 73.5 (CH_2 Bn), 71.0 (C-5), 68.2 (C-6), 64.8 (q, *J* = 34.9 Hz, *C*H_2CF_3); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 97.9 ($J_{H1\text{-}C1}$ = 171 Hz, α); Data of the minor stereoisomer (β product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.93 (d, *J* = 10.9 Hz, 1H), 4.92 (d, *J* = 10.6 Hz, 1H, CHH Bn), 4.68 (d, *J* = 10.7 Hz, 1H, CHH Bn), 4.50 (d, *J* = 7.7 Hz, 1H, H-1), 4.22 (dq, *J* = 12.4, 8.7 Hz, 1H, C*H*$_2CF_3$), 3.50 (dd, *J* = 9.0, 7.6 Hz, 1H, H-2); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 103.8 (C-1), 81.8 (C-3), 75.2 (CH_2 Bn), 75.1 (CH_2 Bn), 68.7 (C-6),

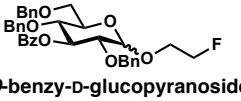
66.2 (q, *J* = 34.9 Hz, *C*H$_2$CF$_3$);^{13}C-GATED NMR (101 MHz, CDCl$_3$): δ 103.8 (J_{H1-C1} = 159 Hz, β); HRMS: [M+Na]$^+$ calcd for $C_{36}H_{37}F_3O_6$ 645.2440, found 645.2455.



1,1,1,3,3,3-Hexafluoro-2-propyl 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside (S41). The title compound was prepared according to general procedure VII. Column chromatography (100:0 → 80:20, pentane:Et$_2$O) yielded the title compound (29 mg, 41 µmol, 41%, colorless oil, α:β; >98:2). TLC: R$_f$ 0.13 (pentane:EtOAc, 95:5, v:v); $[\alpha]_D^{20}$ 20.5° (*c* 1, CHCl$_3$); IR (thin film, cm^{-1}): 687, 696, 736, 1103, 1219, 1287, 1369, 1454, 1498, 2917; ^{1}H NMR (500 MHz, CDCl$_3$, HH-COSY, HSQC, HMBC-Gated, ^{1}H-^{19}F decoupled): δ 7.36 – 7.25 (m, 20H, CH$_{arom}$), 5.14 (d, *J* = 3.8 Hz, 1H, H-1), 4.96 (d, *J* = 10.8 Hz, 1H, C*H*H Bn), 4.82 (dd, *J* = 10.7, 5.5 Hz, 2H, C*H*H Bn, CH*H* Bn), 4.70 (s, 2H, CH$_2$ Bn), 4.60 (d, *J* = 12.1 Hz, 1H, C*H*H Bn), 4.50 – 4.39 (m, 3H, CH*H* Bn, CH*H* Bn, C*H*(CF$_3$)$_2$), 3.96 (t, *J* = 9.5 Hz, 1H, H-3), 3.86 (dt, *J* = 10.1, 2.6 Hz, 1H, H-5), 3.76 (dd, *J* = 10.8, 3.1 Hz, 1H, H-6), 3.63 (dd, *J* = 9.8, 3.8 Hz, 1H, H-2), 3.60 (dd, *J* = 10.8, 2.1 Hz, 1H, H-6); ^{13}C NMR (126 MHz, CDCl$_3$, HSQC, HMBC-Gated): δ 138.7, 138.1, 137.8, 137.7 (C$_{q\text{-}arom}$), 128.6, 128.6, 128.5, 128.2, 128.1, 128.1, 128.0, 128.0, 127.8 (CH$_{arom}$), 99.6 (C-1), 81.3 (C-3), 79.0 (C-2), 77.1 (C-4), 75.9, 75.4, 73.7, 73.5 (CH$_2$ Bn), 72.9 (p, *J* = 33.2, *C*H(CF$_3$)$_2$), 72.0 (C-5), 67.9 (C-6); ^{13}C-GATED NMR (126 MHz, CDCl$_3$): δ 99.6 (J_{H1-C1} = 172 Hz, α); HRMS: [M+Na]$^+$ calcd for $C_{37}H_{36}F_6O_6$ 713.2314, found 713.2329.

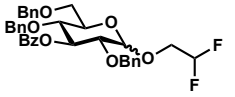


Ethyl 3-*O*-benzoyl-2,4,6-tri-*O*-benzy-D-glucopyranoside (S42). The title compound was prepared according to general procedure VII. Column chromatography (95:5 → 75:25, pentane:Et$_2$O) yielded the title compound (51 mg, 88 µmol, 88%, colorless oil, α:β; 40:60). TLC: R$_f$ 0.15 (pentane:Et$_2$O, 80:20, v:v); IR (thin film, cm^{-1}): 696, 711, 740, 1027, 1047, 1070, 1267, 1452, 1720, 2916, 3031; Data of the major stereoisomer (β product): ^{1}H NMR (500 MHz, CDCl$_3$, HH-COSY, HSQC): δ 7.95 – 6.93 (m, 20H, CH$_{arom}$), 5.49 (t, *J* = 9.5 Hz, 1H, H-4), 4.79 (d, *J* = 11.8 Hz, 1H, C*H*H Bn), 4.58 – 4.34 (m, 6H, H-1, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.03 (dq, *J* = 9.5, 7.1 Hz, 1H, C*H*HCH$_3$ Et), 3.87 – 3.53 (m, 4H, H-4, H-5, H-6, CH*H*CH$_3$ Et), 3.45 (dd, *J* = 9.6, 7.8 Hz, 1H, H-2), 1.31 (t, *J* = 7.1 Hz, 3H, CH$_3$ Et); ^{13}C NMR (126 MHz, CDCl$_3$, HSQC): δ 165.7 (C=O Bz), 138.1, 138.0, 137.6 (C$_{q\text{-}arom}$), 133.1, 131.2, 130.2, 129.9, 129.4, 128.5, 128.5, 128.4, 128.2, 128.2, 127.8, 127.5, 124.9 (CH$_{arom}$), 103.6 (C-1), 78.7 (C-2), 76.4 (C-3), 76.2 (C-4), 74.7 (C-5), 74.6 (CH$_2$ Bn), 73.9 (CH$_2$ Bn), 73.7 (CH$_2$ Bn), 68.7 (C-6), 65.8 (*C*H$_2$CH$_3$ Et), 15.5 (CH$_3$ Et); Data of the minor stereoisomer (α product): ^{1}H NMR (500 MHz, CDCl$_3$, HH-COSY, HSQC): δ 8.03 (dd, *J* = 8.4, 1.4 Hz, 2H, CH$_{arom}$ Bz), 5.82 (dd, *J* = 10.0, 9.1 Hz, 1H, H-3), 4.87 (d, *J* = 3.5 Hz, 1H, H-1), 1.25 (t, *J* = 7.1 Hz, 3H, CH$_3$ Et); ^{13}C NMR (126 MHz, CDCl$_3$, HSQC): δ 165.6 (C=O Bz), 96.5 (C-1), 68.3 (CH$_2$ Bn), 63.7 (C-5), 15.1 (CH$_3$ Et); HRMS: [M+NH$_4$]$^+$ calcd for $C_{36}H_{38}O_7$ 600.29558, found 600.29556.

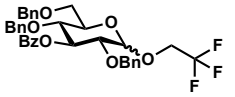


2-Fluoroethyl 3-*O*-benzoyl-2,4,6-tri-*O*-benzy-D-glucopyranoside (S43). The title compound was prepared according to general procedure VII. Column chromatography (95:5 → 75:25, pentane:Et$_2$O) yielded the title compound (57 mg, 95 µmol, 95%, colorless oil, α:β; 44:56). TLC: R$_f$ 0.15 (pentane:Et$_2$O, 70:30, v:v); IR (thin film, cm^{-1}): 697, 711, 742, 1026, 1046, 1070, 1090, 1269, 1452, 1724, 2869, 3030; Data of the major stereoisomer (β product): ^{1}H NMR (500 MHz, CDCl$_3$, HH-COSY, HSQC): δ 8.09 – 6.85 (m, 20H, CH$_{arom}$), 5.50 (t, *J* = 9.4 Hz, 1H, H-3), 4.80 (d, *J* = 11.7 Hz, 1H, C*H*H Bn), 4.57 (d, *J* = 7.6 Hz, 1H, H-1), 4.74 – 4.33 (m, 7H, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, CH$_2$C*H*HF, CH$_2$CH*H*F), 4.14 (dddd, *J* = 32.2, 12.1, 4.8, 2.5 Hz, 1H, C*H*HCH$_2$F), 4.00 – 3.69 (m, 4H, CH*H*CH$_2$F, H-4, H-6, H-6), 3.56 (dt, *J* = 9.8, 3.1 Hz, 1H, H-5), 3.50 (dd, *J* = 9.6, 7.7 Hz, 1H, H-2); ^{13}C NMR (126 MHz, CDCl$_3$, HSQC): δ 165.7 (C=O Bz), 138.0, 137.9, 137.9, 137.8, 137.6, 137.5, 133.1, 133.0, 129.9, 129.9, 129.4, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.3, 128.2, 128.1, 128.0, 128.0, 128.0, 127.9, 127.9, 127.8, 127.8, 127.6 (CH$_{arom}$), 103.9 (C-1), 82.7 (d, *J* = 170.1 Hz, CH$_2$F), 78.4 (C-2), 76.3 (C-3), 76.0 (C-4), 74.8 (C-5), 74.6 (CH$_2$ Bn), 74.6 (CH$_2$ Bn), 73.7 (CH$_2$ Bn), 69.1 (CH$_2$ Bn), 69.0 (d, *J* = 20.1 Hz, CH$_2$*C*H$_2$F), 68.5 (C-6); Data of the minor

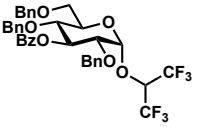
stereoisomer (α product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.82 (dd, *J* = 10.0, 9.2 Hz, 1H, H-3), 4.92 (d, *J* = 3.5 Hz, 1H, H-1); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 165.6 (C=O Bz), 97.2 (C-1), 82.7 (d, *J* = 169.9 Hz, CH_2F), 68.2 (C-6), 67.3 (d, *J* = 20.2 Hz, *C*H_2CH_2F); HRMS: $[M+NH_4]^+$ calcd for $C_{36}H_{37}FO_7$ 618.28616, found 618.28601.



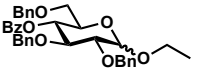
2,2-Difluoroethyl 3-*O*-benzoyl-2,4,6-tri-*O*-benzy-D-glucopyranoside (S44). The title compound was prepared according to general procedure VII. Column chromatography (95:5 → 70:30, pentane:Et_2O) yielded the title compound (60 mg, 97 µmol, 97%, colorless oil, α:β; 58:42). TLC: R_f 0.10 (pentane:Et_2O, 80:20, v:v); IR (thin film, cm^{-1}): 696, 711, 743, 1027, 1070, 1090, 1268, 1452, 1720, 2871, 3031; Data of the major stereoisomer (α product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.17 – 6.80 (m, 20H, CH_{arom}), 5.97 (tt, *J* = 55.5, 4.3 Hz, 1H, CHF_2), 5.78 (dd, *J* = 10.0, 9.1 Hz, 1H, H-3), 4.87 (d, *J* = 3.6 Hz, 1H, H-1), 4.69 – 4.35 (m, 6H, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 3.93 – 3.65 (m, 6H, H-4, H-5, H-6, H-6, C*H*HCHF$_2$, CH*H*CHF$_2$), 3.63 (dd, *J* = 6.5, 3.5 Hz, 1H, H-2); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 165.6 (C=O, Bz), 137.9, 137.7, 137.7, 137.4 ($C_{q\text{-}arom}$), 133.1, 131.2, 130.3, 129.9, 129.4, 128.6, 128.6, 128.4, 128.3, 128.2, 128.1, 128.1, 128.0, 127.9, 127.9, 127.7 (CH_{arom}), 114.2 (t, *J* = 242.0 Hz, CHF_2), 97.7 (C-1), 77.0 (C-2), 76.1 (C-3), 75.8 (C-4), 74.7, 73.8, 72.8 (CH_2 Bn), 70.5 (C-5), 68.1, (C-6) 67.5 (t, *J* = 29.1 Hz, *C*H_2CHF_2); Data of the minor stereoisomer (β product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.49 (t, *J* = 9.4 Hz, 1H, H-3), 4.76 (d, *J* = 11.7 Hz, 1H, C*H*H Bn), 4.69 – 4.35 (m, 6H, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, H-1), 4.05 (dtd, *J* = 18.6, 11.5, 3.3 Hz, 1H, C*H*HCHF$_2$), 3.50 (dd, *J* = 9.5, 7.6 Hz, 1H, H-2); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 165.6 (C=O Bz), 114.2 (t, *J* = 242.0 Hz, CHF_2), 104.1 (C-1), 78.4 (C-2), 76.1 (C-3), 68.8 (dd, *J* = 29.8, 27.4 Hz, *C*H_2CHF_2), 68.3 (C-6); HRMS: $[M+NH_4]^+$ calcd for $C_{36}H_{36}F_2O_7$ 636.27674, found 636.27659.



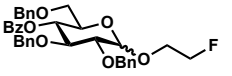
2,2,2-Trifluoroethyl 3-*O*-benzoyl-2,4,6-tri-*O*-benzy-D-glucopyranoside (S45). The title compound was prepared according to general procedure VII. Column chromatography (95:5 → 70:30, pentane:Et_2O) yielded the title compound (58 mg, 91 µmol, 91%, colorless oil, α:β; 76:24). TLC: R_f 0.2 (pentane:Et_2O, 80:20, v:v); IR (thin film, cm^{-1}): 696, 711, 745, 1027, 1072, 1093, 1161, 1270, 1452, 1720, 2926, 3032; Data of the major stereoisomer (α product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.11 – 6.77 (m, 20H, CH_{arom}), 5.79 (dd, *J* = 10.0, 8.8 Hz, 1H, H-3), 4.89 (d, *J* = 3.6 Hz, 1H, H-1), 4.68 – 4.42 (m, 5H, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn), 4.38 (d, *J* = 10.8 Hz, 1H, CH*H* Bn), 3.90 (q, *J* = 8.7 Hz, 2H, C*H*$_2$CF$_3$), 3.88 – 3.86 (m, 1H, H-5), 3.84 (dd, *J* = 10.1, 8.9 Hz, 1H, H-4), 3.77 (dd, *J* = 10.8, 3.0 Hz, 1H, H-6), 3.65 (dd, *J* = 10.1, 3.6 Hz, 1H, H-2), 3.64 (dd, *J* = 9.0, 5.4 Hz, 1H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 165.6 (C=O Bz), 137.9, 137.8, 137.7, 137.5 ($C_{q\text{-}arom}$), 130.3, 130.0, 128.6, 128.6, 128.5, 128.4, 128.3, 128.2, 128.2, 128.2, 128.1, 128.0, 128.0, 127.9, 127.9 (CH_{arom}), 123.7 (q, *J* = 279.0 Hz, CF_3) 97.8 (C-1), 76.8 (C-2), 75.7 (C-4), 74.7 (CH_2 Bn), 73.9 (C-3), 73.8 (CH_2 Bn), 72.7 (CH_2 Bn), 70.8 (C-5), 68.0 (C-6), 65.2 (q, *J* = 35.0 Hz, *C*H_2CF_3); Data of the minor stereoisomer (β product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.49 (t, *J* = 9.4 Hz, 1H, H-3), 4.77 (d, *J* = 11.7 Hz, 1H, C*H*H Bn), 4.68 – 4.42 (m, 5H, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn), 4.60 (d, *J* = 7.6 Hz, 1H, H-1), 4.41 (d, *J* = 10.8 Hz, 1H, CH*H* Bn), 4.24 (dt, *J* = 12.1, 8.7 Hz, 1H, C*H*$_2$CF$_3$), 3.97 (dq, *J* = 12.1, 8.4 Hz, 1H, C*H*$_2$CF$_3$), 3.51 (dd, *J* = 9.5, 7.6 Hz, 1H, H-2); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 165.6 (C=O Bz), 103.7 (C-1), 76.0 (C-3), 74.6 (CH_2 Bn), 73.9 (CH_2 Bn), 73.7 (CH_2 Bn), 68.3 (C-6), 66.3 (q, *J* = 35.1 Hz, *C*H_2CF_3); HRMS: $[M+NH_4]^+$ calcd for $C_{36}H_{35}F_3O_7$ 654.26731, found 654.26721.



1,1,1,3,3,3-Hexafluoro-2-propyl 3-*O*-benzoyl-2,4,6-tri-*O*-benzyl-α-D-glucopyranoside (S46). The title compound was prepared according to general procedure VII. Column chromatography (100:0 → 80:20, pentane:Et_2O) yielded the title compound (20 mg, 28 µmol, 28%, colorless oil, α:β; >98:2). TLC: R_f 0.1 (pentane:Et_2O, 90:10, v:v); $[\alpha]_D^{25}$ 7.6° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 590, 867, 697, 710, 736, 1027, 1070, 1195, 1219, 1266, 1285, 1368, 1452, 1720, 2921, 3032; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.14 – 6.82 (m, 20H, CH_{arom}), 5.75 (t, *J* = 9.7 Hz, 1H, H-3), 5.21 (d, *J* = 3.8 Hz, 1H, H-1), 4.63 (d, *J* = 12.0 Hz, 1H, C*H*H Bn), 4.61 (d, *J* = 12.4 Hz, 1H, C*H*H Bn), 4.51 – 4.42 (m, 4H, C*H*H Bn, CH*H* Bn, CH*H* Bn, C*H*(CF_3)$_2$), 4.39 (d, *J* = 10.8 Hz, 1H, CH*H* Bn), 3.98 (dt, *J* = 10.0, 2.3 Hz, 1H, H-5), 3.85 (t, *J* = 9.7 Hz, 1H, H-4), 3.80 (dd, *J* = 10.9, 2.8 Hz, 1H, H-6), 3.71 (dd, *J* = 10.1, 3.8 Hz, 1H, H-2), 3.62 (dd, *J* = 10.9, 2.1 Hz, 1H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 137.6, 137.4 ($C_{q\text{-}arom}$), 133.3, 133.2, 130.0, 128.7, 128.5, 128.4, 128.3, 128.2, 128.2, 128.1, 127.9 (CH_{arom}), 99.3 (C-1), 75.8 (C-2), 75.4 (C-4), 74.9, 73.9 (CH_2 Bn), 73.6 (C-3), 72.5 (CH_2 Bn), 71.7 (C-5), 67.7 (C-6); HRMS: $[M+NH_4]^+$ calcd for $C_{37}H_{34}F_6O_7$ 722.25470, found 722.25415.

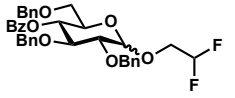


Ethyl 4-*O*-benzoyl-2,3,6-tri-*O*-benzy-D-glucopyranoside (S47). The title compound was prepared according to general procedure VII. Column chromatography 95:5 → 80:20, pentane:Et_2O) yielded the title compound (44 mg, 76 µmol, 76%, colorless oil, α:β; 15:85). TLC: R_f 0.30 (pentane:Et_2O, 80:20, v:v); IR (thin film, cm^{-1}): 696, 711, 735, 1027, 1043, 1266, 1452, 1720, 2869, 3031; Data of the major stereoisomer (β product): ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.00 – 7.00 (m, 20H, CH_{arom}), 5.24 (dd, *J* = 10.0, 9.3 Hz, 1H, H-4), 4.96 (d, *J* = 10.9 Hz, 1H, C*H*H Bn), 4.77 (d, *J* = 11.2 Hz, 1H, C*H*H Bn), 4.74 (d, *J* = 10.9 Hz, 1H, CH*H* Bn), 4.61 (d, *J* = 11.2 Hz, 1H, CH*H* Bn), 4.50 (d, *J* = 7.8 Hz, 1H, H-1), 4.47 (m, 2H, C*H*H Bn, CH*H* Bn), 4.11 – 3.98 (m, 1H, C*H*HCH$_3$ Et), 3.75 (t, *J* = 9.3 Hz, 1H, H-3), 3.72 – 3.59 (m, 4H, H-5, CH*H*CH$_3$ Et, H-6, H-6), 3.56 (dd, *J* = 9.2, 7.8 Hz, 1H, H-2), 1.31 (t, *J* = 7.1 Hz, 3H, CH_3 Et); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 165.5 (C=O Bz), 138.5, 138.4, 138.3, 138.1, 138.0, 137.9 ($C_{q\text{-}arom}$), 133.3, 129.9, 129.8, 128.5, 128.5, 128.3, 128.3, 128.3, 128.3, 128.2, 128.1, 127.9, 127.8, 127.6, 127.6, 127.5 (CH_{arom}), 103.5 (C-1), 82.2 (C-2), 81.6 (C-3), 75.2, 75.1 (CH_2 Bn), 73.8 (C-5), 73.8 (CH_2 Bn), 71.6 (C-4), 70.0 (C-6), 65.9 (*C*H$_2$CH$_3$ Et), 15.5 (CH_3 Et); Data of the minor stereoisomer (α product): ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.32 (dd, *J* = 10.3, 9.3 Hz, 1H, H-4), 4.85 (d, *J* = 11.2 Hz, 1H, C*H*H Bn), 4.79 (d, *J* = 3.6 Hz, 1H, H-1), 4.66 (d, *J* = 12.1 Hz, 1H, CH*H* Bn); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 165.4 (C=O Bz), 96.7 (C-1), 79.8, 79.5 (CH_2 Bn), 71.3 (C-4), 69.2 (C-6), 63.7 (*C*H$_2$CH$_3$ Et), 15.1 (CH_3 Et); HRMS: $[M+NH_4]^+$ calcd for $C_{36}H_{38}O_7$ 600.29558, found 600.29548.

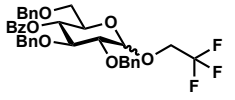


2-Fluoroethyl 4-*O*-benzoyl-2,3,6-tri-*O*-benzy-D-glucopyranoside (S48). The title compound was prepared according to general procedure VII. Column chromatography (90:10 → 60:40, pentane:Et_2O) yielded the title compound (49 mg, 82 µmol, 82%, colorless oil, α:β; 34:66). TLC: R_f 0.2 (pentane:Et_2O, 70:30, v:v); IR (thin film, cm^{-1}): 696, 711, 740, 1027, 1042, 1090, 1268, 1452, 1720, 2867, 3030; Data of the major stereoisomer (β product): ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): 7.97 – 7.12 (m, 20H, CH_{arom}), 5.25 (dd, *J* = 10.0, 9.3 Hz, 1H, H-4), 4.98 (d, *J* = 11.8 Hz, 1H, C*H*H Bn), 4.87 – 4.81 (m, 1H, CH*H* Bn), 4.78 (d, *J* = 11.2 Hz, 1H, C*H*H Bn), 4.73 (d, *J* = 11.8 Hz, 1H, CH*H* Bn), 4.71 – 4.57 (m, 4H, C*H*H Bn, CH*H* Bn, CH$_2$C*H*HF, CH$_2$CH*H*F), 4.55 (d, *J* = 7.8 Hz, 1H, H-1), 4.22 – 3.78 (m, 2H, C*H*HCH$_2$F, CH*H*CH$_2$F), 3.76 (t, *J* = 9.2 Hz, 1H, H-3), 3.75 – 3.65 (m, 1H, H-5), 3.64 – 3.57 (m, 3H, H-6, H-6, H-2); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 165.5 (C=O Bz), 138.3, 138.0, 137.9 ($C_{q\text{-}arom}$), 133.3, 133.2, 131.2, 129.9, 129.7, 129.4, 128.6, 128.5, 128.4, 128.3, 128.1, 128.0, 127.9, 127.8, 127.8, 127.8, 127.7, 127.6, 127.6, 127.5 (CH_{arom}), 103.8 (C-1), 81.7 (d, *J* = 73.4 Hz, CH_2F), 81.5 (C-2), 75.2, 75.1 (CH_2 Bn), 73.8 (C-5), 73.7 (CH_2 Bn), 71.3 (C-4), 69.8 (C-6), 67.0 (d, *J* = 15.2 Hz, *C*H$_2$CH$_2$F); Data of the minor stereoisomer (α product): ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.35 (dd, *J* = 10.3, 9.3 Hz, 1H, H-4), 4.09 (t, *J* = 9.4 Hz, 1H,

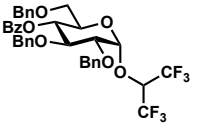
H-3), 4.84 – 4.80 (m, 2H, CH*H* Bn, H-1), 3.51 (dd, *J* = 10.9, 5.0 Hz, 1H, H-2); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 165.4 (C=O Bz), 97.5 (C-1), 79.5 (d, *J* = 56.2 Hz, CH_2F), 71.0 (C-4), 67.4 (d, *J* = 19.9 Hz, *C*H_2CH_2F); HRMS: $[M+NH_4]^+$ calcd for $C_{36}H_{37}FO_7$ 618.28616, found 618.28582.



2,2-Difluoroethyl 4-*O*-benzoyl-2,3,6-tri-*O*-benzy-D-glucopyranoside (S49). The title compound was prepared according to general procedure VII. Column chromatography (95:5 →70:30, pentane:Et_2O) yielded the title compound (43 mg, 70 µmol, 70%, colorless oil, α:β; 48:52). TLC: R_f 0.25 (pentane:Et_2O, 80:20, v:v); IR (thin film, cm^{-1}): 697, 711, 738, 1027, 1093, 1268, 1452, 1720, 2869, 3032; Data of the major stereoisomer (β product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.20 – 7.03 (m, 20H, CH_{arom}), 6.04 (tt, *J* = 55.5, 4.5 Hz, 1H, CHF_2), 5.33 (dd, *J* = 10.3, 9.3 Hz, 1H, H-4), 4.86 – 4.59 (m, 6H, CH_2 Bn, CH_2 Bn, CH_2 Bn, CH_2 Bn, CH_2 Bn, CH_2 Bn), 4.53 (d, *J* = 7.8 Hz, 1H, H-1), 4.13 – 3.96 (m, 1H, C*H*HCHF$_2$), 3.91 – 3.65 (m, 2H, CH*H*CHF$_2$, H-5), 3.75 (t, *J* = 9.2 Hz, 1H, H-3), 3.64 – 3.53 (m, 3H, H-6, H-6, H-2); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 165.4 (C=O Bz), 138.2, 138.2, 138.0, 137.9, 137.8, 137.7 ($C_{q\text{-}arom}$), 129.8, 129.7, 128.6, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, , 128.0, 127.7, 127.6 (CH_{arom}), 114.2 (t, *J* = 241.3 Hz, CHF_2), 104.0 (C-1), 81.9 (C-2), 81.4 (C-3), 75.6 (CH_2 Bn), 75.3 (CH_2 Bn), 73.9 (C-5), 73.8 (CH_2 Bn), 71.2 (C-4), 68.8 (C-6), 67.7 (t, *J* = 28.8 Hz, *C*H_2CHF$_2$); Data of the minor stereoisomer (α product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 6.0 (dddd, *J* = 56.0, 54.8, 5.3, 3.0 Hz, 1H, CHF_2), 5.3 (dd, *J* = 10.0, 9.3 Hz, 1H, H-4), 4.91 (d, *J* = 11.8 Hz, 1H, C*H*H Bn), 4.78 (d, *J* = 3.7 Hz, 1H, H-1), 4.04 (t, *J* = 9.5 Hz, 1H, H-3); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 165.4 (C=O Bz), 114.2 (dd, *J* = 242.2, 239.9 Hz, CHF_2), 98.3 (C-1), 70.8 (C-4), 69.6 (C-6), 68.9 (dd, *J* = 30.4, 26.6 Hz, *C*H_2CHF$_2$); HRMS: $[M+NH_4]^+$ calcd for $C_{36}H_{36}F_2O_7$ 636.27674, found 636.27675.

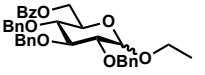


2,2,2-Trifluoroethyl 4-*O*-benzoyl-2,3,6-tri-*O*-benzy-D-glucopyranoside (S50). The title compound was prepared according to general procedure VII. Column chromatography (95:5 → 80:20, pentane:Et_2O) yielded the title compound (49 mg, 76 µmol, 76%, colorless oil, α:β; 79:21). TLC: R_f 0.4 (pentane:Et_2O, 80:20, v:v); IR (thin film, cm^{-1}): 697, 711, 738, 1027, 1070, 1093, 1161, 1270, 1452, 1720, 2959, 2910, 3032; Data of the major stereoisomer (α product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.07 – 6.88 (m, 20H, CH_{arom}), 5.35 (dd, *J* = 10.3, 9.3 Hz, 1H, H-4), 4.87 – 4.78 (m, 3H, C*H*H Bn, CH*H* Bn, H-1), 4.67 – 4.60 (m, 2H, C*H*H Bn, CH*H* Bn), 4.50 – 4.41 (m, 2H, C*H*H Bn, CH*H* Bn), 4.06 (t, *J* = 9.5 Hz, 1H, H-3), 4.00 – 3.87 (m, 3H, CH_2CF$_3$, H-5), 3.70 (dd, *J* = 9.6, 3.6 Hz, 1H, H-2), 3.55 (dd, *J* = 10.9, 2.7 Hz, 1H, H-6), 3.50 (dd, *J* = 10.9, 5.0 Hz, 1H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 165.3 (C=O Bz), 138.2, 138.0, 137.7 ($C_{q\text{-}arom}$), 129.7, 128.6, 128.5, 128.4, 128.3, 128.2, 128.2, 128.0, 127.8, 127.7, 127.6, 127.2, 123.9 (q, *J* = 278.7 Hz, CF_3), 97.9 (C-1), 79.5 (C-2), 78.9 (C-3), 75.6, 73.8, 73.6 (CH_2 Bn), 70.6 (C-4), 69.9 (C-5), 68.7 (C-6), 64.9 (q, *J* = 34.9 Hz, *C*H_2CF$_3$); Data of the minor stereoisomer (β product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.26 (dd, *J* = 10.0, 9.3 Hz, 1H, H-4), 4.93 (d, *J* = 10.6 Hz, 1H, C*H*H Bn), 4.60 (d, *J* = 7.1 Hz, 1H, H-1), 3.75 (t, *J* = 9.2 Hz, 1H, H-3); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 103.6 (C-1), 81.7 (C-2), 81.2 (C-3), 71.0 (C-4) 69.4 (C-6); HRMS: $[M+NH_4]^+$ calcd for $C_{36}H_{35}F_3O_7$ 654.26731, found 654.26708.

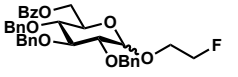


1,1,1,3,3,3-Hexafluoro-2-propyl 4-*O*-benzoyl-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (S51). The title compound was prepared according to general procedure VII. Column chromatography (100:0 → 80:20, pentane:Et_2O) yielded the title compound (13 mg, 19 µmol, 19%, colorless oil, α:β; >98:2). TLC: R_f 0.1 (pentane:Et_2O, 90:10, v:v); $[\alpha]_D^{25}$ 0.7° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 538, 688, 696, 711, 741, 1027, 1068, 1104, 1196, 1219, 1264, 1286, 1452, 1720, 2924, 3032; ^{1}H NMR (500 MHz, CDCl3, HH-COSY, HSQC): δ

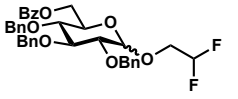
8.42 – 6.93 (m, 20H, CH_{arom}), 5.42 (dd, *J* = 10.3, 9.4 Hz, 1H, H-4), 5.16 (d, *J* = 3.7 Hz, 1H, H-1), 4.82 (d, *J* = 11.1 Hz, 1H, C*H*H Bn), 4.74 (d, *J* = 11.6 Hz, 1H, C*H*H Bn), 4.70 (d, *J* = 11.6 Hz, 1H, CH*H* Bn), 4.61 (d, *J* = 11.1 Hz, 1H, CH*H* Bn), 4.55 – 4.47 (m, 2H, CH*H* Bn, C*H*(CF_3)$_2$), 4.42 (d, *J* = 12.0 Hz, 1H, CH*H* Bn), 4.13 – 4.05 (m, 1H, H-5), 4.04 (t, *J* = 9.6 Hz, 1H, H-3), 3.75 (dd, *J* = 9.8, 3.8 Hz, 1H, H-2), 3.55 (dd, *J* = 11.0, 2.6 Hz, 1H, H-6), 3.50 (dd, *J* = 11.0, 4.4 Hz, 1H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 165.3 (C=O Bz), 133.4, 131.2 ($C_{q\text{-}arom}$), 129.9, 129.5, 128.6, 128.6, 128.4, 128.3, 128.2, 128.2, 128.1, 127.9, 127.7, 127.7 (CH_{arom}), 99.5 (C-1), 77.2 (C-2), 76.9 (C-3), 75.6, 73.8, 73.7 (CH_2 Bn), 70.8 (C-5), 70.1 (C-4), 68.2 (C-6); HRMS: $[M+NH_4]^+$ calcd for $C_{37}H_{34}F_6O_7$ 722.25470, found 722.25434.



Ethyl 6-*O*-benzoyl-2,3,4-tri-*O*-benzy-D-glucopyranoside (S52). The title compound was prepared according to general procedure VII. Column chromatography (95:5 → 75:25, pentane:Et_2O) yielded the title compound (55 mg, 94 µmol, 94%, colorless oil, α:β; 17:83). TLC: R_f 0.30 (pentane:Et_2O, 80:20, v:v); IR (thin film, cm^{-1}): 695, 711, 735, 1026, 1066, 1272, 1720, 2904, 3030; Data of the major stereoisomer (β product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.27 – 7.12 (m, 20H, CH_{arom}), 4.98 (d, *J* = 11.0 Hz, 1H, C*H*H Bn), 4.97 (d, *J* = 10.8 Hz, 1H, C*H*H Bn), 4.89 (d, *J* = 10.7 Hz, 1H, C*H*H Bn), 4.82 (d, *J* = 10.7 Hz, 1H, CH*H* Bn), 4.75 (d, *J* = 10.8 Hz, 1H, CH*H* Bn), 4.60 (m, 2H, CH*H* Bn, H-6), 4.54 – 4.42 (m, 2H, H-6, H-1), 3.98 (dq, *J* = 9.3, 7.2 Hz, 1H, C*H*$_2$CH$_3$ Et), 3.71 (t, *J* = 8.6 Hz, 1H, H-3), 3.71 – 3.55 (m, 3H, C*H*$_2$CH$_3$ Et, H-4, H-5), 3.49 (t, *J* = 8.3 Hz, 1H, H-2), 1.28 (t, *J* = 7.2 Hz, 3H, CH$_2$C*H*$_3$ Et); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 166.4 (C=O Bz), 133.2, 133.1, 130.2 ($C_{q\text{-}arom}$), 129.8, 129.8, 128.6, 128.6, 128.6, 128.5, 128.5, 128.3, 128.2, 128.2, 128.2, 128.1, 128.1, 127.9, 127.9 (CH_{arom}), 103.7 (C-1), 84.8 (C-3), 82.4 (C-2), 77.8 (C-4), 76.0, 75.3, 75.0 (CH_2 Bn), 73.1 (C-5), 65.9 (*C*H$_2$CH$_3$ Et), 63.7 (C-6), 15.5 (CH$_3$ Et); Data of the minor stereoisomer (α product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.04 (d, *J* = 10.6 Hz, 1H, C*H*H Bn), 4.92 (d, *J* = 10.7 Hz, 1H, C*H*H Bn), 4.85 (d, *J* = 10.5 Hz, 1H, CH*H* Bn), 4.77 (signal overlaps with major isomer, 1H, H-1), 4.67 (d, *J* = 12.1 Hz, 1H, CH*H* Bn), 4.08 (t, *J* = 9.2 Hz, 1H, H-3); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 96.5 (C-1), 82.3 (C-3), 80.3 (C-2), 77.8 (C-4), 76.1, 75.4, 73.4 (CH_2 Bn), 68.9 (C-5), 63.6 (*C*H$_2$CH$_3$ Et), 63.6 (C-6), 15.1 (CH$_3$ Et); HRMS: $[M+NH_4]^+$ calcd for $C_{36}H_{38}O_7$ 600.29558, found 600.29595.

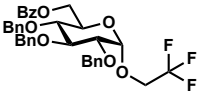


2-Fluoroethyl 6-*O*-benzoyl-2,3,4-tri-*O*-benzy-D-glucopyranoside (S53). The title compound was prepared according to general procedure VII. Column chromatography (90:10 → 60:40, pentane:Et_2O) yielded the title compound (50 mg, 83 µmol, 83%, colorless oil, α:β; 35:65). TLC: R_f 0.2 (pentane:Et_2O, 70:30, v:v); IR (thin film, cm^{-1}): 696, 712, 736, 1026, 1067, 1154, 1273, 1452, 1720; Data of the major stereoisomer (β product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.12 – 6.99 (m, 20H, CH_{arom}), 4.98 (m, 2H, C*H*H Bn, C*H*H Bn), 4.87 (m, 1H, CH*H* Bn), 4.85 – 4.78 (m, 3H, C*H*H Bn, CH*H* Bn, CH*H* Bn), 4.69 – 4.48 (m, 4H, H-6, H-6, CH$_2$C*H*HF, CH$_2$CH*H*F), 4.50 (d, *J* = 7.7 Hz, 1H, H-1), 4.13 – 4.00 (m, 1H, C*H*HCH$_2$F), 3.92 – 3.75 (m, 1H, CH*H*CH$_2$F), 3.72 (t, *J* = 8.8 Hz, 1H, H-3), 3.69 – 3.58 (m, 2H, H-4, H-5), 3.53 (dd, *J* = 8.9, 7.8 Hz, 1H, H-2); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 166.3 (C=O Bz), 138.5, 138.4, 137.7 ($C_{q\text{-}arom}$), 129.8, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.3, 128.1, 128.1, 127.9 (CH_{arom}), 104.0 (C-1), 84.7 (C-3), 82.7 (d, *J* = 169.9 Hz, CH$_2$F) 82.2 (C-2), 77.6 (C-4), 76.0, 75.3, 73.2 (CH_2 Bn), 69.1 (d, *J* = 19.8 Hz, *C*H$_2$CH$_2$F), 63.5 (C-6); Data of the minor stereoisomer (α product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.03 (d, *J* = 10.6 Hz, 1H, C*H*H Bn), 4.81 (d, *J* = 2.0 Hz, 1H, H-1), 4.08 (t, *J* = 9.4 Hz, 1H, H-3); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): 97.3 (C-1), 82.6 (d, *J* = 170.2 Hz, CH$_2$F), 67.2 (d, *J* = 20.2 Hz, *C*H$_2$CH$_2$F), 63.5 (C-6); HRMS: $[M+NH_4]^+$ calcd for $C_{36}H_{37}FO_7$ 618.28616, found 618.28612.

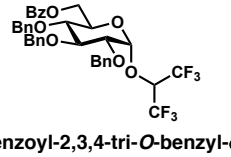


2,2-Difluoroethyl 6-*O*-benzoyl-2,3,4-tri-*O*-benzy-D-glucopyranoside (S54). The title compound was prepared according to general procedure VII. Column chromatography (95:5 → 75:25, pentane:Et_2O) yielded the title compound (51 mg, 82 µmol, 82%, colorless oil, α:β; 77:23). TLC: R_f 0.30 (pentane:Et_2O, 80:20, v:v); IR (thin film, cm^{-1}): 696, 711, 737, 1274, 1452, 1720, 2917, 3032; Data of the major stereoisomer

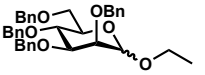
(α product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.07 – 7.04 (m, 20H, CH_{arom}), 5.97 (tt, *J* = 55.5, 4.3 Hz, 1H, CHF_2), 5.01 (d, *J* = 10.6 Hz, 1H, C*H*H Bn), 4.92 (d, *J* = 10.8 Hz, 1H, C*H*H Bn), 4.85 (d, *J* = 10.6 Hz, 1H, CH*H* Bn), 4.81 (d, *J* = 11.9 Hz, 1H CH*H* Bn), 4.75 (d, *J* = 3.6 Hz, 1H, H-1), 4.68 – 4.59 (m, 2H, C*H*H Bn, CH*H* Bn), 4.54 (dd, *J* = 12.0, 2.2 Hz, 1H, H-6), 4.52 – 4.43 (m, 1H, H-6), 4.04 (t, *J* = 9.3 Hz, 1H, H-3), 4.00 (ddd, *J* = 10.2, 4.7, 2.1 Hz, 1H, H-5), 3.86 – 3.56 (m, 4H, H-2, H-4, C*H*HCHF$_2$, CH*H*CHF$_2$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 166.3 (C=O Bz), 138.6, 138.1, 137.7 ($C_{q\text{-}arom}$), 129.7, 128.7, 128.6, 128.6, 128.5, 128.4, 128.2, 128.2, 128.2, 127.9 (CH_{arom}), 114.1 (t, *J* = 241.4 Hz, CHF_2), 97.8 (C-1), 81.9 (C-3), 80.1 (C-2), 77.5 (C-4), 76.1, 75.4, 73.7 (CH_2 Bn), 69.5 (C-5), 67.3 (t, *J* = 28.8 Hz, *C*H$_2$CHF$_2$), 63.4 (C-6); Data of the minor stereoisomer (β product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 6.12 – 5.64 (m, 1H CHF_2), 4.97 (d, *J* = 10.8 Hz, 1H, C*H*H Bn), 4.73 (d, *J* = 10.9 Hz, 1H, CH*H* Bn), 4.49 (d, *J* = 7.8 Hz, 1H, H-1), 3.51 (dd, *J* = 9.0, 7.7 Hz, 1H, H-2); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 104.2 (C-1), 84.6 (C-3), 82.1 (C-2), 76.0, 75.3, 75.1 (CH_2 Bn), 68.9 (dd, *J* = 29.8, 27.3 Hz, *C*H$_2$CHF$_2$), 63.3 (C-6); HRMS: $[M+NH_4]^+$ calcd for $C_{36}H_{36}F_2O_7$ 636.27674, found 636.27645.



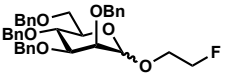
2,2,2-Trifluoroethyl 3-*O*-benzoyl-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (S55). The title compound was prepared according to general procedure VII. Column chromatography (95:5 → 80:20, pentane:Et_2O) yielded the title compound (52 mg, 82 µmol, 82%, colorless oil, α:β; 95:5). TLC: R_f 0.45 (pentane:Et_2O, 80:20, v:v); $[\alpha]_D^{25}$ 40.2° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 696, 711, 736, 1027, 1070, 1273, 1452, 1720, 2920, 3032; Data of the major stereoisomer (α product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.71 – 6.95 (m, 20H, CH_{arom}), 5.02 (d, *J* = 10.6 Hz, 1H, C*H*H Bn), 4.92 (d, *J* = 10.8 Hz, 1H, C*H*H Bn), 4.85 (d, *J* = 10.6 Hz, 1H, CH*H* Bn), 4.85 (d, *J* = 3.6 Hz, 1H, H-1) 4.82 (m, 1H, CH*H* Bn), 4.64 (m, 1H, C*H*H Bn, CH*H* Bn) 4.54 (dd, *J* = 12.0, 2.2 Hz, 1H, H-6), 4.47 (dd, *J* = 12.1, 4.5 Hz, 1H, H-6), 4.05 (dd, *J* = 9.7, 8.9 Hz, 1H, H-3), 3.97 (ddd, *J* = 10.1, 4.5, 2.2 Hz, 1H, H-5), 3.89 (qd, *J* = 8.7, 7.0 Hz, 2H, C*H*$_2$CF$_3$), 3.63 (t, *J* = 10.0 Hz, 1H, H-4), 3.60 (dd, *J* = 9.6, 3.7 Hz, 1H, H-2); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 166.2 (C=O Bz), 138.6, 138.1, 137.7 ($C_{q\text{-}arom}$), 129.9, 129.7, 128.7, 128.7, 128.6, 128.6, 128.6, 128.5, 128.3, 128.2, 128.2, 128.2, 128.2, 128.1, 128.1, 128.0, 127.1 (CH_{arom}), 123.8 (q, *J* = 278.8 Hz, CF_3), 97.7 (C-1), 81.7 (C-3), 80.0 (C-2), 77.3 (C-4), 76.1, 75.4, 73.5 (CH_2 Bn), 65.3 (C-5), 64.9 (q, *J* = 35.0 Hz, *C*H$_2$CF$_3$), 63.2 (C-6); Data of the minor stereoisomer (β product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): 1H NMR (500 MHz, $CDCl_3$): δ 5.06 (d, *J* = 10.7 Hz, 1H, C*H*H Bn), 4.70 (d, *J* = 10.6 Hz, 1H, CH*H* Bn), 4.18 (dq, *J* = 12.3, 8.8 Hz, 1H, C*H*$_2$CF$_3$), 3.53 (dd, *J* = 8.7, 7.7 Hz, 1H, H-2); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): 103.8 (C-1), 84.5 (C-3), 81.9 (C-2); HRMS: $[M+NH_4]^+$ calcd for $C_{36}H_{35}F_3O_7$ 654.26731, found 654.26723.



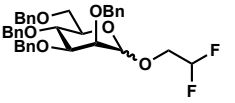
1,1,1,3,3,3-Hexafluoro-2-propyl 6-*O*-benzoyl-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (S56). The title compound was prepared according to general procedure VII. Column chromatography (100:0 → 80:20, pentane:Et_2O) yielded the title compound (21 mg, 30 µmol, 30%, colorless oil, α:β; >98:2). TLC: R_f 0.1 (pentane:Et_2O, 90:10, v:v); $[\alpha]_D^{25}$ 49.0° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 595, 698, 712, 750, 1027, 1105, 1198, 1278, 1454, 1720, 2933, 3035; ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.07 – 7.16 (m, 20H, CH_{arom}), 5.15 (d, *J* = 3.8 Hz, 1H, H-1), 5.00 (d, *J* = 10.6 Hz, 1H, C*H*H Bn), 4.93 (d, *J* = 10.7 Hz, 1H, C*H*H Bn), 4.85 (d, *J* = 10.6 Hz, 1H, CH*H* Bn), 4.76 – 4.66 (m, 2H, C*H*H Bn, CH*H* Bn), 4.63 (d, *J* = 10.7 Hz, 1H, CH*H* Bn), 4.56 (dd, *J* = 12.1, 2.1 Hz, 1H, H-6), 4.46 (m, 2H, H-6, C*H*(CF$_3$)$_2$), 4.09 (ddd, *J* = 10.2, 4.3, 2.1 Hz, 1H, H-5), 4.04 (dd, *J* = 9.8, 9.0 Hz, 1H, H-3), 3.78 – 3.59 (m, 2H, H-4, H-2); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 166.2 (C=O Bz), 138.4, 137.6, 137.5 ($C_{q\text{-}arom}$), 133.4, 129.8, 129.7, 128.7, 128.6, 128.6, 128.3, 128.3, 128.3, 128.2, 128.2, 128.2, 128.0, 127.7 (CH_{arom}), 99.2 (C-1), 81.2 (C-3), 79.2 (C-2), 77.4 (C-4), 76.9, 76.1, 73.7 (CH_2 Bn), 72.9 (p, *J* = 33.6 Hz, *C*H(CF$_3$)$_2$), 62.9 (C-6); HRMS: $[M+NH_4]^+$ calcd for C37H34F6O7 722.25470, found 722.25454.



Ethyl 2,3,4,6-tetra-*O*-benzy-D-mannopyranoside (S57). The title compound was prepared according to general procedure VII. Column chromatography (100:0 → 90:10, pentane:EtOAc) yielded the title compound (40 mg, 70 µmol, 70%, colorless oil, α:β; 33:67). TLC: R_f 0.25 (pentane:EtOAc, 90:10, v:v); Data of the major stereoisomer (β product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.50 – 7.14 (m, 20H, CH_{arom}), 4.99 (d, *J* = 12.5 Hz, 1H, C*H*H Bn), 4.93 – 4.84 (m, 2H, C*H*H Bn, CH*H* Bn), 4.69 – 4.58 (m, 4H, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.44 (d, J = 11.8 Hz, 1H, CH*H* Bn), 4.38 (s, 1H, H-1), 4.07 – 3.97 (m, 1H, C*H*HCH$_3$ Et), 3.97 – 3.67 (m, 5H, CH*H*CH$_3$ Et, H-2, H-4, H-6, H-6), 3.57 – 3.36 (m, 3H, CH*H*CH$_3$ Et, H-5, H-3), 1.27 (t, *J* = 7.0 Hz, 3H, CH$_3$ Et); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 139.0, 138.6, 138.5, 138.3 ($C_{q\text{-}arom}$), 128.6, 128.5, 128.4, 128.4, 128.2, 128.2, 128.0, 127.9, 127.9, 127.8, 127.7, 127.7, 127.6, 127.6, 127.6, 127.5 (CH_{arom}), 101.6 (C-1), 82.5 (C-3), 76.1 (C-5), 75.3 (CH_2 Bn), 75.1 (C-4), 73.9 (CH_2 Bn), 73.9 (H-2), 73.6 (CH_2 Bn), 71.5 (CH_2 Bn), 69.9 (C-6), 65.4 (*C*H$_2$CH$_3$ Et), 15.4 (CH$_3$ Et); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 101.6 ($J_{H1\text{-}C1}$ = 153 Hz, β); Data of the minor stereoisomer (α product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.93 – 4.84 (signals overlap with major isomer, 1H, H-1), 4.76 (d, *J* = 12.5 Hz, 1H, C*H*H Bn), 4.72 (d, *J* = 12.5 Hz, 1H, CH*H* Bn), 1.15 (t, *J* = 7.1 Hz, 3H, CH$_3$ Et); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): 97.8 (C-1), 80.5 (C-3), 69.5 (C-6), 63.0 (*C*H$_2$CH$_3$ Et), 15.1 (CH$_3$ Et); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 97.8 ($J_{H1\text{-}C1}$ = 168 Hz, α); HRMS: $[M+Na]^+$ calcd for $C_{36}H_{40}O_6Na$ 591.27171, found 591.27096.

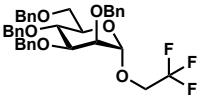


2-Fluoroethyl 2,3,4,6-tetra-*O*-benzy-D-mannopyranoside (S58). The title compound was prepared according to general procedure VII. Column chromatography (97:3 → 90:10, pentane:EtOAc) yielded the title compound (44 mg, 75 µmol, 75%, colorless oil, α:β; 60:40). TLC: R_f 0.24, 0.34 (pentane:EtOAc, 85:15, v:v); IR (thin film, cm^{-1}): 695, 734, 1026, 1073, 1362, 1453, 1496, 2910; Data of the major stereoisomer (α product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): 7.57 – 7.07 (m, 20H, CH_{arom}), 4.98 – 4.83 (m, 2H, C*H*H Bn, CH*H* Bn), 4.93 (d, *J* = 1.9 Hz, 1H, H-1), 4.76 (d, *J* = 12.4 Hz, 1H, C*H*H Bn), 4.72 (d, *J* = 12.5 Hz, 1H, CH*H* Bn), 4.68 – 4.39 (m, 6H, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, CH$_2$C*H*HF, CH$_2$CH*H*F), 4.04 – 3.59 (m, 12H, H-2, H-3, H-4, H-5, H-6, H-6, C*H*HCH$_2$F, CH*H*CH$_2$F); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 138.7, 138.6, 138.4, 138.4 ($C_{q\text{-}arom}$), 128.5, 128.4, 128.4, 128.1, 127.7, 127.6, 127.6, 127.6, 127.6, 127.5 (CH_{arom}), 98.2 (C-1), 82.6 (d, *J* = 169.8 Hz, CH_2F), 80.2 (C-3), 75.3 (CH_2 Bn), 74.9 (C-2), 74.6 (C-4), 73.5, 72.8, 72.2 (CH_2 Bn), 71.9 (C-5), 69.2 (C-6), 66.6 (d, *J* = 19.8 Hz, *C*H$_2$CH$_2$F); ^{13}C-HMBC-GATED NMR (101 MHz, $CDCl_3$): δ 98.2 ($J_{H1\text{-}C1}$ = 170 Hz, α); Data of the minor stereoisomer (β product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.98 (d, *J* = 12.4 Hz, 1H, C*H*H Bn), 4.45 (s, 1H, H-1), 4.11 (dddd, *J* = 35.8, 12.1, 3.9, 2.3 Hz, 1H, C*H*HCH$_2$F), 3.50 (dd, *J* = 9.4, 3.0 Hz, 1H, H-3), 3.46 (ddd, *J* = 9.7, 5.8, 2.1 Hz, 1H, H-5); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 101.7 (C-1), 83.0 (d, *J* = 169.3 Hz, CH_2F), 82.2 (C-3), 69.7 (C-6), 68.7 (d, *J* = 19.7 Hz, *C*H$_2$CH$_2$F); ^{13}C-HMBC-GATED NMR (101 MHz, $CDCl_3$): δ 98.2 ($J_{H1\text{-}C1}$ = 153 Hz, β); HRMS: $[M+Na]^+$ calcd for $C_{36}H_{39}FO_6$ 609.2628, found 609.2635.

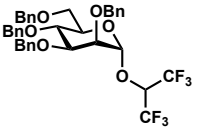


2,2-Difluoroethyl 2,3,4,6-tetra-*O*-benzy-D-mannopyranoside (S59). The title compound was prepared according to general procedure VII. Column chromatography (97:3 → 90:10, pentane:EtOAc) yielded the title compound (39 mg, 65 µmol, 65%, colorless oil, α:β; 80:20). TLC: R_f 0.19, 0.31 (pentane:EtOAc, 90:10, v:v); IR (thin film, cm^{-1}): 695, 734, 1027, 1064, 1363, 1453, 1496, 2916; Data of the major stereoisomer (α product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.71 – 7.10 (m, 20H, CH_{arom}), 5.86 (tdd, *J* = 55.3, 4.8, 3.4 Hz, 1H, CHF_2), 4.95 – 4.80 (m, 3H, C*H*H Bn, CH*H* Bn, C*H*H Bn), 4.90 (d, *J* = 2.0 Hz, 1H, H-1), 4.76 (d, *J* = 12.4 Hz, 1H, CH*H* Bn), 4.70 (d, *J* = 12.4 Hz, 1H, C*H*H Bn), 4.68 – 4.38 (m, 4H, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 3.98 (t, *J* = 9.1 Hz, 1H, H-4), 4.13 – 3.61 (m, 7H, H-2, H-3, H-5, H-6, H-6, C*H*HCHF$_2$, CH*H*CHF$_2$); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 138.6, 138.5, 138.4, 138.3 ($C_{q\text{-}arom}$), 129.5, 128.5, 128.5, 128.0, 127.9, 127.8, 127.8, 127.8, 127.7, 127.7, 127.6 (CH_{arom}), 114.1 (t, *J* = 241.1 Hz, CHF_2), 99.0 (C-1), 80.0 (C-3), 75.3 (C-4), 74.8 (C-2), 74.5, 73.5, 72.9, 72.4 (CH_2 Bn), 72.4 (C-5), 69.2 (C-6), 66.8 (t, *J* = 28.2

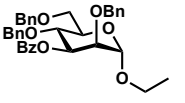
Hz, *C*H$_2$CHF$_2$); ^{13}C-HMBC-GATED NMR (101 MHz, CDCl$_3$): δ 99.0 ($J_{H1\text{-}C1}$ = 171 Hz, α); Data of the minor stereoisomer (β product): ^{1}H NMR (400 MHz, CDCl$_3$, HH-COSY, HSQC): δ 5.94 (dddd, *J* = 56.3, 54.7, 5.6, 2.7 Hz, 1H, CHF$_2$), 4.94 (d, *J* = 12.4 Hz, 1H, C*H*H Bn), 4.68 – 4.38 (signals overlap with major isomer, 1H, H-1), 3.50 (dd, *J* = 9.3, 3.0 Hz, 1H, H-3), 3.45 (ddd, *J* = 9.8, 5.8, 2.2 Hz, 1H, H-5); ^{13}C NMR (101 MHz, CDCl$_3$, HSQC): δ 114.4 (dd, *J* = 242.1, 240.0 Hz, CHF$_2$), 101.8 (C-1), 82.1, 68.5 (dd, *J* = 30.6, 26.2 Hz, *C*H$_2$CHF$_2$); ^{13}C-HMBC-GATED NMR (101 MHz, CDCl$_3$): δ 101.8 ($J_{H1\text{-}C1}$ = 153 Hz, β); HRMS: [M+Na]$^+$ calcd for $C_{36}H_{38}F_2O_6$ 627.2534, found 627.2541.



2,2,2-Trifluoroethyl 2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranoside (S60). The title compound was prepared according to general procedure VII. Column chromatography (97:3 → 90:10, pentane:EtOAc) yielded the title compound (52 mg, 84 µmol, 84%, colorless oil, α:β; >98:2). TLC: R_f 0.45 (pentane:EtOAc, 90:10, v:v); $[\alpha]_D^{20}$ –16.6° (*c* 1, CHCl$_3$); IR (thin film, cm^{-1}): 667, 695, 985, 1069, 1165, 1279, 1362, 1454, 2867; ^{1}H NMR (400 MHz, CDCl$_3$, HH-COSY, HSQC): δ 8.07 – 5.74 (m, 20H, CH$_{arom}$), 4.94 (d, *J* = 1.9 Hz, 1H, H-1), 4.86 (d, *J* = 10.7 Hz, 1H, C*H*H Bn), 4.76 (d, *J* = 12.4 Hz, 1H, C*H*H Bn), 4.69 (d, *J* = 12.3 Hz, 1H, CH*H* Bn), 4.69 – 4.59 (m, 3H, CH*H* Bn, C*H*H Bn, C*H*H Bn), 4.53 (d, *J* = 12.2 Hz, 1H, CH*H* Bn), 4.49 (d, *J* = 10.7 Hz, 1H, CH*H* Bn), 4.00 (t, *J* = 9.1 Hz, 1H, H-4), 3.96 – 3.64 (m, 7H, H-2, H-3, H-5, H-6, H-6, C*H*HCF$_3$, CH*H*CF$_3$); ^{13}C NMR (101 MHz, CDCl$_3$, HSQC): δ 138.4, 138.3, 138.3, 138.1 (C$_{q\text{-}arom}$), 128.5, 128.5, 128.5, 128.1, 128.1, 127.9, 127.8, 127.8, 127.8, 127.8, 127.7, 127.7, 127.7 (CH$_{arom}$), 122.4 (q, *J* = 277.6 Hz, CF$_3$), 98.7 (C-1), 79.8 (C-3), 75.3 (CH$_2$ Bn), 74.6 (C-4), 74.4 (C-2), 73.6, 73.5 (CH$_2$ Bn), 73.1 (C-5), 72.7 (CH$_2$ Bn), 72.5 (C-6), 64.1 (q, *J* = 34.8 Hz, *C*H$_2$CF$_3$); HRMS: [M+Na]$^+$ calcd for $C_{36}H_{37}F_3O_6$ 645.2440, found 645.2452.

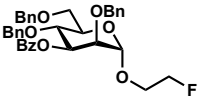


1,1,1,3,3,3-Hexafluoro-2-propyl 2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranoside (S61). The title compound was prepared according to general procedure VII. Column chromatography (100:0 → 80:20, pentane:Et$_2$O) yielded the title compound (26 mg, 39 µmol, 39%, colorless oil, α:β; >98:2). TLC: R_f 0.23 (pentane:EtOAc, 95:5, v:v); $[\alpha]_D^{20}$ 35.7° (*c* 1, CHCl$_3$); IR (thin film, cm^{-1}): 695, 734, 900, 964, 1027, 1101, 1195, 1219, 1288, 1367, 1454, 2917; ^{1}H NMR (500 MHz, CDCl$_3$, HH-COSY, HSQC, HMBC-Gated, ^{1}H-^{19}F Decoupled) δ 7.38 – 7.12 (m, 20H, CH$_{arom}$), 5.07 (d, *J* = 1.8 Hz, 1H, H-1), 4.81 (d, *J* = 10.7 Hz, 1H, C*H*H Bn), 4.75 (d, *J* = 12.3 Hz, 1H, C*H*H Bn), 4.69 – 4.60 (m, 4H, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.50 – 4.39 (m, 3H, CH*H* Bn, CH*H* Bn, C*H*(CF$_3$)$_2$), 4.05 (td, *J* = 9.8, 1.4 Hz, 1H, H-4), 3.87 – 3.79 (m, 3H, H-2, H-3, H-5), 3.77 (dd, *J* = 10.9, 4.5 Hz, 1H, H-6), 3.65 (dd, *J* = 10.9, 1.9 Hz, 1H, H-6); ^{13}C NMR (126 MHz, CDCl$_3$, HSQC, HMBC-Gated) δ 138.3, 138.3, 138.2, 137.8 (C$_{q\text{-}arom}$), 128.6, 128.6, 128.5, 128.5, 128.2, 128.1, 128.0, 127.9, 127.9, 127.7 (CH$_{arom}$), 100.7 (C-1), 79.2 (C-3), 75.1 (CH$_2$ Bn), 74.5 (C-2), 74.3 (C-4), 73.5 (C-5), 73.5, 73.3, 72.8 (CH$_2$ Bn), 72.1 (p, *J* = 32.7 Hz, *C*H(CF$_3$)$_2$), 68.7 (C-6); ^{13}C-GATED NMR (126 MHz, CDCl$_3$): δ 100.7 ($J_{H1\text{-}C1}$ = 174 Hz, α); HRMS: [M+Na]$^+$ calcd for $C_{37}H_{36}F_6O_6$ 713.2314, found 713.2335.

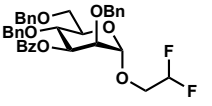


Ethyl 2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranoside (S62). The title compound was prepared according to general procedure VII. Column chromatography (95:5 → 75:25, pentane:Et$_2$O) yielded the title compound (55 mg, 94 µmol, 94%, colorless oil, α:β; >98:2). TLC: R_f 0.30 (pentane:Et$_2$O, 80:20, v:v); $[\alpha]_D^{25}$ –3.6° (*c* 1, CHCl$_3$); IR (thin film, cm^{-1}): 695, 735, 1026, 1059, 1093, 1268, 1452, 1720, 2867, 3030; ^{1}H NMR (500 MHz, CDCl$_3$, HH-COSY, HSQC): δ 8.67 – 6.65 (m, 20H, CH$_{arom}$), 5.55 (dd, *J* = 9.6, 3.3 Hz, 1H, H-3), 4.93 (d, *J* = 1.9 Hz, 1H, H-1), 4.72 (d, *J* = 12.1 Hz, 1H, C*H*H Bn), 4.69 – 4.64 (m, 2H, C*H*H Bn, C*H*H Bn), 4.59 (d, *J* = 12.3 Hz, 1H, CH*H* Bn), 4.54 (d, *J* = 12.1 Hz, 1H, CH*H* Bn), 4.50 (d, *J* = 10.8 Hz, 1H, CH*H* Bn), 4.22 (t, *J* = 9.7 Hz, 1H, H-4), 3.97 (dd, *J* = 3.4, 1.9 Hz, 1H, H-2), 3.91 (ddd, *J* = 9.8, 4.5, 1.9 Hz, 1H, H-5), 3.83 (dd, *J* =

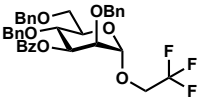
10.8, 4.5 Hz, 1H, H-6), 3.81 – 3.70 (m, 2H, H-6, C*H*HCH$_3$ Et), 3.49 (dq, *J* = 9.7, 7.1 Hz, 1H, CH*H*CH$_3$ Et), 1.20 (t, *J* = 7.1 Hz, 3H, CH$_3$ Et); ^{13}C NMR (126 MHz, CDCl$_3$, HSQC): δ 165.8 (C=O Bz), 138.4, 138.1, 138.0 (C$_{q\text{-arom}}$), 130.2, 128.5, 128.4, 128.4, 128.0, 127.8, 127.8, 127.7, 127.7, 127.7, 127.7 (CH$_{arom}$), 97.8 (C-1), 76.4 (C-2), 75.0 (CH$_2$ Bn), 74.8 (C-3), 73.8 (C-4), 73.6, 73.1 (CH$_2$ Bn), 71.6 (C-5), 69.2 (C-6), 63.3 (*C*H$_2$CH$_3$ Et), 15.1 (CH$_3$ Et); HRMS: [M+NH$_4$]$^+$ calcd for C$_{36}$H$_{38}$O$_7$ 600.29558, found 600.29561.



2-Fluoroethyl 3-*O*-benzoyl-2,4,6-tri-*O*-benzyl-α-D-mannopyranoside (S63). The title compound was prepared according to general procedure VII. Column chromatography (90:10 → 60:40, pentane:Et$_2$O) yielded the title compound (52 mg, 87 µmol, 87%, colorless oil, α:β; >98:2). TLC: R$_f$ 0.20 (pentane:Et$_2$O, 70:30, v:v); $[\alpha]_D^{25}$ –2.6° (*c* 1, CHCl$_3$); IR (thin film, cm^{-1}): 539, 697, 714, 738, 1026, 2046, 170, 1270, 1452 1496, 1601, 1720, 2914, 3031; ^{1}H NMR (500 MHz, CDCl$_3$, HH-COSY, HSQC): 8.28 – 6.76 (m, 20H, CH$_{arom}$), 5.54 (dd, *J* = 9.4, 3.3 Hz, 1H, H-3), 4.98 (d, *J* = 2.0 Hz, 1H, H-1), 4.74 (d, *J* = 11.0 Hz, 1H, C*H*H Bn), 4.67 (d, *J* = 10.8 Hz, 1H, C*H*H Bn), 4.67 (d, *J* = 12.2 Hz, 1H, C*H*H Bn), 4.60 (d, *J* = 12.3 Hz, 1H, CH*H* Bn), 4.62 – 4.46 (m, 2H, C*H*HF, CH*H*F), 4.53 (d, *J* = 12.1 Hz, 1H, CH*H* Bn), 4.50 (d, *J* = 10.7 Hz, 1H, CH*H* Bn), 4.22 (t, *J* = 9.6 Hz, 1H, H-4), 4.04 (dd, *J* = 3.4, 2.0 Hz, 1H, H-2), 3.93 (ddt, *J* = 11.8, 6.7, 2.5 Hz, 2H, H-5), 3.82 (dd, *J* = 10.9, 4.5 Hz, 1H, H-6), 3.91 – 3.67 (m, 2H, C*H*HCH$_2$F, CH*H*CH$_2$F), 3.73 (dd, *J* = 10.9, 1.9 Hz, 1H, H-6); ^{13}C NMR (126 MHz, CDCl$_3$, HSQC): δ 165.7 (C=O Bz), 138.3, 137.9, 133.2, 131.2 (C$_{q\text{-arom}}$), 129.9, 129.4, 128.5, 128.4, 128.4, 128.4, 128.4, 128.0, 128.0, 127.8, 127.8, 127.8, 127.7, 127.7, (CH$_{arom}$) 98.4 (C-1), 82.6 (d, *J* = 169.9 Hz, CH$_2$F), 76.1 (C-2), 74.9 (CH$_2$ Bn), 74.4 (C-3), 73.6 (CH$_2$ Bn), 73.6 (C-4), 73.2 (CH$_2$ Bn), 71.7 (C-5), 69.0 (C-6), 66.8 (d, *J* = 20.2 Hz, *C*H$_2$CH$_2$F); HRMS: [M+NH$_4$]$^+$ calcd for C$_{36}$H$_{37}$FO$_7$ 618.28616, found 618.28583.

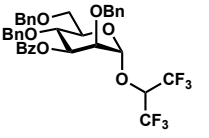


2,2-Difluoroethyl 3-*O*-benzoyl-2,4,6-tri-*O*-benzyl-α-D-mannopyranoside (S64). The title compound was prepared according to general procedure VII. Column chromatography (95:5 → 75:25, pentane:Et$_2$O) yielded the title compound (54 mg, 87 µmol, 87%, colorless oil, α:β; >98:2). TLC: R$_f$ 0.3 (pentane:Et$_2$O, 80:20, v:v); $[\alpha]_D^{25}$ 1.1° (*c* 1, CHCl$_3$); IR (thin film, cm^{-1}): 696, 737, 1269, 1452, 1720, 2926, 3032; ^{1}H NMR (500 MHz, CDCl$_3$, HH-COSY, HSQC): δ 8.40 – 6.70 (m, 20H, CH$_{arom}$), 5.92 (tdd, *J* = 55.5, 4.8, 3.7 Hz, 1H, CHF$_2$), 5.49 (dd, *J* = 9.2, 3.3 Hz, 1H, H-3), 4.96 (d, *J* = 2.1 Hz, 1H, H-1), 4.69 (d, *J* = 12.3 Hz, 1H, C*H*H Bn), 4.69 (d, *J* = 11.2 Hz, 1H, C*H*H Bn), 4.65 (d, *J* = 12.2 Hz, 1H, C*H*H Bn), 4.59 (d, *J* = 12.2 Hz, 1H, CH*H* Bn), 4.53 (d, *J* = 12.0 Hz, 1H, CH*H* Bn), 4.50 (d, *J* = 10.9 Hz, 1H, CH*H* Bn), 4.20 (t, *J* = 9.5 Hz, 1H, H-4), 4.03 (dd, *J* = 3.4, 2.1 Hz, 1H, H-2), 3.93 – 3.68 (m, 5H, H-6, H-6, H-5, C*H*HCH$_2$F, CH*H*CH$_2$F); ^{13}C NMR (126 MHz, CDCl$_3$, HSQC): ^{13}C NMR (126 MHz, CDCl$_3$): δ 165.8 (C=O Bz), 138.2, 137.8, 137.7, 133.3, 130.0, 129.9, 128.6, 128.5, 128.4, 128.4, 128.0, 127.8, 127.8 (CH$_{arom}$), 114.1 (t, *J* = 241.2 Hz, CHF$_2$), 98.9 (C-1), 75.8 (C-2), 74.9 (CH$_2$ Bn), 74.1 (C-3), 73.6 (CH$_2$ Bn), 73.4 (C-4), 73.3 (CH$_2$ Bn), 72.1 (C-5), 68.9 (C-6), 66.9 (t, *J* = 28.7 Hz, *C*H$_2$CHF$_2$); HRMS: [M+NH$_4$]$^+$ calcd for C$_{36}$H$_{36}$F$_2$O$_7$ 636.27674, found 636.27663.

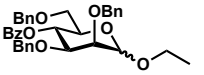


2,2,2-Trifluoroethyl 3-*O*-benzoyl-2,4,6-tri-*O*-benzyl-α-D-mannopyranoside (S65). The title compound was prepared according to general procedure VII. Column chromatography (95:5 → 80:20, pentane:Et$_2$O) yielded the title compound (51 mg, 79 µmol, 79%, colorless oil, α:β; >98:2). TLC: R$_f$ 0.40 (pentane:Et$_2$O, 80:20, v:v); $[\alpha]_D^{25}$ 5.6° (*c* 1, CHCl$_3$); IR (thin film, cm^{-1}): 698, 738, 1027, 1035, 1166, 1253, 1452, 1720, 2866, 3030; ^{1}H NMR (500 MHz, CDCl$_3$, HH-COSY, HSQC): δ 8.53 – 6.76 (m, 20H, CH$_{arom}$), 5.50 (dd, *J* = 9.1, 3.3 Hz, 1H, H-3), 5.00 (d, *J* = 2.1 Hz, 1H, H-1), 4.69 (d, *J* = 12.1 Hz, 1H, C*H*H Bn), 4.68 (d, *J* = 10.9 Hz, 1H, C*H*H Bn), 4.65 (d, *J* = 12.1 Hz, 1H, C*H*H Bn), 4.61 (d, *J* = 12.1 Hz, 1H, CH*H* Bn), 4.52 (d, *J* = 12.1 Hz, 1H, CH*H* Bn), 4.50 (d, *J* = 10.9 Hz, 1H, CH*H* Bn), 4.21 (t, *J* = 9.4 Hz, 1H, H-4), 4.07 (dd, *J* = 3.4, 2.2 Hz, 1H, H-2), 4.06 – 3.83 (m, 3H, C*H*HCF$_3$, CH*H*CF$_3$, H-5), 3.80 (dd, *J* = 10.9, 4.5 Hz, 1H, H-6), 3.71 (dd, *J* = 10.9,

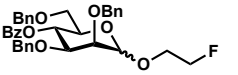
1.9 Hz, 1H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 165.7 (C=O Bz), 138.2, 137.8, 137.6 ($C_{q\text{-arom}}$), 130.0, 128.6, 128.5, 128.4, 128.1, 128.0, 128.0, 128.0, 127.9, 127.8, 127.8, 127.1 (CH_{arom}), 123.8 (q, *J* = 278.4 Hz, CF_3), 98.8 (C-1), 75.6 (C-2), 74.9 (CH_2 Bn), 73.9 (C-3), 73.7 (CH_2 Bn), 73.4 (C-4), 73.4 (CH_2 Bn), 72.3 (C-5), 68.8 (C-6), 64.3 (q, *J* = 35.0 Hz, *C*H_2CF_3); HRMS: $[M+NH_4]^+$ calcd for $C_{36}H_{35}F_3O_7$ 654.26731, found 654.26711.



1,1,1,3,3,3-Hexafluoro-2-propyl 3-*O*-benzoyl-2,4,6-tri-*O*-benzyl-α-D-mannopyranoside (S66). The title compound was prepared according to general procedure VII. Column chromatography (100:0 → 80:20, pentane:Et_2O) yielded the title compound (43 mg, 61 µmol, 61%, colorless oil, α:β; >98:2). TLC: R_f 0.20 (pentane:Et_2O, 90:10, v:v); $[\alpha]_D^{25}$ 19.2° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 688, 696, 712, 738, 974, 1027, 1101, 1195, 1220, 1315, 1367, 1452, 1720, 2926, 3032; ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.22 – 7.03 (m, 20H, CH_{arom}), 5.47 (dd, *J* = 7.9, 3.3 Hz, 1H, H-3), 5.15 (d, *J* = 2.7 Hz, 1H, H-1), 4.71 (d, *J* = 11.0 Hz, 1H, C*H*H Bn), 4.66 (d, *J* = 12.0 Hz, 1H, C*H*H Bn), 4.63 (s, 2H, CH_2 Bn), 4.50 (d, *J* = 10.8 Hz, 1H CH*H* Bn), 4.56 – 4.47 (m, 1H, $CH(CF_3)_2$), 4.44 (d, *J* = 12.0 Hz, 1H, CH*H* Bn), 4.22 (dd, *J* = 9.6, 7.9 Hz, 1H, H-4), 4.10 (dd, *J* = 3.3, 2.7 Hz, 1H, H-2), 3.92 (ddd, *J* = 9.6, 3.9, 2.1 Hz, 1H, H-5), 3.76 (dd, *J* = 11.0, 3.8 Hz, 1H, H-6), 3.66 (dd, *J* = 11.0, 2.1 Hz, 1H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 165.8 (C=O Bz), 138.0, 137.6, 137.2 ($C_{q\text{-arom}}$), 129.9, 128.6, 128.6, 128.5, 128.2, 128.1, 128.1, 128.0, 127.9, 127.8 (CH_{arom}), 100.9 (C-1), 75.1 (C-2), 74.5, 73.6, 73.4 (CH_2 Bn), 73.3 (C-4), 72.9 (C-5), 72.9 (C-3), 72.0 (p, *J* = 34.2 Hz, *C*$H(CF_3)_2$), 68.4 (C-6); ^{13}C-GATED NMR (126 MHz, $CDCl_3$): δ 100.9 ($J_{H1\text{-}C1}$ = 178 Hz, □); HRMS: $[M+NH_4]^+$ calcd for $C_{37}H_{34}F_6O_7$ 722.25470, found 722.25433.

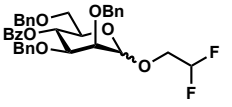


Ethyl 4-*O*-benzoyl-2,3,6-tri-*O*-benzy-D-mannopyranoside (S67). The title compound was prepared according to general procedure VII. Column chromatography (95:5 → 70:30, pentane:Et_2O) yielded the title compound (51 mg, 88 µmol, 88%, colorless oil, α:β; 31:69). TLC: R_f 0.20 (pentane:Et_2O, 80:20, v:v); IR (thin film, cm^{-1}): 595, 695, 735, 1026, 1105, 1266, 1452, 1720, 2869, 3030; Data of the major stereoisomer (β product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.61 – 7.06 (m, 20H, CH_{arom}), 5.55 (t, *J* = 9.7 Hz, 1H, H-4), 4.99 (d, *J* = 12.7 Hz, 1H, C*H*H Bn), 4.90 (d, *J* = 12.6 Hz, 1H, CH*H* Bn), 4.58 – 4.41 (m, 4H, C*H*H Bn, CH*H* Bn, CH*H* Bn, H-1), 4.24 (d, *J* = 12.5 Hz, 1H, CH*H* Bn), 4.05 (dq, *J* = 9.3, 7.1 Hz, 1H, C*H*HCH$_3$ Et), 3.94 (dd, *J* = 3.0, 0.8 Hz, 1H, H-2), 3.81 – 3.60 (m, 3H, H-5, H-6, H-6), 3.56 (dd, *J* = 9.8, 2.9 Hz, 1H, H-3), 3.59 – 3.44 (m, 1H, CH*H*CH$_3$ Et), 1.30 (t, *J* = 7.0 Hz, 3H, CH_3 Et); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 165.7 (C=O Bz), 138.6, 138.2, 137.7 ($C_{q\text{-arom}}$), 129.9, 128.6, 128.4, 128.4, 128.4, 128.2, 127.7, 127.7, 127.6 (CH_{arom}), 101.3 (C-1), 78.8 (C-3), 74.8 (C-5), 74.0, 73.8 (CH_2 Bn), 73.2 (C-2), 71.0 (CH_2 Bn), 70.7 (C-6), 69.8 (C-4), 65.6 (*C*H_2CH$_3$ Et), 15.3 (CH$_3$ Et); Data of the minor stereoisomer (α product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.64 (t, *J* = 9.8 Hz, 1H, H-4), 4.92 (d, *J* = 2.0 Hz, 1H, H-1), 4.80 (d, *J* = 12.5 Hz, 1H, C*H*H Bn), 4.73 (d, *J* = 12.5 Hz, 1H, CH*H* Bn), 3.84 (dd, *J* = 3.1, 2.0 Hz, 1H, H-2); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 98.2 (C-1), 77.5 (C-3), 74.4 (C-2), 73.6, 73.0, 71.9 (CH_2 Bn), 63.4 (*C*H_2CH$_3$ Et), 15.1 (CH$_3$ Et); HRMS: $[M+NH_4]^+$ calcd for $C_{36}H_{38}O_7$ 600.29558, found 600.29575.

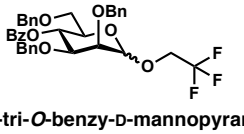


2-Fluoroethyl 4-*O*-benzoyl-2,3,6-tri-*O*-benzy-D-mannopyranoside (S68). The title compound was prepared according to general procedure VII. Column chromatography (90:10 → 60:40, pentane:Et_2O) yielded the title compound (50 mg, 83 µmol, 83%, colorless oil, α:β; 60:40). TLC: R_f 0.20 (pentane:Et_2O, 70:30, v:v); IR (thin film, cm^{-1}): 537, 695, 711, 738, 1027, 1043, 1069, 1088, 1266, 1452, 1724, 2867, 3030; Data of the major stereoisomer (α product): ^{1}H NMR (600 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.05 – 6.98 (m, 20H, CH_{arom}), 5.65 (t, *J* = 9.8 Hz, 1H, H-4), 4.96 (d, *J* = 2.0 Hz, 1H, H-1), 4.80 (d, *J* = 12.4 Hz, 1H, C*H*H Bn), 4.72 (d, *J* = 12.5 Hz, 1H, CH*H* Bn), 4.67 – 4.42 (m, 6H, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*HF,

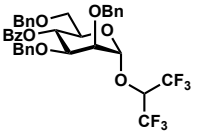
CH*H*F), 4.01 – 3.79 (m, 2H, C*H*HCH$_2$F, CH*H*CH$_2$F), 3.90 (dd, *J* = 3.0, 2.0 Hz, 1H, H-2), 3.79 – 3.64 (m, 3H, H-5, H-6, H-6), 3.62 (dd, *J* = 10.8, 2.8 Hz, 1H, H-2); ^{13}C NMR (151 MHz, $CDCl_3$, HSQC): δ 165.7 (C=O Bz), 138.5, 138.3, 138.2, 138.1, 137.7 ($C_{q\text{-}arom}$), 131.2, 130.0, 129.9, 128.6, 128.4, 128.4, 128.4, 128.4, 128.3, 127.7, 127.5 (CH_{arom}), 98.8 (C-1), 82.6 (d, *J* = 169.6 Hz, *C*H$_2$F), 77.3 (C-3), 74.3 (C-2), 73.6, 73.1, 72.1 (CH$_2$ Bn), 70.9 (C-5), 70.1 (C-6), 69.5 (C-4), 66.9 (d, *J* = 19.7 Hz, *C*H$_2$CH$_2$F); Data of the minor stereoisomer (β product): ^{1}H NMR (600 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.56 (t, *J* = 9.7 Hz, 1H, H-4), 4.98 (d, *J* = 12.5 Hz, 1H, C*H*H Bn), 4.89 (d, *J* = 12.5 Hz, 1H, CH*H* Bn), 4.67 – 4.42 (signals overlap with major isomer, 1H, H-1), 4.26 (d, *J* = 12.5 Hz, 1H, CH*H* Bn), 4.13 (dddd, *J* = 35.8, 12.2, 3.9, 2.3 Hz, 1H, C*H*HCH$_2$F), 3.58 (dd, *J* = 9.7, 3.0 Hz, 1H, H-2); ^{13}C NMR (151 MHz, $CDCl_3$, HSQC): δ 101.5 (C-1), 82.9 (d, *J* = 169.4 Hz, *C*H$_2$F), 74.2, 73.7, 71.1 (CH$_2$ Bn), 70.5 (C-6), 69.6 (C-4), 68.7 (d, *J* = 19.7 Hz, *C*H$_2$CH$_2$F); HRMS: $[M+NH_4]^+$ calcd for $C_{36}H_{37}FO_7$ 618.28616, found 618.28620.



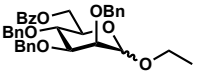
2,2-Difluoroethyl 4-*O*-benzoyl-2,3,6-tri-*O*-benzy-D-mannopyranoside (S69). The title compound was prepared according to general procedure VII. Column chromatography (95:5 → 70:30, pentane:Et$_2$O) yielded the title compound (50 mg, 81 µmol, 81%, colorless oil, α:β; 71:29). TLC: R_f 0.20 (pentane:Et$_2$O, 80:20, v:v); IR (thin film, cm^{-1}): 697, 711, 738, 1027, 1066, 1105, 1266, 1452, 1720, 2870, 3030; Data of the major stereoisomer (α product): ^{1}H NMR (600 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.22 – 6.63 (m, 20H, CH_{arom}), 5.94 (tdd, *J* = 55.3, 4.8, 3.4 Hz, 1H, C*H*F$_2$), 5.63 (t, *J* = 9.7 Hz, 1H, H-4), 4.93 (d, *J* = 2.1 Hz, 1H, H-1), 4.79 (d, *J* = 12.3 Hz, 1H, C*H*H Bn), 4.70 (d, *J* = 12.4 Hz, 1H, CH*H* Bn), 4.60 – 4.42 (m, 4H, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 3.99 (ddd, *J* = 9.7, 6.5, 2.7 Hz, 1H, H-5), 3.94 (dd, *J* = 9.3, 3.0 Hz, 1H, H-3), 3.87 (t, *J* = 2.6 Hz, 1H, H-2), 3.85 – 3.64 (m, 3H, H-6, C*H*HCHF$_2$, CH*H*CHF$_2$), 3.61 (dd, *J* = 10.8, 2.8 Hz, 1H, H-6); ^{13}C NMR (151 MHz, $CDCl_3$, HSQC): δ 165.7 (C=O Bz), 138.4, 138.2, 138.1, 138.1, 138.0, 137.7 ($C_{q\text{-}arom}$), 130.0, 128.6, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 127.9, 127.9, 127.8, 127.8, 127.8, 127.8, 127.8, 127.7 (CH_{arom}), 114.1 (t, *J* = 241.1 Hz, *C*HF$_2$), 99.6 (C-1), 77.2 (C-3), 74.3 (C-2), 73.7, 73.3, 72.2 (CH$_2$ Bn), 71.4 (C-5), 70.0 (C-6), 69.3 (C-4), 67.1 (t, *J* = 28.1 Hz, *C*H$_2$CHF$_2$); Data of the minor stereoisomer (β product): ^{1}H NMR (600 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.55 (t, *J* = 9.5 Hz, 1H, H-4), 4.85 (d, *J* = 12.5 Hz, 1H, CH*H* Bn), 4.53 (s, 1H, H-1), 4.28 (d, *J* = 12.5 Hz, 1H, CH*H* Bn), 4.07 (dddd, *J* = 21.7, 12.1, 9.5, 2.7 Hz, 1H, C*H*HCHF$_2$), 3.58 (dd, *J* = 9.6, 3.0 Hz, 1H, H-3); ^{13}C NMR (151 MHz, $CDCl_3$, HSQC): δ 114.5 (dd, *J* = 242.2, 239.7 Hz, *C*HF$_2$), 101.6 (C-1), 74.3, 73.8, 71.3 (CH$_2$ Bn), 70.4 (C-6), 69.5 (C-4), 68.6 (dd, *J* = 31.0, 25.9 Hz, *C*H$_2$CHF$_2$); HRMS: $[M+NH_4]^+$ calcd for $C_{36}H_{36}F_2O_7$ 636.27674, found 636.27674.



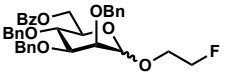
2,2,2-Trifluoroethyl 4-*O*-benzoyl-2,3,6-tri-*O*-benzy-D-mannopyranoside (S70). The title compound was prepared according to general procedure VII. Column chromatography (95:5 → 85:15, pentane:Et$_2$O) yielded the title compound (49 mg, 77 µmol, 77%, colorless oil, α:β; 88:12). TLC: R_f 0.40 (pentane:Et$_2$O, 80:20, v:v); IR (thin film, cm^{-1}): 697, 735, 1027, 1081, 1266, 1452, 1720, 2870, 3031; Data of the major stereoisomer (α product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.47 – 6.78 (m, 20H, CH_{arom}), 5.65 (t, *J* = 9.6 Hz, 1H, H-4), 4.97 (d, *J* = 2.1 Hz, 1H, H-1), 4.80 (d, *J* = 12.3 Hz, 1H, C*H*H Bn), 4.69 (d, *J* = 12.3 Hz, 1H, CH*H* Bn), 4.6 (d, *J* = 12.0 Hz, 1H, C*H*H Bn), 4.53 – 4.41 (m, 3H, C*H*H Bn, CH*H* Bn, CH*H* Bn), 4.09 – 3.83 (m, 5H, H-3, H-4, H-5, C*H*HCF$_3$, CH*H*CF$_3$), 3.67 (dd, *J* = 10.8, 6.2 Hz, 1H, H-6), 3.60 (dd, *J* = 10.8, 2.9 Hz, 1H, H-6); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 165.6 (C=O Bz), 138.1, 138.0, 137.9, 137.5 ($C_{q\text{-}arom}$), 128.4, 127.9, 127.8, 127.8, 127.7, 127.6 (CH_{arom}), 122.5 (q, *J* = 280.0 Hz, *C*F$_3$), 99.1 (C-1), 76.9 (C-3), 74.0 (C-2), 73.6, 73.3, 72.2 (CH$_2$ Bn), 71.6 (C-5), 69.8 (C-6), 69.1 (C-4), 64.3 (q, *J* = 34.9 Hz, *C*H$_2$CF$_3$); Data of the minor stereoisomer (β product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.56 (t, *J* = 9.5 Hz, 1H, H-4), 4.87 (d, *J* = 12.5 Hz, 1H, CH*H* Bn), 4.61 – 4.53 (signals overlap with major isomer, 1H, H-1); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): 101.1 (C-1), 78.5 (C-3), 70.3 (C-6), 69.3 (C-4), 64.3 (q, *J* = 34.9 Hz, *C*H$_2$CF$_3$); HRMS: $[M+NH_4]^+$ calcd for $C_{36}H_{35}F_3O_7$ 654.26731, found 654.26732.



1,1,1,3,3,3-Hexafluoro-2-propyl 4-*O*-benzoyl-2,3,6-tri-*O*-benzyl-α-D-mannopyranoside (S71). The title compound was prepared according to general procedure VII. Column chromatography (100:0 → 80:20, pentane:Et_2O) yielded the title compound (35 mg, 50 µmol, 50%, colorless oil, α:β; >98:2). TLC: R_f 0.10 (pentane:Et_2O, 90:10, v:v); $[\alpha]_D^{25}$ 17.0° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 689, 711, 1027, 1068, 1452, 1727, 2861, 3032; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.08 – 7.09 (m, 20H, CH_{arom}), 5.69 (dd, *J* = 9.9, 8.1 Hz, 1H, H-4), 5.12 (d, *J* = 2.1 Hz, 1H, H-1), 4.77 (d, *J* = 12.3 Hz, 1H, C*H*H Bn), 4.65 (d, *J* = 12.2 Hz, 1H, CH*H* Bn), 4.59 (d, *J* = 12.0 Hz, 1H, C*H*H Bn), 4.53 (d, *J* = 12.0 Hz, 1H, CH*H* Bn), 4.52 – 4.45 (m, 3H, C*H*H Bn, CH*H* Bn, C*H*$(CF_3)_2$), 4.03 (ddd, *J* = 10.0, 5.6, 2.8 Hz, 1H, H-5), 3.93 – 3.84 (m, 2H, H-2, H-3), 3.64 (dd, *J* = 11.0, 5.6 Hz, 1H, H-6), 3.59 (dd, *J* = 11.0, 2.9 Hz, 1H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 165.5 (C=O Bz), 137.9, 137.7, 137.6 ($C_{q\text{-}arom}$), 129.8, 128.5, 128.5, 128.4, 128.4, 128.2, 128.1, 127.9, 127.8, 127.6, 127.6 (CH_{arom}), 100.8 (C-1), 76.5 (C-3), 74.0 (C-2), 73.6, 73.5, 72.4 (CH_2 Bn), 72.3 (C-5), 71.9 (p, *J* = 32.5 Hz, H-1, *C*H$(CF_3)_2$), 69.3 (C-6), 68.6 (C-4); ^{13}C-GATED NMR (126 MHz, $CDCl_3$): δ 100.8 ($J_{H1\text{-}C1}$ = 176 Hz, α); HRMS: $[M+NH_4]^+$ calcd for $C_{37}H_{34}F_6O_7$ 722.25470, found 722.25449.

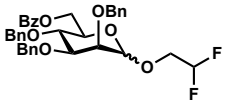


Ethyl 6-*O*-benzoyl-2,3,4-tri-*O*-benzy-D-mannopyranoside (S72). The title compound was prepared according to general procedure VII. Column chromatography (95:5 → 75:25, pentane:Et_2O) yielded the title compound (40 mg, 69 µmol, 69%, colorless oil, α:β; 35:65). TLC: R_f 0.30 (pentane:Et_2O, 80:20, v:v); IR (thin film, cm^{-1}): 696, 712, 737, 1027, 1066, 1104, 1274, 1452, 1496, 1720, 2869, 3030; Data of the major stereoisomer (β product): ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.41 – 7.08 (m, 20H, CH_{arom}), 5.04 (d, *J* = 12.3 Hz, 1H, C*H*H Bn), 5.00 (d, *J* = 10.7 Hz, 1H, C*H*H Bn), 4.91 (d, *J* = 12.3 Hz, 1H, CH*H* Bn), 4.73 – 4.51 (m, 5H, H-6, H-6, C*H*H Bn, CH*H* Bn, CH*H* Bn), 4.47 (s, 1H, H-1), 4.07 (t, *J* = 9.4 Hz, 1H, H-4), 4.05 – 3.99 (m, 1H, C*H*HCH$_3$), 3.97 (d, *J* = 3.1 Hz, 1H, H-2), 3.66 – 3.62 (m, 1H, H-5), 3.61 (dd, *J* = 9.3, 3.0 Hz, 1H, H-3), 3.54 (dq, *J* = 9.8, 7.2 Hz, 1H, CH*H*CH$_3$), 1.28 (t, *J* = 7.1 Hz, 3H, C*H*$_3$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 166.5 (C=O Bz), 139.0, 138.6, 138.2, 138.2 ($C_{q\text{-}arom}$), 130.3, 130.2, 128.5, 128.5, 128.4, 128.4, 128.4, 127.9, 127.9, 127.8, 127.7, 127.7, 127.5 (CH_{arom}), 101.7 (C-1), 82.4 (C-3), 75.4 (CH_2 Bn), 74.8 (C-4), 74.0 (C-2), 73.9 (CH_2 Bn), 73.9 (C-5), 71.6 (CH_2 Bn), 65.6 (*C*H_2CH$_3$), 64.3 (C-6), 15.3 (*C*H$_3$); ^{13}C-GATED NMR (126 MHz, $CDCl_3$): δ 101.7 ($J_{H1\text{-}C1}$ = 153 Hz, β); Data of the minor stereoisomer (α product): ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.94 (d, *J* = 1.9 Hz, 1H, H-1), 4.82 (d, *J* = 12.2 Hz, 1H, C*H*H Bn), 4.14 (t, *J* = 9.6 Hz, 1H, H-4), 3.87 (dd, *J* = 3.1, 1.9 Hz, 1H, H-2), 3.76 (dq, *J* = 9.8, 7.1 Hz, 1H, C*H*HCH$_3$), 3.53 – 3.45 (m, 1H, CH*H*CH$_3$), 1.21 (t, *J* = 7.1 Hz, 3H, C*H*$_3$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 97.7 (C-1), 80.5 (C-3), 75.2 (C-2), 73.9, 72.8, 72.3 (CH_2 Bn), 64.0 (*C*H_2CH$_3$), 63.3 (C-6), 15.1 (*C*H$_3$); ^{13}C-GATED NMR (126 MHz, $CDCl_3$): δ 97.7 ($J_{H1\text{-}C1}$ = 171 Hz, α); HRMS: $[M+NH_4]^+$ calcd for $C_{36}H_{38}O_7$ 600.29558, found 600.29587.

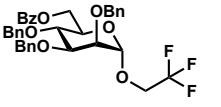


2-Fluoroethyl 6-*O*-benzoyl-2,3,4-tri-*O*-benzy-D-mannopyranoside (S73). The title compound was prepared according to general procedure VII. Column chromatography (90:10 → 60:40, pentane:Et_2O) yielded the title compound (59 mg, 99 µmol, 99%, colorless oil, α:β; 51:49). TLC: R_f 0.20 (pentane:Et_2O, 70:30, v:v); IR (thin film, cm^{-1}): 538, 712, 1027, 1209, 1274, 1720, 2871, 3032; Data of the major stereoisomer (α product): ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.39 – 6.92 (m, 20H, CH_{arom}), 4.99 (d, *J* = 12.2 Hz, 1H, C*H*H Bn), 4.94 (d, *J* = 1.9 Hz, 1H, H-1), 4.87 (d, *J* = 12.2 Hz, 1H, CH*H* Bn), 4.73 – 4.44 (m, 8H, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, H-6, H-6, C*H*HF, CH*H*F), 4.12 (t, *J* = 9.6 Hz, 1H, H-4), 4.02 (dd, *J* = 9.2, 3.0 Hz, 3H, H-3), 3.90 (dd, *J* = 3.1, 1.9 Hz, 1H, H-2), 3.86 – 3.63 (m, 2H, C*H*HCH$_2$F, CH*H*CH$_2$F); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 166.4 (C=O Bz), 138.4, 138.1, 138.1, 138.0 ($C_{q\text{-}arom}$), 131.2, 130.2, 129.8, 128.5, 128.5, 128.4, 128.3, 128.3, 128.2, 127.9, 127.9, 127.8, 127.7, 127.7, 127.5 (CH_{arom}), 98.3 (C-1), 82.9 (d, *J* = 169.3 Hz, *C*H_2F), 80.3 (C-3), 75.4 (CH_2 Bn), 75.0 (C-2), 74.5 (C-4), 74.1,

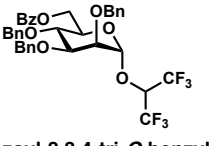
74.0, 72.9 (CH_2 Bn), 70.5 (C-5), 66.8 (d, J = 20.0 Hz, CH_2CH_2F), 64.1 (C-6); ^{13}C-GATED NMR (126 MHz, $CDCl_3$): δ 98.3 ($J_{H1\text{-}C1}$ = 171 Hz, α); Data of the minor stereoisomer (β product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.95 (Signal overlaps with major isomer, 1H, H-1), 4.87 (d, J = 12.2 Hz, 1H, CH*H* Bn), 4.80 (d, J = 3.2 Hz, 1H, H), 4.05 (t, J = 9.5 Hz, 1H, H-4); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): 101.9 (C-1), 82.5 (d, J = 170.2 Hz, CH_2F), 68.7 (d, J = 19.8 Hz, CH_2CH_2); ^{13}C-GATED NMR (126 MHz, $CDCl_3$): δ 101.9 ($J_{H1\text{-}C1}$ = 155 Hz, β); HRMS: $[M+NH_4]^+$ calcd for $C_{36}H_{37}FO_7$ 618.28616, found 618.28604.



2,2-Difluoroethyl 6-*O*-benzoyl-2,3,4-tri-*O*-benzy-D-mannopyranoside (S74). The title compound was prepared according to general procedure VII. Column chromatography (95:5 → 80:20, pentane:Et_2O) yielded the title compound (55 mg, 89 µmol, 89%, colorless oil, α:β; 78:22). TLC: R_f 0.30 (pentane:Et_2O, 80:20, v:v); IR (thin film, cm^{-1}): 696, 1027, 1069, 1273, 1452, 1720, 2924, 3031; Data of the major stereoisomer (α product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.32 – 6.85 (m, 20H, CH_{arom}), 5.87 (tdd, J = 55.3, 4.6, 3.6 Hz, 1H, C*H*F_2), 4.93 (d, J = 10.7 Hz, 1H, C*H*H Bn), 4.91 (d, J = 2.0 Hz, 1H, H-1), 4.79 (d, J = 12.1 Hz, 1H, C*H*H Bn), 4.72 – 4.46 (m, 5H, C*H*H Bn, CH*H* Bn, CH*H* Bn, H-6, H-6), 4.10 (t, J = 9.5 Hz, 1H, H-4), 3.96 (dd, J = 9.3, 3.1 Hz, 1H, H-3), 3.93 (ddd, J = 9.8, 4.3, 2.5 Hz, 1H, H-5), 3.86 (dd, J = 3.1, 2.0 Hz, 1H, H-2), 3.80 (dddd, J = 15.3, 14.1, 11.8, 3.6 Hz, 1H, C*H*HCF$_2$), 3.68 (tdd, J = 13.2, 11.8, 4.6 Hz, 1H, CH*H*CF$_2$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 166.4 (C=O Bz), 138.6, 138.3, 138.2, 137.9 ($C_{q\text{-}arom}$), 130.1, 128.6, 128.5, 128.5, 128.4, 128.3, 128.3, 128.3, 128.0, 128.0, 127.9, 127.9, 127.7, 127.6 (CH_{arom}), 114.0 (t, J = 241.2 Hz, CF_2), 98.8 (C-1), 80.0 (C-3), 75.4 (CH_2 Bn), 74.8 (C-2), 74.3 (C-4), 73.1, 72.5 (CH_2 Bn), 70.9 (C-5), 66.8 (t, J = 28.1 Hz, CH_2CHF_2), 63.7 (C-6); ^{13}C-GATED NMR (126 MHz, $CDCl_3$): δ 98.8 ($J_{H1\text{-}C1}$ = 170 Hz, α); Data of the minor stereoisomer (β product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 6.04 – 5.77 (m, 1H, C*H*F_2), 4.84 (d, J = 12.1 Hz, 1H, CH*H* Bn), 4.50 (signal overlaps with major isomer, 1H, H-1), 4.03 (t, J = 9.4 Hz, 1H, H-4); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 101.9 (C-1), 74.4, 74.1, 73.7 (CH_2 Bn), 68.5 (dd, J = 31.1, 25.9 Hz, CH_2CHF_2), 63.9 (C-6); HRMS: $[M+NH_4]^+$ calcd for $C_{36}H_{36}F_2O_7$ 636.27674, found 636.27662.

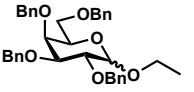


2,2,2-Trifluoroethyl 3-*O*-benzoyl-2,3,4-tri-*O*-benzy-α-D-mannopyranoside (S75). The title compound was prepared according to general procedure VII. Column chromatography (95:5 → 80:20, pentane:Et_2O) yielded the title compound (36 mg, 56 µmol, 56%, colorless oil, α:β; >98:2). TLC: R_f 0.40 (pentane:Et_2O, 80:20, v:v); $[\alpha]_D^{25}$ 34.6° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 697, 712, 1027, 1070, 1166, 1274, 1452, 1720, 2867, 3032; ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.45 – 6.83 (m, 20H, CH_{arom}), 4.93 (s, 1H, H-1), 4.93 (d, J = 10.5 Hz, 1H, C*H*H Bn), 4.79 (d, J = 12.1 Hz, 1H, C*H*H Bn), 4.73 – 4.64 (m, 3H, C*H*H Bn, CH*H* Bn, CH*H* Bn), 4.61 (d, J = 10.8 Hz, 1H, CH*H* Bn), 4.58 – 4.51 (m, 2H, H-6, H-6), 4.11 (t, J = 9.5 Hz, 1H, H-4), 4.01 – 3.80 (m, 5H, H-2, H-3, H-5, C*H*HCF$_3$, CH*H*CF$_3$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 166.4 (C=O Bz), 138.3, 138.1, 138.0 ($C_{q\text{-}arom}$), 130.1, 129.8, 128.6, 128.6, 128.5, 128.3, 128.0, 127.9, 127.9, 127.8, 127.1 (CH_{arom}), 123.8 (q, J = 278.3 Hz, CF_3), 98.7 (C-1), 79.8 (C-3), 75.4 (CH_2 Bn), 74.8 (C-2), 74.2 (C-4), 73.3, 72.6 (CH_2 Bn), 71.2 (C-5), 64.4 (q, J = 35.0 Hz, CH_2CF_3), 63.6 (C-6); HRMS: $[M+NH_4]^+$ calcd for $C_{36}H_{35}F_3O_7$ 654.26731, found 654.26715.

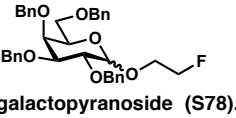


1,1,1,3,3,3-Hexafluoro-2-propyl 6-*O*-benzoyl-2,3,4-tri-*O*-benzyl-α-D-mannopyranoside (S76). The title compound was prepared according to general procedure VII. Column chromatography (100:0 → 85:15, pentane:Et_2O) yielded the title compound (45 mg, 64 µmol, 64%, colorless oil, α:β; >98:2). TLC: R_f 0.25 (pentane:Et_2O, 90:10, v:v); $[\alpha]_D^{25}$ 39.9° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 595, 698, 1027, 1103, 1274, 1720,

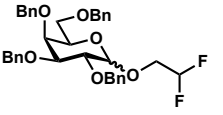
2937, 3034; ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.37 – 6.41 (m, 20H, CH_{arom}), 5.04 (d, *J* = 2.1 Hz, 1H, H-1), 4.90 (d, *J* = 10.7 Hz, 1H, C*H*H Bn), 4.78 (d, *J* = 12.1 Hz, 1H, C*H*H Bn), 4.72 (d, *J* = 11.5 Hz, 1H, C*H*H Bn), 4.68 (d, *J* = 11.6 Hz, 1H, CH*H* Bn), 4.64 – 4.58 (m, 2H, CH*H* Bn, CH*H* Bn), 4.55 (dd, *J* = 12.0, 2.3 Hz, 1H, H-6), 4.51 (dd, *J* = 12.0, 4.3 Hz, 1H, H-6), 4.41 (p, *J* = 5.9 Hz, 1H, C*H*$(CF_3)_2$), 4.11 (t, *J* = 9.3 Hz, 1H, H-4), 3.99 (ddd, *J* = 9.8, 4.1, 2.4 Hz, 1H, H-5), 3.92 (dd, *J* = 8.9, 3.0 Hz, 1H, H-3), 3.86 (dd, *J* = 3.0, 2.1 Hz, 1H, H-2); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 166.1 (C=O Bz), 137.8, 137.5, 137.5 ($C_{q\text{-}arom}$), 129.8, 129.5, 128.4, 128.4, 128.4, 127.9, 127.8, 127.7, 127.7, 127.5 (CH_{arom}), 100.3 (C-1), 79.0 (C-3), 77.2 (CH_2 Bn), 76.9 (C-2), 76.7 (C-4), 75.1, 74.4 (CH_2 Bn), 72.2 (p, *J* = 32.7 Hz, *C*H$(CF_3)_2$) 71.9 (C-5), 63.1 (C-6); HRMS: $[M+NH_4]^+$ calcd for $C_{37}H_{34}F_6O_7$ 722.25470, found 722.25433.



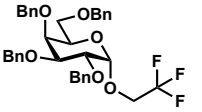
Ethyl 2,3,4,6-tetra-*O*-benzy-D-galactopyranoside (S77). The title compound was prepared according to general procedure VII. Column chromatography (100:0 → 90:10, pentane:EtOAc) yielded the title compound (42 mg, 73 µmol, 73%, colorless oil, α:β; 17:83). TLC: R_f 0.46 (pentane:EtOAc, 90:10, v:v); IR (thin film, cm^{-1}): 731, 1026, 1067, 1092, 1360, 1452, 1497, 2868, 2914; Data of the major stereoisomer (β product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.39 – 7.22 (m, 20H, CH_{arom}), 4.97 – 4.90 (m, 2H, C*H*H Bn, C*H*H Bn), 4.76 (m, 2H, CH*H* Bn, C*H*H Bn), 4.73 – 4.67 (m, 1H, C*H*H Bn), 4.62 (d, *J* = 11.7 Hz, 1H, CH*H* Bn), 4.49 – 4.34 (m, 2H, C*H*H Bn, CH*H* Bn), 4.36 (d, *J* = 7.7 Hz, 1H, H-1), 4.03 – 3.92 (m, 1H, C*H*HCH$_3$), 3.88 (d, *J* = 2.7 Hz, 1H, H-4), 3.81 (t, *J* = 8.7 Hz, 1H, H-2), 3.62 – 3.55 (m, 3H, H-6, H-6, C*H*HCH$_3$), 3.56 – 3.46 (m, 2H, H-3, H-5), 1.26 (t, *J* = 7.1 Hz, 3H, C*H*$_3$); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 139.0, 138.8, 138.7, 138.1 ($C_{q\text{-}arom}$), 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.0, 127.9, 127.7, 127.6, 127.6 (CH_{arom}), 103.9 (C-1), 82.3 (C-3), 79.8 (C-2), 75.3 (CH_2 Bn), 74.6 (CH_2 Bn), 73.7 (CH_2 Bn), 73.6 (C-4), 73.5 (C-5), 73.2 (CH_2 Bn), 69.1 (C-6), 65.6 (*C*H$_2$CH$_3$), 15.4 (*C*H$_3$); Data of the minor stereoisomer (α product): δ 4.86 (d, *J* = 11.9 Hz, 1H, C*H*H Bn), 4.82 (d, *J* = 4.6 Hz, 1H, H-1), 3.70 (dqd, *J* = 10.1, 7.2, 1.0 Hz, 1H, C*H*HCH$_3$); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 97.3 (C-1), 76.7 (C-2), 74.9, 73.4, 69.2 (CH_2 Bn), 63.4 (C-6), 15.1 (CH_3); HRMS: $[M+Na]^+$ calcd for $C_{36}H_{40}O_6Na$ 591.27171, found 591.2710.



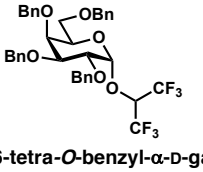
2-Fluoroethyl 2,3,4,6-tetra-*O*-benzy-D-galactopyranoside (S78). The title compound was prepared according to general procedure VII. Column chromatography (97:3 → 85:15, pentane:EtOAc) yielded the title compound (49 mg, 84 µmol, 84%, colorless oil, α:β; 31:69). TLC: R_f 0.36 (pentane:EtOAc, 85:15, v:v); IR (thin film, cm^{-1}): 696, 734, 1027, 1079, 1095, 1347, 1453, 1496, 2914; Data of the major stereoisomer (β product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.67 – 7.17 (m, 20H, CH_{arom}), 4.98 – 4.36 (m, 11H, CH_2 Bn, CH_2 Bn, CH_2 Bn, CH_2 Bn, H-1, CH_2C*H*HF, CH_2CH*H*F), 4.13 – 4.01 (m, 1H, C*H*HCH$_2$F), 3.60 – 3.55 (m, 3H, H-2, H-4, CH*H*CH$_2$F), 3.55 – 3.49 (m, 3H, H-6, H-6, H-3); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 138.8, 138.7, 138.6, 138.0 ($C_{q\text{-}arom}$), 131.1, 129.4, 128.5, 128.5, 128.5, 128.5, 128.4, 128.3, 128.0, 127.7, 127.7, 127.6, 124.9 (CH_{arom}), 104.2 (C-1), 82.7 (d, *J* = 169.8 Hz, *C*H$_2$F), 82.2 (C-3), 79.5 (C-2), 75.3, 74.6, 73.7 (CH_2 Bn), 73.6 (C-4), 73.6 (C-4), 73.5, 73.2 (CH_2 Bn), 69.0 (C-6), 68.8 (d, *J* = 20.2 Hz, *C*H$_2$CH$_2$F); ^{13}C-GATED NMR (126 MHz, $CDCl_3$): δ 104.2 ($J_{H1\text{-}C1}$ = 159 Hz, β); Data of the minor stereoisomer (α product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): 4.86 (d, *J* = 3.6 Hz, 1H, H-1), 4.11 (ddd, *J* = 12.1, 4.4, 2.5, 1H, C*H*HCH$_2$F); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 98.1 (C-1), 82.7 (d, *J* = 169.8 Hz, *C*H$_2$F), 76.6 (C-2), 75.3, 74.9, 73.4 (CH_2 Bn), 69.5 (C-5), 69.1 (C-6), 67.1 (d, *J* = 20.3 Hz, *C*H$_2$CH$_2$F); ^{13}C-GATED NMR (126 MHz, $CDCl_3$): δ 98.1 ($J_{H1\text{-}C1}$ = 171 Hz, α); HRMS: $[M+Na]^+$ calcd for $C_{36}H_{39}FO_6$ 609.2628, found 609.2637.



2,2-Difluoroethyl 2,3,4,6-tetra-*O*-benzy-D-galactopyranoside (S79). The title compound was prepared according to general procedure VII. Column chromatography (97:3 → 85:15, pentane:EtOAc) yielded the title compound (42 mg, 69 µmol, 69%, colorless oil, α:β; 66:34). TLC: R_f 0.21, 0.31 (pentane:EtOAc, 90:10, v:v); IR (thin film, cm^{-1}): 696, 736, 1028, 1056, 1094, 1361, 1453, 1497, 2917; Data of the major stereoisomer (α product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.40 – 7.24 (m, 20H, CH_{arom}), 5.97 (tt, *J* = 55.6, 4.4 Hz, 1H, C*H*F$_2$), 4.94 (dd, *J* = 11.5, 1.3 Hz, 1H, C*H*H Bn), 4.86 – 4.79 (m, 3H, C*H*H Bn, CH*H* Bn, H-1), 4.73 (d, *J* = 11.6 Hz, 1H, C*H*H Bn), 4.65 (d, *J* = 11.9 Hz, 1H, CH*H* Bn), 4.56 (d, *J* = 11.4 Hz, 1H, CH*H* Bn), 4.46 (d, *J* = 11.8 Hz, 1H, C*H*H Bn), 4.43 – 4.37 (m, 1H, CH*H* Bn), 4.05 (dd, *J* = 10.0, 3.7 Hz, 1H, H-2), 3.98 – 3.90 (m, 3H, H-3, H-4, H-5), 3.73 (ddd, *J* = 14.7, 13.0, 4.4 Hz, 1H, C*H*HCHF$_2$), 3.80 – 3.66 (m, 1H, CH*H*CHF$_2$), 3.60 – 3.46 (m, 2H, H-6, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 138.8, 138.6, 138.6, 138.0 ($C_{q\text{-}arom}$), 128.5, 128.4, 128.4, 128.2, 127.8, 127.8, 127.7, 127.6 (CH_{arom}), 114.3 (t, *J* = 241.2 Hz, *C*HF$_2$), 98.9 (C-1), 78.9 (C-3), 76.5 (C-2), 75.1 (C-4), 74.9, 73.7, 73.6, 73.4 (CH_2 Bn), 69.9 (C-5), 69.1 (C-6), 67.5 (t, *J* = 28.9 Hz, *C*H$_2$CHF$_2$); ^{13}C-GATED NMR (126 MHz, $CDCl_3$): δ 98.9 ($J_{H1\text{-}C1}$ = 169 Hz, α); Data of the minor stereoisomer (β product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 5.91 (dddd, *J* = 56.3, 54.7, 5.4, 3.1 Hz, *C*HF$_2$), 4.88 (d, *J* = 10.8 Hz, 1H, C*H*H Bn), 4.61 (d, *J* = 11.6 Hz, 1H, CH*H* Bn), 4.39 (d, *J* = 7.6 Hz, 1H, H-1), 3.83 (dd, *J* = 9.7, 7.6 Hz, 1H, H-2); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 114.4 (dd, *J* = 242.1, 239.7 Hz, *C*HF$_2$), 104.3 (C-1), 79.3 (C-2), 75.4, 74.7 (CH_2 Bn), 73.8 (C-3), 73.7, 73.3 (CH_2 Bn), 68.9 (C-6); ^{13}C-GATED NMR (126 MHz, $CDCl_3$): δ 104.3 ($J_{H1\text{-}C1}$ = 159 Hz, β); HRMS: $[M+Na]^+$ calcd for $C_{36}H_{38}F_2O_6$ 627.2534, found 627.2542.

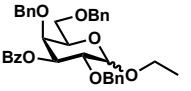


2,2,2-Trifluoroethyl 2,3,4,6-tetra-*O*-benzy-α-D-galactopyranoside (S80). The title compound was prepared according to general procedure VII. Column chromatography (97:3 → 90:10, pentane:EtOAc) yielded the title compound (49 mg, 79 µmol, 79%, colorless oil, α:β; 87:13). TLC: R_f 0.28, 0.47 (pentane:EtOAc, 90:10, v:v); $[\alpha]_D^{20}$ –27.5° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 696, 735, 1079, 1153, 1278, 1351, 1453, 1497, 2915; Data of the major stereoisomer (α product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, ^{13}C-HMBC-Gated): δ 7.52 – 7.05 (m, 20H, CH_{arom}), 4.94 (d, *J* = 11.4 Hz, 1H, C*H*H Bn), 4.88 (d, *J* = 3.7 Hz, 1H, H-1), 4.87 – 4.79 (m, 2H, C*H*H Bn, CH*H* Bn), 4.73 (d, *J* = 11.6 Hz, 1H, CH*H* Bn), 4.65 (d, *J* = 11.9 Hz, 1H, CH*H* Bn), 4.56 (d, *J* = 11.4 Hz, 1H, C*H*H Bn), 4.46 (d, *J* = 11.9 Hz, 1H, C*H*H Bn), 4.39 (d, *J* = 11.8 Hz, 1H, CH*H* Bn), 4.07 (dd, *J* = 10.0, 3.7 Hz, 1H, H-2), 4.00 – 3.87 (m, 5H, C*H*HCF$_3$, CH*H*CF$_3$, H-3, H-4, H-5), 3.55 – 3.48 (m, 2H, H-6, H-6); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, ^{13}C-HMBC-Gated): δ 138.8, 138.6, 138.5, 138.0 ($C_{q\text{-}arom}$), 128.6, 128.6, 128.0, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7, 127.6 (CH_{arom}), 122.6 (q, *J* = 281.9 Hz, *C*F$_3$), 98.3 (C-1), 78.7 (C-3), 76.3 (C-2), 75.0 (CH_2 Bn), 74.9 (C-4), 73.6, 73.5, 73.5 (CH_2 Bn), 70.2 (C-5), 68.9 (C-6), 64.6 (q, *J* = 34.7 Hz, *C*H$_2$CF$_3$); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 98.3 ($J_{H1\text{-}C1}$ = 172 Hz, α); Data of the minor stereoisomer (β product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, ^{13}C-HMBC-Gated): 4.17 (dq, *J* = 12.4, 8.8 Hz, 1H, C*H*HCF$_3$); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, ^{13}C-HMBC-Gated): 104.1 (C-1), 66.0 (q, *J* = 34.8 Hz, *C*H$_2$CF$_3$); HRMS: $[M+Na]^+$ calcd for $C_{36}H_{37}F_3O_6$ 645.2440, found 645.2445.

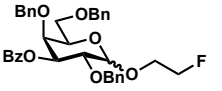


1,1,1,3,3,3-Hexafluoro-2-propyl 2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranoside (S81). The title compound was prepared according to general procedure VII. Column chromatography (100:0 → 80:20, pentane:Et_2O) yielded the title compound (23 mg, 33 µmol, 33%, colorless oil, α:β; >98:2). TLC: R_f 0.38

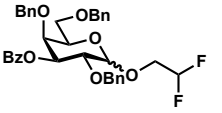
(pentane:EtOAc, 95:5, v:v); $[\alpha]_D^{20}$ 58.8° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 689, 696, 734, 1028, 1051, 1102, 1195, 1218, 1287, 1169, 1454, 1497, 2926; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated, ^1H-^{19}F Decoupled): δ 7.39 – 7.23 (m, 20H, CH_{arom}), 5.15 (d, *J* = 3.8 Hz, 1H, H-1), 4.94 (d, *J* = 11.3 Hz, 1H, C*H*H Bn), 4.84 (d, *J* = 11.5 Hz, 1H, C*H*H Bn), 4.79 – 4.66 (m, 3H, CH*H* Bn, CH*H* Bn, C*H*H Bn), 4.56 (d, *J* = 11.3 Hz, 1H, CH*H* Bn), 4.50 – 4.39 (m, 3H, C*H*H Bn, CH*H* Bn, C*H*$(CF_3)_2$), 4.13 (dd, *J* = 10.2, 3.8 Hz, 1H, H-2), 4.07 – 4.00 (m, 2H, H-4, H-5), 3.94 (dd, *J* = 10.2, 2.7 Hz, 1H, H-3), 3.57 – 3.46 (m, 2H, H-6, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 138.7, 138.5, 138.2, 138.0 ($C_{q\text{-}arom}$), 128.6, 128.5, 128.5, 128.4, 128.3, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7, 127.6 (CH_{arom}), 99.9 (C-1), 78.4 (C-3), 75.5 (C-2), 75.0 (CH_2 Bn), 74.7 (C-4), 73.6, 73.6, 73.4 (CH_2 Bn), 72.5 (p, *J* = 33.3 Hz, C*H*$(CF_3)_2$), 70.9 (C-5), 68.4 (C-6); ^{13}C-GATED NMR (126 MHz, $CDCl_3$): δ 99.9 ($J_{H1\text{-}C1}$ = 174 Hz, α); HRMS: $[M+Na]^+$ calcd for $C_{37}H_{36}F_6O_6$ 713.2314, found 713.2319.



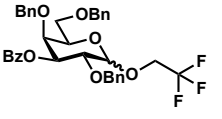
Ethyl 3-*O*-benzoyl-2,4,6-tri-*O*-benzy-D-galactopyranoside (S82). The title compound was prepared according to general procedure VII. Column chromatography (100:0 → 85:15, pentane:Et_2O) yielded the title compound (46 mg, 79 µmol, 79%, colorless oil, α:β; 41:59). TLC: R_f 0.25 (pentane:Et_2O, 80:20, v:v); IR (thin film, cm^{-1}): 695, 735, 1026, 1069, 1270, 1720, 2869, 3063; Data of the major stereoisomer (β product): ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.24 – 6.93 (m, 20H, CH_{arom}), 5.19 (dd, *J* = 10.2, 3.1 Hz, 1H, H-3), 4.86 (d, *J* = 11.5 Hz, 1H, C*H*H Bn), 4.70 (d, *J* = 11.4 Hz, 1H, CH*H* Bn), 4.66 – 4.60 (m, 2H, C*H*H Bn, CH*H* Bn), 4.54 – 4.39 (m, 3H, H-1, C*H*H Bn, CH*H* Bn), 4.22 – 4.12 (m, 1H, H-5), 4.07 (dd, *J* = 3.2, 1.0 Hz, 1H, H-4), 4.02 (dq, *J* = 9.5, 7.1 Hz, 1H, C*H*HCH$_3$), 3.93 (dd, *J* = 10.2, 7.7 Hz, 1H, H-2), 3.69 – 3.58 (m, 2H, H-6, CH*H*CH$_3$), 3.58 – 3.49 (m, 1H, H-6), 1.29 (t, *J* = 7.1 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 166.0 (C=O Bz), 138.4, 138.2, 138.0, 138.0 ($C_{q\text{-}arom}$), 130.1, 129.9, 128.5, 128.4, 128.4, 128.3, 128.1, 128.1, 127.9, 127.9, 127.9, 127.8, 127.8, 127.8, 127.8, 127.8, 127.7, 127.6 (CH_{arom}), 103.9 (C-1), 76.7 (C-2), 75.7 (C-3), 75.0, 74.7 (CH_2 Bn), 74.5 (C-4), 73.6 (CH_2 Bn), 68.8 (C-5), 68.6 (C-6), 65.8 (*C*H$_2$CH$_3$), 15.4 (*C*H$_3$); Data of the minor stereoisomer (α product): ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.57 (dd, *J* = 10.5, 3.1 Hz, 1H, H-3), 4.90 (d, *J* = 3.6 Hz, 1H, H-1), 1.27 (t, *J* = 7.1 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 97.2 (C-1), 75.3 (CH_2 Bn), 74.3 (C-2), 73.5, 73.0 (CH_2 Bn), 68.8 (C-3), 68.7 (C-6), 63.7 (*C*H$_2$CH$_3$), 15.2 (*C*H$_3$); HRMS: $[M+NH_4]^+$ calcd for $C_{36}H_{38}O_7$ 600.29558, found 600.29551.



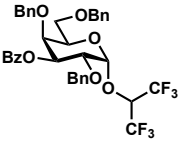
2-Fluoroethyl 3-*O*-benzoyl-2,4,6-tri-*O*-benzy-D-galactopyranoside (S83). The title compound was prepared according to general procedure VII. Column chromatography (90:10 → 60:40, pentane:Et_2O) yielded the title compound (49 mg, 82 µmol, 82%, colorless oil, α:β; 40:60). TLC: R_f 0.20 (pentane:Et_2O, 70:30, v:v); IR (thin film, cm^{-1}): 538, 696, 711, 735, 1026, 1043, 1070, 1077, 1270, 1452, 1720, 1870, 3030; Data of the major stereoisomer (β product): ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.26 – 6.97 (m, 20H, CH_{arom}), 5.19 (dd, *J* = 10.2, 3.1 Hz, 1H, H-3), 4.87 (d, *J* = 11.4 Hz, 1H, C*H*H Bn), 4.76 – 4.58 (m, 3H, C*H*H Bn, C*H*H Bn, C*H*HCH$_2$F), 4.55 (d, *J* = 7.7 Hz, 1H, H-1), 4.59 – 4.39 (m, 4H, CH*H* Bn, CH*H* Bn, CH*H* Bn, CH*H*CH$_2$F), 4.19 – 4.05 (m, 1H, C*H*HF), 4.08 (d, *J* = 2.7 Hz, 1H, H-4), 3.96 (dd, *J* = 10.2, 7.6 Hz, 1H, H-2), 3.94 – 3.81 (m, 1H, CH*H*F), 3.77 (dd, *J* = 7.4, 6.1 Hz, 1H, H-5), 3.60 (t, *J* = 6.3 Hz, 2H, H-6), 3.55 (dd, *J* = 6.6, 1.3 Hz, 1H, H-6); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 165.9 (C=O Bz), 138.2, 138.1, 138.0, 137.9 ($C_{q\text{-}arom}$), 130.0, 129.9, 129.7, 129.4, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.1, 127.6 (CH_{arom}), 104.2 (C-1), 82.7 (d, *J* = 169.8 Hz, *C*H$_2$F), 76.4 (C-2), 75.5 (C-3), 75.1, 74.7 (CH_2 Bn), 74.3 (C-4), 73.6 (CH_2 Bn), 73.4 (C-5), 69.0 (d, *J* = 20.1 Hz, *C*H$_2$CH$_2$F), 68.5 (C-6); Data of the minor stereoisomer (α product): ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.59 (dd, *J* = 10.6, 3.1 Hz, 1H, H-3), 4.95 (d, *J* = 3.6 Hz, 1H, H-1), 4.18 (d, *J* = 3.7 Hz, 1H, H-4); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 97.8 (C-1), 82.7 (d, *J* = 169.7 Hz, *C*H$_2$F), 75.3, 73.4, 73.0 (CH_2 Bn), 67.2 (d, *J* = 20.2 Hz, *C*H$_2$CH$_2$F); HRMS: $[M+NH_4]^+$ calcd for $C_{36}H_{37}FO_7$ 618.28616, found 618.28638.



2,2-Difluoroethyl 3-*O*-benzoyl-2,4,6-tri-*O*-benzy-D-galactopyranoside (S84). The title compound was prepared according to general procedure VII. Column chromatography (95:5 → 75:25, pentane:Et_2O) yielded the title compound (50 mg, 81 µmol, 81%, colorless oil, α:β; 66:34). TLC: R_f 0.20 (pentane:Et_2O, 80:20, v:v); IR (thin film, cm^{-1}): 695, 1026, 1069, 1093, 1270, 1452, 1720, 2869, 3030; Data of the major stereoisomer (α product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.32 – 6.86 (m, 20H, CH_{arom}), 5.99 (tt, *J* = 55.5, 4.3 Hz, 1H, C*H*F_2), 5.55 (dd, *J* = 10.6, 3.0 Hz, 1H, H-3), 4.91 (d, *J* = 3.7 Hz, 1H, H-1), 4.75 – 4.58 (m, 3H, C*H*H Bn, C*H*H Bn, CH*H* Bn), 4.56 – 4.36 (m, 3H, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.23 – 4.11 (m, 3H, H-2, H-3, H-4), 3.89 – 3.68 (m, 2H, C*H*HCHF_2, CH*H*CHF_2), 3.67 – 3.49 (m, 1H, H-6), 3.53 (dd, *J* = 6.5, 5.1 Hz, 2H, H-6); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 165.9 (C=O Bz), 138.1, 138.0, 137.9, 137.8 ($C_{q\text{-}arom}$), 129.9, 129.7, 128.6, 128.5, 128.4, 128.4, 128.3, 128.3, 128.1, 128.0, 128.0, 128.0, 128.0, 127.9, 127.9, 127.8, 127.8 (CH_{arom}), 114.3 (t, *J* = 241.2 Hz, *C*HF_2), 98.4 (C-1), 75.4 (C-2), 75.3 (CH_2 Bn), 74.0 (C-4), 73.5, 73.3 (CH_2 Bn), 72.7 (C-3), 69.4 (C-5), 68.6 (C-6), 67.5 (t, *J* = 29.0 Hz, *C*H_2CHF_2); Data of the minor stereoisomer (β product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.19 (dd, *J* = 10.2, 3.2 Hz, 1H, H-3), 4.82 (d, *J* = 11.4 Hz, 1H, C*H*H Bn), 4.54 (d, *J* = 7.6 Hz, 1H, H-1), 4.08 (d, *J* = 3.2 Hz, 1H, H-4), 3.96 (dd, *J* = 10.2, 7.6 Hz, 1H, H-2); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 114.3 (dd, *J* = 242.0, 240.0 Hz, *C*HF_2), 104.3 (C-1), 76.4 (C-2), 75.1, 74.8, 73.6 (CH_2 Bn), 68.8 (dd, *J* = 30.4, 27.1 Hz, *C*H_2CHF_2), 68.4 (C-6); HRMS: $[M+NH_4]^+$ calcd for $C_{36}H_{36}F_2O_7$ 636.27674, found 636.27661.

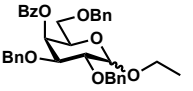


2,2,2-Trifluoroethyl 3-*O*-benzoyl-2,4,6-tri-*O*-benzy-D-galactopyranoside (S85). The title compound was prepared according to general procedure VII. Column chromatography (95:5 → 80:20, pentane:Et_2O) yielded the title compound (49 mg, 77 µmol, 77%, colorless oil, α:β; 86:14). TLC: R_f 0.35 (pentane:Et_2O, 80:20, v:v); IR (thin film, cm^{-1}): 695, 711, 735, 989, 1026, 1096, 1154, 1270, 1452, 1496, 1720, 2923, 3032; Data of the major stereoisomer (α product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.16 – 7.12 (m, 20H, CH_{arom}), 5.53 (dd, *J* = 10.5, 3.1 Hz, 1H, H-3), 4.96 (d, *J* = 3.7 Hz, 1H, H-1), 4.71 (d, *J* = 12.3 Hz, 1H, C*H*H Bn), 4.63 (d, *J* = 11.5 Hz, 1H, C*H*H Bn), 4.62 (d, *J* = 12.2 Hz, 1H, CH*H* Bn), 4.50 (d, *J* = 11.9 Hz, 1H, C*H*H Bn), 4.43 (d, *J* = 11.4 Hz, 1H, CH*H* Bn), 4.47 – 4.39 (m, 1H, CH*H* Bn), 4.27 – 4.17 (m, 2H, H-2, H-4), 4.13 (td, *J* = 6.5, 1.2 Hz, 1H, H-5), 4.03 – 3.85 (m, 2H, C*H*HCF_3, CH*H*CF_3), 3.53 (dd, *J* = 6.6, 2.0 Hz, 2H, H-6, H-6); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 165.9 (C=O Bz), 138.1, 137.9, 137.9, 137.8 ($C_{q\text{-}arom}$), 129.6, 128.6, 128.6, 128.5, 128.4, 128.4, 128.3, 128.0, 128.0, 128.0, 127.9 (CH_{arom}), 123.9 (q, *J* = 278.7 Hz, *C*F_3), 98.2 (C-1), 75.3 (CH_2 Bn), 75.3 (C-2), 73.8 (C-4), 73.5, 73.1 (CH_2 Bn), 72.7 (C-3), 69.7 (C-5), 68.4 (C-6), 64.9 (q, *J* = 34.9 Hz, *C*H_2CF_3); Data of the minor stereoisomer (β product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.18 (dd, *J* = 10.2, 3.1 Hz, 1H, H-3), 4.84 (d, *J* = 11.3 Hz, 1H, C*H*H Bn), 4.60 (d, *J* = 7.5 Hz, 1H, H-1), 4.08 (dd, *J* = 3.2, 1.0 Hz, 1H, H-4); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 104.1 (C-1), 76.1 (C-2), 75.2, 74.7, 73.6 (CH_2 Bn), 68.3 (C-6), 66.2 (d, *J* = 35.1 Hz, *C*H_2CF_3); HRMS: $[M+NH_4]^+$ calcd for $C_{36}H_{35}F_3O_7$ 654.26731, found 654.26738.

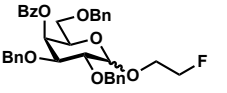


1,1,1,3,3,3-Hexafluoro-2-propyl 3-*O*-benzoyl-2,4,6-tri-*O*-benzyl-α-D-galactopyranoside (S86). The title compound was prepared according to general procedure VII. Column chromatography (100:0 → 80:20, pentane:Et_2O) yielded the title compound (38 mg, 55 µmol, 55%, colorless oil, α:β; >98:2). TLC: R_f 0.15 (pentane:Et_2O, 90:10, v:v); $[\alpha]_D^{25}$ 42.2° (*c* 1, $CHCl_3$); 687, 697, 735, 1105, 1196, 1219, 1315, 1452, 1496, 1720, 2363, 2868, 2936, 3065; ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.22 – 7.13 (m, 20H, CH_{arom}), 5.51 (dd, *J* = 10.7, 3.0 Hz, 1H, H-3), 5.24 (d, *J* = 3.8 Hz, 1H, H-1), 4.69 (d, *J* = 12.1 Hz, 1H, C*H*H

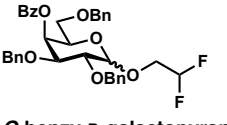
Bn), 4.63 (d, *J* = 12.0 Hz, 1H, CH*H* Bn), 4.61 (d, *J* = 11.3 Hz, 1H, C*H*H Bn), 4.50 (d, *J* = 12.1 Hz, 1H, CH*H* Bn), 4.49 – 4.41 (m, 3H, C*H*H Bn, CH*H* Bn, C*H*(CF_3)$_2$), 4.28 (dd, *J* = 10.7, 3.8 Hz, 1H, H-2), 4.26 – 4.22 (m, 2H, H-4, H-5), 3.60 – 3.48 (m, 2H, H-6, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 165.9 (C=O Bz), 137.9, 137.6 ($C_{q\text{-arom}}$), 129.8, 128.6, 128.6, 128.5, 128.5, 128.2, 128.1, 128.0, 127.9, 127.9, 127.7 (CH_{arom}), 99.7 (C-1), 75.4 (CH_2 Bn), 75.0 (C-4), 73.5, 73.1 (CH_2 Bn), 72.9 (C-2), 72.4 (C-3), 70.3 (C-5), 68.0 (C-6); HRMS: $[M+NH_4]^+$ calcd for $C_{37}H_{34}F_6O_7$ 722.25470, found 722.25438.



Ethyl 4-*O*-benzoyl-2,3,6-tri-*O*-benzy-D-galactopyranoside (S87). The title compound was prepared according to general procedure VII. Column chromatography (95:5 → 70:30, pentane:Et_2O) yielded the title compound (50 mg, 86 µmol, 86%, colorless oil, α:β; 45:55). TLC: R_f 0.25 (pentane:Et_2O, 80:20x, v:v); IR (thin film, cm^{-1}): 696, 711, 1026, 1068, 1271, 1173, 1720, 2866, 3032; Data of the major stereoisomer (β product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.29 – 7.03 (m, 20H, CH_{arom}), 5.83 (d, *J* = 1.9 Hz, 1H, H-4), 4.92 – 4.80 (m, 2H, C*H*H Bn, C*H*H Bn), 4.73 (d, *J* = 10.8 Hz, 1H, CH*H* Bn), 4.57 (d, *J* = 11.6 Hz, 1H, CH*H* Bn), 4.51 (d, *J* = 11.8 Hz, 1H, CH*H* Bn), 4.49 (d, *J* = 11.8 Hz, 1H, C*H*H Bn), 4.45 (d, *J* = 7.6 Hz, 1H, H-1), 4.04 (dq, *J* = 9.6, 7.1 Hz, 1H, C*H*HCH$_3$), 3.82 (ddd, *J* = 7.0, 5.9, 1.1 Hz, 1H, H-5), 3.71 – 3.57 (m, 3H, H-2, H-3, CH*H*CH$_3$), 3.53 (m, 2H, H-6, H-6), 1.32 (t, *J* = 7.1 Hz, 3H, C*H*$_3$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 166.0 (C=O Bz), 138.8, 138.7, 138.1, 137.8 ($C_{q\text{-arom}}$), 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.2, 128.1, 128.0, 127.7, 127.7, 127.5 (CH_{arom}), 103.9 (C-1), 79.5 (C-3/C-2), 76.7 (C-2/C-3), 75.5, 73.9 (CH_2 Bn), 72.6 (C-5), 72.0 (CH_2 Bn), 68.6 (C-6), 67.6 (C-4), 66.1 (*C*H$_2$CH$_3$), 15.5 (*C*H$_3$); Data of the minor stereoisomer (α product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.86 (dd, *J* = 3.5, 1.2 Hz, 1H, H-4), 4.92 – 4.80 (signal overlaps with major isomer, 1H, H-1), 4.65 (d, *J* = 12.1 Hz, 1H, CH*H* Bn), 4.22 (td, *J* = 6.3, 1.1 Hz, 1H, H-5), 4.10 (dd, *J* = 10.0, 3.3 Hz, 1H, H-3), 3.89 (dd, *J* = 10.0, 3.7 Hz, 1H, H-2), 3.76 (dq, *J* = 10.0, 7.1 Hz, 1H, C*H*HCH$_3$), 1.28 (t, *J* = 7.1 Hz, 3H, CH$_3$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 97.7 (C-1), 76.7 (C-3), 75.3 (C-2), 73.7, 73.6, 72.1 (CH_2 Bn), 68.9 (C-6), 68.1 (C-4), 15.1 (*C*H$_3$); HRMS: $[M+NH_4]^+$ calcd for $C_{36}H_{38}O_7$ 600.29558, found 600.29569.

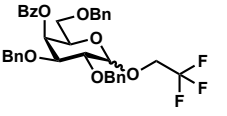


2-Fluoroethyl 4-*O*-benzoyl-2,3,6-tri-*O*-benzy-D-galactopyranoside (S88). The title compound was prepared according to general procedure VII. Column chromatography (90:10 → 60:40, pentane:Et_2O) yielded the title compound (50 mg, 84 µmol, 84%, colorless oil, α:β; 63:37). TLC: R_f 0.20 (pentane:Et_2O, 70:30, v:v); IR (thin film, cm^{-1}): 536, 712, 740, 1090, 1270, 1720, 2870, 3032; Data of the major stereoisomer (α product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.15 – 7.02 (m, 20H, CH_{arom}), 5.87 (dd, *J* = 3.4, 1.3 Hz, 1H, H-4), 4.95 (d, *J* = 3.7 Hz, 1H, H-1), 4.87 – 4.80 (m, 2H, C*H*H Bn, C*H*H Bn), 4.69 – 4.54 (m, 4H, CH*H* Bn, CH*H* Bn, C*H*HF, CH*H*F), 4.53 – 4.38 (m, 2H, C*H*H Bn, CH*H* Bn), 4.27 (td, *J* = 6.3, 1.3 Hz, 1H, H-5), 4.11 (dd, *J* = 10.1, 3.2 Hz, 1H, H-3), 3.92 (dd, *J* = 9.9, 3.7 Hz, 1H, H-2), 3.90 – 3.74 (m, 2H, C*H*HCH$_2$F, CHHCH$_2$F), 3.60 – 3.49 (m, 2H, H-6, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 165.9 (C=O Bz), 138.6, 138.5, 138.0, 137.8 ($C_{q\text{-arom}}$), 129.9, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.2, 128.1, 127.8, 127.8, 127.7, 127.6 (CH_{arom}), 98.4 (C-1), 82.8 (d, *J* = 169.8 Hz, *C*H$_2$F), 76.5 (C-3), 75.2 (C-2), 73.7, 73.6, 72.1 (CH_2 Bn), 68.8 (C-4), 68.8 (C-6), 68.2 (C-5), 67.3 (d, *J* = 20.1 Hz, *C*H$_2$CH$_2$F); Data of the minor stereoisomer (β product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.82 (dd, *J* = 3.3, 1.1 Hz, 1H, H-4), 4.50 (d, *J* = 7.4 Hz, 1H, H-1); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): 104.2 (C-1), 69.3 (d, *J* = 20.1 Hz, *C*H$_2$CH$_2$F), 67.5 (C-4); HRMS: $[M+NH_4]^+$ calcd for $C_{36}H_{37}FO_7$ 618.28616, found 618.28617.

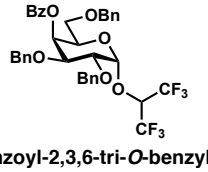


2,2-Difluoroethyl 4-*O*-benzoyl-2,3,6-tri-*O*-benzy-D-galactopyranoside (S89). The title compound was prepared according to general procedure VII. Column chromatography (95:5 → 80:20, pentane:Et_2O) yielded the title compound (40 mg, 65 µmol, 65%, colorless oil, α:β; 44:56). TLC: R_f 0.30 (pentane:Et_2O,

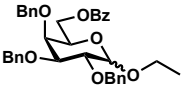
80:20, v:v); IR (thin film, cm^{-1}): 738, 1026, 1267, 1720, 2869, 3032; Data of the major stereoisomer (β product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.44 – 7.02 (m, 20H, CH_{arom}), 6.02 (tt, *J* = 55.5, 4.3 Hz, 1H, C*H*F_2), 5.86 (dd, *J* = 3.4, 1.2 Hz, 1H, H-4), 4.91 (d, *J* = 3.7 Hz, 1H, H-1), 4.85 (d, *J* = 11.2 Hz, 1H, C*H*H Bn), 4.83 (d, *J* = 11.9 Hz, 1H, C*H*H Bn), 4.64 (d, *J* = 11.9 Hz, 1H, CH*H* Bn), 4.58 (d, *J* = 11.2 Hz, 1H, CH*H* Bn), 4.49 (d, *J* = 11.8 Hz, 1H, C*H*H Bn), 4.41 (d, *J* = 11.9 Hz, 1H, CH*H* Bn), 4.21 (td, *J* = 6.3, 1.3 Hz, 1H, H-5), 4.07 (dd, *J* = 10.1, 3.2 Hz, 1H, H-3), 3.92 (dd, *J* = 10.1, 3.6 Hz, 1H, H-2), 3.80 (m, 2H, C*H*HCHF_2, CH*H*CHF_2), 3.53 (m, 2H, H-6, H-6); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 165.8 (C=O Bz), 138.3, 138.1, 137.7 ($C_{q\text{-}arom}$), 128.5, 128.5, 128.4, 128.4, 128.4, 128.2, 128.1, 128.0, 127.9, 127.8, 127.8, 127.6 (CH_{arom}), 114.3 (t, *J* = 241.3 Hz, *C*HF_2), 99.1 (C-1), 76.3 (C-3), 75.1 (C-2), 73.9, 73.7, 72.1 (CH_2 Bn), 68.7 (C-6), 68.6 (C-5), 67.7 (t, *J* = 28.9 Hz, *C*H_2CHF_2); Data of the minor stereoisomer (α product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.82 (dd, *J* = 2.9, 1.1 Hz, 1H, H-4), 4.72 (d, *J* = 10.7 Hz, 1H, CH*H* Bn), 4.52-4.46 (signal overlaps with major isomer, 1H, H-1); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 104.3 (C-1), 72.1 (CH_2 Bn); HRMS: $[M+NH_4]^+$ calcd for $C_{36}H_{36}F_2O_7$ 636.27674, found 636.27679.



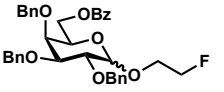
2,2,2-Trifluoroethyl 4-*O*-benzoyl-2,3,6-tri-*O*-benzy-D-galactopyranoside (S90). The title compound was prepared according to general procedure VII. Column chromatography (95:5 → 85:15, pentane:Et_2O) yielded the title compound (51 mg, 79 µmol, 79%, colorless oil, α:β; 97:3). TLC: R_f 0.40 (pentane:Et_2O, 80:20, v:v); IR (thin film, cm^{-1}): 596, 696, 735, 1054, 1267, 1720, 2873, 3032; Data of the major stereoisomer (α product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.43 – 6.88 (m, 20H, CH_{arom}), 5.87 (dd, *J* = 3.4, 1.2 Hz, 1H, H-4), 4.97 (d, *J* = 3.7 Hz, 1H, H-1), 4.85 (d, *J* = 11.1 Hz, 1H, C*H*H Bn), 4.82 (d, *J* = 11.9 Hz, 1H, C*H*H Bn), 4.63 (d, *J* = 12.0 Hz, 1H, CH*H* Bn), 4.58 (d, *J* = 11.1 Hz, 1H, CH*H* Bn), 4.49 (d, *J* = 11.9 Hz, 1H, C*H*H Bn), 4.41 (d, *J* = 11.9 Hz, 1H, CH*H* Bn), 4.19 (td, *J* = 6.3, 1.3 Hz, 1H, H-5), 4.08 (dd, *J* = 10.1, 3.3 Hz, 1H, H-3), 4.00 – 3.91 (m, 3H, H-2, C*H*HCF_3, CH*H*CF_3), 3.60 – 3.46 (m, 2H, H-6, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 165.8 (C=O Bz), 138.4, 138.2, 137.7 ($C_{q\text{-}arom}$), 130.0, 128.5, 128.5, 128.5, 128.4, 128.4, 128.3, 128.1, 128.0, 127.9, 127.9, 127.8, 127.8, 127.2 (CH_{arom}), 123.9z (q, *J* = 278.8 Hz, *C*F_3), 98.7 (C-1), 76.1 (C-3), 75.0 (C-2), 73.7, 73.7, 72.2 (CH_2 Bn), 68.9 (C-5), 68.6 (C-6), 68.5 (C-4), 64.9 (q, *J* = 34.9 Hz, *C*H_2CF_3); Data of the minor stereoisomer (β product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.72 (d, *J* = 3.9 Hz, 1H, H-4), 4.55 (d, *J* = 7.4 Hz, 1H, H-1); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 104.0 (C-1), 75.6, 73.9 (CH_2 Bn); HRMS: $[M+NH_4]^+$ calcd for $C_{36}H_{35}F_3O_7$ 654.26731, found 654.26699.



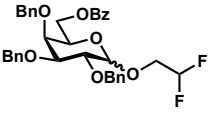
1,1,1,3,3,3-Hexafluoro-2-propyl 4-*O*-benzoyl-2,3,6-tri-*O*-benzyl-α-D-galactopyranoside (S91). The title compound was prepared according to general procedure VII. Column chromatography (100:0 → 85:15, pentane:Et_2O) yielded the title compound (39 mg, 55 µmol, 55%, colorless oil, α:β; >98:2). TLC: R_f 0.20 (pentane:Et_2O, 90:10, v:v); $[\alpha]_D^{25}$ 4.5° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 538, 685, 749, 1101, 1269, 1720, 2850, 3032; ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.55 – 7.03 (m, 20H, CH_{arom}), 5.99 – 5.88 (m, 1H, H-4), 5.22 (d, *J* = 3.8 Hz, 1H, H-1), 4.86 (d, *J* = 10.9 Hz, 1H, C*H*H Bn), 4.78 (d, *J* = 11.8 Hz, 1H, C*H*H Bn), 4.66 (d, *J* = 11.7 Hz, 1H, CH*H* Bn), 4.58 (d, *J* = 10.9 Hz, 1H, CH*H* Bn), 4.53 – 4.46 (m, 2H, C*H*H Bn, C*H*$(CF_3)_2$), 4.41 (d, *J* = 11.9 Hz, 1H, CH*H* Bn), 4.30 (dd, *J* = 7.0, 5.7 Hz, 1H, H-5), 4.09 (dd, *J* = 10.2, 3.2 Hz, 1H, H-3), 3.98 (dd, *J* = 10.2, 3.8 Hz, 1H, H-2), 3.57 – 3.46 (m, 2H, H-6, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 136.7, 133.8 ($C_{q\text{-}arom}$), 130.0, 129.6, 128.9, 128.6, 128.5, 128.5, 128.4, 128.1, 128.1, 127.9, 127.9, 127.8, 127.7, 127.7 (CH_{arom}), 100.2 (C-1), 76.0 (C-3), 74.3 (C-2), 73.9, 73.7, 72.1 (CH_2 Bn), 69.6 (C-5), 68.2 (C-4), 68.2 (C-6); HRMS: $[M+NH_4]^+$ calcd for $C_{37}H_{34}F_6O_7$ 722.25470, found 722.25409.



Ethyl 6-*O*-benzoyl-2,3,4-tri-*O*-benzy-D-galactopyranoside (S92). The title compound was prepared according to general procedure VII. Column chromatography (95:5 → 75:25, pentane:Et_2O) yielded the title compound (51 mg, 88 µmol, 88%, colorless oil, α:β; 15:85). TLC: R_f 0.25 (pentane:Et_2O, 80:20, v:v); IR (thin film, cm^{-1}): 696, 1027, 1070, 1270, 1452, 1720, 2871, 3032; Data of the major stereoisomer (β product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.54 – 7.08 (m, 20H, CH_{arom}), 5.00 (d, *J* = 11.6 Hz, 1H, C*H*H Bn), 4.95 (d, *J* = 10.9 Hz, 1H, C*H*H Bn), 4.84 (d, *J* = 11.7 Hz, 1H, C*H*H Bn), 4.78 (d, *J* = 10.9 Hz, 1H, CH*H* Bn), 4.74 (d, *J* = 11.8 Hz, 1H, CH*H* Bn), 4.70 (d, *J* = 11.6 Hz, 1H, CH*H* Bn), 4.48 (dd, *J* = 11.0, 6.5 Hz, 1H, H-6), 4.39 (d, *J* = 7.7 Hz, 1H, H-1), 4.33 (dd, *J* = 11.0, 6.5 Hz, 1H, H-6), 3.99 (dq, *J* = 9.5, 7.0 Hz, 1H, C*H*HCH$_3$), 3.87 (dd, *J* = 9.7, 7.7 Hz, 1H, H-2), 3.85 (dd, *J* = 2.9, 1.1 Hz, 1H, H-4), 3.67 (td, *J* = 6.5, 1.1 Hz, 1H, H-5), 3.65 – 3.57 (m, 1H, CH*H*CH$_3$), 3.55 (dd, *J* = 9.8, 2.9 Hz, 1H, H-3); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 166.2 (C=O Bz), 138.9, 138.6, 138.4 ($C_{q\text{-}arom}$), 130.0, 128.6, 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 128.2, 127.8, 127.8, 127.7, 127.7, 127.7 (CH_{arom}), 104.0 (C-1), 82.4 (C-3), 79.7 (C-2), 75.3, 74.5, 73.7 (CH_2 Bn), 73.3 (C-4), 72.1 (C-5), 65.7 (*C*H_2CH$_3$), 63.4 (C-6), 15.4 (CH$_3$); Data of the minor stereoisomer (α product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.92 (d, *J* = 11.8 Hz, 1H, C*H*H Bn), 4.86 – 4.81 (signal overlaps with major isomer, 1H, H-1), 4.66 (d, *J* = 11.6 Hz, 1H, CH*H* Bn), 4.26 (dd, *J* = 11.1, 5.7 Hz, 1H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 97.3 (C-1), 74.7, 73.8, 73.6 (CH_2 Bn), 15.1 (*C*H$_3$); HRMS: $[M+NH_4]^+$ calcd for $C_{36}H_{38}O_7$ 600.29558, found 600.29557.

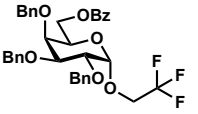


2-Fluoroethyl 6-*O*-benzoyl-2,3,4-tri-*O*-benzy-D-galactopyranoside (S93). The title compound was prepared according to general procedure VII. Column chromatography (95:5 → 60:40, pentane:Et_2O) yielded the title compound (50 mg, 81 µmol, 81%, colorless oil, α:β; 33:67). TLC: R_f 0.20 (pentane:Et_2O, 70:30, v:v); IR (thin film, cm^{-1}): 711, 734, 1026, 1270, 1452, 1720, 2900; Data of the major stereoisomer (β product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.01 – 7.03 (m, 20H, CH_{arom}), 5.00 (d, *J* = 11.7 Hz, 1H, C*H*H Bn), 4.97 (d, *J* = 10.8 Hz, 1H, C*H*H Bn), 4.85 (d, *J* = 11.8 Hz, 1H, C*H*H Bn), 4.80 – 4.55 (m, 5H, CH*H* Bn, CH*H* Bn, CH*H* Bn, C*H*HF, CH*H*F), 4.48 (dd, *J* = 11.1, 6.5 Hz, 1H, H-6), 4.45 (d, *J* = 7.7 Hz, 1H, H-1), 4.31 (dd, *J* = 11.1, 6.4 Hz, 1H, H-6), 3.90 (dd, *J* = 9.8, 7.7 Hz, 1H, H-2), 3.89 – 3.73 (m, 2H, C*H*HCH$_2$F, CH*H*CH$_2$F), 3.85 (dd, *J* = 2.8, 0.8 Hz, 1H, H-4), 3.68 (td, *J* = 6.5, 1.1 Hz, 1H, H-5), 3.56 (dd, *J* = 9.7, 2.9 Hz, 1H, H-3); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 166.2 (C=O Bz), 138.9, 138.7, 138.6, 138.5, 138.3, 138.2 ($C_{q\text{-}arom}$), 130.0, 129.9, 128.6, 128.5, 128.5, 128.5, 128.4, 128.2, 127.9, 127.8, 127.8, 127.7 (CH_{arom}), 104.3 (C-1), 82.8 (d, *J* = 169.7 Hz, *C*H$_2$F), 82.2 (C-3), 79.5 (C-2), 75.4, 74.5, 73.7 (CH_2 Bn), 73.2 (C-4), 72.3 (C-5), 68.9 (d, *J* = 20.2 Hz, *C*H$_2$CH$_2$F), 63.3 (C-6); Data of the minor stereoisomer (α product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.92 (d, *J* = 11.7 Hz, 1H, C*H*H Bn), 4.88 (d, *J* = 3.6 Hz, 1H, H-1), 4.41 (dd, *J* = 11.2, 7.1 Hz, 1H, H-6), 4.25 (dd, *J* = 11.2, 5.5 Hz, 1H, H-6), 4.02 (dd, *J* = 10.1, 2.8 Hz, 1H, H-2), 3.96 (dd, *J* = 2.8, 1.3 Hz, 1H, H-4).; ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 98.1 (C-1), 82.7 (d, *J* = 169.8 Hz, *C*H$_2$F), 76.6 (C-2), 74.8, 73.8, 73.7 (CH_2 Bn), 67.2 (d, *J* = 20.2 Hz, *C*H$_2$CH$_2$F), 64.0 (C-6); HRMS: $[M+NH_4]^+$ calcd for $C_{36}H_{37}FO_7$ 618.28616, found 618.28635.

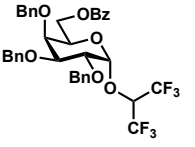


2,2-Difluoroethyl 6-*O*-benzoyl-2,3,4-tri-*O*-benzy-D-galactopyranoside (S94). The title compound was prepared according to general procedure VII. Column chromatography (95:5 → 75:25, pentane:Et_2O) yielded the title compound (50 mg, 81 µmol, 81%, colorless oil, α:β; 61:39). TLC: R_f 0.30 (pentane:Et_2O, 80:20, v:v); IR (thin film, cm^{-1}): 711, 735, 1270, 1452, 1717, 2916, 3032; Data of the major stereoisomer (α product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.47 – 6.72 (m, 20H, CH_{arom}), 5.95 (tt, *J* = 55.4, 4.3 Hz, 1H, C*H*F$_2$), 5.00 (d, *J* = 10.9 Hz, 1H, C*H*H Bn), 4.91 (d, *J* = 11.7 Hz, 1H, C*H*H Bn), 4.85 (d, *J* = 12.1 Hz, 1H, CH*H* Bn), 4.77 (d, *J* = 11.6 Hz, 1H, C*H*H Bn), 4.67 (d, *J* = 12.0 Hz, 1H, CH*H* Bn), 4.65 (d, *J* = 11.4 Hz, 1H, CH*H* Bn), 4.43 (d, *J* = 7.7 Hz, 1H, H-1), 4.41 (dd, *J* = 11.3, 7.3 Hz, 1H, H-6), 4.24 (dd, *J* = 11.3, 5.1

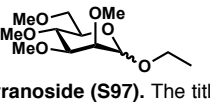
Hz, 1H, H-6), 4.14 – 4.05 (m, 2H, H-2, H-5), 4.00 – 3.94 (m, 2H, H-3, H-4), 3.80 – 3.65 (m, 2H, C*H*HCHF$_2$, CH*H*CHF$_2$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 166.3 (C=O Bz), 138.7, 138.5, 138.4, 138.1 ($C_{q\text{-arom}}$), 129.9, 129.8, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.2, 128.0, 127.9, 127.8, 127.8, 127.8, 127.7 (CH_{arom}), 114.2 (t, *J* = 241.3 Hz *C*HF$_2$), 98.7 (C-1), 78.9 (C-3), 76.4 (C-2), 74.9 (C-4), 74.8, 73.9, 73.8 (CH_2 Bn), 69.2 (C-5), 67.5 (t, *J* = 28.9 Hz, *C*H$_2$CHF$_2$), 64.1 (C-6); Data of the minor stereoisomer (β product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.47 (dd, *J* = 11.2, 6.7 Hz, 1H, H-6), 4.43 (d, *J* = 7.7 Hz, 1H, H-1), 4.32 (dd, *J* = 11.2, 6.1 Hz, 1H, H-6), 3.90 (dd, *J* = 9.7, 7.6 Hz, 1H, H-2), 3.85 (dd, *J* = 2.9, 1.1 Hz, 1H, H-4), 3.56 (dd, *J* = 9.7, 2.8 Hz, 1H, H-3); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 114.4 (dd, *J* = 241.1, 239.3 Hz, *C*HF$_2$), 104.4 (C-1), 82.2 (C-3), 79.3 (C-2), 75.5, 74.6, 73.8 (CH_2 Bn), 73.2 (C-4), 68.8 (dd, *J* = 30.8, 26.5 Hz, *C*H$_2$CHF$_2$), 63.3 (C-6); HRMS: [M+NH$_4$]$^+$ calcd for $C_{36}H_{36}F_2O_7$ 636.27674, found 636.27668.



2,2,2-Trifluoroethyl 3-*O*-benzoyl-2,3,4-tri-*O*-benzy-α-D-galactopyranoside (S95). The title compound was prepared according to general procedure VII. Column chromatography (95:5 → 80:20, pentane:Et$_2$O) yielded the title compound (47 mg, 74 µmol, 74%, colorless oil, α:β; 89:11). TLC: R_f 0.40 (pentane:Et$_2$O, 80:20, v:v); $[\alpha]_D^{25}$ 6.7° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 549, 711, 735, 1026, 1101, 1273, 1452, 1720, 2917, 3030; Data of the major stereoisomer (α product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.34 – 7.02 (m, 20H, CH_{arom}), 5.00 (d, *J* = 11.4 Hz, 1H, C*H*H Bn), 4.91 (d, *J* = 11.4 Hz, 1H, C*H*H Bn), 4.89 (d, *J* = 3.7 Hz, 1H, H-1), 4.84 (d, *J* = 11.9 Hz, 1H, C*H*H Bn), 4.77 (d, *J* = 11.7 Hz, 1H, CH*H* Bn), 4.67 (d, *J* = 11.9 Hz, 1H, CH*H* Bn), 4.65 (d, *J* = 11.4 Hz, 1H, CH*H* Bn), 4.42 (dd, *J* = 11.3, 7.1 Hz, 1H, H-6), 4.24 (dd, *J* = 11.3, 5.4 Hz, 1H, H-6), 4.12 (dd, *J* = 9.8, 3.7 Hz, 1H, H-2), 4.06 (ddd, *J* = 6.8, 5.1, 1.1 Hz, 1H, H-5), 4.02 – 3.94 (m, 2H, H-3, H-4), 3.94 – 3.83 (m, 2H, C*H*HCF$_3$, CH*H*CF$_3$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 166.2 (C=O Bz), 138.7, 138.5, 138.4, 138.1 ($C_{q\text{-arom}}$), 129.8, 129.8, 129.7, 128.6, 128.6, 128.5, 128.5, 128.4, 128.1, 127.9, 127.9, 127.9, 127.7, 127.7, 127.7, 127.2 (CH_{arom}), 123.9 (q, *J* = 278.6 Hz, *C*F$_3$), 98.4 (C-1), 78.7 (C-3), 76.3 (C-2), 74.8 (CH_2 Bn), 74.8 (C-4), 73.9, 73.7 (CH_2 Bn), 64.7 (q, *J* = 34.9 Hz, *C*H$_2$CF$_3$), 63.8 (C-6); Data of the minor stereoisomer (β product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.51 (d, *J* = 7.6 Hz, 1H, H-1), 3.56 (dd, *J* = 9.7, 2.9 Hz, 1H, H-3); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 104.1 (C-1), 75.5, 74.6, 73.8 (CH_2 Bn), 66.0 (q, *J* = 35.0 Hz, CH_2CF_3), 63.2 (C-6); HRMS: [M+NH$_4$]$^+$ calcd for $C_{36}H_{35}F_3O_7$ 654.26731, found 654.26715.

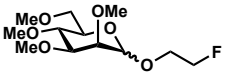


1,1,1,3,3,3-Hexafluoro-2-propyl 6-*O*-benzoyl-2,3,4-tri-*O*-benzyl-α-D-galactopyranoside (S96). The title compound was prepared according to general procedure VII. Column chromatography (100:0 → 85:15, pentane:Et$_2$O) yielded the title compound (40 mg, 57 µmol, 57%, colorless oil, α:β; >98:2). TLC: R_f 0.15 (pentane:Et$_2$O, 90:10, v:v); $[\alpha]_D^{25}$ –47.0° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 538, 595, 697, 1027, 1104, 1196, 1274, 1452, 1720, 2924, 3032; ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.07 – 7.03 (m, 20H, CH_{arom}), 5.21 (d, *J* = 3.8 Hz, 1H, H-1), 5.00 (d, *J* = 11.3 Hz, 1H, C*H*H Bn), 4.91 (d, *J* = 11.5 Hz, 1H, C*H*H Bn), 4.79 – 4.69 (m, 3H, C*H*H Bn, CH*H* Bn, CH*H* Bn), 4.65 (d, *J* = 11.3 Hz, 1H, CH*H* Bn), 4.47 (dt, *J* = 11.9, 5.9 Hz, 1H, C*H*(CF$_3$)$_2$), 4.42 (dd, *J* = 11.4, 7.2 Hz, 1H, H-6), 4.25 (dd, *J* = 11.5, 4.9 Hz, 1H, H-6), 4.21 – 4.15 (m, 2H, H-2, H-5), 4.01 (t, *J* = 1.9 Hz, 1H, H-4), 3.99 (dd, *J* = 10.0, 2.7 Hz, 1H, H-2); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 166.2 (C=O Bz), 138.5, 138.0 ($C_{q\text{-arom}}$), 129.7, 129.6, 128.9, 128.6, 128.6, 128.5, 128.1, 128.0, 127.7, 127.6 (CH_{arom}), 99.8 (C-1), 78.3 (C-3), 75.4 (C-2), 74.9 (CH_2 Bn), 74.7 (C-4), 73.8, 73.7 (CH_2 Bn), 70.5 (C-5), 64.0 (C-6); HRMS: [M+NH$_4$]$^+$ calcd for $C_{37}H_{34}F_6O_7$ 722.25470, found 722.25408.

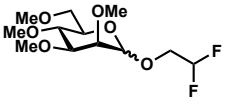


Ethyl 2,3,4,6-tetra-*O*-methyl-D-mannopyranoside (S97). The title compound was prepared according to general procedure VII. Column chromatography (80:20 → 70:30, pentane:EtOAc) yielded the title

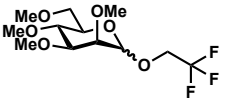
compound (18.2 mg, 69 µmol, 69%, colorless oil, α:β; 51:49). TLC: R_f 0.30, (pentane:EtOAc, 60:40, v:v); IR (thin film, cm^{-1}): 926, 1069, 1110, 1377, 2973; Data of the major stereoisomer (α product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.92 (d, *J* = 1.6 Hz, 1H, H-1), 3.79 – 3.71 (m, 1H, C*H*H Et), 3.70 – 3.46 (m, 18H, H-2, H-3, H-4, H-5, 2x H-6, CH*H* Et, 3x CH_3 Me), 3.40 (s, 3H, CH_3 Me), 1.22 – 1.18 (m, 3H, CH_3 Et); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 96.6 (C-1), 81.3 (C-3), 77.4, 77.1 (C-2/C-4), 71.9 (C-6), 71.3 (C-5), 63.1 (CH_2 Et), 60.9, 59.4, 59.3, 57.8 (CH_3 Me), 15.1 (CH_3 Et); ^{13}C-HMBC-GATED NMR (101 MHz, $CDCl_3$): δ 96.6 ($J_{H1\text{-}C1}$ = 167 Hz, α); Data of the minor stereoisomer (β product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.39 (d, *J* = 0.8 Hz, 1H, H-1), 3.99 (dq, *J* = 9.4, 7.1 Hz, 1H, C*H*H Et), 3.64 (s, 3H, CH_3 Me), 3.19 (dd, *J* = 8.9, 3.2 Hz, 1H, H-3), 1.26 – 1.22 (m, 3H, CH_3 Et); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 101.3 (C-1), 84.2 (C-3), 72.2 (C-6), 65.3 (CH_2 Et), 15.2 (CH_3 Et); ^{13}C-HMBC-GATED NMR (101 MHz, $CDCl_3$): δ 101.3 ($J_{H1\text{-}C1}$ = 154 Hz, β) ; HRMS: $[M+NH_4]^+$ calcd for $C_{13}H_{28}NO_7$ 282.19111, found 282.19093.



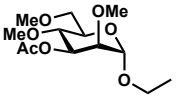
2-Fluoroethyl 2,3,4,6-tetra-*O*-methyl-D-mannopyranoside (S98). The title compound was prepared according to general procedure VII. Column chromatography (70:30 → 60:40, pentane:EtOAc) yielded the title compound (21 mg, 74 µmol, 74%, colorless oil, α:β; 64:36). TLC: R_f 0.21, (pentane:EtOAc, 60:40, v:v); IR (thin film, cm^{-1}): 730, 912, 1083, 1110, 2898; Data of the major stereoisomer (α product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.96 (d, *J* = 1.8 Hz, 1H, H-1), 4.63 (dd, *J* = 4.9, 3.4 Hz, 1H, CH_2CHHF), 4.51 (dd, *J* = 4.8, 3.5 Hz, 1H, CH_2CHHF), 3.97 – 3.82 (m, 1H, C*H*HCH_2F), 3.81 – 3.67 (m, 2H, H-4, CH*H*CH_2F), 3.64 – 3.61 (m, 1H, H-2), 3.60 – 3.58 (m, 3H, H-5, 2x H-6), 3.58 – 3.53 (m, 1H, H-3), 3.53 (s, 3H, CH_3 Me) 3.51 (s, 3H, CH_3 Me), 3.49 (s, 3H, CH_3 Me), 3.40 (s, 3H, CH_3 Me); ^{13}C NMR (101 MHz, $CDCl_3$): δ 97.2 (C-1), 82.6 (d, *J* = 169.6 Hz, CH_2CH_2F), 81.2 (C-3), 77.1 (C-2), 76.5 (C-4), 71.8 (C-6), 71.5 (C-5), 66.7 (d, *J* = 19.7 Hz, CH_2CH_2F), 60.8, 59.4, 59.1, 57.9 (CH_3 Me); ^{13}C-HMBC-GATED NMR (101 MHz, $CDCl_3$): δ 97.2 ($J_{H1\text{-}C1}$ = 169 Hz, α); Data of the minor stereoisomer (β product): ^{1}H NMR (400 MHz, $CDCl_3$ HH-COSY, HSQC): δ 4.46 (d, *J* = 0.8 Hz, 1H, H-1), 4.10 (dddd, *J* = 36.7, 12.2, 3.7, 2.3 Hz, 1H, C*H*HCH_2F), 3.65 (s, 3H, CH_3 Me), 3.52 (s, 3H, CH_3 Me), 3.50 (s, 2H, CH_3 Me), 3.39 (s, 3H, CH_3 Me), 3.20 (dd, *J* = 8.9, 3.2 Hz, 1H, H-3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 101.6 (C-1), 83.0 (d, *J* = 169.1 Hz, CH_2CH_2F), 82.2 (C-3), 68.7 (d, *J* = 19.6 Hz, CH_2CH_2F) 61.9, 60.9, 59.4, 57.5 (4x CH_3 Me); ^{13}C-HMBC-GATED NMR (101 MHz, $CDCl_3$): δ 101.6 ($J_{H1\text{-}C1}$ = 155 Hz, β); HRMS: $[M+NH_4]^+$ calcd for $C_{13}H_{27}NO_7F$ 300.18169, found 300.18153.



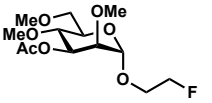
2,2-Difluoroethyl 2,3,4,6-tetra-*O*-methyl-D-mannopyranoside (S99). The title compound was prepared according to general procedure VII. Column chromatography (85:15 → 75:25, pentane:EtOAc) yielded the title compound (15.5 mg, 52 µmol, 52%, colorless oil, α:β; 76:24). TLC: R_f 0.35, (pentane:EtOAc, 60:40, v:v); IR (thin film, cm^{-1}): 730, 909, 1072, 1111; Data of the major stereoisomer (α product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.92 (tdd, *J* = 55.3, 4.8, 3.4 Hz, 1H, CH_2CHF_2), 4.95 (d, *J* = 1.9 Hz, 1H, H-1), 3.90 – 3.64 (m, 2H, CH_2CHF_2), 3.63 – 3.57 (m, 5H, H-2, H-3, H-5, 2x H-6), 3.52 (s, 3H, CH_3 Me), 3.51 (s, 3H, CH_3 Me), 3.50 – 3.47 (m, 4H, H-4, CH_3 Me), 3.40 (s, 3H, CH_3 Me); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 117.5 – 110.0 (m, CH_2CHF_2), 97.9 (C-1), 81.0 (C-4), 76.8, 76.3 (C-2/C-3), 71.9 (C-5), 71.7 (C-6), 66.8 (t, J = 28.0 Hz, CH_2CHF_2), 60.8, 59.4, 59.2, 58.0 (CH_3 Me): ^{13}C-HMBC-GATED NMR (101 MHz, $CDCl_3$): δ 97.9 ($J_{H1\text{-}C1}$ = 170 Hz, α); Data of the minor stereoisomer (β product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 6.10 – 5.76 (m, 1H, CH_2CHF_2), 4.46 (d, *J* = 0.8 Hz, 1H, H-1), 4.06 (dddd, *J* = 22.5, 11.7, 9.9, 2.7 Hz, 1H, C*H*HCHF_2), 3.50 (s, 3H, CH_3 Me), 3.19 (dd, *J* = 9.1, 3.1 Hz, 1H, H-3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 101.8 (C-1), 83.9 (C-3), 68.8 – 68.0 (m, CH_2CHF_2), 61.9, 60.9, 59.4, 57.7 (4x CH_3 Me); ^{13}C-HMBC-GATED NMR (101 MHz, $CDCl_3$): δ 101.8 ($J_{H1\text{-}C1}$ = 156 Hz, β); HRMS: $[M+Na]^+$ calcd for $C_{13}H_{22}NaO_7F_2$ 323.12767, found 323.12723.



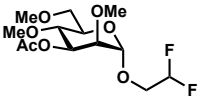
2,2,2-Trifluoroethyl 2,3,4,6-tetra-*O*-methyl-D-mannopyranoside (S100). The title compound was prepared according to general procedure VII. Column chromatography (85:15 pentane:EtOAc) yielded the title compound (18 mg, 57 µmol, 57%, colorless oil, α:β; 93:7). TLC: R_f 0.40, (pentane:EtOAc, 60:40, v:v); IR (thin film, cm^{-1}): 732, 985, 1081, 1164, 1280; Data of the major stereoisomer (α product): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.99 (d, *J* = 1.8 Hz, 1H, H-1), 4.04 – 3.94 (m, 1H, C*H*HCF$_3$), 3.94 – 3.84 (m, 1H, CH*H*CF$_3$), 3.66 – 3.62 (m, 1H, H-2), 3.63 – 3.53 (m, 3H, H-5, H-6, H-6), 3.53 (s, 3H, CH_3 Me), 3.52 (s, 3H, CH_3 Me), 3.51 – 3.45 (m, 5H, H-2, H-4, CH_3 Me), 3.40 (s, 3H, CH_3 Me); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 123.9 (q, *J* = 278.2 Hz, CH_2CF_3), 97.7 (C-1), 80.9 (C-4), 76.8 (C-2), 76.2 (C-3), 72.2 (C-5), 71.6 (C-6), 64.2 (q, *J* = 34.8 Hz, CH_2CF_3), 60.8, 59.4, 59.3, 58.1 (CH_3 Me); HMBC-GATED NMR (101 MHz, $CDCl_3$): δ 97.7 ($J_{H1\text{-}C1}$ = 170 Hz, α); Data of the minor stereoisomer (β product): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.52 (s, 1H, H-1), 4.21 (dq, *J* = 12.6, 8.9 Hz, 1H, C*H*HCF$_3$), 3.76 (dd, *J* = 3.1, 0.8 Hz, 1H, H-2), 3.19 (dd, *J* = 9.1, 3.2 Hz, 1H, H-3) ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 101.4 (C-1), 61.9, 59.4, 57.7 (3x CH_3 Me); HRMS: $[M+Na]^+$ calcd for $C_{13}H_{21}NaO_7F_3$ 341.11824, found 341.11811.



Ethyl 3-*O*-acetyl-2,4,6-tri-*O*-methyl-α-D-mannopyranoside (S101). The title compound was prepared according to general procedure VII. Column chromatography (85:15 → 75:25, pentane:EtOAc) yielded the title compound (19.1 mg, 65 µmol, 65%, colorless oil, α:β; >98:2). TLC: R_f 0.29, (pentane:EtOAc, 60:40, v:v); $[\alpha]_D^{25}$ 69.0° (*c* 0.10 $CHCl_3$); IR (thin film, cm^{-1}): 730, 909,1067, 1101, 1238, 1733; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.17 (dd, *J* = 9.5, 3.4 Hz, 1H, H-3), 4.87 (d, *J* = 1.9 Hz, 1H, H-1), 3.75 (dt, *J* = 9.8, 7.1 Hz, 1H, C*H*H Et), 3.71 – 3.66 (m, 1H, H-6), 3.64 – 3.56 (m, 4H, H-2, H-4, H-5 ,CH*H* Et), 3.52 – 3.47 (m, 1H, H-6), 3.46 (s, 3H, CH_3 Me), 3.44 (s, 3H, CH_3 Me), 3.41 (s, 3H, CH_3 Me), 2.15 (s, 3H, CH_3 Ac), 1.20 (t, *J* = 7.1 Hz, 3H, CH_3 Et); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 170.5 (C=O), 97.0 (C-1), 78.7 (C-2), 74.9 (C-4), 74.0 (C-3), 71.5 (CH_2 Et), 71.1 (C-5), 63.3 (C-6), 60.5, 59.4, 59.3 (CH_3 Me), 21.4 (CH_3 Ac), 15.1 (CH_3 Et); HMBC-GATED NMR (101 MHz, $CDCl_3$): δ 97.0 ($J_{H1\text{-}C1}$ = 169 Hz, α); HRMS: $[M+Na]^+$ calcd for $C_{13}H_{24}NaO_7$ 315.14142, found 315.14126.

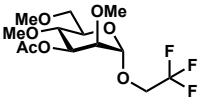


2-Fluoroethyl 3-*O*-acetyl-2,4,6-tri-*O*-methyl-α-D-mannopyranoside (S102). The title compound was prepared according to general procedure VII. Column chromatography (80:20 → 60:40, pentane:EtOAc) yielded the title compound (24.7 mg, 80 µmol, 80%, colorless oil, α:β; >98:2). TLC: R_f 0.23, (pentane:EtOAc, 60:40, v:v); $[\alpha]_D^{25}$ 52.4° (*c* 0.29 $CHCl_3$); IR (thin film, cm^{-1}): 1047, 1101, 1123, 1238, 1369, 1739; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.17 (dd, *J* = 9.5, 3.4 Hz, 1H, H-3), 4.92 (d, *J* = 1.9 Hz, 1H, H-1), 4.65 – 4.60 (m, 1H, CH_2CHHF), 4.54 – 4.48 (m, 1H, CH_2CHHF), 3.97 – 3.82 (m, 1H, C*H*HCH$_2$F), 3.81 – 3.69 (m, 2H, H-6, CH*H*CH$_2$F), 3.68 – 3.56 (m, 4H, H-2, H-4, H-5, H-6), 3.46 (s, 3H, CH_3 Me), 3.44 (s, 3H, CH_3 Me), 3.41 (s, 3H, CH_3 Me), 2.15 (s, 3H, CH_3 Ac); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 170.4 (C=O), 97.6 (C-1) 82.6 (d, *J* = 169.9 Hz, CH_2CH_2F), 78.4 (H-2), 74.7 (C-4), 73.7 (C-3), 71.4 (C-6), 71.3 (C-5), 66.8 (d, *J* = 20.0 Hz, CH_2CH_2F), 60.5, 59.4, 59.4 (CH_3 Me), 21.4 (CH_3 Ac); HMBC-GATED NMR (101 MHz, $CDCl_3$): δ 97.6 ($J_{H1\text{-}C1}$ = 170 Hz, α); HRMS: $[M+Na]^+$ calcd for $C_{13}H_{23}NaO_7F$ 333.13200, found 333.13176.



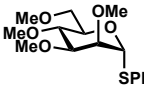
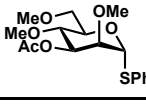
2,2-Difluoroethyl 3-*O*-acetyl-2,4,6-tri-*O*-methyl-α-D-mannopyranoside (S103). The title compound was prepared according to general procedure VII. Column chromatography (90:10 → 75:25, pentane:EtOAc)

yielded the title compound (18.6 mg, 57 µmol, 57%, colorless oil, α:β; >98:2). TLC: R_f 0.35, (pentane:EtOAc, 60:40, v:v); $[\alpha]_D^{25}$ 59.3° (*c* 0.14 $CHCl_3$); IR (thin film, cm^{-1}): 731, 909, 1070, 1100, 1240, 1739; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.93 (tdd, *J* = 55.4, 4.8, 3.6 Hz, 1H, CH_2CHF_2), 5.12 (dd, *J* = 8.9, 3.3 Hz, 1H, H-3), 4.91 (d, *J* = 2.0 Hz, 1H, H-1), 3.90 – 3.78 (m, 1H, $CHHCHF_2$), 3.78 – 3.70 (m, 1H, $CHHCHF_2$), 3.69 – 3.57 (m, 5H, H-2, H-4, H-5, H-6, H-6), 3.46 (s, 3H, CH_3 Me), 3.44 (s, 3H, CH_3 Me), 3.41 (s, 3H, CH_3 Me), 2.15 (s, 3H, CH_3 Ac) ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 170.4 (C=O), 114.1 (t, *J* = 241.1 Hz, CH_2CHF_2), 98.2 (C-1), 78.1 (C-2), 74.6 (C-4), 73.5 (C-3), 71.7 (C-5), 71.3 (C-6), 66.9 (t, *J* = 28.6 Hz, CH_2CHF_2), 60.5, 59.5, 59.4 (CH_3 Me), 21.3 (CH_3 Ac); HMBC-GATED NMR (101 MHz, $CDCl_3$): δ 98.2 ($J_{H1\text{-}C1}$ = 170 Hz, α); HRMS: $[M+Na]^+$ calcd for $C_{13}H_{22}NaO_7F_2$ 351.12258, found 351.12233.



2,2,2-Trifluoroethyl 3-*O*-acetyl-2,4,6-tri-*O*-methyl-α-D-mannopyranoside (S104). The title compound was prepared according to general procedure VII. Column chromatography (85:15, pentane:EtOAc) yielded the title compound (15.5 mg, 45 µmol, 45%, colorless oil, α:β; >98:2). TLC: R_f 0.39, (pentane:EtOAc, 60:40, v:v); $[\alpha]_D^{25}$ 59.0° (*c* 0.5 $CHCl_3$); IR (thin film, cm^{-1}): 730, 910, 1083, 1103, 1238, 1745, 2933; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, $HSC_{q\text{-}arom}$): δ 5.17 – 5.11 (m, 1H, H-3), 4.95 (d, *J* = 2.1 Hz, 1H, H-1), 3.95 (qq, *J* = 12.4, 8.6 Hz, 2H, CH_2CF_3), 3.69 (dd, *J* = 3.4, 2.1 Hz, 1H, H-2), 3.67 – 3.63 (m, 2H, H-4, H-5), 3.63 – 3.56 (m, 2H, H-6, H-6), 3.47 (s, 3H, CH_3 Me), 3.45 (s, 3H, CH_3 Me), 3.41 (s, 3H, CH_3 Me), 2.15 (s, 3H, CH_3 Ac); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 170.4 (C=O), 98.1 (C-1), 77.9 (C-2), 74.5 (C-4), 73.2 (C-3), 71.9 (C-5), 71.2 (C-6), 64.3 (q, *J* = 35.0 Hz, CH_2CF_3), 60.5, 59.6, 59.4 (CH_3 Me), 21.3 (CH_3 Ac); HMBC-GATED NMR (101 MHz, $CDCl_3$): δ 98.1 ($J_{H1\text{-}C1}$ = 170 Hz, α); HRMS: $[M+Na]^+$ calcd for $C_{13}H_{21}NaO_7F_3$ 369.11316, found 369.11324.

Table S1. Experimentally found stereoselectivity for glycosylation reactions for Ac-Me-protected donors with model acceptors. The stereoselectivity is expressed as α:β ratios and were established by ^1H-NMR spectroscopy of the crude and purified reaction mixtures.

Entry	donor	HO–CF_3	HO–CH(F)–CHF$_2$	HO–CH$_2$–CH$_2$F	HO–Et
1		93:7 (57%)	76:24 (52%)	64:36 (74%)	51:49 (69%)
2		>98:2 (45%)	>98:2 (57%)	>98:2 (80%)	>98:2 (65%)

>90:10	>80:20	>60:40	>50:50	<50:50	<40:60	<20:80	<10:90	(α:β)

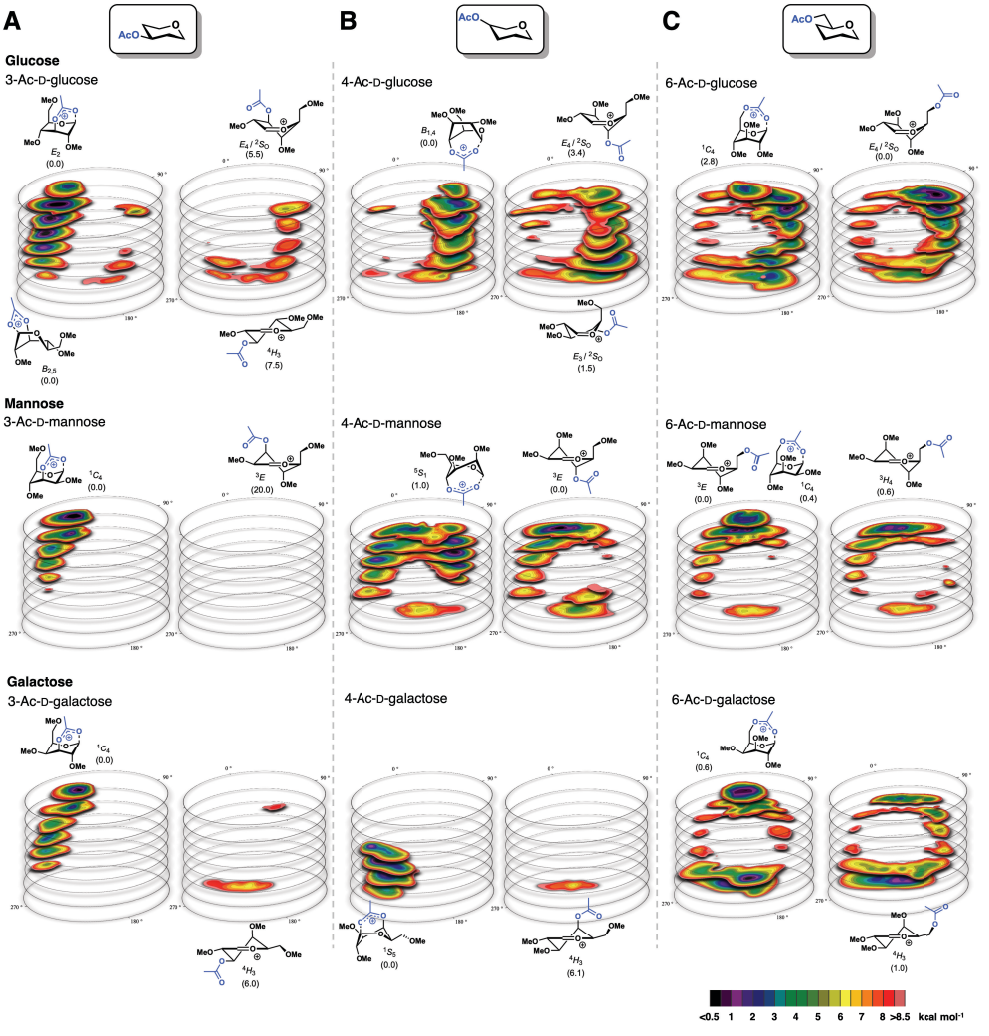


Figure S14. Gas-phase CEL maps of selected pyranosyl oxocarbenium ions in which the found local minima are shown and indicated with their respective energy. Two acetyl ester rotamers (R1 = left and R2 = right) were considered for all computed oxocarbenium ions generating two CEL maps. All energies are as calculated in the gas-phase at B3LYP/6-311G(d,p) at *T*=293.15 K and expressed as Gibbs free energy. (A) CEL maps for the C3-acetyl pyranosyl ions; (B) CEL maps for the C4-acetyl pyranosyl ions; (C) CEL maps for the C6-acetyl pyranosyl ions.

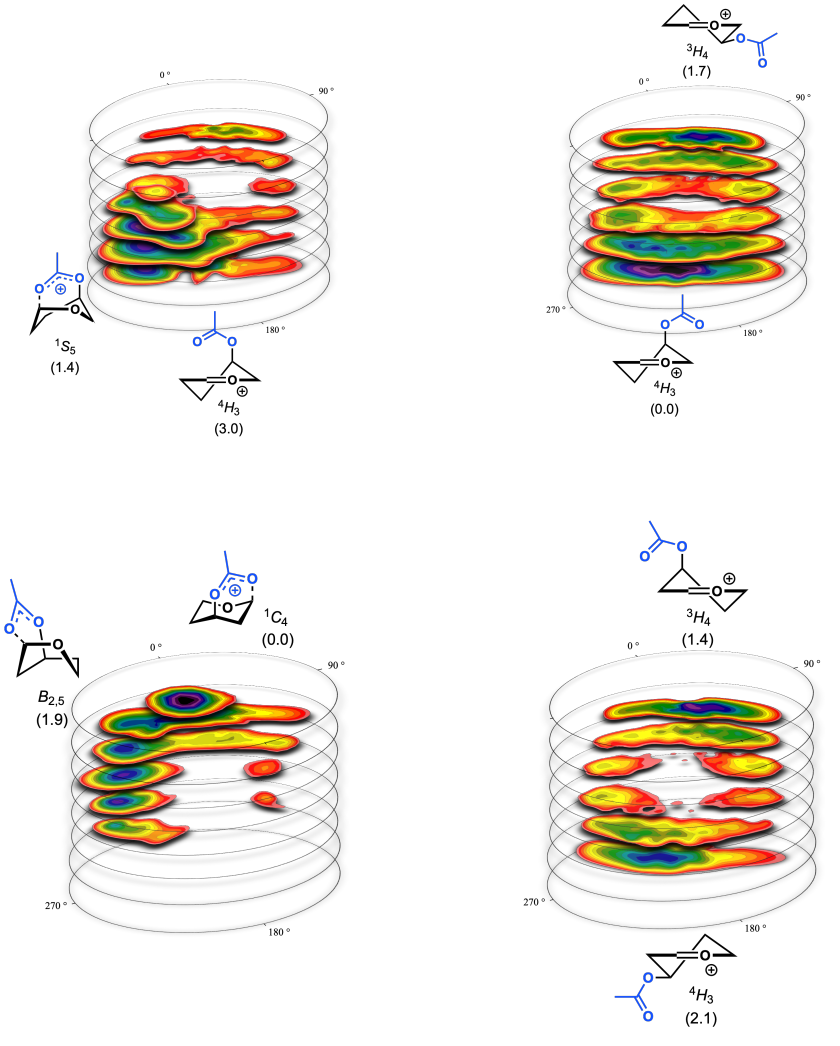


Figure S15. CEL maps of **S105** and **S106**. Two acetyl ester rotamers (R1 = left and R2 = right) were considered for all computed oxocarbenium ions generating two CEL maps. All energies are as calculated in the gas-phase at B3LYP/6-311G(d,p) at *T*=293.15 K and expressed as Gibbs free energy.

References

(1) Leng, W.-L.; Yao, H.; He, J.-X.; Liu, X.-W. Venturing beyond Donor-Controlled Glycosylation: New Perspectives toward Anomeric Selectivity. *Acc. Chem. Res.* **2018**, *51* (3), 628–639.

(2) Zhu, X.; Schmidt, R. R. New Principles for Glycoside-Bond Formation. *Angew. Chem. Int. Ed.* **2009**, *48* (11), 1900–1934.

(3) Nigudkar, S. S.; Demchenko, A. V. Stereocontrolled 1,2-*Cis* Glycosylation as the Driving Force of Progress in Synthetic Carbohydrate Chemistry. *Chem. Sci.* **2015**, *6* (5), 2687–2704.

(4) Bohé, L.; Crich, D. A Propos of Glycosyl Cations and the Mechanism of Chemical Glycosylation; the Current State of the Art. *Carbohydr. Res.* **2015**, *403*, 48–59.

(5) Crich, D.; Li, M. Revisiting the Armed−Disarmed Concept: The Importance of Anomeric Configuration in the Activation of *S*-Benzoxazolyl Glycosides. *Org. Lett.* **2007**, *9* (21), 4115–4118.

(6) Poulsen, L. T.; Heuckendorff, M.; Jensen, H. H. Effect of 2-*O*-Benzoyl Para-Substituents on Glycosylation Rates. *ACS Omega* **2018**, *3* (6), 7117–7123.

(7) Pittman, C. U.; McManus, S. P.; Larsen, J. W. 1,3-Dioxolan-2-Ylium and Related Heterocyclic Cations. *Chem. Rev.* **1972**, *72* (4), 357–438.

(8) Plante, O. J.; Palmacci, E. R.; Seeberger, P. H. Automated Solid-Phase Synthesis of Oligosaccharides. *Science* **2001**, *291* (5508), 1523–1527.

(9) Wu, Y.; Xiong, D.-C.; Chen, S.-C.; Wang, Y.-S.; Ye, X.-S. Total Synthesis of Mycobacterial Arabinogalactan Containing 92 Monosaccharide Units. *Nat. Commun.* **2017**, *8* (1), 1–7.

(10) Cheng, Y.-P.; Chen, H.-T.; Lin, C.-C. A Convenient and Highly Stereoselective Approach for α-Galactosylation Performed by Galactopyranosyl Dibenzyl Phosphite with Remote Participating Groups. *Tet. Lett.* **2002**, *43* (43).

(11) Baek, J. Y.; Lee, B.-Y.; Jo, M. G.; Kim, K. S. β-Directing Effect of Electron-Withdrawing Groups at *O*-3, *O*-4, and *O*-6 Positions and α-Directing Effect by Remote Participation of 3-*O*-Acyl and 6-*O*-Acetyl Groups of Donors in Mannopyranosylations. *J. Am. Chem. Soc.* **2009**, *131* (48), 17705–17713.

(12) Crich, D.; Vinod, A. U.; Picione, J. The 3,4-*O*-Carbonate Protecting Group as a β-Directing Group in Rhamnopyranosylation in Both Homogeneous and Heterogeneous Glycosylations As Compared to the Chameleon-like 2,3-*O*-Carbonates. *J. Org. Chem.* **2003**, *68* (22), 8453–8458.

(13) Lei, J.-C.; Ruan, Y.-X.; Luo, S.; Yang, J.-S. Stereodirecting Effect of C3-Ester Groups on the Glycosylation Stereochemistry of L-Rhamnopyranose Thioglycoside Donors: Stereoselective Synthesis of α- and β-L-Rhamnopyranosides. *Eur. J. Org. Chem.* **2019**, *2019* (37), 6377–6382.

(14) Demchenko, A. V.; Rousson, E.; Boons, G.-J. Stereoselective 1,2-*Cis*-Galactosylation Assisted by Remote Neighboring Group Participation and Solvent Effects. *Tet. Lett.* **1999**, *40* (36), 6523–6526.

(15) Baek, J. Y.; Kwon, H.-W.; Myung, S. J.; Park, J. J.; Kim, M. Y.; Rathwell, D. C. K.; Jeon, H. B.; Seeberger, P. H.; Kim, K. S. Directing Effect by Remote Electron-Withdrawing Protecting Groups at *O*-3 or *O*-4 Position of Donors in Glucosylations and Galactosylations. *Tetrahedron* **2015**, *71* (33), 5315–5320.

(16) Ayala, L.; Lucero, C. G.; Romero, J. A. C.; Tabacco, S. A.; Woerpel, K. A. Stereochemistry of Nucleophilic Substitution Reactions Depending upon Substituent: Evidence for Electrostatic Stabilization of Pseudoaxial Conformers of Oxocarbenium Ions by Heteroatom Substituents. *J. Am. Chem. Soc.* **2003**, *125* (50), 15521–15528.

(17) Ma, Y.; Lian, G.; Li, Y.; Yu, B. Identification of 3,6-Di-*O*-Acetyl-1,2,4-*O*-Orthoacetyl-α-D-Glucopyranose as a Direct Evidence for the 4-*O*-Acyl Group Participation in Glycosylation. *Chem. Commun.* **2011**, *47* (26), 7515–7517.

(18) Komarova, B. S.; Orekhova, M. V.; Tsvetkov, Y. E.; Nifantiev, N. E. Is an Acyl Group at *O*-3 in Glucosyl Donors Able to Control α-Stereoselectivity of Glycosylation? The Role of Conformational Mobility and the Protecting Group at *O*-6. *Carbohydr. Res.* **2014**, *384*, 70–86.

(19) Frechet, J. M.; Schuerch, C. Solid-Phase Synthesis of Oligosaccharides. II. Steric Control by *C*-6 Substituents in Glucoside Syntheses. *J. Am. Chem. Soc.* **1972**, *94* (2), 604–609.

(20) Dejter-Juszynski, M.; Flowers, H. M. Studies on the Koenigs-Knorr Reaction: Part IV: The Effect of Participating Groups on the Stereochemistry of Disaccharide Formation. *Carbohydr. Res.* **1973**, *28* (1), 61–74.

(21) Tokimoto, H.; Fujimoto, Y.; Fukase, K.; Kusumoto, S. Stereoselective Glycosylation Using the Long-Range Effect of a [2-(4-Phenylbenzyl)Oxycarbonyl]Benzoyl Group. *Tet. Asym.* **2005**, *16* (2), 441–447.

(22) Meo, C. D.; Kamat, M. N.; Demchenko, A. V. Remote Participation-Assisted Synthesis of β-Mannosides. *Eur. J. Org. Chem.* **2005**, *2005* (4), 706–711.

(23) Hagen, B.; Ali, S.; Overkleeft, H. S.; van der Marel, G. A.; Codée, J. D. C. Mapping the Reactivity and Selectivity of 2-Azidofucosyl Donors for the Assembly of *N*-Acetylfucosamine-Containing Bacterial Oligosaccharides. *J. Org. Chem.* **2017**, *82* (2), 848–868.

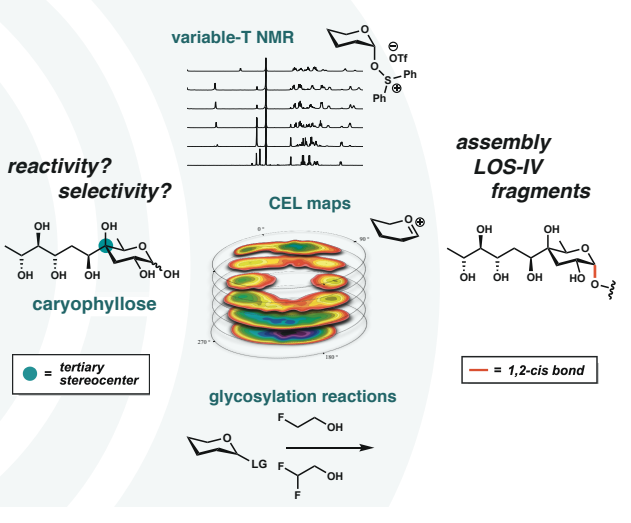
(24) Crich, D.; Hu, T.; Cai, F. Does Neighboring Group Participation by Non-Vicinal Esters Play a Role in Glycosylation Reactions? Effective Probes for the Detection of Bridging Intermediates. *J. Org. Chem.* **2008**, *73* (22), 8942–8953.

(25) Paulsen, H.; Trautwein, W.-P.; Espinosa, F. G.; Heyns, K. Darstellung stabiler 1,2-acetoxonium-salze acetylierter hexosen und pentosen. *Tet. Lett.* **1966**, *7* (34), 4131–4135.
(26) Crich, D.; Dai, Z.; Gastaldi, S. On the Role of Neighboring Group Participation and Ortho Esters in β-Xylosylation: ^{13}C NMR Observation of a Bridging 2-Phenyl-1,3-Dioxalenium Ion. *J. Org. Chem.* **1999**, *64* (14), 5224–5229.
(27) Martin, A.; Arda, A.; Désiré, J.; Martin-Mingot, A.; Probst, N.; Sinaÿ, P.; Jiménez-Barbero, J.; Thibaudeau, S.; Blériot, Y. Catching Elusive Glycosyl Cations in a Condensed Phase with HF/SbF_5 Superacid. *Nat. Chem.* **2016**, *8* (2), 186–191.
(28) Lebedel, L.; Ardá, A.; Martin, A.; Désiré, J.; Mingot, A.; Aufiero, M.; Aiguabella Font, N.; Gilmour, R.; Jiménez-Barbero, J.; Blériot, Y.; Thibaudeau, S. Structural and Computational Analysis of 2-Halogeno-Glycosyl Cations in the Presence of a Superacid: An Expansive Platform. *Angew. Chem. Int. Ed.* **2019**, *58* (39), 13758–13762.
(29) Hansen, T.; Lebedel, L.; Remmerswaal, W. A.; van der Vorm, S.; Wander, D. P. A.; Somers, M.; Overkleeft, H. S.; Filippov, D. V.; Désiré, J.; Mingot, A.; Bleriot, Y.; van der Marel, G. A.; Thibaudeau, S.; Codée, J. D. C. Defining the S_N1 Side of Glycosylation Reactions: Stereoselectivity of Glycopyranosyl Cations. *ACS Cent. Sci.* **2019**, *5* (5), 781–788.
(30) Frihed, T. G.; Bols, M.; Pedersen, C. M. Mechanisms of Glycosylation Reactions Studied by Low-Temperature Nuclear Magnetic Resonance. *Chem. Rev.* **2015**, *115* (11), 4963–5013.
(31) Mucha, E.; Marianski, M.; Xu, F.-F.; Thomas, D. A.; Meijer, G.; von Helden, G.; Seeberger, P. H.; Pagel, K. Unravelling the Structure of Glycosyl Cations via Cold-Ion Infrared Spectroscopy. *Nat. Commun.* **2018**, *9* (1), 1–5.
(32) Elferink, H.; Severijnen, M. E.; Martens, J.; Mensink, R. A.; Berden, G.; Oomens, J.; Rutjes, F. P. J. T.; Rijs, A. M.; Boltje, T. J. Direct Experimental Characterization of Glycosyl Cations by Infrared Ion Spectroscopy. *J. Am. Chem. Soc.* **2018**, *140* (19), 6034–6038.
(33) Elferink, H.; Mensink, R. A.; Castelijns, W. W. A.; Jansen, O.; Bruekers, J. P. J.; Martens, J.; Oomens, J.; Rijs, A. M.; Boltje, T. J. The Glycosylation Mechanisms of 6,3-Uronic Acid Lactones. *Angew. Chem. Int. Ed.* **2019**, *58* (26), 8746–8751.
(34) Marianski, M.; Mucha, E.; Greis, K.; Moon, S.; Pardo, A.; Kirschbaum, C.; Thomas, D. A.; Meijer, G.; Helden, G. von; Gilmore, K.; Seeberger, P. H.; Pagel, K. Remote Participation during Glycosylation Reactions of Galactose Building Blocks: Direct Evidence from Cryogenic Vibrational Spectroscopy. *Angew. Chem. Int. Ed.* **2020**, *59* (15), 6166–6171.
(35) Zhang, Z.; Ollmann, I. R.; Ye, X.-S.; Wischnat, R.; Baasov, T.; Wong, C.-H. Programmable One-Pot Oligosaccharide Synthesis. *J. Am. Chem. Soc.* **1999**, *121* (4), 734–753.
(36) Chang, C.-W.; Wu, C.-H.; Lin, M.-H.; Liao, P.-H.; Chang, C.-C.; Chuang, H.-H.; Lin, S.-C.; Lam, S.; Verma, V. P.; Hsu, C.-P.; Wang, C.-C. Establishment of Guidelines for the Control of Glycosylation Reactions and Intermediates by Quantitative Assessment of Reactivity. *Angew. Chem. Int. Edition* **2019**, *58* (47), 16775–16779.
(37) Martens, J.; Berden, G.; Gebhardt, C. R.; Oomens, J. Infrared Ion Spectroscopy in a Modified Quadrupole Ion Trap Mass Spectrometer at the FELIX Free Electron Laser Laboratory. *Rev. Sci. Instrum.* **2016**, *87* (10), 103108.
(38) Rijs, A.; Oomens, J. *Gas-Phase IR Spectroscopy and Structure of Biological Molecules*. Topics in Current Chemistry; Springer International Publishing, **2015**.
(39) Madern, J. M.; Hansen, T.; van Rijssel, E. R.; Kistemaker, H. A. V.; van der Vorm, S.; Overkleeft, H. S.; van der Marel, G. A.; Filippov, D. V.; Codée, J. D. C. Synthesis, Reactivity, and Stereoselectivity of 4-Thiofuranosides. *J. Org. Chem.* **2019**, *84* (3), 1218–1227.
(40) van der Vorm, S.; Hansen, T.; van Rijssel, E. R.; Dekkers, R.; Madern, J. M.; Overkleeft, H. S.; Filippov, D. V.; van der Marel, G. A.; Codée, J. D. C. Furanosyl Oxocarbenium Ion Conformational Energy Landscape Maps as a Tool to Study the Glycosylation Stereoselectivity of 2-Azidofuranoses, 2-Fluorofuranoses and Methyl Furanosyl Uronates. *Chem. Eur. J.* **2019**, *25* (29), 7149–7157.
(41) van Rijssel, E. R.; van Delft, P.; Lodder, G.; Overkleeft, H. S.; van der Marel, G. A.; Filippov, D. V.; Codée, J. D. C. Furanosyl Oxocarbenium Ion Stability and Stereoselectivity. *Angew. Chem. Int. Ed.* **2014**, *53* (39), 10381–10385.
(42) Vorm, S. van der; Hansen, T.; Overkleeft, H. S.; Marel, G. A. van der; Codée, J. D. C. The Influence of Acceptor Nucleophilicity on the Glycosylation Reaction Mechanism. *Chem. Sci.* **2017**, *8* (3), 1867–1875.
(43) Vorm, S. van der; Hansen, T.; Hengst, J. M. A. van; S. Overkleeft, H.; Marel, G. A. van der; C. Codée, J. D. Acceptor Reactivity in Glycosylation Reactions. *Chem. Soc. Rev.* **2019**, *48* (17), 4688–4706.
(44) Codée, J. D. C.; Litjens, R. E. J. N.; den Heeten, R.; Overkleeft, H. S.; van Boom, J. H.; van der Marel, G. A. Ph_2SO/Tf_2O: A Powerful Promotor System in Chemoselective Glycosylations Using Thioglycosides. *Org. Lett.* **2003**, *5* (9), 1519–1522.
(45) Liu, H.; Hansen, T.; Zhou, S.-Y.; Wen, G.-E.; Liu, X.-X.; Zhang, Q.-J.; Codée, J. D. C.; Schmidt, R. R.; Sun, J.-S. Dual-Participation Protecting Group Solves the Anomeric Stereocontrol Problems in Glycosylation Reactions. *Org. Lett.* **2019**, *21* (21), 8713–8717.

(46) Hahm, H. S.; Hurevich, M.; Seeberger, P. H. Automated Assembly of Oligosaccharides Containing Multiple *Cis*-Glycosidic Linkages. *Nat. Commun.* **2016**, *7* (1), 1–8.
(47) van Outersterp, R. E.; Houthuijs, K. J.; Berden, G.; Engelke, U. F.; Kluijtmans, L. A. J.; Wevers, R. A.; Coene, K. L. M.; Oomens, J.; Martens, J. Reference-Standard Free Metabolite Identification Using Infrared Ion Spectroscopy. *Int. J. Mass. Spectrom.* **2019**, *443*, 77–85.
(48) Landrum, G. (**2006**). RDKit: Open-Source Cheminformatics.
(49) Tosco, P.; Stiefl, N.; Landrum, G. Bringing the MMFF Force Field to the RDKit: Implementation and Validation. *J. Cheminformatics* **2014**, *6* (1), 37.
(50) Ebejer, J.-P.; Morris, G. M.; Deane, C. M. Freely Available Conformer Generation Methods: How Good Are They? *J. Chem. Inf. Model.* **2012**, *52* (5), 1146–1158.
(51) Gaussian 16, Revision A.03, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. V. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. J. Bearpark, J. J. Heyd, E. N. Brothers, K. N. Kudin, V. N. Staroverov, T. A. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. P. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman, and D. J. Fox, *Gaussian, Inc.*, Wallingford CT, **2016**.
(52) Gaussian 09, Revision D.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, *Gaussian, Inc.*, Wallingford CT, **2013**.
(53) Ribeiro, R. F.; Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. Use of Solution-Phase Vibrational Frequencies in Continuum Models for the Free Energy of Solvation. *J. Phys. Chem. B* **2011**, *115* (49), 14556–14562.
(54) Legault, C.Y.; CYLview, 1.0b, Université de Sherbrooke, **2009** (www.cylview.org).
(55) Gómez, A. M.; Casillas, M.; Barrio, A.; Gawel, A.; López, J. C. Synthesis of Pyranoid and Furanoid Glycals from Glycosyl Sulfoxides by Treatment with Organolithium Reagents. *Eur. J. Org. Chem.* **2008**, *2008* (23), 3933–3942.
(56) Chaube, M. A.; Sarpe, V. A.; Jana, S.; Kulkarni, S. S. First Total Synthesis of Trehalose Containing Tetrasaccharides from Mycobacterium Smegmatis. *Org. Biomol. Chem.* **2016**, *14* (24), 5595–5598.
(57) Pozsgay, V. Large Scale Synthesis of 2-Azidodeoxy Glucosyl Donors. *J. Carbohydr. Chem.* **2001**, *20* (7–8), 659–665.
(58) Deng, S.; Gangadharmath, U.; Chang, C.-W. T. Sonochemistry: A Powerful Way of Enhancing the Efficiency of Carbohydrate Synthesis. *J. Org. Chem.* **2006**, *71* (14), 5179–5185.
(59) Blom, P.; Ruttens, B.; Van Hoof, S.; Hubrecht, I.; Van der Eycken, J.; Sas, B.; Van hemel, J.; Vandenkerckhove, J. A Convergent Ring-Closing Metathesis Approach to Carbohydrate-Based Macrolides with Potential Antibiotic Activity. *J. Org. Chem.* **2005**, *70* (24), 10109–10112.
(60) Uriel, C.; Ventura, J.; Gómez, A. M.; López, J. C.; Fraser-Reid, B. Methyl 1,2-Orthoesters as Useful Glycosyl Donors in Glycosylation Reactions: A Comparison with *n*-Pent-4-Enyl 1,2-Orthoesters. *Eur. J. Org. Chem.* **2012**, *2012* (16), 3122–3131.

Chapter 5

Reactivity-Stereoselectivity Mapping for the Assembly of *Mycobacterium Marinum* Lipooligosaccharides



Abstract | The assembly of complex bacterial glycans presenting rare structural motifs and cis-glycosidic linkages is significantly obstructed by the lack of knowledge of the reactivity of the constituting building blocks and the stereoselectivity of the reactions in which they partake. We here report a strategy to map the reactivity of carbohydrate building blocks and apply it to understand the reactivity of the bacterial sugars, caryophyllose, a rare C12-monosaccharide, containing a characteristic tetrasubstituted stereocenter. We mapped reactivity-stereoselectivity relationships for caryophyllose donor and acceptor glycosides, by a systematic series of glycosylations in combination with the detection and characterization of different reactive intermediates using experimental and computational techniques. The insights garnered from these studies enabled the rational design of building blocks with the required properties to assemble Mycobacterial lipooligosaccharide fragments of *M. marinum*.

Published | Hansen, T.[‡]; Ofman, T. P.[‡]; Vlaming, J.G.C.[‡]; Gagarinov, I.; van Beek, J.; Goté, T. A.; Tichem, J. A.; Ruijgrok, G., Overkleeft, H. S.; Filippov, D. V.; van der Marel, G. A.; Codée, J. C. D. *Angewandte Chemie International Edition*, **2020**, *Accepted*.

Introduction

The bacterial glycan repertoire is equally vast and diverse.[1–5] As opposed to the mammalian carbohydrate biosynthesis machinery that employs a limited set of 9 monosaccharides[6] to build oligosaccharides and glycoconjugates, the bacterial biomachinery can introduce a wide variety of substitution patterns.[1–5] Bacterial monosaccharides can feature diversely substituted amino groups, deoxy centers, carbonyl groups, and tetrasubstituted tertiary carbon atoms at various positions on the carbohydrate ring. Tertiary-*C* sugars can be found in various natural products, having attractive biological properties.[7–10] They are part of the structure of erythromycin, gentamicin, vancomycin, saccharomicin, and anthracyclines.

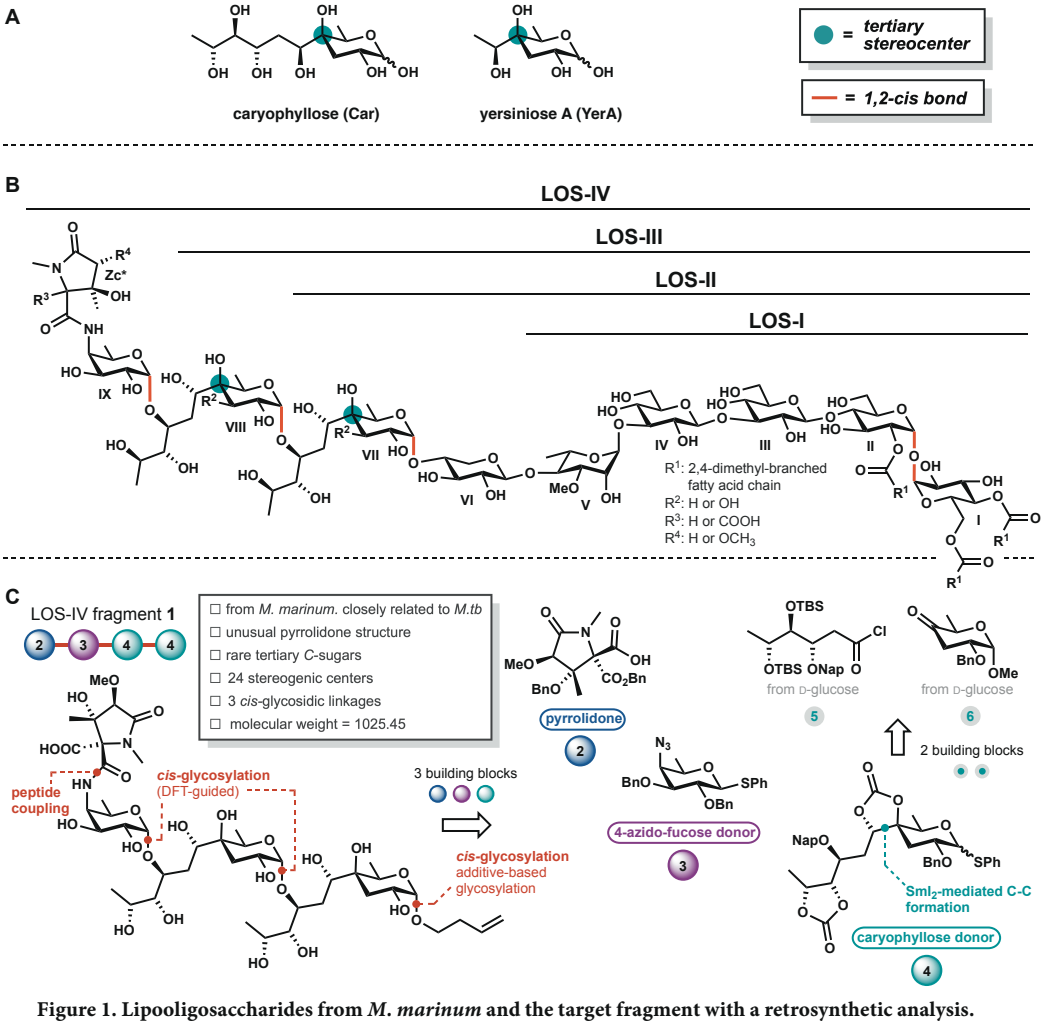


Figure 1. Lipooligosaccharides from *M. marinum* and the target fragment with a retrosynthetic analysis. (A) Tertiary *C*-sugar caryophyllose (Car) found in mycobacterial lipooligosaccharides and the related smaller yersiniose A (YerA); (B) LOS-IV, LOS-III, LOS-II and LOS-I from *M. marinum*. with numbering introduced by Rombouts *et al.*;[11-13] (C) Retrosynthetic analysis for LOS-IV fragment **1**.

Often these tertiary *C*-atoms are substituted with a small alkyl group, commonly a methyl substituent, but more complex architectures in which functionalized alkyl chains are attached can be found as well. For example, the tertiary *C*-sugar caryophyllose (Car, see Figure 1A) is found in mycobacterial lipooligosaccharides (LOSs).[11–13] This unique structure bears a hydroxylated C6-chain at the tetrasubstituted tertiary C4-atom.

The mycobacterial LOSs are major constituents of the thick and waxy cell wall of mycobacteria.[11–16] Being at the host-pathogen interface, they play an important role in the interaction with the immune system. Because it is exceedingly laborious to purify these lipophilic compounds from the bacterial cell wall, it has proven difficult to establish the precise role of these glycolipids in shaping an immune response. In addition, the LOS-structures contain subtle structural variations, making it even more difficult to establish structure-activity-relationships (SAR) at the molecular level. *Mycobacterium marinum* is a waterborne pathogen that is most closely related to *Mycobacterium tuberculosis*, and causes tuberculosis-like infections. As such it is often used as a surrogate to study host-pathogen interactions involved in *Mt.b* infections. *M. marinum* produces four LOS structures (LOS-I–IV; Figure 1B), which all share an acylated trehalose core functionalized with species-specific glycans. The LOS-II, LOS-III, and LOS-IV structures of *M. marinum* contain several unusual carbohydrate monosaccharides, including the tertiary *C*-sugar caryophyllose as well as an *N*-acylated 4-amino-4-deoxy-D-fucose (FucNAc).[11–13,17–19] Structural variation in the LOS structures of *M. marinum* has been found. The caryophyllose can be hydroxylated at the C3 position (R^2), and the terminal pyrrolidone structure can vary on two positions of the ring, with structures having a carboxylate and a methylether at R^3 and R^4, respectively, being the most prevalent pyrrolidone. LOS structures have been implicated in multiple processes involved in the pathogenesis of *M. marinum* and it has been shown that the mutants expressing truncated LOS-structures (LOS-I) are less virulent and can be cleared more easily by the immune system.[12] The complex carbohydrates of the higher LOS-structures thus seem to play an important role in immune evasion although the exact mode of action of these remains ill-understood.

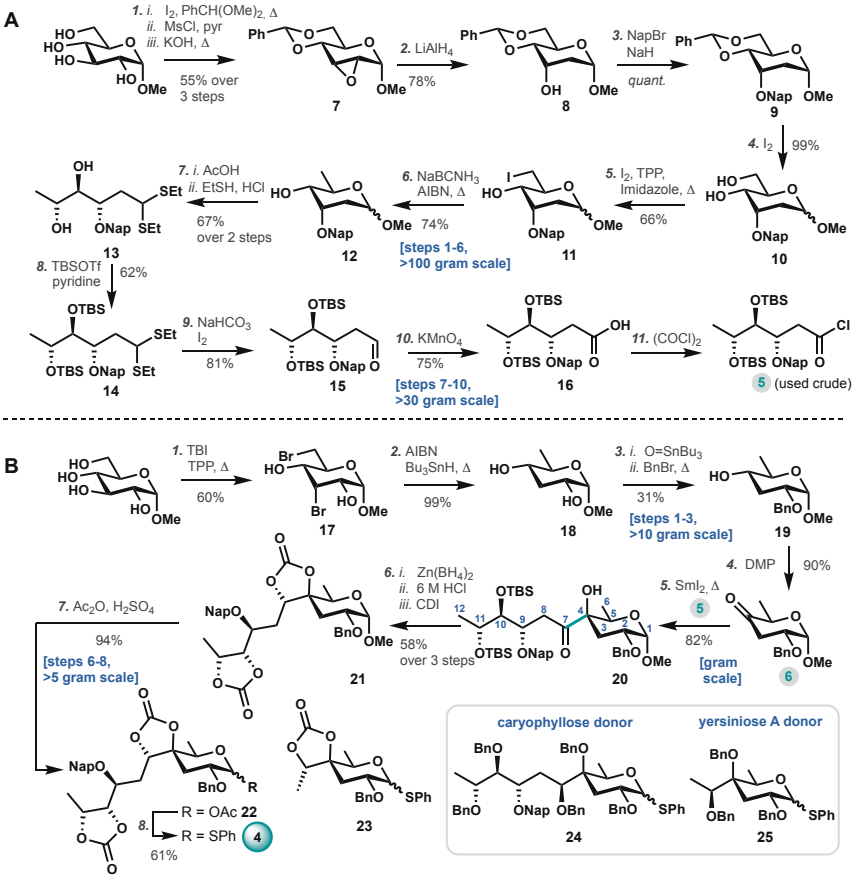
The compelling bioactivity, intriguing structural features, and the fact that well-defined pure LOS structures cannot be obtained from natural sources in sufficient amounts for biological studies was an incentive to develop synthetic chemistry to attain these complex structures to generate probes for SAR-studies. Although great progress has been made in oligosaccharide synthesis, the assembly of bacterial glycans presenting rare structural modifications and challenging *cis*-glycosidic linkages still presents a major obstacle as the reactivity of the required building blocks is not well understood.[20–33] This chapter reports an approach to map the reactivity-stereoselectivity relationships for the tertiary *C*-sugar caryophyllose and its truncated counterpart yersiniose A (YerA; Figure 1A). This in turn has allowed to effectively construct the Car-Car-FucNAc LOS-IV fragment **1** (Figure 1C), and related shorter fragments, equipped with an alkene spacer for future conjugation purposes. The approach taken to understand the reactivity and stereoselectivity of these rare and challenging bacterial monosaccharides hinges on the detection and

characterization of different reactive intermediates using experimental and computational techniques. These combined studies have enabled the rational design of building blocks with the desired reactivity and selectivity to assemble the spacer equipped Car-Car-NAcFuc LOS-IV fragment **1** with complete stereoselectivity. The disclosed intrinsic reactivity of tertiary-*C* Car donors can act as a prototype for related tertiary-*C* sugars, thereby fueling ensuing biological research.

Results and discussion

The Car-Car-FucNAc carbohydrate **1** (Figure 1C) was assembled from the three key monomeric building blocks, pyrrolidone **2**, 4-amino-4-deoxy-D-fucose **3** and caryophyllose **4** (Figure 1C). The design of the latter building block was based on reactivity studies, as outlined below. Pyrrolidone **2** can be synthesized based on the work of the Lowary group from D-serine and the 4-azido-fucose donor **3** can be made from D-glucose by deoxygenation of C6 and an inversion of the C4 position, following established procedures.[34] Car donor **4** can be synthesized from building blocks **5** and **6** by a SmI_2-mediated C-C bond formation, as originally described by Prandi and co-workers.[35,36]

Our first goal was the generation of sufficient amounts of the Car donor glycosides, required to map the reactivity of these building blocks and build the target LOS fragment **1**. To this end acid chloride **5** and 2,6-dideoxy-4-keto-glucose **6** were assembled. The synthesis of **5** is depicted in Scheme 1A and started from methyl-α-D-glucopyranose. Epoxide **7** was readily prepared in three steps, which could easily be performed on >150 gram scale. Regioselective opening of the epoxide with $LiAlH_4$ afforded digitoxose-configured **8** in good yield (78%, >120 gram scale). Installation of the temporary 2-methylnaphthyl protecting group, which can be removed at a later stage to afford the appropriate acceptor glycoside, was achieved using standard Williamson etherification conditions resulting in fully protected **9**. The 4,6-*O*-benzylidene protecting group was removed using a catalytic amount of I_2 to yield diol **10** (99%), and the primary alcohol was converted into iodide **11** with an Appel reaction using triphenylphosphine, iodide and imidazole. Radical reduction using $NaBCNH_3$ and AIBN yielded the partially protected D-digitoxose **12** (74%, >100 gram scale). Hydrolysis of D-digitoxose **12** with 25% v:v aq. AcOH under reflux conditions, followed by the treatment with an excess of ethanethiol and concentrated HCl afforded the linear diethyl dithioacetal **13** (67% over two steps, 50 gram scale). Subsequently, both hydroxyl functions of the dithioacetal were protected with a TBS group using TBSOTf and pyridine to yield the fully protected dithioacetal **14** (62%).



Scheme 1. Synthesis of **4**, **5**, **6**, **23**, **24**, and **25**. (A) Synthesis of building block **5**. *Reagents and conditions:* (1) *i.* benzaldehyde dimethyl acetal, I_2, CH_3CN; *ii.* MsCl, pyridine; *iii.* KOH, THF/MeOH (55% over three steps); (2) $LiAlH_4$, Et_2O (78%); (3) NapBr, NaH, DMF (*quant.*); (4) I_2, MeOH (99%); (5) imidazole, triphenylphosphine, I_2, toluene, 75 °C (66%); (6) $NaBCNH_3$, AIBN, *t*-BuOH, 80 °C (74%); (7) *i.* aq. 25% AcOH, reflux; *ii.* EtSH, aq. 37% HCl (67% over 2 steps); (8) TBSOTf, pyridine, DCM (62%); (9) I_2, $NaHCO_3$, acetone, H_2O (81%); (10) $KMnO_4$ aq., NaH_2PO_4 aq., *t*-BuOH (75%); (11) $(COCl)_2$, pyridine (B) Synthesis of building block **6** following by SmI_2-mediated coupling reactions to generate donor **4** and **23**. *Reagents and conditions:* (1) tribromoimidazole, triphenylphosphine, toluene, reflux (60%); (2) AIBN, Bu_3SnH, toluene, reflux (99%); (3) *i.* tributyltin oxide, toluene, reflux; *ii.* benzyl bromide, reflux (31%); (4) DMP, DCM (91%); (5); SmI_2, **5**, THF, 50 °C, 15 min (82%); (6) *i.* $Zn(BH_4)_2$, THF; *ii.* 6 M HCl, MeOH; *iii.* CDI, DCM (58% over three steps); (7) Ac_2O, H_2SO_4, 1 min (94%); (8) thiophenol, $BF_3{\cdot}OEt_2$, DCM (61%).

Treating dithioacetal **14** with I_2 and $NaHCO_3$ in acetone/water delivered the corresponding aldehyde **15** in 81% yield (30 gram scale). Oxidation with buffered potassium permanganate in *t*-BuOH/water of aldehyde **15** furnished the protected acid **16** (75%), which could be easily converted to building block **5** by pyridine and oxalyl chloride.

As depicted in Scheme 1B building block **6** was also synthesized from methyl-α-D-glucopyranoside, starting with a regioselective bromination of the C3- and C6-position using tribromoimidazole in good yield (60%, >30 gram scale). Removal of the bromides

through a radical reduction with tributyltin hydride and AIBN afforded the required dideoxy glucoside **18** in excellent yield (99%, 15 gram scale). The reaction of **18** with tributyltin oxide, followed by benzyl bromide provided the benzylated glucoside **19** in 31% yield. Oxidation of the C4-alcohol in **19** with Dess-Martin periodinane then afforded key building block **6** (90%).

To build the tertiary *C*-sugar having the required Car-configuration, a SmI_2-promoted C-C bond coupling was employed using acyl chloride **5** and ketone **6** (Scheme 1B).[35,36] The best yield for this cross-coupling was obtained by premixing both coupling partners and quickly adding them, by canula, to a warm (50 °C) solution of SmI_2 in THF under completely inert atmosphere. This procedure reliably delivered ketone **20** with the required stereochemistry at C4 in 82% yield (gram scale). A chelation controlled reduction of ketone **20** with $Zn(BH_4)_2$ in THF then afforded free alcohol. After removal of the silyl protection groups using acidic conditions and protection of the two vicinal diols using carbonyldiimidazole afforded caryophyllose **21** in 58% (over three steps, 15 gram scale). Proof for the stereochemistry of the C7 position was obtained by NOESY NMR experiments showing strong NOE interactions between $H3_{eq}$-H7 and H6-H8 for **21** (see SI). The anomeric methoxy group of caryophyllose **21** was then converted to an acetyl group using H_2SO_4 in acetic anhydride. A short reaction time (80 seconds) proved crucial to maintain the C9-methylnaphthyl protecting group. The anomeric acetate **22** was formed in excellent yield (94%, >5 gram scale) and subsequently transformed into the key caryophyllose thioglycoside **4** under the aegis of thiophenol and $BF_3{\cdot}OEt_2$. Following a highly similar route the per-*O*-Bn caryophyllose thioglycoside **24** was constructed (see SI). Additionally, yersiniose A (YerA) donors **23** and **25** were assembled, to be used as model donors to map the reactivity-selectivity of these type of donors (see SI).

With all donors in hand, the glycosylation properties of the building blocks could be studied under pre-activation conditions (Figure 2A). To do so, first the possible reactive intermediates that can play a role during the glycosylation of these donors were investigated. Covalent species, such as anomeric triflates are formed, which can undergo a S_N2-like substitution or serve as a reservoir for more reactive oxocarbenium ion type species that partake in substitution reactions with more S_N1-character. The investigation started with the detection of the formation of reactive covalent species by the use of variable-T NMR. Per-*O*-benzyl donor **24** was first tested. To this end a mixture of **24** and Ph_2SO (1.3 eq.) in CD_2Cl_2 was treated with Tf_2O (1.3 eq.) at −80 °C (Figure 2B).[37] Directly after the addition, NMR data (^1H, HSQC, COSY) were recorded, to reveal the generation of a single new species.

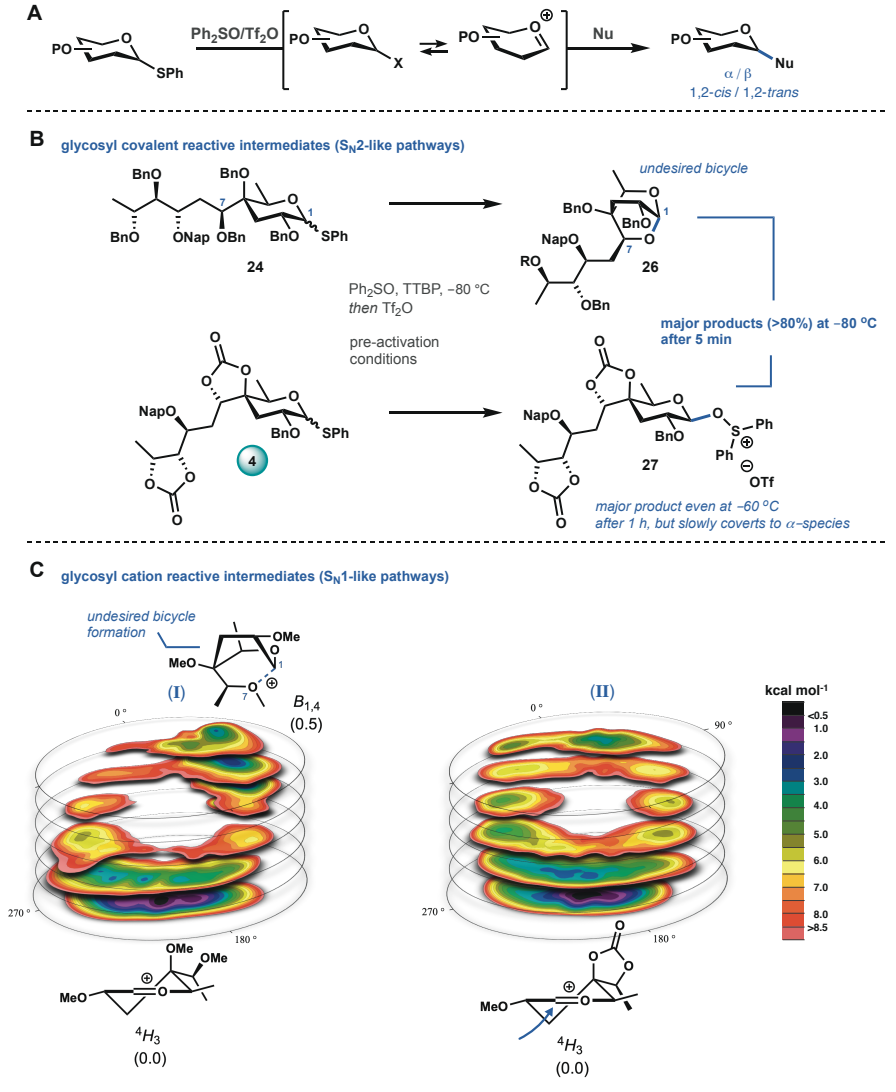


Figure 2. Mapping the relevant reactive intermediates by a combined experimental and computational approach. (A) The reaction mechanism continuum operational during glycosylation reactions. Glycosylation reactions are best considered as taking place at a continuum between two formal extremes of the mechanisms, including the S_N1 and S_N2 mechanism; (B) Upon activation with Ph_2SO/Tf_2O of donor **24**, the undesired fused bicycle **26** was formed. This side reaction makes these per-*O*-benzylated caryophyllose donors unsuitable for efficient glycosylation reactions; (C) Conformational energy landscape (CEL) maps of selected pyranosyl oxocarbenium ions in which the found local minima are indicated with their respective energy. All energies are as computed at PCM(CH_2Cl_2)-B3LYP/6-311G(d,p) at T=213.15 K and expressed as solution-phase Gibbs free energy.

The signals of the anomeric H and C atoms appeared at δ 4.7 ppm and δ 90.4 ppm for ^{1}H and ^{13}C respectively, which is significantly upfield from signals corresponding to an anomeric triflate or oxosulfonium triflate species (*i.e.*, generally found at ^{1}H: δ ~5-6.5 ppm and ^{13}C: δ ~105-110 ppm).[38–42] Warming the sample did not lead to the degradation of the

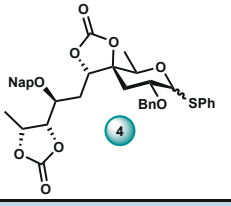
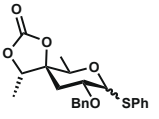
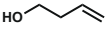
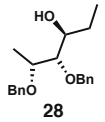
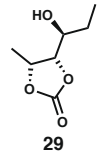
initially formed product, and therefore it could be isolated. NMR analysis (^{1}H, ^{13}C, HSQC, COSY, NOESY and HMBC) identified the formed species to be bicyclic compound **26**. Similarly, upon activation of the structurally simpler yersiniose donor **25**, a corresponding bicycle was formed. These bicycles are formed by nucleophilic attack of the oxygen atom in the C7 benzyl ether on the activated C1 position. Cyclization reactions on activated glycosyl donors have been reported before (*e.g.*, from a C6-OBn to form a 1,6-anhydrosugar), but the rate with which the caryophyllose/yersiniose cyclization takes place is striking. Apparently, the architecture in these systems is intrinsically geared for this intramolecular nucleophilic cyclization. To prevent this cyclization, the C7-OH was tethered to the C4-hydoxyl by the use of a carbonate protection group. Activation of the thus obtained donor **4**, using the conditions described above, resulted in the formation of several species, amongst which the anomeric β-oxosulfonium triflate **27** species (^{1}H: δ 5.8 ppm; ^{13}C: δ 107.6 ppm) as the dominant reactive intermediate (±80% based on ^{1}H-NMR). To support that this is indeed the oxosulfonium triflate, more Ph_2SO (+1.7 eq.) was added after the activation, which led to the increase of the oxosulfonium signals and the disappearance of the signals corresponding to the anomeric triflate. Upon slow warming of the mixture, this species gradually converted into the anomeric α-triflate and α-oxosulfonium triflate species (see SI Figure S2-S8 for all variable-T NMR spectra).

To study the reactive intermediates on the other side of the reaction mechanism continuum, the caryophyllose and yersiniose oxocarbenium ions were subjected to DFT computations. As explained in Chapter 2, a DFT protocol was developed to compute the relative energy of all possible glycopyranosyl oxocarbenium ion conformers, filling the complete conformational space these ions can occupy generating conformational energy landscape (CEL) maps.[43–45] Based on these CEL maps, a prediction can be made on the stereochemical preference of the glycosyl cations. Figure 2C shows the CEL maps of the two yersiniose oxocarbenium ions (these were selected as the substituted C6-chain of caryophyllose would demand a significant increase in computing cost). The lowest energy structures are shown next to the CEL maps with their corresponding energy (with the lowest energy depicted in black/purple). The CEL map of oxocarbenium ion **I** (Figure 2C, left) shows that this species preferentially takes up a $^{4}H_3$ conformation. A second local minimum was found on the other side of the CEL map, revealing the $B_{1,4}$ conformer to be only slightly higher in energy ($\Delta G_{CH_2Cl_2}$ = 0.5 kcal mol^{-1}). This latter conformer explains the rapid formation of the bicycles found upon activation of donors **24** and **25** as the C7 ether is perfectly positioned to attack the C1 position in this cation. The CEL map of oxocarbenium ion **II** (Figure 2C, right) reveals a single minimal energy conformer. This $^{4}H_3$ conformer is preferentially attacked from the diastereotopic face that leads to a chair-like transition state, and thus based on this analysis this cation is predicted to serve as a 1,2-*cis*-selective glycosylating species.

Next, donors **4** and **23** were probed for their stereoselectivity in glycosylation (Table 1). To this end, a matrix of glycosylation reactions was performed with a set of model alcohol

nucleophiles of gradually decreasing nucleophilicity.[46,47] The trends observed relate to changes from an S_N2-type substitution reaction of the covalent intermediate for the most nucleophilic alcohols (*i.e.*, EtOH and MFE), to reactions involving more oxocarbenium character (for the poorest nucleophiles; *i.e.*, TFE, HFIP and TES-*d*). The glycosylation reactions were performed under pre-activation conditions using diphenyl sulfoxide (Ph_2SO)/triflic anhydride (Tf_2O) as the activator.[37]

Table 1. Experimentally found stereoselectivities for model glycosylation reactions with ethanol, 2-fluoroethanol, 2,2-difluoroethanol, 2,2,2-trifluoroethanol, 1,1,1,3,3,3-hexafluoro-2-propanol, triethylsilane-*d*, 1-buten-4-ol, **28** and **29**. The stereoselectivity of the reaction is expressed as 1,2-*cis*:1,2-*trans* and based on the ^{1}H-NMR spectroscopy. Experimental conditions: pre-activation based glycosylation conditions; Ph_2SO (1.3 eq.), TTBP (2.5 eq.), DCM (0.05 M), *then* Tf_2O (1.3 eq.), *then* nucleophile (2 eq.), –80 °C to –60 °C.

	 **4**	 **23**
	67:33 (94%)	50:50 (60%)
	83:17 (100%)	66:34 (76%)
	87:13 (63%)	80:20 (100%)
	>98:2 (76%)	>98:2 (77%)
	>98:2 (16%)	>98:2 (28%)
	*donor hydrolysis*	>98:2 (54%)
	63:37 (97%)	59:41 (86%)
 **28**	77:23 (50%)	61:39 (63%)
 **29**	>98:2 (54%)	>98:2 (74%)

>90:10	>80:20	>60:40	>50:50	<50:50	<40:60	<20:80	<10:90	(1,2-*cis*:1,2-*trans*)

The outcome of the glycosylation reactions for both the caryophyllose and yersiniose donor show clear trends with changing nucleophilicity of the used acceptors. The caryophyllose donor **4** and yersiniose donor **23** behave very similarly and with decreasing nucleophilicity the 1,2-*cis*-selectivity increases for both systems. Even with strong nucleophiles, somewhat more of the 1,2-*cis*-product is formed, which may be explained by the direct displacement of the β-oxosulfonium triflate **27** species. The increasing 1,2-*cis* selectivity can be accounted for by an increase of S_N1 character in the glycosylation reaction, as the weaker nucleophiles require a more electrophilic glycosylating agent. The CEL maps revealed the $^4H_3$ oxocarbenium ion conformers to be most stable and a stereoselective addition to these ions can explain the formation of the α-products. To test the nucleophiles relevant for the assembly of LOS IV-fragment **1**, three acceptors (*i.e.*, 1-buten-4-ol, **28**, and **29**) were probed. Acceptor **28** and **29** represent truncated versions of the caryophyllose acceptor, and 1-buten-4-ol will be used to serve as a conjugation-ready linker moiety. Acceptor **28** is protected with benzyl groups, known to be electronically neutral (*i.e.*, nor electron-withdrawing, nor electron-donating), while **29** is protected with an electron-withdrawing carbonate group. The difference in reactivity between these two acceptors is mirrored in the stereoselectivity of the glycosylation reactions with donors **4** and **23**, with the more nucleophilic dibenzylated alcohol **28** providing an α/β-mixture, while the less nucleophilic alcohol **29**, bearing the cyclic carbonate protecting group, exclusively formed the 1,2-*cis*-products. These results indicate the need for an electron-withdrawing protecting group on the caryophyllose building block, when employed as an acceptor. The cyclic carbonate spanning hydroxyl groups at C10 and C11 in the synthesized caryophyllose building blocks thus serves this purpose.

After having established the glycosylation properties of the designed donors, the construction of the target Car-Car-FucNAc LOS-IV fragment **1** from building blocks **2**, **3** and **4** was undertaken (Figure 3A). Because of the high reactivity of 3-butene-1-ol, modifying the reactivity of the reactive intermediates formed upon activation of the donor glycoside was required. To this end, an additive mediated glycosylation strategy was used. Various strategies have recently been developed to use exogenous nucleophiles to generate reactive intermediates of which the reactivity can be tuned to match the reactivity of the nucleophile that is to be glycosylated. Based on the work of Mukaiyama and co-workers[48–51] and others[52], triphenylphosphine oxide[53] was introduced to modulate the reactivity of anomeric iodides, and used to stereoselectively glycosylate reactive alcohols (see SI Table S2 for the complete reactivity-selectivity mapping study with additives).

Thus, caryophyllose **4** was pre-activated in the usual manner, after which a mixture of tetrabutylammonium iodide and triphenyl phosphine oxide was added to the 3-butene-1-ol. This led to the generation of the spacer-equipped caryophyllose **30** in 60% yield and excellent stereoselectivity (>98:2; *cis*:*trans*). Subsequent HCl-mediated deprotection of the 2-methylnaphthyl protection group according to an adapted procedure of Volbeda *et al.* yielded the caryophyllose acceptor **31** (61%).[54]

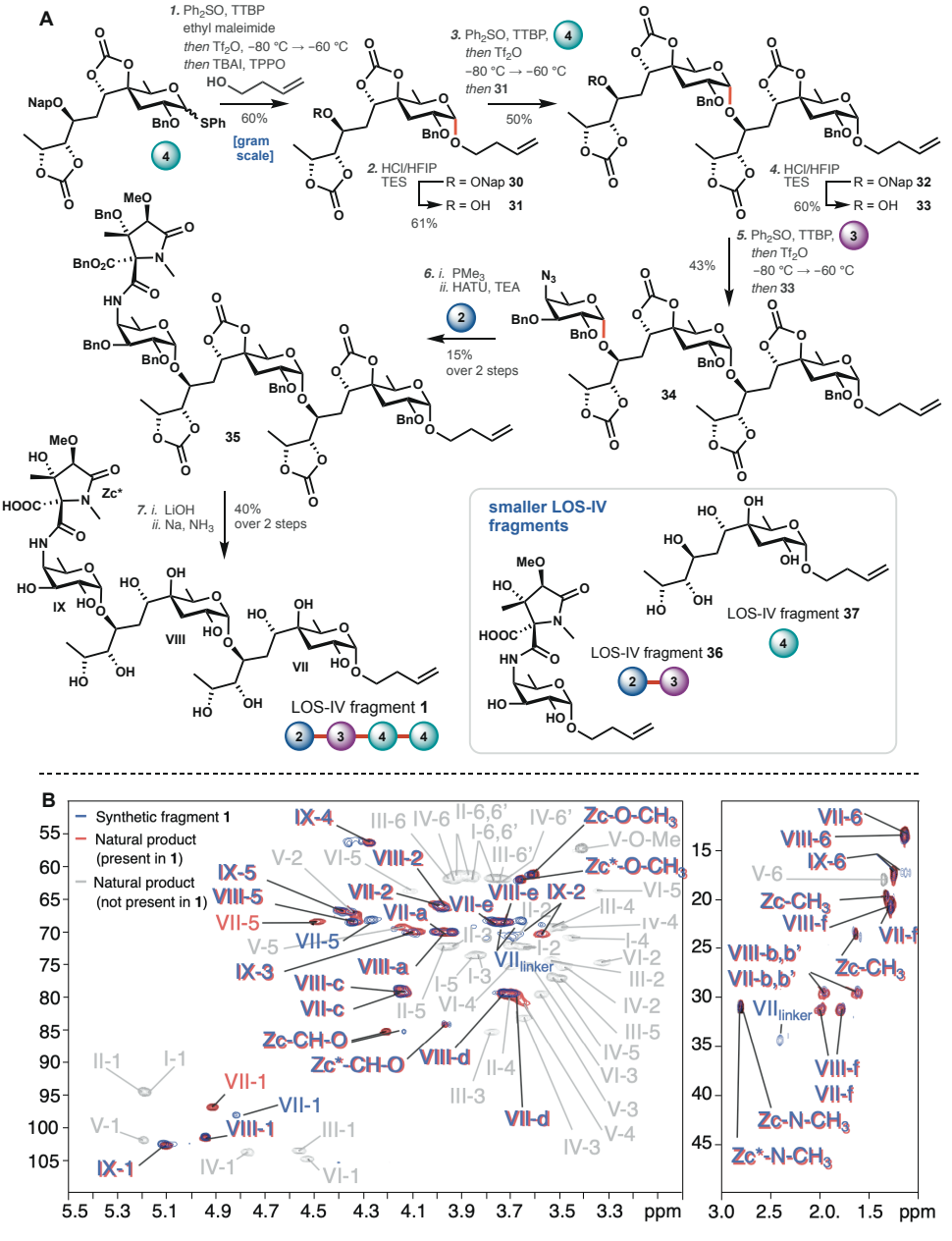


Figure 3. (A) Assembly of LOS-IV fragment **1**. *Reagents and conditions:* (1) Ph_2SO, TTBP, *N*-ethyl maleimide, *then* Tf_2O, *then* TBAI, TPPO, *then* 3-buten-1-ol, –80 °C to 40 °C (60%); (2) HCl/HFIP, TES, DCM (61%); (3) Ph_2SO, TTBP, DCM, *then* Tf_2O, *then* **31**, –80 °C to –60 °C (50%); (4) HCl/HFIP, TES, DCM (60%); (5) Ph_2SO, TTBP, DCM, *then* Tf_2O, *then* **33**, –80 °C to –60 °C (43%); (6) *i.* trimethylphosphine, THF *ii.* **2**, TEA, HATU, CH_3CN (15% over 2 steps); (7) *i.* LiOH, H_2O, THF *ii.* Na, NH_3, *t*-BuOH, THF (40% over 2 steps); (B) ^{1}H-^{13}C HSQC NMR overlay of the acidic OS-IV fraction isolated by Rombouts *et al.* (red = residues of the natural product present in the synthesized fragment **1**, and grey = residues of the natural product absent in **1**), and synthesized **1** (blue). I to IX correspond to the nine monosaccharides of the OS-IV. In the overlay most signals overlap. Only signals close to the linker on VII are slightly off, because this area is different from the natural compound, which is linked to a xylose.

Coupling of this acceptor with donor **4** using pre-activation conditions afforded disaccharide **32** in 50% yield and with complete 1,2-*cis* selectivity, in line with the results obtained above with the model acceptors. Deprotection of the 2-methylnaphthyl protection group of Car-Car **32** required more acid compared to the deprotection of **30**, because of the presence of more Lewis basic entities in the substrate, but furnished acceptor **33** in a similar yield (60%). Coupling of acceptor **33** to 4-azidofucose donor **3** under pre-activation conditions provided **32** in 43% yield with the exclusive formation of the 1,2-*cis* product (see SI Figure S1 and Table S1 for the complete reactivity-selectivity mapping study performed with this donor). A Staudinger reduction was used to generated the free amine. Surprisingly, this transformation proceeded very sluggishly (reduction of the 4-azido fucose monosaccharide proceeded readily with TPP in 79% yield, see SI) even with the more reactive trimethyl phosphine. The crude product was directly coupled to the pyrrolidone **2**, to yield the completely protected Car-Car- FucNAc LOS-IV fragment **35**. Deprotection was done by saponification of the carbonate protection groups and the benzyl ester on the pyrrolidone, followed by debenzylation under Birch condition, to successfully yield the target structure **1** in 40% yield over the two deprotection steps.

The structure and purity of compound **1**, were confirmed by NMR and HRMS analysis. It was observed that **1** exists as a mixture of atropisomers, in line with the behavior of related pyrrolidone-4-aminofucose monosaccharides, prepared by Lowary and co-workers.[34,55] Figure 3B compares the ^{1}H-^{13}C HSQC NMR spectra of the synthetic Car-Car-FucNAc LOS-IV fragment **1** with the natural product, isolated by Rombouts *et al.*[12] The blue signals originate from the synthesized compound, the red signals are from the natural product, and all residues from the natural product that are absent in the synthetic fragment are grey. From the overlay it is apparent that the spectra match very well, indicating that the assembled fragment resembles the natural product well.

Conclusion

In conclusion, this chapter reports a systematic evaluation of tertiary-*C* sugar building blocks, caryophyllose and yersiniose. An integrated approach, consisting of a systematic series of glycosylation reactions in combination with the detection and characterization of different reactive intermediates using variable-T NMR and conformational energy landscape computations, were used to assess reactivity-stereoselectivity relationships. It has been found for these 4-*C*-branched sugars that ether functionalities in the appended side-chain readily attack the activated anomeric center of the caryophyllose and yersiniose donors, leading to unproductive glycosylation reactions. This surprising behavior has been explained using the conformational preference of oxocarbenium ion intermediates that can form. Prevention of this nucleophilic attack is a prerequisite to generate effective donor glycosides and could be achieved by tethering of the C4 side-chain. It was found that tethered Car and YerA donors can efficiently form the desired 1,2-*cis* linkages, as long as

weak nucleophiles are employed in the glycosylation. In order to achieve 1,2-*cis* selectivity, the reactivity of the Car-acceptors was tuned using electron-withdrawing protecting groups. The rationally designed building blocks enabled the first effective and stereoselective assembly of a Car-Car-FucNAc LOS-IV fragment, and related shorter fragments. The approach taken here can serve as a blueprint to uncover the reactivity of rare bacterial saccharides. The insight gathered will be a solid base to inform future syntheses of bacterial oligosaccharides and glycoconjugates to fuel immunological- and biological research.

Supporting information

Reactivity-selectivity mapping for FucNAc donor 3

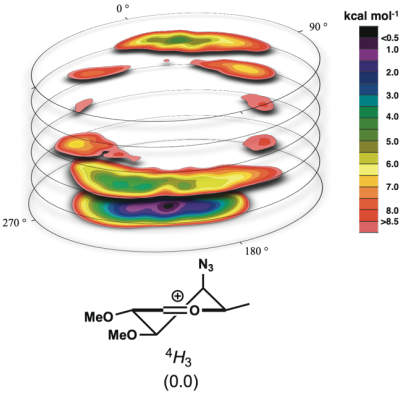
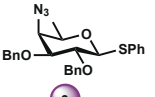


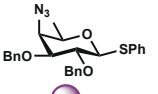
Figure S1. Conformational energy landscape (CEL) maps of 4-azidofucose pyranosyl oxocarbenium ions in which the found local minima are indicated with their respective energy. All energies are as computed at PCM(CH_2Cl_2)-B3LYP/6-311G(d,p) at *T*=213.15 K and expressed as solution-phase Gibbs free energy.

Table S1. Experimentally found stereoselectivities for model glycosylation reactions with ethanol, 2-fluoroethanol, 2,2-difluoroethanol, 2,2,2-trifluoroethanol, 1,1,1,3,3,3-hexafluoro-2-propanol, triethylsilane-*d*, 1-buten-4-ol, **28** and **29**. The stereoselectivity of the reaction is expressed as 1,2-*cis*:1,2-*trans* and based on the ^{1}H-NMR spectroscopy. Results of the glycosylation study. Experimental conditions: pre-activation based glycosylation conditions; Ph_2SO (1.3 eq.), TTBP (2.5 eq.), DCM (0.05 M), *then* Tf_2O (1.3 eq.), *then* nucleophile (2 eq.), –80 °C to –60 °C.



3

HO	36:64 (87%)
HO, F	48:52 (100%)
HO, F, F	77:23 (91%)
HO, CF_3	>98:2 (70%)
CF_3, HO, CF_3	>98:2 (69%)
D–Si	>98:2 (82%)



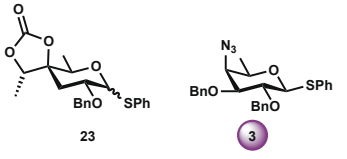
3

HO	39:61 (85%)
HO, BnO, OBn	58:42 (76%)
HO, O, O, O	>98:2 (66%)

>90:10 | >80:20 | >60:40 | >50:50 | <50:50 | <40:60 | <20:80 | <10:90 (1,2-*cis*:1,2-*trans*)

Additives controlled model glycosylation reactions

Table S2. Experimentally found stereoselectivities for model glycosylation reactions with additives including DMF (16 eq) and TBAI (8 eq). The stereoselectivity of the reaction is expressed as 1,2-*cis*:1,2-*trans* and based on the ^{1}H-NMR spectroscopy. Experimental conditions: pre-activation based glycosylation conditions; Ph_2SO (1.3 eq.), TTBP (2.5 eq.), DCM (0.05 M), *then* Tf_2O (1.3 eq.), *then* nucleophile (2 eq.), –80 °C to –60 °C.

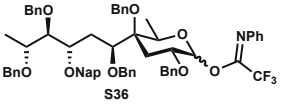


Entry	donor	HO CF3	HO F F	HO F	HO	HO
1	**23**	>98:2 (77%)	80:20 (100%)	66:34 (76%)	50:50 (60%)	60:40 (86%)
2	+ DMF	>98:2 (36%)	88:12 (100%)	81:19 (85%)	63:37 (72%)	67:33 (55%)
3	+ TBAI	*donor hydrolysis*	>98:2 (16%)	>98:2 (65%)	>98:2 (62%)	>98:2 (61%)
4	**3**	>98:2 (70%)	77:23 (91%)	48:52 (100%)	36:64 (87%)	39:61 (85%)
5	+ DMF	>98:2 (73%)	>98:2 (85%)	81:19 (100%)	62:38 (93%)	63:37 (61%)
6	+ TBAI	*donor hydrolysis*	>98:2 (81%)	>98:2 (79%)	>98:2 (75%)	>98:2 (95%)

>90:10 | >80:20 | >60:40 | >50:50 | <50:50 | <40:60 | <20:80 | <10:90 (1,2-*cis*:1,2-*trans*)

Model glycosylation reaction with imidate donor

Table S3. Experimentally found stereoselectivities for model glycosylation reactions. The stereoselectivity of the reaction is expressed as 1,2-*cis*:1,2-*trans* and based on the ^{1}H-NMR spectroscopy. Experimental conditions: acceptor (2.0 eq.), DCM (0.05 M), *then* TMSOTf (0.5 M solution in DCM) (2 eq.), –80 °C to –10 °C.



S36

Entry	donor	D–Si	HO, CF3, CF3	HO, CF3	HO, F, F	HO, F	HO
1	**25**	*by-product* **26**	*by-product* **26**	>98:2 (68%)	63:37 (86%)	33:67 (70%)	25:75 (100%)

DFT calculations

General procedure I: conformational energy landscape calculation of glycosyl cations • To keep the calculation time manageable, large protection groups (*i.e.*, *O*-Bn) were substituted with electronically comparable smaller groups (*i.e.*, *O*-Me). The initial structure for the conformational energy landscape (CEL) was optimized by starting from a 'conformer distribution search' option included in the Spartan 10 program by utilizing DFT as the level of theory and the hybrid functional B3LYP in gas phase with 6-31G(d) as the basis set. All generated gas-phase geometries were re-optimized with Gaussian 09 rev. D.01 by using B3LYP/6-311G(d,p), after which a vibrational analysis was computed to obtain the thermodynamic properties. The gas-phase structures were than solvated by using the PCM implicit solvation model, with CH_2Cl_2 as solvent. Solvent effects were explicitly used in the solving of the SCF equations and during the optimization of the geometry. The geometry with the lowest solvated energy was selected as the starting point for the CEL map. A complete survey of the possible conformational space was done by scanning three dihedral angles ranging from –60° to 60°, including the C1-C2-C3-C4 (D1), C3-C4-C5-O (D3) and C5-O-C1-C2 (D5). The resolution of this survey is determined by the step size which was set to 15° per puckering parameter, giving a total of 729 pre-fixed conformations per six-membered oxocarbenium ion spanning the entire conformational landscape. All other internal coordinates were unconstrained. With the exception of a C2-substituent being present on the oxocarbenium ring of interest, then the C2-H2 bond length was fixed based on the optimized structure to counteract rearrangements occurring for higher energy conformers. The 729 structures were computed with Gaussian 09 again with a two-step procedure. First, the structures were optimized in the gas-phase with B3LYP/6-311G(d,p), after which a vibrational analysis was computed to obtain the thermodynamic properties. The gas-phase structures were than solvated by using the PCM implicit solvation model, with CH_2Cl_2 as solvent. Solvent effects were explicitly used in the solving of the SCF equations and during the optimization of the geometry. The final denoted free Gibbs energy was calculated using Equation S1 in which ΔE_{gas} is the gas-phase energy (*i.e.*, electronic energy), $\Delta G^T_{gas,QH}$ (T = reaction temperature and p = 1 atm.) is the sum of corrections from the electronic energy to free Gibbs energy in the quasi-harmonic oscillator approximation also including zero-point energy (ZPE), and ΔG_{solv} is their corresponding free solvation Gibbs energy. The $\Delta G^T_{gas,QH}$ were computed using the quasi-harmonic approximation in the gas phase according to the work of Truhlar.

$$\Delta G^T_{CH_2Cl_2} = \Delta E_{gas} + \Delta G^T_{gas,QH} + \Delta G_{solv} \qquad \text{(Eq. S1)}$$

$$= \Delta G^T_{gas} + \Delta G_{solv}$$

The quasi-harmonic approximation is the same as the harmonic oscillator approximation except that vibrational frequencies lower than 100 cm^{-1} were raised to 100 cm^{-1} as a way to correct for the breakdown of the harmonic oscillator model for the free energies of low-frequency vibrational modes. All found minima

were checked for imaginary frequencies. To visualize the energy levels of the conformers on the Cremer-Pople sphere, slices were generated dissecting the sphere that combine closely associated conformers (Figure S1). The OriginPro software was employed to produce the energy heat maps, contoured at 0.5 kcal mol^{-1}. For ease of visualization, the Cremer-Pople globe is turned 180° with respect to its common representation and both poles (the $^4C_1$ and $^1C_4$ structures) are omitted as these conformations are very high in energy. Visualization of conformations of interest was done with CYLview.

Variable-temperature NMR

General procedure II: pre-activation Tf_2O/Ph_2SO based variable-temperature NMR • A mixture of the donor (30 µmol, 1 eq.), Ph_2SO (8.0 mg, 39 µmol, 1.3 eq.) and TTBP (19 mg, 75 µmol, 2.5 eq.) were co-evaporated with toluene (3x). Under a nitrogen atmosphere, CD_2Cl_2 was added after which the mixture was transferred to a nitrogen flushed NMR tube that was then closed with an NMR septum. The NMR magnet was cooled to −80 °C, locked and shimmed prior to activation. The sample was cooled in an ethanol bath of −80 °C, upon which Tf_2O (6.6 µL, 39 µmol, 1.3 eq.) was added, the tube was shaken three times, wiped clean and rapidly inserted back in the NMR magnet. The sample was then re-shimmed and spectra were recorded with 10 °C intervals, securing the temperature to be stable. At −60 °C full characterization of the reactive species was performed by taking ^{13}C, HH-COSY, HSQC, and ^{19}F NMR. ^1H spectra were recorded with increasing temperature until degradation was observed.

Results of compound **25**

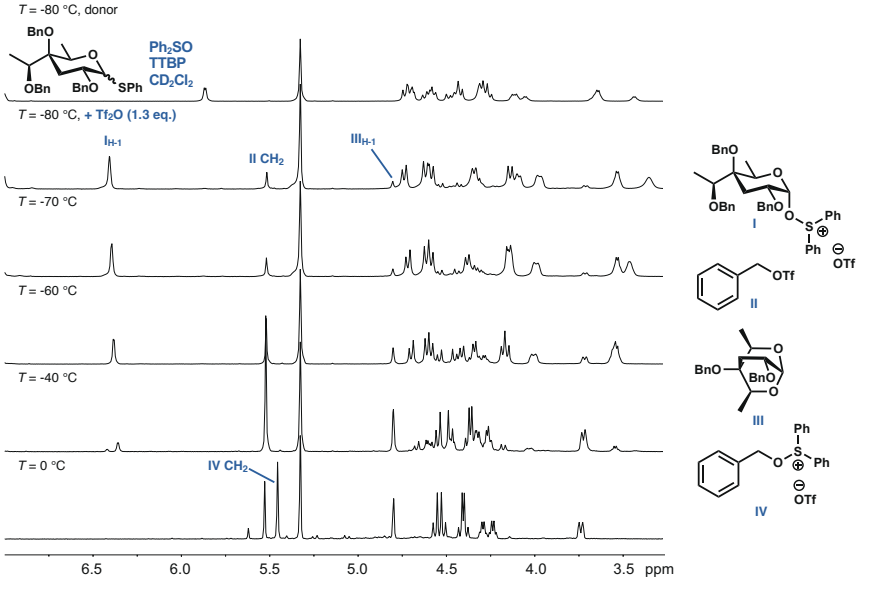


Figure S2. Variable-T NMR of donor **25** under pre-activation conditions.

Results of compound **24**

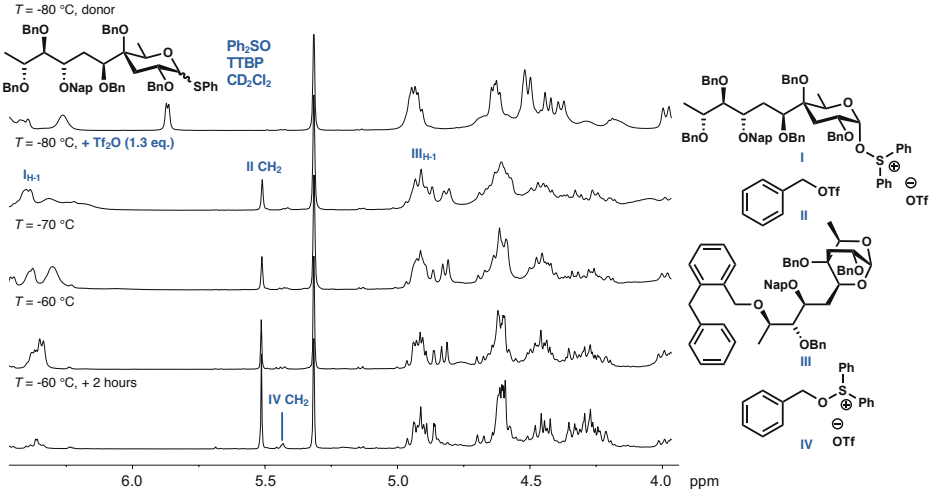


Figure S3. Variable-T NMR of donor **24** under pre-activation conditions.

Results of compound **3**

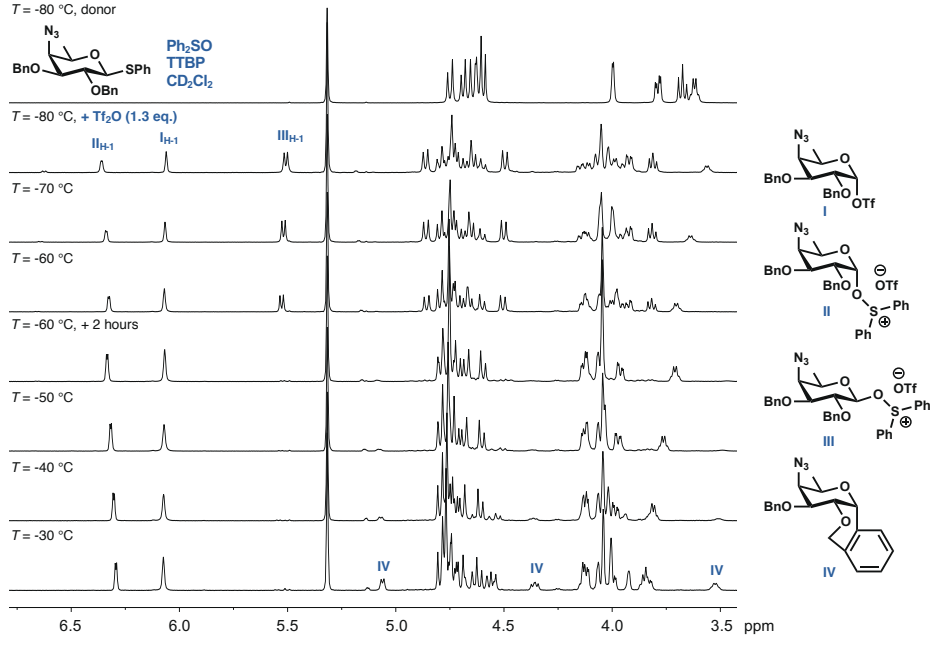


Figure S4. Variable-T NMR of donor **3** under pre-activation conditions.

Results of compound **3** (+DMF)

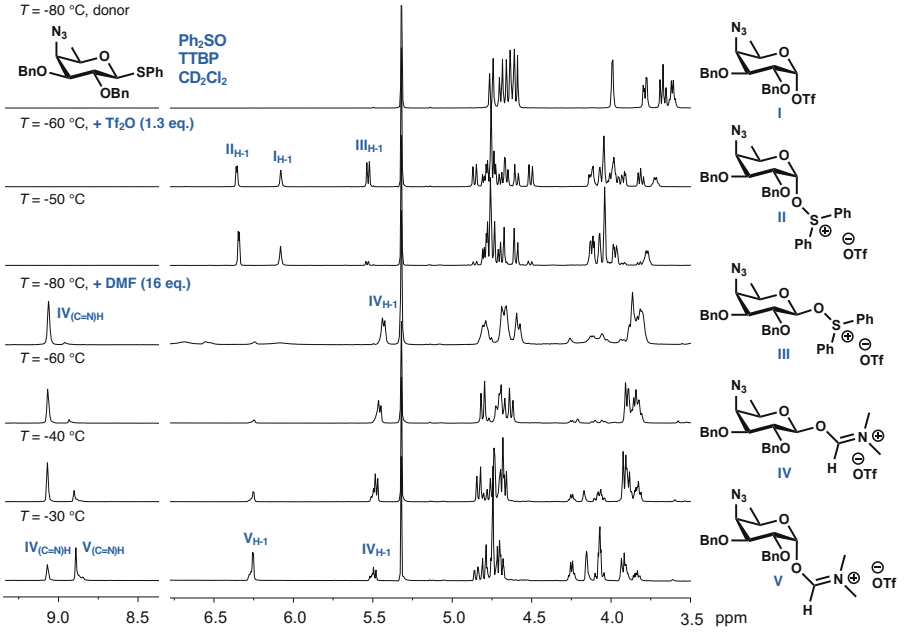


Figure S5. Variable-T NMR of donor **3** under pre-activation conditions with DMF as additive.

Results of compound **23**

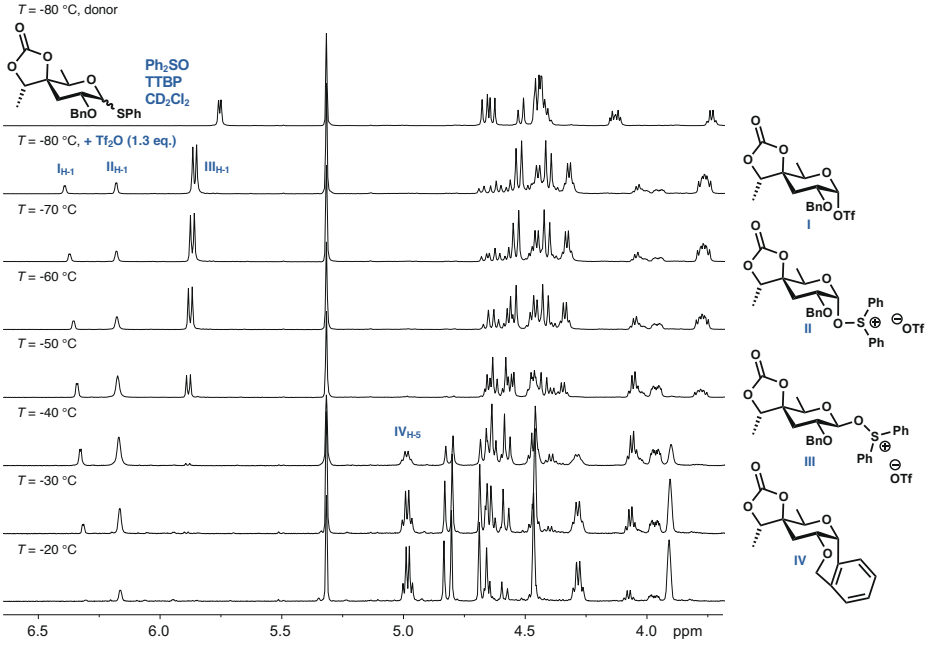


Figure S6. Variable-T NMR of donor **23** under pre-activation conditions.

Results of compound **23** (+1.7 eq. extra Ph_2SO)

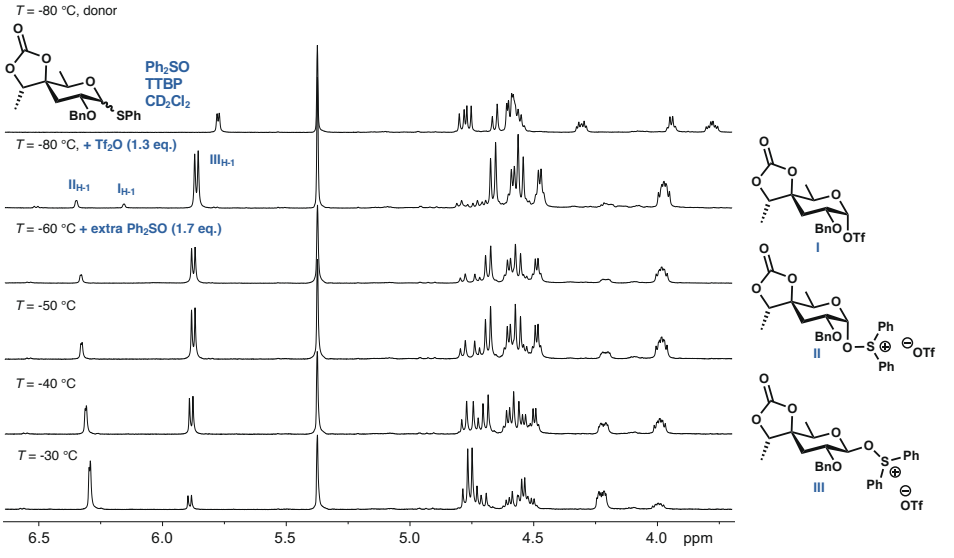


Figure S7. Variable-T NMR of donor **23** under pre-activation conditions with +1.7 eq. extra Ph_2SO.

Results of compound **4**

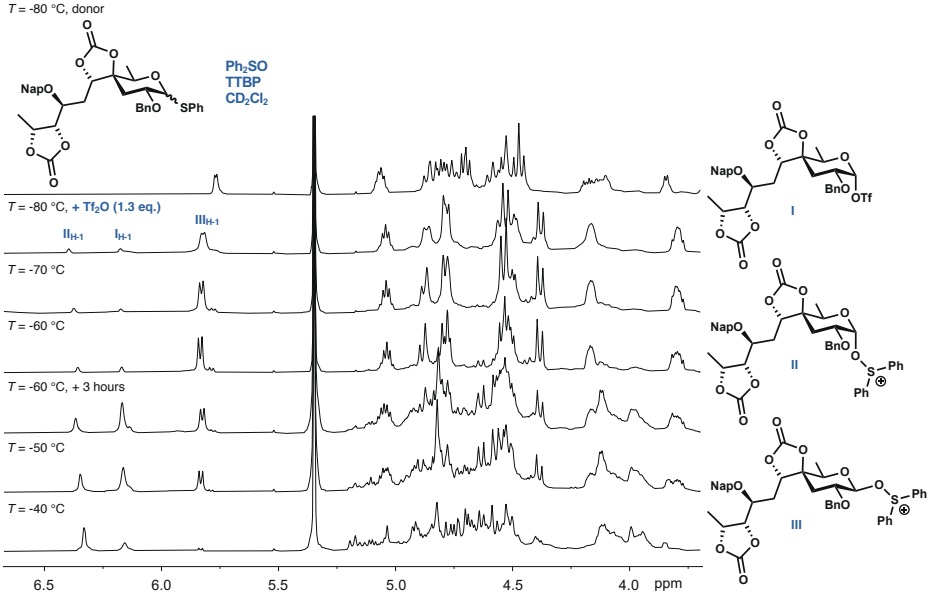


Figure S8. Variable-T NMR of donor **4** under pre-activation conditions.

Organic synthesis

General experimental procedures • All chemicals (Merck, Sigma-Aldrich, Alfa Aesar, Honeywell, Boom and Merck KGaA) were of commercial grade and were used as received unless stated otherwise. Dichloromethane, tetrahydrofuran and toluene were stored over activated 4 Å molecular sieves (beads, 8-12 mesh, Sigma-Aldrich). Before use traces of water present in the donor, diphenyl sulfoxide (Ph_2SO) and tri-*tert*-butylpyrimidine (TTBP) were removed by co-evaporation with dry toluene. The acceptors used in the model glycosylation reactions (ethanol, 2-fluoroethanol, 2,2-difluoroethanol and 2,2,2,-trifluoroethanol, 1,1,1,3,3,3-hexafluoro-2-propanol, triethylsilane-*d*, and 3-buten-1-ol) were stored in stock solutions (DCM, 0.5 M) over activated 3 Å molecular rods (rods, size 1/16 in., Sigma Aldrich). Trifluoromethanesulfonic anhydride (Tf_2O) was distilled over P_2O_5 and stored at –20 °C under a nitrogen atmosphere. Deuterated chloroform was stored over activated 3 Å molecular rods (rods, size 1/16 in., Sigma Aldrich) and potassium carbonate. Flash column chromatography was performed on silica gel 60 Å (0.04 – 0.063 mm, Screening Devices B.V.). Size exclusion chromatography was performed on SephadexTM (LH-20, GE Healthcare Life Sciences) by isocratic elution with DCM:MeOH (1:1, v:v). TLC analysis was performed on TLC Silica gel 60 (Kieselgel 60 F254, Merck) with UV detection (254 nm) and by spraying with 20% H_2SO_4 in ethanol followed by charring at ± 260 °C or by spraying with a solution of $(NH_4)_6Mo_7O_{24}{\cdot}H_2O$ (25 g/L) and $(NH_4)_4Ce(SO_4)_4{\cdot}2H_2O$ (10 g/L) in 10% sulfuric acid in water followed by charring at ± 260 °C. TLC-MS analysis was performed on a Camag TLC-MS Interface coupled with an API165 (SCIEX) mass spectrometer (eluted with *tert*-butylmethylether/EtOAc/MeOH, 5/4/1, v/v/v +0.1% formic acid, flow rate 0.12 mL/min). High-resolution mass spectra (HRMS) were recorded on a Waters Synapt G2-Si (TOF) equipped with an electrospray ion source in positive mode (source voltage 3.5 kV) and an internal lock mass LeuEnk ($M+H^+$ = 556.2771) or on a Thermo Finnigan LTQ Orbitrap mass spectrometer equipped with an electrospray ion source in positive mode (source voltage 3.5 kV, sheath gas flow 10, capillary temperature 275 °C) with resolution R=60.000 at m/z=400 (mass range = 150-4000). Amberlite resin (Sigma Aldrich Amberlite IR120 H^+ form or Amberlite IRA-67 free base) was pre-washed with MeOH. ^1H and ^{13}C NMR spectra were recorded on a Bruker AV-400 NMR instrument (400 and 101 MHz respectively), a Bruker AV-500 NMR instrument (500 and 126 MHz respectively), a Bruker AV-600 NMR instrument (600 and 151 MHz respectively) or a Bruker AV-850 NMR instrument (850 and 214 MHz respectively. All samples were measured in $CDCl_3$, unless stated otherwise. Chemical shifts (δ) are given in ppm relative to tetramethylsilane as internal standard or the residual signal of the deuterated solvent. Coupling constants (*J*) are given in Hz. To get better resolution of signals with small coupling constants or overlapping signals a gaussian window function (LB = ± -1 and GB = ± 0.5) was used on the ^1H NMR spectrum. All given ^{13}C APT spectra are proton decoupled. NMR peak assignment was accomplished using COSY, HSQC. If necessary, additional NOESY, HMBC, and HMBC-gated experiments were used to further elucidate the structure. Stereochemical product ratios were based on integration of ^1H NMR (crude and purified). IR spectra were recorded on a Shimadzu FTIR-8300 IR spectrometer and are reported in cm^{-1}. Specific rotations were measured on an Anton Paar Polarimeter MCP 100 in $CHCl_3$ (10 mg/mL) at 589 nm, unless stated otherwise.

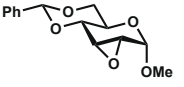
General procedure III: pre-activation Tf_2O/Ph_2SO based glycosylation • To a solution of the donor (50 µmol, 1 eq.) in DCM (1 mL, 0.05 M), Ph_2SO (13 mg, 65 µmol, 1.3 eq.) and TTBP (31 mg, 125 µmol, 2.5 eq.) were added. The solution was stirred over activated 3 Å molecular sieves (rods, size 1/16 in., Sigma Aldrich) for 30 min. The solution was cooled to –80 °C upon which Tf_2O (11 µL, 65 µmol, 1.3 eq.) was added slowly (5 seconds). Subsequently, the solution was allowed to attain to –60 °C to secure full activation of the donor followed by cooling back to –80 °C after which the acceptor was added (0.2 mL, 0.5 M solution, 2.0 eq.). The reaction was stirred for 16 h at –60 °C (for ethanol, 2-fluoroethanol, 2,2-difluoroethanol and 2,2,2-trifluoroethanol) or for 40 h at –60 °C (for 1,1,1,3,3,3-hexafluoro-2-propanol and triethylsilane-*d*). The reaction was quenched with sat. aq. $NaHCO_3$ followed by the dilution with EtOAc. The aqueous layer was extracted three times with EtOAc. The aqueous layer was extracted three times with EtOAc. The combined organic layers were washed with H_2O and brine, dried over $MgSO_4$, filtered off and concentrated under reduced pressure. Purification was performed by flash column chromatography to afford the corresponding coupled glycoside.

General procedure IV: DMF assisted pre-activation Tf_2O/Ph_2SO based glycosylation • To a solution of the donor (50 µmol, 1 eq.) in DCM (1 mL, 0.05 M), Ph_2SO (13 mg, 65 µmol, 1.3 eq.) and TTBP (31 mg, 125 µmol, 2.5 eq.) were added. The solution was stirred over activated 3 Å molecular sieves (rods, size 1/16 in., Sigma Aldrich) for 30 min. The solution was cooled to –80 °C upon which Tf_2O (11 µL, 65 µmol,

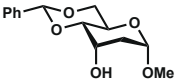
1.3 eq.) was added slowly. Subsequently, the solution was allowed to attain to −60 °C to secure full activation of the donor followed by cooling back to −80 °C after which DMF (61 µL, 0.8 mmol, 16 eq.) was added. The solution was stirred for 15 min at −80 °C followed by the addition of the acceptor (0.2 mL, 0.5 M solution, 2.0 eq.). The reaction was stirred overnight at 0 °C upon which the reaction was quenched with sat. aq. $NaHCO_3$ followed by the dilution with EtOAc. The aqueous layer was extracted three times with EtOAc. The combined organic layers were washed with H_2O and brine, dried over $MgSO_4$, filtered off and concentrated under reduced pressure. Purification was performed by flash column chromatography to afford the corresponding coupled glycoside.

General procedure V: TBAI assisted pre-activation Tf_2O/Ph_2SO based glycosylation • To a solution of the donor (50 µmol, 1 eq.) in DCM (1 mL, 0.05 M), Ph_2SO (13 mg, 65 µmol, 1.3 eq.), TTBP (31 mg, 125 µmol, 2.5 eq.) and ethyl maleimide (12.5 mg, 100 µmol, 2.0 eq) were added. The solution was stirred over activated 3 Å molecular sieves (rods, size 1/16 in., Sigma Aldrich) for 30 min. The solution was cooled to −80 °C upon which Tf_2O (11 µL, 65 µmol, 1.3 eq.) was added slowly. Subsequently, the solution was allowed to attain to −60 °C to secure full activation of the donor followed by cooling back to −80 °C after which TBAI (148 mg, 0.4 mmol, 8 eq.) was added. The solution was stirred for 15 min at −80 °C followed by the addition of the acceptor (0.2 mL, 0.5 M solution, 2.0 eq.). The reaction was stirred overnight at 0 °C upon which the reaction was quenched with sat. aq. $NaHCO_3$ and sat. aq. thiosulfate sol. followed by the dilution with EtOAc. The combined organic layers were washed with H_2O and brine, dried over $MgSO_4$, filtered off and concentrated under reduced pressure. Purification was performed by flash column chromatography to afford the corresponding coupled glycoside.

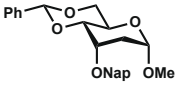
General procedure VI: TMSOTf activation based glycosylation of imidates • A solution of the donor (22.5 µmol, 1.0 eq.) and acceptor (45 µmol, 2.0 eq.) in DCM (450 µL, 0.05 M) was stirred over activated 3 Å molecular sieves (rods, size 1/16 in., Sigma Aldrich) for 30 min. The solution was cooled to −80 °C upon which TMSOTf (9.0 µL of a 0.5 M solution, 0.2 eq.) was added slowly. Subsequently, the solution was allowed to attain to −10 °C and stirred for 16 h. The reaction was quenched with sat. aq. $NaHCO_3$ followed by the dilution with EtOAc. The aqueous layer was extracted three times with EtOAc. The combined organic layers were washed with H_2O and brine, dried over $MgSO_4$, filtered off and concentrated under reduced pressure. Purification was performed by flash column chromatography to afford the corresponding coupled glycoside.



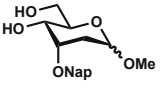
Methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-allopyranoside (7). Methyl α-D-glucopyranoside (167 g, 860 mmol) was dissolved in dry acetonitrile (1.7 L, 0.5 M), $PhCH(OMe)_2$ (142 mL, 950 mmol, 1.1 eq.) and iodine (21.8 g, 86 mmol, 0.1 eq.) were added. The mixture was stirred for 3 h at 50 °C. The solution was concentrated *in vacuo* and co-evaporated with toluene. The crude solid was recrystallized from EtOAc/pentane to give a white solid. The solid was dissolved in pyridine (1.7 L, 0.5 M), the solution was cooled on ice followed by the dropwise addition of MsCl (200 mL, 2.6 mol, 3.0 eq.), the solution was stirred for 15 h at room temperature. The solution was quenched by diluting with ice water (15 L). The resulting suspension was filtered, followed by washing with water. Co-evaporation with toluene yielded the crude product as a light brown solid. The crude product was divided into two equal portions. The brown solid was dissolved in a 2:3 mixture of THF/MeOH (3.4 L, 0.125 M), KOH (72.4 g, 1290 mmol, 3.0 eq.) was added, and the solution was refluxed at 80 °C for 15 h, resulting in a thick brown suspension. After cooling to room temperature, both suspensions were combined and diluted with cold water (60 L). Filtration followed by washing with water yielded the crude product. Recrystallization (EtOAc/pentane) yielded the title compound as a white solid (124.7 g, 471.8 mmol, 55% over 3 steps). TLC: R_f 0.4 (pentane:EtOAc, 4:6, v:v); $[\alpha]_D^{20}$ 217.6° (c 0.125, $CHCl_3$); IR (neat, cm^{-1}): 1074, 1144, 1391, 2988; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.53 – 7.48 (m, 2H, CH_{arom}), 7.41 – 7.34 (m, 3H, CH_{arom}), 5.58 (s, 1H, CHPh), 4.90 (d, *J* = 2.7 Hz, 1H, H-1), 4.25 (ddd, *J* = 10.1, 5.0, 0.8 Hz, 1H, H-6), 4.09 (ddd, *J* = 10.3, 9.1, 5.0 Hz, 1H, H-5), 3.96 (dd, *J* = 9.1, 1.2 Hz, 1H, H-4), 3.69 (t, *J* = 10.3 Hz, 1H, H-6), 3.53 (d, *J* = 4.4 Hz, 1H, H-3), 3.50 (dd, *J* = 4.3, 2.8 Hz, 1H, H-2), 3.48 (s, 3H, CH_3 OMe); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 137.2 ($C_{q\text{-}arom}$), 129.4, 128.5, 126.5 (CH_{arom}), 102.9 (CHPh), 95.5 (C-1), 78.0 (C-4), 69.1 (C-6), 60.2 (C-5), 56.1 (CH_3 OMe), 53.3 (C-2), 50.9 (C-3); HRMS: $[M+Na]^+$ calcd for $C_{14}H_{16}O_5Na$ 287.0895, found 287.0897.



Methyl 4,6-*O*-benzylidene-2-deoxy-D-altropyranoside (8). Compound **7** (124.7 g, 471.8 mmol) was divided into two equal portions of 236 mmol. Compound **7** was dissolved in Et_2O (3.9 L, 0.06 M), and $LiAlH_4$ (119 mL, 476 mmol, 2 eq., 4 M solution in THF) was then added drop-wise. After 2 h of refluxing at 45 °C the mixture was led to cool to room temperature and quenched with 20 mL of water. The excess water was removed by drying over $MgSO_4$, after which the mixture was filtered, and concentrated *in vacuo* to yield a white crystalline solid. The crude products were combined and recrystallized (Et_2O) to afford the title compound (98.5 grams, 369.9 mmol, 78%) as a white solid. TLC: R_f 0.5 (pentane:EtOAc, 4:6, v:v); $[\alpha]_D^{20}$ 84.2° (c 0.5, $CHCl_3$); IR (neat, cm^{-1}): 1045, 1099, 1381, 2932, 3510; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.53 – 7.49 (m, 2H, CH_{arom}), 7.40 – 7.33 (m, 3H, CH_{arom}), 5.63 (s, 1H, CHPh), 4.80 (d, *J* = 3.9 Hz, 1H, H-1), 4.33 (dd, *J* = 10.1, 5.1 Hz, 1H, H-6), 4.28 – 4.22 (m, 1H, H-5), 4.19 (dq, *J* = 6.3, 3.1 Hz, 1H, H-3), 3.78 (t, *J* = 10.2 Hz, 1H. H-6), 3.62 (dd, *J* = 9.6, 2.8 Hz, 1H, H-4), 3.42 (s, 3H, CH_3 OMe), 3.03 (d, *J* = 6.7 Hz, 1H, 3-OH), 2.20 (ddd, *J* = 14.9, 3.2, 1.0 Hz, 1H, H-2), 2.01 (dt, *J* = 14.9, 3.7 Hz, 1H, H-2); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 137.4 ($C_{q\text{-}arom}$), 129.2, 128.4, 126.4 (CH_{arom}), 102.2 (CHPh), 98.8 (C-1), 79.8 (C-4), 69.5 (C-6), 65.2 (C-3), 58.3 (C-5), 55.6 (CH_3 OMe), 35.6 (C-2); HRMS: $[M+Na]^+$ calcd for $C_{14}H_{18}O_5Na$ 289.1052, found 289.1068.

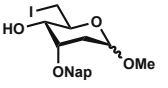


Methyl 4,6-*O*-benzylidene-2-deoxy-3-*O*-(2-methylnaphtalene)-α-D-altropyranoside (9). Compound **8** (98.5 g, 369.9 mmol) was dissolved in DMF (925 mL, 0.4 M) under N_2 atmosphere and cooled on ice. NaH (17.8 g, 443.9 mmol, 1.2 eq., 60% dispersion in mineral oil) was added portion-wise. Subsequently, 2-(bromomethyl)naphthalene (98.1 g, 443.9 mmol, 1.2 eq.) was added portion-wise over a time span of 30 min. The solution was stirred for 1 h after which the solution was concentrated to 1/5th of its original volume. The solution was then quenched with H_2O followed by further dilution with Et_2O and H_2O. The aqueous layer was extracted 5 times with Et_2O after which the combined organic layers were washed with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. The organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product as a colorless oil. Flash column chromatography (90:10 → 70:30; pentane:EtOAc) yielded the title compound (150.4 g, 369.9 mmol, *quant.*) as a yellow oil. TLC: R_f 0.7 (pentane:EtOAc, 1:1, v:v); $[\alpha]_D^{20}$ 44.3° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 474, 699, 748, 1007, 1044, 1099, 1128; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.94 – 7.62 (m, 4H, CH_{arom}), 7.60 – 7.33 (m, 8H, CH_{arom}), 5.57 (s, 1H, CHPh), 4.97 (s, 2H, CH_2 Nap), 4.74 (d, *J* = 4.6 Hz, 1H, H-1), 4.49 (td, *J* = 10.1, 5.3 Hz, 1H, H-5), 4.34 (dd, *J* = 10.3, 5.3 Hz, 1H, H-6), 4.01 (q, *J* = 3.0 Hz, 1H, H-3), 3.73 (t, *J* = 10.4 Hz, 1H, H-6), 3.70 (dd, *J* = 9.5, 2.9 Hz, 1H, H-4), 3.44 (s, 3H, CH_3 OMe), 2.24 (dd, *J* = 14.7, 2.5 Hz, 1H, H-2), 1.92 (ddd, *J* = 15.0, 4.6, 3.8 Hz, 1H, H-2); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 138.0, 136.7, 133.4, 133.0 ($C_{q\text{-}arom}$), 129.2, 128.5, 128.0, 128.0, 127.8, 126.5, 126.4, 126.0, 126.0, 125.7 (CH_{arom}), 102.4 (CHPh), 98.1 (C-1), 80.5 (C-4), 72.3 (CH_2 Nap), 70.3 (C-3), 69.8 (C-6), 58.4 (C-5), 55.8 (CH_3 OMe), 34.6 (C-2); HRMS: $[M+Na]^+$ calcd for $C_{25}H_{26}O_5Na$ 429.1678, found 429.1680.

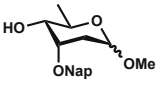


Methyl 2-deoxy-3-*O*-(2-methylnaphtalene)-D-altropyranoside (10). Iodine (9.4 g, 37 mmol, 0.1 eq.) was added to a stirred solution of **9** (150.4 g, 369.9 mmol) in MeOH (1.8 L, 0.2 M). The solution was stirred at room temperature for 18 h after which the reaction was quenched with sat. aq. $Na_2S_2O_3$ and diluted with EtOAc and H_2O. The aqueous layer was extensively extracted with EtOAc, followed by drying the combined organic layers over $MgSO_4$. The organic layer was then filtered, and concentrated *in vacuo* to yield the crude product as a yellow oil. Flash column chromatography (50:50 → 20:80; pentane:EtOAc) yielded the title compound (117.1 g, 368 mmol, 99%, α:β; 50:50) as a colorless oil. TLC: R_f 0.3 (pentane:EtOAc, 1:4, v:v); IR (neat, cm^{-1}): 750, 817, 1041, 2924, 3354; Data of the major stereoisomer (α-anomer): ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.89 – 7.75 (m, 4H, CH_{arom}), 7.54 – 7.42 (m, 3H, CH_{arom}), 4.95 (d, *J* = 11.5 Hz, 1H, C*H*H Nap), 4.75 (d, *J* = 3.5 Hz, 2H, H-1), 4.56 (d, *J* = 11.5 Hz, 1H, CH*H* Nap), 4.05 – 3.57 (m,

5H, H-3, H-4, H-5, H-6, H-6), 3.40 (s, 3H, CH_3 OMe), 2.72 (bs, 1H, OH), 2.52 (bs, 1H, OH), 2.37 (ddd, *J* = 15.2, 3.0, 0.9 Hz, 1H, H-2), 1.75 (ddd, *J* = 15.2, 4.6, 3.4 Hz, 1H, H-2); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 135.4, 133.2, 133.0 ($C_{q\text{-arom}}$), 128.3, 127.9, 127.7, 126.8, 126.2, 126.0, 126.0 (CH_{arom}), 97.4 (C-1), 72.8 (C-3), 70.6 (CH_2 Nap), 68.2 (C-4), 67.6 (C-5), 63.1 (C-6), 55.3 (CH_3 OMe), 31.2 (C-2); Diagnostic signals of the minor stereoisomer (β-anomer): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.89 (d, *J* = 11.7 Hz, 1H, C*H*H Nap), 4.77 (d, *J* = 2.0 Hz, 1H, H-1), 4.66 (d, *J* = 11.7 Hz, 1H, CH*H* Nap), 3.50 (s, 3H, CH_3 OMe), 2.31 (ddd, *J* = 14.2, 3.7, 2.1 Hz, 1H, H-2), 1.62 (ddd, *J* = 14.1, 9.4, 2.6 Hz, 1H, H-2); ^{13}C NMR (101 MHz, $CDCl_3$ HSQC): δ 99.1 (C-1), 71.7 (CH_2 Nap), 56.7 (CH_3 OMe), 34.0 (C-2); HRMS: $[M+Na]^+$ calcd for $C_{18}H_{22}O_5Na$ 341.1365, found 341.1364.

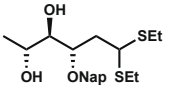


Methyl 2,6-dideoxy-6-*C*-iodo-3-*O*-(2-methylnaphtalene)-D-altropyranoside (11). To a stirred solution of **10** (114.6 g, 360 mmol) in toluene (2.5 L, 0.12 M), imidazole (71.4 g, 1.1 mol, 3.0 eq.) and triphenylphosphine (141.6 g, 540 mmol, 1.5 eq.) were added. The solution was heated to 75 °C upon which an iodine (127.9 g, 504 mmol, 1.4 eq.) solution in toluene (500 mL) was added dropwise over a time span of 15 min. After stirring for 30 min at 75 °C the solution was allowed to cool down to room temperature and quenched with sat. aq. $NaHCO_3$ and sat. aq. $Na_2S_2O_3$ and further diluted with EtOAc. The organic layer was washed with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (90:10 → 60:40; pentane:EtOAc) yielded the title compound (101.7 g, 237.4 mmol, 66%, α:β; 67:33) as a colorless oil. TLC: R_f 0.6 (pentane:EtOAc, 4:1, v:v); IR (neat, cm^{-1}): 750, 815, 1018, 1080, 2926, 3402; Data of the major stereoisomer (α-anomer): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.07 – 7.68 (m, 4H, CH_{arom}), 7.63 – 7.38 (m, 3H, CH_{arom}), 4.94 (d, *J* = 11.4 Hz, 1H, C*H*H Nap), 4.78 (d, *J* = 4.4 Hz, 1H, H-1), 4.54 (d, *J* = 11.4 Hz, 1H, CH*H* Nap), 3.88 (q, *J* = 3.2 Hz, 1H, H-3), 3.79 (ddd, *J* = 9.7, 7.7, 2.4 Hz, 1H, H-5), 3.64 (dd, *J* = 10.7, 2.5 Hz, 1H, H-6), 3.49 (s, 3H, CH_3 OMe), 3.40 (td, *J* = 10.3, 3.7 Hz, 1H, H-4), 3.34 (dd, *J* = 10.6, 7.6 Hz, 1H, H-6), 2.69 (d, *J* = 10.8 Hz, 1H, 4-OH), 2.38 (ddd, *J* = 15.2, 2.9, 1.0 Hz, 1H, H-2), 1.77 (ddd, *J* = 15.2, 4.5, 3.4 Hz, 1H, H-2); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 135.3, 133.2, 133.1 ($C_{q\text{-arom}}$), 128.4, 127.9, 127.8, 126.9, 126.3, 126.1, 126.0 (CH_{arom}), 97.7 (C-1), 72.8 (C-3), 71.1 (C-4), 70.7 (CH_2 Nap), 67.9 (C-5), 55.7(CH_3 OMe), 31.4 (C-2), 8.9 (C-6); Diagnostic signals of the minor stereoisomer (β-anomer): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.87 (d, *J* = 11.6 Hz, 1H, C*H*H Nap), 4.75 (dd, *J* = 9.6, 2.0 Hz, 1H, H-1), 4.60 (d, *J* = 11.6 Hz, 1H, CH*H* Nap), 3.93 (q, *J* = 3.3 Hz, 1H, H-3), 3.56 (s, 3H, CH_3 OMe), 3.27 (dd, *J* = 10.2, 8.1 Hz, 1H, H-6), 2.47 (d, *J* = 10.7 Hz, 1H, 4-OH), 2.32 (ddd, *J* = 14.2, 3.4, 2.1 Hz, 1H, H-2), 1.64 (ddd, *J* = 14.2, 9.6, 2.6 Hz, 1H, H-2); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 99.1 (C-1), 75.3 (C-3), 74.4 (C-4), 71.8 (CH_2 Nap), 71.3 (C-5), 56.7 (CH_3 OMe), 34.2 (C-2), 7.7 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{18}H_{21}IO_4Na$ 451.0382, found 451.0385.

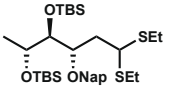


Methyl 2,6-dideoxy-3-*O*-(2-methylnaphtalene)-D-altropyranoside (12). Compound **11** (101.7 g, 237.4 mmol) was dissolved in dry *t*-BuOH (3.4 L, 0.07 M) and stirred under N_2 atmosphere. Subsequently, $NaBH_3CN$ (22.4 g, 356.1 mmol, 1.5 eq) and AIBN (46.8 g, 284.9 mmol, 1.2 eq.) were added. The solution was refluxed at 85 °C for 17 h. After cooling to room temperature, the solution was concentrated to a tenth of its original volume and diluted with EtOAc an H_2O, the aqueous layer was extracted twice, followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product as a yellow oil. Flash column chromatography (80:20 → 60:40; pentane:EtOAc) yielded the title compound (52.9 g, 175 mmol, 74%, α:β; 67:33) as a colorless oil. TLC: R_f 0.3 (pentane:EtOAc, 4:1, v:v); IR (neat, cm^{-1}): 748, 817, 1055, 1128, 2927; Data of the major stereoisomer (α-anomer): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.94 – 7.75 (m, 4H, CH_{arom}), 7.57 – 7.42 (m, 3H, CH_{arom}), 4.95 (d, *J* = 11.6 Hz, 1H, C*H*H Nap), 4.70 (d, *J* = 4.8 Hz, 1H, H-1), 4.57 (d, *J* = 11.6 Hz, 1H, CH*H* Nap), 3.99 (dq, *J* = 9.4, 6.4 Hz, 1H, H-5), 3.88 (q, *J* = 3.4 Hz, 1H, H-3), 3.40 (s, 3H, CH_3 OMe), 3.28 (dd, *J* = 9.4, 3.6 Hz, 1H, H-4), 2.61 – 2.49 (bs, 1H, 4-OH), 2.36 (ddd, *J* = 15.0, 3.1, 1.2 Hz, 1H, H-2), 1.78 (ddd, *J* = 15.1, 4.5, 3.5 Hz, 1H, H-2), 1.29 (d, *J* = 6.4 Hz, 3H, H-6); ^{13}C NMR (101 MHz, $CDCl_3$ HSQC): δ 135.6, 133.3, 133.1 ($C_{q\text{-arom}}$), 128.4, 128.0,

127.9, 127.8, 126.9, 126.3, 126.1 (CH_{arom}), 97.4 (C-1), 73.0 (C-3), 72.3 (C-4), 70.7(CH_2 Nap), 64.6 (C-5), 55.4 (CH_3 OMe), 31.6 (C-2), 18.0 (C-6); Diagnostic signals of the minor stereoisomer (β-anomer): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.89 (d, *J* = 11.6 Hz, 1H, C*H*H Nap), 4.63 (d, *J* = 11.6 Hz, 1H, CH*H* Nap), 3.72 (dq, *J* = 9.4, 6.3 Hz, 1H, H-5), 3.50 (s, 3H, CH_3 OMe), 1.64 (ddd, *J* = 14.1, 9.5, 2.7 Hz, 1H, H-2), 1.33 (d, *J* = 6.3 Hz, 3H, H-6); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 99.0 (C-1), 75.5 (C-3), 72.7 (C-4), 71.7 (CH_2 Nap), 71.0 (C-5), 56.6 (CH_3 OMe), 34.3 (C-2), 18.3 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{18}H_{22}O_4Na$ 325.1416, found 325.1418.

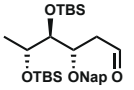


2,6-Dideoxy-1,1-diethyl-thioacetal-3-*O*-(2-methylnaphtalene)-D-altrose (13). Compound **12** (52.9 g, 175 mmol) was dissolved in 25% v:v aqueous acetic acid (3.5 L, 0.05 M) and refluxed at 100 °C for 1 h after which the solution was cooled to 0 °C. Subsequently, solid $NaHCO_3$ (583.8 g, 6.95 mol) was added to quench 50% of the acetic acid. The solution was then extracted with EtOAc (3x) and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product as an orange oil. TLC: R_f 0.3 (pentane:EtOAc, 1:1, v:v). The crude product was suspended in ethanethiol (69.4 mL, 962.4 mmol, 5.5 eq.) and cooled on ice, HCl (29.7 mL, 962.4 mmol, 5.5 eq., 37% aqueous solution) was added while stirring vigorously. The solution was stirred for 3 h at 0 °C upon which the reaction was neutralized with sat. aq. $NaHCO_3$ and diluted with EtOAc and H_2O. The aqueous layer was extracted 3x with EtOAc and the combined organic layers were washed with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (90:10 → 50:50; pentane:EtOAc) yielded the title compound (46.1 g, 116.8 mmol, 67%) as a yellow oil. TLC: R_f 0.6 (pentane:EtOAc, 1:1, v:v); $[\alpha]_D^{20}$ –13.3° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 750, 815, 1064, 1265, 1373, 1450, 2926, 2968, 3459; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.87 – 7.77 (m, 4H, CH_{arom}), 7.53 – 7.43 (m, 3H, CH_{arom}), 4.78 (d, *J* = 11.5 Hz, 1H, C*H*H Nap), 4.74 (d, *J* = 11.5 Hz, 1H, CH*H* Nap), 4.08 – 4.02 (m, 2H, H-1, H-3), 3.87 (p, *J* = 6.2 Hz, 1H, H-5), 3.75 (dd, *J* = 6.3, 4.3 Hz, 1H, H-4), 2.96 (bs, 1H, 4-OH), 2.75 – 2.50 (m, 5H, C*H*$_2$CH$_3$, C*H*$_2$CH$_3$, 5-OH), 2.29 – 2.07 (m, 2H, H-2), 1.29 – 1.21 (m, 6H, H-6, CH_2CH_3), 1.19 (t, *J* = 7.5 Hz, 3H, CH_2CH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 135.4, 133.2, 133.0 ($C_{q\text{-}arom}$), 128.3, 127.9, 127.7, 126.8, 126.2, 126.0, 125.9 (CH_{arom}), 77.8 (C-1/C-3), 75.1 (C-4), 72.1 (CH_2 Nap), 68.1 (C-5), 47.8 (C-3/C-1), 36.5 (C-2), 24.4 (*C*H_2CH$_3$), 23.6 (*C*H_2CH$_3$), 19.3 (C-6), 14.5 (CH_2*C*H_3), 14.3 (CH_2*C*H_3); HRMS: $[M+Na]^+$ calcd for $C_{21}H_{30}O_3S_2Na$ 417.1534, found 417.1533.

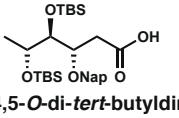


2,6-Dideoxy-1,1-diethyl-thioacetal-3-*O*-(2-methylnaphthalene)-4,5-*O*-di-*tert*-butyldimethylsilyl-D-altrose (14). Pyridine (140 mL, 75 mmol, 15.0 eq.) was added to a solution of compound **13** (46 g, 116.5 mmol) in DCM (1.2 L, 0.1 M), pyridine (140 mL, 75 mmol, 15.0 eq.), after which the solution was cooled on ice, and TBSOTf (80 mL, 350 mmol, 3.0 eq.) was added dropwise. After stirring for 10 min on ice the reaction was refluxed at 40 °C for 6 h. The reaction mixture was then concentrated to 1/4th of its original volume and quenched with sat. aq. $NaHCO_3$ followed by further dilution with Et_2O and H_2O. The aqueous layer was extracted with Et_2O (3x) followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (98:2 → 95:5; pentane: Et_2O) yielded the title compound (45 g, 72.2 mmol, 62%) as a colorless oil. TLC: R_f 0.5 (pentane:toluene, 9:1, v:v); $[\alpha]_D^{20}$ – 31.1° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 756, 835, 1105, 1253, 2927; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.87 – 7.76 (m, 4H, CH_{arom}), 7.51 – 7.43 (m, 3H, CH_{arom}), 4.87 (dd, *J* = 11.8, 0.8 Hz, 1H, CH*H* Nap), 4.66 (dd, *J* = 11.7, 0.8 Hz, 1H, C*H*H Nap), 4.09 – 3.97 (m, 2H, H-1, H-3), 3.79 (p, *J* = 6.1 Hz, 1H, H-5), 3.70 (dd, *J* = 6.0, 2.4 Hz, 1H, H-4), 2.70 – 2.44 (m, 4H, C*H*$_2$CH$_3$, C*H*$_2$CH$_3$), 2.26 (ddd, *J* = 14.9, 10.4, 3.5 Hz, 1H, H-2), 1.90 (ddd, *J* = 14.9, 11.3, 2.5 Hz, 1H, H-2), 1.25 (t, *J* = 7.4 Hz, 3H, CH_2CH_3), 1.21 (d, *J* = 6.1 Hz, 3H, H-6), 1.13 (t, *J* = 7.4 Hz, 3H, CH_2CH_3), 1.02 – 0.84 (m, 18H, $C(CH_3)_3$, $C(CH_3)_3$), 0.18 – 0.06 (m, 12H, $SiCH_3$, $SiCH_3$, $SiCH_3$, $SiCH_3$); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 136.5, 133.4, 133.0 ($C_{q\text{-}arom}$), 128.0, 128.0, 127.8, 126.3, 126.1, 126.0, 125.8 (CH_{arom}), 78.8 (C-4), 78.6 (C-1/C-3), 72.4 (CH_2 Nap), 69.8

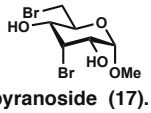
(C-5), 48.1 (C-3/C-1), 37.4 (C-2), 26.3 (C(CH_3)$_3$), 25.8 (C(CH_3)$_3$), 24.5 (CH_2CH_3), 24.2 (CH_2CH_3), 20.8 (C-6), 18.5 ($C(CH_3)_3$), 18.2 ($C(CH_3)_3$), 14.8 (CH_2CH_3), 14.4 (CH_2CH_3), -2.8 ($SiCH_3$), -3.7 ($SiCH_3$), -3.9 ($SiCH_3$), -4.3 ($SiCH_3$); HRMS: $[M+Na]^+$ calcd for $C_{33}H_{58}O_3S_2Si_2Na$ 645.3264, found 645.3258.



2,6-Dideoxy-3-*O*-(2-methylnaphthalene)-4,5-*O*-di-*tert*-butyldimethylsilyl-D-altrose (15). Compound **14** (45 g, 72.2 mmol) was dissolved in acetone (480 mL, 0.15 M) and H_2O (11 mL, 0.6 mol, 8.5 eq.) and cooled on ice. $NaHCO_3$ (27.3 g, 325 mmol, 4.5 eq.) and iodine (40.3 g, 160 mmol, 2.2 eq.) were added and the mixture was allowed to reach room temperature. After stirring for 6 h the mixture was quenched with sat. aq. $Na_2S_2O_3$ and further diluted with Et_2O and H_2O. The aqueous layer was extracted with Et_2O (3x) followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product as a colorless oil. Flash column chromatography (99:1 → 90:10; pentane:Et_2O) yielded the title compound (30.1 g, 58.2 mmol, 81%) as a colorless oil. TLC: R_f 0.2 (pentane,Et_2O, 40:1, v:v); $[\alpha]_D^{20}$ –23.2° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 775, 835, 1101, 1253, 1471, 1728, 2927; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 9.79 (dd, *J* = 2.8, 1.6 Hz, 1H, H-1), 7.86 – 7.72 (m, 4H, CH_{arom}), 7.54 – 7.40 (m, 3H, CH_{arom}), 4.76 (d, *J* = 11.7 Hz, 1H, CH*H* Nap), 4.66 (d, *J* = 11.8 Hz, 1H, C*H*H Nap), 4.24 (ddd, *J* = 8.4, 3.2, 2.5 Hz, 1H, H-3), 3.76 (dd, *J* = 6.2, 2.5 Hz, 1H, H-4), 3.69 (p, *J* = 6.1 Hz, 1H, H-5), 2.75 (ddd, *J* = 16.9, 8.4, 2.8 Hz, 1H, H-2), 2.60 (ddd, *J* = 17.0, 3.3, 1.6 Hz, 1H, H-2), 1.17 (d, *J* = 6.0 Hz, 3H, H-6), 0.87 (d, *J* = 22.8 Hz, 18H, C(CH_3)$_3$, C(CH_3)$_3$), 0.10 (d, *J* = 4.1 Hz, 12H, $SiCH_3$, $SiCH_3$, $SiCH_3$, $SiCH_3$); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 202.0 (C-1), 135.6, 133.3, 133.1 ($C_{q\text{-}arom}$), 128.2, 128.0, 127.8, 126.7, 126.1, 126.0, 125.9 (CH_{arom}), 78.1 (C-4), 75.2 (C-3), 71.8 (CH_2 Nap), 70.0 (C-5), 44.3 (C-2), 26.2 (C(CH_3)$_3$), 26.0 (C(CH_3)$_3$), 20.7 (C-6), 18.4 ($C(CH_3)_3$), 18.0 ($C(CH_3)_3$), -3.9 ($SiCH_3$), -4.0 ($SiCH_3$), -4.3 ($SiCH_3$), -4.7 ($SiCH_3$); HRMS: $[M+Na]^+$ calcd for $C_{29}H_{48}O_4Si_2Na$ 539.2989, found 539.2986.

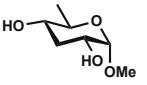


2,6-Dideoxy-3-*O*-(2-methylnaphthalene)-4,5-*O*-di-*tert*-butyldimethylsilyl-D-altronic acid (16). To a stirred solution of **15** (30 g, 58 mmol) in *t*-BuOH (0.5 L, 0.12 M) and aq. NaH_2PO_4 (266 mL, 5% w:w) an aqueous $KMnO_4$ solution (157 mL, 157 mmol, 2.7 eq., 1 M) was added. The reaction mixture was stirred for 3 h after which an excess of solid $Na_2S_2O_3$ was added. After the mixture had turned brown the solution was filtered over Celite© Hyflo Supercel (Merck) and was rinsed with Et_2O and H_2O. The aqueous layer was extracted with Et_2O (3x) followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product as a colorless oil. Flash column chromatography (95:5 → 80:20; pentane:Et_2O) yielded the title compound (23.4 g, 43.9 mmol, 75%) as a colorless oil. TLC: R_f 0.3 (pentane:EtOAc, 9:1, v:v); $[\alpha]_D^{20}$ –20.1° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 775, 829, 948, 1107, 1253, 1710, 2927; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.89 – 7.73 (m, 4H, CH_{arom}), 7.50 – 7.39 (m, 3H, CH_{arom}), 4.76 (d, *J* = 11.6 Hz, 1H, CH*H* Nap), 4.70 (d, *J* = 11.5 Hz, 1H, C*H*H Nap), 4.20 (td, *J* = 6.1, 2.0 Hz, 1H, H-3), 3.75 – 3.67 (m, 2H, H-4, H-5), 2.68 (d, *J* = 6.1 Hz, 2H, H-2), 1.17 (d, *J* = 5.8 Hz, 3H, H-6), 0.91 – 0.85 (m, 18H, C(CH_3)$_3$, C(CH_3)$_3$), 0.11 – 0.04 (m, 12H, $SiCH_3$, $SiCH_3$, $SiCH_3$, $SiCH_3$); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 178.4 (C-1), 135.8, 133.3, 133.0 ($C_{q\text{-}arom}$), 128.1, 128.0, 127.8, 126.6, 126.1, 126.1, 125.8 (CH_{arom}), 78.1 (C-4/C-5), 77.1 (C-3), 72.4 (CH_2 Nap), 70.0 (C-5/C-4), 35.8 (C-2), 26.2 (C(CH_3)$_3$), 26.0 (C(CH_3)$_3$), 20.6 (C-6), 18.5 ($C(CH_3)_3$), 18.1 ($C(CH_3)_3$), -3.9 ($SiCH_3$),-4.0 ($SiCH_3$), -4.4 ($SiCH_3$), -4.7 ($SiCH_3$); HRMS: $[M+Na]^+$ calcd for $C_{29}H_{48}O_5Si_2Na$ 555.2938, found 345.1316.

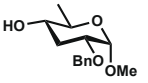


Methyl 3,6-dibromo-3,6-dideoxy-α-D-allopyranoside (17). A mixture of methyl α-D-glucopyranoside (32.5 g, 167 mmol), 2,4,5-tribromoimidazole (102 g, 335 mmol, 2.0 eq.) and triphenylphosphine (87.8 g, 335 mmol, 2.0 eq.) in toluene (2.7 L, 63 mM) was refluxed at 125 °C for 6 h. The mixture was allowed to

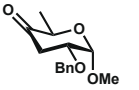
cool to room temperature and concentrated *in vacuo*, yielding a dark brown syrup. Flash column chromatography (90:10 → 60:40; pentane:EtOAc) yielded the product as a mixture of methyl 3,6-dibromo-3,6-dideoxy-α-D-allopyranoside and triphenylphosphine oxide. The mixture could be separated by flash column chromatography (60:40 → 40:60; pentane:Et_2O) to yield the title compound (32 g, 100 mmol, 60%) as a white solid. TLC: R_f 0.5 (pentane:EtOAc, 4:6, v:v); $[\alpha]_D^{20}$ 63.3° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 1161, 1209, 1263, 2909, 3451; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.82 (t, *J* = 3.9 Hz, 1H, H-3), 4.79 (d, *J* = 4.3 Hz, 1H, H-1), 3.95 (ddd, *J* = 8.9, 6.2, 2.4 Hz, 1H, H-5), 3.90 (dt, *J* = 12.0, 4.3 Hz, 1H, H-2), 3.77 (dd, *J* = 11.1, 2.4 Hz, 1H, H-6), 3.62 (dd, *J* = 11.1, 6.2 Hz, 1H, H-6), 3.58 (ddd, *J* = 10.8, 9.3, 3.4 Hz, 1H, H-4), 3.48 (s, 3H, CH_3 OMe), 2.74 (d, *J* = 11.9 Hz, 1H, 2-OH), 2.27 (d, *J* = 10.9 Hz, 1H, 4-OH); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 99.0 (C-1), 68.2 (C-4), 67.9 (C-5), 67.1 (C-2), 62.9 (C-3), 56.2 (CH_3 OMe), 33.0 (C-6); HRMS: $[M+Na]^+$ calcd for $C_7H_{12}Br_2O_4Na$ 342.8980, found 342.8985.



Methyl 3,6-dideoxy-α-D-allopyranoside (18). Compound **17** (16.6 g, 52 mmol) was dissolved in dry toluene (580 mL, 0.09 M) under N_2 atmosphere. Bu_3SnH (37.8 mL, 140 mmol, 2.7 eq.) and AIBN (0.85 g, 5.2 mmol, 0.1 eq.) were added respectively. The solution was refluxed at 120 °C for 17 h, and upon full conversion, the solution was concentrated *in vacuo*. Flash column chromatography (50:50 → 10:90; pentane:EtOAc) yielded the title compound (8.4 g, 51.5 mmol, 99%) as a colorless oil. TLC: R_f 0.25 (pentane:EtOAc, 4:6, v:v); $[\alpha]_D^{20}$ 39.3° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 1150, 2934, 3385; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.60 (d, *J* = 3.6 Hz, 1H, H-1), 3.71 (dt, *J* = 11.8, 4.6 Hz, 1H, H-2), 3.51 (dq, *J* = 9.2, 6.3 Hz, 1H, H-5), 3.44 (s, 3H, CH_3 OMe), 3.28 (ddd, *J* = 11.1, 9.1, 4.5 Hz, 1H, H-4), 2.19 (dt, *J* = 11.6, 4.7 Hz, 1H, H-3), 1.65 (q, *J* = 11.4 Hz, 1H H-3), 1.26 (d, *J* = 6.2 Hz, 3H, H-6); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 98.4 (C-1), 70.8 (C-4), 68.7 (C-5), 67.7 (C-2), 55.2 (CH_3 OMe), 37.0 (C-3), 17.5 (C-6); HRMS: $[M+Na]^+$ calcd for $C_7H_{14}O_4Na$ 185.0790, found 185.0790.

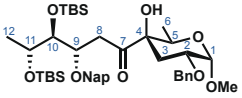


Methyl 2-*O*-benzyl-3,6-dideoxy-α-D-allopyranoside (19). Compound **18** (13.7 g, 84.6 mmol) and tributyltin oxide (86.2 mL, 169 mmol, 2.0 eq.) were dissolved in dry toluene (560 mL, 0.15 M, the solution was refluxed for 20 h under positive N_2 flow in a flask equipped with a Dean-Stark apparatus. The reaction was concentrated in *vacuo* upon which benzyl bromide (60.3 mL, 508 mmol, 6.0 eq.) was added to the residue. The mixture was stirred at 95 °C for 16 h, where after the reaction was cooled to room temperature and purified by flash column chromatography on silica gel. Flash column chromatography (100:0 → 50:50; pentane:EtOAc) yielded the title compound (6.56 g, 26 mmol, 31%) as a colorless oil. TLC: R_f 0.3 (pentane:acetone, 8:2, v:v); $[\alpha]_D^{20}$ 44.5° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 1050, 1090, 1454, 2935; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.37 – 7.27 (m, 5H, CH_{arom}), 4.63 (d, *J* = 12.4 Hz, 1H, C*H*H Bn), 4.61 (d, *J* = 3.1 Hz, 1H, H-1), 4.57 (d, *J* = 12.4 Hz, 1H, CH*H* Bn), 3.57 – 3.48 (m, 2H, H-2, H-5), 3.42 (s, 3H, CH_3 OMe), 3.23 (ddd, *J* = 11.2, 9.3, 4.6 Hz, 1H, H-4), 2.23 – 2.13 (m, 1H, H-3), 1.81 (q, *J* = 11.6 Hz, 1H, H-3), 1.23 (d, *J* = 6.2 Hz, 3H, H-6); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 138.2 ($C_{q\text{-}arom}$), 128.6, 128.0, 128.0 (CH_{arom}), 97.2 (C-1), 74.0 (C-2), 71.3 (C-4), 71.2 (CH_2 Bn), 68.7 (C-5), 55.0 (CH_3 OMe), 33.7 (C-3), 17.5 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{14}H_{20}O_4Na$ 275.1259, found 275.1254.



Methyl 2-*O*-benzyl-3,6-dideoxy-α-D-erythropyranosid-4-ulose (6). Compound **19** (6.5 g, 26 mmol) was dissolved in DCM (153 mL, 0.17 M) under N_2 atmosphere. Dess-Martin periodinane (16.5 g, 39 mmol, 1.5 eq.) was added and the mixture was stirred for 2.5 h upon the reaction was quenched with water. The aqueous layer was extracted with DCM (3x) followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product as a white oil. Flash column chromatography (95:5 → 90:10; pentane:Et_2O) yielded the title compound (5.8 g, 23.3 mmol, 90%) as a colorless oil. TLC: R_f 0.7

(pentane:acetone, 8:2, v:v); $[\alpha]_D^{20}$ 73.6° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 1047, 1077, 1454, 1724, 2938; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.39 – 7.28 (m, 5H, CH_{arom}), 4.82 (d, *J* = 3.2 Hz, 1H, H-1), 4.65 (d, *J* = 12.4 Hz, 1H, C*H*H Bn), 4.58 (d, *J* = 12.3 Hz, 1H, CH*H* Bn), 4.13 (q, *J* = 6.7 Hz, 1H, H-5), 3.83 (ddd, *J* = 10.6, 6.4, 3.3 Hz, 1H, H-2), 3.51 (s, 3H, CH_3 OMe), 2.83 – 2.69 (m, 2H, H-3, H-3), 1.26 (d, *J* = 6.7 Hz, 3H, H-6); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 206.1 (C=O), 137.7 ($C_{q\text{-}arom}$), 128.7, 128.2, 128.0 (CH_{arom}), 97.4 (C-1), 74.4 (C-2), 71.7 (CH_2 Bn), 70.2 (C-5), 56.0 (CH_3 OMe), 41.1 (C-3), 14.6 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{14}H_{18}O_4Na$ 273.1103, found 273.1097.



Methyl 2-*O*-benzyl-3,6-dideoxy-4-*C*-([9*S*,10*S*,11*R*]-9-*O*-[2-methylnaphthalene]-10,11-*O*-di-*tert*-butyldimethylsilyl-hexan-7-one)-α-D-galactopyranoside (20). Carboxylic acid **16** (2.66 g, 5.0 mmol) was dissolved in dry THF (50 mL, 0.1 M). This solution was cooled to 0 °C, and while stirring pyridine (604 µL, 7.5 mmol, 1.5 eq.), DMF (77 µL, 1.0 mmol, 0.2 eq.) and oxalyl chloride (557 µL, 6.5 mmol, 1.3 eq.) were added respectively. The solution was stirred for 10 min on ice. The suspension was diluted with pentane and filtered into a flask containing ketone **6** (938.6 mg, 3.75 mmol, 0.75 eq.), resulting in a clear liquid that was concentrated *in vacuo* under N_2 atmosphere to yield the crude acid chloride **5** combined with ketone **6** as a yellow oil. A solution of samarium(II)iodide (175 mL, 17.5 mmol, 3.5 eq. [0.1 M solution in THF, stabilized by samarium chips, Sigma-Aldrich]) was added to a flame dried flask which was under a constant gas flow of nitrogen. The samarium(II)iodide solution was heated to 50 °C followed by the addition of the crude acid chloride **5** and ketone **6** using a cannula. After 10 min the heat source was removed and the solution was quenched with air and diluted with EtOAc, aq. 1.0 M HCl and stirred for 30 min. The aqueous layer was extracted with EtOAc (3x) followed by washing the combined organic layers with sat. aq. NaS_2O_3. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product as a colorless oil. Flash column chromatography (90:10; pentane:Et_2O) afforded the title compound (2.21 g, 2.88 mmol, 82% based on **6**) as a colorless oil. TLC: R_f 0.6 (pentane:acetone, 9:1, v:v); $[\alpha]_D^{20}$ – 10.3° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 777, 811, 1108, 1255, 1472, 1706, 2856, 2929; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC):δ 7.84 – 7.18 (m, 12H, CH_{arom}), 4.73 (d, *J* = 11.5 Hz, 1H, C*H*H Bn/Nap), 4.68 (d, *J* = 3.3 Hz, 1H, H-1), 4.56 (d, *J* = 11.5 Hz, 1H, CH*H* Bn/Nap), 4.48 (d, *J* = 12.4 Hz, 1H, C*H*H Bn/Nap), 4.39 – 4.35 (m, 1H, H-9), 4.34 (d, *J* = 12.4 Hz, 1H, CH*H* Bn/Nap), 4.23 (q, *J* = 6.4 Hz, 1H, H-5), 3.89 (s, 1H, 4-OH), 3.83 (ddd, *J* = 11.7, 4.7, 3.3 Hz, 1H, H-2), 3.72 – 3.65 (m, 2H, H-10, H-11), 3.44 (s, 3H, CH_3 OMe), 3.27 (dd, *J* = 16.9, 10.1 Hz, 1H, H-8), 2.43 – 2.35 (m, 2H, H-3, H-8), 1.63 (dd, *J* = 12.4, 4.7 Hz, 1H, H-3), 1.18 (d, *J* = 5.8 Hz, 3H, H-12), 0.96 – 0.88 (m, 21H, H-6, $C(CH_3)_3$, $C(CH_3)_3$), 0.15 – 0.04 (m, 12H, $SiCH_3$, $SiCH_3$, $SiCH_3$, $SiCH_3$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 210.2 (C-7), 138.3, 135.8, 133.4, 133.0 ($C_{q\text{-}arom}$), 128.5, 128.1, 128.0, 127.9, 127.8, 126.3, 126.1, 125.9 (CH_{arom}), 98.1 (C-1), 81.1 (C-4), 78.1 (C-10/C-11), 77.2 (C-9), 72.8 (CH_2 Bn/Nap), 71.6 (C-2), 71.0 (CH_2 Bn/Nap), 70.1 (C-11/C-10), 65.2 (C-5), 55.4 (CH_3 OMe), 38.2 (C-8), 32.9 (C-3), 26.2, 26.0 (C(*C*H_3)$_3$), 20.8 (C-12), 18.5, 18.2 (*C*(CH_3)$_3$), 14.4 (C-6), -3.8, -4.0, -4.3, -4.6 ($SiCH_3$); HRMS: $[M+Na]^+$ calcd for $C_{43}H_{66}O_8Si_2Na$ 789.4194, found 789.4188.

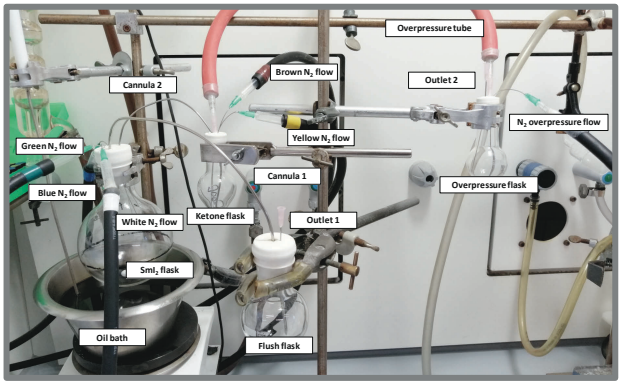


Figure S9. General setup of SmI_2-promoted C-C bond coupling.

Extra experimental details

Due to the direct oxidation of Sm(II) to the unreactive and more stable Sm(III) in the presence of oxygen, the C-C couplings have to be executed with great care and under completely inert conditions. The experimental setup can be found in Figure S8. The general procedure employed in the C-C couplings was as follows: Both the ketone flask and the SmI_2 flask seen in Figure S8 were flame dried, subsequently, the entire setup was flushed with N_2 (30 mbar overpressure) for 18 h. Then, pyranulose **6** was co-evaporated with toluene under N_2 atmosphere in a flame dried flask. Using an N_2 flushed syringe, the ketone was transferred to the ketone flask in THF. Subsequently, the acid chloride (1.33 eq.) was added to the ketone flask and N_2 was bubbled through the solution of ketone and acid chloride for 30 min through cannula 2 by closing the yellow, brown and overpressure N_2 flow and removing outlet 1. Simultaneously, SmI_2 (3.0 eq.) was added to the SmI_2 flask by transferring the flush flask side of cannula 1 and the green and white N_2 flow to a 0.1 M solution SmI_2 in THF, and closing the blue N_2 flow (Figure S9). Once the necessary amount of SmI_2 was transferred to the SmI_2 flask, cannula 1 was transferred from the 0.1 M solution SmI_2 in THF to the flush flask and the green and white N_2 flow tubes were transferred back to the SmI_2 flask. The SmI_2 flask was then heated to 50 °C using the oil bath. Once the SmI_2 flask reached a temperature of 50 °C, the solution of ketone and acid chloride was added to the SmI_2 flask through cannula 2 over a time span of approximately 10 seconds by removing outlet 2 and installing outlet 1, opening the yellow, brown and overpressure N_2 flows, and closing the green and white N_2 flows. After 15 min, the positive nitrogen flow was removed and a 1 M aq. HCl solution and EtOAc were added, followed by standard workup procedures.

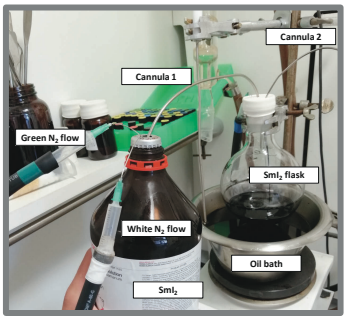
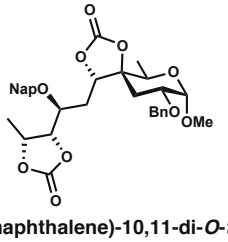
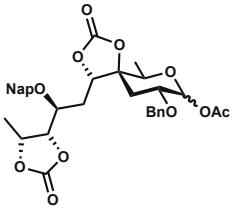


Figure S10. General setup for the addition of SmI_2 to the SmI_2 flask needed for the SmI_2-promoted C-C bond coupling.

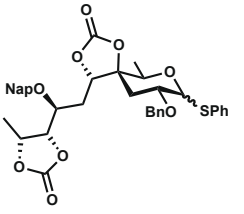


Methyl 2-*O*-benzyl-9-*O*-(2-methylnaphthalene)-10,11-di-*O*-*tert*-butyldimethylsilyl-α-D-caryophyllo-side (21). A $Zn(BH_4)_2$ solution was prepared by dissolving anhydrous $ZnCl_2$ (12.1 g, 88.5 mmol, 4.2 eq.) in dry THF (177 mL, 0.5 M), at 0 °C $NaBH_4$ (8.4 g, 221.3 mmol, 10.5 eq.) was added and the solution was stirred for 1 h. **20** (16.2 g, 21.1 mmol, 1.0 eq.) was dissolved in dry THF (422 mL, 0.05 M) after which it was cooled on ice, the $Zn(BH_4)_2$ solution was added. The solution was allowed to warm to room temperature and stirred for 16 h. The reaction was quenched with sat. aq. NH_4Cl and diluted with EtOAc and brine, the aqueous layer was extracted with EtOAc (3x) followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude products as an inseparable mixture. The mixture (14.9 g, 19.3 mmol, 1.0 eq.) was dissolved in methanol (568 mL, 0.034 M), a 6 M HCl aq. solution (32 mL, 10 eq.) was added and the mixture was stirred for 18 h upon which the reaction was quenched by neutralizing the acid with NaOMe. The reaction mixture was concentrated *in vacuo* to yield the crude products as an inseparable mixture. The mixture (8.4 g, 15.5 mmol) was dissolved in DCM (310 mL, 0.05 M) and CDI (7.6 g, 46.6 mmol, 3 eq.) was added. The resulting mixture was refluxed for 24 h. Upon full conversion, the reaction mixture

was concentrated in vacuo. Flash column chromatography (90:10 → 40:60; pentane:EtOAc) afforded the title compound (7.2 g, 12.2 mmol, 58% over 3 steps) as a white foam. TLC: R_f 0.7 (pentane:EtOAc, 4:6, v:v); $[\alpha]_D^{20}$ 149.0° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 1056, 1121, 1800; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.94 – 7.28 (m, 12H, CH_{arom}), 4.92 (p, *J* = 6.7 Hz, 1H, H-11), 4.79 (s, 2H, CH_2 Bn/Nap), 4.67 – 4.62 (m, 2H, H-1, H-10), 4.57 (d, *J* = 12.1 Hz, 1H, C*H*H Bn/Nap), 4.49 (d, *J* = 12.1 Hz, 1H, CH*H* Bn/Nap), 4.33 (dd, *J* = 11.4, 1.8 Hz, 1H, H-7), 4.03 (ddd, *J* = 9.5, 6.7, 3.1 Hz, 1H, H-9), 3.86 (q, *J* = 6.3 Hz, 1H, H-5), 3.75 (ddd, *J* = 11.7, 4.9, 3.5 Hz, 1H, H-2), 3.42 (s, 3H, CH_3 OMe), 2.12 (ddd, *J* = 14.7, 11.5, 3.1 Hz, 1H, H-8), 2.03 (dd, *J* = 13.4, 11.8 Hz, 1H, H-3), 1.95 (ddd, *J* = 14.9, 8.6, 1.9 Hz, 1H, H-8), 1.83 (dd, *J* = 13.5, 4.9 Hz, 1H, H-3), 1.46 (d, *J* = 6.7 Hz, 3H, H-12), 1.24 (d, *J* = 6.3 Hz, 3H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 153.6, 153.5 (O(C=O)O), 137.8, 134.2, 133.3, 133.3 ($C_{q\text{-}arom}$), 128.9, 128.7, 128.2, 128.1, 128.0, 127.9, 126.8, 126.8, 126.6, 125.4 (CH_{arom}), 96.9 (C-1), 84.8 (C-4), 81.0 (C-7), 79.0 (C-10), 75.8 (C-11), 73.9 (C-9), 73.7, 71.7 (CH_2 Bn/Nap), 71.4 (C-2), 64.7 (C-5), 55.9 (CH_3 OMe), 33.6 (C-3), 29.8 (C-8), 15.3 (C-12), 15.0 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{33}H_{36}O_{10}Na$ 615.2206, found 615.2215.



Acetyl 2-*O*-benzyl-4,7,10,11-di-*O*-carbonate-9-*O*-(2-methylnaphthalene)-D-caryophylloside (22). Compound **21** (6.4 g, 10.8 mmol) was dissolved in Ac_2O (216 mL, 0.05 M) and cooled on ice. H_2SO_4 (1.15 mL, 21.6 mmol, 2.0 eq.) was dissolved in Ac_2O (10 mL) and dropwise added to the solution of compound **21**. After stirring the solution for exactly 80 sec, the reaction mixture was poured into a mixture of sat. aq. $NaHCO_3$ and ice, and stirred for another 15 min. The aqueous layer was extracted twice with EtOAc followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (70:30 → 50:50; pentane:EtOAc) yielded the title compound (6.3 g, 10.2 mmol, 94%, α:β; 63:37) as a white foam. TLC: R_f 0.2 (pentane:EtOAc, 7:3, v:v); IR (neat, cm^{-1}): 752, 1054, 1086, 1200, 1229, 1751, 1797; Data of the major stereoisomer (α-anomer): ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.22 – 6.97 (m, 12H, CH_{arom}), 6.34 (d, *J* = 3.0 Hz, 1H, H-1), 4.95 (p, *J* = 6.9 Hz, 1H, H-11), 4.88 – 4.41 (m, 6H, H-7, H-10, CH_2 Bn/Nap, CH_2 Bn/Nap), 4.11 – 3.85 (m, 3H, H-2, H-5, H-9), 2.20 (s, 3H, CH_3 OAc), 2.16 – 1.96 (m, 4H, H-3, H-3, H-8, H-8), 1.48 (d, *J* = 6.6 Hz, 3H, H-12), 1.29 (d, *J* = 6.2 Hz, 3H, H-6); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 169.5 (C=O Ac), 153.6, 153.2(O(C=O)O), 137.3, 134.2, 134.0, 133.2 ($C_{q\text{-}arom}$), 128.8, 128.7, 128.7, 128.6, 127.9, 127.9, 127.7, 127.0, 126.7, 126.7, 125.6, 125.6 (CH_{arom}), 88.4 (C-1), 84.2 (C-4), 80.8 (C-7), 78.5 (C-10), 75.8 (C-11), 73.5 (C-9), 73.4, 71.8 (CH_2 Bn/Nap), 70.2 (C-2), 67.3 (C-5), 33.8 (C-3), 29.2 (C-8), 21.2 (CH_3 Ac), 15.1 (C-12), 15.0 (C-6); Diagnostic signals of the minor stereoisomer (β-isomer): ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.65 (d, *J* = 6.5 Hz, 1H, H-1), 2.13 (s, 3H, CH_3 Ac), 1.35 (d, *J* = 6.4 Hz, 3H, H-6); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 169.4 (C=O Ac), 153.7, 153.0 (O(C=O)O), 93.8 (C-1), 83.2 (C-4), 36.5 (C-3), 29.5 (C-8), 21.2 (CH_3 OAc), 15.8 (C-12), 15.2 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{34}H_{36}O_{11}Na$ 643.2155, found 643.2164.

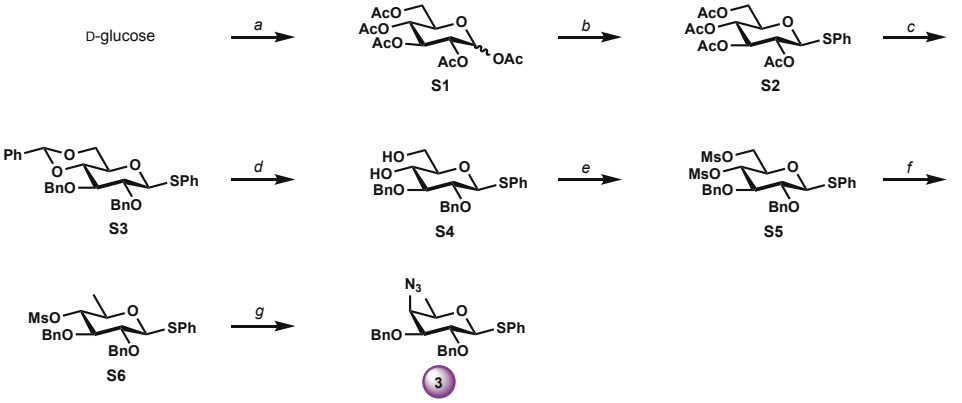


Phenyl 2-*O*-benzyl-4,7,10,11-di-*O*-carbonate-9-*O*-(2-methylnaphthalene)-1-thio-D-caryophylloside (4). Compound **22** (6.3 g, 10.15 mmol) was dissolved in DCM (101.5 mL, 0.1 M) and thiophenol (1.14 mL, 11.16 mmol, 1.1 eq.). Subsequently, the reaction mixture was cooled to –80 °C followed by the dropwise addition of $BF_3{\cdot}OEt_2$ (1.5 mL, 12.18 mmol, 1.2 eq.) and allowed to warm to room temperature overnight.

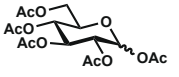
Upon full conversion, sat. aq. $NaHCO_3$ and EtOAc were added. The aqueous layer was extracted twice with EtOAc followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (80:20 → 70:30; pentane:EtOAc) yielded the title compound (4.2 g, 6.2 mmol, 61%, α:β; 49:51) as a white foam. TLC: R_f 0.7 (pentane:EtOAc, 6:4, v:v); IR (neat, cm^{-1}): 746, 1014, 1027, 1801; Data of the major stereoisomer (β-anomer): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.17 – 6.95 (m, 12H, CH_{arom}), 4.94 – 4.85 (m, 1H, H-11), 4.67 – 4.60 (m, 3H, C*H*H Bn/Nap, CH*H* Bn/Nap, H-10), 4.58 (d, *J* = 9.0 Hz, 1H, H-1), 4.52 – 4.44 (m, 2H, C*H*H Bn/Nap, CH*H* Bn/Nap), 4.11 – 3.97 (m, 2H, H-7, H-9), 3.70 – 3.55 (m, 2H, H-2, H-5), 2.21 – 2.10 (m, 1H, H-3), 2.10 – 2.02 (m, 1H, H-8), 1.98 – 1.88 (m, 2H, H-3, H-8), 1.44 (d, *J* = 6.7 Hz, 3H, H-12), 1.33 (d, *J* = 6.1 Hz, 3H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 153.6, 153.2 (O(C=O)O), 137.6, 137.2, 134.1, 133.3 ($C_{q\text{-}arom}$), 132.5, 131.5, 129.1, 128.6, 128.1, 127.9, 127.5, 127.0, 126.8, 126.7, 125.6, 125.5 (CH_{arom}), 88.5 (C-1), 84.2 (C-4), 78.7 (C-10), 75.7 (C-11), 74.9 (C-2/C-5), 74.0 (C-7/C-9), 73.9 (C-7/C-9), 72.9 (CH_2 Bn/Nap), 72.5 (C-2/C-5), 71.5 (CH_2 Bn/Nap), 39.5 (C-3), 29.4 (C-8), 15.7 (C-6), 15.2 (C-12); Diagnostic signals of the minor stereoisomer (α-isomer): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.62 (d, *J* = 4.8 Hz, 1H, H-1), 1.71 (dd, *J* = 14.1, 10.3 Hz, 1H, H-3), 1.46 (d, *J* = 6.6 Hz, 3H, H-12), 1.24 (d, *J* = 6.3 Hz, 3H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 153.6, 153.3 (O(C=O)O), 86.5 (C-1), 84.3 (C-4), 73.8, 73.7 (CH_2 Bn/Nap), 35.7 (C-3), 29.9 (C-8), 15.4 (C-6), 14.9 (C-12); HRMS: $[M+Na]^+$ calcd for $C_{38}H_{38}O_9SNa$ 693.2134, found 693.2145.

Preparation of donor 3

Scheme S1. Synthesis of 4,6-dideoxy-4-galactosazide donor **3**.

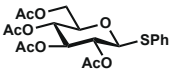


Reagents and conditions: a) Ac_2O, NaOAc, reflux (75%); b) PhSH, $BF_3{\cdot}OEt_2$, DCM (72%); c) *i.* NaOMe, MeOH; *ii.* $PhCH(OMe)_2$, *p*TsOH, 50 °C; *iii.* NaH, BnBr, DMF (91% over 3 steps); d) CSA, MeOH (71%); e) MsCl, pyridine (95%); f) $NaBH_4$, DMSO, 85 °C (67%); g) NaN_3, 1,3-dimethyl-3,4,5,6-tetrahydro-2-(*H*)-pyrimidone, 125 °C (62%).

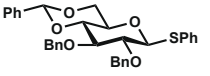


1,2,3,4,6-Penta-*O*-acetyl-D-glucopyranoside (S1). Sodium acetate (8.2 g, 100 mmol, 0.5 eq.) was dissolved in acetic anhydride (190 mL, 2.0 mol, 10 eq.) and heated to 140 °C. D-glucose (36.0 g, 200 mmol) was added portion-wise after which the solution was stirred another 15 min at 140 °C. After the solution had attained room temperature it was poured into a beaker containing ice water. The white precipitate formed on the bottom was collected and dissolved in DCM. The organic layer was washed with water (2x) followed by washing with a sat. aq. brine solution. The organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield a white crystalline solid. Recrystallized from hot EtOH yielded the title compound (58.3 g, 149 mmol, 75%, α:β; 8:92) as a white fluffy solid. TLC: R_f 0.5 (pentane:EtOAc, 9:1, v:v); IR (neat, cm^{-1}): 1036, 1075, 1213, 1367, 1750; Data of the major stereoisomer (β-anomer): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.70 (d, *J* = 8.3 Hz, 1H, H-1), 5.23 (t, *J* = 9.4 Hz, 1H, H-3), 5.16 – 5.01 (m, 2H, H-2, H-4), 4.27 (dd, *J* = 12.5, 4.5 Hz, 1H, H-6), 4.09 (dd, *J* = 12.5, 2.2 Hz, 1H, H-6), 3.82 (ddd, *J* = 10.1, 4.5, 2.2 Hz, 1H, H-5), 2.23 – 1.76 (m, 15H, $COCH_3$); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 170.7, 170.2, 169.5, 169.3,

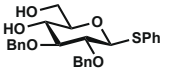
169.0 (*C*OCH$_3$), 91.8 (C-1), 72.9 (C-3), 72.8 (C-5), 70.3 (C-4/C-2), 67.9 (C-4/C-2), 61.6 (C-6), 20.9, 20.8, 20.7, 20.6, 20.5 (CO*C*H$_3$); Diagnostic signals of the minor stereoisomer (α-anomer): δ 6.31 (d, *J* = 3.7 Hz, 1H, H-1), 5.55 – 5.35 (t, *J* = 9.9 Hz, 1H , 1H, H-3); ^{13}C NMR (101 MHz, CDCl$_3$, HSQC): δ 170.3, 169.7, 168.8 (*C*OCH$_3$), 89.2 (C-1), 69.9 (C-4), 69.3 (C-2), 68.0 (C-6), 21.0, 20.8 (CO$_2$*C*H$_3$); HRMS: [M+Na]$^+$ calcd for $C_{16}H_{22}O_{11}Na$ 413.1060, found 413.1054.



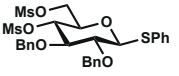
Phenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (S2). Compound **S1** (58.3 g, 149 mmol) was dissolved in DCM (0.5 M, 300 mL) and cooled on ice. While stirring, $BF_3{\cdot}OEt_2$ (27.3 mL, 223 mmol, 1.5 eq.) and thiophenol (22.9 mL, 223 mmol, 1.5 eq.) were added and consequently refluxed for 16 h. After cooling to room temperature, the solution was diluted with sat. aq. $NaHCO_3$ and Et_2O. The aqueous layer was extracted with Et_2O followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product as a white crystalline solid. Recrystallization from EtOAc/pentane yielded the title compound (44.9 g, 106 mmol, 72%) as a white fluffy solid. TLC: R_f 0.6 (pentane:EtOAc, 9:1, v:v); $[\alpha]_D^{20}$ – 10.4° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 1038, 1220, 1367, 1749; ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.53 – 7.44 (m, 2H, CH_{arom}), 7.32 (m, 3H, CH_{arom}), 5.22 (t, *J* = 9.4 Hz, 1H, H-3), 5.04 (t, *J* = 9.8 Hz, 1H, H-4), 4.97 (t, *J* = 9.7 Hz, 1H, H-2), 4.70 (d, *J* = 10.1 Hz, 1H, H-1), 4.20 (qd, *J* = 12.3, 3.8 Hz, 2H, H-6), 3.72 (ddd, *J* = 10.1, 5.1, 2.5 Hz, 1H, H-5), 2.10 – 1.97 (m, 12H, $COCH_3$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 170.7, 170.3, 169.5, 169.4 (*C*OCH$_3$), 133.2 (CH_{arom}), 131.8 ($C_{q\text{-}arom}$), 129.1, 128.5 (CH_{arom}), 85.9 (C-1), 75.9 (C-5), 74.1 (C-3), 70.1 (C-2), 68.3 (C-4), 62.3 (C-6), 20.9, 20.9, 20.7, 20.7 (CO*C*H$_3$); HRMS: [M+Na]$^+$ calcd for $C_{20}H_{24}O_9SNa$ 463.1039, found 463.1035.



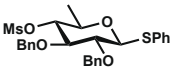
Phenyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (S3). Compound **S2** (44.9 g, 106 mmol) was dissolved in MeOH (0.2 M, 530 mL) followed by the addition of NaOMe (0.6 g, 10.6 mmol, 0.1 eq.). The solution was stirred for 18 h upon which the reaction was neutralized with amberlite H$^+$ (Sigma Aldrich Amberlite IR120 H$^+$ form, pre-washed with MeOH) and filtered over Celite© Hyflo Supercel (Merck). The methanol was removed under reduced pressure to yield the crude product **27** as a colorless oil. TLC: R_f 0.6 (EtOH:EtOAc, 1:2, v:v). The crude product **27** was then dissolved in DMF (56 mL) and CH_3CN (225 mL) followed by the addition of $PhCH(OMe)_2$ (22.3 mL, 148 mmol, 1.4 eq.) and *p*TsOH (1.0 g, 5.3 mmol, 0.05 eq.). After stirring for 5 h at 50 °C the reaction was quenched with solid $NaHCO_3$ (1.0 g). The solution was concentrated under reduced pressure to a fifth of its original volume and consequently diluted with EtOAc and water. The aqueous layer was extracted with Et_2O followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product as a brown oil. TLC: R_f 0.9 (EtOH:EtOAc, 1:2, v:v). The crude product was dissolved in DMF (0.3M, 350 mL) and cooled on ice. NaH (21.4 g, 530 mmol, 5.0 eq., 60% in mineral oil) was added followed by the portion-wise addition of BnBr (50.4 mL, 424 mmol, 4.0 eq.). The reaction mixture was allowed to reach room temperature and was stirred vigorously for 18 h. The reaction was quenched with water upon which the solution was diluted with EtOAc and water. The aqueous layer was extracted with EtOAc followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product as a yellow solid. Recrystallization from EtOAc/pentane yielded the title compound (52.0 g, 96.3 mmol, 91% over 3 steps) as a white crystalline solid. TLC: R_f 0.6 (pentane:EtOAc, 9:1, v:v); $[\alpha]_D^{20}$ –19.7° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 697, 747, 1028, 1092, 2872; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.65 – 7.28 (m, 20H, CH_{arom}), 5.60 (s, 1H, CHPh), 4.95 (d, *J* = 11.1 Hz, 1H, CH*H* Bn), 4.87 (d, *J* = 10.2 Hz, 1H, C*H*H Bn), 4.82 (d, *J* = 10.3 Hz, 1H, CH*H* Bn), 4.79 (d, *J* = 9.9 Hz, 1H, C*H*H Bn), 4.77 (d, *J* = 8.6 Hz, 1H, H-1), 4.40 (dd, *J* = 10.5, 5.0 Hz, 1H, H-6), 3.88 – 3.78 (m, 2H, H-6, H-3), 3.72 (t, *J* = 9.4 Hz, 1H, H-4), 3.52 (dd, *J* = 9.8, 8.3 Hz, 1H, H-2), 3.48 (dq, *J* = 9.8, 5.1 Hz, 1H, H-5); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 138.4, 138.1, 137.3, 133.2 ($C_{q\text{-}arom}$), 132.5, 129.2, 129.1, 128.5, 128.5, 128.4, 128.4, 128.3, 128.0, 128.0, 127.9, 126.1 (CH_{arom}), 101.2 (CHPh), 88.4 (C-1), 83.1 (C-3), 81.6 (C-4), 80.5 (C-2), 76.0, 75.5 (CH_2 Bn), 70.4 (C-5), 68.8 (C-6); HRMS: [M+Na]$^+$ calcd for $C_{33}H_{32}O_5SNa$ 563.1868, found.



Phenyl 2,3-di-*O*-benzyl-1-thio-β-D-glucopyranoside (S4). Compound **S3** (10.8 g, 20 mmol) was dissolved in MeOH (0.1 M, 200 mL), CSA (2.3 g, 10 mmol, 0.5 eq.) was added and the solution was stirred for 18 h at room temperature. Upon full conversion, solid $NaHCO_3$ was added and the solution was concentrated under reduced pressure to a fifth of its original volume upon which the mixture was diluted with EtOAc and water. The aqueous layer was extracted with EtOAc followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product as a colorless solid. Flash column chromatography (75:25 → 50:50; pentane:EtOAc) yielded the title compound (6.36 g, 14.1 mmol, 71%) as a colorless oil. TLC: R_f 0.3 (pentane:EtOAc, 1:1, v:v); $[\alpha]_D^{20}$ –30.8° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 695, 739, 1027, 1058, 1124, 2941, 3410; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.55 – 7.28 (m, 15H, CH_{arom}), 4.98 (m, 1H, CH*H* Bn), 4.95 (m, 1H, C*H*H Bn), 4.76 (d, *J* = 10.3 Hz, 1H, CH*H* Bn), 4.73 (d, *J* = 9.4 Hz, 1H, H-1), 4.71 (d, *J* = 11.5 Hz, 1H, C*H*H Bn), 3.88 (ddd, *J* = 11.8, 6.7, 3.5 Hz, 1H, H-6), 3.75 (ddd, *J* = 12.1, 6.8, 5.5 Hz, 1H, H-6), 3.58 (td, *J* = 9.1, 2.5 Hz, 1H, H-5), 3.56 – 3.47 (m, 2H, H-2, H-3), 3.38 – 3.33 (m, 1H, H-5), 2.20 (d, *J* = 2.6 Hz, 1H, 4-OH), 1.98 (t, *J* = 6.7 Hz, 1H, 6-OH); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 138.4, 137.9, 133.6 ($C_{q\text{-}arom}$), 131.9, 129.2, 128.9, 128.6, 128.4, 128.3, 128.2, 128.1, 127.9 (CH_{arom}), 87.9 (C-1), 86.2 (C-3), 81.1(C-2), 79.2 (C-5), 75.6, 75.6 (CH_2 Bn), 70.6 (C-4), 63.0 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{26}H_{28}O_5SNa$ 475.1555, found 475.1548.

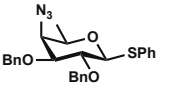


Phenyl 2,3-di-*O*-benzyl-4,6-di-*O*-methylsulfonyl-1-thio-β-D-glucopyranoside (S5). Compound **S4** (5.7 g, 12.7 mmol) was dissolved in pyridine (42 mL, 0.3 M) and cooled on ice. MsCl (3.9 mL, 50.8 mmol, 4.0 eq.) was added dropwise while stirring vigorously. The mixture was stirred for 2 h while attaining room temperature. Upon full conversion, the mixture was slowly poured on ice and EtOAc was added. The aqueous layer was extracted with EtOAc followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product as a yellow oil. Flash column chromatography (75:25 → 60:40; pentane:EtOAc) yielded the title compound (7.3 g, 12.0 mmol, 95%) as a colorless oil. TLC: R_f 0.5 (pentane:EtOAc, 2:1, v:v); $[\alpha]_D^{20}$ 13.2° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 699, 750, 817, 957, 996, 1175, 1356; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.60 – 7.53 (m, 2H, CH_{arom}), 7.41 – 7.27 (m, 13H, CH_{arom}), 4.99 (m, 2H, CH*H* Bn, C*H*H Bn), 4.77 – 4.66 (m, 3H, CH*H* Bn, C*H*H Bn, H-1), 4.57 (dd, *J* = 11.5, 2.4 Hz, 1H, H-6), 4.52 (t, *J* = 9.6 Hz, 1H, H-4), 4.38 (dd, *J* = 11.5, 5.8 Hz, 1H, H-6), 3.79 – 3.72 (m, 2H, H-5, H-3), 3.58 (dd, *J* = 9.7, 8.8 Hz, 1H, H-2), 3.02 (s, 3H, SO_2CH_3), 2.83 (s, 3H, SO_2CH_3); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 137.4, 137.3, 132.6 ($C_{q\text{-}arom}$), 132.5, 129.4, 128.7, 128.7, 128.4, 128.4, 128.3, 128.2, 127.6 (CH_{arom}), 87.8 (C-1), 83.2 (C-3), 81.1 (c-2), 76.8 (C-4), 75.9 (C-5), 75.7, 75.6 (CH_2 Bn), 68.0 (C-6), 38.7 (SO_2CH_3), 37.8 (SO_2CH_3); HRMS: $[M+Na]^+$ calcd for $C_{28}H_{32}O_9S_3Na$ 631.1106, found 631.1108.



Phenyl 2,3-di-*O*-benzyl-4-*O*-methylsulfonyl-6-deoxy-1-thio-β-D-glucopyranoside (S6). Compound **S5** (6.7 g, 11.0 mmol) was dissolved in DMSO (37 mL, 0.3 M) and subsequently $NaBH_4$ (2.3 g, 60.5 mmol, 5.5 eq.) was added. The reaction mixture was heated to 85 °C and stirred for 2 h. Upon full conversion, the reaction mixture was led to attain room temperature and poured out on ice and sat. aq. NH_4Cl. The mixture was filtered and rinsed with pentane to yield the crude product as a white crystalline solid. Recrystallization from EtOAc/pentane yielded the title compound (3.8 g, 7.4 mmol, 67%) as a white solid. TLC: R_f 0.8 (pentane:EtOAc, 2:1, v:v); $[\alpha]_D^{20}$ 15.9° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 698, 751, 813, 958, 1040, 1070, 1094, 1177, 1355, 2930; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.58 – 7.52 (m, 2H, CH_{arom}), 7.38 – 7.28 (m, 13H, CH_{arom}), 5.00 (m, 2H, CH*H* Bn, C*H*H Bn), 4.69 (m, 2H, CH*H* Bn, C*H*H Bn), 4.65 (d, *J* = 9.8 Hz, 1H, H-1), 4.30 (t, *J* = 9.5 Hz, 1H, H-4), 3.78 – 3.65 (m, 1H, H-3), 3.59 – 3.52 (m, 2H, H-5, H-2), 2.80 (s, 3H, SO_2CH_3), 1.44 (d, *J* = 6.2 Hz, 3H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 137.7, 137.6, 133.3 ($C_{q\text{-}arom}$), 132.4, 129.2, 128.7, 128.7, 128.4, 128.2, 128.1, 128.1, 127.5 (CH_{arom}), 87.7 (C-1), 83.5 (C-3), 82.5

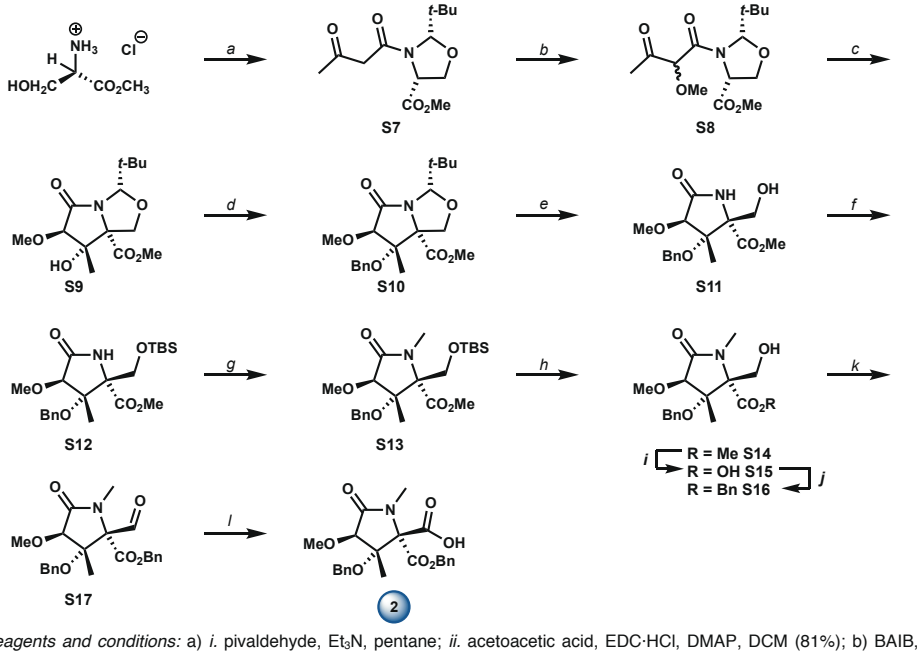
(C-4), 81.7 (C-2), 75.6, 75.6 (CH_2 Bn), 74.7 (C-5), 38.9 (SO_2CH_3), 18.2 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{27}H_{30}O_6S_2Na$ 537.1381, found 537.1379.



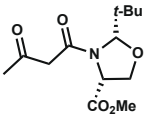
Phenyl 2,3-di-*O*-benzyl-4-azido-4,6-dideoxy-1-thio-β-D-galactopyranoside (3). Compound **S6** (3.81 g, 7.44 mmol) was dissolved in 1,3-dimethyl-3,4,5,6-tetrahydro-2-(*H*)-pyrimidone (15 mL, 0.5 M) and NaN_3 (725 mg, 11.2 mmol, 1.5 eq.) was added. The reaction mixture was heated to 125 °C and stirred for 18 h. Upon full conversion, the reaction was led to attain room temperature and diluted with water and EtOAc. The aqueous layer was extracted with EtOAc followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product as a white crystalline solid. Recrystallization from EtOH/pentane yielded the title compound (2.1 g, 4.6 mmol, 62%) as a white solid. TLC: R_f 0.5 (pentane:EtOAc, 9:1, v:v); $[\alpha]_D^{20}$ 15.7° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 697, 740, 1077, 1275, 1358, 1454, 2104; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.62 – 7.53 (m, 2H, CH_{arom}), 7.45 – 7.27 (m, 13H, CH_{arom}), 4.81 (d, *J* = 10.2 Hz, 1H, CH*H* Bn), 4.76 – 4.73 (m, 3H, C*H*H Bn, CH*H* Bn, C*H*H Bn), 4.67 – 4.44 (m, 1H, H-1), 3.86 – 3.65 (m, 3H, H-2, H-3, H-4), 3.57 (qd, *J* = 6.2, 0.9 Hz, 1H, H-5), 1.34 (d, *J* = 6.3 Hz, 3H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 138.2, 137.7, 133.8 ($C_{q\text{-}arom}$), 132.1, 128.9, 128.7, 128.5, 128.4, 128.1, 128.0, 127.9, 127.6 (CH_{arom}), 87.8 (C-1), 83.2 (C-3), 77.0 (C-2), 75.9 (CH_2 Bn), 73.3 (C-5), 72.9 (CH_2 Bn), 63.8 (C-4), 18.0 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{26}H_{27}O_3N_3SNa$ 484.1671, found 484.1668.

Preparation of compound 2

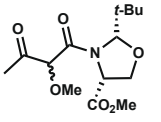
Scheme S2. Synthesis of compound **2**.



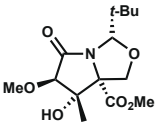
Reagents and conditions: a) *i.* pivaldehyde, Et_3N, pentane; *ii.* acetoacetic acid, EDC·HCl, DMAP, DCM (81%); b) BAIB, $BF_3{\cdot}OEt_2$, MeOH (64%); c) DBU, toluene (61%); d) BnBr, NaH, TBAI, DMF (95%); e) 1,3-propanedithiol, 37% HCl, TFE (*quant.*); f) TBSCl, imidazole, DCM (93%); g) MeI, NaH, DMF (95%); h) TBAF, THF (76%); i) LiOH·H_2O, THF, H_2O (*quant.*); j) *i.* Cs_2CO_3, MeOH, H_2O; *ii.* BnBr, DMF (*quant.*); k) TPAP, NMO, 4 Å MS, DCM (72%); l) $NaClO_2$, 20% aq. NaH_2PO_4, 2-methyl-2-butene, *t*-BuOH (*quant.*).



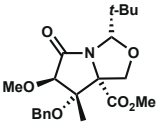
(2*S*,4*R*)-Methyl-2-(*tert*-butyl)-3-(3-oxobutanoyl)oxazolidine-4-carboxylate (S7). D-serine methyl ester hydrochloride (23 g, 150 mmol) was added to a stirred solution of pentane (750 mL, 0.2 M), Et_3N (27 mL, 195 mmol, 1.3 eq.) and *t*-butyl aldehyde (21 mL, 195 mmol, 1.3 eq.) at room temperature. The mixture was refluxed for 18 h using a Dean-Stark apparatus, upon cooling back to room temperature the emulsion was filtered off and the residue thoroughly washed with pentane. The combined filtrate was concentrated to yield crude product as a clear oil. Subsequently, the crude product was dissolved in dry DCM and cooled on ice. Acetoacetic acid (18.4 g, 180 mmol, 1.2 eq.), EDC·HCl (34.5 g, 180 mmol, 1.2 eq.) and DMAP (1.8 g, 15.0 mmol, 0.1 eq.) were added and the mixture was stirred for 18 h at room temperature. Upon full conversion, the solution was diluted with water and EtOAc, the aqueous layer was extracted with EtOAc followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (80:20 → 40:60; pentane:EtOAc) yielded the title compound (32.8 g, 121 mmol, 81% over 2 steps, keto-enol tautomers; 58:42) as a colorless oil. TLC: R_f 0.5 (pentane:EtOAc, 1:1, v:v); IR (neat, cm^{-1}): 1176, 1329, 1634, 1668, 1745, 2957; NMR data for keto form: ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.30 (s, 1H, C*H*C$(CH_3)_3$), 4.62 (d, *J* = 5.7 Hz, 1H, C*H*CO_2CH_3), 4.56 – 4.43 (m, 1H, OCH_2), 4.10 – 3.95 (m, 1H, OCH_2), 3.78 (s, 3H, CO_2CH_3) 3.74 (s, 2H, CH_2C=ON), 2.30 (s, 3H, CH_3CO), 0.91 (s, 9H, C$(CH_3)_3$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 202.8 (CH_3C=O), 170.1 (*C*O_2CH_3), 168.2 (NC=O), 96.8 (*C*HC$(CH_3)_3$), 68.0 (OCH_2), 59.6 (*C*HCO_2CH_3), 52.8 (*C*O_2CH_3), 52.0 (*C*H_2C=ON), 37.5 (*C*(CH_3), 25.9 (*C*H_3C=O), 25.8 (C(*C*H_3); data for enol form: ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): 5.09 (s, 1H, C*H*C$(CH_3)_3$), 4.56 – 4.43 (m, 1H, OCH_2), 4.10 – 3.95 (m, 1H, OCH_2), 3.79 (s, 2H, CO_2CH_3), 1.97 (s, 3H, CH_3CO), 0.92 (s, 9H, C$(CH_3)_3$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 176.6 (NC=O), 170.5 (*C*O_2CH_3), 89.7 (*C*CH$(CH_3)_3$, 68.0 (OCH_2), 52.9 (*C*O_2CH_3), 30.8 (*C*(CH_3), 26.5 (C(*C*H_3), 22.1 (CH_3C=O); HRMS: $[M+Na]^+$ calcd for $C_{13}H_{21}O_5NNa$ 294.1317, found 294.1317.



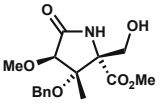
(2*S*,4*R*)-Methyl-2-(*tert*-butyl)-3-(2-methoxy-3-oxobutanoyl)oxazolidine-4-carboxylate (S8). To a vigorously stirred solution of BAIB (50.7 g, 157 mmol, 1.3 eq) in dry methanol (605 mL, 0.2 M) was dropwise added BF_3·OEt_2 (19.4 mL, 157 mmol, 1.3 eq.). After the solution became clear, **S7** (32.8 g, 121 mmol) in methanol (85 mL, 1.4 M) was added dropwise. The mixture was stirred for 18 h and subsequently concentrated until a fifth of its original volume. The BF_3·OEt_2 was quenched by the addition of a sat. aq. $NaHCO_3$ solution, the aqueous layer was extracted with EtOAc followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (90:10 → 70:30; pentane:EtOAc) yielded the title compound (23.3 g, 77 mmol, 64%, keto-enol tautomers; 95:5, diastereomeric mixture; 62:38) as a colorless oil. TLC: R_f 0.2 (pentane:EtOAc, 8:2, v:v); IR (neat, cm^{-1}): 1100, 1118, 1169, 1672, 1742, 2957; NMR data for major isomer: ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.27 (s, 1H, C*H*C$(CH_3)_3$), 5.26 (dd, *J* = 6.9, 1.8 Hz, 1H, C*H*CO_2CH_3), 4.69 (s, 1H, C*H*OCH_3), 4.56 (dd, *J* = 8.8, 1.7 Hz, 1H, OCH_2), 3.94 (dd, *J* = 8.9, 6.7 Hz, 1H, OCH_2), 3.78 (s, 3H, CO_2CH_3), 3.47 (s, 3H, $CHOCH_3$), 2.31 (s, 3H, CH_3C=O), 0.90 (s, 9H, C$(CH_3)_3$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 207.2 (CH_3C=O), 170.2 (*C*O_2CH_3), 168.0 (NC=O), 97.2 ((*C*HC(CH_3), 86.9 (*C*HOCH_3), 67.8 (OCH_2), 58.3 ($CH_2CO_2CH_3$), 57.6 (OCH_3), 52.8 (CO_2CH_3), 37.3 ((*C*$(CH_3)_3$), 26.9 (*C*H_3C=O), 25.9 ((C(*C*$H_3)_3$); NMR data for minor isomer: ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.35 (s, 1H, C*H*C$(CH_3)_3$), 4.75 (dd, *J* = 7.0, 2.3 Hz, 1H, C*H*CO_2CH_3), 4.59 (s, 1H, C*H*OCH_3), 4.42 (dd, *J* = 8.8, 2.4 Hz, 1H, OCH_2), 3.90 (dd, *J* = 8.8, 7.0 Hz, 1H, OCH_2), 3.78 (s, 3H, CO_2CH_3), 3.45 (s, 1H, CHOC*H*$_3$), 2.27 (s, 3H, CH_3C=O), 0.95 (s, 9H, C$(CH_3)_3$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 202.7 (CH_3CO), 170.1 (*C*O_2CH_3), 168.7 (NC=O), 97.7 (*C*HC$(CH_3)_3$), 88.9 (*C*HOCH_3), 69.9 (OCH_2), 59.4 (*C*HCO_2CH_3), 58.7 (OCH_3), 52.7 (CO_2CH_3), 37.2 (*C*$(CH_3)_3$), 27.1 (*C*H_3C=O), 26.1 (C(*C*$H_3)_3$); HRMS: $[M+Na]^+$ calcd for $C_{14}H_{23}O_6NNa$ 324.1423, found 324.1423.



(3*S*,6*R*,7*S*,7a*S*)-Methyl-3-(*tert*-butyl)-7-hydroxy-6-methoxy-7-methyl-5-oxohexahydropyrrolo [1,2-c]oxazole-7a-carboxylate (S9). Compound **S8** (23.3 g, 77.3 mmol) was dissolved in dry toluene (1.55 L, 0.05 M), after which DBU (5.8 mL, 38.7 mmol, 0.5 eq.) was added. After stirring for 18 h at 60 °C the solution was concentrated under reduced pressure to yield the crude product as a brown solid. Flash column chromatography (90:10 → 50:50; pentane:EtOAc) yielded the title compound (14.3 g, 47.4 mmol, 61%) as a colorless oil. TLC: R_f 0.4 (pentane:EtOAc, 4:6, v:v); IR (neat, cm^{-1}): 1095, 1215, 1290, 1320, 1730, 2958; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.84 (s, 1H, C*H*C(CH_3)$_3$), 4.57 (d, *J* = 9.4 Hz, 1H, OCH_2), 4.54 (s, 1H, C*H*OCH_3), 3.89 (d, *J* = 9.4 Hz, 1H, OCH_2), 3.74 (s, 3H, CO_2CH_3), 3.71 (s, 1H, OH), 3.58 (s, 3H, OCH_3), 1.25 (s, 3H, CCH_3), 0.80 (s, 9H, C(CH_3)$_3$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 173.4 (NC=O), 171.3 (*C*O_2CH_3), 95.9 (*C*HC(CH_3)$_3$), 85.7 (CH_3OCH), 81.3 (HO*C*CH_3), 76.1 (*C*CO_2CH_3), 69.0 (OCH_2), 59.7 (OCH_3), 52.7 (CO_2CH_3), 36.4 (*C*(CH_3)$_3$), 24.9 (C(*C*H_3)$_3$), 18.1 (C*C*H_3); HRMS: $[M+Na]^+$ calcd for $C_{14}H_{23}O_6NNa$ 324.1423, found 324.1425.

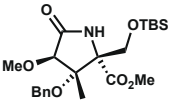


(3*S*,6*R*,7*S*,7a*S*)-Methyl-7-*O*-benzyl-3-(*tert*-butyl)-6-methoxy-7-methyl-5-oxohexahydro pyrrolo [1,2-c]oxazole-7a-carboxylate (S10). To a stirred solution of **S9** (14.3 g, 47.4 mmol) in DMF (66 mL, 0.7 M) and benzyl bromide (200 mL, 1.66 mol, 35 eq.) was added TBAI (21 g, 56.9 mmol, 1.2eq.). The solution was cooled to –15 °C and NaH (2.9 g, 71.1 mmol, 1.5 eq., 60% in mineral oil) was added in two portions. The solution was allowed to attain 0 °C followed by quenching the reaction with a sat. aq. NH_4Cl solution. The aqueous layer was extracted with EtOAc followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (95:5 → 80:20; pentane:EtOAc) yielded the title compound (17.6 g, 45.0 mmol, 95%) as a colorless oil. TLC: R_f 0.6 (pentane:EtOAc, 8:2, v:v); IR (neat, cm^{-1}): 1100, 1136, 1733, 2957; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.42 – 7.22 (m, 5H, CH_{arom}), 4.93 (s, 1H, C*H*C(CH_3)$_3$), 4.75 (d, *J* = 9.4 Hz, 1H, OCH_2), 4.73 (s, 1H, CH_3OCH), 4.55 (d, *J* = 11.1 Hz, 1H, CH*H* Bn), 4.48 (d, *J* = 11.1 Hz, 1H, C*H*H Bn), 4.01 (d, *J* = 9.4 Hz, 1H, OCH_2), 3.68 (s, 3H, CO_2CH_3), 3.65 (s, 3H, OCH_3), 1.37 (s, 3H, CCH_3), 0.89 (s, 9H, C(CH_3)$_3$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 173.4 (NC=O), 171.1 (*C*O_2CH_3), 137.9 ($C_{q\text{-}arom}$), 128.5, 127.8, 127.2 (CH_{arom}), 96.0 (*C*HC(CH_3)$_3$), 86.1 (*C*CH_3), 85.6 (CH_3OCH), 75.9 (*C*CO_2CH_3), 69.2 (OCH_2), 67.1 (CH_2 Bn), 59.4 (OCH_3), 52.8 (CO_2CH_3), 36.6 (*C*(CH_3), 25.1 (C(*C*H_3)$_3$), 14.0 (C*C*H_3); HRMS: $[M+Na]^+$ calcd for $C_{21}H_{29}O_6NNa$ 414.1893, found 414.1889.

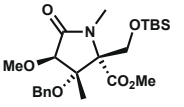


(2*S*,3*S*,4*R*)-Methyl-3-*O*-benzyl-2-(hydroxymethyl)-4-methoxy-3-methyl-5-oxopyrrolidine-2-carboxylate (S11). To a stirred solution of **S10** (17.6 g, 45.0 mmol) in CF_3CH_2OH (100 mL, 0.45 M) was added 1,3-propanedithiol (100 mL, 0.45 M) and 37% HCl aq. (1.4 mL, 17 mmol, 0.4 eq.). The solution was stirred for 2 h at 60 °C. Upon full conversion, the solution was allowed to attain room temperature and concentrated under reduced pressure to yield the crude product as a yellow oil subsequently. Flash column chromatography (40:60 → 10:90; pentane:EtOAc) yielded the title compound (14.3 g, 45.0 mmol, *quant.*) as a colorless oil. TLC: R_f 0.2 (pentane:EtOAc, 2:8, v:v); IR (neat, cm^{-1}): 1101, 1124, 1229, 1712, 3337; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.42 – 6.94 (m, 5H, CH_{arom}), 7.03 (s, 1H, NH) 4.58 (d, *J* = 11.4 Hz, 1H, CH*H* Bn), 4.47 (d, *J* = 11.4 Hz, 1H, C*H*H Bn), 4.22 (dd, *J* = 11.1, 6.5 Hz, 1H, CCH_2OH), 3.99 (s, 1H, CH_3OCH), 3.77 (dd, *J* = 11.1, 6.1 Hz, 1H, CCH_2OH), 3.71 (s, 3H, CO_2CH_3), 3.63 (s, 3H, OCH_3), 3.30 (t, *J* = 6.4 Hz, 1H, OH), 1.42 (s, 3H, CCH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 173.6 (NC=O), 171.1 (*C*O_2CH_3), 138.0 ($C_{q\text{-}arom}$), 128.4, 127.6, 126.9 (CH_{arom}), 84.4 (*C*CH_3), 82.6 (CH_3OCH), 72.7 (*C*CO_2CH_3),

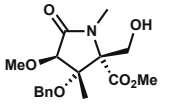
65.8 (CH_2 Bn), 64.6 (CCH_2OH), 59.5 (OCH_3), 52.9 (CO_2CH_3), 12.7(CCH_3); HRMS: $[M+Na]^+$ calcd for $C_{16}H_{21}O_6NNa$ 346.1267, found 346.1261.



(2*S*,3*S*,4*R*)-Methyl-3-*O*-benzyl-2-(*O*-(*tert*-butyldimethylsilyl)methyl)-4-methoxy-3-methyl-5-oxopyrrolidine-2-carboxylate (S12). Compound **S11** (14.3 g, 45.0 mmol) was dissolved in DCM (900 mL, 0.05 M) followed by the addition of TBSCl (10.2 g, 67.5 mmol, 1.5 eq.) and imidazole (4.6 g, 67.5 mmol, 1.5 eq.). The solution was stirred for 16 h at room temperature, and upon full conversion, the mixture was diluted with water and brine. The aqueous layer was extracted with EtOAc followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (90:10 → 70:30; pentane:EtOAc) yielded the title compound (18.0 g, 42.0 mmol, 93%) as a colorless oil. TLC: R_f 0.5 (pentane:EtOAc, 8:2, v:v); IR (neat, cm^{-1}): 837, 1088, 1252, 1720, 2951; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.42 – 7.18 (m, 5H, CH_{arom}), 6.21 (s, 1H, NH), 4.57 (d, J = 11.5 Hz, 1H, C*H*H Bn), 4.48 (d, J = 11.5 Hz, 1H, CH*H* Bn), 4.23 (d, J = 9.1 Hz, 1H, CCH_2OTBS), 3.88 (s, 1H, CH_3OCH), 3.68 (d, J = 9.0 Hz, 1H, CCH_2OTBS), 3.68 (s, 3H, CO_2CH_3), 3.63 (s, 3H, OCH_3), 1.41 (s, 3H, CCH_3), 0.85 (s, 9H, $SiC(CH_3)_3$), 0.05 (d, J = 6.4 Hz, 6H, $SiCH_3$, $SiCH_3$); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 172.6 (NC=O), 170.7 (CO_2CH_3), 138.1 ($C_{q\text{-}arom}$), 128.4, 127.6, 126.9 (CH_{arom}), 83.9 (CCH_3), 82.3 (CH_3OCH), 73.1 (CCO_2CH_3), 65.6 (CH_2 Bn), 65.6 (CCH_2OTBS), 59.4 (OCH_3), 52.6 (CO_2CH_3), 25.8 ($SiC(CH_3)_3$), 18.2 ($SiC(CH_3)_3$), 12.9 (CCH_3), -5.3 ($SiCH_3$), -5.6 ($SiCH_3$); HRMS: $[M+Na]^+$ calcd for $C_{22}H_{35}O_6NSiNa$ 460.2131, found 460.2127.

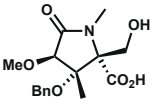


(2*S*,3*S*,4*R*)-Methyl-3-*O*-benzyl-2-(*O*-(*tert*-butyldimethylsilyl)methyl)-4-methoxy-1,3-dimethyl-5-oxopyrrolidine-2-carboxylate (S13). To a stirred solution of **S12** (530 mg, 1.23 mmol) in DMF (25 mL, 0.05 M) was added MeI (0.77 mL, 12.3 mL, 10.0 eq.). The mixture was cooled to 0 °C and NaH (128 mg, 3.2 mmol, 2.6 eq., 60% in mineral oil) was added. The mixture was allowed to attain room temperature, and upon full conversion, quenched with a sat. aq. NH_4Cl solution. The aqueous layer was extracted with EtOAc followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (90:10 → 70:30; pentane:EtOAc) yielded the title compound (518 mg, 1.16 mmol, 95%) as a colorless oil. TLC: R_f 0.4 (pentane:EtOAc, 9:1, v:v); IR (neat, cm^{-1}): 837, 1098, 1249, 1715, 2952; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.39 – 7.18 (m, 5H, CH_{arom}), 4.62 (d, J = 11.5 Hz, 1H, C*H*H Bn), 4.51 (d, J = 11.5 Hz, 1H, CH*H* Bn), 4.21 (d, J = 10.8 Hz, 1H, CCH_2OTBS), 3.99 (s, 1H, CH_3OCH), 3.96 (d, J = 10.8 Hz, 1H, CCH_2OTBS), 3.67 (s, 3H, OCH_3), 3.66 (s, 3H, CO_2CH_3), 2.92 (s, 3H, NCH_3), 1.39 (s, 3H, CCH_3), 0.87 (s, 9H, $SiC(CH_3)_3$), 0.08 (S, 3H, $SiCH_3$), 0.08 (S, 3H, $SiCH_3$); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 172.6 (NC=O), 170.3 (CO_2CH_3), 138.4 ($C_{q\text{-}arom}$), 128.4, 127.6, 126.9 (CH_{arom}), 83.3 (CCH_3), 82.5 (CH_3OCH), 75.2 (CCO_2CH_3), 65.9 (CH_2 Bn), 63.2 (CCH_2OTBS), 59.5 (OCH_3), 52.4 (CO_2CH_3), 28.5 (NCH_3), 25.8 ($SiC(CH_3)_3$), 18.1 ($SiC(CH_3)_3$), 13.4 (CCH_3), -5.6 ($SiCH_3$), -5.8 ($SiCH_3$); HRMS: $[M+Na]^+$ calcd for $C_{23}H_{37}O_6NSiNa$ 474.2288, found 474.2287.

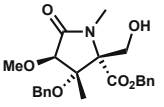


(2*S*,3*S*,4*R*)-Methyl-3-*O*-benzyl-2-(hydroxymethyl)-4-methoxy-1,3-dimethyl-5-oxopyrrolidine-2-carboxylate (S14). To a stirred solution of **S13** (18.7 g, 42 mmol) in THF (500 mL, 0.05 M) TBAF (210 mL, 1.0 M, 5.0 eq.) was added. The mixture was stirred for 3 h, and upon full conversion, quenched with water. The aqueous layer was extracted with EtOAc followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered,

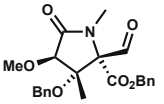
and concentrated *in vacuo* to yield the crude product. Flash column chromatography (70:30 → 30:70; pentane:EtOAc) yielded the title compound (10.5 g, 32.0 mmol, 76%) as a colorless oil. TLC: R_f 0.1 (pentane:EtOAc, 7:3, v:v); $[\alpha]_D^{20}$ 55.7° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 1099, 1273, 1700, 1736, 3427; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.38 – 7.18 (m, 5H, CH_{arom}), 4.64 (d, *J* = 11.6 Hz, 1H, C*H*H Bn), 4.50 (d, *J* = 11.6 Hz, 1H, CH*H* Bn), 4.09 (d, *J* = 12.2 Hz, 1H, CH_2OH), 4.07 (s, 1H, CH_3CH), 3.98 (d, *J* = 12.2 Hz, 1H, CH_2OH), 3.72 (s, 3H, CO_2CH_3), 3.70 (s, 3H, OCH_3), 2.89 (s, 3H, NCH_3), 2.76 (s, 1H, OH), 1.44 (s, 3H, CCH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 172.6 (NC=O), 167.9 (CO_2CH_3), 137.5 ($C_{q\text{-}arom}$), 128.6, 128.0, 127.1 (CH_{arom}), 84.5 (CCH_3), 82.4 (CH_3OCH), 80.3 (CCO_2CH_3), 67.0 (CH_2 Bn), 62.6 (CH_2OH), 59.5 (OCH_3), 53.4 (CO_2CH_3), 29.1 (NCH_3), 14.4 (CCH_3); HRMS: $[M+Na]^+$ calcd for $C_{17}H_{23}O_6NNa$ 360.1423, found 360.1421.



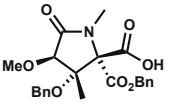
(2*S*,3*S*,4*R*)-3-*O*-Benzyl-2-(hydroxymethyl)-4-methoxy-1,3-dimethyl-5-oxopyrrolidine-2-carboxylic acid (S15). Compound **S14** (1.65 g, 5.0 mmol) was dissolved in THF (50 mL, 0.1 M) and H_2O (50 mL, 0.1 M), LiOH·H_2O (1.05 g, 25.0 mmol, 5.0 eq.) was added and the mixture was stirred for 18 h. Upon full conversion, the pH was adjusted with 1 M aq. HCl until a pH = 1 was obtained. The aqueous layer was extracted with EtOAc followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the product (1.58 g, 5.0 mmol, *quant.*) as a white solid. TLC: R_f 0.5 (DCM:MeOH, 8:2, v:v); $[\alpha]_D^{20}$ 29.0° (c 0.5, $CHCl_3$); IR (neat, cm^{-1}): 1099, 1213, 1453, 1691, 2944, 3434; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.34 – 7.16 (m, 5H, CH_{arom}), 4.62 (d, *J* = 11.7 Hz, 1H, C*H*H Bn), 4.49 (d, *J* = 11.7 Hz, 1H, CH*H* Bn), 4.14 – 4.05 (m, 2H, CH_2OH, CH_3CH), 3.98 (d, *J* = 12.4 Hz, 1H, CH_2OH), 3.64 (s, 3H, OCH_3), 2.89 (s, 3H, NCH_3), 1.44 (s, 3H, CCH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 173.7 (CO_2H), 172.7 (NC=O), 138.0 ($C_{q\text{-}arom}$), 128.4, 127.6, 126.8 (CH_{arom}), 83.5 (CCH_3), 81.9 (CH_3OCH), 74.8 (CCO_2H), 66.1 (CH_2 Bn), 62.3 (CH_2OH), 59.6 (OCH_3), 28.0 (NCH_3), 12.9 (CCH_3); HRMS: $[M+Na]^+$ calcd for $C_{16}H_{21}O_6NNa$ 346.1267, found 346.1261.



Benzyl-(2*S*,3*S*,4*R*)-Methyl-3-*O*-benzyl-2-(hydroxymethyl)-4-methoxy-1,3-dimethyl-5-oxopyrrolidine-2-carboxylate (S16). To a stirred solution of **S15** (535 mg, 1.7 mmol) in MeOH:H_2O (5:1, 3.4 mL, 0.5 M) was added Cs_2CO_3 (276 mg, 0.85 mmol, 0.5 eq.), after 30 min the mixture was concentrated under reduced pressure, co-evaporated to dryness with toluene (3x) and dissolved in DMF (8.5 mL, 0.2 M). The solution was cooled on ice and consequently BnBr (240 µL, 2.0 mmol, 1.2 eq.) was added. Upon 18 h of stirring the mixture was quenched with a sat. aq. NH_4Cl solution, the aqueous layer was extracted with EtOAc followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (50:50; pentane:EtOAc) yielded the title compound (889 mg, 1.7 mmol, *quant.*) as a colorless oil. TLC: R_f 0.4 (pentane:EtOAc, 1:1, v:v); $[\alpha]_D^{20}$ 69.3° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 1098, 1217, 1454, 1700, 3430; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.40 – 7.08 (m, 10H, CH_{arom}), 5.16 (d, *J* = 12.1 Hz, 1H, C*H*H Bn), 5.08 (d, *J* = 12.1 Hz, 1H, CH*H* Bn), 4.60 (d, *J* = 11.5 Hz, 1H, C*H*H Bn), 4.43 (d, *J* = 11.5 Hz, 1H, CH*H* Bn), 4.10 (dd, *J* = 12.4, 7.9 Hz, 1H, CH_2OH), 4.04 (s, 1H, CH_3OCH), 3.98 (dd, *J* = 12.4, 6.0 Hz, 1H, CH_2OH), 3.65 (s, 3H, OCH_3), 2.88 (s, 3H, NCH_3), 2.77 (dd, *J* = 7.9, 6.1 Hz, 1H, OH), 1.43 (s, 3H, CCH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 172.4 (CO_2H), 170.2 (NC=O), 138.1, 134.8 ($C_{q\text{-}arom}$), 128.8, 128.7, 128.5, 127.6, 127.0 (CH_{arom}), 83.5 (CCH_3), 82.1 (CH_3OCH), 74.9 (CCO_2Bn), 67.8, 66.1 (CH_2 Bn), 62.5 (CH_2OH), 59.5 (OCH_3), 27.9 (NCH_3), 12.9 (CCH_3); HRMS: $[M+Na]^+$ calcd for $C_{23}H_{27}O_6NNa$ 436.1736, found 436.1731.



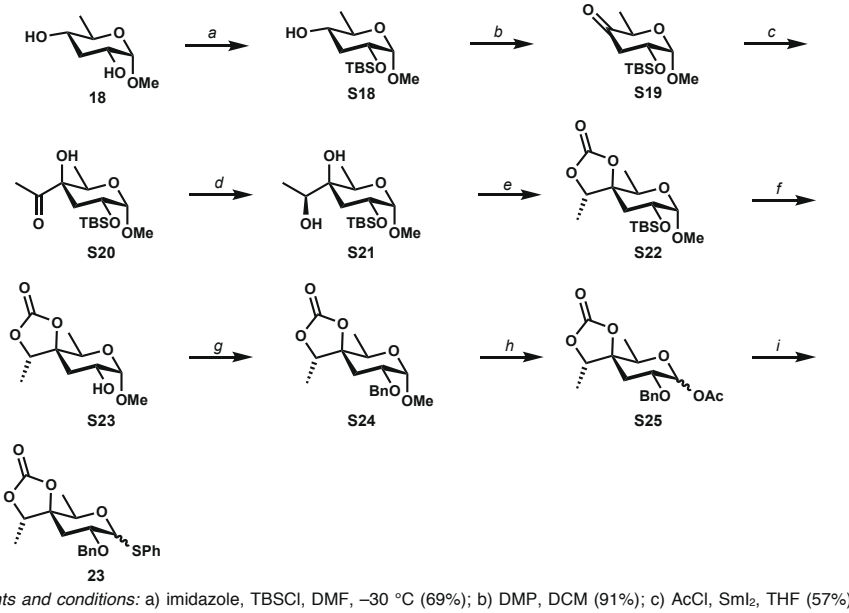
Benzyl-(2*R*,3*S*,4*R*)-Methyl-3-*O*-benzyl-2-formyl-4-methoxy-1,3-dimethyl-5-oxopyrrolidine-2-carboxylate (S17). Compound **S16** (774 mg, 1.9 mmol) was dissolved in dry DCM (38 mL, 0.05 M) and 4 Å molecular sieves were added. After stirring the solution for 30 min under an inert atmosphere, NMO (333 mg, 2.9 mmol, 1.5 eq.) and TPAP (33 mg, 0.1 mmol, 0.05 eq.) were added. Full conversion was achieved in approximately 6 h upon which the solution was concentrated to yield the crude product as a black oil. Flash column chromatography (90:10 → 80:20; pentane:EtOAc) yielded the title compound (551 mg, 1.37 mmol, 72%) as a colorless oil. TLC: R_f 0.8 (pentane:acetone, 8:2, v:v); $[\alpha]_D^{20}$ 56.9° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 1101, 1218, 1722, 3033; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 10.07 (s, 1H, CHO), 7.46 – 7.07 (m, 10H, CH_{arom}), 5.23 (d, *J* = 12.0 Hz, 1H, C*H*H Bn), 5.16 (d, *J* = 12.0 Hz, 1H, CH*H* Bn), 4.62 (d, *J* = 11.2 Hz, 1H, C*H*H Bn), 4.52 (d, *J* = 11.2 Hz, 1H, CH*H* Bn), 4.17 (s, 1H, CH_3OCH), 3.65 (s, 3H, OCH_3), 2.83 (s, 3H, NCH_3), 1.33 (s, 3H, CCH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 194.4 (CHO), 172.6 (CO_2Bn), 167.3 (NC=O), 137.5, 134.4 ($C_{q\text{-}arom}$), 128.9, 128.8, 128.6, 128.6, 128.0, 127.3 (CH_{arom}), 84.5 (*C*CH_3), 82.3 (CH_3OCH), 80.3 (*C*CO_2Bn), 68.5, 67.0 (CH_2 Bn), 59.5 (OCH_3), 29.1 (NCH_3), 14.4 (C*C*H_3); HRMS: $[M+Na]^+$ calcd for $C_{23}H_{25}O_6NNa$ 434.1580, found 434.1576.



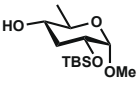
Benzyl-(2*R*,3*S*,4*R*)-3-*O*-benzyl-4-methoxy-2-(methoxycarbonyl)-1,3-dimethyl-5-oxopyrrolidine-2-carboxylic acid (2). A stirred solution of **S17** (551 mg, 1.37 mmol) in *t*-BuOH (15.6 mL, 0.1 M) and 2-methyl-2-butene (9.6 mL) was treated with an aqueous solution of $NaClO_2$ (1.23 g, 13.7 mmol, 10 eq.) in 20% NaH_2PO_4 (9.6 mL). After 2 h the mixture was quenched by adding sat. aq. NaS_2O_3 and sat. aq. NH_4Cl. The aqueous layer was extracted twice with EtOAc followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (50:50; pentane:EtOAc) yielded the title compound (889 mg, 1.7 mmol, *quant.*) as a colorless oil. TLC: R_f 0.4 (pentane:EtOAc, 1:1, v:v); $[\alpha]_D^{20}$ 64.3° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 1050, 1095, 1134, 1274, 1727, 2937; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.41 – 7.12 (m, 10H, CH_{arom}), 5.28 (d, *J* = 11.9 Hz, 1H, C*H*H Ph), 5.22 (d, *J* = 11.9 Hz, 1H, CH*H* Ph), 4.67 (d, *J* = 11.6 Hz, 1H, C*H*H Ph), 4.41 (d, *J* = 11.6 Hz, 1H, CH*H* Ph), 4.00 (s, 1H, CH_3OCH), 3.62 (s, 3H, OCH_3), 2.82 (s, 3H, NCH_3), 1.46 (s, 3H, CCH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 172.2 (NC=O), 170.4 (CO_2Bn), 164.8 (CO_2H), 137.4, 133.7 ($C_{q\text{-}arom}$), 129.4, 129.0, 128.9, 128.6, 128.0, 127.1 (CH_{arom}), 84.5 (*C*CH_3), 82.6 (CH_3OCH), 78.2 (*C*CO_2Bn), 69.8, 66.9 (CH_2 Bn), 59.6 (OCH_3), 28.9 (NCH_3), 15.3 (C*C*H_3); HRMS: $[M+Na]^+$ calcd for $C_{23}H_{25}O_7NNa$ 450.1529, found 450.1524.

Preparation of compound 23

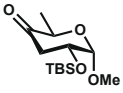
Scheme S3. Synthesis of compound **23**.



Reagents and conditions: a) imidazole, TBSCl, DMF, –30 °C (69%); b) DMP, DCM (91%); c) AcCl, SmI_2, THF (57%); d) $ZnBH_4$, THF (86%); e) triphosgene, pyridine, DCM (78%); f) HCl aq., MeOH (91%); g) benzyl 2,2,2-trichloroacetimidate, TfOH, dioxane (*quant.*); h) Ac_2O, H_2SO_4 (98%); i) thiophenol, $BF_3{\cdot}OEt_2$, DCM (97%).

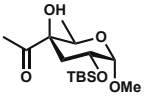


Methyl 3,6-dideoxy-2-*O*-*tert*-butyldimethylsilyl-α-D-allopyranoside (S18). Compound **18** (8.4 g, 51.5 mmol) and imidazole (6.8 g, 103 mmol, 2.0 eq.) were dissolved in DMF (103 mL, 0.5 M), the solution was cooled to –30 °C upon which TBSCl (8.2 g, 54 mmol, 1.05 eq.) was added. The mixture was stirred for 2 h while the mixture was allowed to warm to room temperature. Upon full conversion, the reaction was quenched with water and diluted with Et_2O. The aqueous layer was extracted with Et_2O (3x) followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product as a colorless oil. Flash column chromatography (95:5 → 80:20; pentane:EtOAc) yielded the title compound (9.9 g, 35.7 mmol, 69%) as a colorless oil. TLC: R_f 0.8 (pentane:EtOAc, 7:3, v:v); $[\alpha]_D^{20}$ 36.4° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 1260, 2930, 3445; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.48 (d, *J* = 3.4 Hz, 1H, H-1), 3.78 (ddd, *J* = 11.7, 4.7, 3.5 Hz, 1H, H-2), 3.53 (dq, *J* = 9.0, 6.2 Hz, 1H, H-5), 3.42 (s, 3H, CH_3 OMe), 3.28 (ddd, *J* = 11.2, 9.2, 4.6 Hz, 1H, H-4), 2.03 (dt, *J* = 11.6, 4.6 Hz, 1H, H-3), 1.90 (s, 1H, 4-OH), 1.82 (q, *J* = 11.5 Hz, 1H, H-3), 1.25 (d, *J* = 6.2 Hz, 3H, H-6), 0.89 (s, 9H, $C(CH_3)_3$), 0.08 (s, 6H, $Si(CH_3)_2$); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 99.3 (C-1), 71.2 (C-4), 68.9 (C-2), 68.5 (C-5), 55.2 (CH_3 OMe), 36.8 (C-3), 26.0 ($C(CH_3)_3$), 18.4 ($C(CH_3)_3$), 17.5 (C-6), -4.5 ($SiCH_3$), -4.6 ($SiCH_3$); HRMS: $[M+Na]^+$ calcd for $C_{13}H_{28}O_4SiNa$ 299.1655, found 299.1654.

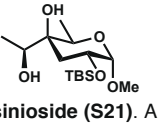


Methyl 3,6-dideoxy-2-*O*-*tert*-butyldimethylsilyl-α-D-erythropyranosid-4-ulose (S19). Compound **S18** (9.8 g, 35.7 mmol) was dissolved in DCM (210 mL, 0.17 M) under N_2 atmosphere. Dess-Martin periodinane (22.7 g, 53.6 mmol, 1.5 eq.) was added and the mixture was stirred for 4.5 h upon the reaction was quenched with water. The aqueous layer was extracted with DCM (3x) followed by washing the combined

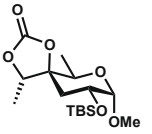
organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product as a white oil. Flash column chromatography (95:5 → 90:10; pentane:Et_2O) yielded the title compound (8.9 g, 32.5 mmol, 91%) as a colorless oil. TLC: R_f 0.5 (pentane:Et_2O, 9:1, v:v); $[\alpha]_D^{20}$ –8.0° (c 0.5, $CHCl_3$); IR (neat, cm^{-1}): 1119, 1261, 1728, 1794, 2857, 2930; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.71 (d, *J* = 3.3 Hz, 1H, H-1), 4.17 – 4.07 (m, 2H, H-5 and H-2), 3.53 (s, 3H, CH_3 OMe), 2.76 (dd, *J* = 15.2, 10.8 Hz, 1H, H-3), 2.61 (dd, *J* = 15.3, 5.6 Hz, 1H, H-3), 1.27 (d, *J* = 6.7 Hz, 3H, CH_3 H-6), 0.89 (s, 9H, $C(CH_3)_3$), 0.09 (s, 3H, $SiCH_3$), 0.08 (s, 3H, $SiCH_3$); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 206.8 (C-4), 99.4 (C-1), 70.1 (C-5), 69.3 (C-2), 56.1 (CH_3 OMe), 44.0 (C-3), 25.9 ($C(CH_3)_3$), 18.3 ($(C(CH_3)_3$), 14.6 (C-6), -4.6 ($SiCH_3$); HRMS: $[M+Na]^+$ calcd for $C_{13}H_{26}O_4SiNa$ 297.1498, found 297.1496.



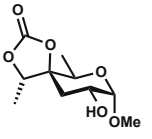
Methyl 4-*C*-acetyl-3,6-dideoxy-2-*O*-*tert*-butyldimethylsilyl-α-D-galactopyranoside (S20). Compound **S19** (221 mg, 0.8 mmol) was co-evaporated with dry toluene once under N_2 atmosphere. Glycoside **S19** was dissolved in THF (1.6 mL, 0.5 M) and cooled to –80 °C. The solution was flushed with N_2 with 30 mbar overpressure for 25 min, after which AcCl (143 µL, 2 mmol, 2.5 eq.) was added and the solution was flushed with N_2 with 30 mbar overpressure for another 5 min. A flame-dried flask was flushed with N_2 by using a Schlenk line for 16 h. After flushing the flask, it was filled with SmI_2 (28 mL, 2.8 mmol, 3.5 eq, [0.1 M solution in THF, stabilized by samarium chips, Sigma-Aldrich]) by using a pre-flushed cannula. The flask with SmI_2 was heated to 40 °C and the solution of ketone **S19** and AcCl in THF was added with a syringe. The reaction was quenched after 10 min with 20 mL 1 M HCl, diluted with 20 mL EtOAc and stirred for 30 min. The mixture was washed with H_2O, sat. aq. $Na_2S_2O_3$ and brine, respectively. The organic phase was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Flash column chromatography (90:10; pentane:EtOAc) afforded the title compound (145 mg, 455 µmol, 57%) as a colorless oil. TLC: R_f 0.3 (pentane:Et_2O, 8:2, v:v); $[\alpha]_D^{20}$ 42.4° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 1115, 1263, 1709, 2930, 3455; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC): δ 4.63 (d, *J* = 3.4 Hz, 1H, H-1), 4.23 (q, *J* = 6.4 Hz, 1H, H-5), 4.17 (ddd, *J* = 11.5, 4.9, 3.5 Hz, 1H, H-2), 3.95 (s, 1H, 4-OH), 3.50 (s, 3H, CH_3 OMe), 2.32 (t, *J* = 11.9 Hz, 1H, H-3), 2.25 (s, 3H, H-8), 1.60 (ddd, *J* = 12.3, 4.9, 0.9 Hz, 1H, H-3), 0.96 (d, *J* = 6.5 Hz, 3H, H-6), 0.89 (s, 9H, $C(CH_3)_3$), 0.09 (s, 3H, $SiCH_3$), 0.08 (1s, 3H, $SiCH_3$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC): δ 208.5 (C-7), 100.0 (C-1), 81.1 (C-4), 66.0 (C-2), 65.3 (C-5), 55.9 (CH_3 OMe), 36.4 (C-3), 25.9 ($C(CH_3)_3$), 24.5 (C-8), 18.3 ($C(CH_3)_3$), 14.1 (C-6), -4.5 ($SiCH_3$), -4.6 ($SiCH_3$); HRMS: $[M+Na]^+$ calcd for $C_{15}H_{30}O_5SiNa$ 341.1759, found 341.1760.



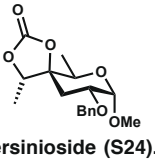
Methyl 2-*O*-*tert*-butyldimethylsilyl-α-D-yersinioside (S21). A solution of $ZnBH_4$ was made by dissolving ZnCl (572 mg, 4.2 mmol, 4.2 eq.) and $NaBH_4$ (397 mg, 10.5 mmol, 10.5 eq.) in THF (8.4 mL, 0.5 M) at 0 °C. This solution was stirred for 1 h at 0 °C. A solution of glycoside S20 (325 mg, 1.0 mmol) in THF (20 mL, 50 mM) was cooled to 0 °C and the $ZnBH_4$ solution was added. The reaction mixture was stirred for 24 h at room temperature and quenched with sat. NH_4Cl. The aqueous layer was extracted with EtOAc (2x), followed by washing the combined organic layers with brine. The organic phase was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash column chromatography (80:20 → 60:40, pentane:EtOAc) afforded the title compound (275 mg, 860 µmol, 86%) as a colorless oil. TLC: R_f 0.4 (pentane:EtOAc, 6:4, v:v); $[\alpha]_D^{20}$ 40.9° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 1263, 2930, 3424; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.54 (d, *J* = 3.7 Hz, 1H, H-1), 4.06 (q, *J* = 5.9, 5.1 Hz, 1H, H-5), 4.03 (ddd, *J* = 9.0, 6.3, 4.4 Hz, 1H, H-2), 3.68 (m, *J* = 13.5, 6.6 Hz, 1H, H-7), 3.43 (s, 3H, CH_3 OMe), 2.38 (s, 1H, 4-OH), 2.12 (s, 1H, 7-OH), 1.89 (m, 1H, H-3), 1.59 (ddd, *J* = 12.7, 5.3, 0.9 Hz, 1H, H-3), 1.22 (d, *J* = 6.6 Hz, 3H, H-8), 1.19 (d, *J* = 6.5 Hz, 3H, H-6), 0.90 (s, 9H, $C(CH_3)_3$), 0.09 (s, 6H, $SiCH_3$, $SiCH_3$); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 99.6 (C-1), 74.9 (C-4), 72.1 (C-7), 67.0 (C-2), 65.7 (C-5), 55.6 (CH_3 OMe), 35.4 (C-3), 26.0 ($C(CH_3)_3$), 18.4 ($C(CH_3)_3$), 17.2 (C-8), 14.5 (C-6), -4.5 ($SiCH_3$), -4.5 ($SiCH_3$); HRMS: $[M+Na]^+$ calcd for $C_{15}H_{32}O_5SiNa$ 343.1916, found 343.1917.



Methyl 2-*O*-*tert*-butyldimethylsilyl-4,7-*O*-carbonate-α-D-yersinioside (S22). Compound **S21** (270 mg, 840 µmol) was dissolved in dry DCM (1 mL, 0.4 M) and pyridine (0.5 mL, 6.3 mmol, 7.5 eq.) and cooled on ice. While stirring, triphosgene (124 mg, 0.42 mmol, 0.5 eq.) dissolved in 1.1 mL dry DCM was added dropwise and the mixture was stirred at 0 °C for 16 h. Upon full conversion, the reaction was quenched with ice-cooled sat. aq. NH_4Cl and diluted with EtOAc. The aqueous layer was extracted twice with EtOAc followed by washing the combined organic layers with brine. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (95:5 → 80:20; pentane:EtOAc) yielded the title compound (226 mg, 650 µmol, 78%) as a white solid. TLC: R_f 0.7 (pentane:EtOAc, 8:2, v:v); $[\alpha]_D^{20}$ 67.0° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 1007, 1054, 1066, 1088, 1812, 2929; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, NOESY) δ 4.55 (d, *J* = 3.4 Hz, 1H, H-1), 4.34 (q, *J* = 6.9 Hz, 1H, H-7), 4.05 (ddd, *J* = 11.6, 5.0, 3.5 Hz, 1H, H-2), 3.90 (q, *J* = 6.3 Hz, 1H, H-5), 3.44 (s, 3H, OCH_3), 2.07 (dd, *J* = 13.5, 11.7 Hz, 1H, H-3), 1.84 (dd, *J* = 13.5, 4.9 Hz, 1H, H-3), 1.44 (d, *J* = 6.9 Hz, 3H, H-8), 1.28 (d, *J* = 6.4 Hz, 3H, H-6), 0.89 (s, 9H, $SiC(CH_3)_3$), 0.08 (s, 6H, $SiCH_3$, $SiCH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.2 (O(C=O)O), 99.0 (C-1), 85.0 (C-4), 81.5 (C-7), 66.0 (C-2), 64.6 (C-5), 55.9 (OCH_3), 36.4 (C-3), 25.8 ($SiC(CH_3)_3$), 18.2 ($SiC(CH_3)_3$),14.7 (C-6), 13.1 (C-8), -4.6 ($SiCH_3$), -4.6 ($SiCH_3$); HRMS: $[M+Na]^+$ calcd for $C_{16}H_{30}O_6SiNa$ 369.1709, found 369.1710.

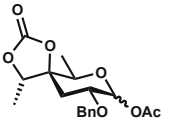


Methyl 4,7-*O*-carbonate-α-D-yersinioside (S23). To a stirred solution of **S22** (230 mg, 660 µmol) in MeOH (19.4 mL, 0.034 M) was added a 6 M aq. HCl solution (1.1 mL, 6.6 mmol, 10 eq.). Upon full conversion, the mixture was neutralized by addition of Amberlite IRA-67 (Sigma Aldrich Amberlite IRA-67 free base, pre-washed with MeOH), filtered, and concentrated under reduced pressure to yield the crude product. Flash column chromatography (50:50 → 0:100; pentane:EtOAc) yielded the title compound (139.3 mg, 0.6 mmol, 91%) as a white solid. TLC: R_f 0.1 (pentane:EtOAc, 1:1, v:v); $[\alpha]_D^{20}$ 125.2° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 1008, 1051, 1063, 1201, 1788, 1807, 3460; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.68 (d, *J* = 3.7 Hz, 1H, H-1), 4.36 (q, *J* = 6.9 Hz, 1H, H-7), 3.97 (dddd, *J* = 11.4, 10.2, 5.1, 3.7 Hz, 1H, H-2), 3.87 (q, *J* = 6.3 Hz, 1H, H-5), 3.46 (s, 3H, CH_3 OCH_3), 2.04 (dd, *J* = 13.4, 5.1 Hz, 1H, H-3), 1.98 (d, *J* = 10.2 Hz, 1H, 2-OH), 1.90 (dd, *J* = 13.4, 11.5 Hz, 1H, H-3), 1.45 (d, *J* = 6.9 Hz, 3H, H-8), 1.29 (d, *J* = 6.4 Hz, 2H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$): δ 154.1 (O(C=O)O), 98.1 (C-1), 84.6 (C-4), 81.6 (C-7), 65.0 (C-2), 64.8 (C-5), 55.8 (CH_3 OCH_3), 36.4 (C-3), 14.8 (C-6), 13.1 (C-8); HRMS: $[M+Na]^+$ calcd for $C_{10}H_{16}O_6Na$ 255.0845, found 255.0845.

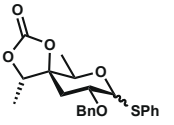


Methyl 2-*O*-benzyl-4,7-*O*-carbonate-α-D-yersinioside (S24). To a stirred solution of **S23** (251 mg, 1.1 mmol) in dioxane (10.8 mL, 0.1 M) was added benzyl 2,2,2-trichloroacetimidate (0.4 mL, 2.2 mmol, 2.0 eq.) followed by the addition of TfOH (19.1 µL, 216 µmol, 0.2 eq.). After stirring for 60 min at room temperature the reaction was quenched by addition of sat. aq. $NaHCO_3$ and diluted with EtOAc. The aqueous layer was extracted twice with EtOAc followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (80:20 → 50:50; pentane:EtOAc) yielded the title compound (354 mg, 1.1 mmol, *quant.*) as a white solid. TLC: R_f 0.5 (pentane:EtOAc, 1:1, v:v); $[\alpha]_D^{20}$ 55.9° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 1008, 1052, 1065, 1086, 1206, 1273, 1727, 1792, 1807; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.38 – 7.27 (m, 5H, CH_{arom}), 4.65 (d, *J* = 3.3 Hz, 1H, H-1), 4.61 (d,

J = 12.1 Hz, 1H, C*H*H Bn), 4.56 (d, *J* = 12.1 Hz, 1H, CH*H* Bn), 4.33 (q, *J* = 6.9 Hz, 1H, H-7), 3.89 (q, *J* = 6.3 Hz, 1H, H-5), 3.81 (ddd, *J* = 11.7, 5.0, 3.4 Hz, 1H, H-2), 3.41 (s, 3H,CH_3 OCH_3), 2.07 (dd, *J* = 13.4, 11.8 Hz, 1H, H-3), 1.98 (dd, *J* = 13.5, 5.0 Hz, 1H, H-3), 1.44 (d, *J* = 6.9 Hz, 3H, H-8), 1.26 (d, *J* = 6.4 Hz, 3H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 154.1 (O(C=O)O), 137.8 ($C_{q\text{-}arom}$), 128.7, 128.2, 128.0 (CH_{arom}), 96.9 (C-1), 84.8 (C-4), 81.5 (C-7), 71.8 (CH_2 Bn), 71.6 (C-2), 64.8 (C-5), 55.7 (CH_3 OCH_3), 33.6 (C-3), 14.8 (C-6), 13.1 (C-8); HRMS: $[M+Na]^+$ calcd for $C_{17}H_{22}O_6Na$ 345.1314, found 345.1316.



Acetyl 2-*O*-benzyl-4,7-*O*-carbonate-D-yersinioside (S25). Compound **S24** (83 mg, 260 µmol) was dissolved in Ac_2O (4.7 mL, 0.05 M) and cooled on ice. Subsequently, H_2SO_4 (28 µL, 0.5 mmol, 2.0 eq.) was dissolved in 0.5 mL Ac_2O and added dropwise to the mixture. After stirring the solution for exactly 2 min, sat. aq. $NaHCO_3$ and EtOAc were added dropwise and stirred for another 15 min. The aqueous layer was extracted twice with EtOAc followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (80:20 → 50:50; pentane:EtOAc yielded the title compound (89 mg, 254 µmol, 98%, α:β; 66:34) as a white solid. TLC: R_f 0.5 (pentane:EtOAc, 1:1, v:v); IR (neat, cm^{-1}): 1009, 1064, 1091, 1227, 1751, 1805; Data of the major stereoisomer (α-anomer): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.39 – 7.24 (m, 5H, CH_{arom}), 6.33 (d, *J* = 3.3 Hz, 1H, H-1), 4.63 (d, *J* = 11.6 Hz, 1H, C*H*H Bn), 4.52 (d, *J* = 11.6 Hz, 1H, CH*H* Bn), 4.38 (q, *J* = 6.9 Hz, 1H, H-7), 4.00 (q, *J* = 6.3 Hz, 1H, H-5), 3.93 (ddd, *J* = 9.9, 6.9, 3.4 Hz, 1H, H-2), 2.16 (s, 3H, $COCH_3$), 2.10 – 2.06 (m, 2H, H-3, H-3), 1.47 (d, *J* = 6.9 Hz, 3H, H-8), 1.28 (d, *J* = 6.3 Hz, 3H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 169.4 (C=O OAc), 153.8 (O(C=O)O), 137.4 ($C_{q\text{-}arom}$), 128.7, 128.7,128.2, 127.9, 127.7 (CH_{arom}), 88.6 (C-1), 81.5 (C-7), 72.0 (CH_2 Bn), 70.4 (C-2), 67.5 (C-5), 33.9 (C-3), 21.1 (CH_3 Ac), 14.9 (C-6), 13.2 (C-8); Diagnostic signals of the minor stereoisomer (β-anomer): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.60 (d, *J* = 7.3 Hz, 1H, H-1), 4.47 (q, *J* = 6.8 Hz, 1H, H-7), 3.75 (ddd, *J* = 10.2, 7.2, 5.1 Hz, 1H, H-2), 2.34 (dd, *J* = 14.3, 5.1 Hz, 1H, H-3), 2.12 (s, 3H, $COCH_3$), 1.85 (dd, *J* = 14.3, 10.2 Hz, 1H, H-3), 1.45 (d, *J* = 6.9 Hz, 3H, H-8), 1.35 (d, *J* = 6.3 Hz, 3H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 169.6 (C=O OAc), 153.7 (O(C=O)O), 137.7 ($C_{q\text{-}arom}$), 94.4 (C-1), 80.8 (C-7), 73.1 (CH_2 Bn), 72.8 (C-2), 72.6 (C-5), 37.6 (C-3), 21.2 (CH_3 Ac), 15.4 (C-6), 13.3 (C-8); HRMS: $[M+Na]^+$ calcd for $C_{18}H_{22}O_7Na$ 373.1263, found 373.1259.

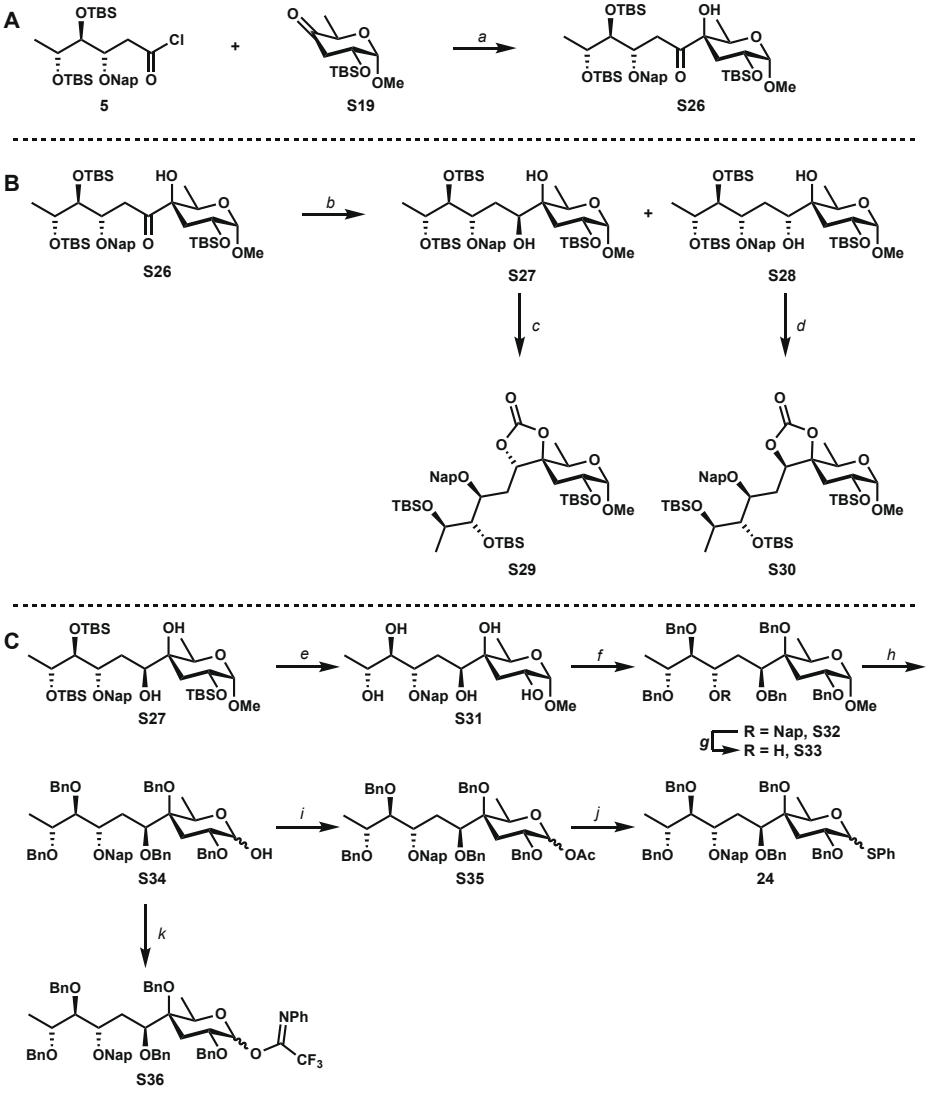


Phenyl 2-*O*-benzyl-4,7-*O*-carbonate-1-thio-D-yersinioside (23). Compound **S25** (347 mg, 990 µmol) was dissolved in DCM (9.9 mL, 0.1 M) and thiophenol (111 µL, 1.1 mmol, 1.1 eq.) was added. Subsequently, the solution was cooled to –80 °C and $BF_3{\cdot}OEt_2$ (147 µL, 1.2 mmol, 1.2 eq.) was added dropwise, the solution was stirred for 16 h while attaining to 0 °C. Upon full conversion, the reaction was quenched with sat. aq. $NaHCO_3$ and diluted with EtOAc. The aqueous layer was extracted twice with EtOAc followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (90:10 → 60:40; pentane:EtOAc) yielded the title compound (383 mg, 956 µmol, 97%, α:β; 56:44) as a colorless oil. TLC: R_f 0.2 (pentane:EtOAc, 9:1, v:v); IR (neat, cm^{-1}): 693, 1009, 1069, 1199, 1793, 1805; Data of the major stereoisomer (α-anomer): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.64 – 7.23 (m, 10H, CH_{arom}), 5.68 (d, *J* = 4.6 Hz, 1H, H-1), 4.71 (d, *J* = 11.5 Hz, 1H, C*H*H Bn), 4.55 (d, *J* = 11.5 Hz, 1H, H-3 CH*H* Bn), 4.45 (q, *J* = 6.3 Hz, 1H, H-5), 4.39 (q, *J* = 6.6 Hz, 1H, H-7), 4.15 (dt, *J* = 11.3, 4.9 Hz, 1H, H-2), 2.16 – 1.98 (m, 2H, H-3, H-3), 1.51 (d, *J* = 6.9 Hz, 3H, H-8), 1.28 (d, *J* = 6.3 Hz, 3H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$): δ 154.0 (O(C=O)O), 137.7, 133.1 ($C_{q\text{-}arom}$), 132.6, 131.4, 129.2, 129.1, 128.7, 128.7, 128.3, 128.2, 128.1, 127.4 (CH_{arom}), 86.6 (C-1), 84.5 (C-4), 81.6 (C-7), 71.5 (C-2), 71.5 (CH_2 Bn), 66.1 (C-5), 35.8 (C-3), 14.8 (C-6), 13.3 (C-8); Diagnostic signals of the minor stereoisomer (β-anomer): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.70 (d, *J* = 11.3 Hz, 1H, C*H*H Bn), 4.58 (d, *J* = 9.3 Hz, 1H, H-1), 4.53 (d, *J* = 11.3 Hz, 1H, CH*H* Bn), 4.35 (q, *J* = 6.7 Hz, 1H, H-7), 3.72 – 3.65 (m, 2H, H-

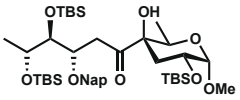
2, H-5), 2.33 (dd, *J* = 14.1, 5.0 Hz, 1H, H-3), 1.77 (dd, *J* = 14.1, 10.6 Hz, 1H, H-3), 1.42 (d, *J* = 6.9 Hz, 3H, H-8), 1.37 (d, *J* = 6.2 Hz, 3H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 153.9 (O(C=O)O), 137.3, 133.9 ($C_{q\text{-arom}}$), 88.6 (C-1), 84.2 (C-4), 80.9 (C-7), 75.3 (C-2/C-5), 73.2 (CH_2 Bn), 72.5 (C-2/C-5), 39.9 (C-3), 15.5 (C-6), 13.1 (C-8); HRMS: $[M+Na]^+$ calcd for $C_{22}H_{24}O_5SNa$ 423.1242, found 423.1237.

Preparation of compound 24 and S36

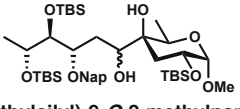
Scheme S4. Synthesis of compound **24** and **S36**.



Reagents and conditions: a) SmI_2, THF, 40 °C, 15 min (70%); b) $Zn(BH_4)_2$, THF (82%, and 10% for the C-7 epimer); c) and d) $COCl_2$, Et_3N, THF (79% and 48% for the C-7 epimer); e) 6 M HCl, MeOH (*quant.*); f) BnBr, NaH, DMF (74%); g) DDQ, DCM/MeOH 4:1 (70%); h) $SrCl_2{\cdot}H_2O$, aq. HCOOH 80%, dioxane (68%); i) Ac_2O, pyridine (85%); j) thiophenol, $BF_3{\cdot}OEt_2$, DCM (61%); k) 2,2,2,-trifluoro-*N*-phenylacetimidoyl chloride, $CsCO_3$, acetone (85%).

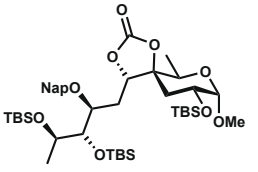


Methyl 2-*O*-*tert*-butyldimethylsilyl-3,6-dideoxy-4-C-((3*S*,4*S*,5*R*)-4,5-*O*-bis((*tert*-butyldimethylsilyl)oxy)-3-*O*-2-methylnaphthalene-hexan-1-one)-α-D-galacto-hexapyranoside (S26). Acid **5** (1.06 g, 2.0 mmol) was dissolved in dry THF (20 mL, 0.1 M). This solution was cooled to 0 °C while stirring, pyridine (242 µL, 3.0 mmol, 1.5 eq.) and oxalyl chloride (220 µL, 2.6 mmol, 1.3 eq.) were added respectively. The solution was stirred for 30 min on ice after which it was warmed to room temperature over a time span of 15 min. The suspension was diluted with pentane and filtered into a flask containing ketone **S19** (457 mg, 1.67 mmol, 0.8 eq.), resulting in a clear liquid which was concentrated *in vacuo* to yield the crude acid chloride **5** combined with ketone **S19** as a colorless oil. While gently stirring, a constant gas flow of nitrogen was applied for 20 min after which the mixture was heated to 40 °C followed by the addition of a solution of samarium(II)iodide (0.1 M) in THF (59 mL, 5.85 mmol, 3.5 eq.). After 10 min the heat source was removed and the solution was quenched with air and diluted with EtOAc, aq. 1.0 M HCl and stirred for 30 min. The aqueous layer was extracted with EtOAc (3x) followed by washing the combined organic layers with sat. aq. NaS_2O_3. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product as a colorless oil. Flash column chromatography (97:3 → 95:5; pentane:Et_2O) yielded the title compound (850 mg, 1.08 mmol, 65% based on **S19**) as a colorless oil. TLC: R_f 0.5 (pentane:Et_2O, 9:1, v:v); $[\alpha]_D^{20}$ 15.7° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 775, 835, 1112, 1253, 1471, 1707, 2856, 2929; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.83 – 7.65 (m, 4H, CH_{arom}), 7.48 – 7.30 (m, 3H, CH_{arom}), 4.70 (d, *J* = 11.6 Hz, 1H, CH*H* Nap), 4.59 (m, 1H, C*H*H Nap), 4.57 (s, 1H, H-1), 4.33 (dt, *J* = 10.0, 2.5 Hz, 1H, H-9), 4.23 (q, *J* = 6.4 Hz, 1H, H-5), 4.11 (ddd, *J* = 11.5, 4.8, 3.4 Hz, 1H, H-2), 3.94 (s, 1H, 4-OH), 3.77 – 3.67 (m, 2H, H-10, H-11), 3.45 (s, 3H, CH_3 OMe), 3.29 (dd, *J* = 17.1, 10.0 Hz, 1H, H-8), 2.47 – 2.35 (m, 2H, H-8, H-3), 1.50 (dd, *J* = 12.3, 4.6 Hz, 1H, H-3), 1.18 (d, *J* = 5.8 Hz, 3H, H-12), 0.93 (d, *J* = 2.6 Hz, 3H, H-6) 0.92 – 0.78 (m, 27H, $C(CH_3)_3$, $C(CH_3)_3$, $C(CH_3)_3$), 0.14 – -0.07 (m, 18H, $SiCH_3$, $SiCH_3$, $SiCH_3$, $SiCH_3$, $SiCH_3$, $SiCH_3$); ^{13}C NMR (101 MHz, $CDCl_3$ HSQC): δ 210.2 (C-7), 135.7, 133.3, 133.0 ($C_{q\text{-}arom}$), 128.0, 128.0, 127.8, 126.4, 126.1, 126.0, 125.8 (CH_{arom}), 100.1 (C-1), 81.4 (C-4), 78.2 (C-10/C-11), 77.0 (C-9), 72.9 (CH_2 Nap), 70.0 (C-11/C-10), 66.2 (C-2), 65.0 (C-5), 55.7 (CH_3 OMe), 38.3 (C-8), 36.1 (C-3), 26.2 ($C(CH_3)_3$), 26.0 ($C(CH_3)_3$), 25.9 ($C(CH_3)_3$), 20.5 (C-12), 18.5 ($C(CH_3)_3$), 18.2 ($C(CH_3)_3$), 18.2 ($C(CH_3)_3$), 14.3 (C-6), -4.0 ($SiCH_3$), -4.1 ($SiCH_3$), -4.2 ($SiCH_3$), -4.6 ($SiCH_3$), -4.6 ($SiCH_3$), -4.6 ($SiCH_3$); HRMS: $[M+Na]^+$ calcd for $C_{42}H_{74}O_8Si_3Na$ 813.4589, found 813.4598.

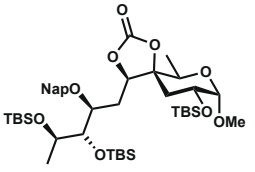


Methyl 2,10,11-tris-*O*-(*tert*-butyldimethylsilyl)-9-*O*-2-methylnaphthalene-α-D-caryophylloside (S27) and **Methyl 7-epi-2,10,11-tris-*O*-(*tert*-butyldimethylsilyl)-9-*O*-2-methylnaphthalene-α-D-caryophylloside (S28).** A $Zn(BH_4)_2$ solution was prepared by dissolving anhydrous $ZnCl_2$ (209 mg, 1.54 mmol) in dry THF (2.95 mL), at 0 °C $NaBH_4$ (148 mg, 3.9 mmol) was added and the solution was stirred for 18 h. **S26** (47.4 mg, 60 µmol) was dissolved in dry THF (2.4 mL, 0.025 M) after which it was cooled on ice, 0.6 mL of the $Zn(BH_4)_2$ solution (0.31 mmol, 5.2 eq.) was added. The solution was led to warm to room temperature and stirred for 18 h. The reaction was quenched with sat. aq. NH_4Cl and diluted with EtOAc and brine, the aqueous layer was extracted with EtOAc (3x) followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude products as a separable diastereomeric mixture. Flash column chromatography (95:5 → 90:10; pentane:Et_2O) yielded the C-7 epimer **S28** and the caryophyllose **S27** in an 11:89 ratio respectively. Yielding caryophyllose **S27** (39 mg, 49 µmol, 82%) and the C-7 epimer **S28** (5 mg, 6 µmol, 10%) both as colorless oils. TLC: R_f 0.2 and 0.5 for the caryophyllose **S27** and C-7 epimer **S28** respectively (pentane:EtOAc, 9:1, v:v); Data of the major stereoisomer caryophyllose **S27**: $[\alpha]_D^{20}$ 13.3° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 775, 835, 1056, 1104, 1252, 2928, 3483; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.01 – 7.65 (m, 4H, CH_{arom}), 7.47 (m, 3H, CH_{arom}), 4.79 (d, *J* = 11.9 Hz, 1H, CH*H* Nap), 4.64 (d, *J* = 11.9 Hz, 1H, C*H*H Nap), 4.52 (d, *J* = 3.6 Hz, 1H, H-1), 4.12 – 3.99 (m, 2H, H-2, H-5), 3.92 – 3.79 (m, 2H, H-9, H-11), 3.75 (dd, *J* = 5.5, 3.6 Hz, 1H, H-10), 3.67 (d, *J* = 10.4 Hz, 1H, H-7), 3.39 (s, 3H, CH_3 OMe), 2.35 (d, *J* = 4.2 Hz, 1H, 4-OH), 2.28 (s, 1H, 7-OH), 2.00 – 1.91 (m, 2H, H-3, H-8), 1.66 – 1.54 (m, 2H, H-3, H-8), 1.17 (d, *J* = 6.1 Hz, 3H, H-12), 1.11 (d, *J* = 6.5 Hz, 3H, H-6), 0.93

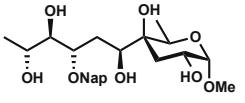
– 0.85 (m, 27H, C(CH_3)$_3$, C(CH_3)$_3$, C(CH_3)$_3$), 0.14 – 0.02 (m, 18H, $SiCH_3$, $SiCH_3$, $SiCH_3$, $SiCH_3$, $SiCH_3$, $SiCH_3$); ^{13}C NMR (101 MHz, $CDCl_3$ HSQC): δ 135.9, 133.4, 133.1 ($C_{q\text{-arom}}$), 128.3, 128.0, 127.8, 126.8, 126.3, 126.1, 126.0 (CH_{arom}), 99.7 (C-1), 79.0 (C-10), 77.6 (C-11), 74.7 (C-4), 72.4 (C-7), 72.1 (CH_2 Nap), 69.8 (C-9), 67.1 (C-2), 66.0 (C-5), 55.4 (CH_3 OMe), 34.5 (C-3/C-8), 31.4 (C-8/C-3), 26.3 (C(*C*H_3)$_3$), 26.1 (C(*C*H_3)$_3$), 26.0 (C(*C*H_3)$_3$), 20.3 (C-12), 18.5 (*C*(CH_3)$_3$), 18.4 (*C*(CH_3)$_3$), 18.2 (*C*(CH_3)$_3$), 14.1 (C-6), -4.0 ($SiCH_3$), -4.0 ($SiCH_3$), -4.1 ($SiCH_3$), -4.4 ($SiCH_3$), -4.4 ($SiCH_3$), -4.4 ($SiCH_3$); HRMS: [M+Na]$^+$ calcd for $C_{42}H_{76}O_8Si_3Na$ 815.4746, found 815.4746. Data of the minor stereoisomer C-7 epimer **S28**: $[\alpha]_D^{20}$ 6.4° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 776, 835, 1052, 1104, 1252, 2928, 3502; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.87 – 7.74 (m, 4H, CH_{arom}), 7.52 – 7.42 (m, 3H, CH_{arom}), 4.85 (d, *J* = 11.6 Hz, 1H, CH*H* Nap), 4.58 (d, *J* = 11.6 Hz, 1H, H-1), 4.55 (m, 1H, C*H*H Nap), 4.33 (d, *J* = 1.5 Hz, 1H, 7-OH), 4.16 (ddd, *J* = 11.3, 5.2, 3.5 Hz, 1H, H-2), 3.97 (ddd, *J* = 8.9, 3.9, 1.7 Hz, 1H, H-7), 3.76 – 3.69 (m, 2H, H-5, H-10), 3.69 – 3.58 (m, 2H, H-9, H-11), 3.40 (s, 3H, CH_3 OMe), 2.95 (d, *J* = 1.0 Hz, 1H, 4-OH), 1.87 – 1.69 (m, 3H, H-3, H-3, H-8), 1.53 (dd, *J* = 15.1, 3.9 Hz, 1H, H-8), 1.22 (d, *J* = 6.0 Hz, 3H, H-12), 1.08 (d, *J* = 6.5 Hz, 3H, H-6), 0.93 – 0.78 (m, 27H, C(CH_3)$_3$, C(CH_3)$_3$, C(CH_3)$_3$), 0.14 – -0.04 (m, 18H, $SiCH_3$, $SiCH_3$, $SiCH_3$, $SiCH_3$, $SiCH_3$, $SiCH_3$); ^{13}C NMR (101 MHz, $CDCl_3$ HSQC): δ 134.8, 133.3, 133.2 ($C_{q\text{-arom}}$), 128.6, 128.1, 127.8, 127.4, 126.4, 126.3, 126.1 (CH_{arom}), 99.9 (C-1), 80.0 (C-7), 77.9 (C-4), 74.7 (C-10/C-5), 72.2 (C-9/C-11), 72.0 (CH_2 Nap), 69.6 (C-11/C-9), 67.1 (C-2), 66.6 (C-5/C-10), 55.4 (CH_3 OMe), 33.3 (C-3), 30.1 (C-8), 26.3 (C(*C*H_3)$_3$), 26.1 (C(*C*H_3)$_3$), 26.0 (C(*C*H_3)$_3$), 21.6 (C-12), 18.6 (*C*(CH_3)$_3$), 18.4 (*C*(CH_3)$_3$), 18.0 (*C*(CH_3)$_3$), 14.3 (*C*(CH_3)$_3$), -3.5 ($SiCH_3$), -3.6 ($SiCH_3$), -4.4 ($SiCH_3$), -4.4 ($SiCH_3$), -4.5 ($SiCH_3$), -4.6 ($SiCH_3$); HRMS: [M+Na]$^+$ calcd for $C_{42}H_{76}O_8Si_3Na$ 815.4746, found 815.4722.



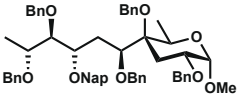
Methyl 2,10,11-tris-*O*-(*tert*-butyldimethylsilyl)-9-*O*-2-methylnaphthalene-4,7-carbonate-α-D-caryophylloside (S29). A phosgene solution was prepared by diluting a 20% phosgene in hexane solution (0.95 mL, 1.75 mmol, 5 eq.) with dry THF (1 mL). The caryophyllose **S27** (280 mg, 0.35 mmol) was dissolved in THF (2.5 mL, 0.1 M) and Et_3N (242 µL, 1.75 mmol, 5.0 eq.) and cooled on ice. The phosgene solution was added dropwise, after which the solution was stirred for 1 h at 0 °C followed by 1 h on room temperature. The reaction was quenched by adding 1 mL of sat. aq. $NaHCO_3$ followed by diluting the mixture with Et_2O and water. The aqueous layer was extracted with Et_2O (3x) followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product as a colorless oil. Flash column chromatography (99:1 → 97:3; pentane:EtOAc) yielded the title compound (227 mg, 0.28 mmol, 79%) as a colorless oil. TLC: R_f 0.2 (pentane:EtOAc, 9:1, v:v); $[\alpha]_D^{20}$ 8.4° (c 0.5, $CHCl_3$); IR (neat, cm^{-1}): 776, 835, 1059, 1098, 1253, 1812, 2928; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, NOESY): δ 7.83 (dt, *J* = 11.6, 4.0 Hz, 4H, CH_{arom}), 7.53 – 7.43 (m, 3H, CH_{arom}), 4.74 (d, *J* = 11.8 Hz, 1H, CH*H* Nap), 4.60 (d, *J* = 11.7 Hz, 1H, C*H*H Nap), 4.52 (d, *J* = 3.2 Hz, 1H, H-1), 4.36 (dd, *J* = 9.6, 3.9 Hz, 1H, H-7), 4.02 (ddd, *J* = 11.5, 4.7, 3.3 Hz, 1H, H-2), 3.84 (p, *J* = 6.1 Hz, 1H, H-11), 3.77 – 3.67 (m, 2H, H-9, H-10), 3.56 (q, *J* = 6.4 Hz, 1H, H-5), 3.34 (s, 3H, CH_3 OMe), 2.08 (ddd, *J* = 15.4, 9.6, 6.2 Hz, 1H, H-8), 2.00 (dd, *J* = 13.2, 11.5 Hz, 1H, H-3), 1.94 – 1.86 (m, 2H, H-3, H-8), 1.12 (d, *J* = 6.2 Hz, 3H, H-12), 1.09 (d, *J* = 6.4 Hz, 3H, H-6), 0.93 – 0.82 (m, 27H, C(CH_3)$_3$, C(CH_3)$_3$, C(CH_3)$_3$), 0.12 – 0.03 (m, 18H, $SiCH_3$, $SiCH_3$, $SiCH_3$, $SiCH_3$, $SiCH_3$, $SiCH_3$); ^{13}C NMR (101 MHz, $CDCl_3$ HSQC): δ 153.9 (O(C=O)O), 135.5, 133.4, 133.1 ($C_{q\text{-arom}}$), 128.3, 128.1, 127.8, 127.0, 126.3, 126.2, 126.1 (CH_{arom}), 99.3 (C-1), 85.3 (C-4), 78.7 (C-7/C-10), 78.7 (C-10/C-7), 77.1 (C-9), 71.9 (CH_2 Nap), 70.1 (C-11), 66.5 (C-5), 66.3 (C-2), 55.7 (CH_3 OMe), 32.8 (C-3), 30.8 (C-8), 26.3 (C(*C*H_3)$_3$), 26.1 (C(*C*H_3)$_3$), 25.9 (C(*C*H_3)$_3$), 19.9 (C-12), 18.5 (*C*(CH_3)$_3$), 18.3 (*C*(CH_3)$_3$), 18.3 (*C*(CH_3)$_3$), 13.2 (C-6), -4.0 ($SiCH_3$), -4.0 ($SiCH_3$), -4.1 ($SiCH_3$), -4.4 ($SiCH_3$), -4.5 ($SiCH_3$), -4.6 ($SiCH_3$); HRMS: [M+Na]$^+$ calcd for $C_{43}H_{74}O_9Si_3Na$ 841.4538, found 841.4532.



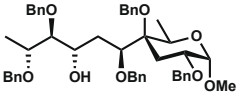
Methyl 7-epi-2,10,11-tris-*O*-(*tert*-butyldimethylsilyl)-9-*O*-2-methylnaphthalene-4,7-carbonate-α-D-caryophylloside (S30). A phosgene solution was prepared by diluting a 20% phosgene in hexane solution (265 µL, 334 µmol, 10 eq.) with dry THF (1.5 mL). The C-7 epimer **S28** (26.5 mg, 33 µmol) was dissolved in THF (0.33 mL, 0.1 M) and Et_3N (90 µL, 660 µmol, 20 eq.) and cooled on ice. The phosgene solution was added dropwise after which the solution was stirred for 1 h at 0 °C followed by 1 h on room temperature. The reaction was quenched by adding 1 mL of sat. aq. $NaHCO_3$ followed by diluting the mixture with Et_2O and water. The aqueous layer was extracted with Et_2O (3x) followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product as a colorless oil. Flash column chromatography (99:1 → 97:3; pentane:EtOAc) yielded the title compound (12.9 mg, 16.0 µmol, 48%) as a colorless oil. TLC: R_f 0.3 (pentane:EtOAc, 9:1, v:v); $[\alpha]_D^{20}$ 32.0° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 776, 835, 1034, 1066, 1086, 1110, 1471, 1809, 2929; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, NOESY): δ 7.86 – 7.75 (m, 4H, CH_{arom}), 7.52 – 7.37 (m, 3H, CH_{arom}), 4.84 (d, *J* = 11.9 Hz, 1H, CH*H* Nap), 4.58 (d, *J* = 11.8 Hz, 1H, C*H*H Nap), 4.54 (d, *J* = 3.3 Hz, 1H, H-1), 4.44 – 4.38 (m, 1H, H-7), 4.02 (ddd, *J* = 11.7, 4.9, 3.4 Hz, 1H, H-2), 3.94 – 3.82 (m, 2H, H-9, H-11), 3.70 (m, 2H, H-5, H-10), 3.40 (s, 2H, CH_3 OMe), 2.12 (dd, *J* = 13.5, 11.9 Hz, 1H, H-3), 1.91 – 1.83 (m, 2H, H-3, H-8), 1.76 (dd, *J* = 13.5, 4.8 Hz, 1H, H-8), 1.26 (d, *J* = 6.4 Hz, 3H, H-12), 1.19 (d, *J* = 5.7 Hz, 3H, H-6), 0.97 – 0.79 (m, 27H, $C(CH_3)_3$, $C(CH_3)_3$, $C(CH_3)_3$), 0.19 – 0.03 (m, 18H, $SiCH_3$, $SiCH_3$, $SiCH_3$, $SiCH_3$, $SiCH_3$, $SiCH_3$); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 154.2 (C-13), 135.6, 133.4, 133.0 ($C_{q\text{-}arom}$), 128.3, 128.0, 127.8, 126.4, 126.3, 126.1, 125.7 (CH_{arom}), 99.0 (C-1), 85.1 (C-4), 82.4 (C-7), 78.3 (C-5), 77.0 (C-9), 72.6 (CH_2 Nap), 69.7 (C-10), 66.2 (C-2), 64.8 (C-11), 55.6 (CH_3 OMe), 36.3 (C-3), 28.7 (C-8), 26.2 ($C(CH_3)_3$), 26.1 ($C(CH_3)_3$), 26.0 ($C(CH_3)_3$), 20.8 (C-6), 18.5 ($C(CH_3)_3$), 18.4 ($C(CH_3)_3$), 18.2 ($C(CH_3)_3$), 15.0 (C-12), -3.9 ($SiCH_3$), -3.9 ($SiCH_3$), -4.3 ($SiCH_3$), -4.5 ($SiCH_3$), -4.5 ($SiCH_3$), -4.6 ($SiCH_3$); HRMS: $[M+Na]^+$ calcd for $C_{43}H_{74}O_9Si_3Na$ 841.4538, found 841.4538.



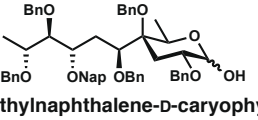
Methyl 9-*O*-2-methylnaphthalene-α-D-caryophylloside (S31). Compound **S30** (400 mg, 0.5 mmol) was dissolved in methanol (15 mL, 0.034 M), a 6 M HCl aq. solution (0.9 mL, 10 eq.) was added and the mixture was stirred for 18 h upon which the reaction was quenched by neutralizing the acid with Amberlite IRA-67 (Sigma Aldrich Amberlite IRA-67 free base, pre-washed with MeOH). The reaction mixture was filtered off and rinsed with excess methanol, concentration of the filtrate yielded the crude product as a colorless oil. Flash column chromatography (50:50 → 0:100; pentane:acetone) yielded the title compound (225 mg, 0.5 mmol, *quant.*) as a colorless oil. TLC: R_f 0.6 (acetone, 9:1, v:v); $[\alpha]_D^{20}$ 31.7° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 972, 1052, 1695, 2928, 3352; ^1H NMR (400 MHz, CD_3OD, HH-COSY, HSQC): δ 7.92 – 7.38 (m, 7H, CH_{arom}), 4.82 (d, *J* = 11.5 Hz, 1H, CH*H* Nap), 4.69 (d, *J* = 11.5 Hz, 1H, *CH*H Nap), 4.55 (d, *J* = 3.6 Hz, 1H, H-1), 4.12 (q, *J* = 6.5 Hz, 1H, H-5), 3.99 – 3.89 (m, 2H, H-2, H-7), 3.79 – 3.67 (m, 3H, H-9, H-10, H-11), 3.38 (s, 3H, CH_3 OMe), 2.08 – 1.92 (m, 2H, H-3, H-8), 1.68 (dd, *J* = 12.5, 5.1 Hz, 1H, H-3), 1.61 (ddd, *J* = 14.1, 10.7, 2.7 Hz, 1H, H-8), 1.23 (d, *J* = 5.7 Hz, 3H, H-12), 1.11 (d, *J* = 6.5 Hz, 3H, H-6); ^{13}C NMR (101 MHz, MeOD, HSQC): δ 137.5, 134.8, 134.4 ($C_{q\text{-}arom}$), 129.0, 128.9, 128.7, 127.7, 127.2, 127.1, 126.9 (CH_{arom}), 100.5 (C-1), 78.7 (C-2/C-7), 77.2 (C-9), 75.7 (C-4), 72.8 (CH_2 Nap), 72.0 (C-11/C-10), 68.7 (C-10/C-11), 67.6 (C-5), 66.4 (C-2/C-7), 55.4 (CH_3 OMe), 32.8 (C-3), 31.2 (C-8), 19.8 (C-12), 13.6 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{24}H_{34}O_8Na$ 473.2151, found 473.2148.



Methyl 2,4,7,10,11-penta-*O*-benzyl-9-*O*-2-methylnaphthalene-α-D-caryophylloside (S32). Compound **S31** (225 mg, 0.5 mmol) was dissolved in DMF (5 ml, 0.1 M) and cooled on ice. NaH (1.0 g, 25.0 mmol, 50.0 eq., 60% dispersion in mineral oil) was added slowly. Consequently, BnBr (3.0 mL, 25.0 mmol, 50.0 eq.) was added and the mixture was stirred for 18 h at 40 °C. Upon full conversion, the reaction mixture was quenched with water and the suspension was diluted with water and Et_2O. The aqueous layer was extracted with Et_2O (3x) followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product as a colorless oil. Flash column chromatography (90:10 → 80:20; pentane:EtOAc) yielded the title compound (335 mg, 0.37 mmol, 74%) as a colorless oil. TLC: R_f 0.2 (pentane:EtOAc, 9:1, v:v); $[\alpha]_D^{20}$ –3.0° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 1047, 1072, 1095, 1454; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.90 – 6.78 (m, 32H, CH_{arom}), 4.88 (d, *J* = 12.3 Hz, 1H, CH*H* Ph), 4.84 (d, *J* = 11.4 Hz, 1H, CH*H* Ph), 4.71 (s, 1H, CH*H* Ph), 4.68 (d, *J* = 3.4 Hz, 1H, H-1), 4.65 (d, *J* = 11.4 Hz, 1H, CH*H* Ph), 4.57 (d, *J* = 12.2 Hz, 1H, CH*H* Ph), 4.53 (m, 2H, CH*H* Ph, CH*H* Ph), 4.50 (m, 1H, CH*H* Ph), 4.46 (m, 1H, CH*H* Ph), 4.43 (m, 1H, CH*H* Ph), 4.18 (d, *J* = 11.5 Hz, 1H, CH*H* Ph), 4.07 – 3.96 (m, 3H, H-5, H-9, CH*H* Ph), 3.81 – 3.72 (m, 3H, H-2, H-10, CH*H* Ph), 3.56 (d, *J* = 9.5 Hz, 1H, H-7), 3.43 (dd, *J* = 7.6, 6.2 Hz, 1H, H-11) 3.36 (s, 3H, CH_3 OMe), 2.24 – 2.09 (m, 3H, H-3, H-8), 1.65 (dd, *J* = 13.9, 9.9 Hz, 1H, H-8), 1.29 (d, *J* = 6.4 Hz, 3H, H-12), 1.26 (d, *J* = 8.5 Hz, 3H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 139.5, 138.9, 138.8, 138.5, 138.4, 136.2, 133.4, 133.1 ($C_{q\text{-}arom}$), 128.7, 128.5, 128.4, 128.4, 128.3, 128.2, 128.2, 128.2, 128.1, 127.9, 127.9, 127.8, 127.7, 127.5, 127.3, 127.1, 127.0, 126.8, 126.6, 126.4, 126.4, 126.2 (CH_{arom}), 97.4 (C-1), 82.0 (C-2), 80.3 (C-4), 79.1 (C-7), 76.8 (C-9), 74.9 (C-11), 74.2, 74.0 (CH_2 Bn), 72.0 (C-10), 71.3, 71.0, 70.7 (CH_2 Bn), 68.0 (C-5), 65.4 (CH_2 Bn), 55.1 (CH_3 OMe), 32.4 (C-8), 27.9 (C-3), 16.9 (C-12), 15.3 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{59}H_{64}O_8Na$ 923.4499, found 923.4507.

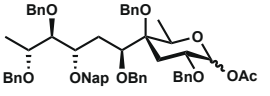


Methyl 2,4,7,10,11-penta-*O*-benzyl-α-D-caryophylloside (S33). Compound **S32** (15.3 mg, 17 µmol) was dissolved in 4:1 DCM:MeOH (340 µL, 0.05 mL) and the solution was cooled on ice. Subsequently DDQ (7.7 mg, 34 µmol, 2.0 eq.) was added. The mixture was stirred for 3 h at room temperature, and upon full conversion, diluted with H_2O and EtOAc. The aqueous layer was extracted (3x) with EtOAc followed by washing the combined organic layer with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product as a colorless oil. Flash column chromatography (80:20 → 70:30; pentane:Et_2O) yielded the title compound (108 mg, 102 µmol, 85%) as a colorless oil. TLC: R_f 0.5 (pentane:EtOAc, 9:1, v:v); IR (neat, cm^{-1}): 696, 735, 1047, 1071, 1092, 1453; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.39 – 7.15 (m, 25H, CH_{arom}), 4.71 (d, *J* = 3.6 Hz, 1H, H-1), 4.68 (d, *J* = 11.5 Hz, 1H, CH*H* Ph), 4.57 (m, 7H, CH*H* Ph, CH*H* Ph, CH*H* Ph, CH*H* Ph, C*H*H Ph, C*H*H Ph, C*H*H Ph), 4.50 (d, *J* = 11.6 Hz, 1H, C*H*H Ph), 4.37 (d, *J* = 11.6 Hz, 1H, C*H*H Ph), 4.10 (q, *J* = 6.5 Hz, 1H, H-5), 3.94 (dt, *J* = 9.3, 4.7 Hz, 1H, H-9), 3.79 (ddd, *J* = 10.3, 7.0, 3.6 Hz, 1H, H-2), 3.76 – 3.71 (m, 1H, H-7), 3.68 (p, *J* = 6.1 Hz, 1H, H-11), 3.40 (s, 3H, CH_3 OMe), 3.34 (t, *J* = 5.6 Hz, 1H, H-10), 2.64 (s, 1H, 9-OH), 2.21 – 2.16 (m, 2H, H-3), 1.86 (dt, *J* = 7.4, 3.6 Hz, 2H, H-8), 1.28 (d, *J* = 6.2 Hz, 3H, H-6/H-12), 1.26 (d, *J* = 6.0 Hz, 3H, H-6/H-12); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 139.1, 138.9, 138.5, 138.4, 138.3 ($C_{q\text{-}arom}$), 128.6, 128.5, 128.4, 128.4, 128.1, 128.0, 128.0, 127.9, 127.8, 127.7, 127.5, 127.4, 127.2, 126.8 (CH_{arom}), 97.3 (C-1), 85.1 (C-10), 80.2 (C-4), 78.8 (C-7), 76.6 (C-11), 74.5, 74.3 (CH_2 Bn), 72.1 (C-2), 71.3, 71.0 (CH_2 Bn), 70.1 (C-9), 67.9 (C-5), 65.9 (CH_2 Bn), 55.1 (CH_3 OMe), 34.2 (C-8), 28.0 (C-3), 16.3 (C-12), 15.1 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{48}H_{56}O_8Na$ 783.3873, found 783.3890.

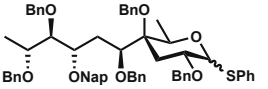


2,4,7,10,11-Penta-*O*-benzyl-9-*O*-2-methylnaphthalene-D-caryophylloside (S34). Compound **S32** (335 mg, 0.37 mmol) was dissolved in formic acid (6.5 mL, 0.05 M, 80% in water) and dioxane (6.5 mL, 0.05 M).

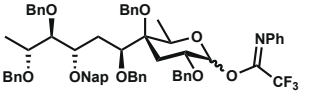
$SrCl_2 \cdot 6H_2O$ (88 mg, 0.33 mmol, 1.0 eq) was added and the solution was stirred for 40 h at 60 °C and 250 mbar. The solution was diluted with water and EtOAc, the aqueous layer was extracted with EtOAc (3x) followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product as a colorless oil. Flash column chromatography (90:10 → 80:20; pentane:EtOAc) yielded the title compound (199 mg, 0.22 mmol, 68%, α:β; 47:53) as a colorless oil. Starting material was recovered (33.3 mg, 0.037 mmol, 11%) which resulted in a 79% yield based on recovered starting material. TLC: R_f 0.2 (pentane:EtOAc, 8:2, v:v); IR (neat, cm^{-1}): 696, 734, 1028, 1072, 1093; Data of the major stereoisomer (β-anomer): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.86 – 6.76 (m, 32H), 4.91 – 4.81 (m, 3H, CH*H* Ph, CH*H* Ph, CH*H* Ph), 4.75 – 4.57 (m, 4H, CH*H* Ph, C*H*H Ph, C*H*H Ph, H-1), 4.54 – 4.43 (m, 2H, C*H*H Ph, C*H*H Ph), 4.29 (q, *J* = 6.4 Hz, 1H, H-5), 4.22 (d, *J* = 10.1 Hz, 1H, C*H*H Ph), 4.19 (d, *J* = 10.2 Hz, 1H, C*H*H Ph), 4.06 (dt, *J* = 11.0, 2.5 Hz, 1H, H-9), 3.95 (d, *J* = 12.0 Hz, 1H, CH*H* Ph), 3.89 – 3.71 (m, 1H, H-10), 3.65 – 3.53 (m, 2H, H-2, H-7), 3.46 (ddd, *J* = 10.3, 7.7, 6.1 Hz, 1H, H-11), 3.17 (d, *J* = 5.1 Hz, 1H, 1-OH), 2.35 (dd, *J* = 14.6, 5.4 Hz, 1H, H-3), 2.29 – 2.18 (m, 2H, H-3, H-8), 1.90 (dd, *J* = 14.5, 11.7 Hz, 1H, H-3), 1.70 – 1.58 (m, 1H, H-8), 1.34 – 1.28 (m, 6H, H-6, H-12); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 139.4, 138.7, 138.6, 138.4, 138.3, 138.0, 136.1, 133.3 ($C_{q\text{-}arom}$), 128.6, 128.5, 128.4, 128.4, 128.4, 128.3, 128.2, 128.2, 128.2, 128.1, 128.1, 128.1, 128.1, 128.0, 128.0, 128.0, 127.8, 127.8, 127.7, 127.7, 127.7, 127.6, 127.5, 127.5, 127.2, 127.1, 127.1, 126.8, 126.8, 126.5, 126.1, 126.1 (CH_{arom}), 99.0 (C-1), 81.9 (C-10), 79.9 (C-4), 78.3 (C-7), 76.5 (C-9), 76.1 (C-2), 74.7 (C-11), 74.2, 74.1, 72.5, 71.0, 70.8 (CH_2 Bn), 68.2 (C-3), 66.5 (CH_2 Bn), 32.6 (C-3), 31.9 (C-8), 16.7 (C-6/C-12), 15.3 (C-6/C-12); Diagnostic signals of the minor stereoisomer (α-isomer): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.27 (d, *J* = 3.0 Hz, 1H, H-1), 2.85 (s, 1H, 1-OH), 1.90 (dd, *J* = 14.5, 11.7 Hz, 1H, H-3); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 90.3 (C-1), 81.9 (C-10), 79.8 (C-4), 78.8 (C-7), 76.7 (C-9), 76.0 (C-5), 74.8 (C-11), 73.9, 73.6 (CH_2 Bn), 72.2 (C-2), 70.9, 70.7, 70.5, 65.5 (CH_2 Bn), 32.3 (C-8), 27.3 (C-3), 16.8 (C-12), 15.4 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{58}H_{62}O_8Na$ 909.4342, found 909.4354.



Acetyl 2,4,7,10,11-penta-*O*-benzyl-9-*O*-2-methylnaphthalene-D-caryophylloside (S35). Compound **S34** (44.6 mg, 50 µmol) was dissolved in pyridine (0.5 mL, 0.1 M) and cooled on ice. Ac_2O (15.3 µL, 150 µmol, 3.0 eq.) was added and the reaction was stirred for 18 h and subsequently quenched with water. The mixture was diluted with EtOAc, the aqueous layer was extracted with EtOAc (3x) followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product as a colorless oil. Flash column chromatography (95:5 → 90:10; pentane:EtOAc) yielded the title compound (38.8 mg, 42.3 µmol, 85%, α:β; 20:80) as a colorless oil. TLC: R_f 0.6 (pentane:EtOAc, 8:2, v:v); IR (neat, cm^{-1}): 696, 734, 1053, 1095, 1751; Data of the major stereoisomer (β-anomer): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.94 – 6.74 (m, 32H,CH_{arom}), 5.55 (d, *J* = 8.1 Hz, 1H, H-1), 4.84 (m, 2H, CH*H* Ph, CH*H* Ph), 4.69 – 4.43 (m, 7H, C*H*H Ph, C*H*H Ph, C*H*H Ph, C*H*H Ph, CH*H* Ph, CH*H* Ph, CH*H* Ph), 4.22 (d, *J* = 11.6 Hz, 1H, C*H*H Ph), 4.05 (dt, *J* = 10.9, 1.8 Hz, 1H, H-9), 4.00 (d, *J* = 11.8 Hz, 1H, CH*H* Ph), 3.95 (q, *J* = 6.6 Hz, 1H, H-5), 3.83 (d, *J* = 11.8 Hz, 1H, C*H*H Ph), 3.77 – 3.70 (m, 2H, H-2, H-10), 3.60 (dd, *J* = 9.7, 1.2 Hz, 1H, H-7), 3.47 (dd, *J* = 7.8, 6.0 Hz, 1H, H-11), 2.40 (dd, *J* = 14.5, 5.4 Hz, 1H, H-3), 2.26 – 2.19 (m, 1H, H-8), 2.11 (s, 3H, $COCH_3$), 1.91 (dd, *J* = 14.5, 11.6 Hz, 1H, H-3), 1.62 (ddd, *J* = 14.9, 9.7, 1.8 Hz, 1H, H-8), 1.33 (d, *J* = 6.5 Hz, 3H, H-6), 1.30 (d, *J* = 6.0 Hz, 3H, H-12); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 169.7(*C*OCH_3), 139.3, 138.7, 138.5, 138.4, 136.1, 133.4, 133.1 ($C_{q\text{-}arom}$), 128.6, 128.6, 128.5, 128.4, 128.4, 128.3, 128.3, 128.3, 128.2, 128.2, 128.1, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7, 127.6, 127.6, 127.5, 127.4, 127.2, 127.2, 127.1, 127.1, 126.9, 126.8, 126.7, 126.4, 126.4, 126.3, 126.2 (CH_{arom}), 96.3 (C-1), 82.0 (C-10), 79.8 (C-4), 78.3 (C-7), 76.9 (C-5), 76.6 (C-9), 74.7 (C-11), 74.2, 73.7 (CH_2 Bn), 73.6 (C-2), 72.6, 70.9, 70.6, 66.4 (CH_2 Bn), 33.0 (C-3), 32.1 (C-8), 21.4 (CO*C*H_3), 16.8 (C-12), 15.3 (C-6); Diagnostic signals of the minor stereoisomer (α-isomer): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 6.31 (d, *J* = 3.4 Hz, 1H, H-1), 4.12 (q, *J* = 7.1 Hz, 1H, H-5), 2.04 (s, 3H, $COCH_3$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 170.0 (*C*OCH_3), 89.6 (C-1), 79.8 (C-4), 32.1 (C-3), 28.3 (C-8), 21.2 (CO*C*H_3), 16.9 (C-12), 15.4 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{60}H_{64}O_9Na$ 951.4448, found 951.4462.



Thiophenol 2,4,7,10,11-penta-*O*-benzyl-9-*O*-2-methylnaphthalene-D-caryophylloside (24). Compound **S35** (38.8 mg, 42.3 µmol) was dissolved in DCM (0.43 mL, 0.1 M), thiophenol (4.8 µL, 47 µmol, 1.1 eq.) was added and subsequently cooled to –80 °C. $BF_3{\cdot}OEt_2$ (6.2 µL, 50.8 µmol, 1.2 eq.) was added and the solution was allowed to attain 0 °C. Upon full conversion, the solution was quenched by adding sat. aq. $NaHCO_3$. The solution was diluted with EtOAc, the aqueous layer was extracted with EtOAc (3x) followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product as a colorless oil. Flash column chromatography (95:5 → 80:10; pentane:EtOAc) yielded the title compound (30.1 mg, 32.0 µmol, 61%, α:β; 65:35) as a colorless oil. TLC: R_f 0.7 (pentane:EtOAc, 8:2, v:v); IR (neat, cm^{-1}): 696, 734, 1028, 1072, 1091; Data of the major stereoisomer (α-anomer): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.83 – 6.65 (m, 37H, CH_{arom}), 5.69 (d, *J* = 5.0 Hz, 1H, H-1), 4.84 – 4.74 (m, 3H, CH*H* Ph, CH*H* Ph, C*H*H Ph), 4.63 – 4.35 (m, 5H, CH*H* Ph, CH*H* Ph, CH*H* Ph, C*H*H Ph, C*H*H Ph), 4.16 – 4.10 (m, 1H, H-2), 4.05 (m, 1H, C*H*H Ph), 4.00 – 3.94 (m, 2H, H-9, CH*H* Ph), 3.77 – 3.65 (m, 3H, H-10, C*H*H Ph, C*H*H Ph), 3.54 (d, *J* = 9.1 Hz, 1H, H-7), 3.43 – 3.33 (m, 1H, H-11), 2.24 – 2.11 (m, 2H, H-3, H-8), 1.99 (dd, *J* = 14.2, 12.2 Hz, 1H, H-3), 1.60 (dd, *J* = 13.7, 9.5 Hz, 1H, H-8), 1.24 (d, *J* = 4.5 Hz, 3H, H-6/H-12), 1.21 (d, *J* = 6.0 Hz, 3H, H-6/H-12); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 139.3, 138.8, 138.7, 138.4, 138.0, 136.1, 135.3, 133.3, 133.1 ($C_{q\text{-}arom}$), 132.1, 131.3, 128.9, 128.8, 128.6, 128.5, 128.4, 128.3, 128.3, 128.3, 128.2, 128.1, 128.1, 128.0, 127.8, 127.8, 127.7, 127.6, 127.5, 127.4, 127.2, 127.1, 127.1, 126.9, 126.8, 126.7, 126.6, 126.4, 126.4, 126.2 (CH_{arom}), 87.6 (C-1), 82.0 (C-10), 80.0 (C-4), 78.7 (C-7), 76.8 (C-9), 74.9 (C-11), 74.2, 73.9 (CH_2 Bn), 71.9 (C-2), 71.0, 70.9, 70.7 (CH_2 Bn), 69.4 (C-5), 65.4 (CH_2 Bn), 32.4 (C-8), 30.4 (C-3), 16.9 (C-6/C-12), 15.3 (C-6/C-12); Diagnostic signals of the minor stereoisomer (β-isomer): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 3.86 (d, *J* = 11.9 Hz, 1H, CH*H* Ph), 3.61 (td, *J* = 10.9, 5.3 Hz, 1H, H-2), 3.50 (d, *J* = 9.2 Hz, 1H, H-7), 2.32 (dd, *J* = 14.4, 5.4 Hz, 1H, H-3), 1.84 (dd, *J* = 14.4, 11.1 Hz, 1H, H-3), 1.52 (dd, *J* = 13.2, 9.7 Hz, 1H, H-8), 1.28 (d, *J* = 6.5 Hz, 3H, H-6/H-12), 1.24 (d, *J* = 6.1 Hz, 3H, H-6/H-12); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 88.4 (C-1), 82.0 (C-10), 79.7 (C-4), 79.1 (C-7), 78.5 (C-9), 76.5 (C-11), 74.6 (C-2), 74.2, 73.7, 73.0, 72.3 (CH_2 Bn), 70.7 (C-5), 66.4 (CH_2 Bn), 34.3 (C-8), 31.8 (C-3), 16.8 (C-12), 15.7 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{64}H_{66}O_7SNa$ 1001.4427, found 1001.4418.

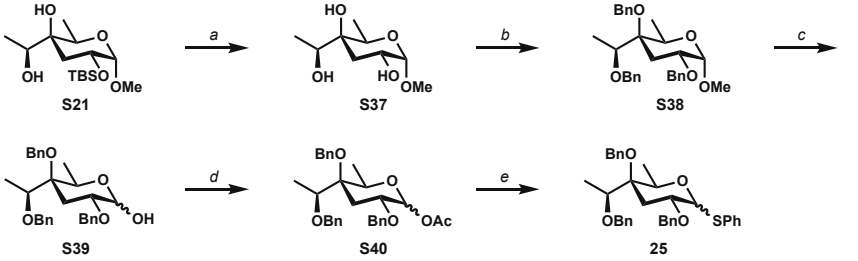


2,2,2-Trifluoro-*N*-phenylacetimido-yl 2,4,7,10,11-penta-*O*-benzyl-9-*O*-2-methylnaphthalene-D-caryophylloside (S36). Compound **S34** (105 mg, 0.12 mmol) was dissolved in acetone (1.2 mL, 0.1 M) and cooled on ice. Subsequently, $CsCO_3$ (40.1 mg, 0.12 mmol, 1.1 eq.) and 2,2,2-trifluoro-*N*-phenylacetimido-yl chloride (37.7 µL, 0.24 mmol, 2.0 eq.) were added and the solution was allowed to attain room temperature. After stirring for 18 h, the solution was diluted with H_2O and EtOAc. The aqueous layer was extracted (3x) with EtOAc followed by washing the combined organic layer with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product as a colorless oil. Flash column chromatography (95:5 → 80:20; pentane:Et_2O) yielded the title compound (10.3 mg, 13.5 µmol, 80%, α:β; 28:72) as a colorless oil. TLC: R_f 0.2 (pentane:EtOAc, 8:2, v:v); IR (neat, cm^{-1}): 695, 734, 1027, 1093, 1207, 1453, 1717; Data of the major stereoisomer (β-anomer): ^{1}H NMR (400 MHz, toluene-d_8, HH-COSY, HSQC, *T* = 333 K): δ 7.94 – 6.64 (m, 37H, CH_{arom}), 4.89 – 4.74 (m, 4H, CH*H* Ph, CH*H* Ph, C*H*H Ph, C*H*H Ph), 5.64 (d, *J* = 7.5 Hz, 1H), 4.59 (s, 6H, CH*H* Ph, CH*H* Ph, CH*H* Ph, C*H*H Ph, C*H*H Ph, C*H*H Ph), 4.26 (m, 2H, CH*H* Ph, C*H*H Ph), 4.12 – 3.92 (m, 2H, H-5, H-9), 3.78 (dt, *J* = 12.1, 6.6 Hz, 1H, H-2), 3.71 (dd, *J* = 6.9, 2.0 Hz, 1H, H-10), 3.58 (d, *J* = 9.2 Hz, 1H, H-7), 3.55 – 3.48 (m, 1H, H-11), 2.32 (dd, *J* = 14.6, 5.5 Hz, 1H, H-3), 2.18 (dd, *J* = 10.2, 5.0 Hz, 1H, H-8), 1.86 (dd, *J* = 14.7, 11.4 Hz, 1H, H-3), 1.62 (dd, *J* = 14.9, 9.4 Hz, 1H, H-8), 1.37 – 1.20 (m, 6H, H-6, H-12); ^{13}C NMR (101 MHz, toluene-d_8, *T* = 333 K): δ 137.8 (C=N), 129.0 (t, *J* = 23.7 Hz, CF_3), 128.8, 128.7, 128.6, 128.5, 128.0, 127.8, 127.6, 126.9, 126.7, 126.5, 126.4, 126.3, 125.9, 125.7, 124.6, 124.4, 120.3 (CH_{arom}), 101.1 (C-1), 84.0 (C-10), 80.0 (C-4), 78.4 (C-7), 77.6 (C-11), 76.0, 74.8 (CH_2 Bn), 74.6 (C-2), 74.5, 73.1 (CH_2 Bn), 72.6 C-9), 71.8 (C-5), 71.4, 67.4 (CH_2 Bn), 33.6 (C-3/C-8), 33.5 (C-3/C-8), 16.8 (C-12), 15.7 (C-6); Diagnostic signals of the minor stereoisomer (α-isomer): ^{1}H NMR (400 MHz, toluene-d_8,

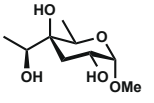
HH-COSY, HSQC, T = 333 K): δ 6.53 (d, J = 3.4 Hz, 1H, H-1), 1.94 (dd, J = 14.9, 9.2 Hz, 1H, H-8); ^{13}C NMR (101 MHz, toluene-d_8, T = 333 K): δ 125.43 (t, J = 24.2 Hz, CF_3), 94.9 (C-1).

Preparation of compound 25

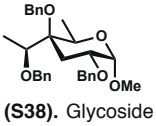
Scheme S5. Synthesis of compound **25**.



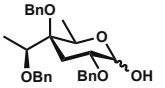
Reagents and conditions: a) HCl, MeOH (*quant.*); b) BnBr, NaH, DMF (53%); c) Ac_2O, H_2SO_4 (88%); d) PhSH, $BF_3{\cdot}OEt_2$, DCM (77%).



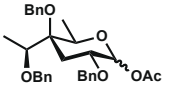
Methyl α-D-yersinioside (S37). Compound **S21** (1.0 g, 3.1 mmol) was dissolved in MeOH (62 mL, 0.05 M). 6 M aq. HCl was added (5.2 mL, 31 mmol, 10 eq.) and the mixture was stirred at room temperature for 3 h. Upon full conversion, the reaction was quenched with basic Amberlite IRA-67 resin (Sigma Aldrich Amberlite IRA-67 free base, pre-washed with MeOH). After filtration, the mixture was concentrated *in vacuo*. Purification by flash column chromatography (80:20 → 60:40; pentane:EtOAc) afforded the title compound (639 mg, 3.1 mmol, *quant.*) as a colorless oil. TLC: R_f 0.7 (acetone); $[\alpha]_D^{20}$ 74.9° (c 1.0, MeOH); IR (neat, cm^{-1}): 1035, 2939, 3383; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.67 (d, J = 3.9 Hz, 1H, H-1), 4.05 (q, J = 6.6 Hz, 1H, H-5), 3.92 (dddd, J = 10.9, 9.5, 6.7, 4.7 Hz, 1H, H-2), 3.69 (qd, J = 6.6, 3.6 Hz, 1H, H-7), 3.45 (s, 3H, CH_3 OMe), 2.24 (s, 1H, OH), 1.95 (d, J = 3.7 Hz, 1H, OH), 1.90 (d, J = 10.8 Hz, 1H, OH), 1.83 (ddd, J = 12.5, 5.6, 0.8 Hz, 1H, H-3), 1.71 (dd, J = 12.6, 11.7 Hz, 1H, H-3), 1.21 (m, 6H, H-6, H-8); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 98.6 (C-1), 74.5 (C-7), 71.5 (C-3), 66.1 (C-5), 65.7 (C-2), 55.4 (CH_3 OMe), 34.7 (C-3), 17.1 (C-8), 14.0 (C-6); HRMS: $[M+Na]^+$ calcd for $C_9H_{18}O_5Na$ 229.1046, found 229.1049.



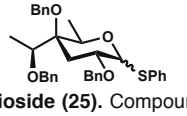
Methyl 2,4,7-tri-*O*-benzyl-α-D-yersinioside (S38). Glycoside **S37** (190 mg, 920 µmol) was dissolved in DMF (9.2 mL, 0.1 M) and BnBr (4.4 mL, 36.8 mmol, 40 eq.) and NaH (1.5 g, 36.8 mmol, 40 eq., 60% dispersion in mineral oil) were added at 0 °C. The mixture was stirred for 96 h at 40 °C and the reaction was quenched with H_2O at 0 °C. The organic phase was washed with sat. aq. $NaHCO_3$ and brine respectively, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Flash column chromatography (95:5 → 80:20; pentane:EtOAc) yielded the title compound (233 mg, 920 µmol, 53%) as a colorless oil. TLC: R_f 0.7 (pentane:EtOAc, 9:1, v:v); $[\alpha]_D^{20}$ 47.8° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 734, 1046, 1454, 2936; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.38 – 7.22 (m, 15H, CH_{arom}), 4.72 – 4.53 (m, 5H, CH_2 Bn, CH_2 Bn, H-1), 4.36 (dd, J = 23.6, 11.6 Hz, 2H, CH_2 Bn), 4.14 (q, J = 6.5 Hz, 1H, H-7), 3.79 (ddd, J = 12.0, 5.0, 3.6 Hz, 1H, H-2), 3.53 (q, J = 6.3 Hz, 1H, H-5), 3.42 (s, 3H, CH_3 OMe), 2.22 – 2.14 (m, 1H, H-3), 2.07 (dd, J = 13.9, 12.0 Hz, 1H, H-3), 1.25 (d, J = 6.4 Hz, 3H, H-8), 1.21 (d, J = 6.6 Hz, 3H, H-6); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 139.3, 138.6, 138.3 ($C_{q\text{-}arom}$), 128.6, 128.4, 128.3, 128.2, 128.1, 127.8, 127.7, 127.4, 127.3, 127.0, 127.0, 126.9 (CH_{arom}), 97.2 (C-1), 79.2 (C-4), 76.8 (C-7), 72.0 (C-2), 71.2, 71.0 (CH_2 Bn), 67.4 (C-5), 65.0 (CH_2 Bn), 55.0 (CH_3 OMe), 27.5 (C-3), 14.7 (C-8), 14.3 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{30}H_{36}O_5Na$ 499.2460, found 499.2459.



2,4,7-Tri-*O*-benzyl-D-yersinioside (S39). Compound **S38** (100 mg, 210 µmol) was dissolved in 80% aq. HCOOH (2.1 mL, 0.1 M) and $SrCl_2 \cdot 6H_2O$ (6.7 mg, 42 µmol, 0.2 eq.) was added. The mixture was stirred for 24 h at 40 °C, and the reaction was quenched with H_2O at 0 °C. The organic phase was washed with sat. aq. $NaHCO_3$ and brine respectively, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Flash column chromatography (90:10 → 70:30; pentane:EtOAc) yielded the title compound (43 mg, 94 µmol, 47%, α:β; 34:66) as a colorless oil. TLC: R_f 0.2 (pentane:EtOAc, 8:2, v:v); IR (neat, cm^{-1}): 696, 734, 1027, 1074, 1453, 3399; Data of the major stereoisomer (β-anomer): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.42 – 7.18 (m, 15H, CH_{arom}), 4.79 (d, *J* = 11.7 Hz, 2H, CH_2 Bn), 4.75 – 4.53 (m, 5H, CH_2 Bn, CH_2 Bn, H-1), 4.11 (q, *J* = 6.5 Hz, 1H, H-7), 3.68 – 3.60 (m, 1H, H-2), 3.48 (q, *J* = 6.1 Hz, 1H, H-5), 2.95 (d, *J* = 5.1 Hz, 1H, 1-OH), 2.35 (dd, *J* = 14.7, 5.7 Hz, 1H, H-3), 1.96 (dd, *J* = 14.6, 11.6 Hz, 1H, H-3), 1.24 (d, *J* = 6.2 Hz, 3H, H-8), 1.18 (d, *J* = 6.4 Hz, 3H, H-6); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 139.3, 138.6, 138.3 ($C_{q\text{-}arom}$), 128.5, 128.4, 128.3, 128.2, 128.1, 127.8, 127.7, 127.4, 127.3, 127.0, 127.0, 126.9 (CH_{arom}), 98.9 (C-1), 79.1 (C-4), 76.3 (C-2), 76.1 (C-7), 75.7 (C-5), 72.4, 72.2, 71.0 (CH_2 Bn), 31.9 (C-3), 14.6 (C-6), 14.3 (C-8); Diagnostic signals of the minor stereoisomer (α-anomer): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.29 (d, *J* = 3.6 Hz, 1H, H-1), 4.49 (d, *J* = 11.4 Hz, 1H, C*H*H Bn), 4.43 (q, *J* = 6.5 Hz, 1H, H-5), 4.33 (t, *J* = 12.2 Hz, 2H, CH_2 Bn), 3.84 (ddd, *J* = 11.4, 5.3, 3.6 Hz, 1H, H-2), 2.89 (s, 1H, 1-OH), 2.21 (dd, *J* = 13.9, 5.1 Hz, 1H, H-3), 2.16 – 2.02 (m, 1H, H-3), 1.27 (d, *J* = 6.3 Hz, 3H, H-6), 1.21 (d, *J* = 6.6 Hz, 3H, H-8); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 128.5, 127.6, 127.4, 127.2, 126.9 (CH_{arom}), 90.1 (C-1), 70.7, 67.0, 65.6 (CH_2 Bn), 26.8 (C-3), 13.9 (C-8), 13.4 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{29}H_{34}O_5Na$ 485.2298, found 485.2299.

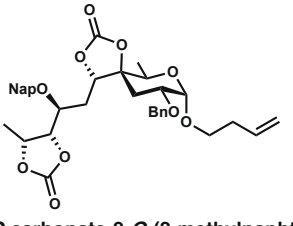


Acetyl 2,4,7-tri-*O*-benzyl-D-yersinioside (S40). Compound **S39** (69 mg, 150 µmol) was dissolved in pyridine (0.4 mL, 0.4 M) and Ac_2O (45 µL, 450 µmol, 3.0 eq.) was added at 0 °C. The reaction mixture was stirred for 24 h and quenched with sat. aq. $NaHCO_3$ upon full conversion. The organic phase was washed with sat. aq. $NaHCO_3$ and brine, respectively. The organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Flash column chromatography (90:10; pentane:EtOAc) yielded the title compound **74** (66 mg, 130 µmol, 87%, α:β; 24:76) as a colorless oil. TLC: R_f 0.5 (pentane:EtOAc, 9:1, v:v); IR (neat, cm^{-1}): 696, 734, 1053, 1088, 1228, 1453, 1748; Data of the major stereoisomer (β-anomer): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.42 – 7.16 (m, 15H, CH_{arom}), 5.61 (d, *J* = 8.1 Hz, 1H, H-1), 4.67 – 4.56 (m, 3H, C*H*H Bn, C*H*H Bn, CH*H* Bn), 4.46 (m, 1H, CH*H* Bn), 4.36 – 4.30 (m, 2H, C*H*H Bn, CH*H* Bn), 4.18 (q, *J* = 6.4 Hz, 1H, H-7), 3.79 (ddd, *J* = 11.5, 8.1, 5.7 Hz, 1H, H-2), 3.48 (q, *J* = 6.2 Hz, 1H, H-5), 2.39 (dd, *J* = 14.6, 5.7 Hz, 1H, H-3), 2.12 (s, 3H, $COCH_3$), 2.00 (dd, *J* = 14.7, 11.5 Hz, 1H, H-3), 1.23 (d, *J* = 6.2 Hz, 3H, H-6), 1.18 (d, *J* = 6.4 Hz, 3H, H-8); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 169.7 (*C*OCH_3), 139.3, 138.4, 138.2 ($C_{q\text{-}arom}$), 128.6, 128.6, 128.5, 128.4, 128.4, 128.0, 127.9, 127.9, 127.9, 127.8, 127.6, 127.4, 127.3, 127.3, 127.1 (CH_{arom}), 96.3 (C-1), 79.0 (C-4), 76.7 (C-7), 76.0 (C-5), 73.9 (C-2), 72.6, 70.9, 66.9 (CH_2 Bn), 32.2 (C-3), 21.4 (CO*C*H_3), 14.4 (C-8), 13.6 (C-6); Diagnostic signals of the minor stereoisomer (α-anomer): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 6.33 (d, *J* = 3.6 Hz, 1H, H-1), 3.89 (ddd, *J* = 12.1, 5.2, 3.5 Hz, 1H, H-2), 3.56 (q, *J* = 6.3 Hz, 1H, H-5), 2.23 (ddd, *J* = 13.9, 4.6, 0.8 Hz, 1H, H-3), 2.12 (s, 3H, $COCH_3$), 1.28 (d, *J* = 6.3 Hz, 3H, H-6), 1.21 (d, *J* = 6.6 Hz, 3H, H-8);^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 170.1 (*C*OCH_3), 139.2, 138.6, 138.0 ($C_{q\text{-}arom}$), 89.6 (C-1), 79.0 (C-4), 76.8 (C-7), 71.5, 71.1 (CH_2 Bn), 71.0 (C-2), 70.3 (C-5), 65.7 (CH_2 Bn), 27.8 (C-3), 21.3 (CO*C*H_3), 14.7 (C-8), 14.1 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{31}H_{36}O_6Na$ 527.2404, found 527.2410.

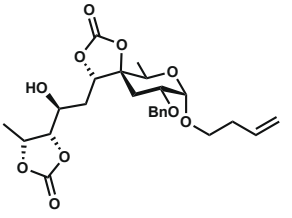


Phenyl 2,4,7-tri-*O*-benzyl-1-thio-D-yersinioside (25). Compound **S40** (66 mg, 130 µmol) was dissolved in DCM (1.3 mL, 0.1 M) and cooled to –80 °C upon which thiophenol (14.6 µL, 143 µmol, 1.1 eq.) and $BF_3 \cdot OEt_2$ (19.3 µL, 156 µmol, 1.2 eq.) were added. The reaction mixture was stirred for 2 h and was allowed to warm to room temperature. The reaction was quenched with sat. aq. $NaHCO_3$ and the organic phase

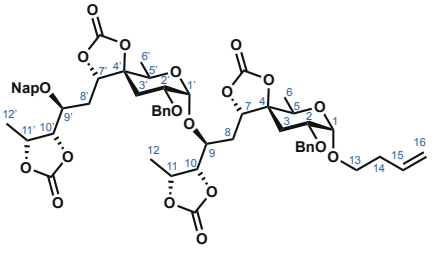
was washed with sat. aq. $NaHCO_3$ and brine, respectively. The organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Flash column chromatography (99:1 → 95:5; pentane:EtOAc) yielded the title compound (55 mg, 100 µmol, 77%, α:β; 65:35) as a colorless oil. TLC: R_f 0.7 (pentane:EtOAc, 9.5:0.5, v:v); IR (neat, cm^{-1}): 694, 733, 1026, 1073, 1453; Data of the major stereoisomer (α-anomer): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.70 – 7.12 (m, 15H), 5.78 (d, *J* = 5.1 Hz, 1H, H-1), 4.75 – 4.61 (m, 3H, CH*H* Ph, C*H*H Ph, H-7), 4.57 (d, *J* = 10.0 Hz, 1H, CH*H* Ph), 4.50 (d, *J* = 10.0 Hz, 1H, C*H*H Ph), 4.47 – 4.40 (m, 1H, CH*H* Ph), 4.36 (d, *J* = 11.9 Hz, 1H, C*H*H Ph), 4.15 (dt, *J* = 11.9, 4.9 Hz, 1H, H-2), 3.60 (q, *J* = 6.2 Hz, 1H, H-5), 2.29 (dd, *J* = 14.3, 4.6 Hz, 1H, H-3), 2.07 (dd, *J* = 14.4, 11.9 Hz, 1H, H-3), 1.29 (d, *J* = 6.2 Hz, 3H, H-8), 1.23 – 1.17 (m, 3H, H-6); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 139.2, 138.5, 137.8, 135.2 ($C_{q\text{-}arom}$), 132.1, 131.3, 128.8, 128.7, 128.5, 128.4, 128.4, 128.3, 128.2, 128.0, 127.9, 127.8, 127.7, 127.6, 127.4, 127.4, 127.2, 127.1, 127.1, 126.9 (CH_{arom}), 87.3 (C-1), 79.0 (C-4), 78.9 (C-7), 72.3 (CH_2 Bn), 72.0 (C-2), 70.9, 70.8 (CH_2 Bn), 69.1 (C-5), 29.7 (C-3), 14.6 (C-8), 14.1 (C-6); Diagnostic signals of the minor stereoisomer (β-anomer): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.65 (d, *J* = 8.3 Hz, 1H, H-1), 4.05 (q, *J* = 6.4 Hz, 1H, H-7), 3.72 (td, *J* = 10.3, 5.5 Hz, 1H, H-2), 3.45 (q, *J* = 6.2 Hz, 1H, H-5), 2.37 (dd, *J* = 14.5, 5.6 Hz, 1H, H-3), 1.97 (dd, *J* = 14.5, 11.0 Hz, 1H, H-3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 88.3 (C-1), 78.9 (C-4), 78.8 (C-7), 76.1 (C-5), 73.2 (C-2), 72.1, 70.7, 66.9 (CH_2 Bn), 33.4 (C-3), 14.7 (C-8), 13.3 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{35}H_{38}O_4SNa$ 577.2383, found 577.2389.



3-Butene 2-*O*-benzyl-4,7,10,11-di-*O*-carbonate-9-*O*-(2-methylnaphthalene)-α-D-caryophylloside (30). Compound **4** (1.68 g, 2.5 mmol) was dissolved in DCM (50 mL, 0.05 M) in a flame dried flask containing activated 3 Å molecular sieves (rods, size 1/16 in., Sigma Aldrich). Ph_2SO (650 mg, 3.25 mmol, 1.3 eq.), ethyl maleimide (625 mg 5.0 mmol, 2 eq) and TTBP (1.55 g, 6.25 mmol, 2.5 eq.) were added. The solution was stirred at room temperature for 30 min. The solution was cooled to –80 °C upon which Tf_2O (550 µL, 3.25 mmol, 1.3 eq.) was added slowly. Subsequently, the solution was allowed to attain to –65 °C to secure full activation of the donor followed by cooling back to –80 °C after which TBAI (7.4 g, 20 mmol, 8 eq.) was added. The solution was stirred for 5 min at –80 °C followed by the addition of the acceptor (5.4 mL, 62.5 mmol, 25 eq.) and triphenylphosphine oxide (4.17 g, 15 mmol, 6.0 eq.). The reaction was refluxed for 40 h upon which the reaction was quenched with sat. aq. $NaHCO_3$ followed by the dilution with EtOAc and sat. aq. $Na_2S_2O_3$. The aqueous layer was extracted three times with EtOAc. The organic layer was washed with H_2O and brine, dried over $MgSO_4$, filtered off and concentrated under reduced pressure. Flash column chromatography (80:20 → 60:40; pentane:EtOAc) yielded the title compound (943 mg, 1.49 mmol, 60%, α:β; >98:2) as a white foam. TLC: R_f 0.6 (pentane:EtOAc, 6:4, v:v); $[\alpha]_D^{20}$ 66.1° (c 0.5, $CHCl_3$); IR (neat, cm^{-1}): 1055, 1202, 1797; ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC): δ 7.89 – 7.27 (m, 12H, CH_{arom}), 5.83 (ddt, *J* = 17.1, 10.3, 6.8 Hz, 1H, H-15), 5.14 (dq, *J* = 17.2, 1.6 Hz, 1H, H-16), 5.09 (ddt, *J* = 10.2, 2.1, 1.2 Hz, 1H, H-16), 4.95 – 4.88 (m, 1H, H-11), 4.78 (d, *J* = 2.0 Hz, 2H, CH_2 Bn/Nap), 4.77 (d, *J* = 3.3 Hz, 1H, H-1), 4.63 (dd, *J* = 7.4, 6.4 Hz, 1H, H-10), 4.55 (d, *J* = 12.1 Hz, 1H, C*H*H Bn/Nap), 4.50 (d, *J* = 12.0 Hz, 1H, CH*H* Bn/Nap), 4.33 (dd, *J* = 11.4, 1.9 Hz, 1H, H-7), 4.02 (ddd, *J* = 8.5, 6.4, 3.1 Hz, 1H, H-9), 3.92 (q, *J* = 6.3 Hz, 1H, H-5), 3.75 (ddd, *J* = 11.7, 4.8, 3.3 Hz, 1H, H-2), 3.69 (dt, *J* = 9.8, 6.9 Hz, 1H, H-13), 3.55 (dt, *J* = 9.9, 6.4 Hz, 1H, H-13), 2.40 (ttd, *J* = 8.0, 6.7, 1.4 Hz, 2H, H-14), 2.13 – 2.03 (m, 2H, H-3, H-8), 1.92 (ddd, *J* = 14.9, 8.6, 2.0 Hz, 1H, H-8), 1.83 (dd, *J* = 13.5, 4.8 Hz, 1H, H-3), 1.46 (d, *J* = 6.7 Hz, 3H, H-12), 1.22 (d, *J* = 6.3 Hz, 3H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC): δ 153.6, 153.5 (O(C=O)O), 137.9 ($C_{q\text{-}arom}$), 135.2 (C-15), 134.1, 133.3, 133.3 ($C_{q\text{-}arom}$), 128.9, 128.6, 128.1, 128.0, 127.9, 126.8, 126.8, 126.7, 125.4 (CH_{arom}), 117.1 (C-16), 95.5 (C-1), 84.9 (C-4), 81.0 (C-7), 78.9 (C-10), 75.8 (C-11), 73.8 (C-9), 73.7, 71.5 (CH_2 Bn/Nap), 71.5 (C-2), 67.7 (C-13), 64.8 (C-5), 34.0 (C-14), 33.7 (C-3), 29.7 (C-8), 15.3 (C-12), 14.9 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{36}H_{40}O_{10}Na$ 655.2519, found 655.2514.

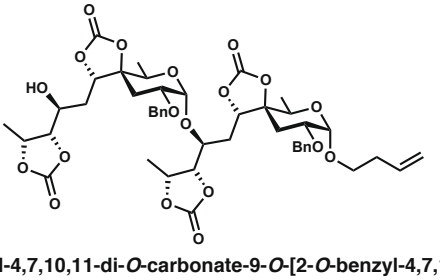


3-Butene 2-*O*-benzyl-4,7,10,11-di-*O*-carbonate-α-D-caryophylloside (31). Compound **30** (943 mg, 1.49 mmol) was divided into 15 equal portions of 0.1 mmol. Compound **30** (0.1 mmol, 63.3 mg, 1.0 eq.) was dissolved in 1:1 (v:v) DCM:HFIP (2.0 mL, 0.05 M) and TES (50 µL, 0.3 mmol, 3.0 eq.) was added. Then 0.5 M solution of HCl in HFIP (3.0 mL, 1.5 mmol, 15 eq.) was added and the reaction mixture was stirred for 2 h. Upon completion, the reaction was quenched with sat. aq. $NaHCO_3$. The aqueous layer was extracted twice with EtOAc followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (70:30 → 40:60; pentane:EtOAc) yielded the title compound (454 mg, 0.92 mmol, 61%) as a white foam. TLC: R_f 0.7 (pentane:EtOAc, 1:1, v:v); $[\alpha]_D^{20}$ 32.1° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 1058, 1205, 1357, 1800, 2918, 3477; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC): δ 7.38 – 7.28 (m, 5H, CH_{arom}), 5.83 (ddt, *J* = 17.1, 10.2, 6.8 Hz, 1H, H-15), 5.18 – 5.05 (m, 2H, H-16, H-16), 4.97 (p, *J* = 6.7 Hz, 1H, H-11), 4.80 (d, *J* = 3.3 Hz, 1H, H-1), 4.59 (d, *J* = 1.5 Hz, 2H, CH_2 Bn), 4.53 (dd, *J* = 11.9, 2.1 Hz, 1H, H-7), 4.40 (dd, *J* = 9.0, 7.3 Hz, 1H, H-10), 4.08 (q, *J* = 8.5 Hz, 1H, H-9), 3.93 (q, *J* = 6.3 Hz, 1H, H-5), 3.81 (ddd, *J* = 11.4, 5.0, 3.3 Hz, 1H, H-2), 3.71 (dt, *J* = 9.8, 6.9 Hz, 1H, H-13), 3.55 (dt, *J* = 9.8, 6.4 Hz, 1H, H-13), 2.99 (d, *J* = 7.0 Hz, 1H, 9-OH), 2.40 (tdt, *J* = 8.7, 7.9, 4.4, 1.3 Hz, 2H, H-14), 2.18 – 1.99 (m, 3H, H-3, H-3, H-8), 1.70 (ddd, *J* = 14.8, 10.5, 2.1 Hz, 1H, H-8), 1.49 (d, *J* = 6.7 Hz, 3H, H-12), 1.24 (d, *J* = 6.3 Hz, 3H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC): δ 154.0, 153.9 (O(C=O)O), 137.9 ($C_{q\text{-}arom}$), 135.1 (C-15), 128.7, 128.2, 128.0 (CH_{arom}), 117.1 (C-16), 95.5 (C-1), 85.2 (C-4), 80.9 (C-7), 80.0 (C-10), 76.2 (C-11), 71.7 (CH_2 Bn), 71.7 (C-2), 67.7 (C-13), 65.1 (C-5), 64.8 (C-9), 34.1 (C-14), 33.7 (C-3), 32.1 (C-8), 15.0 (C-12), 14.8 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{25}H_{32}O_{10}Na$ 515.1893, found 515.1888.

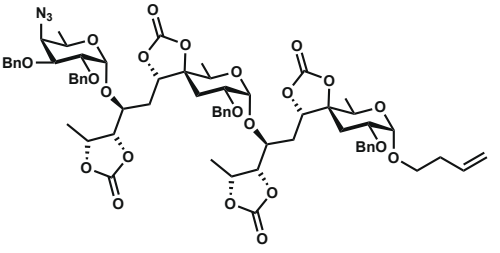


3-Butene 2-*O*-benzyl-4,7,10,11-di-*O*-carbonate-9-*O*-[2-*O*-benzyl-4,7,10,11-di-*O*-carbonate-9-*O*-(2-methylnaphthalene)-α-D-caryophyllosyl]-α-D-caryophylloside (32). Compound **4** (335 mg, 0.5 mmol, 1 eq.) was dissolved in DCM (10 mL, 0.05 M) in a flame dried flask containing activated 3 Å molecular sieves (rods, size 1/16 in., Sigma Aldrich). Ph_2SO (110 mg, 0.55 mmol, 1.1 eq.) and TTBP (310 mg, 1.25 mmol, 2.5 eq.) were added. The solution was stirred at room temperature for 30 min. The solution was cooled to –80 °C upon which Tf_2O (93.5 µL, 0.55 mmol, 1.1 eq.) was added slowly. Subsequently, the solution was allowed to attain to –65 °C to secure full activation of the donor followed by cooling back to –80 °C after which acceptor **31** (2.0 mL of a 0.5 M solution, 2.0 eq.) was added. The reaction was stirred for 20 h at –65 °C upon which the reaction was quenched with sat. aq. $NaHCO_3$ followed by the dilution with DCM. The aqueous layer was extracted three times with EtOAc. The organic layer was washed with H_2O and brine, dried over $MgSO_4$, filtered off and concentrated under reduced pressure. Size exclusion chromatography by isocratic elution with DCM:MeOH (1:1, v:v) followed by flash column chromatography (80:20 → 70:30; pentane:acetone) yielded the title compound (262 mg, 249 µmol, 50%, α:β; >98:2) as a white foam. TLC: R_f 0.4 (pentane:acetone, 7:3, v:v); $[\alpha]_D^{20}$ 42.6° (c 0.5, $CHCl_3$); IR (neat, cm^{-1}): 754, 1062, 1201, 1802; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC): δ 7.90 – 7.28 (m, 17H, CH_{arom}), 5.79 (ddt, *J* = 17.1, 10.2, 6.7 Hz, 1H, H-15), 5.14 – 5.04 (m, 2H, H-16, H-16), 4.99 – 4.87 (m, 3H, H-1, H-11, H-11'), 4.85 – 4.75 (m, 3H, C*H*H Bn/Nap, CH*H* Bn/Nap, H-10), 4.71 (d, *J* = 3.3 Hz, 1H, H-1'), 4.70 – 4.58 (m, 2H, H-7, H-10'),

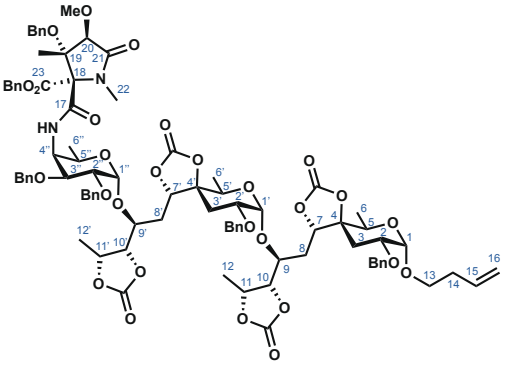
4.53 – 4.32 (m, 5H, C*H*H Bn/Nap, C*H*H Bn/Nap, CH*H* Bn/Nap, CH*H* Bn/Nap, H-7'), 4.10 (td, *J* = 8.8, 3.0 Hz, 1H, H-9'), 4.04 – 3.93 (m, 2H, H-5', H-9), 3.83 – 3.75 (m, 2H, H-2', H-5), 3.65 (dt, *J* = 9.9, 6.9 Hz, 1H, H-13), 3.55 (dt, *J* = 11.8, 4.4 Hz, 1H, H-2), 3.48 (dt, *J* = 9.9, 6.4 Hz, 1H, H-13), 2.35 (q, *J* = 7.7 Hz, 2H, H-14), 2.19 – 1.96 (m, 3H, H-8, H-8', H-8'), 1.95 – 1.78 (m, 5H, H-3, H-3', H-3, H-3', H-8), 1.54 – 1.48 (m, 6H, H-12, H-12'), 1.25 (d, *J* = 6.3 Hz, 3H, H-6'), 1.16 (d, *J* = 6.3 Hz, 3H, H-6); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC): δ 153.7, 153.6, 153.4, 153.1 (O(C=O)O), 137.9, 137.1 ($C_{q\text{-}arom}$), 135.0 (C-15), 134.3, 133.2 ($C_{q\text{-}arom}$), 129.0, 128.7, 128.6, 128.4, 128.1, 128.0, 127.9, 127.8, 126.8, 126.7, 126.6, 125.5 (CH_{arom}), 117.0 (C-16), 98.3 (C-1'), 95.3 (C-1), 84.5 (C-4'), 84.0 (C-4), 80.9 (C-7'), 80.2 (C-7), 79.9 (C-10), 79.0 (C-10'), 76.3 (C-9), 75.9 (C-11/C-11'), 75.6 (C11'/C-11), 73.8 (C-9'), 73.8 (CH_2 Bn/Nap), 72.0 (C-2'), 71.9 (CH_2 Bn/Nap), 71.5 (C-2), 71.5 (CH_2 Bn/Nap), 67.7 (C-13), 66.3 (C-5'), 64.7 (C-5), 33.9 (C-14), 32.9 (C-3'/C-3), 32.8 (C-3/C-3'), 29.6 (C-8'), 29.3 (C-8), 15.3 (C-12'/C-12), 15.1 (C-12/C-12'), 14.9 (C-6, C-6'); HRMS: $[M+Na]^+$ calcd for $C_{57}H_{54}O_{19}Na$ 1075.3939, found 1075.3934.



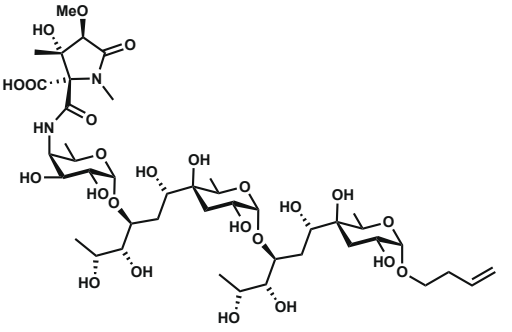
3-Butene 2-*O*-benzyl-4,7,10,11-di-*O*-carbonate-9-*O*-[2-*O*-benzyl-4,7,10,11-di-*O*-carbonate-α-D-caryophyllosyl]-α-D-caryophylloside (33). Compound **32** (84 mg, 80 µmol) was dissolved in 1:1 DCM:HFIP (1.6 mL, 0.05 M) and TES (40 µL, 240 µmol, 3.0 eq.) was added. Then 1.0 M solution of HCl in HFIP (2.4 mL, 2.4 mmol, 30 eq.) was added and the reaction mixture was stirred for 1.5 h. Upon completion the reaction was quenched with sat. aq. $NaHCO_3$. The aqueous layer was extracted twice with EtOAc followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (70:30 → 40:60; pentane:EtOAc) yielded the title compound (44 mg, 48 µmol, 60%) as a white foam. TLC: R_f 0.3 (toluene:EtOAc, 1:1, v:v); $[\alpha]_D^{20}$ –102.8° (c 0.25, $CHCl_3$); IR (neat, cm^{-1}): 753, 1052, 1201, 1368, 1804, 2923; ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.40 – 7.27 (m, 10H, CH_{arom}), 5.80 (ddt, *J* = 17.1, 10.3, 6.7 Hz, 1H, H-15), 5.14 – 5.04 (m, 2H, H-16, H-16), 5.02 – 4.95 (m, 2H, H-11, H-11'), 4.92 (d, *J* = 3.4 Hz, 1H, H-1'), 4.86 (dd, *J* = 7.5, 3.8 Hz, 1H, H-10), 4.72 (d, *J* = 3.3 Hz, 1H, H-1), 4.63 – 4.55 (m, 3H, H-7, H-7', H-10'), 4.55 – 4.43 (m, 4H, C*H*H Bn, C*H*H Bn, CH*H* Bn, CH*H* Bn), 4.06 – 3.98 (m, 3H, H-5, H-5', H-9), 3.87 (ddd, *J* = 11.8, 4.9, 3.3 Hz, 1H, H-2'), 3.79 (q, *J* = 6.2 Hz, 1H, H-5), 3.66 (dt, *J* = 10.0, 6.9 Hz, 1H, H-13), 3.59 (ddd, *J* = 11.8, 4.8, 3.3 Hz, 1H, H-2), 3.50 (dt, *J* = 10.0, 6.4 Hz, 1H, H-13), 3.08 (d, *J* = 8.4 Hz, 1H, 9'-OH), 2.36 (dddd, *J* = 9.5, 7.8, 5.4, 1.3 Hz, 2H, H-14), 2.22 – 1.82 (m, 8H, H-3, H-3', H-3, H-3', H-8, H-8', H-8, H-8'), 1.56 – 1.48 (m, 6H, H-12, H-12'), 1.27 (d, *J* = 6.3 Hz, 3H, H-6'), 1.15 (d, *J* = 6.3 Hz, 3H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 154.2, 154.1, 153.6, 153.6 (O(C=O)O), 137.9, 137.3 ($C_{q\text{-}arom}$), 135.1 (C-15), 129.1, 129.0, 129.0, 128.7, 128.6, 128.4, 128.2, 128.1, 128.1, 128.0, 127.9, 127.9, 127.9 (CH_{arom}), 117.1 (C-16), 97.4 (C-1'), 95.5 (C-1), 84.8 (C-4'), 84.4 (C-4), 81.2 (C-7'), 80.7 (C-7), 80.0 (C-10), 79.9 (C-10'), 76.4 (C-11, C-11'), 75.9 (C-9), 72.2 (C-2'), 72.1, 71.6 (CH_2 Bn), 71.6 (C-2), 67.8 (C-13), 66.5 (C-9'), 65.2 (C-5'), 64.7 (C-5), 34.0 (C-14), 33.1 (C-3), 33.1, (C-3'), 32.5 (C-8'), 28.8 (C-8), 15.1 (C-12'/C-12), 15.0 (C-12/C-12'), 15.0 (C-6/C-6'), 14.9 (C-6'/C-6); HRMS: $[M+Na]^+$ calcd for $C_{46}H_{56}O_{19}Na$ 935.3313, found 935.3308.



3-Butene 2-*O*-benzyl-4,7,10,11-di-*O*-carbonate-9-*O*-[2-*O*-benzyl-4,7,10,11-di-*O*-carbonate-9-*O*-[4-azido-2,3-di-*O*-benzyl-4,6-dideoxy-α-D-galactopyranosyl]-α-D-caryophyllosyl]-α-D-caryophylloside (34). Compound **3** (150 µmol, 69.2 mg, 3 eq.) was dissolved in DCM (1.0 mL, 0.05 M) in a flame dried flask containing activated 3 Å molecular sieves (rods, size 1/16 in., Sigma Aldrich). Ph_2SO (29 mg, 145 µmol, 2.9 eq.) and TTBP (31 mg, 125 µmol, 2.5 eq.) were added. The solution was stirred at room temperature for 30 min. The solution was cooled to –80 °C upon which Tf_2O (24.5 µL, 145 µmol, 2.9 eq.) was added slowly. Subsequently, the solution was allowed to attain to –65 °C to secure full activation of the donor followed by cooling back to –80 °C after which acceptor **33** (0.1 mL of a 0.5 M solution, 1.0 eq.) was added. The reaction was stirred for 20 h at –65 °C upon which the reaction was quenched with sat. aq. $NaHCO_3$ followed by the dilution with DCM. The aqueous layer was extracted three times with EtOAc. The organic layer was washed with H_2O and brine, dried over $MgSO_4$, filtered off and concentrated under reduced pressure. Size exclusion chromatography by isocratic elution with DCM:MeOH (1:1, v:v) followed by flash column chromatography (70:30 → 50:50; pentane:acetone) yielded the title compound (27.1 mg, 21.4 µmol, 43%, α:β; >98:2) as a white foam. TLC: R_f 0.6 (EtOAc:toluene, 1:1, v:v); ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC): δ 7.44 – 7.27 (m, 20H, CH_{arom}), 5.79 (ddt, *J* = 17.0, 10.3, 6.7 Hz, 1H, H-15), 5.13 – 5.04 (m, 2H, H-16, H-16), 4.97 (d, *J* = 3.9 Hz, 1H, H-1''), 4.94 – 4.82 (m, 5H, H-1', H-7', H-11, H-11', C*H*H Bn), 4.79 (s, 2H, CH_2 Bn), 4.72 – 4.68 (m, 3H, H-1, H-10, H-10'), 4.61 – 4.53 (m, 2H, H-7, CH*H* Bn), 4.48 (d, *J* = 11.8 Hz, 1H, C*H*H Bn), 4.42 (d, *J* = 11.9 Hz, 1H, CH*H* Bn), 4.38 (d, *J* = 10.7 Hz, 1H, C*H*H Bn), 4.32 (d, *J* = 10.8 Hz, 1H, CH*H* Bn), 4.09 – 4.03 (m, 2H, H-3'', H-5''), 3.99 – 3.91 (m, 3H, H-2'', H-9, H-9'), 3.82 – 3.73 (m, 3H, H-4'',H-5, H-5'), 3.65 (dt, *J* = 9.9, 6.8 Hz, 1H, H-2'), 3.57 (ddd, *J* = 12.0, 4.7, 3.5 Hz, 1H, H-13), 3.54 – 3.50 (m, 1H, H-2), 3.47 (dt, *J* = 10.0, 6.5 Hz, 1H, H-13), 2.35 (qd, *J* = 6.7, 6.2, 2.9 Hz, 2H, H-14), 1.94 – 1.89 (m, 2H, H-8', H-8'), 1.83 (ddd, *J* = 9.1, 6.1, 3.2 Hz, 2H, H-8, H-8), 1.76 (dd, *J* = 13.6, 11.9 Hz, 1H, H-3), 1.68 (dd, *J* = 13.5, 11.9 Hz, 1H, H-3'), 1.48 (d, *J* = 6.7 Hz, 6H, H-12, H-12'), 1.27 (d, *J* = 6.4 Hz, 3H, H-6''), 1.21 (d, *J* = 6.2 Hz, 3H, H-6'), 1.15 (d, *J* = 6.3 Hz, 3H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 153.7, 153.7, 153.4, 153.3 (O(C=O)O), 138.0, 138.0, 137.7, 137.3 ($C_{q\text{-}arom}$), 135.0 (C-15), 129.1, 129.1, 129.1, 128.8, 128.6, 128.6, 128.5, 128.5, 128.4, 128.3, 128.2, 128.1, 127.9, 127.9, 127.8, 127.8, 127.7 (CH_{arom}), 117.1 (C-16), 100.9 (C-1''), 98.3 (C-1'), 95.4 (C-1), 84.5 (C-4'), 83.8 (C-4), 80.4 (C-10, C-10'), 80.1 (C-7'), 80.0 (C-7), 78.3 (C-3''), 76.3 (C-9'/C-9), 76.0 (C-9/C-9'), 75.9 (C-2''), 75.9 (C-11'/C-11), 75.6 (C-11/C-11'), 75.3, 72.6 (CH_2 Bn), 72.2 (C-2'), 72.1 (CH_2 Bn), 71.6 (C-2), 71.5 (CH_2 Bn), 67.8 (C-13), 66.4 (C-5'), 66.0 (C-5''), 64.8 (C-4''), 64.1 (C-5), 33.9 (C-14), 32.9 (C-3), 32.0 (C-3'), 29.8 (C-8'), 29.3 (C-8), 17.6 (C-6''), 15.2 (C-12'/C-12), 15.1 (C-12/C-12'), 15.0 (C-6, C-6'); HRMS: $[M+Na]^+$ calcd for $C_{66}H_{77}O_{22}N_3Na$ 1286.4896, found 1286.4890.



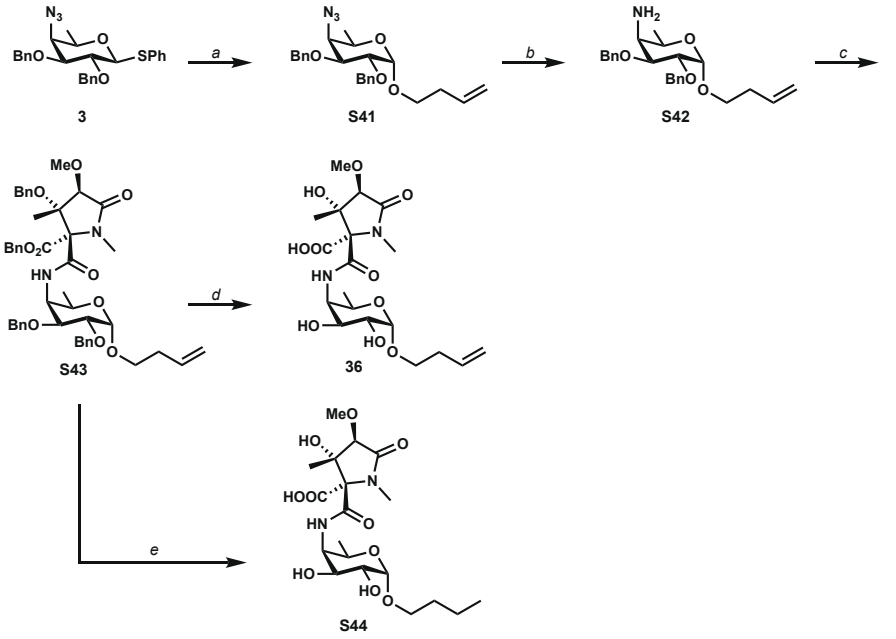
3-Butene 2-*O*-benzyl-4,7,10,11-di-*O*-carbonate-9-*O*-[2-*O*-benzyl-4,7,10,11-di-*O*-carbonate-9-*O*-[4-[(2'*S*,3'*S*,4'*R*)-3'-*O*-Benzyl-2'-(benzyloxycarbonyl)-4'-methoxy-1',3'-dimethyl-5'-oxopyrrolidine-2'-carboxamido]-2,3-di-*O*-benzyl-4,6-dideoxy-α-D-galactopyranosyl]-α-D-caryophyllosyl]-α-D-caryophylloside (35). Compound **34** (26.5 mg, 21 µmol, 1.0 eq.) was dissolved in THF (200 µL, 0.1 M) followed by the addition of trimethylphosphine (23.1 µL, 23.1 µmol, 1.1 eq. [1.0 M solution in THF, Sigma-Aldrich]). The mixture was stirred for 3 h at room temperature upon which H_2O (4.7 µL, 262 µmol, 12.5 eq.) was added and the reaction was stirred for another 18 h. Upon completion, the reaction was concentrated *in vacuo* to yield the crude galactosamine. To a stirred solution of pyrrolidone **2** (10.9 mg, 26.3 µmol, 1.25 eq.) and triethylamine (7.3 µL, 53 µmol, 2.5 eq.) in CH_3CN (0.2 mL, 0.1 M) was added HATU (10.5 mg, 27.7 µmol, 1.3 eq.). The solution was stirred for 30 min at room temperature followed by the addition of the galactosamine in 0.2 mL CH_3CN. The reaction was stirred for 3 h at room temperature upon which 1M HCl and EtOAc were added. The aqueous layer was extracted with EtOAc (3x) followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product as a colorless oil. Size exclusion chromatography by isocratic elution with DCM:MeOH (1:1, v:v) yielded the title compound (5 mg, 3 µmol, 15%, over 2 steps) as a colorless oil. TLC: R_f 0.5 (toluene:acetone, 7:3, v:v); ^{1}H NMR (600 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.08 (d, *J* = 10.1 Hz, 1H, NH), 7.39 – 7.13 (m, 30H, CH_{arom}), 5.78 (ddt, *J* = 17.1, 10.3, 6.7 Hz, 1H, H-15), 5.21 (d, *J* = 12.0 Hz, 1H, C*H*H Bn), 5.15 – 5.05 (m, 3H, CH*H* Bn, H-16, H-16), 4.96 (d, *J* = 4.1 Hz, 1H, H-1''), 4.93 – 4.82 (m, 5H, H-1', H-7', H-11', H-11, C*H*H Bn), 4.72 – 4.67 (m, 3H, H-1, H-10', H-10), 4.65 – 4.60 (m, 2H, H-4'', C*H*H Bn), 4.59 – 4.53 (m, 2H, H-7, CH*H* Bn), 4.51 – 4.46 (m, 2H, CH*H* Bn, C*H*H Bn), 4.41 (d, *J* = 11.8 Hz, 1H, CH*H* Bn), 4.37 (d, *J* = 11.6 Hz, 1H, CH*H* Bn), 4.34 (d, *J* = 10.6 Hz, 1H, C*H*H Bn), 4.29 (d, *J* = 10.5 Hz, 1H, CH*H* Bn), 4.23 (q, *J* = 6.6, 3.7 Hz, 1H, H-5''), 4.03 (dd, *J* = 10.2, 3.9 Hz, 1H, H-3''), 3.99 (q, *J* = 5.9 Hz, 1H, H-9'), 3.94 (dt, *J* = 10.0, 3.6 Hz, 1H, H-9), 3.91 (s, 1H, H-20), 3.79 (q, *J* = 6.2 Hz, 1H, H-5'), 3.73 (q, *J* = 6.2 Hz, 1H, H-5), 3.67 – 3.55 (m, 5H, H-2'', H-13, OCH_3), 3.55 – 3.42 (m, 3H, H-2, H-2', H-13), 2.58 (s, 3H, NCH_3), 2.34 (ddt, *J* = 6.4, 3.0, 1.4 Hz, 2H, H-14), 1.93 – 1.61 (m, 8H, H-3, H-3', H-3, H-3', H-8, H-8', H-8, H-8'), 1.52 (d, *J* = 6.6 Hz, 3H, H-12'), 1.47 (d, *J* = 6.6 Hz, 3H, H-12), 1.44 (s, 3H, 19-CH_3), 1.22 (d, *J* = 6.2 Hz, 3H, H-6'), 1.19 (d, *J* = 6.4 Hz, 3H, H-6''), 1.13 (d, *J* = 6.3 Hz, 3H, H-6); ^{13}C NMR (151 MHz, $CDCl_3$, HSQC): δ 172.7 (C=O ester), 169.1, 164.5 (C=O amide), 153.6, 153.4 (O(C=O)O), 138.3, 138.2, 137.9, 137.8, 137.2 ($C_{q\text{-}arom}$), 135.0 (C-15), 134.4 ($C_{q\text{-}arom}$), 129.2, 129.1, 129.0, 128.8, 128.7, 128.7, 128.6, 128.6, 128.6, 128.5, 128.4, 128.2, 128.2, 127.9, 127.8, 127.8, 127.7, 127.1 (CH_{arom}), 117.1 (C-16), 101.4 (C-1''), 97.8 (C-1'), 95.3 (C-1), 84.4 (C-4'), 84.0 (C-19), 83.8 (C-4), 82.5 (C-20), 80.5 (C-10'), 80.1 (C-10), 80.0 (C-7'), 79.8 (C-7), 78.9 (C-18), 77.6 (C-3''), 76.5 (C-9'/C-9), 76.3 (C-2''), 76.0 (C-9/C-9'), 75.9 (C-11'/C-11), 75.6 (CH_2 Bn), 75.6 (C-11/C-11'), 72.2 (C-2'), 72.1, 71.6 (CH_2 Bn), 71.5 (C-2), 71.4, 68.7, 67.8, 66.5 (CH_2 Bn), 66.5 (C-5'), 65.7 (C-5''), 64.7 (C-5), 59.5 (CH_3 OMe), 51.4 (C-4''), 33.9 (C-14), 32.8 (C-3'), 31.8 (C-3), 30.0 (C-8'), 29.8 (C-8), 29.2 (CH_3 NMe), 17.6 (C-6''), 15.3 (C-12'/C-12), 15.2 (C-12/C-12'), 15.0 (C-6'/C-6), 15.0 (C-6/C-6'), 14.9 (CH_3); HRMS: $[M+Na]^+$ calcd for $C_{89}H_{102}O_{28}N_2Na$ 1669.6517, found 1669.6511.



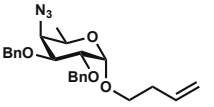
3-Butene 9-*O*-[9-*O*-[4-[(2'*S*,3'*S*,4'*R*)-2'-carboxyl-3'-hydroxy-4'-methoxy-1',3'-dimethyl-5'-oxopyrrolidine-2'-carboxamido]-4,6-dideoxy-α-D-galactopyranosyl]-α-D-caryophyllosyl]-α-D-caryophylloside (1). The protected target structure **35** (4.9 mg, 3 µmol) was dissolved in 0.6 mL 1:1 v:v THF:H_2O (0.005 M). LiOH·H_2O (12.6 mg, 300 µmol, 100 eq.) was added and the resulting mixture was stirred at room temperature for 20 h. Upon completion, 80% of the LiOH was quenched with 0.1 M HCl (2.4 mL) and the mixture was concentrated under reduced pressure to yield the crude product. The crude product was then co-evaporated twice with dry toluene. 3 mL ammonia was condensed at –70 °C, sodium (3.45 mg, 150 µmol, 50 eq.) was added and the resulting suspension was stirred for 30 min. The crude product was dissolved in 0.5 mL THF, hexene (50 µL, used for scales from 1-25 µmol) and *t*-BuOH (2.85 µL, 30 µmol, 10 eq.) and the solution was added to the suspension of sodium in ammonia. The reaction mixture was stirred at –70 °C for 15 min, upon which the reaction was quenched with water. The reaction mixture was then stirred at room temperature until all ammonia had evaporated. The mixture was concentrated *in vacuo* to yield the crude product as a colorless oil. Flash column chromatography (30:70 → 50:50; MeOH:DCM) followed by size exclusion over a 250x10 mm column filled with Biogel P2 media (Bio-Rad) yielded the title compound **1** (1.2 mg, 1.2 µmol, 40% over two steps) as a colorless oil. The NMR data showed the presence of four atropisomers in D_2O. Data for atropisomeric mixture: ^{1}H NMR (850 MHz, D_2O, HH-COSY, HSQC): δ 6.10 (td, *J* = 10.4, 6.7 Hz, 1H, H-15), 5.35 (d, *J* = 17.5, 1.7 Hz, 1H, H-16), 5.30 – 5.26 (m, 2H, H-1'', H-16), 5.13 – 5.09 (m, 1H, H-1'), 4.98 (d, *J* = 3.7 Hz, 1H, H-1), 4.59 – 4.39 (m, 4H, H-4'', H-5'', H-5', H-5), 4.34 – 4.22 (m, 3H, H-3'', H-9', H-9), 4.19 – 4.05 (m, 5H, H-2', H-2, H-7', H-7, H-20), 3.98 – 3.71 (m, 10H, H-2'', H-10', H-10, H-11', H-11, H-13, H-13, CH_3 OMe), 3.01 – 2.93 (m, 3H, CH_3 NMe), 2.58 (p, *J* = 7.0 Hz, 2H, H-14), 2.19 – 2.05 (m, 4H, H-8', H-8, H-3', H-3), 2.00 – 1.91 (m, 2H, H-8', H-8), 1.84 – 1.74 (m, 2H, H-3', H-3), 1.51 – 1.36 (m, 9H, H-12', H-12, 19-CH_3), 1.35 – 1.23 (m, 9H, H-6'', H-6', H-6); ^{13}C NMR (214 MHz, D_2O, HSQC): δ 172.2, 172.1, 170.0, 169.9 (C=O amide), 136.9 (C-15), 117.4 (C-16), 102.2 (C-1''), 101.0 (C-1'), 98.1 (C-1), 85.6, 85.1, 83.7 (C-20), 80.2, 80.2 (C-19), 78.9 (C-9', C-9), 78.9 (C-9, C-9'), 78.7 (C-10', C-10), 78.3 (C-10, C-10'), 75.9 (C-4', C-4), 75.8 (C-4, C-4'), 70.8, 70.5 (C-2''), 70.1, 70.0 (C-3''), 69.9 (C-7', C-7), 69.8 (C-7, C-7'), 68.5 (C-18), 68.2 (C-5', C-5), 68.2 (C-11', C-11), 68.1 (C-11, C-11'), 68.0 (C-13), 67.7 (C-5, C-5'), 66.8, 66.3 (C-5''), 65.9 (C-2', C-2), 65.5 (C-2, C-2'), 60.9, 60.8 (CH_3 OMe), 56.0, 55.5 (C-4''), 34.1 (C-14), 31.1 (C-8', C-8), 31.0 (C-8, C-8'), 30.7, 30.6, 30.5 (CH_3 NMe), 29.3 (C-3', C-3), 29.2 (C-3, C-3'), 20.1 (C-12', C-12), 19.9 (C-12, C-12'), 19.0, 17.2 (CH_3), 16.6 (C-6''), 13.0 (C-6', C-6), 12.9 (C-6, C-6'); HRMS: $[M+Na]^+$ calcd for $C_{43}H_{74}O_{24}N_2Na$ 1025.4529, found 1025.4524.

Preparation of compound 36

Scheme S6. Synthesis of compound **36** and **S44**.

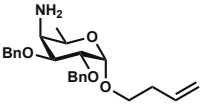


Reagents and conditions: a) Ph_2SO, TTBP, ethyl maleimide, Tf_2O, TBAI, 3-buten-1-ol (95%); b) triphenylphosphine, THF (79%); c) pyrralidone **2**, TEA, HATU, CH_3CN (88%); d) Na, NH_3, *t*-BuOH, THF (44%); e) H_2, $Pd(OH)_2$/C, THF, *t*-BuOH, H_2O (13%).

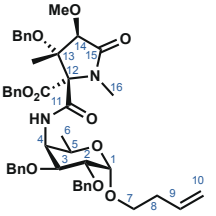


3-Butene 4-azido-2,3-di-*O*-benzyl-4,6-dideoxy-α-D-galactopyranoside (S41). To a solution of the donor **3** (23 mg, 50 µmol, 1 eq.) in DCM (1 mL, 0.05 M), Ph_2SO (13 mg, 65 µmol, 1.3 eq.), TTBP (31 mg, 125 µmol, 2.5 eq.) and ethyl maleimide (12.5 mg, 100 µmol, 2.0 eq) were added. The solution was stirred over activated 3 Å molecular sieves (rods, size 1/16 in., Sigma Aldrich) for 30 min. The solution was cooled to –80 °C upon which Tf_2O (11 µL, 65 µmol, 1.3 eq.) was added slowly. Subsequently, the solution was allowed to attain to –50 °C to secure full activation of the donor followed by cooling back to –80 °C after which TBAI (148 mg, 0.4 mmol, 8 eq.) was added. The solution was stirred for 15 min at –80 °C followed by the addition of the acceptor 3-buten-1-ol (0.2 mL of a 0.5 M solution, 2.0 eq.). The reaction was stirred for 16 h at 0 °C upon which the reaction was quenched with sat. aq. $NaHCO_3$ followed by the dilution with EtOAc. The organic layer was washed with H_2O and brine, dried over $MgSO_4$, filtered off and concentrated under reduced pressure. Flash column chromatography (95:5 → 92:8; pentane:Et_2O) yielded the title compound **S41** (19.1 mg, 45 µmol, 95%, α:β; >98:2) as a colorless oil. TLC: R_f 0.6 (pentane:Et_2O, 9:1, v:v); $[\alpha]_D^{20}$ 24.3° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 697, 1045, 1105, 1709, 2109, 2916; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.42 – 7.27 (m, 10H, CH_{arom}), 5.81 (ddt, *J* = 17.0, 10.2, 6.7 Hz, 1H, H-9), 5.10 (dq, *J* = 17.2, 1.6 Hz, 1H, H-10), 5.08 – 5.00 (m, 1H, H-10), 4.85 (d, *J* = 11.7 Hz, 1H, C*H*H Bn), 4.81 (d, *J* = 12.0 Hz, 1H, C*H*H Bn), 4.74 (d, *J* = 11.7 Hz, 1H, CH*H* Bn), 4.70 (d, *J* = 3.8 Hz, 1H, H-1), 4.64 (d, *J* = 12.0 Hz, 1H, CH*H* Bn), 4.03 (dd, *J* = 9.9, 3.7 Hz, 1H, H-3), 3.96 (qd, *J* = 6.5, 1.6 Hz, 1H, H-5), 3.83 (dd, *J* = 9.9, 3.8 Hz, 1H, H-2), 3.72 (dd, *J* = 3.8, 1.5 Hz, 1H, H-4), 3.56 (ddt, *J* = 44.4, 9.9, 7.0 Hz, 2H, H-7, H-7), 2.37 (qt, *J* = 7.0, 1.4 Hz, 2H, H-8, H-8), 1.21 (d, *J* = 6.5 Hz, 3H, H-6); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 138.6, 138.4 ($C_{q\text{-}arom}$), 135.1 (C-9), 128.6, 128.5, 128.1, 127.9, 127.9, 127.8 (CH_{arom}), 116.8 (C-10), 97.5 (C-1), 78.2 (C-3), 76.2

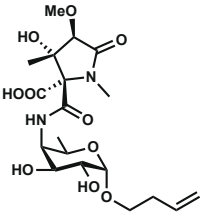
(C-2), 73.6, 73.3 (CH_2 Bn), 67.7 (C-7), 65.2 (C-4), 64.5 (C-5), 34.0 (C-8), 17.4 (C-6). HRMS: $[M+Na]^+$ calcd for $C_{24}H_{29}O_4N_3Na$ 446.2056, found 446.2050.



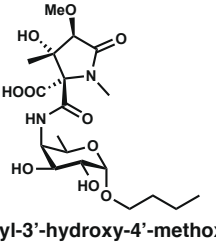
3-Butene 4-amine-2,3-di-*O*-benzyl-4,6-dideoxy-α-D-galactopyranoside (S42). Azide **S41** (42.4 mg, 0.1 mmol, 1 eq.) was dissolved in THF (250 µL, 0.4 M) followed by the addition of polymer bound triphenylphosphine (66.7 mg, 0.2 mmol, 2 eq.; 100-200 mesh, 3 mmol/gr). The mixture was stirred for 3 h at room temperature upon which H_2O (22.6 µL, 1.25 mmol, 12.5 eq.) was added and the reaction was stirred for another 16 h. Upon completion, the reaction was filtered, rinsed with $CHCl_3$, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (10:90 → 0:100; pentane:EtOAc) yielded the title compound (31.3 mg, 78.7 µmol, 79%) as a colorless oil. TLC: R_f 0.1 (pentane:EtOAc, 1:9, v:v); $[\alpha]_D^{20}$ 39.6° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 698, 1042, 1100, 2928; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.73 – 7.26 (m, 10H, CH_{arom}), 5.84 (ddt, *J* = 17.0, 10.2, 6.7 Hz, 1H, H-9), 5.11 (dq, *J* = 17.2, 1.6 Hz, 1H, H-10), 5.05 (ddt, *J* = 10.2, 2.1, 1.2 Hz, 1H, H-10), 4.79 (d, *J* = 12.1 Hz, 1H, C*H*H Bn), 4.77 – 4.73 (m, 2H, C*H*H Bn, H-1), 4.70 – 4.62 (m, 2H, CH*H* Bn, CH*H* Bn), 4.02 (qd, *J* = 6.6, 1.7 Hz, 1H, H-5), 3.86 (dd, *J* = 9.9, 4.0 Hz, 1H, H-3), 3.74 (dd, *J* = 10.0, 3.9 Hz, 1H, H-2), 3.59 (ddt, *J* = 55.2, 9.9, 7.0 Hz, 2H, H-7, H-7), 3.16 (dd, *J* = 4.1, 1.8 Hz, 1H, H-4), 2.40 (qt, *J* = 7.0, 1.4 Hz, 2H, H-8, H-8), 1.21 (d, *J* = 6.6 Hz, 3H, H-6); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 138.8 ($C_{q\text{-}arom}$), 135.2 (C-9), 128.5, 128.5, 128.0, 127.8, 127.8 (CH_{arom}), 116.7 (C-10), 97.5 (C-1), 78.6 (C-3), 75.5 (C-2), 73.2, 72.5 (CH_2 Bn), 67.5 (C-7), 65.3 (C-5), 53.5 (C-4), 34.1 (C-8), 16.8 (C-6); HRMS: $[M+H]^+$ calcd for $C_{24}H_{32}O_4N$ 398.2331, found 398.2326.



3-Butene 4-[(2'*S*,3'*S*,4'*R*)-3'-*O*-Benzyl-2'-(benzyloxycarbonyl)-4'-methoxy-1',3'-dimethyl-5'-oxopyrrolidine-2'-carboxamido] 2,3-di-*O*-benzyl-4,6-dideoxy-α-D-galactopyranoside (S43). To a stirred solution of pyrrolidone **2** (63.7 mg, 154 µmol, 1.25 eq.) and triethylamine (42.7 µL, 308 µmol, 2.5 eq.) in CH_3CN (0.4 mL, 0.15 M) was added HATU (62 mg, 163 µmol, 1.3 eq.). The solution was stirred for 30 min at room temperature followed by the addition of galactosamine **S42** in 0.4 mL CH_3CN. The reaction was stirred for 3 h at room temperature upon which 1M HCl and EtOAc were added. The aqueous layer was extracted with EtOAc (3x) followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine, respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product as a colorless oil. Flash column chromatography (80:20 → 60:40; pentane:EtOAc) yielded the title compound (86 mg, 108 µmol, 88%) as a colorless oil. TLC: R_f 0.6 (pentane:EtOAc, 1:1, v:v); $[\alpha]_D^{20}$ 79.4° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 698, 1046, 1097, 1686, 1717, 2926; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.13 (d, *J* = 10.0 Hz, 1H, NH), 7.38 – 7.13 (m, 20H, CH_{arom}), 5.84 (ddt, *J* = 17.0, 10.2, 6.7 Hz, 1H, H-9), 5.17 (d, *J* = 12.1 Hz, 1H, C*H*H Bn), 5.15 – 5.04 (m, 3H, C*H*H Bn, H-10, H-10), 4.84 (d, *J* = 10.9 Hz, 1H, C*H*H Bn), 4.78 (d, *J* = 12.2 Hz, 1H, C*H*H Bn), 4.74 (d, *J* = 3.9 Hz, 1H, H-1), 4.61 (d, *J* = 6.3 Hz, 1H, CH*H* Bn), 4.60 – 4.51 (m, 3H, CH*H* Bn, CH*H* Bn, H-4), 4.35 (d, *J* = 11.6 Hz, 1H, CH*H* Bn), 4.18 (tt, *J* = 7.4, 3.5 Hz, 1H, H-5), 3.98 (dd, *J* = 10.1, 4.1 Hz, 1H, H-3), 3.84 (s, 1H, H-14), 3.72 – 3.62 (m, 1H, H-7), 3.59 – 3.48 (m, 5H, H-2, H-7, CH_3 OMe), 2.65 (s, 3H, CH_3 NMe), 2.40 (qt, *J* = 7.0, 1.4 Hz, 2H, H-8), 1.45 (s, 3H, CH_3), 1.15 (d, *J* = 6.5 Hz, 3H, H-6); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 172.4 (C=O ester), 168.8, 164.7 (C=O amide), 138.8, 138.7, 137.8 ($C_{q\text{-}arom}$), 135.0 (C-9), 134.7($C_{q\text{-}arom}$), 128.8, 128.7, 128.5, 128.5, 128.4, 128.2, 128.1, 127.9, 127.7, 127.5, 127.1 (CH_{arom}), 116.9 (C-10), 97.6 (C-1), 83.9 (C-13), 82.4 (C-14), 79.5 (C-12), 77.6 (C-3), 75.6 (C-2), 73.4, 71.9, 68.3 (CH_2 Bn), 67.8 (C-7), 66.3 (CH_2 Ph), 64.2 (C-5), 59.5 (CH_3 OMe), 52.0 (C-4), 34.0 (C-8), 29.2 (CH_3 NMe), 17.4 (C-6), 14.8 (CH_3); HRMS: $[M+H]^+$ calcd for $C_{47}H_{55}O_{10}N_2$ 807.3857, found 807.3851.

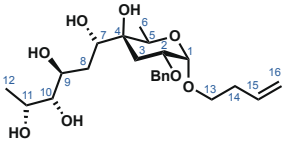


3-Butene 4-[(2'*S*,3'*S*,4'*R*)-2'-carboxyl-3'-hydroxy-4'-methoxy-1',3'-dimethyl-5'-oxopyrrolidine-2'-carboxamido]-4,6-dideoxy-α-D-galactopyranoside (36). The protected galactopyranoside **S43** (19.8 mg, 25 µmol) was co-evaporated twice with dry toluene. 20 mL ammonia was condensed at –70 °C, sodium (22.5 mg, 0.98 mmol, 40 eq.) was added and the resulting suspension was stirred for 30 min. Galactopyranoside was dissolved in 4 mL THF, 3-buten-1-ol (100 µL, used for scales from 10-100 µmol) and *t*-BuOH (24 µL, 250 µmol, 10 eq.) and the solution was added to the suspension of sodium in ammonia. The reaction mixture was stirred at –70 °C for 15 min, upon which the reaction was quenched with water. The reaction mixture was then stirred at room temperature until all ammonia had evaporated. The mixture was concentrated *in vacuo* to yield the crude product as a colorless oil. Flash column chromatography (30:70 → 50:50; MeOH:DCM) yielded the title compound (4.9 mg, 11 µmol, 44%) as a colorless oil. TLC: R_f 0.2 (DCM:MeOH, 7:3, v:v); The NMR data showed the presence of two atropisomers in D_2O in a 60:40 ratio. Data for atropisomeric mixture: ^{1}H NMR (500 MHz, D_2O, HH-COSY, HSQC: δ 5.89 (ddt, *J* = 17.1, 10.4, 6.7 Hz, 1H, H-9), 5.15 (dt, *J* = 17.3, 1.9 Hz, 1H, H-10), 5.11 – 5.06 (m, 1H, H-10), 4.98 – 4.93 (m, 1H, H-1), 4.30 (ddd, *J* = 13.0, 6.5, 1.6 Hz, 1H, H-5), 4.24 – 4.21 (m, 1H, H-4), 4.15 – 4.13 (m, 0.4H, H-14*), 4.03 (ddd, *J* = 10.8, 6.7, 4.2 Hz, 1H, H-3), 3.91 (t, *J* = 0.7 Hz, 0.6H, H-14), 3.74 (dt, *J* = 10.0, 6.8 Hz, 1H, H-7), 3.68 – 3.57 (m, 5H, H-2, H-7, OCH_3), 2.80 – 2.74 (m, 3H, NMe, 2.39 (d, *J* = 6.6 Hz, 2H, H-8), 1.56 (s, 1.8H, CH_3), 1.24 – 1.17 (m, 4.2H, H-6, CH_3*); ^{13}C NMR (126 MHz, D_2O, HSQC): δ 174.8 (C=O acid), 173.9 (C=O acid*), 171.7 (C=O amide), 171.3, 168.6 (C=O amide*), 167.9 (C=O amide), 135.7 (C-9), 116.7 (C-10), 98.4 (C-1), 84.7 (C-14*), 83.1 (C-14), 79.4 (C-13*), 76.2 (C-13), 69.2 (C-3*), 69.0 (C-3), 68.7 (OCH_3), 68.5 (OCH_3*), 67.8 (C-7), 65.7 (C-5), 65.2 (C-5*), 60.8 (C-2), 60.0 (C-2*), 54.9 (C-4*), 54.6 (C-4), 33.2 (C-8), 29.8 (NMe*), 29.7 (NMe), 22.5 (CH_3), 18.2 (CH_3*), 16.3 (C-6*), 16.0 (C-6); HRMS: $[M+H]^+$ calcd for $C_{19}H_{31}O_{10}N_2$ 447.1979, found 447.1973.



Butane 4-[(2'*S*,3'*S*,4'*R*)-2'-carboxyl-3'-hydroxy-4'-methoxy-1',3'-dimethyl-5'-oxopyrrolidine-2'-carboxamido]-4,6-dideoxy-α-D-galactopyranoside (S44). The protected galactopyranoside **S43** (19.8 mg, 25 µmol) was co-evaporated twice with dry toluene. It was then dissolved in 5 mL of a mixture of THF, *t*-BuOH and water (13:13:30). 3 drops of acetic acid were added and the solution was treated with palladium hydroxide on charcoal (52.7 mg, 20 % loading, Sigma-Aldrich) and subjected to hydrogen atmosphere for 20 h. The mixture was filtered through Celite© Hyflo Supercel (Merck) and the filtrate was concentrated *in vacuo*. Flash column chromatography (C18 column, gradient 100:0 → 50:50 CH_3OH–H_2O) yielded the title compound (1.5 mg, 3.4 µmol, 13%) as a white solid. TLC: R_f 0.2 (DCM:MeOH, 7:3, v:v); The NMR data showed the presence of two atropisomers in D_2O in a 60:40 ratio. Data for atropisomeric mixture: ^{1}H NMR (850 MHz, D_2O, HH-COSY, HSQC): δ 5.00 – 4.97 (m, 1H, H-1), 4.36 – 4.30 (m, 1H, H-5), 4.27 – 4.25 (m, 1H, H-4), 4.17 (s, 0.4H, H-14*), 4.09 – 4.05 (m, 1H, H-3), 3.95 (s, 0.6H, H-14), 3.75 – 3.55 (m, 6H, H-2, H-7, OMe), 2.83 – 2.80 (m, 3H, NMe), 1.68 – 1.58 (m, 3.8H, H-8, CH_3), 1.45 – 1.36 (m, 2H, H-9), 1.27 – 1.21 (m, 4.2H, H-6, CH_3*), 0.93 (t, *J* = 7.4 Hz, 3H, H-10); ^{13}C NMR (214 MHz, D_2O, HSQC): δ 174.7, 173.9 (C=O acid, C=O acid*), 171.6, 171.3, 168.5, 167.9 (C=O amide, C=O amide*), 98.3 (C-1*), 98.3 (C-1), 84.6 (C-14*), 83.1 (C-14), 81.3, 79.5 (C-14/C-13), 79.3, 76.2 (C-13/C-14, C-13*/C-14), 69.2 (C-3*), 69.0 (C-3), 68.6 (C-2), 68.4 (C-2*), 68.4 (C-7), 65.5 (C-5), 65.0 (C-5*), 60.8 (OCH_3), 59.9 (OCH_3*), 54.8 (C-4*), 54.6 (C-4),

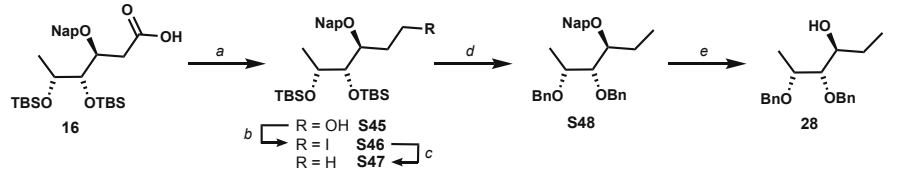
30.7 (C-8), 29.7 (NMe*), 29.7 (NMe), 22.4 (CH_3), 18.7 (C-9), 18.1 (CH_3*), 16.3 (C-6*), 16.0 (C-6), 13.0 (C-10); HRMS: $[M+H]^+$ calcd for $C_{19}H_{33}O_{10}N_2$ 449.2135, found 449.2130.



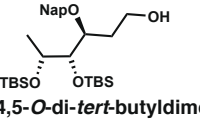
3-Butene caryophylloside (37). The protected glycoside **30** (33 mg, 50 µmol) was dissolved in 10 mL 1:1 v:v THF:H_2O (0.005 M). LiOH·H_2O (210 mg, 5.0 mmol, 100 eq.) was added and the resulting mixture was stirred at rt for 20 h. Upon completion 80% of the LiOH was quenched with 0.1 M HCl (40 mL) and the mixture was concentrated under reduced pressure to yield the crude product. The crude product was then co-evaporated twice with dry toluene. 3 mL ammonia was condensed at –70 °C, sodium (23 mg, 1.0 mmol, 20 eq.) was added and the resulting suspension was stirred for 30 min. The crude product was dissolved in 0.5 mL THF, 3-butenol (50 µL, 1.0 mmol, 20 eq.) and *t*-BuOH (50 µL, 500 µmol, 10 eq.) and the solution was added to the suspension of sodium in ammonia. The reaction mixture was stirred at –70 °C for 15 min, upon which the reaction was quenched with water. The reaction mixture was then stirred at room temperature until all ammonia had evaporated. The mixture was concentrated in vacuo to yield the crude product as a colorless oil. Flash column chromatography (5:95 → 20:80; MeOH:DCM) followed by size exclusion over a 250x10 mm column filled with Biogel P2 media (Bio-Rad) yielded the title compound (4.6 mg, 13 µmol, 26% over two steps) as a colorless oil. ^{1}H NMR (500 MHz, D_2O, HH-COSY, HSQC): δ 5.90 (ddt, *J* = 17.1, 10.3, 6.7 Hz, 1H, H-15), 5.16 (dq, *J* = 17.3, 1.7 Hz, 1H, H-16), 5.08 (dd, *J* = 10.3, 2.1 Hz, 1H, H-16), 4.80 (H-1, value from HSQC due to overlap with the solvent signal) 4.25 (q, *J* = 6.5 Hz, 1H, H-5), 3.98 (ddd, *J* = 12.3, 5.1, 3.7 Hz, 1H, H-2), 3.93 (dt, *J* = 12.5, 6.3 Hz, 1H, H-11), 3.81 (td, *J* = 7.4, 6.2, 2.2 Hz, 1H, H-9), 3.77 – 3.70 (m, 2H, H-7, H-13), 3.63 (dt, *J* = 9.8, 5.9 Hz, 1H, H-1'), 3.50 (t, *J* = 5.9 Hz, 1H, H-10), 2.43 – 2.36 (m, 2H, H-14), 1.93 (t, *J* = 12.6 Hz, 1H, H-3), 1.77 – 1.61 (m, 3H, H-3, H-8), 1.20 (d, *J* = 6.4 Hz, 3H, H-12), 1.13 (d, *J* = 6.6 Hz, 3H, H-6); ^{13}C NMR (126 MHz, D2O, HSQC): δ 135.9 (C-15), 116.6 (C-16), 97.1 (C-1), 77.4 (C-10), 74.8 (C-4), 69.6 (C-7), 67.9 (C-9), 67.5 (C-11), 67.1 (C-13), 66.9 (C-5), 64.6 (C-2), 33.3 (C-14), 31.9 (C-8), 30.4 (C-3), 16.9 (C-12), 11.3 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{16}H_{30}O_8Na$ 373.1838, found 373.1833.

Preparation of compound 28

Scheme S7. Synthesis of compound **28**.

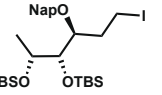


Reagents and conditions: a) BH_3·THF, THF (75%); b) triphenylphosphine, imidazole, iodine, THF (92%); c) $LiAlH_4$, THF (72%); d) *i.* HF-pyridine, pyridine; *ii.* NaH, BnBr, DMF (91%); e) DDQ, DCM (67%).

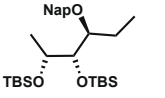


2,6-Dideoxy-3-*O*-(2-methylnaphthalene)-4,5-*O*-di-*tert*-butyldimethylsilyl-D-altritol (S45). Carboxylate **16** (2.96 g, 5.5 mmol) was dissolved in THF (10 mL), followed by adding BH_3·THF (17 mL, 1.0 M in THF, 3.0 eq) at 0 °C. The reaction mixture was left stirring at room temperature for 16 h, after which it was concentrated *in vacuo* to a thick syrup, which was absorbed on silica gel and chromatographed using pentane:Et_2O (75:25) as a mobile phase. The product was obtained as a clear oil (2.1 g, 75%). TLC: R_f 0.3 (pentane:Et_2O, 75:25); ^{1}H NMR (300 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.89 – 7.80 (m, 4H, CH_{arom}), 7.53 – 7.47 (m, 3H, CH_{arom}), 4.83 (d, *J* = 12.3 Hz, 1H, CH*H* Nap), 4.64 (d, *J* = 12.3 Hz, 1H, CH*H* Nap), 3.92 (m, 1H, H-3), 3.81 – 3.71 (m, 4H, H-5, H-4, H-1 x 2), 1.98 (m, 1H, H-2_a), 1.78 (m, 1H, H-2_b), 1.21 (d, *J* = 6.9 Hz,

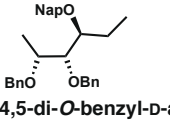
3H, H-6), 0.93 (s, 9H, $C(CH_3)_3$), 0.87 (s, 9H, $C(CH_3)_3$), 0.16 – 0.03 (m, 12H, $SiCH_3$, $SiCH_3$, $SiCH_3$, $SiCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$, HSQC): δ 135.5, 133.2, 133.0 ($C_{q\text{-arom}}$), 128.3, 127.9, 127.9, 127.7, 127.7, 127.7, 126.8, 126.8, 126.8, 126.1, 126.0, 125.9 (CH_{arom}), 79.5 (C-3), 77.8, 71.6 (CH_2 Nap), 69.6, 69.6, 60.8 (C-1), 31.1 (C-2), 26.1 ($C(CH_3)_3$), 26.1 ($C(CH_3)_3$), 25.8 ($C(CH_3)_3$), 20.8 (C-6), -3.9, -4.0, -4.4, -4.5, -4.8 ($SiCH_3$); HRMS: $[M+H]^+$ calcd for $C_{29}H_{51}O_4Si_2$ 519.3326, found 519.3323.



2,6-Dideoxy-1-deoxy-1-iodo-3-*O*-(2-methylnaphthalene)-4,5-*O*-di-*tert*-butyldimethylsilyl-D-altritol (S46). Alcohol **S45** (2.1 g, 4.04 mmol) was dissolved in THF (10 mL), followed by adding imidazole (884 mg, 13 mmol,1.5 eq), PPh_3 (1.75 g, 6.07 mmol, 1.5 eq.), and I_2 (1.5 g, 6.07 mmol, 1.5 eq.) sequentially at room temperature. The reaction mixture was heated at 60 °C for 1 h, after which it was quenched with sat. $Na_2S_2O_3$, diluted with CH_2Cl_2 and washed with H_2O. The organic layer was then dried over $MgSO_4$, filtered, and concentrated *in vacuo* to give the crude product as an oil, which was loaded on silica gel and chromatographed using pentane:Et_2O (90:10) as a mobile phase. The product was obtained as a clear oil (2.32 g, 92%). TLC: R_f 0.7 (pentane:Et_2O, 75:25); ^1H NMR (300 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.89 – 7.82 (m, 4H, CH_{arom}), 7.54 – 7.48 (m, 3H, CH_{arom}), 4.85 (d, *J* = 12.3 Hz, 1H, CH*H* Nap), 4.66 (d, *J* = 12.3 Hz, 1H, CH*H* Nap), 3.80 (m, 1H, H-5), 3.74 (m, 2H, H-4, H-3), 3.40 (m, 1H, C*H*H I), 3.28 (m, 1H, CH*H* I), 1.21 (d, *J* = 6.9 Hz, 3H, H-6), 0.93 (s, 9H, $C(CH_3)_3$), 0.87 (s, 9H, $C(CH_3)_3$), 0.16 – 0.03 (m, 12H, $SiCH_3$, $SiCH_3$, $SiCH_3$, $SiCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$, HSQC): δ 135.9, 133.3, 132.9 ($C_{q\text{-arom}}$), 128.1, 127.9, 127.7, 126.5, 126.0, 126.0, 125.8 (CH_{arom}), 80.3, 78.0, 72.3 (CH_2 Nap), 69.7 (C-5), 34.2 (C-2), 26.1($C(CH_3)_3$), 26.0 ($C(CH_3)_3$), 20.5 (C-6), 4.1 (CH_2I), -3.9, -4.1, -4.4, -4.5 ($SiCH_3$); HRMS: $[M+H]^+$ calcd for $C_{29}H_{50}IO_3Si_2$ 629.2342, found 629.2337.

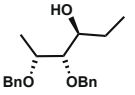


1,2,6-Trideoxy-3-*O*-(2-methylnaphthalene)-4,5-*O*-di-*tert*-butyldimethylsilyl-D-altritol (S47). Iodide **S46** (2.32 g, 3.75 mmol) was dissolved in dry THF (20 mL), and $LiAlH_4$ (1.5 mL, 4.0 M in Et_2O, 1.5 eq.) was added at 0 °C, and the reaction mixture was then left stirring at room temperature for 1 h. It was then carefully quenched with H_2O, after which saturated solution of Rochelle's salt was added, and stirring was continued at room temperature for 1 h. The reaction mixture was then diluted with Et_2O, and the organic layer was separated and dried over $MgSO_4$, filtered, and concentrated *in vacuo* to give the crude product as an oil, which was loaded on silica gel and chromatographed using pentane:Et_2O (90:10) as a mobile phase. The product was obtained as a clear oil (1.35 g, 72%). TLC: R_f 0.7 (pentane:Et_2O, 75:25); ^1H NMR (300 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.87 – 7.82 (m, 4H, CH_{arom}), 7.52 – 7.45 (m, 3H, CH_{arom}), 4.77 (d, *J* = 12.3 Hz, 1H, CH*H* Nap), 4.65 (d, *J* = 12.3 Hz, 1H, CH*H* Nap), 3.92 (m, 1H, H-5), 3.73 (dd, *J* = 4.3, 4.8 Hz, 1H, H-4), 3.50 (m, 1H, H-3), 1.65 (m, 2H, H-2), 1.17 (d, 3H, *J* = 5.8 Hz, H-6), 1.00 (t, *J* = 7.5 Hz, 3H, H-1), 0.93 (s, 9H, $C(CH_3)_3$), 0.87 (s, 9H, $C(CH_3)_3$), 0.16 – 0.03 (m, 12H, $SiCH_3$, $SiCH_3$, $SiCH_3$, $SiCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$, HSQC): δ 136.5, 133.3, 132.9 ($C_{q\text{-arom}}$), 127.9, 127.7, 126.2, 126.0, 125.9, 125.6 (CH_{arom}), 81.7 (C-3), 78.2 (C-4), 71.9 (CH_2 Nap), 69.6 (C-5), 26.1 ($C(CH_3)_3$), 26.0 ($C(CH_3)_3$), 22.3 (C-2), 19.6 (C-6), 10.1 (C-1), -4.2, -4.2, -4.4, -4.7 ($SiCH_3$); HRMS: $[M+H]^+$ calcd for $C_{29}H_{51}O_3Si_2$ 503.3377, found 503.3374.



1,2,6-Trideoxy-3-*O*-(2-methylnaphthalene)-4,5-di-*O*-benzyl-D-altritol (S48). To a solution of compound **S47** (830 mg, 1.65 mmol) in pyridine (5 mL) was added a solution of HF-pyridine (5 mL, 5 mL of 70% HF-pyridine diluted with 5 mL of pyridine), and the reaction mixture was left stirring at rt for 16 h. The reaction mixture was diluted with CH_2Cl_2, washed with water, sat. $NaHCO_3$, and the organic phase was separated, dried over $MgSO_4$, filtered, and concentrated *in vacuo* to give the crude intermediate as an oil. This material was dissolved in DMF (10 mL), after which BnBr (600 µL, 5 mmol, 3.0 eq) and NaH (200 mg, 5.0 mmol, 3.0

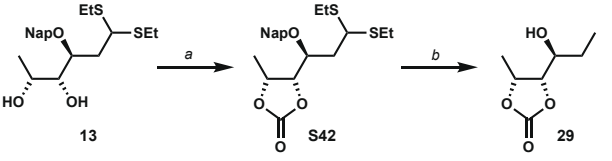
eq, 60% dispersion in mineral oil) were added at 0 °C, and the reaction mixture was left stirring at room temperature for 4 h, after which it was quenched with methanol, concentrated *in vacuo*, loaded on silica gel, and chromatographed using hexane:EtOAc (90:10) as a mobile phase to give the desired product as a clear oil (710 mg, 91% over two steps). TLC: R_f 0.7 (pentane:EtOAc, 75:25); ^{1}H NMR (300 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.89 – 7.79 (m, 4H, CH_{arom}), 7.54 – 7.47 (m, 3H, CH_{arom}), 7.42 – 7.38 (m, 9H, CH_{arom}), 4.85 (d, *J* = 11.5 Hz, 1H, CH*H* Bn), 4.80 (d, *J* = 11.5 Hz, 1H, CH*H* Bn), 4.74 (s, 2H, CH_2Ar), 4.65 (d, *J* = 12.2 Hz, 1H, CH*H* Bn), 4.52 (d, *J* = 12.2 Hz, 1H, CH*H* Bn), 3.86 – 3.76 (m, 2H, H-4, H-5), 3.63 (m, 1H, H-3), 1.74 (m, 2H, H-2), 1.32 (d, *J* = 6.1 Hz, 2H, H-2), 0.99 (t, *J* = 7.4 Hz, 3H, H-1); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.9, 138.8, 136.2, 133.3, 132.9 ($C_{q\text{-}arom}$), 128.3, 128.3, 128.0, 128.0, 127.9, 127.7, 127.6, 127.5, 126.5, 126.1, 126.0, 125.8 (CH_{arom}), 81.6 (C-5), 80.5 (C-3), 75.5 (C-4), 73.9 (CH_2Ar), 71.8 (CH_2Ar), 70.8 (CH_2Ar), 22.7 (C-2), 15.4 (C-6), 9.8 (C-1); HRMS: $[M+H]^+$ calcd for $C_{31}H_{35}O_3$ 455.2586, found 455.2580.



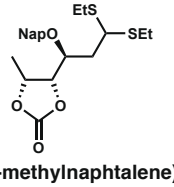
1,2,6-Trideoxy-4,5-di-*O*-benzyl-D-altritol (28). To a solution of **S48** (740 mg, 1.62 mmol) in CH_2Cl_2 (10 mL) was added water (1 mL) and DDQ (544 mg, 2.44 mmol, 1.5 eq) at rt. The reaction mixture was left stirring at that temperature for 1 h, after which it was quenched with sat. $NaHCO_3$. The organic phase was separated, dried over $MgSO_4$, and concentrated *in vacuo* to give a crude product. Column chromatography on silica gel using pentane:Et_2O (90:10) gave the title product as a clear oil (340 mg, 67%). TLC: R_f 0.7 (pentane:EtOAc, 75:25); ^{1}H NMR (300 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.39 – 7.29 (m, 10H, CH_{arom}), 4.77 (d, *J* = 11.4 Hz, 1H, CH*H* Bn), 4.69 (d, *J* = 5.5 Hz, 1H, CH*H* Bn), 4.65 (d, *J* = 5.5 Hz, 1H, CH*H* Bn), 4.51 (d, *J* = 11.4 Hz, 1H, CH*H* Bn), 3.83 (m, 1H, H-5), 3.71 (m, 1H, H-3), 3.42 (m, *J* = 5.1 Hz, 1H, H-4), 1.73 (m, 1H, H-2_a), 1.50 (m, 1H, H-2_b), 1.37 (d, J = 6.4 Hz, 3H, H-6), 1.00 (t, J = 7.0 Hz, 3H, H-1); ^{13}C NMR (75 MHz, $CDCl_3$): δ 128.4, 128.4, 127.9, 127.7 127.7, 127.6 (CH_{arom}), 84.1 (C-4), 76.6 (C-5), 74.2 (C-3), 74.1 (CH_2Ar), 70.7 (CH_2Ar), 26.0 (C-2), 16.1 (C-6), 10.3 (C-1); HRMS: $[M+H]^+$ calcd for $C_{20}H_{27}O_3$ 315.1960, found 319.1955.

Preparation of compound 29

Scheme S8. Synthesis of compound **29**.

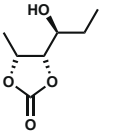


Reagents and conditions: a) BH_3·THF, THF (75%); b) triphenylphosphine, imidazole, iodine, THF (92%); c) $LiAlH_4$, THF (72%); d) *i.* HF-pyridine, pyridine; *ii.* NaH, BnBr, DMF (91%); e) DDQ, DCM (67%).

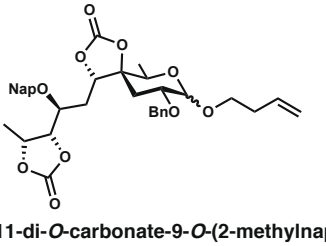


2,6-Dideoxy-1,1-diethyl-thioacetal-3-*O*-(2-methylnaphtalene)-4,5-*O*-carbonate-D-altritol (S42). A phosgene solution was prepared by diluting a 20% phosgene in hexane solution (1.35 mL) with dry THF (1.5 mL). **13** (190 mg, 0.50 mmol) was dissolved in THF (3.6 mL, 0.1 M) and Et_3N (346 µL, 2.5 mmol, 5.0 eq.) and cooled on ice. The phosgene solution was added dropwise after which the solution was stirred for 3 h at room temperature. The reaction was quenched by adding 1 mL of sat. aq. $NaHCO_3$ followed by diluting the mixture with Et_2O and water. The aqueous layer was extracted with Et_2O (3x) followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo* to yield the crude product as a colorless oil. Flash column chromatography (99:1 → 70:30; pentane:Et_2O) yielded the title compound (150

mg, 0.37 mmol, 74%) as a colorless oil. TLC: R_f 0.2 (pentane:Et_2O, 8:2, v:v); IR (neat, cm^{-1}): 817, 1092, 1125, 1348, 1804, 2870, 2928, 2970; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.92 – 7.38 (m, 7H, CH_{arom}), 4.98 – 4.87 (m, 1H, H-5), 4.85 (d, *J* = 11.5 Hz, 1H, CH*H* Nap), 4.76 (d, *J* = 11.5 Hz, 1H, CH*H* Nap), 4.72 (t, *J* = 7.1 Hz, 1H, H-4), 4.21 (ddd, *J* = 6.8, 6.1, 5.0 Hz, 1H, H-3), 3.98 (dd, *J* = 7.9, 6.8 Hz, 1H, H-1), 2.77 – 2.54 (m, 4H, S*CH*$_2$CH$_3$, S*CH*$_2$CH$_3$), 2.30 (ddd, *J* = 15.0, 6.8, 6.1 Hz, 1H, H-2), 2.18 (ddd, *J* = 15.0, 7.9, 5.0 Hz, 1H, H-2), 1.49 (d, *J* = 6.6 Hz, 3H, H-6), 1.25 (td, *J* = 7.4, 2.2 Hz, 6H, SCH$_2$C*H*$_3$, SCH$_2$C*H*$_3$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 154.1 (O(C=O)O), 134.8, 133.3, 133.2 ($C_{q\text{-}arom}$), 128.5, 128.0, 127.8, 126.8, 126.5, 126.3, 125.7 (CH_{arom}), 80.1 (C-4), 76.2 (C-5), 74.6 (C-3), 72.5 (CH_2 Nap), 47.3 (C-1), 38.5 (C-2), 24.5 (S*CH*$_2$CH$_3$), 24.1 (S*CH*$_2$CH$_3$), 15.2 (C-6), 14.4 (SCH$_2$*CH*$_3$); HRMS: $[M+Na]^+$ calcd for $C_{22}H_{28}O_4NaS_2$ 443.1321, found 443.1320.

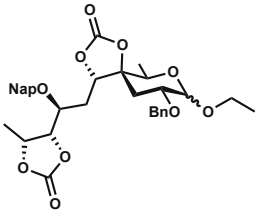


1,2,6-Trideoxy-4,5-*O*-carbonate-D-altritol (29). S49 was converted to **29** according to a modified literature procedure.[56] **S49** (100 mg, 0.24 mmol) was dissolved in 3 mL EtOH and 1 mL H_2O, followed by the addition of sodium hypophosphite monohydrate (0.25 g, 2.38 mmol, 10 eq.) in 1 mL EtOH. Subsequently, 20 spoon tips of pre-washed (with H_2O; pH ± 7) Raney®-Nickel (Sigma-Aldrich, W.R. Grace and Co. Raney® 2800, slurry, in H_2O, active catalyst) was added. The resulting suspension was stirred for 16 h at room temperature and the work-up was performed by filtration over Celite© Hyflo Supercel (Merck). After washing the Celite© with EtOH and H_2O, the filtrate was diluted with DCM. The aqueous layer was extracted with DCM (3x) followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo* to yield the crude product as a colorless oil. Flash column chromatography (10:90 → 40:60; pentane: EtOAc) yielded the title compound (33 mg, 0.21 mmol, 87%) as a colorless oil. TLC: R_f 0.3 (pentane:EtOAc, 8:2, v:v); IR (neat, cm^{-1}): 810, 1080, 1120, 1320, 1803, 2879, 2928; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.94 (p, *J* = 6.7 Hz, 1H, H-5), 4.41 (dd, *J* = 9.0, 7.2 Hz, 1H, H-4), 3.82 (tdd, *J* = 8.6, 5.3, 3.1 Hz, 1H, H-3), 1.87 (dqd, *J* = 14.4, 7.6, 3.0 Hz, 1H, H-2), 1.66 (d, *J* = 5.5 Hz, 1H, 3-OH), 1.59 – 1.51 (m, 1H, H-2), 1.51 (d, *J* = 6.6 Hz, 3H, H-6), 1.05 (t, *J* = 7.5 Hz, 3H, H-1); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 154.3 (O(C=O)O), 80.0 (C-4), 76.4 (C-5), 69.9 (C-3), 27.4 (C-2), 15.0 (C-6), 8.9 (C-1); HRMS: $[M+Na]^+$ calcd for $C_7H_{12}O_4Na$ 183.0628, found 183.0623.

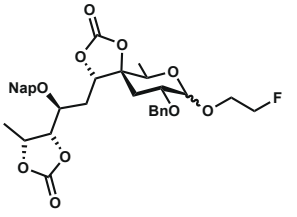


3-Butene 2-*O*-benzyl-4,7,10,11-di-*O*-carbonate-9-*O*-(2-methylnaphthalene)-α-D-caryophylloside (S51). The title compound was prepared according to general procedure III (30.6 mg, 48 µmol, 97%, α:β; 63:37). Flash column chromatography (80:20 → 60:40; pentane:EtOAc) yielded the title compound as a white foam. TLC: R_f 0.6 (pentane:EtOAc, 6:4, v:v); IR (neat, cm^{-1}): 1055, 1202, 1797; NMR data reported as a mixture of α- and β-anomers; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC): ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.89 – 7.27 (m, 19.2H, CH_{arom}), 5.89 – 5.76 (m, 1.6H, H-15$_\alpha$, H-15$_\beta$), 5.23 – 4.97 (m, 3.2H, H-16$_\alpha$, H-16$_\beta$), 4.92 – 4.86 (m, 1.6H, H-11$_\alpha$, H-11$_\beta$), 4.79 – 4.75 (m, 4.2H, H-1$_\alpha$, CH_2 Bn/Nap$_\alpha$, CH_2 Bn/Nap$_\beta$), 4.65 – 4.60 (m, 1.6H, H-10$_\alpha$, H-10$_\beta$), 4.57 – 4.43 (m, 3.8H, C*H*H Bn/Nap$_\alpha$, C*H*H Bn/Nap$_\beta$, CH*H* Bn/Nap$_\alpha$, CH*H* Bn/Nap$_\beta$, H-7$_\beta$), 4.36 – 4.30 (m, 1.6H, H-1$_\beta$, H-7$_\alpha$), 4.05 – 3.88 (m, 3.2H, H-5$_\alpha$, H-9$_\alpha$, H-9$_\beta$, H-13$_\beta$), 3.77 – 3.51 (m, 4.8H, H-2$_\alpha$, H-2$_\beta$, H-5$_\beta$, H-13$_\alpha$, H-13$_\alpha$, H-13$_\beta$), 2.45 – 2.32 (m, 3.2H, H-14$_\alpha$, H-14$_\beta$), 2.16 (dd, *J* = 14.3, 5.1 Hz, 0.6H, H-3$_\beta$), 2.11 – 2.02 (m, 3.2H, H-3$_\alpha$, H-8$_\alpha$, H-8$_\beta$, H-8$_\beta$), 1.92 (ddd, *J* = 14.9, 8.5, 2.0 Hz, 1H, H-8$_\alpha$), 1.83 (dd, *J* = 13.5, 4.8 Hz, 1H, H-3$_\alpha$), 1.74 (dd, *J* = 14.3, 10.2 Hz, 0.6H, H-3$_\beta$), 1.47 – 1.41 (m, 4.8H, H-12$_\alpha$, H-12$_\beta$), 1.33 (d, *J* = 6.3 Hz, 1.8H, H-6$_\beta$), 1.22 (d, *J* = 6.3 Hz, 3H, H-6$_\alpha$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 153.7, 153.6, 153.5, 153.3 (O(C=O)O), 138.1, 137.9 ($C_{q\text{-}arom}$),

135.2 (C-15$_\alpha$), 135.0 (C-15$_\beta$), 134.2, 134.1, 133.3, 133.3 (C$_{q\text{-arom}}$), 132.4, 128.8, 128.8, 128.6, 128.6, 128.1, 128.1, 128.1, 127.9, 127.9, 127.9, 127.9, 127.0, 126.8, 126.7, 126.7, 126.6, 125.6, 125.5 (CH$_{arom}$), 117.1 (C-16$_\alpha$), 116.9 (C-16$_\beta$), 103.6 (C-1$_\beta$), 95.6 (C-1$_\alpha$), 84.9 (C-4$_\alpha$), 84.0 (C-4$_\beta$), 81.0 (C-7$_\alpha$), 80.2 (C-7$_\beta$), 78.9 (C-10$_\alpha$), 78.7 (C-10$_\beta$), 75.8 (C-11$_\beta$), 75.8 (C-11$_\alpha$), 73.9 (C-9$_\beta$), 73.8 (C-9$_\alpha$), 73.7, 73.5 (CH$_2$ Bn/Nap), 73.3 (C-2$_\beta$), 73.2 (CH$_2$ Bn/Nap), 71.5 (C-2$_\alpha$), 68.7 (C-13$_\beta$), 67.7 (C-13$_\alpha$), 64.9 (C-5$_\alpha$), 37.6 (C-3$_\beta$), 34.2 (C-14$_\beta$), 34.0 (C-14$_\alpha$), 33.7 (C-3$_\alpha$), 29.7 (C-8$_\alpha$), 29.4 (C-8$_\beta$), 15.6 (C-6$_\beta$), 15.3 (C-12$_\alpha$), 15.2 (C-12$_\beta$), 14.9 (C-6$_\alpha$); HRMS: [M+Na]$^+$ calcd for $C_{36}H_{40}O_{10}Na$ 655.2519, found 655.2514.

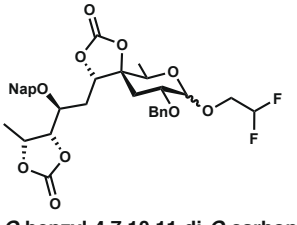


Ethyl 2-*O*-benzyl-4,7,10,11-di-*O*-carbonate-9-*O*-(2-methylnaphthalene)-D-caryophylloside (S52). The title compound was prepared according to general procedure III (28.5 mg, 47 µmol, 94%, α:β; 67:33). Flash column chromatography (80:20 → 50:50; pentane:EtOAc) yielded the title compound as a colorless oil. TLC: R$_f$ 0.3 (pentane:EtOAc, 7:3, v:v); IR (neat, cm^{-1}): 756, 1059, 1090, 1202, 1382, 1802, 2929; NMR data reported as a mixture of α- and β-anomers; ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.87 – 7.26 (m, 18H, CH$_{arom}$), 4.95 – 4.86 (m, 1.5H, H-11$_\alpha$, H-11$_\beta$), 4.79 – 4.76 (m, 4H, H-1$_\alpha$, CH$_2$ Bn/Nap$_\alpha$, CH$_2$ Bn/Nap$_\beta$), 4.66 – 4.61 (m, 1.5H, H-10$_\alpha$, H-10$_\beta$), 4.58 – 4.54 (m, 1.5H, C*H*H Bn/Nap$_\alpha$, C*H*H Bn/Nap$_\beta$), 4.51 – 4.47 (m, 2H, CH*H* Bn/Nap$_\alpha$, CH*H* Bn/Nap$_\beta$, H-7$_\beta$), 4.37 – 4.31 (m, 1.5H, H-1$_\beta$, H-7$_\alpha$), 4.05 – 3.97 (m, 1.5H, H-9$_\alpha$, H-9$_\beta$), 3.94 (dd, *J* = 9.5, 7.1 Hz, 1H, C*H*$_2$CH$_{3\beta}$), 3.89 (q, *J* = 6.4 Hz, 1H, H-5$_\alpha$), 3.78 – 3.69 (m, 2.5H, H-2$_\alpha$, H-5$_\beta$, C*H*$_2$CH$_{3\alpha}$), 3.60 – 3.50 (m, 2H, H-2$_\beta$, C*H*$_2$CH$_{3\alpha}$, C*H*$_2$CH$_{3\beta}$), 2.20 – 2.04 (m, 3H, H-3$_\alpha$, H-3$_\beta$, H-8$_\alpha$, H-8$_\beta$), 1.95 (ddd, *J* = 14.9, 8.6, 2.1 Hz, 1H, H-8$_\alpha$), 1.84 (dd, *J* = 13.5, 4.8 Hz, 1H, H-3$_\alpha$), 1.75 (dd, *J* = 14.3, 10.1 Hz, 0.5H, H-3$_\beta$), 1.47 – 1.42 (m, 4.5H, H-12$_\alpha$, H-12$_\beta$), 1.34 (d, *J* = 6.3 Hz, 1.5H, H-6$_\beta$), 1.26 (m, 1.28 – 1.24, 4.5H, CH$_2$C*H*$_{3\alpha}$, CH$_2$C*H*$_{3\beta}$), 1.23 (d, *J* = 6.3 Hz, 3H, H-6$_\alpha$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 153.7 153.7, 153.5, 153.3 (O(C=O)O), 138.2, 137.9, 134.2, 134.1, 133.3 (C$_{q\text{-arom}}$), 128.8, 128.8, 128.7, 128.6, 128.6, 128.2, 128.1, 128.1, 128.1, 128.0, 127.9, 127.9, 127.9, 127.0, 126.8, 126.7, 126.7, 126.7, 126.6, 126.6, 125.6, 125.4 (CH$_{arom}$), 103.3 (C-1$_\beta$), 95.3 (C-1$_\alpha$), 84.9 (C-4$_\alpha$), 84.0 (C-4$_\beta$), 80.9 (C-7$_\alpha$), 80.3 (C-7$_\beta$), 79.0 (C-10$_\alpha$), 78.8 (C-10$_\beta$), 75.8 (C-11$_\alpha$), 75.8 (C-11$_\beta$), 73.9 (C-9$_\beta$), 73.8 (C-9$_\alpha$), 73.7 (CH$_2$ Bn/Nap$_\alpha$), 73.5 (CH$_2$ Bn/Nap$_\beta$), 73.4 (C-2$_\beta$), 73.2 (CH$_2$ Bn/Nap$_\beta$), 71.5 (CH$_2$ Bn/Nap$_\alpha$), 71.4 (C-5$_\beta$), 71.4 (C-2$_\alpha$), 65.0 (C*H*$_2$CH$_{3\beta}$), 64.7 (C-5$_\alpha$), 63.9 (C*H*$_2$CH$_{3\alpha}$), 37.5 (C-3$_\beta$), 33.7 (C-3$_\alpha$), 29.7 (C-8$_\alpha$), 29.5 (C-8$_\beta$), 15.6 (C-6$_\beta$), 15.3 (C-12$_\beta$), 15.3 (C-12$_\alpha$), 15.2 (CH$_2$C*H*$_{3\alpha}$, CH$_2$C*H*$_{3\beta}$), 15.0 (C-6$_\alpha$); HRMS: [M+Na]$^+$ calcd for $C_{34}H_{36}O_{10}Na$ 629.2363, found 629.2357.

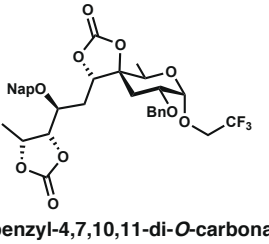


2-Fluoroethyl 2-*O*-benzyl-4,7,10,11-di-*O*-carbonate-9-*O*-(2-methylnaphthalene)-D-caryophylloside (S53). The title compound was prepared according to general procedure III (31 mg, 50 µmol, *quant.*, α:β; 83:17). Flash column chromatography (60:40 → 40:60; pentane:EtOAc) yielded the title compound as a colorless oil. TLC: R$_f$ 0.4 (pentane:EtOAc, 1:1, v:v); IR (neat, cm^{-1}): 700, 753, 819, 1070, 1202, 1455, 1802; NMR data reported as a mixture of α- and β-anomers; ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.89 – 7.27 (m, 14.4H, CH$_{arom}$), 4.99 – 4.85 (m, 1.2H, H-11$_\alpha$, H-11$_\beta$), 4.81 (d, *J* = 3.2 Hz, 1H, H-1$_\alpha$), 4.78 (s, 2H, CH$_2$ Bn/Nap$_\alpha$), 4.74 – 4.46 (m, 6.6H, H-7$_\beta$, H-10$_\alpha$, H-10$_\beta$, CH$_2$F$_\alpha$, CH$_2$F$_\beta$, CH$_2$ Bn/Nap$_\alpha$, CH$_2$ Bn/Nap$_\beta$, CH$_2$ Bn/Nap$_\beta$), 4.42 (d, *J* = 6.6 Hz, 0.2H, H-1$_\beta$), 4.32 (d, *J* = 11.0 Hz, 1H, H-7$_\alpha$), 4.08 (dd, *J* = 12.5, 4.1 Hz, 0.2H, H-9$_\beta$), 4.06 – 3.95 (m, 2H, H-5$_\alpha$, H-9$_\alpha$), 3.95 – 3.66 (m, 3.6H, H-2$_\alpha$, H-5$_\beta$, C*H*$_2$CH$_2$F$_\alpha$, C*H*$_2$CH$_2$F$_\beta$), 3.61

(dt, *J* = 10.8, 5.8 Hz, 0.2H, H-2β), 2.22 – 2.15 (m, 0.4H, H-3β, H-8β), 2.14 – 2.04 (m, 2.2H, H-3α, H-8α, H-8β), 1.95 (dd, *J* = 14.8, 8.2 Hz, 1H, H-8α), 1.84 (dd, *J* = 13.6, 4.9 Hz, 1H, H-3α), 1.76 (dd, *J* = 14.4, 10.1 Hz, 0.2H, H-3β), 1.46 (d, *J* = 6.7 Hz, 3H, H-12α), 1.44 (d, *J* = 6.7 Hz, 0.6H, H-12β), 1.34 (d, *J* = 6.2 Hz, 0.6H, H-6β), 1.23 (d, *J* = 6.3 Hz, 3H, H-6α); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 153.7, 153.7, 153.5, 153.2 (O(C=O)O), 138.0, 137.8, 134.2, 134.1, 133.8, 133.3 ($C_{q\text{-}arom}$), 128.8, 128.8, 128.7, 128.7, 128.6, 128.2, 128.2, 128.1, 128.1, 128.1, 128.0, 128.0, 128.0, 127.9, 127.2, 127.0, 126.8, 126.8, 126.7, 126.7, 126.6, 126.6, 125.7, 125.6, 125.5 (CH_{arom}), 103.6 (C-1β), 95.6 (C-1α), 84.9 (C-4β), 84.7 (C-4α), 82.8 (d, *J* = 169.5 Hz, CH_2F_α), 82.7 (d, *J* = 169.8 Hz, CH_2F_β), 80.9 (C-7α), 80.3 (C-7β), 79.0 (C-10α), 78.7 (C-10β), 75.9 (C-11α), 75.8 (C-11β), 73.9 (C-9α), 73.8 (C-9β), 73.7 (CH_2 Bn/Nap$_\alpha$), 73.5, 73.3 (CH_2 Bn/Nap$_\beta$), 73.2 (C-2β), 71.6 (CH_2 Bn/Nap$_\alpha$), 71.4 (C-2α), 68.3 (d, *J* = 19.8 Hz, *C*$H_2CH_2F_\beta$), 67.0 (d, *J* = 19.5 Hz, *C*$H_2CH_2F_\alpha$), 66.7 (C-5β), 64.8 (C-5α), 37.4 (C-3β), 33.5 (C-3α), 29.6 (C-8β), 29.5 (C-8α), 15.6 (C-12β), 15.2 (C-12α), 15.2 (C-6α), 14.9 (C-12β); HRMS: $[M+Na]^+$ calcd for $C_{34}H_{37}FO_{10}Na$ 647.2268, found 647.2263.

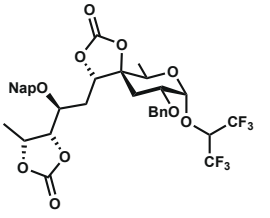


2,2-Difluoroethyl 2-*O*-benzyl-4,7,10,11-di-*O*-carbonate-9-*O*-(2-methylnaphthalene)-D-caryophylloside (S54). The title compound was prepared according to general procedure III (20.1 mg, 31 µmol, 63%, α:β; 87:13). Flash column chromatography (80:20 → 60:40; pentane:EtOAc) yielded the title compound as a colorless oil. TLC: R_f 0.7 (pentane:EtOAc, 1:1, v:v); IR (neat, cm^{-1}): 700, 754, 819, 1063, 1202, 1364, 1802; Data of the major stereoisomer (α-anomer): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.93 – 7.28 (m, 12H, CH_{arom}), 5.95 (tt, *J* = 55.3, 4.2 Hz, 1H, CHF_2), 4.93 (h, *J* = 6.6 Hz, 1H, H-11), 4.82 – 4.74 (m, 3H, H-1, CH_2 Bn/Nap), 4.62 (t, *J* = 7.0 Hz, 1H, H-10), 4.57 (d, *J* = 12.1 Hz, 1H, C*H*H Bn/Nap), 4.48 (d, *J* = 12.0 Hz, 1H, CH*H* Bn/Nap), 4.33 (dd, *J* = 11.1, 2.1 Hz, 1H, H-7), 4.03 (ddd, *J* = 8.2, 6.5, 3.2 Hz, 1H, H-9), 3.91 (q, *J* = 6.3 Hz, 1H, H-5), 3.82 – 3.69 (m, 3H, H-2, C*H*$_2$CHF$_2$), 2.15 – 2.01 (m, 2H, H-3, H-8), 1.93 (ddd, *J* = 14.7, 8.1, 2.1 Hz, 1H, H-8), 1.85 (dd, *J* = 13.6, 4.9 Hz, 1H, H-3), 1.46 (d, *J* = 6.6 Hz, 3H, H-12), 1.24 (d, *J* = 6.3 Hz, 3H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 153.6, 153.3 (O(C=O)O), 137.7, 134.1, 133.3, 133.3 ($C_{q\text{-}arom}$), 128.8, 128.7, 128.7, 128.3, 128.1, 128.0, 127.9, 127.9, 126.9, 126.7, 126.6, 125.5 (CH_{arom}), 114.1 (t, *J* = 241.2 Hz, CHF_2), 96.3 (C-1), 84.5 (C-4), 80.9 (C-7), 78.8 (C-10), 75.8 (C-11), 73.8 (C-9), 73.7, 71.8 (CH_2 Bn/Nap), 71.3 (C-2), 67.1 (t, *J* = 28.2 Hz, *C*H_2CHF$_2$), 65.3 (C-5), 33.4 (C-3), 29.5 (C-8), 15.2 (C-12), 14.9 (C-6); Diagnostic signals of the minor stereoisomer (β-anomer): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.91 (tt, *J* = 55.4, 4.1 Hz, 1H, CHF_2), 3.59 (q, *J* = 6.4 Hz, 1H, H-5), 1.41 (d, *J* = 6.6 Hz, 3H, H-12), 1.11 (d, *J* = 6.4 Hz, 3H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 96.7 (C-1), 84.7 (C-4), 78.9 (C-10), 72.7 (C-9), 71.9, 71.9 (CH_2 Bn/Nap), 71.6 (C-2), 31.3 (C-3), 29.8 (C-8), 14.8 (C-12), 13.3 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{34}H_{36}F_2O_{10}Na$ 665.2174, found 665.2169.

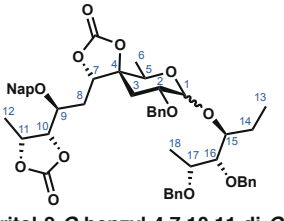


2,2,2-Trifluoroethyl 2-*O*-benzyl-4,7,10,11-di-*O*-carbonate-9-*O*-(2-methylnaphthalene)-α-D-caryophylloside (S55). The title compound was prepared according to general procedure III (25 mg, 38 µmol, 76%, α:β; >98:2). Flash column chromatography (90:10 → 70:30; pentane:EtOAc) yielded the title compound as a colorless oil. TLC: R_f 0.8 (pentane:EtOAc, 1:1, v:v); $[\alpha]_D^{20}$ 21.0° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 701, 753, 819, 1067, 1155, 1279, 1804; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.91 – 7.27 (m, 12H, CH_{arom}), 4.91 (p, *J* = 6.8 Hz, 1H, H-11), 4.83 (d, *J* = 3.3 Hz, 1H, H-1), 4.78 (d, *J* = 2.5 Hz, 2H, CH_2 Bn/Nap), 4.62 (dd, *J* = 7.3, 6.5 Hz, 1H, H-10), 4.55 (d, *J* = 11.8 Hz, 1H, C*H*H Bn/Nap), 4.49 (d, *J* = 11.8 Hz,

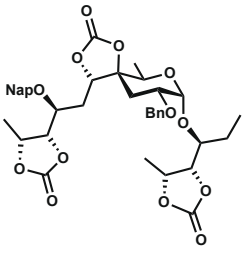
1H, CH*H* Bn/Nap), 4.32 (dd, *J* = 11.2, 2.1 Hz, 1H, H-7), 4.03 (ddd, *J* = 8.5, 6.5, 3.1 Hz, 1H, H-9), 3.99 – 3.85 (m, 3H, H-5, CH_2CF_3), 3.78 (ddd, *J* = 11.7, 4.9, 3.3 Hz, 1H, H-2), 2.14 – 2.00 (m, 2H, H-3, H-8), 1.92 (ddd, *J* = 14.9, 8.5, 2.1 Hz, 1H, H-8), 1.85 (dd, *J* = 13.7, 4.9 Hz, 1H, H-3), 1.46 (d, *J* = 6.7 Hz, 3H, H-12), 1.24 (d, *J* = 6.4 Hz, 3H, H-6); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 153.6, 153.3 (O(C=O)O), 137.6, 134.2, 133.3, 133.3 ($C_{q\text{-arom}}$), 128.9, 128.7, 128.7, 128.2, 128.1, 128.0, 127.9, 126.8, 126.8, 126.6, 125.5 (CH_{arom}), 123.8 (d, *J* = 278.7 Hz, CF_3), 96.4 (C-1), 84.3 (C-4), 81.0 (C-7), 79.0 (C-10), 75.8 (C-11), 73.9 (C-9), 73.8, 71.7 (CH_2 Bn/Nap), 71.1 (C-2), 65.7 (C-5), 65.1 (d, *J* = 35.0 Hz, *C*H_2CF_3), 33.3 (C-3), 29.7 (C-8), 15.3 (C-12), 14.9 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{34}H_{35}F_3O_{10}Na$ 683.2080, found 683.2075.



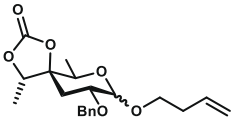
1,1,1,3,3,3-Hexafluoropropyl 2-*O*-benzyl-4,7,10,11-di-*O*-carbonate-9-*O*-(2-methylnaphthalene)-α-D-caryophylloside (S56). The title compound was prepared according to general procedure III (5.2 mg, 7.2 µmol, 16%, α:β; >98:2). Flash column chromatography (90:10 → 70:30; pentane:EtOAc) yielded the title compound as a colorless oil. TLC: R_f 0.8 (pentane:EtOAc, 1:1, v:v); IR (neat, cm^{-1}): 700, 754, 819, 1066, 1204, 1311, 1803; ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.89 – 7.27 (m, 12H, CH_{arom}), 5.10 (d, *J* = 3.4 Hz, 1H, H-1), 4.92 (p, *J* = 6.8 Hz, 1H, H-11), 4.81 (d, *J* = 11.6 Hz, 1H, C*H*H Bn/Nap), 4.75 (d, *J* = 11.6 Hz, 1H, CH*H* Bn/Nap), 4.59 (t, *J* = 7.0 Hz, 1H, H-10), 4.55 (d, *J* = 11.5 Hz, 1H, C*H*H Bn/Nap), 4.52 – 4.43 (m, 2H, CH*H* Bn/Nap, $CH(CF_3)_2$), 4.31 (dd, *J* = 11.5, 2.0 Hz, 1H, H-7), 4.04 (ddd, *J* = 9.3, 6.7, 3.1 Hz, 1H, H-9), 3.99 (q, *J* = 6.2 Hz, 1H, H-5), 3.82 (ddd, *J* = 11.4, 4.7, 3.6 Hz, 1H, H-2), 2.07 – 1.99 (m, 2H, H-3, H-8), 1.92 – 1.87 (m, 1H, H-8), 1.84 (dd, *J* = 13.8, 4.7 Hz, 1H, H-3), 1.47 (d, *J* = 6.7 Hz, 3H, H-12), 1.25 – 1.23 (m, 3H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 137.3, 134.2, 133.3, 133.3 ($C_{q\text{-arom}}$), 128.9, 128.7, 128.3, 128.1, 127.9, 127.8, 126.9, 126.8, 126.7, 125.5 (CH_{arom}), 97.9 (C-1), 84.0 (C-4), 81.2 (C-7), 79.0 (C-10), 75.8 (C-11), 74.0 (C-9), 74.0, 71.8 (CH_2 Bn/Nap), 70.5 (C-2), 66.7 (C-5), 33.3 (C-3), 29.8 (C-8), 15.3 (C-12), 14.8 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{35}H_{34}F_6O_{10}Na$ 751.1954, found 751.1948.



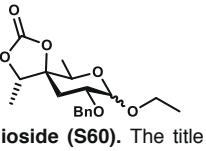
1,2,6-Trideoxy-4,5-di-*O*-benzyl-D-altritol-2-*O*-benzyl-4,7,10,11-di-*O*-carbonyl-9-*O*-(2-methylnaphthalene)-α-D-caryophylloside (S57). The title compound was prepared according to the general procedure III giving the product as a white solid (11.5 mg, 50%, α:β; 77:23) TLC: R_f 0.8 (pentane:EtOAc, 3:2, v:v); Data of the major stereoisomer (α-anomer): ^{1}H NMR (600 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.87 – 7.14 (m, 22H, CH_{arom}), 4.98 (d, *J* = 3.2 Hz, 1H, H-1), 4.79 (m, 1H, H-11), 4.76 – 4.64 (m, 2H, CH_2 Bn/Nap), 4.56 – 4.48 (m, 2H, CH_2 Bn/Nap), 4.37 (t, *J* = 6.8 Hz, H-10), 4.27 (dd, *J* = 11.6, 1.6 Hz, 1H, H-7), 4.22 (q, *J* = 6.8 Hz, 1H, H-17), 3.92 (m, 1H, H-9), 3.85 (m, 1H, H-15), 3.78 (m, 1H, H-2), 3.67 (m, 1H, H-16), 2.22 (m, 1H, H-8), 2.04 –1.96 (m, 2H, H-3, H-8), 1.87 (dd, *J* = 13.6, 4.5 Hz, 1H, H-3), 1.82 (m, 1H, H-2), 1.43 (d, *J* = 6.4 Hz, 3H, H-12), 1.41 (d, *J* = 6.4 Hz, 3H, H-6), 1.07 (d, *J* = 6.4 Hz, 3H, H-18), 0.95 (t, *J* = 8.2 Hz, 1H, H-13); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 153.5, 153.4, 138.7, 137.8, 134.0, 133.2 ($C_{q\text{-arom}}$), 128.7, 128.5, 128.4, 128.0, 128.0, 127.9, 127.8, 127.6, 127.6, 127.5, 127.5, 127.0, 126.5, 126.4, 125.6 (CH_{arom}), 93.0 (C-1), 82.2 (C-16), 80.6 (C-7), 78.3 (C-10), 78.2, 75.7 (CH_2 Bn/Nap), 75.6 (C-11), 75.0 (C-15), 73.5 (C-9), 71.4 (C-2), 70.8 (CH_2 Bn/Nap), 64.8 (C-5), 33.7 (C-3), 29.7 (C-8), 22.7 (C-14), 16.3 (C-6), 15.0 (C-12), 14.9 (C-18), 10.0 (C-13); Diagnostic signals of the minor stereoisomer (β-anomer): ^{1}H NMR (600 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.45 (d, *J* = 7.0 Hz, 1H, H-1); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 102.3 (C-1); HRMS: $[M+Na]^+$ calcd for $C_{52}H_{58}O_{12}N_a$ 897.3826, found 897.3816.



1,2,6-Trideoxy-4,5-di-*O*-carbonyl-D-altritol-2-*O*-benzyl-4,7,10,11-di-*O*-carbonyl-9-*O*-(2-methylnaphthalene)-α-D-caryophylloside (S58). The title compound was prepared according to the general procedure III giving the product as a white solid (12.0 mg, 54%, α:β; >98:2). TLC: R_f 0.4 (pentane:EtOAc, 3:2, v:v); ^{1}H NMR (600 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.88 – 7.89 (m, 4H, CH_{arom}), 7.39 (m, 2H, CH_{arom}), 7.44 (m, 2H, CH_{arom}), 7.37 – 7.30 (m, 4H, CH_{arom}), 5.01 – 4.95 (m, 3H, H-1, H-5, H-11), 4.90 (d, *J* = 11.9 Hz, 1H, C*H*H Bn/Nap), 4.79 (d, *J* = 11.9 Hz, 1H, C*H*H Bn/Nap), 4.71 (m, 2H, H-10, H-16), 4.52 (d, *J* = 11.9 Hz, 1H, C*H*H Bn/Nap), 4.35 (dd, *J* = 11.8, 1.42 Hz, 1H, H-7), 4.16 (m, 1H, H-9), 4.00 (m, 2H, H-17, H-15), 3.81 (m, 1H, H-2), 2.22 (m, 1H, H-8), 2.04 -1.96 (m, 2H, H-3, H-8), 1.87 (dd, *J* = 13.6, 4.5 Hz, 1H, H-3), 1.82 (m, 1H, H-14), 1.66 (d, *J* = 6.3 Hz, H-6), 1.60 (m, 3H, H-14), 1.56 (d, *J* = 7.1 Hz, 1H, H-12), 1.27 (d, *J* = 7.1 Hz, 1H, H-18), 1.02 (t, *J* = 8.2 Hz, 1H, H-13); ^{13}C NMR (151 MHz, $CDCl_3$, HSQC): δ 155.8, 155.0, 154.4, 138.7, 135.6, 134.2, 134.1 ($C_{q\text{-}arom}$), 129.5, 129.5, 129.0, 128.9, 128.7, 128.5, 127.8, 127.4, 127.3, 126.6 (CH_{arom}), 93.4 (C-1), 82.3 (C-7), 80.5 (C-16), 79.6 (C-10), 78.1 (C-15), 77.3 (C-11/C-17) 77.2 (C-17/C-11), 75.0 (C-9), 74.7, 72.3 (CH_2 Bn/Nap), 72.2 (C-2), 66.6 (C-5), 34.1 (C-3), 30.0 (C-8), 23.0 (C-14), 16.4 (C-12), 16.3 (C-6), 15.9 (C-18), 11.5 (C-13); HRMS: $[M+Na]^+$ calcd for $C_{39}H_{44}O_{13}Na$ 743.2680, found 743.2672.

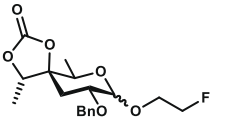


But-3-ylene 2-*O*-benzyl-4,7-carbonate-D-yersinioside (S59). The title compound was prepared according to general procedure III (15.6 mg, 43 µmol, 86%, α:β; 59:41) as a colorless oil. The title compound was also prepared according to general procedure IV (10 mg, 27 µmol, 55%, α:β; 67:33). The title compound was also prepared according to general procedure V (11 mg, 30 µmol, 61%, α:β; >98:2). TLC: R_f 0.4 (pentane:EtOAc, 8:2, v:v); $[\alpha]_D^{20}$ 28.3° (c 0.5, $CHCl_3$; α-anomer); IR (neat, cm^{-1}): 746, 1008, 1066, 1089, 1808, 2925; Data of the α-anomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 – 7.28 (m, 5H, CH_{arom}), 5.83 (ddt, *J* = 17.1, 10.2, 6.8 Hz, 1H, H-11), 5.13 (dq, *J* = 17.2, 1.7 Hz, 1H, H-12), 5.06 (ddt, *J* = 10.2, 2.1, 1.2 Hz, 1H, H-12), 4.78 (d, *J* = 3.3 Hz, 1H, H-1), 4.61 (d, *J* = 12.1 Hz, 1H, C*H*H Bn), 4.56 (d, *J* = 12.0 Hz, 1H, CH*H* Bn), 4.33 (q, *J* = 6.9 Hz, 1H, H-5), 3.95 (q, *J* = 6.3 Hz, 1H, H-7), 3.81 (ddd, *J* = 11.8, 5.0, 3.3 Hz, 1H, H-2), 3.73 – 3.51 (m, 2H, H-9), 2.55 – 2.28 (m, 2H, H-10), 2.11 (dd, *J* = 13.5, 11.8 Hz, 1H, H-3), 1.97 (dd, *J* = 13.5, 4.9 Hz, 1H, H-3), 1.43 (d, *J* = 6.9 Hz, 3H, H-6), 1.25 (d, *J* = 6.3 Hz, 3H, H-8); ^{13}C NMR (101 MHz, $CDCl_3$): δ 154.2 (O(C=O)O), 138.0 ($C_{q\text{-}arom}$), 135.2 (C-11), 129.5, 128.7, 128.1, 127.9 (CH_{arom}), 117.0 (C-12), 95.6 (C-1), 84.9 (C-4), 81.5 (C-5), 71.8 (CH_2 Bn), 71.7 (C-2), 67.6 (C-9), 65.0 (C-7), 34.1 (C-10), 33.7 (C-3), 14.7 (C-8), 13.1 (C-6); Diagnostic signals of the β-anomer: ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.36 (d, *J* = 7.2 Hz, 1H, H-1); ^{13}C NMR (126 MHz): δ 104.1 (C-1), 73.8 (CH_2 Bn), 68.9 (C-9); HRMS: $[M+Na]^+$ calcd for $C_{20}H_{26}O_6Na$ 385.1627, found 385.1622.

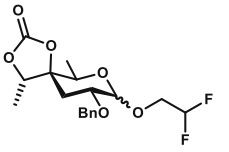


Ethyl 2-*O*-benzyl-4,7-carbonate-D-yersinioside (S60). The title compound was prepared according to general procedure III (10 mg, 30 µmol, 60%, α:β; 50:50) as a colorless oil. The title compound was also prepared according to general procedure IV (12 mg, 36 µmol, 72%, α:β; 63:37). The title compound was also prepared according to general procedure V (10 mg, 30 µmol, 60%, α:β; >98:2). TLC: R_f 0.5 (pentane:EtOAc, 7:3, v:v); $[\alpha]_D^{20}$ 69.8° (c 0.5, $CHCl_3$; α-anomer); IR (neat, cm^{-1}): 1007, 1066, 1804, 2923;

NMR data reported as a mixture of α- and β-anomers; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 – 7.28 (m, 10H, CH_{arom}), 4.86 (d, *J* = 11.6 Hz, 1H, C*H*H Bn), 4.79 (d, *J* = 3.3 Hz, 1H, H-1$_\alpha$), 4.65 – 4.59 (m, 2H, C*H*H Bn, CH*H* Bn), 4.56 (d, *J* = 12.1 Hz, 1H, , CH*H* Bn), 4.47 – 4.30 (m, 3H, H-1$_\beta$, H-7$_\beta$, H-7$_\alpha$), 4.02 – 3.90 (m, 2H, H-9$_\beta$, H-9$_\alpha$), 3.81 (ddd, *J* = 11.8, 5.0, 3.4 Hz, 1H, H-2$_\alpha$), 3.76 – 3.68 (m, 2H, H-5$_\beta$, H-5$_\alpha$), 3.65 – 3.50 (m, 3H, H-2$_\beta$, H-9$_\beta$, H-9$_\alpha$), 2.25 (dd, *J* = 14.2, 5.2 Hz, 1H, H-3$_\beta$), 2.16 – 2.04 (m, 1H, H-3$_\alpha$), 1.97 (dd, *J* = 13.5, 5.0 Hz, 1H, H-3$_\alpha$), 1.76 (dd, *J* = 14.3, 10.8 Hz, 1H, H-3$_\beta$), 1.48 – 1.42 (m, *J* = 6.9, 3.3 Hz, 6H, H-8$_\beta$, H-8$_\alpha$), 1.36 (d, *J* = 6.3 Hz, 3H H-10$_\alpha$/H-10$_\beta$), 1.27 – 1.24 (m, 9H, H-6$_\beta$, H-6$_\alpha$, H-10$_\beta$/H-10$_\alpha$); ^{13}C NMR (101 MHz, $CDCl_3$): δ 138.0, 137.9 ($C_{q\text{-}arom}$), 131.2, 129.5, 128.7, 128.6, 128.1, 128.0, 128.0, 127.9, 124.9 (CH_{arom}), 104.0 (C-1$_\beta$), 95.3 (C-1$_\alpha$), 85.0 (C-4$_\alpha$/C-4$_\beta$), 84.2(C-4$_\beta$/C-4$_\alpha$), 81.5 (C-7$_\alpha$/C-7$_\beta$), 80.6 (C-7$_\beta$/C-7$_\alpha$), 73.4(C-2$_\beta$), 73.4 (CH_2 Bn), 71.9(C-2$_\alpha$), 71.7 (CH_2 Bn), 65.1 (C-9$_\beta$/C-9$_\alpha$), 64.9 (C-5$_\beta$/C-5$_\alpha$), 63.8 (C-9$_\alpha$/C-9$_\beta$), 38.3 (C-3$_\beta$), 33.8 (C-3$_\alpha$), 15.4 (C-6$_\beta$/C-6$_\alpha$), 15.4 (C-6$_\alpha$/C-6$_\beta$), 15.2 (C-10$_\alpha$/C-10$_\beta$), 14.8 (C-10$_\beta$/C-10$_\alpha$), 13.2 (C-8$_\beta$/C-8$_\alpha$), 13.2 (C-8$_\alpha$/C-8$_\beta$); HRMS: $[M+Na]^+$ calcd for $C_{18}H_{24}O_6Na$ 359.1471, found 359.1465.

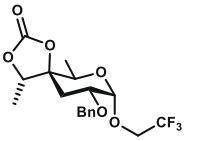


2-Fluoroethyl 2-*O*-benzyl-4,7-carbonate-D-yersinioside (S61). The title compound was prepared according to general procedure III (13 mg, 38 µmol, 76%, α:β; 66:34) as a colorless oil. The title compound was also prepared according to general procedure IV (14 mg, 42 µmol, 85%, α:β; 81:19). The title compound was also prepared according to general procedure V (11 mg, 33 µmol, 65%, α:β; >98:2); TLC: R_f 0.1 (pentane:EtOAc, 8:2, v:v); $[\alpha]_D^{20}$ 57.6° (c 0.5, $CHCl_3$; α-anomer); IR (neat, cm^{-1}): 1008, 1066, 1793, 1805; Data of the anomer: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.45 – 7.19 (m, 5H, CH_{arom}), 4.82 (d, *J* = 3.2 Hz, 1H, H-1), 4.72 – 4.50 (m, 4H, CH_2F, CH*H* Bn, C*H*H Bn), 4.34 (q, *J* = 6.9 Hz, 1H, H-7), 4.01 (q, *J* = 6.4 Hz, 1H, H-5), 3.96 – 3.68 (m, 3H, H-3, C*H*$_2$$CH_2F$), 2.14 (dd, *J* = 13.5, 11.9 Hz, 1H, H-3), 1.99 (dd, *J* = 13.5, 4.9 Hz, 1H, H-3), 1.43 (d, *J* = 6.9 Hz, 3H, H-8), 1.25 (d, *J* = 6.3 Hz, 3H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$): δ 154.1 (O(C=O)O), 137.9 ($C_{q\text{-}arom}$), 128.7, 128.6, 128.2, 128.0, 128.0 (CH_{arom}), 95.8 (C-1), 84.8 (C-4), 82.7 (d, *J* = 169.8 Hz, CH_2F), 81.6 (C-7), 72.0 (C-2), 71.8 (C-5), 71.7 (CH_2 Bn), 67.1 (d, *J* = 19.7 Hz, C*H*$_2$$CH_2F$), 33.6 (C-3), 14.8 (C-6), 13.1 (C-8); Diagnostic signals of the β-isomer: ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.86 (d, *J* = 11.5 Hz, 1H, C*H*H Bn), 4.46 – 4.39 (m, 2H, H-1, H-7), 3.65 (ddd, *J* = 11.1, 6.9, 5.3 Hz, 2H, H-2), 2.27 (dd, *J* = 14.3, 5.3 Hz, 1H, H-3), 1.78 (dd, *J* = 14.3, 10.7 Hz, 1H, H-3), 1.36 (d, *J* = 6.3 Hz, 3H, H-6); ^{13}C NMR (126 MHz): δ 153.8 (O(C=O)O), 138.2 ($C_{q\text{-}arom}$), 104.2 (C-1), 84.1 (C-4), 82.84 (d, *J* = 169.8 Hz, CH_2F), 80.6 (C-7), 73.5 (CH_2 Bn), 73.2 (C-2), 68.27 (d, *J* = 20.0 Hz, *C*H_2CH_2F), 65.0 (C-5), 38.1 (C-3), 15.3 (C-6), 13.2 (C-8); HRMS: $[M+Na]^+$ calcd for $C_{18}H_{23}O_6Na$ 377.1376, found 377.1368.

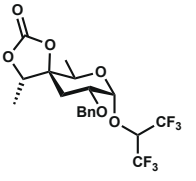


2,2-Di-fluoroethyl 2-*O*-benzyl-4,7-carbonate-D-yersinioside (S62). The title compound was prepared according to general procedure III (18 mg, 50 µmol, *quant.*, α:β; 80:20) as a colorless oil. The title compound was also prepared according to general procedure IV (18 mg, 50 µmol, *quant.*, α:β; 88:12). The title compound was also prepared according to general procedure V (3.0 mg, 8 µmol, 16%, α:β; >98:2); TLC: R_f 0.2 (pentane:EtOAc, 8:2, v:v); IR (neat, cm^{-1}): 696, 1009, 1063, 1091, 1793, 1808; Data of the major stereoisomer (α-anomer): ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.10 – 7.16 (m, 15H, CH_{arom}), 5.94 (tt, *J* = 55.4, 4.2 Hz, 1H, CHF_2), 4.79 (d, *J* = 3.3 Hz, 1H, H-1), 4.63 (d, *J* = 12.1 Hz, 1H, CH*H* Bn), 4.55 (d, *J* = 12.0 Hz, 1H, C*H*H Bn), 4.35 (q, *J* = 6.9 Hz, 1H, H-7), 3.95 (q, *J* = 6.3 Hz, 1H, H-5), 3.87 – 3.70 (m, 3H, H-2, C*H*$_2$$CHF_2$), 2.09 (d, *J* = 11.8 Hz, 1H, H-3), 2.00 (dd, *J* = 13.6, 5.0 Hz, 1H, H-3), 1.43 (d, *J* = 6.9 Hz, 3H, H-8), 1.26 (d, *J* = 6.3 Hz, 3H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$): δ 154.0 (O(C=O)O), 137.8 ($C_{q\text{-}arom}$), 131.2, 129.5, 128.7, 128.0, 124.9 (CH_{arom}), 114.1 (t, *J* = 241.5 Hz, CHF_2), 96.4 (C-1), 84.5 (C-4), 81.5 (C-7), 71.9 (CH_2 Bn), 71.6 (C-2), 67.2 (t, *J* = 28.5 Hz, *C*H_2CHF_2), 65.5 (C-5), 33.5 (C-3), 14.8 (C-6), 13.1 (C-8); Diagnostic signals of the minor stereoisomer (β-isomer): ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.46 – 4.39 (m, 2H, H-1, H-7), 3.64 (ddd, *J* = 10.8, 7.1, 5.3 Hz, 1H), 2.26 (dd, *J* = 14.4, 5.3 Hz, 1H, H-3), 1.78 (dd, *J* = 14.3, 10.8 Hz, 1H, H-3), 1.36

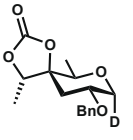
(d, *J* = 6.2 Hz, 1H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$): δ 145.8 (O(C=O)O), 138.0 ($C_{q\text{-arom}}$), 104.3 (C-1), 83.9 (C-4), 80.6 (C-7), 73.5 (CH_2 Bn), 73.1 (C-2), 72.2 (C-5), 38.0 (C-3), 15.3 (C-6), 13.2 (C-8); HRMS: $[M+Na]^+$ calcd for $C_{18}H_{22}O_6F_2Na$ 395.1282, found 395.1284.



2,2,2-Tri-fluoroethyl 2-*O*-benzyl-4,7-carbonate-α-D-yersinioside (S63). The title compound was prepared according to general procedure III (15 mg, 38 µmol, 77%, α:β; >98:2) as a colorless oil. The title compound was also prepared according to general procedure IV (7.0 mg, 18 µmol, 36%, α:β; >98:2). TLC: R_f 0.8 (pentane:EtOAc, 7:3, v:v); $[\alpha]_D^{20}$ 25.7° (c 0.5, $CHCl_3$); IR (neat, cm^{-1}): 1009, 1063, 1275, 1793, 1809, 2925; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 – 7.28 (m, 5H, CH_{arom}), 4.83 (d, *J* = 3.3 Hz, 1H, H-1), 4.63 (d, *J* = 11.9 Hz, 1H, C*H*H Bn), 4.56 (d, *J* = 11.9 Hz, 1H, CH*H* Bn), 4.36 (q, *J* = 6.9 Hz, 1H, H-7), 3.98 – 3.80 (m, 4H, H-2, H-5, CH_2CF$_3$), 2.13 (dd, *J* = 13.6, 11.8 Hz, 1H, H-3), 2.02 (ddd, *J* = 13.6, 5.1, 0.8 Hz, 1H, H-3), 1.44 (d, *J* = 5.2 Hz, 3H, H-8), 1.27 (d, *J* = 6.4 Hz, 3H, H-6); ^{13}C NMR (101 MHz, $CDCl_3$): δ 153.9 (O(C=O)O), 137.8 ($C_{q\text{-arom}}$), 131.2, 129.5, 128.7, 128.3, 128.0, 125.7, 124.9 (CH_{arom}), 96.4 (C-1), 84.4 (C-4), 81.5 (C-7), 71.9 (CH_2 Bn), 71.4 (C-2), 65.8 (C-5), 65.3, 65.0 (C-9), 33.4 (C-3), 14.7 (C-6), 13.1 (C-8); HRMS: $[M+Na]^+$ calcd for $C_{18}H_{21}F_3O_6Na$ 413.1188, found 413.1182.

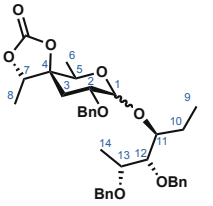


1,1,1,3,3,3-Hexafluoropropyl 2-*O*-benzyl-4,7-carbonate-α-D-yersinioside (S64). The title compound was prepared according to general procedure III yieldingthe title compound (6.5 mg, 14 µmol, 28%, α:β; >98:2). Flash column chromatography (80:20 → 60:40; pentane:Et_2O) yielded the title compound as a colourless oil. TLC: R_f 0.8 (pentane:EtOAc, 8:2, v:v); $[\alpha]_D^{20}$ 42.5° (c 0.5, $CHCl_3$); IR (neat, cm^{-1}): 1008, 1064, 1105, 1197, 1796, 1813, 2923; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.39 – 7.29 (m, 5H, CH_{arom}), 5.15 (d, *J* = 3.4 Hz, 1H, H-1), 4.63 (d, *J* = 11.5 Hz, 1H, C*H*H Bn), 4.54 (d, *J* = 11.5 Hz, 1H, CH*H* Bn), 4.53 – 4.45 (m, 1H, H-9), 4.39 (q, *J* = 6.9 Hz, 1H, H-7), 4.04 (q, *J* = 6.3 Hz, 1H, H-5), 3.90 (ddd, *J* = 11.6, 5.2, 3.4 Hz, 1H, H-2), 2.14 (dd, *J* = 13.7, 11.6 Hz, 1H, H-3), 2.06 (dd, *J* = 13.7, 4.7 Hz, 1H, H-3), 1.43 (d, *J* = 2.9 Hz, 3H, H-8), 1.28 (d, *J* = 6.3 Hz, 3H, H-6); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 137.3 ($C_{q\text{-arom}}$), 128.7, 128.3, 127.8 (CH_{arom}), 97.9 (C-1), 84.1 (C-4), 81.6 (C-7), 73.4, 73.1 (C-9), 71.7 (CH_2 Bn), 70.7 (C-2), 66.8 (C-5), 33.2 (C-3), 14.7 (C-6), 13.0 (C-8); HRMS: $[M+Na]^+$ calcd for $C_{19}H_{20}F_6O_6Na$ 481.1062, found 481.1056.

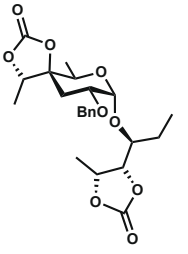


2-*O*-Benzyl-4,7-carbonate-1-α-deuterio-D-yersinioside (S65). The title compound was prepared according to general procedure III yielding the title compound (7.9 mg, 27 µmol, 54%, α:β; >98:2). Flash column chromatography (80:20 → 60:40; pentane:Et_2O) yielded the title compound as a colorless oil. TLC: R_f 0.5 (pentane:EtOAc, 8:2, v:v); $[\alpha]_D^{20}$ 12.5° (c 0.5, $CHCl_3$); IR (neat, cm^{-1}): 1008, 1065, 1093, 1793, 2923; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.38 – 7.29 (m, 5H, CH_{arom}), 4.56 (s, 2H, CH_2 Bn), 4.49 (q, *J* = 6.8 Hz, 1H, H-7), 4.00 (dd, *J* = 4.5, 1.8 Hz, 1H, H-1), 3.81 (dt, *J* = 9.2, 4.5 Hz, 1H, H-2), 3.64 (q, *J* = 6.3 Hz, 1H, H-5), 2.31 (ddd, *J* = 13.8, 4.6, 1.9 Hz, 1H, H-3), 1.76 (dd, *J* = 13.7, 9.5 Hz, 1H, H-3), 1.47 (d, *J* = 6.8 Hz, 3H, H-8), 1.31 (d, *J* = 6.3 Hz, 3H, H-6); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 154.0 (O(C=O)O), 137.9 ($C_{q\text{-arom}}$), 128.7, 128.2, 127.8 (CH_{arom}), 83.8 (C-4), 81.8 (C-7), 73.4 (C-5), 71.5 (CH_2 Bn), 70.5 (C-2),

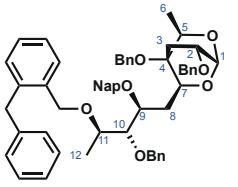
67.8, 67.6, 67.4 (C-1), 38.3 (C-3), 14.9 (C-6), 13.4 (C-8); HRMS: $[M+Na]^+$ calcd for $C_{16}H_{19}DO_5Na$ 316.1271, found 316.1266.



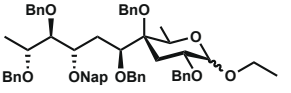
1,2,6-Trideoxy-4,5-di-*O*-benzyl-D-altritol-2-*O*-benzyl-4,7-carbonyl-D-yersinioside (S66). The title compound was prepared according to the general procedure III giving the product as a white solid (10.4 mg, 63%, α:β; 61:39). TLC: R_f 0.5 (pentane:EtOAc, 4:1, v:v) for α-isomer. TLC: R_f 0.2 (pentane:EtOAc, 4:1, v:v) for β-isomer; NMR data reported as a mixture of α- and β-anomers; ^{1}H NMR (850 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.41 – 7.17 (m, 15H, CH_{arom}), 4.95 (d, *J* = 3.3 Hz, 1H, H-1$_\alpha$), 4.76 (m, 2H, CH*H* Bn$_\alpha$, CH*H* Bn$_\beta$), 4.71 (d, *J* = 11.8 Hz, 1H, CH*H* Bn$_\beta$), 4.67 – 4.49 (m, 7H, CH*H* Bn$_\alpha$, CH*H* Bn$_\alpha$, CH*H* Bn$_\beta$, C*H*H Bn$_\alpha$, C*H*H Bn$_\alpha$, C*H*H Bn$_\beta$, C*H*H Bn$_\beta$), 4.43 (d, *J* = 7.5 Hz, 1H, H-1$_\beta$), 4.38 – 4.33 (m, 1H, C*H*H Bn$_\beta$, H-13$_\beta$), 4.22 (q, *J* = 6.9 Hz, 1H, H-7$_\alpha$/H-5$_\alpha$), 4.13 – 4.05 (m, 2H, H-5$_\alpha$/H-7$_\alpha$, H-5$_\beta$/H-7$_\beta$), 3.91 (dt, *J* = 8.3, 3.6 Hz, 1H, H-11$_\beta$), 3.87 (ddd, *J* = 6.9, 5.3, 3.8 Hz, 1H, H-11$_\alpha$), 3.82 – 3.77 (m, 2H, H-2$_\alpha$, H-12$_\alpha$), 3.69 – 3.67 (m, 1H, H-12$_\beta$), 3.62 (dd, *J* = 6.2, 3.6 Hz, 1H, H-13$_\alpha$), 3.61 – 3.58 (m, 1H, H-2$_\beta$, H-5$_\beta$/H-7$_\beta$), 3.55 (q, *J* = 6.2 Hz, 1H, H-5$_\beta$/H-7$_\beta$), 2.07 – 1.98 (m, 2H, H-3$_\alpha$), 1.92 (ddd, *J* = 13.4, 4.8, 1.0 Hz, 1H, H-3$_\alpha$), 1.77 – 1.66 (m, 2H, H-10$_\alpha$, H-10$_\beta$, H-10$_\beta$), 1.64 – 1.59 (m, 3H, H-10$_\alpha$, H-3$_\beta$, H-3$_\beta$), 1.39 – 1.37 (m, 2H, H-14$_\beta$), 1.36 – 1.32 (m, 4H, H-14$_\alpha$), 1.29 – 1.27 (m, 5H, H-6$_\beta$/H-8$_\beta$), 1.12 (d, *J* = 6.9 Hz, 3H, H-6$_\alpha$/H-8$_\alpha$), 1.00 (d, *J* = 6.3 Hz, 3H, H-6$_\alpha$/H-8$_\alpha$), 0.97 (t, *J* = 7.4 Hz, 2H, H-9$_\beta$), 0.92 (t, *J* = 7.5 Hz, 3H, H-9$_\alpha$), 0.88 (td, *J* = 7.2, 0.9 Hz, 2H, H-6$_\beta$/H-8$_\beta$); ^{13}C NMR (214 MHz, $CDCl_3$, HSQC): δ 154.2, 154.1, 152.3, 147.2, 139.0, 138.8, 138.7, 138.2, 138.0, 136.0 ($C_{q\text{-}arom}$), 131.3, 128.6, 128.5, 128.4, 128.3, 128.1, 128.0, 127.8, 127.7, 127.6, 127.5, 124.9, 114.2 (CH_{arom}), 102.4 (C-1$_\beta$), 93.3 (C-1$_\alpha$), 85.0, 84.5, 83.2, 81.7 (C-12), 81.6 (C-5$_\alpha$), 80.6, 80.6, 80.2, 80.1, 77.9 (C-11), 77.9, 75.4 (C-13), 75.4, 75.1, 74.2, 73.8 (C-2$_\beta$), 73.6, 73.0, 72.0 (C-13), 72.0, 71.9 (C-2$_\alpha$), 71.9, 71.6, 71.4, 71.4, 71.0, 70.8, 70.8, 70.8, 65.1 (C-5$_\beta$), 64.8, 38.8 (C-3$_\beta$), 36.7, 34.4, 33.9 (C-3$_\alpha$), 32.1, 31.6, 31.2, 30.5, 30.3, 29.8, 29.7, 29.5, 29.4, 29.3, 29.1, 28.8, 26.1, 23.4, 22.8, 22.6, 16.1, 16.0, 15.2, 14.6 (C-6$_\beta$), 14.3, 13.1, 12.9, 12.9 (C-6$_\alpha$), 10.5 (C-9), 9.9 (C-9); HRMS: $[M+Na]^+$ calcd for $C_{36}H_{44}O_8Na$ 627.2934, found 627.2928.



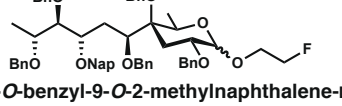
1,2,6-Trideoxy-4,5-*O*-carbonate-D-altritol-2-*O*-benzyl-4,7-carbonate-α-D-yersinioside (S67). The title compound was prepared according to general procedure III (17 mg, 37 µmol, 74%, α:β; >98:2). Flash column chromatography (80:20 → 60:40; pentane:EtOAc) yielded the title compound as a colorless oil. TLC: R_f 0.3 (pentane:EtOAc, 7:3, v:v); $[\alpha]_D^{20}$ 48.2° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 1006, 1063, 1790, 2923; ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC): δ 7.37 – 7.27 (m, 5H, CH_{arom}), 4.98 (d, *J* = 3.4 Hz, 1H, H-1), 4.95 – 4.88 (m, 1H, H-13), 4.70 (dd, *J* = 7.5, 3.5 Hz, 1H, H-12), 4.58 (d, *J* = 11.8 Hz, 1H, C*H*H Bn), 4.53 (d, *J* = 11.8 Hz, 1H, CH*H* Bn), 4.37 (q, *J* = 6.8 Hz, 1H, H-7), 4.03 (q, *J* = 6.3 Hz, 1H, H-5), 3.95 (ddd, *J* = 7.5, 5.6, 3.4 Hz, 1H, H-9), 3.86 (ddd, *J* = 11.2, 5.4, 3.4 Hz, 1H, H-2), 2.07 – 2.01 (m, 2H, H-3, H-3), 1.81 (dqd, *J* = 15.2, 7.6, 4.9 Hz, 1H, H-10'), 1.62 – 1.58 (m, 4H, H-10, H-14), 1.50 (d, *J* = 6.9 Hz, 3H, H-8), 1.27 (d, *J* = 6.3 Hz, 3H, H-6), 1.01 (t, *J* = 7.5 Hz, 3H, H-11); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 154.6, 154.1 (O(C=O)O), 137.9 ($C_{q\text{-}arom}$), 128.6, 128.0, 127.6 (CH_{arom}), 93.0 (C-1), 82.0 (C-7), 78.7 (C-12), 77.2 (C-9), 76.1 (C-13), 71.7 (C-2), 71.6 (CH_2 Bn), 65.9 (C-5), 33.5 (C-3), 22.2 (C-10), 15.3 (C-14), 14.9 (C-6), 13.1 (C-8), 10.3 (C-11); HRMS: $[M+Na]^+$ calcd for $C_{23}H_{30}O_9Na$ 473.1788, found 473.1782.



(1*R*,3*S*,4*R*,5*R*,7*S*)-3-((2*S*,3*R*,4*R*)-4-((2-Benzylbenzyl)oxy)-3-*O*-benzyl-2-*O*-2-methylnaphthalene)pentyl)-4,7-di-*O*-benzyl-5-methyl-2,6-dioxabicyclo[2.2.2]octane (26). The title compound was prepared according to general procedure III (16.7 mg, 19 µmol, 85%). Flash column chromatography (90:10 → 80:20; pentane:Et_2O) yielded the title compound as a colorless oil. TLC: R_f 0.3 (pentane:EtOAc, 9:1, v:v); $[\alpha]_D^{20}$ 5.6° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 696, 734, 804, 1027, 1071, 1088, 1260, 1453; ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.87 – 6.95 (m, 31H, CH_{arom}), 4.89 – 4.81 (m, 2H, CH*H* Ph, C*H*H Ph), 4.74 (d, *J* = 2.3 Hz, 1H, H-1), 4.65 (m, 2H, CH*H* Ph, C*H*H Ph), 4.56 (d, *J* = 10.3 Hz, 1H, CH*H* Ph), 4.52 (d, *J* = 11.7 Hz, 1H, H-7), 4.43 (d, *J* = 11.7 Hz, 1H, CH*H* Ph), 4.36 (d, *J* = 11.7 Hz, 1H, C*H*H Ph), 4.30 – 4.20 (m, 5H, H-5, H-9, CH*H* Ph, C*H*H Ph, C*H*H Ph), 3.97 (s, 2H, CH_2Bn), 3.75 – 3.66 (m, 2H, H-2, H-10), 3.42 (dq, *J* = 7.7, 6.0 Hz, 1H, H-11), 2.31 – 2.22 (m, 2H, H-3, H-8), 2.15 (dd, *J* = 14.4, 10.8 Hz, 1H, H-8), 1.98 (ddd, *J* = 13.8, 2.8, 1.5 Hz, 1H, H-3), 1.24 (d, *J* = 6.4 Hz, 3H, H-6), 1.20 (d, *J* = 6.1 Hz, 3H, H-12); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 140.9, 139.3, 139.0, 138.0, 137.9, 136.8, 136.7 ($C_{q\text{-}arom}$), 133.4, 132.9, 130.2, 129.8, 129.1, 128.6, 128.5, 128.4, 128.1, 128.0, 127.8, 127.8, 127.8, 127.5, 126.5, 126.1, 126.1, 125.9, 125.8, 125.7 (CH_{arom}), 90.4 (C-1), 82.4 (C-10), 77.9 (C-9), 75.5 (C-11), 75.1 (C-7), 74.2 (CH_2 Bn), 73.6 (C-5), 72.7 (C-2), 72.3 (CH_2 Bn), 71.7 (C-4), 70.7, 69.3, 64.4, 38.1 (CH_2 Bn), 30.4 (C-8), 28.4 (C-3), 16.9 (C-12), 15.8 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{58}H_{60}O_7Na$ 891.4237, found 891.4240.

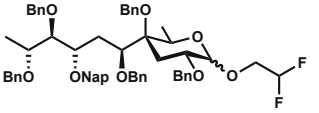


Ethyl 2,4,7,10,11-penta-*O*-benzyl-9-*O*-2-methylnaphthalene-D-caryophylloside (S68). The title compound was prepared according to general procedure III (20.6 mg, 22.5 µmol, *quant.*, α:β; 25:75). Flash column chromatography (95:5 → 90:10; pentane:Et_2O) yielded the title compound as a colorless oil. TLC: R_f 0.8 (pentane:EtOAc, 8:2, v:v); IR (neat, cm^{-1}): 696, 733, 1028, 1051, 1073, 1093, 1453; Data of the major stereoisomer (β-anomer): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.94 – 6.68 (m, 32H, CH_{arom}), 4.89 – 4.40 (m, 11H, CH*H* Ph, CH*H* Ph, CH*H* Ph, CH*H* Ph, C*H*H Ph, C*H*H Ph, CH*H* Ph, C*H*H Ph, CH*H* Ph, C*H*H Ph), 4.30 (d, *J* = 7.7 Hz, 1H, H-1), 4.21 (d, *J* = 11.5 Hz, 1H, C*H*H Ph), 4.05 – 3.94 (m, 2H, H-9, C*H*$_2$CH$_3$), 3.86 – 3.71 (m, 2H, H-5, H-10), 3.66 (ddd, *J* = 11.5, 7.9, 6.3 Hz, 1H, H-2), 3.60 – 3.54 (m, 2H, H-7, C*H*$_2$CH$_3$), 3.47 (dd, *J* = 7.7, 6.1 Hz, 1H, H-11), 2.30 (dd, *J* = 14.6, 5.6 Hz, 1H, H-3), 2.24 (dd, *J* = 14.5, 10.7 Hz, 1H, H-8), 1.96 (dd, *J* = 14.6, 11.7 Hz, 1H, H-3), 1.63 (ddd, *J* = 14.8, 9.8, 1.6 Hz, 1H, H-8), 1.34 – 1.25 (m, 9H, CH$_2$C*H*$_3$, H-6, H-12); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 139.6, 139.0, 138.8, 138.8, 138.4, 136.2, 133.4 ($C_{q\text{-}arom}$), 128.5, 128.5, 128.4, 128.3, 128.3, 128.2, 128.2, 128.2, 128.2, 128.1, 128.1, 128.1, 128.0, 127.8, 127.8, 127.8, 127.7, 127.7, 127.6, 127.6, 127.5, 127.5, 127.3, 127.1, 127.1, 127.0, 126.9, 126.8, 126.6, 126.4, 126.4, 126.3, 126.2, 126.1 (CH_{arom}), 105.5 (C-1), 81.9 (C-10), 80.0 (C-4), 78.4 (C-7), 76.6 (C-9), 75.6 (C-5), 74.8 (C-2), 74.8 (C-11), 74.1, 73.5, 73.1, 70.9, 70.4, 66.7 (CH_2 Bn), 65.1 (*C*H$_2$CH$_3$), 33.2 (C-3), 31.9 (C-8), 16.8 (CH$_2$*C*H$_3$), 15.5 (C-12), 15.2 (C-6); Diagnostic signals of the minor stereoisomer (α-isomer): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.82 (d, *J* = 4.2 Hz, 1H, H-1); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 95.8 (H-1), 80.3 (C-4), 32.4 (C-3), 27.9 (C-8), 16.9 (CH$_2$*C*H$_3$), 15.3 (C-12), 15.2 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{60}H_{66}O_8Na$ 937.4655, found 937.4667.

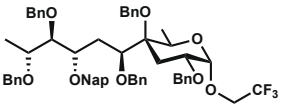


2-Fluoroethyl 2,4,7,10,11-penta-*O*-benzyl-9-*O*-2-methylnaphthalene-D-caryophylloside (S69). The title compound was prepared according to general procedure III (14.6 mg, 15.6 µmol, 70%, α:β; 33:67). Flash column chromatography (90:10 → 80:20; pentane:Et_2O) yielded the title compound as a colorless oil. TLC: R_f 0.6 (pentane:EtOAc, 9:1, v:v); IR (neat, cm^{-1}): 696, 734, 1028, 1071, 1094, 1453; Data of the

major stereoisomer (β-anomer): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.02 – 6.63 (m, 32H, CH_{arom}), 4.90 – 4.40 (m, 13H, CH_2F, CH*H* Ph, CH*H* Ph, CH*H* Ph, CH*H* Ph, CH*H* Ph, CH*H* Ph, C*H*H Ph, C*H*H Ph, C*H*H Ph, C*H*H Ph, C*H*H Ph), 4.35 (d, *J* = 7.7 Hz, 1H, H-1), 4.21 (d, *J* = 11.5 Hz, 1H, C*H*H Ph), 4.08 – 3.96 (m, 3H, H-5, C$H_2$$CH_2F$), 3.88 – 3.71 (m, 4H, H-9, H-10), 3.67 (ddd, *J* = 13.1, 7.6, 5.7 Hz, 1H, H-2), 3.59 (d, *J* = 9.3 Hz, 1H, H-7), 3.51 – 3.44 (m, 1H, H-11), 2.32 (dd, *J* = 14.7, 5.7 Hz, 1H, H-3), 2.27 – 2.20 (m, 1H, H-8), 1.95 (dd, *J* = 14.6, 11.7 Hz, 1H, H-3), 1.63 (dd, *J* = 13.8, 10.2 Hz, 1H, H-8), 1.32 – 1.28 (m, 6H, H-6, H-12); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 139.5, 138.9, 138.7, 138.4, 136.2, 136.1, 133.4, 133.1 ($C_{q\text{-}arom}$), 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 128.2, 128.2, 128.2, 128.1, 128.1, 127.9, 127.8, 127.8, 127.8, 127.7, 127.7, 127.6, 127.6, 127.5, 127.3, 127.1, 127.1, 127.1, 127.0, 126.9, 126.8, 126.7, 126.6, 126.4, 126.4, 126.3, 126.2, 126.1 (CH_{arom}), 105.8 (C-1), 83.0 (d, *J* = 169.4 Hz, CH_2F), 81.9 (C-9/C-10), 79.9 (C-4), 78.4 (C-7), 76.6 (C-5), 75.8 (C-9/C-10), 74.8 (C-2), 74.6, 74.1, 73.2, 70.9, 68.3, 66.7 (CH_2 Bn), 33.1 (C-3), 31.9 (C-8), 16.8 (C-12), 15.2 (C-6); Diagnostic signals of the minor stereoisomer (α-isomer): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.85 (d, *J* = 3.8 Hz, 1H, H-1); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 96.5 (C-1), 82.8 (d, *J* = 169.5 Hz, CH_2F), 80.3 (C-4); HRMS: $[M+Na]^+$ calcd for $C_{60}H_{65}O_8FNa$ 955.4561, found 955.4578.

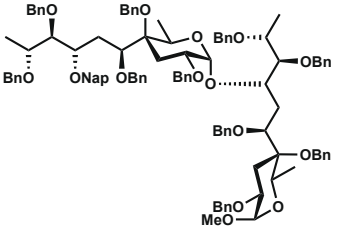


2,2-Difluoroethyl 2,4,7,10,11-penta-*O*-benzyl-9-*O*-2-methylnaphthalene-D-caryophylloside (S70). The title compound was prepared according to general procedure III (18.4 mg, 19.3 µmol, 86%, α:β; 63:37). Flash column chromatography (95:5 → 80:20; pentane:Et_2O) yielded the title compound as a colourless oil. TLC: R_f 0.5 (pentane:EtOAc, 9:1, v:v); IR (neat, cm^{-1}): 696, 732, 1028, 1070, 1453; Data of the major stereoisomer (α-anomer): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.28 – 6.49 (m, 32H, CH_{arom}), 5.86 (tt, *J* = 55.7, 4.4 Hz, 1H, CHF_2), 4.89 – 4.83 (m, 2H, C*H*H Ph, C*H*H Ph), 4.81 (d, *J* = 2.7 Hz, 1H, H-1), 4.71 – 4.41 (m, 8H, C*H*H Ph, C*H*H Ph, C*H*H Ph, C*H*H Ph), 4.24 – 4.16 (m, 2H, CH*H* Ph, CH*H* Ph), 4.08 – 3.93 (m, 4H, H-5, H-9), 3.81 – 3.67 (m, 6H, H-2, H-10, C$H_2$$CHF_2$), 3.54 (d, *J* = 9.3 Hz, 1H, H-7), 3.50 – 3.40 (m, 1H, H-11), 2.24 – 2.16 (m, 3H, H-8, H-3), 2.10 – 2.04 (m, 1H, H-3), 1.36 – 1.25 (m, 6H, H-6, H-12); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 139.3, 138.8, 138.8, 138.5, 138.3, 136.1, 133.4, 133.1 ($C_{q\text{-}arom}$), 128.6, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.1, 128.1, 128.0, 127.8, 127.8, 127.8, 127.8, 127.7, 127.6, 127.6, 127.5, 127.4, 127.2, 127.1, 127.1, 126.9, 126.8, 126.7, 126.6, 126.4, 126.4, 126.3, 126.2, 126.2 (CH_{arom}), 114.5 (t, *J* = 241.2 Hz, CHF_2), 97.0 (C-1), 82.0 (C-10), 80.2 (C-4), 79.0 (C-7), 76.7 (C-5/C-9), 75.0 (C-11), 74.1, 73.9 (CH_2 Bn), 71.9 (C-2), 71.4, 71.0, 70.7 (CH_2 Bn), 68.9 (C-5/C-9), 66.8 (d, *J* = 45.7 Hz, *C*$H_2$$CHF_2$), 65.3 ($CH_2$ Bn), 32.5 (C-8), 27.9 (C-3), 16.9 (C-12), 15.3 (C-6); Diagnostic signals of the minor stereoisomer (β-isomer): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.34 (d, *J* = 7.6 Hz, 1H, H-1), 3.64 (ddd, *J* = 13.3, 7.7, 5.8 Hz, 2H, H-2), 3.59 (d, *J* = 9.1 Hz, 1H, H-7), 2.32 (dd, *J* = 14.6, 5.7 Hz, 1H, H-3), 1.92 (dd, *J* = 14.6, 11.7 Hz, 1H, H-3), 1.65 (dd, *J* = 13.8, 9.7 Hz, 2H, H-8); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 114.6 (t, *J* = 241.2 Hz, CHF_2), 105.9 (C-1), 79.8 (C-4), 66.99 (d, *J* = 57.6 Hz), 33.0 (C-8), 31.9 (C-3), 16.8 (C-12), 15.2 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{60}H_{64}O_8F_2Na$ 973.4467, found 973.4478.

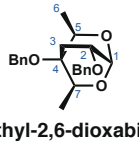


2,2,2-Trifluoroethyl 2,4,7,10,11-penta-*O*-benzyl-9-*O*-2-methylnaphthalene-D-caryophylloside (S71). The title compound was prepared according to general procedure III (14.3 mg, 15.3 µmol, 68%, α:β; >98:2). Flash column chromatography (95:5 → 90:10; pentane:EtOAc) yielded the title compound as a colorless oil. TLC: R_f 0.8 (pentane:EtOAc, 8:2, v:v); $[\alpha]_D^{20}$ 3.2° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 696, 734, 1028, 1071, 1095, 1159, 1278, 1453; ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.89 – 6.74 (m, 32H, CH_{arom}), 4.89 (d, *J* = 3.4 Hz, 1H, H-1), 4.88 – 4.81 (m, 2H, C*H*H Ph, C*H*H Ph), 4.68 – 4.41 (m, 9H, C*H*H Ph, C*H*H Ph, C*H*H Ph, C*H*H Ph, CH*H* Ph, CH*H* Ph, CH*H* Ph, CH*H* Ph, CH*H* Ph), 4.17 (d, *J* = 11.5 Hz, 1H, CH*H* Ph), 4.05– 3.92 (m, 2H, H-5, H-9), 3.88 (dd, *J* = 11.7, 8.8 Hz, 1H, CH_2CF_3), 3.77 (ddd, *J* = 12.2, 4.7, 3.6 Hz, 1H, H-2), 3.74 – 3.71 (m, 1H, H-10), 3.54 (d, *J* = 9.1 Hz, 1H, H-7), 3.43 (dt, *J* = 11.6, 5.8 Hz, 1H, H-11), 2.27 – 2.17 (m, 2H, H-3, H-8), 2.10 (dd, *J* = 13.8, 12.4 Hz, 1H, H-3), 1.65 (dd, *J* = 13.7, 9.6 Hz, 1H, H-8), 1.30 (d,

J = 1.3 Hz, 3H, H-12), 1.29 (d, *J* = 1.9 Hz, 3H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$) δ 139.2, 138.8, 138.7, 138.5, 138.3, 136.0, 133.3, 133.1 ($C_{q\text{-arom}}$), 130.2, 129.8, 129.1, 128.6, 128.6, 128.5, 128.4, 128.4, 128.4, 128.3, 128.2, 128.1, 128.1, 128.0, 128.0, 128.0, 127.9, 127.8, 127.8, 127.7, 127.6, 127.5, 127.4, 127.1, 127.0, 126.8, 126.7, 126.6, 126.4, 126.2, 126.1, 126.1, 125.9, 125.8, 125.7 (CH_{arom}), 96.9 (C-1), 82.0 (C-10), 80.1 (C-4), 78.9 (C-7), 76.7 (C-9), 75.0 (C-11), 74.1, 73.9 (CH_2 Bn), 71.7 (C-2), 71.2, 71.0, 70.7 (CH_2 Bn), 69.2 (C-5), 65.3 (CH_2 Bn), 64.7 (dd, *J* = 69.1, 38.4 Hz, CH_2CF_3), 32.5 (C-8), 27.8 (C-3), 16.9 (C-12), 15.3 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{60}H_{63}O_8F_3Na$ 991.4373, found 991.4390.

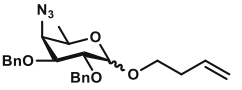


Methyl 2,4,7,10,11-penta-*O*-benzyl-9-*O*-[2,4,7,10,11-penta-*O*-benzyl-9-*O*-2-methylnaphthalene-α-D-caryophyllosyl]-α-D-caryophylloside (S72). The title compound was prepared according to general procedure VI with acceptor **S33** (1.2 eq. acceptor used instead of 2.0 eq.) yielding title compound (7.3 mg, 4.5 µmol, 20%, α:β; >98:2). Flash column chromatography (95:5 → 80:20; pentane:EtOAc) yielded the title compound as a colorless oil. TLC: R_f 0.7 (pentane:EtOAc, 9:1, v:v); $[\alpha]_D^{20}$ 2.1° (c 0.4, $CHCl_3$); IR (neat, cm^{-1}): 696, 734, 1028, 1072, 1096, 1453; ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.84 – 6.74 (m, 57H, CH_{arom}), 5.02 (d, *J* = 3.5 Hz, 1H, H-1'), 4.82 – 4.72 (m, 2H, CH*H* Ph, CH*H* Ph), 4.67 (d, *J* = 3.4 Hz, 1H, H-1), 4.63 – 4.32 (m, 20H, CH*H* Ph, CH*H* Ph, CH*H* Ph, CH*H* Ph, CH*H* Ph, CH*H* Ph, CH*H* Ph, CH*H* Ph, C*H*H Ph, C*H*H Ph, C*H*H Ph, C*H*H Ph, C*H*H Ph, C*H*H Ph, C *H*H Ph, C*H*H Ph, C*H*H Ph, C*H*H Ph, C*H*H Ph, CH*H* Ph), 4.28 – 4.19 (m, 3H, H-5, H-9, H-9'), 4.10 (m, *2*H, H-10, H-10'), 3.99 (m, *2*H, H-5', H-7'), 3.80 (dd, *J* = 9.8, 5.9 Hz, 1H, H-2'), 3.76 – 3.66 (m, 1H, H-2), 3.60 (d, *J* = 9.6 Hz, 1H, H-7), 3.45 (p, *J* = 6.3 Hz, 1H, H-11), 3.35 (td, *J* = 6.7, 6.3, 3.3 Hz, 1H, H-11'), 3.31 (s, 3H, CH_3 OMe), 2.40 – 2.32 (m, 3H, H-3, H-3', H-8'), 2.26 (dd, *J* = 14.6, 11.1 Hz, 1H, H-8), 2.09 – 1.98 (m, 2H, H-3, H-3'), 1.83 (dd, *J* = 14.1, 9.6 Hz, 1H, H-8'), 1.65 (dd, *J* = 14.0, 9.7 Hz, 1H, H-8), 1.30 (d, *J* = 6.5 Hz, 3H, H-6), 1.30 (d, *J* = 6.4 Hz, 3H, H-6'), 1.21 (d, *J* = 6.1 Hz, 3H, H-12'), 1.15 (d, *J* = 6.2 Hz, 3H, H-12); ^{13}C NMR (126 MHz, $CDCl_3$) δ 139.4, 139.3, 139.1, 139.0, 138.9, 138.9, 138.6, 138.5, 138.4, 136.0, 135.3, 133.0 ($C_{q\text{-arom}}$), 128.7, 128.5, 128.4, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.2, 128.2, 128.2, 128.1, 128.1, 128.0, 128.0, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 127.6, 127.5, 127.4, 127.3, 127.3, 127.2, 127.2, 127.1, 127.1, 127.0, 127.0, 127.0, 126.9, 126.9, 126.8, 126.5, 126.4, 126.3, 126.3, 126.3, 126.2, 126.1, 125.4 (CH_{arom}), 98.3 (C-1), 97.5 (C-1'), 85.3 (C-2'), 81.7 (C-2), 80.6, 80.4 (C-4, C-4'), 80.2 (C-5'), 79.7 (C-5), 79.4 (C-7), 76.7 (C-7'), 75.2, 74.9 (C-11, C-11'), 74.9, 74.2, 74.0, 73.8, 72.6 (CH_2 Bn), 72.5, 72.0 (C-10, C-10'), 71.2, 70.9, 70.8, 70.7, 70.6 (CH_2 Bn), 69.8, 68.8 (C-9, C-9'), 65.7, 65.2 (CH_2 Bn), 55.0 (CH_3 OMe), 33.4 (C-8'), 32.7 (C-8), 27.6, 22.5 (C-3, C-3'), 16.8 (C-12'), 16.7 (C-12), 15.5, 15.3 (C-6, C-6'); HRMS: $[M+Na]^+$ calcd for $C_{106}H_{116}O_{15}Na$ 1651.8212, found 1651.8168.

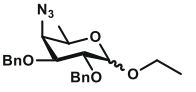


(1*R*,3*R*,4*R*,5*S*,7*S*)-4,7-Di-*O*-benzyl-3,5-dimethyl-2,6-dioxabicyclo[2.2.2]octane (S73). The title compound was prepared according to general procedure III (on a 30 µmol scale) yielding title compound (8.8 mg, 25 µmol, 83%). Flash column chromatography (95:5 → 80:20; pentane:Et_2O) yielded the title compound as a colorless oil. TLC: R_f 0.2 (pentane:Et_2O, 8:2, v:v); $[\alpha]_D^{20}$ –2.4° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 696, 1027, 1066, 1091, 1127; ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.40 – 7.19 (m, 10H, CH_{arom}), 4.86 (d, *J* = 2.1 Hz, 1H, H-1), 4.58 (s, 2H, CH_2Bn), 4.44 (d, *J* = 10.6 Hz, 1H, C*H*H Ph), 4.41 (d, *J* = 10.6 Hz, 1H, CH*H* Ph), 4.32 (qd, *J* = 6.4, 2.0 Hz, 1H, H-7), 4.25 (qd, *J* = 6.4, 1.6 Hz, 1H, H-5), 3.74 (ddd, *J* = 10.0, 3.3, 2.1 Hz, 1H, H-2), 2.29 (ddd, *J* = 13.7, 10.0, 2.1 Hz, 1H, H-3), 2.02 (ddd, *J* = 13.7, 3.3, 1.7 Hz, 1H, H-3), 1.46 (d, *J* = 6.4 Hz, 3H, H-8), 1.26 (d, *J* = 6.4 Hz, 3H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 138.1, 137.8 ($C_{q\text{-arom}}$), 128.7, 128.6, 128.0, 127.9, 127.8, 127.5 (CH_{arom}), 90.7 (C-1), 75.1 (C-7), 74.3 (C-

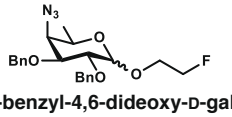
5), 72.6 (C-2), 72.3 (C-4), 70.7 (4-OCH_2Bn), 64.9 (2-OCH_2Bn), 27.2 (C-3), 16.1 (C-6), 15.4 (C-8); HRMS: $[M+Na]^+$ calcd for $C_{22}H_{26}O_4Na$ 377.1729, found 377.1729.



3-Butene 4-azido-2,3-di-*O*-benzyl-4,6-dideoxy-D-galactopyranoside (S74). The title compound was prepared according to general procedure III (18 mg, 42 µmol, 85%, α:β; 39:61) as a colorless oil. The title compound was also prepared according to general procedure IV (13 mg, 61 µmol, 61%, α:β; 62:38). The title compound was also prepared according to general procedure V (19 mg, 45 µmol, 95%, α:β; >98:2). TLC: R_f 0.6 (pentane:Et_2O, 9:1, v:v); $[\alpha]_D^{20}$ 24.3° (c 1.0, $CHCl_3$, α-anomer); IR (neat, cm^{-1}): 697, 1045, 1105, 1709, 2109, 2916; Data of the α-anomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 – 7.27 (m, 10H, CH_{arom}), 5.81 (ddt, *J* = 17.0, 10.2, 6.7 Hz, 1H, H-9), 5.10 (dq, *J* = 17.2, 1.6 Hz, 1H, H-10), 5.08 – 5.00 (m, 1H, H-10), 4.85 (d, *J* = 11.7 Hz, 1H, C*H*H Bn), 4.81 (d, *J* = 12.0 Hz, 1H, C*H*H Bn), 4.74 (d, *J* = 11.7 Hz, 1H, CH*H* Bn), 4.70 (d, *J* = 3.8 Hz, 1H, H-1), 4.64 (d, *J* = 12.0 Hz, 1H, CH*H* Bn), 4.03 (dd, *J* = 9.9, 3.7 Hz, 1H, H-3), 3.96 (qd, *J* = 6.5, 1.6 Hz, 1H, H-5), 3.83 (dd, *J* = 9.9, 3.8 Hz, 1H, H-2), 3.72 (dd, *J* = 3.8, 1.5 Hz, 1H, H-4), 3.56 (ddt, *J* = 44.4, 9.9, 7.0 Hz, 2H, H-7), 2.37 (qt, *J* = 7.0, 1.4 Hz, 2H, H-8, H-8), 1.21 (d, *J* = 6.5 Hz, 3H, H-6); ^{13}C NMR (101 MHz, $CDCl_3$): δ 138.6, 138.4 ($C_{q\text{-}arom}$), 135.1 (C-9), 128.6, 128.5, 128.1, 127.9, 127.9, 127.8 (CH_{arom}), 116.8 (C-10), 97.5 (C-1), 78.2 (C-3), 76.2 (C-2), 73.6, 73.3 (CH_2 Bn), 67.7 (C-7), 65.2 (C-4), 64.5 (C-5), 34.0 (C-8), 17.4 (C-6); Diagnostic signals of the β-anomer: ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.30 (d, *J* = 7.6 Hz, 1H, H-1); ^{13}C NMR (101 MHz, $CDCl_3$): δ 103.7 (C-1), 73.6, 73.3 (CH_2 Bn), 67.7 (C-7); HRMS: $[M+Na]^+$ calcd for $C_{24}H_{29}O_4N_3Na$ 446.2056, found 446.2050.

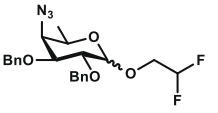


Ethyl 4-azido-2,3-di-*O*-benzyl-4,6-dideoxy-D-galactopyranoside (S75). The title compound was prepared according to general procedure III (18 mg, 44 µmol, 87%, α:β; 36:64) as a colorless oil. The title compound was also prepared according to general procedure IV (19 mg, 47 µmol, 93%, α:β; 62:38). The title compound was also prepared according to general procedure V (15 mg, 38 µmol, 75%, α:β; >98:2). TLC: R_f 0.7 (pentane:EtOAc, 9:1, v:v); IR (neat, cm^{-1}): 696, 1028, 1045, 1061, 2102; Data of the β-anomer: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.48 – 7.23 (m, 10H, CH_{arom}), 4.91 (d, *J* = 10.8 Hz, 1H, C*H*H Ph), 4.76 (d, *J* = 10.2 Hz, 1H, C*H*H Ph), 4.74 (d, *J* = 10.9 Hz, 1H, CH*H* Ph), 4.64 (d, *J* = 12.1 Hz, 1H, CH*H* Ph), 4.29 (d, *J* = 7.3 Hz, 1H, H-1), 3.96 (dq, *J* = 9.4, 7.1 Hz, 1H, C*H*$_2$$CH_3$), 3.66 – 3.62 (m, 3H, H-2, H-3, H-4), 3.56 (dd, *J* = 9.5, 7.1 Hz, 1H, C*H*$_2$$CH_3$), 3.53 – 3.49 (m, 1H, H-5), 1.30 (d, *J* = 6.3 Hz, 3H, H-6), 1.26 (t, *J* = 7.1 Hz, 3H, CH_2C*H*$_3$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 138.7, 138.1 ($C_{q\text{-}arom}$), 128.6, 128.5, 128.4, 128.2, 128.1, 127.9, 127.9, 127.7 (CH_{arom}), 103.5 (C-1), 81.1 (C-2/C-3), 79.3 (C-2/C-3), 75.4, 73.1 (CH_2 Bn), 68.9 (C-5), 65.5 (*C*$H_2$$CH_3$), 64.0 (C-4), 17.7 (C-6), 15.4 (CH_2*C*H_3); Diagnostic signals of the α-anomer: ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.85 (d, *J* = 11.7 Hz, 1H, C*H*H Ph), 4.82 (d, *J* = 12.1 Hz, 1H, C*H*H Ph), 4.74 (d, *J* = 10.9 Hz, 1H, CH*H* Ph), 4.69 (d, *J* = 3.8 Hz, 1H, H-1), 4.04 (dd, *J* = 9.9, 3.7 Hz, 1H, H-3), 3.82 (dd, *J* = 9.9, 3.8 Hz, 1H, H-2), 3.72 (dd, *J* = 3.8, 1.5 Hz, 1H, H-4), 1.22 (t, *J* = 7.1 Hz, 3H, CH_2C*H*$_3$), 1.21 (d, *J* = 6.5 Hz, 2H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 138.5, 138.4 ($C_{q\text{-}arom}$), 97.1 (C-1), 78.3 (C-3), 76.2 (C-2), 73.6, 73.3 (CH_2 Bn), 65.2 (C-4), 64.3 (C-5), 63.6 (*C*$H_2$$CH_3$), 17.4 (C-6), 15.1 ($CH_2$*C*$H_3$); HRMS: $[M+Na]^+$ calcd for $C_{22}H_{27}O_4N_3Na$ 420.1899, found 420.1892.

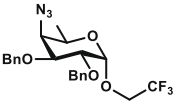


2-Mono-fluoroethyl 4-azido-2,3-di-*O*-benzyl-4,6-dideoxy-D-galactopyranoside (S76). The title compound was prepared according to general procedure III (21 mg, 50 µmol, *quant.*, α:β; 48:52) as a colorless oil. The title compound was also prepared according to general procedure IV (21 mg, 50 µmol, *quant.*, α:β; 81:19). The title compound was also prepared according to general procedure V (17 mg, 38 µmol, 79%, α:β; >98:2). TLC: R_f 0.3 (pentane:EtOAc, 9:1, v:v); IR (neat, cm^{-1}): 1041, 1089, 2102; Data of the β-anomer: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75 – 7.12 (m, 10H, CH_{arom}), 4.93 (d, *J* = 10.6 Hz, 1H, C*H*H Ph), 4.85 (d, *J* = 11.7 Hz, 1H, C*H*H Ph), 4.77 (m, 1H, CH*H* Ph), 4.72 (d, *J* = 10.8 Hz, 1H, CH*H* Ph), 4.70 –

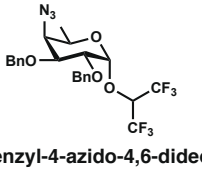
4.48 (m, 2H, CH_2F), 4.36 (d, J = 7.0 Hz, 1H, H-1), 4.13 – 3.98 (m, 1H, C$H_2$$CH_2F$), 3.88 – 3.62 (m, 4H, H-2, H-3, H-4, C$H_2$$CH_2F$), 3.53 (qd, J = 6.3, 1.1 Hz, 1H, H-5), 1.31 (d, J = 6.3 Hz, 3H, H-6); ^{13}C NMR (126 MHz) δ 138.5, 138.0 ($C_{q\text{-arom}}$), 131.2, 129.4, 128.6, 128.5, 128.4, 128.1, 127.8, 127.7 (CH_{arom}), 103.8 (C-1), 83.38 (d, J = 5.1 Hz, CH_2F), 81.0 (C-2/C-3), 79.0 (C-2/C-3), 73.3, 73.2 (CH_2 Bn), 69.0 (C-5), 67.21 (d, J = 20.0 Hz, $C$$H_2$$CHF_2$), 63.8 (C-4), 17.6 (C-6); Diagnostic signals of the α-anomer: ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.72 (d, J = 5.8 Hz, 1H, H-1), 1.21 (d, J = 6.5 Hz, 3H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.4, 138.3 ($C_{q\text{-arom}}$), 97.8 (C-1), 82.0 (d, J = 5.2 Hz, CH_2F), 78.1 (C-3), 76.1 (C-2), 75.4, 73.7 (CH_2 Bn), 68.7 (d, J = 20.2 Hz, $C$$H_2$$CHF_2$), 65.0 (C-4), 64.6 (C-5), 17.4 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{22}H_{26}O_4N_3FNa$ 438.1805, found 438.1800.



2,2-Di-fluoroethyl 4-azido-2,3-di-*O*-benzyl-4,6-dideoxy-D-galactopyranoside (S77). The title compound was prepared according to general procedure III (20 mg, 46 µmol, 91%, α:β; 77:23) as a colorless oil. The title compound was also prepared according to general procedure IV (19 mg, 43 µmol, 85%, α:β; >98:2). The title compound was also prepared according to general procedure V (17 mg, 41 µmol, 81%, α:β; >98:2). TLC: R_f 0.7 (pentane:EtOAc, 9:1, v:v); IR (neat, cm^{-1}): 696, 1046, 1067, 1091, 2104; Data of the α-anomer: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.80 – 7.22 (m, 10H, CH_{arom}), 5.92 (tt, J = 55.6, 4.4 Hz, 1H, CHF_2), 4.85 (m, 1H, CHH Bn), 4.82 (m, 1H, CHH Bn), 4.74 (d, J = 11.7 Hz, 1H, CHH Bn), 4.69 (d, J = 3.8 Hz, 1H, H-1), 4.62 (d, J = 11.9 Hz, 1H, CHH Bn), 4.02 (dd, J = 9.9, 3.6 Hz, 1H, H-3), 3.95 (qd, J = 6.6, 1.5 Hz, 1H, H-5), 3.86 (dd, J = 9.9, 3.8 Hz, 1H, H-2), 3.74 – 3.64 (m, 3H, C$H_2$$CHF_2$, H-4), 1.22 (d, J = 6.5 Hz, 3H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$): δ 138.3, 138.2 ($C_{q\text{-arom}}$), 128.6, 128.5, 128.4, 128.1, 128.0, 127.9, 127.9, 127.7 (CH_{arom}), 114.1 (t, J = 241.3 Hz, CHF_2), 98.5 (C-1), 77.9 (C-3), 75.9 (C-2), 73.9, 73.3 (CH_2 Bn), 67.4 (t, J = 28.7 Hz, $C$$H_2$$CHF_2$), 65.0 (C-5), 64.8 (C-4), 17.3 (C-6); Diagnostic signals of the β-anomer: ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.85 (tt, J = 55.1, 4.1 Hz, 1H, CHF_2), 4.34 (d, J = 7.2 Hz, 1H, H-1), 4.14 (tdd, J = 13.7, 11.9, 3.9 Hz, 1H, C$H_2$$CHF_2$), 3.53 (qd, J = 6.3, 1.1 Hz, 1H, H-5), 1.31 (d, J = 6.3 Hz, 3H, H-6); ^{13}C NMR (126 MHz) δ 138.3, 137.8 ($C_{q\text{-arom}}$), 114.3 (dd, J = 242.3, 239.7 Hz, CHF_2), 103.9 (C-1), 80.9 (C-3), 78.8 (C-2), 75.5, 73.2 (CH_2 Bn), 68.5 (dd, J = 30.8, 26.4 Hz, $C$$H_2$$CHF_2$), 68.3 (C-5), 63.7 (C-4), 17.5 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{22}H_{25}O_4N_3F_2Na$ 456.1711, found 456.1704.

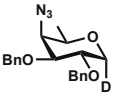


2,2,2-Tri-fluoroethyl 4-azido-2,3-di-*O*-benzyl-4,6-dideoxy-α-D-galactopyranoside (S78). The title compound was prepared according to general procedure III (16 mg, 35 µmol, 70%, α:β; >98:2) as a colorless oil. The title compound was also prepared according to general procedure IV (17 mg, 37 µmol, 73%, α:β; >98:2). TLC: R_f 0.8 (pentane:EtOAc, 9:1, v:v); IR (neat, cm^{-1}): 1103, 1156, 1277, 2109; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 – 7.28 (m, 10H, CH_{arom}), 4.84 (m, 2H, CHH Bn, CHH Bn), 4.76 (d, J = 5.5 Hz, 1H, H-1), 4.74 (m, 1H, CHH Bn), 4.63 (d, J = 11.9 Hz, 1H, CHH Bn), 4.04 (dd, J = 9.9, 3.6 Hz, 1H, H-3), 3.95 (qd, J = 6.5, 1.3 Hz, 1H, H-5), 3.92 – 3.82 (m, 3H, H-2, CH_2CF_3), 3.75 (dd, J = 3.6, 1.4 Hz, 1H, H-4), 1.23 (d, J = 6.5 Hz, 3H, H-6); ^{13}C NMR (101 MHz): δ 138.3, 138.2 ($C_{q\text{-arom}}$), 129.6, 129.4, 129.1, 128.9, 128.7, 128.6, 128.6, 128.1, 128.0, 127.9 (CH_{arom}), 122.5 (CF_3), 98.5 (C-1), 77.8 (C-3), 75.8 (C-2), 73.8, 73.4 (CH_2 Bn), 65.3 (C-5), 65.2 (q, J = 34.9 Hz, $C$$H_2$$CF_3$), 64.8 (C-4), 17.3 (C-6); ^{19}F NMR (471 MHz, $CDCl_3$): δ –73.7 (t, J = 8.3 Hz); HRMS: $[M+Na]^+$ calcd for $C_{22}H_{24}O_4N_3F_3Na$ 474.1617, found 474.1614.

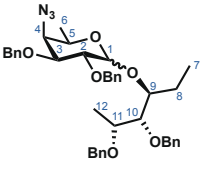


1,1,1,3,3,3-Hexafluoropropyl 2,3-di-*O*-benzyl-4-azido-4,6-dideoxy-α-D-galactopyranoside (S79). The title compound was prepared according to general procedure III (18 mg, 35 µmol, 69%, α:β; >98:2) as a

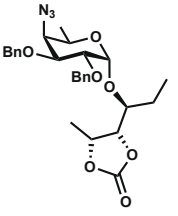
colorless oil. Flash column chromatography (95:5 → 80:20; pentane:Et_2O) yielded the title compound. TLC: R_f 0.8 (pentane:EtOAc, 9:1, v:v); $[\alpha]_D^{20}$ 47.0° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 1105, 1196, 1287, 2110; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.90 – 7.28 (m, 10H), 5.06 (d, *J* = 3.9 Hz, 1H, H-1), 4.84 (d, *J* = 11.5 Hz, 1H, CH*H* Bn), 4.76 (m, 1H, C*H*H Bn), 4.74 (m, 1H, CH*H* Bn), 4.69 (d, *J* = 11.5 Hz, 1H, C*H*H Bn), 4.41 (hept, *J* = 5.9 Hz, 1H, $CH(CF_3)_2$), 4.10 – 4.00 (m, 2H, H-3, H-4), 3.94 (dd, *J* = 10.0, 3.9 Hz, 1H, H-2), 3.79 (dd, *J* = 3.4, 1.3 Hz, 1H, H-5), 1.24 (d, *J* = 6.4 Hz, 3H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 138.0, 137.9 ($C_{q\text{-arom}}$), 136.7, 135.5, 133.7, 131.7, 130.4, 129.6, 129.1, 128.9, 128.6, 127.7 (CH_{arom}), 100.1 (C-1), 77.6 (C-3/C-4), 75.1 (C-2), 73.8, 73.4 (CH_2 Bn), 73.1 (p, *J* = 33.0 Hz, *C*H(CF_3)), 66.4 (C-3/C-4), 64.5 (C-5), 17.2 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{23}H_{23}O_4N_3F_6Na$ 542.1490, found 542.1489.



2,3-Di-*O*-benzyl-4-azido-1,4,6-trideoxy-1-α-deuterio-D-galactopyranoside (S80). The title compound was prepared according to general procedure III (15 mg, 41 µmol, 82%, α:β; >98:2) as a colorless oil. Flash column chromatography (90:10 → 80:20; pentane:EtOAc) yielded the title compound. TLC: R_f 0.5 (pentane:EtOAc, 9:1, v:v); $[\alpha]_D^{20}$ 11.4° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 1093, 1124, 2108; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.44 – 7.26 (m, 10H, CH_{arom}), 4.87 – 4.76 (m, 3H, CH_2 Bn), 4.64 (d, *J* = 11.5 Hz, 1H, CH_2 Bn), 3.97 (d, *J* = 5.6 Hz, 1H, H-1), 3.89 (dd, *J* = 9.0, 5.6 Hz, 1H, H-2), 3.72 (dd, *J* = 3.7, 1.3 Hz, 1H, H-4), 3.67 (dd, *J* = 9.1, 3.7 Hz, 1H, H-3), 3.47 (qd, *J* = 6.3, 1.3 Hz, 1H, H-5), 1.27 (d, *J* = 6.3 Hz, 3H, H-6); ^2H NMR (77 MHz, $CDCl_3$) δ 3.12 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 138.4, 138.1 ($C_{q\text{-arom}}$), 129.5, 128.6, 128.6, 128.0, 127.9, 127.9, 127.9, 124.9 (CH_{arom}), 82.8 (C-3), 74.6 (C-2), 73.9 (CH_2 Bn), 73.8 (C-5), 72.7 (CH_2 Bn), 68.34 (t, *J* = 21.5 Hz, C-1), 64.3 (C-4), 18.0 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{19}H_{20}O_3N_3DNa$ 377.1700, found 377.1697.



1,2,6-Trideoxy-4,5-di-*O*-benzyl-D-altritol-2,3-di-*O*-benzyl-4-azido-4,6-dideoxy-D-galactopyranoside (S81). The title compound was prepared according to the general procedure III giving title glycoside as a white solid (25.2 mg, 76%, α:β; 58:42). TLC: R_f 0.5 (pentane:Et_2O, 4:1, v:v) for α-isomer; TLC: R_f 0.2 (pentane:Et_2O, 4:1, v:v); NMR data reported as a mixture of α- and β-anomers; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.39 – 7.20 (m, 40H, CH_{arom}), 4.87 (d, *J* = 4.0 Hz, 1H, H-1α), 4.83 – 4.65 (m, 2H, CH_2 Bn), 4.59 (d, *J* = 11.6 Hz, 1H, CH*H* Bn), 4.51 – 4.47 (m, 2H, CH_2 Bn), 4.37 (d, *J* = 7.1 Hz, H-1β), 4.32 (d, *J* = 11.6 Hz, 1H, CH*H* Bn), 3.94 (m, 1H, H-9β), 3.91 (dd, *J* = 3.6, 9.9 Hz, 1H, H-3α), 3.85 – 3.81 (m, 2H, H-9α, H-2α), 3.77 (m, 1H, H-5β), 3.72 (m, 1H, H-9), 3.70 – 3.65 (m, 2H, H-11, H-5β), 3.65 – 3.59 (m, 2H, H-2β, H-4β), 3.58 (dd, *J* = 3.4, 1.5 Hz, 1H, H-4α), 3.46 (m, 1H, H-5α), 1.74 – 1.56 (m, 4H, H-8β, H-8β, H-8α, H-8α),1.29 – 1.65 (m, 6H, H-6α, H-12), 1.04 (d, *J* = 6.4 Hz, 3H, H-6β), 0.98 (t, *J* = 7.4 Hz, 3H, H-7), 0.91 (t, *J* = 7.6 Hz, 3H, H-7); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 139.0, 138.9, 138.8, 138.8, 138.7, 138.5, 138.3, 137.8 ($C_{q\text{-arom}}$), 128.6, 128.5, 128.4, 128.4, 128.4, 128.3, 128.0, 128.0, 127.9, 127.9, 127.8, 127.7, 127.7, 127.6, 127.6, 127.6, 127.5, 127.4 (CH_{arom}), 102.0 (C-1β), 96.1 (C-1α), 83.0, 81.9, 81.6, 80.7, 79.1, 78.5 (C-9), 77.8 (C-3α), 76.2 (C-2α), 75.4, 75.2, 75.1, 74.0, 73.7, 73.4, 72.9, 70.7, 70.6, 68.9, 65.1 (C-4α), 64.9 (C-5β), 63.7, 29.8, 23.5, 22.3 (C-8), 17.6 (C-6β), 17.3, 15.8, 15.5, 10.3 (C-7), 9.6 (C-7); HRMS: $[M+Na]^+$ calcd for $C_{40}H_{47}N_3O_6Na$ 688.3363, found 688.3357.



1,2,6-Trideoxy-4,5-*O*-carbonate-D-altritol-4-azido-2,3-di-*O*-benzyl-4,6-dideoxy-α-D-galactopyranoside (S82). The title compound was prepared according to general procedure III (17 mg, 33 µmol, 66%, α:β; >98:2). Flash column chromatography (90:10 → 70:30; pentane:EtOAc) yielded the title compound as a colorless oil. TLC: R_f 0.6 (pentane:EtOAc, 7:3, v:v); $[\alpha]_D^{20}$ 45.2° (c 1.0, $CHCl_3$); IR (neat, cm^{-1}): 698, 737, 1012, 1053, 1093, 1800, 2106, 2928; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC): δ 7.43 – 7.30 (m, 10H, CH_{arom}), 4.89 (d, *J* = 3.9 Hz, 1H, H-1), 4.88 – 4.82 (m, 2H, C*H*H Ph, H-9), 4.81 – 4.74 (m, 2H, CH_2 Bn), 4.67 – 4.61 (m, 2H, CH*H* Bn, H-8), 4.05 – 3.95 (m, 2H, H-3, H-5), 3.87 (dd, *J* = 10.0, 3.8 Hz, 1H, H-2), 3.83 (q, *J* = 5.6 Hz, 1H, H-7), 3.78 (dd, *J* = 3.6, 1.6 Hz, 1H, H-4), 1.75 (dqd, *J* = 14.9, 7.5, 5.8 Hz, 1H, H-11), 1.65 (dqd, *J* = 14.8, 7.4, 5.9 Hz, 1H, H-11'), 1.50 (d, *J* = 6.7 Hz, 3H, H-10), 1.24 (d, *J* = 6.5 Hz, 3H, H-6), 1.00 (t, *J* = 7.5 Hz, 3H, H-12); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 154.5 (O(C=O)O), 138.4, 138.0 ($C_{q\text{-}arom}$), 131.2, 129.5, 128.7, 128.6, 128.5, 128.0, 127.9, 127.9, 124.9 (CH_{arom}), 96.3 (C-1), 78.8 (C-8), 78.0 (C-3), 77.2 (C-7), 76.1 (C-9), 75.8 (C-2), 74.1, 73.0 (CH_2 Bn), 65.5 (C-5), 64.7 (C-4), 22.7 (C-11), 17.5 (C-6), 15.1 (C-10), 9.6 (C-12); HRMS: $[M+Na]^+$ calcd for $C_{27}H_{33}O_7Na$ 534.2216, found 534.2211.

Structural proofs

Compound 21

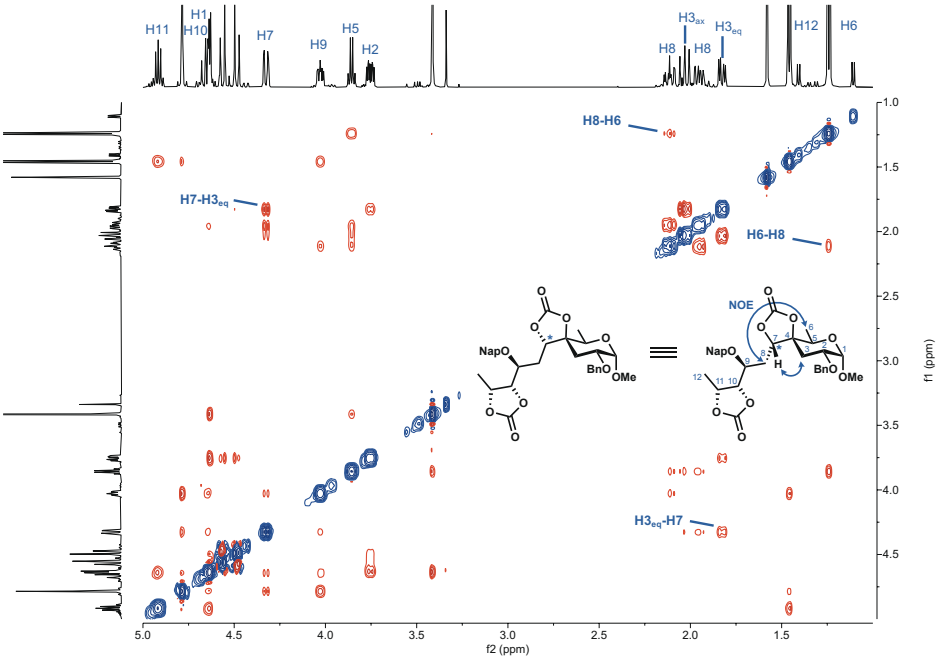


Figure S11. NOESY spectrum of compound **21**. The key NOE interactions for **21** can be found between $H3_{eq}$-H7 and H6-H8.

Compound S29 and S30

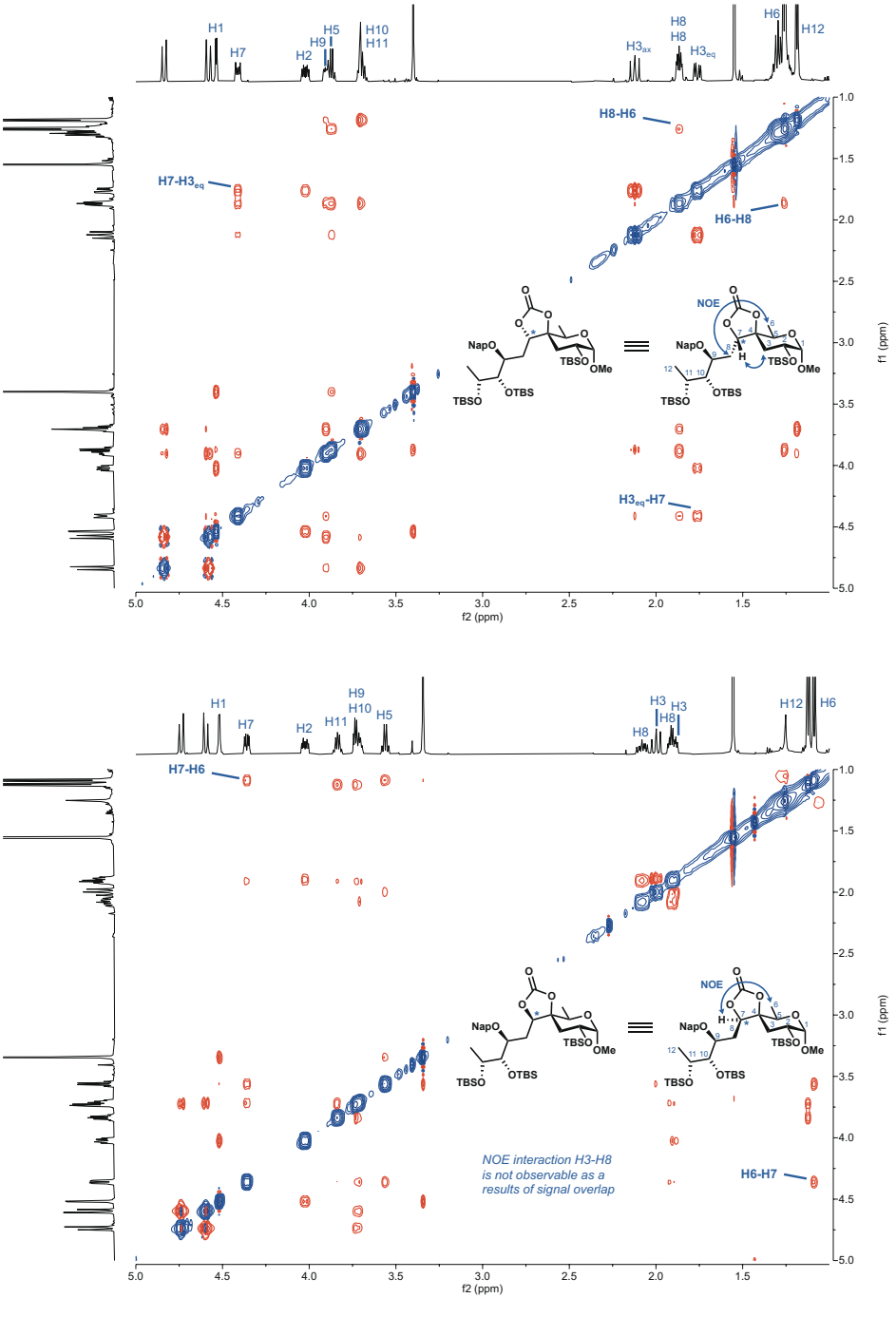
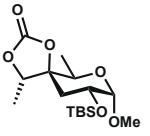


Figure S12. NOESY spectra of compound **S29** and **S30**. (A) The key NOE interactions for **S29** can be found between $H3_{eq}$-H7 and H6-H8. (B) The key NOE interaction for **S30** can be found between H6-H7.

Compound S22

^{1}H NMR H-H coupling constants



H-1: d, J = 3.4 Hz (eq^{H-1}-ax^{H-2})
H-2: ddd, J = 3.5 Hz (ax^{H-2}-eq^{H-1}), 5.0 Hz (ax^{H-2}-eq^{H-3}), 11.6 Hz (ax^{H-2}-ax^{H-3})
H-3$_{ax}$: dd, J = 11.6 Hz (ax^{H-3}-ax^{H-2}), 13.5 Hz (ax^{H-3}-eq^{H-3})
H-3$_{eq}$: dd, J = 4.9 Hz (eq^{H-3}-ax^{H-2}), 13.5 Hz (eq^{H-3}-ax^{H-3})
H-5: q, J = 6.4 Hz (ax^{H-5}-H-6)

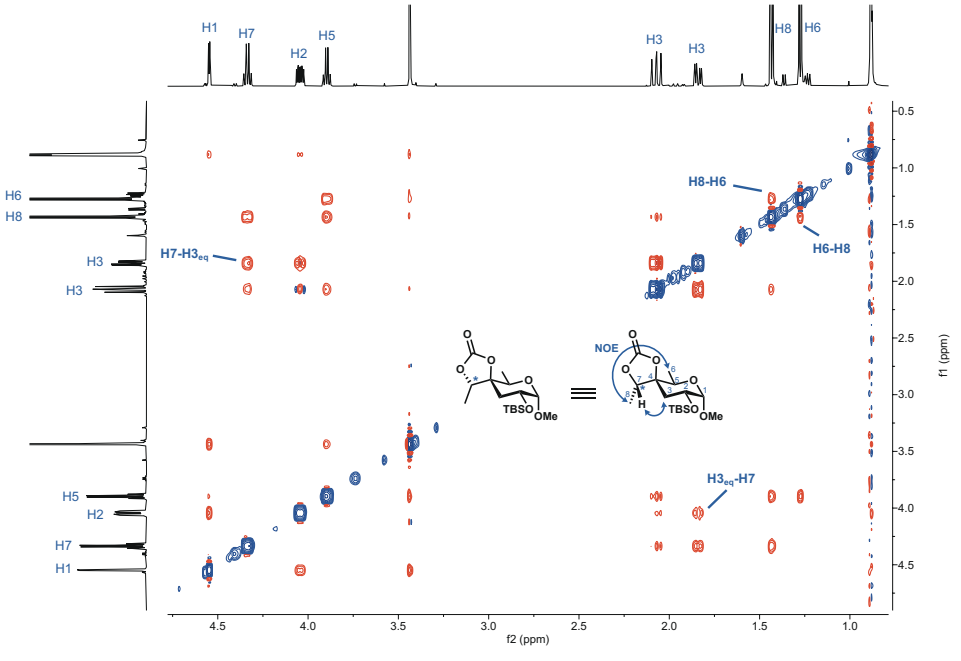
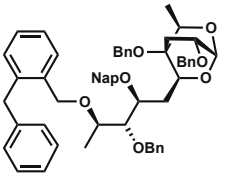


Figure S13. NOESY spectra of compound **S22**. The key NOE interactions for **S22** can be found between $H3_{eq}$-H7 and H6-H8.

Compound 24

^{1}H NMR H-H coupling constants



H-1: d, *J* = 2.3 Hz (eq$^{H\text{-}1}$-ax$^{H\text{-}2}$)
H-2: overlaps with H-10
H-3$_{ax}$: overlaps with H-8
H-3$_{eq}$: dd, *J* = 2.8 Hz (eq$^{H\text{-}3}$-ax$^{H\text{-}2}$), 13.8 Hz (eq$^{H\text{-}3}$-ax$^{H\text{-}3}$)
H-5: overlaps with H-9

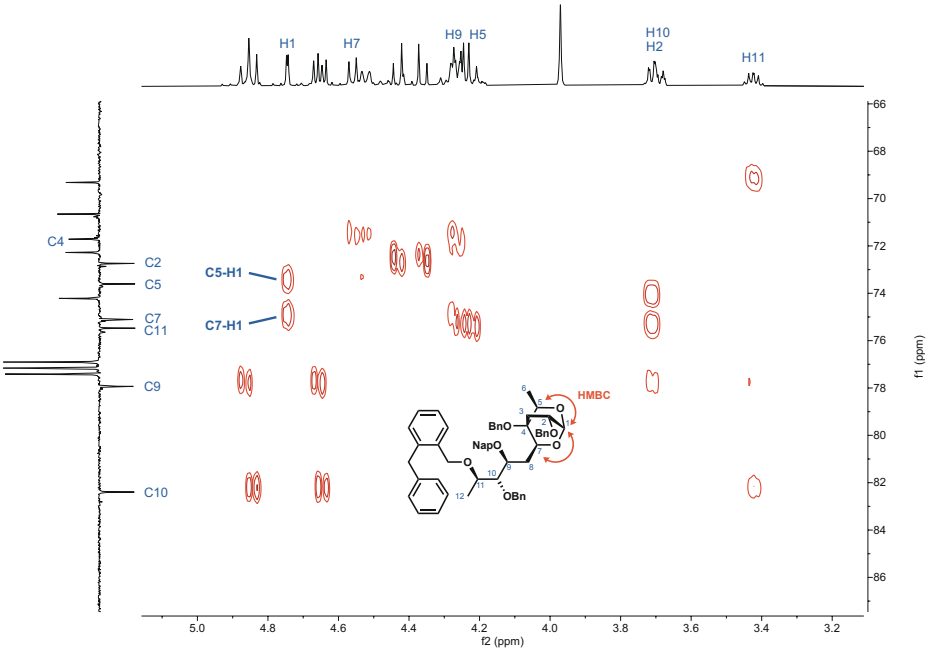


Figure S14. HMBC spectrum of compound **24**. The key long-range heteronuclear correlation for **24** can be found between C5-H1 and C7-H1.

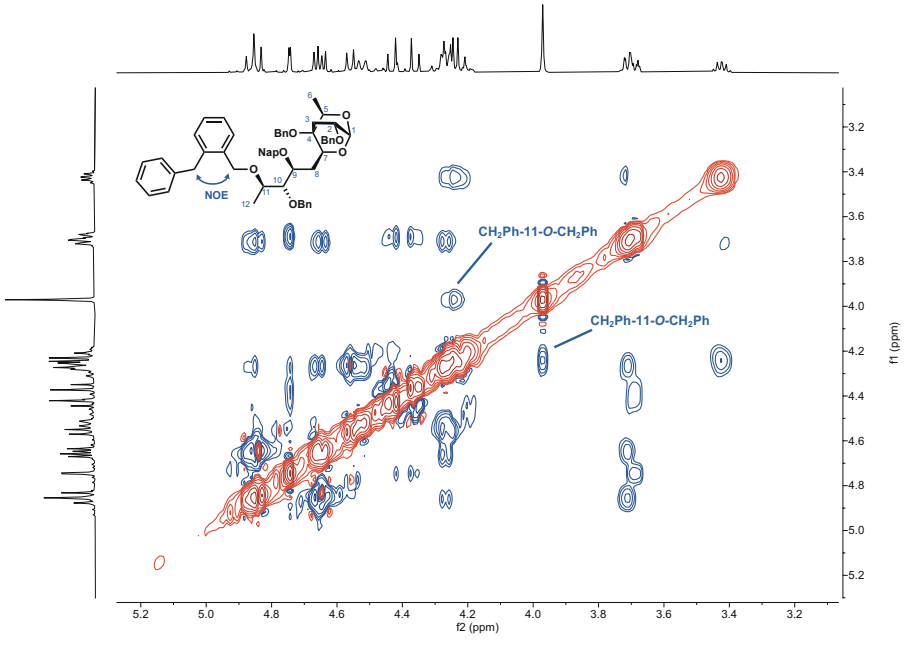


Figure S15. NOESY spectra of compound **24**. The key NOE interactions for **24** can be found between CH_2Bn and 11-*O*-CH_2Bn.

References

(1) Tytgat, H. L. P.; Lebeer, S. The Sweet Tooth of Bacteria: Common Themes in Bacterial Glycoconjugates. *Microbiol. Mol. Biol. Rev.* **2014**, *78* (3), 372–417.

(2) Herget, S.; Toukach, P. V.; Ranzinger, R.; Hull, W. E.; Knirel, Y. A.; von der Lieth, C.-W. Statistical Analysis of the Bacterial Carbohydrate Structure Data Base (BCSDB): Characteristics and Diversity of Bacterial Carbohydrates in Comparison with Mammalian Glycans. *BMC Struc. Biol.* **2008**, *8* (1), 35.

(3) Elshahawi, S. I.; Shaaban, K. A.; Kharel, M. K.; Thorson, J. S. A Comprehensive Review of Glycosylated Bacterial Natural Products. *Chem. Soc. Rev.* **2015**, *44* (21), 7591–7697.

(4) Thibodeaux, C. J.; Melançon, C. E.; Liu, H. Natural-Product Sugar Biosynthesis and Enzymatic Glycodiversification. *Angew. Chem. Int. Ed.* **2008**, *47* (51), 9814–9859.

(5) Thibodeaux, C. J.; Melançon, C. E.; Liu, H. Unusual Sugar Biosynthesis and Natural Product Glycodiversification. *Nature* **2007**, *446* (7139), 1008–1016.

(6) Werz, D. B.; Ranzinger, R.; Herget, S.; Adibekian, A.; von der Lieth, C.-W.; Seeberger, P. H. Exploring the Structural Diversity of Mammalian Carbohydrates ("Glycospace") by Statistical Databank Analysis. *ACS Chem. Biol.* **2007**, *2* (10), 685–691.

(7) Zeng, J.; Sun, G.; Yao, W.; Zhu, Y.; Wang, R.; Cai, L.; Liu, K.; Zhang, Q.; Liu, X.-W.; Wan, Q. 3-Aminodeoxypyranoses in Glycosylation: Diversity-Oriented Synthesis and Assembly in Oligosaccharides. *Angew. Chem. Int. Ed. Engl.* **2017**, *56* (19), 5227–5231.

(8) Bera, S.; Chatterjee, B.; Mondal, D. Construction of Quaternary Stereocentres on Carbohydrate Scaffolds. *RSC Adv.* **2016**, *6* (81), 77212–77242.

(9) Wang, S.; Sun, J.; Zhang, Q.; Cao, X.; Zhao, Y.; Tang, G.; Yu, B. Amipurimycin: Total Synthesis of the Proposed Structures and Diastereoisomers. *Angew. Chem. Int. Ed.* **2018**, *57* (11), 2884–2888.

(10) Nicolaou, K. C.; Renaud, J.; Nantermet, P. G.; Couladouros, E. A.; Guy, R. K.; Wrasidlo, W. Chemical Synthesis and Biological Evaluation of C-2 Taxoids. *J. Am. Chem. Soc.* **1995**, *117* (9), 2409–2420.

(11) Rombouts, Y.; Burguière, A.; Maes, E.; Coddeville, B.; Elass, E.; Guérardel, Y.; Kremer, L. Mycobacterium Marinum Lipooligosaccharides Are Unique Caryophyllose-Containing Cell Wall Glycolipids That Inhibit Tumor Necrosis Factor-α Secretion in Macrophages. *J. Biol. Chem.* **2009**, *284* (31), 20975–20988.

(12) Rombouts, Y.; Elass, E.; Biot, C.; Maes, E.; Coddeville, B.; Burguière, A.; Tokarski, C.; Buisine, E.; Trivelli, X.; Kremer, L.; Guérardel, Y. Structural Analysis of an Unusual Bioactive *N*-Acylated Lipo-Oligosaccharide LOS-IV in Mycobacterium Marinum. *J. Am. Chem. Soc.* **2010**, *132* (45), 16073–16084.

(13) Rombouts, Y.; Alibaud, L.; Carrère-Kremer, S.; Maes, E.; Tokarski, C.; Elass, E.; Kremer, L.; Guérardel, Y. Fatty Acyl Chains of Mycobacterium Marinum Lipooligosaccharides strucuture, localization and acelation by PapA4 (MMAR_2343) protein. *J. Biol. Chem.* **2011**, *286* (38), 33678–33688.

(14) Lowary, T. L. Twenty Years of Mycobacterial Glycans: Furanosides and Beyond. *Acc. Chem. Res.* **2016**, *49* (7), 1379–1388.

(15) Bai, B.; Chu, C.; Lowary, T. L. Lipooligosaccharides from Mycobacteria: Structure, Function, and Synthesis. *Isr. J. Chem.* **2015**, *55* (3–4), 360–372. (16) Nobre, A.; Alarico, S.; Maranha, A.; Mendes, V.; Empadinhas, N. The Molecular Biology of Mycobacterial Trehalose in the Quest for Advanced Tuberculosis Therapies. *Microbiology,* **2014**, *160* (8), 1547–1570.

(17) Burguière, A.; Hitchen, P. G.; Dover, L. G.; Kremer, L.; Ridell, M.; Alexander, D. C.; Liu, J.; Morris, H. R.; Minnikin, D. E.; Dell, A.; Besra, G. S. LosA, a Key Glycosyltransferase Involved in the Biosynthesis of a Novel Family of Glycosylated Acyltrehalose Lipooligosaccharides from Mycobacterium Marinum. *J. Biol. Chem.* **2005**, *280* (51), 42124–42133.

(18) Ren, H.; Dover, L. G.; Islam, S. T.; Alexander, D. C.; Chen, J. M.; Besra, G. S.; Liu, J. Identification of the Lipooligosaccharide Biosynthetic Gene Cluster from Mycobacterium Marinum. *Mol. Microbiol.* **2007**, *63* (5), 1345–1359.

(19) Sarkar, D.; Sidhu, M.; Singh, A.; Chen, J.; Lammas, D. A.; van der Sar, A. M.; Besra, G. S.; Bhatt, A. Identification of a Glycosyltransferase from Mycobacterium Marinum Involved in Addition of a Caryophyllose Moiety in Lipooligosaccharides. *J. Bacteriol.* **2011**, *193* (9), 2336–2340.

(20) Nigudkar, S. S.; Demchenko, A. V. Stereocontrolled 1,2-Cis Glycosylation as the Driving Force of Progress in Synthetic Carbohydrate Chemistry. *Chem. Sci.* **2015**, *6* (5), 2687–2704.

(21) Demchenko, A. V. General Aspects of the Glycosidic Bond Formation. In *Handbook of Chemical Glycosylation*; Demchenko, A. V., Ed.; Wiley-VCH Verlag GmbH & Co. KGaA, 2008; pp 1–27.

(22) Adero, P. O.; Amarasekara, H.; Wen, P.; Bohé, L.; Crich, D. The Experimental Evidence in Support of Glycosylation Mechanisms at the S_N1–S_N2 Interface. *Chem. Rev.* **2018**, *118* (17), 8242–8284.

(23) Hahm, H. S.; Hurevich, M.; Seeberger, P. H. Automated Assembly of Oligosaccharides Containing Multiple *Cis*- Glycosidic Linkages. *Nat. Commun.* **2016**, *7* (1), 1–8.

(24) Mensink, R. A.; Boltje, T. J. Advances in Stereoselective 1,2-*Cis* Glycosylation Using C-2 Auxiliaries. *Chem. Eur. J.* **2017**, *23* (70), 17637–17653.

(25) Leng, W.-L.; Yao, H.; He, J.-X.; Liu, X.-W. Venturing beyond Donor-Controlled Glycosylation: New Perspectives toward Anomeric Selectivity. *Acc. Chem. Res.* **2018**, *51* (3), 628–639.

(26) Wang, C.-C.; Lee, J.-C.; Luo, S.-Y.; Kulkarni, S. S.; Huang, Y.-W.; Lee, C.-C.; Chang, K.-L.; Hung, S.-C. Regioselective One-Pot Protection of Carbohydrates. *Nature* **2007**, *446* (7138), 896–899.

(27) Zhu, X.; Schmidt, R. R. New Principles for Glycoside-Bond Formation. *Angew. Chem. Int. Ed.* **2009**, *48* (11), 1900–1934.

(28) Vorm, S. van der; Hansen, T.; Hengst, J. M. A. van; S. Overkleeft, H.; Marel, G. A. van der; C. Codée, J. D. Acceptor Reactivity in Glycosylation Reactions. *Chem. Soc. Rev.* **2019**, *48* (17), 4688–4706.

(29) Hansen, T.; Elferink, H.; Hengst, J. M. A. van; Houthuijs, K.; Remmerswaal, W. A.; Kromm, A.; Berden, G.; Vorm, S. van der; Rijs, A.; Overkleeft, H. S.; Filippov, D.; Rutjes, F. P. J. T.; Marel, G. van der; Martens, J.; Oomens, J.; Codée, J. D. C.; Boltje, T. Characterization of Glycosyl Dioxolenium Ions and Their Role in Glycosylation Reactions. **2019**.

(30) Liu, H.; Hansen, T.; Zhou, S.-Y.; Wen, G.-E.; Liu, X.-X.; Zhang, Q.-J.; Codée, J. D. C.; Schmidt, R. R.; Sun, J.-S. Dual-Participation Protecting Group Solves the Anomeric Stereocontrol Problems in Glycosylation Reactions. *Org. Lett.* **2019**, *21* (21), 8713–8717.

(31) Hagen, B.; van der Vorm, S.; Hansen, T.; van der Marel, G. A.; Codée, J. D. C. Stereoselective Glycosylations – Additions to Oxocarbenium Ions. In *Selective Glycosylations: Synthetic Methods and Catalysts*; Bennett, C. S., Ed.; Wiley-VCH Verlag GmbH & Co. KGaA, 2017; pp 1–28.

(32) Bohé, L.; Crich, D. A Propos of Glycosyl Cations and the Mechanism of Chemical Glycosylation; the Current State of the Art. *Carbohydr. Res.* **2015**, *403*, 48–59.

(33) Zhang, Q.; Gimeno, A.; Santana, D.; Wang, Z.; Valdés-Balbin, Y.; Rodríguez-Noda, L. M.; Hansen, T.; Kong, L.; Shen, M.; Overkleeft, H. S.; Vérez-Bencomo, V.; van der Marel, G. A.; Jiménez-Barbero, J.; Chiodo, F.; Codée, J. D. C. Synthetic, Zwitterionic *Sp1* Oligosaccharides Adopt a Helical Structure Crucial for Antibody Interaction. *ACS Cent. Sci.* **2019**, *5* (8), 1407–1416.

(34) Wang, L.; Dong, M.; Lowary, T. L. Synthesis of Unusual *N*-Acylated Aminosugar Fragments of Mycobacterium Marinum Lipooligosaccharide IV. *J. Org. Chem.* **2015**, *80* (5), 2767–2780.

(35) Prandi, J. A General Route to 4-*C*-Branched Sugars. Synthesis of Methyl α-Caryophylloside. *Carbohydr. Res.* **2001**, *332* (3), 241–247.

(36) Prandi, J.; Couturier, G. Synthesis of Methyl α-Caryophylloside. *Tet. Lett.* **2000**, *41* (1), 49–52.

(37) Codée, J. D. C.; Litjens, R. E. J. N.; den Heeten, R.; Overkleeft, H. S.; van Boom, J. H.; van der Marel, G. A. Ph_2SO/Tf_2O: A Powerful Promotor System in Chemoselective Glycosylations Using Thioglycosides. *Org. Lett.* **2003**, *5* (9), 1519–1522.

(38) Frihed, T. G.; Bols, M.; Pedersen, C. M. Mechanisms of Glycosylation Reactions Studied by Low-Temperature Nuclear Magnetic Resonance. *Chem. Rev.* **2015**.

(39) Hagen, B.; Ali, S.; Overkleeft, H. S.; van der Marel, G. A.; Codée, J. D. C. Mapping the Reactivity and Selectivity of 2-Azidofucosyl Donors for the Assembly of *N*-Acetylfucosamine-Containing Bacterial Oligosaccharides. *J. Org. Chem.* **2017**, *82* (2), 848–868.

(40) van der Vorm, S.; Overkleeft, H. S.; van der Marel, G. A.; Codée, J. D. C. Stereoselectivity of Conformationally Restricted Glucosazide Donors. *J. Org. Chem.* **2017**, *82* (9), 4793–4811.

(41) Crich, D.; Cai, W. Chemistry of 4,6-*O*-Benzylidene-D-Glycopyranosyl Triflates: Contrasting Behavior between the Gluco and Manno Series. *J. Org. Chem.* **1999**, *64* (13), 4926–4930.

(42) Crich, D.; Sun, S. Are Glycosyl Triflates Intermediates in the Sulfoxide Glycosylation Method? A Chemical and ^{1}H, ^{13}C, and ^{1}F NMR Spectroscopic Investigation. *J. Am. Chem. Soc.* **1997**, *119* (46), 11217–11223.

(43) Hansen, T.; Lebedel, L.; Remmerswaal, W. A.; van der Vorm, S.; Wander, D. P. A.; Somers, M.; Overkleeft, H. S.; Filippov, D. V.; Désiré, J.; Mingot, A.; Bleriot, Y.; van der Marel, G. A.; Thibaudeau, S.; Codée, J. D. C. Defining the S_N1 Side of Glycosylation Reactions: Stereoselectivity of Glycopyranosyl Cations. *ACS Cent. Sci.* **2019**, *5* (5), 781–788.

(44) van der Vorm, S.; Hansen, T.; van Rijssel, E. R.; Dekkers, R.; Madern, J. M.; Overkleeft, H. S.; Filippov, D. V.; van der Marel, G. A.; Codée, J. D. C. Furanosyl Oxocarbenium Ion Conformational Energy Landscape Maps as a Tool to Study the Glycosylation Stereoselectivity of 2-Azidofuranoses, 2-Fluorofuranoses and Methyl Furanosyl Uronates. *Chem. Eur. J.* **2019**, *25* (29), 7149–7157.

(45) Madern, J. M.; Hansen, T.; van Rijssel, E. R.; Kistemaker, H. A. V.; van der Vorm, S.; Overkleeft, H. S.; van der Marel, G. A.; Filippov, D. V.; Codée, J. D. C. Synthesis, Reactivity, and Stereoselectivity of 4-Thiofuranosides. *J. Org. Chem.* **2019**, *84* (3), 1218–1227.

(46) Vorm, S. van der; Hansen, T.; Overkleeft, H. S.; Marel, G. A. van der; Codée, J. D. C. The Influence of Acceptor Nucleophilicity on the Glycosylation Reaction Mechanism. *Chem. Sci.* **2017**, *8* (3), 1867–1875.

(47) Beaver, M. G.; Woerpel, K. A. Erosion of Stereochemical Control with Increasing Nucleophilicity: *O*-Glycosylation at the Diffusion Limit. *J. Org. Chem.* **2010**, *75* (4), 1107–1118.

(48) Mukaiyama, T.; Kobashi, Y.; Shintou, T. A New Method for α-Selective Glycosylation Using a Donor, Glycosyl Methyldiphenylphosphonium Iodide, without Any Assistance of Acid Promoters. *Chem. Lett.* **2003**, *32* (10), 900–901.

(49) Mukaiyama, T.; Kobashi, Y. Highly α-Selective Synthesis of Disaccharide Using Glycosyl Bromide by the Promotion of Phosphine Oxide. *Chem. Lett.* **2003**, *33* (1), 10–11.

(50) Kobashi, Y.; Mukaiyama, T. Glycosyl Phosphonium Halide as a Reactive Intermediate in Highly α-Selective Glycosylation. *BCSJ* **2005**, *78* (5), 910–916.
(51) Kobashi, Y.; Mukaiyama, T. Highly α-Selective Glycosylation with Glycosyl Acetate via Glycosyl Phosphonium Iodide. *Chem. Lett.* **2004**, *33* (7), 874–875.
(52) Chu, A.-H. A.; Nguyen, S. H.; Sisel, J. A.; Minciunescu, A.; Bennett, C. S. Selective Synthesis of 1,2-*Cis*-α-Glycosides without Directing Groups. Application to Iterative Oligosaccharide Synthesis. *Org. Lett.* **2013**, *15* (10), 2566–2569.
(53) Wang, L.; Overkleeft, H. S.; van der Marel, G. A.; Codée, J. D. C. Reagent Controlled Stereoselective Synthesis of α-Glucans. *J. Am. Chem. Soc.* **2018**, *140* (13), 4632–4638.
(54) Volbeda, A. G.; Kistemaker, H. A. V.; Overkleeft, H. S.; van der Marel, G. A.; Filippov, D. V.; Codée, J. D. C. Chemoselective Cleavage of P-Methoxybenzyl and 2-Naphthylmethyl Ethers Using a Catalytic Amount of HCl in Hexafluoro-2-Propanol. *J. Org. Chem.* **2015**, *80* (17), 8796–8806.
(55) Reisberg, S. H.; Gao, Y.; Walker, A. S.; Helfrich, E. J. N.; Clardy, J.; Baran, P. S. Total Synthesis Reveals Atypical Atropisomerism in a Small-Molecule Natural Product, Tryptorubin A. *Science* **2020**, *367* (6476), 458–463.
(56) Sommer, R.; Exner, T. E.; Titz, A. A Biophysical Study with Carbohydrate Derivatives Explains the Molecular Basis of Monosaccharide Selectivity of the Pseudomonas Aeruginosa Lectin LecB. *PLOS ONE* **2014**, *9* (11).

Chapter 6

Summary and Perspectives

Summary

The central reaction in synthetic carbohydrate chemistry is the glycosylation reaction, in which two building blocks are united to form more complex carbohydrates. Insufficient knowledge of this reaction thwarts the routine assembly of synthetic oligosaccharides. In essence, the glycosylation reaction is a substitution reaction between a nucleophile and an electrophile. Figure 1 depicts the general mechanism for the glycosylation reaction, in which the first step consists of the activation of a donor molecule by a promotor system. This activation leads to an array of reactive intermediates, including covalent species which can partake in S_N2-like pathways, while cationic intermediates can undergo S_N1-type substitutions. Glycosyl cations, also known as glycosyl oxocarbenium ions, are key reactive intermediates in the S_N1-like pathways of the glycosylation reaction. Although significant progress has been made in the field, studying these highly reactive intermediate remains to date a daunting challenge and lies at the forefront of current efforts to advance glycosylation chemistry.

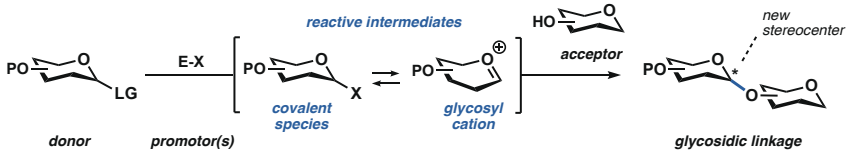


Figure 1. General overview of the glycosylation reaction. Glycosylation reactions are best considered as taking place at a continuum between two formal extremes of the mechanisms, the S_N1- and S_N2-mechanism; LG = leaving group; P = protection group; E-X = promoter system.

The research described in this thesis aimed to gain more insight into the mechanisms of chemical glycosylation reactions and their reactive intermediates. Chapter 1 provides an overview of research directed at understanding the behavior of glycosyl cations in terms of stability, selectivity and conformational preference.

The study described in Chapter 2 is focused on the development of a novel computational approach to investigate the stability and reactivity of glycosyl cations in a quantitative manner. The developed computational method probes the complete conformational space of these flexible six-membered ring cations (Figure 2A). This was accomplished by systematically scanning three dihedral angles (*i.e.*, C1–C2–C3–C4, C3–C4–C5–O5, and C5–O5–C1–C2) and computing their geometries and energies by DFT (Figure 2B). Based on the conformational preference of the intermediate ions, a prediction of the product stereoselectivity, formed in model S_N1 glycosylation reactions, could be made.

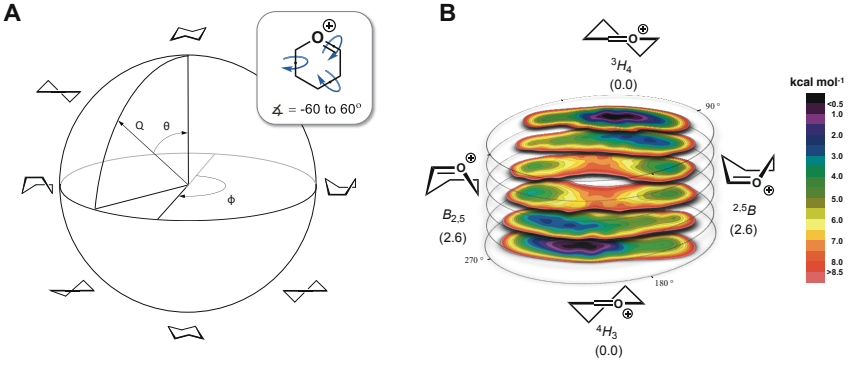


Figure 2. The developed method probes the complete conformational space of these highly flexible six-membered ring cations. (A) The complete conformational space of a six membered ring was scanned by computing 729 pre-fixed structures; A few canonical conformations (chair, half-chair, envelope and boat) are depicted; (B) The associated energies were graphed on slices dividing the Cremer-Pople sphere. All energies are computed at PCM(CH_2Cl_2)-B3LYP/6-311G(d,p) at T=213.15 K and expressed as solution-phase Gibbs free energy.

More than 30 different glycosyl oxocarbenium ions with varying substitution patterns were evaluated. The stability, reactivity and conformational mobility of these glycosyl oxocarbenium ions could be fully understood by computing the complete conformational

energy landscape (CEL), and the conformational preference of the cations could be directly related to the experimental stereochemical outcome of addition reactions with a typical S_N1-nucleophile, triethylsilane-*d*. The CEL maps showed in detail how the stereoelectronic effects of various ring substituents (halogens, chalcogens, azides, and carbon-based substituents) determine the overall shape of the cations and thereby the stereochemical course of the reactions. To obtain direct experimental evidence for the computed conformations using the CEL mapping method two 2-deoxy diacetylated oxocarbenium were generated and studied in 'non'-nucleophilic superacid media (*i.e.*, HF/SbF_5). The simulated NMR spectra of the selected cations, reconstituted by using the Boltzmann weighted averaged coupling constants determined by the CEL mapping method, perfectly matched the experimental ones obtained in superacid.

Where glycosyl oxocarbenium ions were previously thought to be at the basis of non-selective coupling reactions because of their high reactivity, the findings described in Chapter 2 show that these species – including the glycosyl cations derived from L-fucose, L-rhamnose, D-glucose, D-mannose and D-galactose – have an intrinsic preference to generate the challenging 1,2-*cis*-linkages. Chapter 2 firmly establishes the CEL mapping method as valuable tool for future research towards flexible six-membered ring oxocarbenium ion intermediates.

Chapter 3 expands on Chapter 2 with the focus on the reaction between the glycosyl cations and different S_N1-type nucleophiles. By performing model glycosylation reactions with two typical S_N1-nucleophiles, allyltrimethylsilane (allyl-TMS) and triethylsilane-*d* (TES-*d*), it was experimentally found that most of the substituted glycosyl cations react with similar stereoselectivities with both nucleophiles.

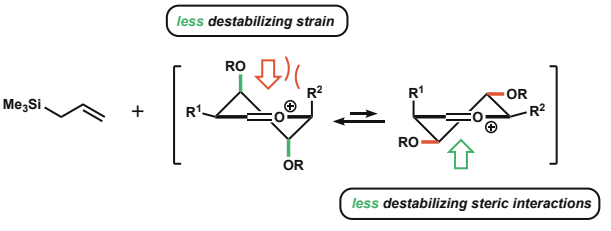


Figure 3. Schematic representation of the controlling factors (green = stabilizing; red = destabilizing factors) of the stereoselectivity of *C*-glycosylation reactions, in which the strain is always less destabilizing for the more stable conformer (*i.e.*,$^3H_4$), while the Pauli repulsion is also always more destabilizing for this conformation; R^1 = H or OBn and R^2 = H, Me or CH_2OBn.

In parallel, computational studies showed that most of these cations react via barrierless reaction pathways, and therefore the conformational preference of these glycosyl cations dictates the stereochemical outcome of addition reactions to these cations. However, a selected number of glycosyl cations reacted in a different stereoselective manner. For these latter cases, addition barriers were computationally found and Curtin-Hammett analyses of these reactions showed that these activation barriers are strongly influenced by the nature

of the nucleophile. By performing activation strain and Kohn-Sham molecular orbital analyses, it was found that the disparate stereoselectivity originated from (i) the stability of the different glycosyl cation conformers; (ii) the steric repulsion between the nucleophile and the glycosyl cation; and (iii) the position of the transition state along the reaction coordinate. (Figure 3).

The subject of Chapter 4 covered the possible formation of dioxolenium ions from their parent oxocarbenium ion through participation of remote acyl groups present on donor molecules (Figure 4). This long-range participation can steer the stereochemical outcome of glycosylation reactions. In this Chapter a three-pronged approach consisting of infrared ion spectroscopy (IRIS), CEL computations, and model glycosylation reactions, was used to assess the effect of long-range participation (LRP) in a set of glycosyl donors. First, the DFT protocol, developed as described in Chapter 2, was used to compute the relative stability of the dioxolenium ions, to analyze which systems were susceptible for LRP.

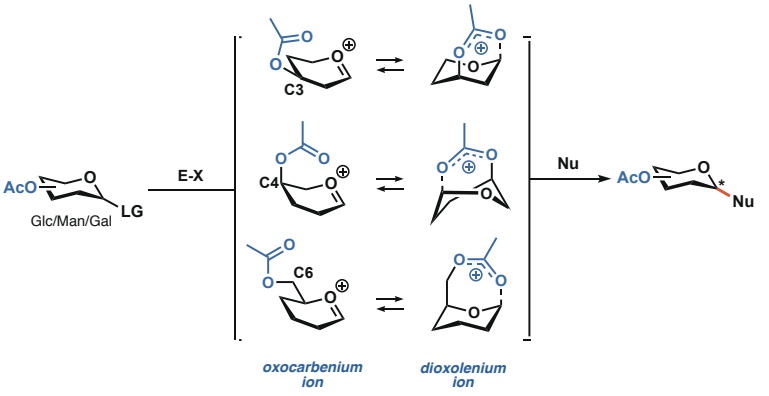


Figure 4. LRP in glycosylation reactions offers an opportunity to control the stereoselectivity of glycosylations. P = protection group; E-X = promoter system; and Nu = nucleophile.

To get direct experimental support for the computed reactive intermediates, IRIS was performed. In this method, glycosyl donors are introduced into the mass spectrometer via electrospray ionization (ESI) and, in a tandem-mass spectrometric (MS^2) scheme, glycosyl cations could be formed from the isolated donors by collision induced dissociation (CID). This allowed the generation of "naked" glycosyl cations, and characterization using multi photon infrared ion spectroscopy. In order to verify if the postulated LRP based on the DFT computations and IRIS measurements could also be found in a relevant experimental setup for glycosylation chemistry, an array of glycosylation experiments was performed.

Together these studies confirm that LRP can play a decisive role in shaping the stereochemical outcome of a glycosylation reaction. LRP plays a major role in glycosylations of C-3 acyl mannosides and to a somewhat lesser extent with C-4 acyl galactosides. C-3 acyl groups in glucose and galactosyl donors can engage in LRP but this anchimeric assistance has relatively little influence on the stereochemical course of

glycosylations of these donors. No important role for C-6 acyl LRP has been found. The strength of LRP thus follows the order: 3-Ac-Man >> 4-Ac-Gal > 3-Ac-Glc ~ 3-Ac-Gal > 4-Ac-Glc > 4-Ac-Man ~ 6-Ac-Glc/Gal/Man.

The research described in Chapter 5 implements the fundamental insights gained in the previous chapters in the assembly of a biologically relevant complex mycobacterial glycolipid, built up from (amongst others) rare and complex monosaccharides, featuring tetrasubstituted tertiary carbon stereocenters (Figure 5A). An integrated approach, consisting of a systematic series of glycosylation reactions in combination with the detection and characterization of different reactive intermediates using variable-T NMR and CEL computations, were used to assess reactivity-stereoselectivity relationships.

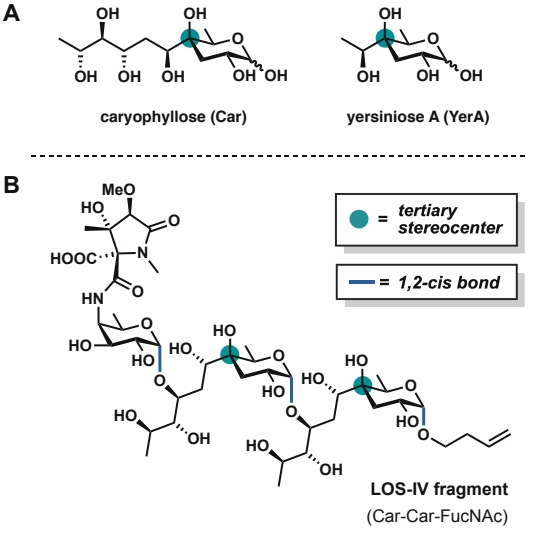


Figure 5. Tetrasubstituted tertiary-*C* sugars present in lipooligosaccharides from *M. marinum*. (A) Tertiary *C*-sugar caryophyllose (Car) found in mycobacterial lipooligosaccharides and the related smaller Yersiniose A (YerA); (B) Synthesized fragment of a lipooligosaccharide from *M. marinum*.

Pre-activation of these donors revealed that the protected oxygen of the ether functionalities in the appended side chain of caryophyllose (Car) and yersioniose (YerA) readily attack the activated anomeric center of the donors, providing bridged structures leading to unproductive glycosylation reactions. This behavior has been explained using the structural preference of the oxocarbenium ion intermediates that can form. Prevention of this nucleophilic attack is a prerequisite to generate effective donor glycosides, and this could be achieved by tethering of the C4 side-chain. It was found that Car and YerA donors, equipped with a tethering carbonate protecting group, can efficiently form the desired 1,2-*cis* linkages, as long as weak nucleophiles are employed in the glycosylation. In order to achieve 1,2-*cis* selectivity, the reactivity of the Car-acceptors was tuned using electron-withdrawing protecting groups. The rationally designed building blocks enabled the

effective and stereoselective assembly of a Car-Car-FucNAc LOS-IV fragment, and related shorter fragments (Figure 5B).

/ In conclusion, this thesis describes the use of a combined approach of computational and experimental techniques to gain novel insights to understand the glycosylation reaction and its reactive intermediates. The research in this thesis shows that glycosyl cations can act as reactive intermediates in glycosylation reactions for the introduction of glycosidic linkages. Furthermore, computational and experimental evidence has been provided showing that dioxolenium ions, formed by participation of remote acyl groups, are relevant reactive intermediates and can effectively steer the stereochemical course of glycosylation reactions. Ultimately, the techniques developed and insights gained in these studies were used in the synthesis of a complex mycobacterial glycolipid. The fundamental knowledge presented in this thesis can be further exploited in future synthetic endeavors, delivering more and more complex glycans to fuel glycobiological and glycomedical research. /

Future perspectives

The main goal of this thesis was to shed light on the glycosylation reaction mechanisms and especially its reactive intermediates that can form during these reactions. The insights gained during these studies will have to be applied in target-oriented syntheses, delivering new oligosaccharides and glycoconjugates for further study. This section describes several studies to extend the presented work and translate the fundamental insights to synthetic applications.

Further applications of the CEL mapping method

The developed CEL mapping method can be applied to a wide range of systems to understand the conformational behavior of these six membered rings. The method can be applied to popular donors used in synthetic chemistry, such as cyclic protected donors (Figure 6A). It can also be applied to probe cations of differently substituted glycosyl donors, derived from bacterial monosaccharides[1] or sialic acid derivatives (Figure 6C-D). Also, the effect of a counter ion on the structure of intermediates can be studied (Figure 6B). The role of the counter ion is largely debated, and it is to date exceedingly difficult to experimentally or computationally study these elusive species.[2–8]

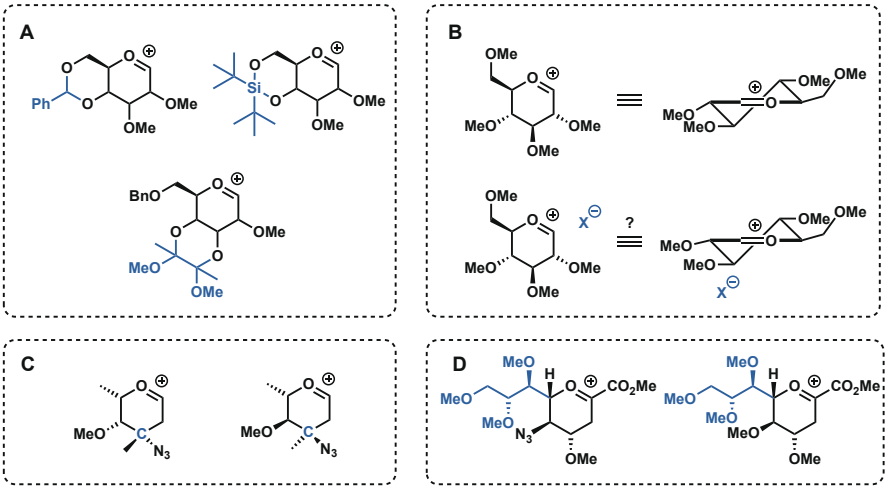


Figure 6. Further applications of the CEL mapping method for studying oxocarbenium ions. (A) Studying the influence of cyclic protection groups; (B) Presence of a counter-ion; (C) Tertiary-*C* motives; (D) Appended side-chains.

A selection of the endeavors towards these applications is shown in Figure 7, in which the CEL maps of two popular donors used in synthetic chemistry, benzylidene protected glucose **1** and mannose **2** are presented. The CEL maps of the cations formed from these donors, support the currently accepted model, in which the glucosyl cation **1** preferably adopts a $^{4}H_{3}/^{4}E$-like structure, while mannosyl ion **2** takes up a $B_{2,5}$ conformation. This conformational preference translates to the 1,2-*cis* selectivity observed in glycosylations of these donors, in which glucosyl cation **1** is attacked at the bottom-face of the $^{4}H_{3}/^{4}E$-like conformer and mannosyl cation **2** by a top-face addition at the $B_{2,5}$ intermediate.[9,10]

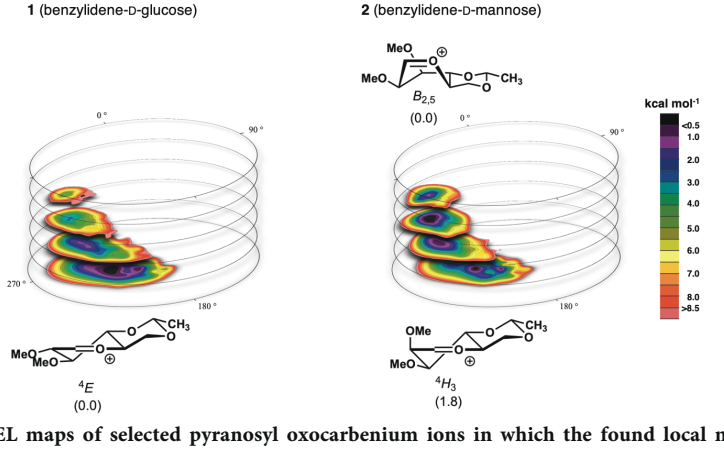
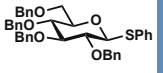
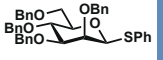
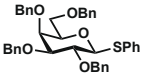
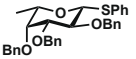
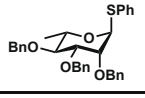
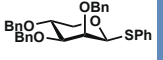
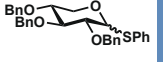
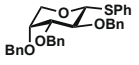
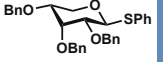
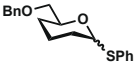


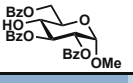
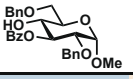
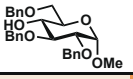
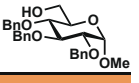
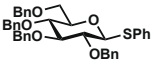
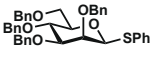
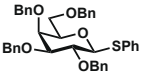
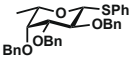
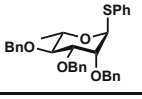
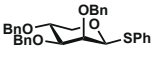
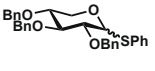
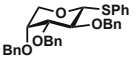
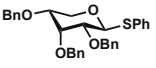
Figure 7. CEL maps of selected pyranosyl oxocarbenium ions in which the found local minima are indicated with their respective energy. CEL maps of benzylidene protected pyranosyl oxocarbenium ions **1** and **2**. All energies are as computed at PCM(CH_2Cl_2)-B3LYP/6-311G(d,p) and expressed as solution-phase Gibbs free energy.

Table 1. Experimentally found stereoselectivity for glycosylation reactions on a series of mono- and multi-substituted donors with a variety of model *d*-, *C*- and *O*-nucleophiles. For the mono-substituted pyranosides the *cis*:*trans* ratio is expressed as the relationship between the substituent and the coupled nucleophile; for the other glycopyranosides the *cis*:*trans* ratio is expressed as the relationship between the substituent on C-2 and the coupled nucleophile. The experimental results for the *gluco*-, *manno*-, and *galacto*-entries are from Chapter 4.

	TES-*d*	TMS	CF_3 HO CF_3	HO CF_3	HO F F	HO F	HO
	>98:2 (70%)	>98:2 (71%)	>98:2 (41%)	75:25 (80%)	48:52 (58%)	36:64 (75%)	15:85 (70%)
	>98:2 (93%)	34:66 (80%)	<2:98 (39%)	<2:98 (84%)	20:80 (58%)	40:60 (75%)	67:33 (70%)
	>98:2 (86%)	>98:2 (80%)	>98:2 (33%)	87:13 (79%)	66:34 (69%)	33:67 (84%)	17:83 (73%)
	>98:2 (74%)	>98:2 (76%)	>98:2 (33%)	100:0 (89%)	67:33 (82%)	40:60 (100%)	29:71 (100%)
	>98:2 (79%)	23:77 (70%)	<2:98 (46%)	8:92 (95%)	30:70 (70%)	77:23 (92%)	54:46 (86%)
	>98:2 (81%)	>98:2 (76%)	>98:2 (46%)	59:41 (62%)	64:36 (93%)	73:27 (100%)	53:47 (87%)
	>98:2 (86%)	>98:2 (72%)	34:66 (55%)	34:66 (78 %)	33:67 (89%)	29:71 (100%)	15:85 (89%)
	>98:2 (79%)	>98:2 (68%)	>98:2 (26%)	88:12 (90%)	62:38 (54%)	56:44 (96%)	18:82 (100%)
	>98:2 (69%)	>98:2 (70%)	>98:2 (36%)	52:48 (68%)	50:50 (72%)	39:61 (100%)	28:72 (100%)
	<2:98 (80%)	<2:98 (79%)	<2:98 (100%)	<2:98 (20%)	22:88 (73%)	50:50 (63%)	52:48 (40%)

>90:10 >80:20 >60:40 >50:50 <50:50 <40:60 <20:80 <10:90 (1,2-*cis*:1,2-*trans*)

Table 2. Experimentally found stereoselectivity for glycosylation reactions on a series of mono- and multi-substituted donors with a variety of model carbohydrate acceptors. The *cis*:*trans* ratio is expressed as the relationship between the substituent on C-2 and the coupled nucleophile.

				
	88:12 (58%)	61:39 (62%)	42:58 (91%)	15:85 (76%)
	<2:98 (59%)	<2:98 (77%)	<2:98 (70%)	77:23 (79%)
	>98:2 (66%)	92:8 (70%)	70:30 (70%)	30:70 (75%)
	>98:2 (76%)	93:7 (85%)	90:10 (75%)	45:55 (90%)
	<2:98 (51%)	10:90 (78%)	12:88 (84%)	66:34 (91%)
	61:39 (67%)	55:45 (74%)	90:10 (84%)	60:40 (95%)
	60:40 (54%)	60:40 (91%)	60:40 (70%)	38:62 (90%)
	78:22 (59%)	75:25 (79%)	53:47 (84%)	30:70 (93%)
	50:50 (67%)	40:60 (61%)	40:60 (75%)	35:65 (63%)

>90:10 | >80:20 | >60:40 | >50:50 | <50:50 | <40:60 | <20:80 | <10:90 (1,2-*cis*:1,2-*trans*)

Glycosylation reaction with *O*-nucleophiles

Chapter 2 and 3 focused on the use of typical S_N1-nucleophiles (*d*- and *C*-nucleophiles; TES-*d* and allyl-TMS). An important extension of these studies is the investigation in reactions involving *O*-nucleophiles, since these types of acceptors are mainly used in synthetically relevant glycosylation reactions. To this end, an array of glycosylation reactions was performed with a set of pyranosyl donors in combination with a set of model alcohol nucleophiles (for their use see also Chapter 4), of gradually decreasing nucleophilicity. The glycosylation reactions were performed under pre-activation

conditions using diphenyl sulfoxide (Ph_2SO)/triflic anhydride (Tf_2O) as an activator.[11] A panel of 10 benzyl protected donors was selected, ranging from mono-substituted pyranoses to fully decorated donors. The results are summarized in Table 1. Based on earlier work, the changes in stereochemistry of the reactions can be related to changes in mechanism.[10] Strong nucleophiles (*i.e.*, EtOH and MFE) generally show direct displacement, in a S_N2-type substitution fashion, of the covalent intermediate (*e.g.*, α-triflate) to form the β-product. Weaker *O*-nucleophiles (*i.e.*, HFIP and TFE) are expected to follow a reaction pathway with significant oxocarbenium ion character, reacting in S_N1-like fashion. In most cases the results support this and the obtained stereoselectivities for HFIP are in agreement with allyl-TMS and TES-*d*, the typical S_N1-nucleophiles. However, in some cases the stereochemical results deviate. This suggests that the mechanism of these reactions involving the weak *O*-nucleophiles could be differing from the established S_N1-like mechanisms. Perhaps these nucleophiles follow more of a S_Ni-like pathway (*i.e.*, S_N2-f), which has been established for enzyme-catalyzed glycosylations.[12–14] In this type of nucleophilic substitution, the incoming acceptor is assisted by the departing leaving group by forming a hydrogen bond. Whitfield and co-workers supported this concept by stretching the importance of hydrogen bonding in the glycosylation reaction by the use of DFT computations.[15] In the future, DFT calculations (similar to the ones described in Chapter 3) can be used to shed light on the exact mechanism(s) at play investigating different transition states through which the reactions may proceed. The study with *O*-nucleophiles was further extended by the use of a set of carbohydrate acceptors and these results are summarized in Table 2. These carbohydrate acceptors also represent a set of nucleophiles of gradually decreasing nucleophilicity. The trends found for the model ethanol acceptors translates well to the carbohydrate acceptors. This further supports the use of these model acceptors as surrogates for carbohydrate acceptors.[10,16,17]

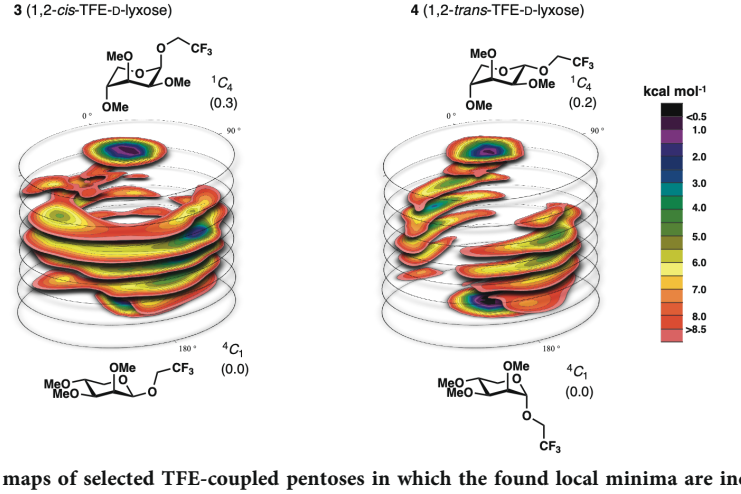


Figure 8. CEL maps of selected TFE-coupled pentoses in which the found local minima are indicated with their respective energy. CEL maps of trifluoroethanol coupled lyxose **3** and **4**. All energies are as computed at PCM($CHCl_3$)-B3LYP/6-311G(d,p) and expressed as solution-phase Gibbs free energy.

Several glycosylation products were exceptionally difficult to characterize by NMR spectroscopy because the pentose systems proved to be highly flexible, leading to coupling constants for the ring protons, deviating from values, commonly obtained for the canonical $^{1}C_{4}$ or $^{4}C_{1}$ chair conformer. In order to probe the conformational space that was available for these molecules, the CEL mapping method was applied. From the generated maps (Figure 8), it becomes apparent that for lyxose products **3** and **4**, a mixture of conformers can be expected, in accounting for the *J*-values found in the NMR analysis.

Novel remote-participating groups

Chapter 4 establishes dioxolenium ion intermediates as relevant reactive intermediates in glycosylation reactions. With the gained fundamental knowledge described in this chapter these species can be exploited by searching for groups that could potentially strengthen the LRP effect and allow for full control over the stereochemical preference of the glycosylation reaction. This is supported by the work of the group of Boons (Figure 9).[18] They showed that by placing a variety of ester groups, which differ in electron-withdrawing character, a clear trend in stereoselectivity was found.

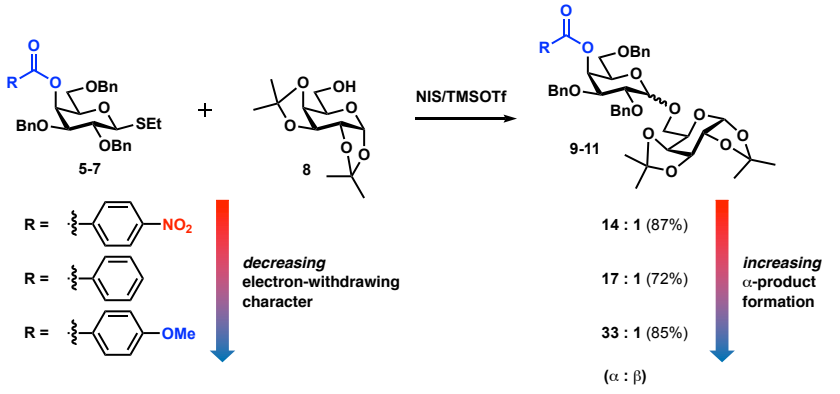


Figure 9. Using ester groups with varying electron-withdrawing character provides a way to steer the stereoselectivity of the reaction.[18]

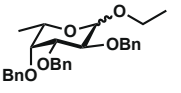
The stereoselectivity of these three couplings can be traced back to the stability of the corresponding dioxolenium ions, which can form upon activation. This suggests that it is possible to manipulate the stability of the dioxolenium ion by tuning the properties of the appended acyl esters, to steer glycosylation reactions. Early attempts in this direction show promising results. The 2,2-dimethyl-2-(*ortho*-nitrophenyl)acetyl (DMNPA) group was used as protection group, which showed more efficient LRP control compared to a classical benzoyl group.[19,20]

Supporting information

Organic synthesis

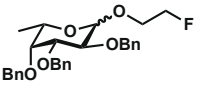
General experimental procedures. All chemicals (Merck, Sigma-Aldrich, Alfa Aesar, Honeywell, Boom and Merck KGaA) were of commercial grade and were used as received unless stated otherwise. Dichloromethane, tetrahydrofuran and toluene were stored over activated 4 Å molecular sieves (beads, 8-12 mesh, Sigma-Aldrich). Deuterated chloroform was stored over activated 3 Å molecular rods (rods, size 1/16 in., Sigma Aldrich) and potassium carbonate. Flash column chromatography was performed on silica gel 60 Å (0.04 – 0.063 mm, Screening Devices B.V.). Size exclusion chromatography was performed on SephadexTM (LH-20, GE Healthcare Life Sciences) by isocratic elution with DCM:MeOH (1:1, v:v). TLC-analysis was performed on TLC Silica gel 60 (Kieselgel 60 F254, Merck) with UV detection (254 nm) and by spraying with 20% H_2SO_4 in ethanol followed by charring at ± 260 °C or by spraying with a solution of $(NH_4)_6Mo_7O_{24}{\cdot}H_2O$ (25 g/L) and $(NH_4)_4Ce(SO_4)_4{\cdot}2H_2O$ (10 g/L) in 10% sulfuric acid in water followed by charring at ± 260 °C. TLC-MS analysis was performed on a Camag TLC-MS Interface coupled with an API165 (SCIEX) mass spectrometer (eluted with *tert*-butylmethylether/EtOAc/MeOH, 5/4/1, v/v/v +0.1% formic acid, flow rate 0.12 mL/min). High-resolution mass spectra (HRMS) were recorded on a Waters Synapt G2-Si (TOF) equipped with an electrospray ion source in positive mode (source voltage 3.5 kV) and an internal lock mass LeuEnk ($M+H^+$ = 556.2771). Amberlite resin (Sigma Aldrich Amberlite IR120 H^+ form, Amberlite IRA-67 free base) was pre-washed with MeOH. ^1H and ^{13}C NMR spectra were recorded on a Bruker AV-400 NMR instrument (400 and 101 MHz respectively), a Bruker AV-500 NMR instrument (500 and 126 MHz respectively), a Bruker AV-600 NMR instrument (600 and 151 MHz respectively) or a Bruker AV-850 NMR instrument (850 and 214 MHz respectively. All samples were measured in $CDCl_3$, unless stated otherwise. Chemical shifts (δ) are given in ppm relative to tetramethylsilane as internal standard or the residual signal of the deuterated solvent. Coupling constants (J) are given in Hz. All given ^{13}C APT spectra are proton decoupled. NMR peak assignment was accomplished using COSY, HSQC. If necessary, an additional NOESY, HMBC, and HMBC-gated experiment were used to further elucidate the structure. Stereochemical product ratios were based on integration of ^1H NMR (crude and purified). IR spectra were recorded on a Shimadzu FTIR-8300 IR spectrometer and are reported in cm^{-1}. Specific rotations were measured on an Anton Paar Polarimeter MCP 100 in $CHCl_3$ (10 mg/mL) at 589 nm, unless stated otherwise.

General procedure I: pre-activation Tf_2O/Ph_2SO based glycosylation
To a solution of the donor (100 µmol, 1 eq.) in DCM (2 mL, 0.05 M), Ph_2SO (26 mg, 130 µmol, 1.3 eq.) and TTBP (62 mg, 250 µmol, 2.5 eq.) were added. The solution was stirred over activated 3 Å molecular sieves (rods, size 1/16 in., Sigma Aldrich) for 30 minutes. The solution was cooled to −80 °C upon which Tf_2O (22 µL, 130 µmol, 1.3 eq.) was added slowly (5 seconds). Subsequently, the solution was allowed to attain to −60 °C to secure full activation of the donor followed by cooling back to −80 °C after which the acceptor was added (0.2 mL, 0.5 M solution, 2.0 eq.). The reaction was stirred for 16 hours at −60 °C (for ethanol, 2-fluoroethanol, 2,2-difluoroethanol and 2,2,2-trifluoroethanol) or for 40 hours at −60 °C (for 1,1,1,3,3,3-hexafluoro-2-propanol). The reaction was quenched with sat. aq. $NaHCO_3$ followed by the dilution with EtOAc. The aqueous layer was extracted three times with EtOAc. The organic layer was washed with H_2O and brine, dried over $MgSO_4$, filtered off and concentrated under reduced pressure. Purification was performed by flash column chromatography to afford the corresponding coupled glycoside.

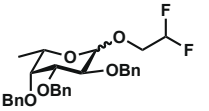


Ethyl 2,3,4-tri-*O*-benzyl-L-fucopyranoside (S1). The title compound was prepared according to general procedure I. The reaction was quenched after 2 h. Flash column chromatography (97:3 → 85:15, pentane:EtOAc) afforded the title compound (46 mg, 100 µmol, *quant.*, colorless oil, 1,2-*cis*:1,2-*trans*; 29:71). TLC: R_f 0.49 (pentane:EtOAc, 90:10, v:v); IR (thin film, cm^{-1}): 695, 731, 1027, 1064, 1092, 1360, 1453, 2892; Data for the major stereoisomer (1,2-*trans*): ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.44 – 7.22 (m, 15H, CH_{arom}), 5.01 – 4.92 (m, 2H, C*H*H Bn, C*H*H Bn), 4.82 – 4.65 (m, 6H, CH*H* Bn, CH*H* Bn, CH_2 Bn, CH_2 Bn), 4.32 (d, J = 7.7 Hz, 1H, H-1), 4.05 – 3.92 (m, 2H, C*H*H Et), 3.80 (dd, J = 9.7, 7.7 Hz, 1H, H-2), 3.60 – 3.53 (m, 2H, H-4, CH*H* Et), 3.50 (dd, J = 9.7, 3.0 Hz, 1H, H-3), 3.44 (qd, J = 6.4, 1.0 Hz, 1H, H-5), 1.26 (t, J = 7.0 Hz, 3H, CH_3 Et), 1.17 (d, J = 6.4 Hz, 3H, CH_3); ^{13}C NMR (101 MHz,

$CDCl_3$ HSQC, HMBC-Gated): δ 139.1, 138.8, 138.7 ($C_{q\text{-}arom}$), 128.6, 128.5, 128.4, 128.3, 128.2, 127.6, 127.6 (CH_{arom}), 103.7 (C-1), 82.6 (C-3), 79.6 (C-2), 76.4 (C-4), 75.2, 74.6, 73.3 (CH_2 Bn), 70.3 (C-5), 65.4 (CH_2 Et), 17.0 (CH_3 Et), 15.4 (CH_3); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 103.7 ($J_{H1\text{-}C1}$ = 157 Hz, 1,2-*trans*); Data for the minor stereoisomer (1,2-*cis*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.44 – 7.22 (m, 15H), 4.89 (d, *J* = 11.8 Hz, 1H, C*H*H Bn), 3.88 (qd, *J* = 6.4, 0.9 Hz, 1H, H-5), 3.71 – 3.61 (m, 2H, C*H*H Et, H-3/H-4), 1.25 – 1.20 (m, 3H, CH_3 Et), 1.10 (d, *J* = 6.5 Hz, 2H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 139.2, 138.8, 138.8 ($C_{q\text{-}arom}$), 128.5, 128.4, 128.3, 128.1, 127.7, 127.6, 127.5 (CH_{arom}), 97.2 (C-1), 79.6, 78.0 (C-3/C-4), 76.6 (C-2), 74.9, 73.5, 73.4 (CH_2 Bn), 66.2 (C-5), 63.3 (CH_2 Et), 16.8 (CH_3 Et), 15.2 (CH_3); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 97.2 ($J_{H1\text{-}C1}$ = 167 Hz, 1,2-*cis*); HRMS: $[M+Na]^+$ calcd for $C_{29}H_{34}O_5$ 485.2304, found 485.2307.

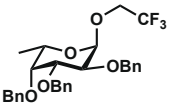


2-Fluoroethyl 2,3,4-tri-*O*-benzyl-L-fucopyranoside (S2). The title compound was prepared according to general procedure I. The reaction was quenched after 2 h. Flash column chromatography (97:3 → 85:15, pentane:EtOAc) afforded the title compound (48 mg, 100 µmol, *quant.*, colorless oil, 1,2-*cis*:1,2-*trans*; 40:60). TLC: R_f 0.32, 0.40 (pentane:EtOAc, 85:15, v:v); IR (thin film, cm^{-1}): 694, 732, 913, 1027, 1042, 1089, 1360, 1497, 2919; Data for the major stereoisomer (1,2-*trans*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.44 – 7.21 (m, 15H, CH_{arom}), 5.03 – 4.45 (m, 8H, CH_2 Bn, CH_2 Bn, CH_2 Bn, $CH_2C\mathit{H}_2F$), 4.38 (d, *J* = 7.7 Hz, 1H, H-1), 4.16 – 4.01 (m, 1H, $C\mathit{H}_2CH_2F$), 3.90 – 3.72 (m, 1H, H-2), 3.55 (dd, *J* = 3.0, 1.0 Hz, 1H, H-4), 3.51 (dd, *J* = 9.7, 2.9 Hz, 1H, H-3), 3.45 (qd, *J* = 6.4, 0.8 Hz, 1H, H-5), 1.16 (d, *J* = 6.4 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 138.8, 138.7, 138.6 ($C_{q\text{-}arom}$), 128.7, 128.5, 128.4, 128.3, 127.7, 127.7, 127.6 (CH_{arom}), 104.1 (C-1), 82.9 (d, *J* = 169.5 Hz, $CH_2\mathit{CH}_2F$), 82.5 (C-3), 79.4 (C-2), 76.2 (C-4), 75.3, 74.6, 73.4 (CH_3 Bn), 70.5 (C-5), 68.6 (d, *J* = 20.1 Hz, CH_2CH_2F), 16.9 (CH_3); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 104.1 ($J_{H1\text{-}C1}$ = 158 Hz, 1,2-*trans*); Data for the minor stereoisomer (1,2-*cis*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.44 – 7.21 (m, 15H, CH_{arom}), 4.05 (dd, *J* = 10.1, 3.6 Hz, 1H, H-2), 4.01 – 3.88 (m, 2H, H-4, H-5), 1.10 (d, *J* = 6.5 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 139.1, 138.7, 138.7 ($C_{q\text{-}arom}$), 128.6, 128.5, 128.4, 128.3, 128.2, 127.8, 127.6 (CH_{arom}), 98.0 (C-1), 82.8 (d, *J* = 169.4 Hz, $CH_2\mathit{CH}_2F$), 79.4 (C-4), 77.8 (C-3), 76.4 (C-2), 75.0, 73.5, 73.5 (CH_2 Bn), 67.0 (d, *J* = 20.1 Hz, CH_2CH_2F), 66.4 (C-5), 16.7 (CH_3); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 98.0 ($J_{H1\text{-}C1}$ = 168 Hz, 1,2-*cis*); HRMS: $[M+Na]^+$ calcd for $C_{29}H_{33}FO_5$ 503.2210, found 503.2217.

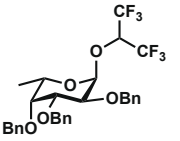


2,2-Difluoroethyl 2,3,4-tri-*O*-benzyl-L-fucopyranoside (S3). The title compound was prepared according to general procedure I. The reaction was quenched after 2 h. Flash column chromatography (97:3 → 85:15, pentane:EtOAc) afforded the title compound (41 mg, 82 µmol, 82%, colorless oil, 1,2-*cis*:1,2-*trans*; 67:33). TLC: R_f 0.29, 0.42 (pentane:EtOAc, 90:10, v:v); IR (thin film, cm^{-1}): 695, 732, 1027, 1047, 1097, 1168, 1361, 1453, 1497, 2934; Data for the major stereoisomer (1,2-*cis*): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.42 – 7.24 (m, 15H, CH_{arom}), 6.07 – 5.79 (m, 1H, CHF_2), 4.98 (d, *J* = 11.6 Hz, 1H, C*H*H Bn), 4.89 – 4.80 (m, 2H, CH_2 Bn), 4.79 – 4.70 (m, 1H, C*H*H Bn), 4.73 (d, *J* = 3.7 Hz, 1H, H-1), 4.70 – 4.62 (m, 2H, CH*H* Bn, CH*H* Bn), 4.05 (dd, *J* = 10.2, 3.7 Hz, 1H, H-2), 3.92 (dd, *J* = 10.2, 2.9 Hz, 1H, H-3), 3.88 (q, *J* = 6.5 Hz, 1H, H-5), 3.71 (ddd, *J* = 14.3, 12.9, 4.4 Hz, 2H, CH_2CHF_2) 3.66 (m, 1H, H-4), 1.11 (d, *J* = 6.5 Hz, 3H, CH_3); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 138.9, 138.6, 138.6 ($C_{q\text{-}arom}$), 128.5, 128.5, 128.5, 128.3, 128.1, 127.7, 127.6 (CH_{arom}), 114.3 (t, *J* = 241.2 Hz, $CH_2\mathit{CH}F_2$) , 98.7 (C-1), 79.2 (C-3), 77.7 (C-4), 76.3 (C-2), 75.0, 73.7, 73.5 (CH_2 Bn), 67.3 (t, *J* = 28.8 Hz), 66.9 (C-5) 16.6 (CH_3); ^{13}C-GATED NMR (126 MHz, $CDCl_3$): δ 98.7 ($J_{H1\text{-}C1}$ = 170 Hz, 1,2-*cis*); Data for the minor stereoisomer (1,2-*trans*): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.42 – 7.24 (m, 15H, CH_{arom}), 6.07 – 5.79 (m, 1H, CHF_2), 4.37 (d, *J* = 7.7 Hz, 1H, H-1), 3.83 (dd, *J* = 9.7, 7.6 Hz, 1H, H-2), 3.55 (dd, *J* = 3.0, 1.0 Hz, 1H, H-4), 3.51 (dd, *J* = 9.7, 2.9 Hz, 1H, H-3), 3.45 (t, *J* = 6.4, 1.0 Hz, 1H, H-5), 1.17 (d, *J* = 6.4 Hz, 3H, CH_3); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 138.7, 138.6, 138.5, 128.7, 128.4, 128.4, 128.4, 128.3, 127.9, 127.7, 127.7, 127.6 ($C_{q\text{-}arom}$), 114.5 (dd, *J* = 242.3, 239.4 Hz, $CH_2\mathit{CH}F_2$) (CHF_2), 104.2 (C-1), 82.4

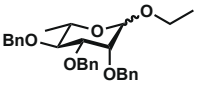
(C-3), 79.2 (C-2), 76.1 (C-4), 75.3, 74.7, 73.4 (CH_3 Bn), 70.7 (C-5), 68.5 (dd, J = 30.9, 26.4 Hz), 16.9 (CH_3); ^{13}C-GATED NMR (126 MHz, $CDCl_3$): δ 104.2 ($J_{H1\text{-}C1}$ = 157 Hz, 1,2-*trans*); HRMS: $[M+Na]^+$ calcd for $C_{29}H_{32}F_2O_5$ 521.2116, found 521.2122.



2,2,2-Trifluoroethyl 2,3,4-tri-*O*-benzyl-1,2-*cis*-L-fucopyranoside (S4). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Flash column chromatography (97:3 → 85:15, pentane:EtOAc) afforded the title compound (46 mg, 89 µmol, 89%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). TLC: R_f 0.55 (pentane:EtOAc, 90:10, v:v); $[\alpha]_D^{20}$ –44.1° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 696, 736, 969, 1045, 1079, 1160, 1276, 1454, 1717, 2916; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.47 – 7.18 (m, 15H, CH_{arom}), 4.98 (d, J = 11.5 Hz, 1H, C*H*H Bn), 4.88 (d, J = 11.8 Hz, 1H, C*H*H Bn), 4.85 – 4.79 (m, 2H, H-1, CH*H* Bn), 4.74 (d, J = 11.7 Hz, 1H, CH*H* Bn), 4.65 (dd, J = 11.7, 4.5 Hz, 2H, C*H*H Bn, CH*H* Bn), 4.07 (dd, J = 10.1, 3.7 Hz, 1H, H-2), 3.98 – 3.81 (m, 4H, H-3, H-5, C*H*HCF$_3$, CH*H*CF$_3$), 3.67 (dd, J = 2.9, 1.2 Hz, 1H, H-4), 1.11 (d, J = 6.5 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 138.9, 138.6, 138.5 ($C_{q\text{-}arom}$), 128.6, 128.5, 128.5, 128.4, 128.1, 127.9, 127.8, 127.7, 127.6 (CH_{arom}), 98.6 (C-1), 79.0 (C-3), 77.6 (C-4), 76.2 (C-2), 75.0, 73.6, 73.5 (CH_2 Bn), 67.2 (C-5), 64.9 (q, J = 34.7 Hz, *C*H$_2$CF$_3$), 16.6 (CH_3); ^{13}C-GATED NMR (101 MHz, $CDCl_3$) δ 98.6 ($J_{H1\text{-}C1}$= 170 Hz, 1,2-*cis*); HRMS: $[M+Na]^+$ calcd for $C_{29}H_{31}F_3O_5$ 539.2021, found 539.2026.

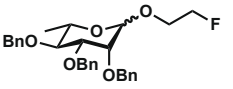


1,1,1,3,3,3-Hexafluoro-2-propyl 2,3,4-tri-*O*-benzyl-1,2-*cis*-L-fucopyranoside (S5). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Flash column chromatography (97:3 → 85:15, pentane:EtOAc) afforded the title compound (19 mg, 33 µmol, 33%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). TLC: R_f 0.48 (pentane:EtOAc, 95:5, v:v); $[\alpha]_D^{20}$ –22.6° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 960, 1071, 1105, 1143, 12201, 1290, 1375, 1440, 2915; ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated, NOESY): δ 7.72 – 7.13 (m, 15H, CH_{arom}), 5.13 (d, J = 3.9 Hz, 1H, H-1), 4.98 (d, J = 11.5 Hz, 1H, C*H*H Bn), 4.87 (d, J = 11.6 Hz, 1H, C*H*H Bn), 4.79 – 4.67 (m, 3H, CH*H* Bn, CH*H* Bn, C*H*H Bn), 4.65 (d, J = 11.5 Hz, 1H, CH*H* Bn), 4.45 (hept, J = 6.0 Hz, 1H, CH(CF$_3$)$_2$), 4.13 (dd, J = 10.3, 3.9 Hz, 1H, H-2), 4.01 – 3.89 (m, 2H, H-3, H-5), 3.71 (dd, J = 2.8, 1.2 Hz, 1H, H-4); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 138.8, 138.4, 138.2 ($C_{q\text{-}arom}$), 128.6, 128.5, 128.5, 128.4, 128.1, 127.9, 127.9, 127.7, 127.6 (CH_{arom}), 100.1 (C-1), 78.8 (C-3), 77.3 (C-4), 75.4 (C-2), 75.0 (CH_2 Bn), 73.5 (CH_2 Bn, CH_2 Bn), 72.6 (dt, J = 65.0, 32.4 Hz, *C*H(CF$_3$)$_2$), 68.3 (C-5), 16.5 (CH_3); ^{13}C-GATED NMR (126 MHz, $CDCl_3$) δ 100.1 ($J_{H1\text{-}C1}$= 174 Hz, 1,2-*cis*); HRMS: $[M+Na]^+$ calcd for $C_{29}H_{31}F_3O_5$ 539.2021, found 539.2026.

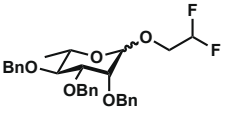


Ethyl 2,3,4-tri-*O*-benzyl-L-rhamnopyranoside (S6). The title compound was prepared according to general procedure I. The reaction was quenched after 2 h. Flash column chromatography (97:3 → 85:15, pentane:EtOAc) afforded the title compound (40 mg, 86 µmol, 86%, colorless oil, 1,2-*cis*:1,2-*trans*; 54:46). TLC: R_f 0.53, 0.69 (pentane:EtOAc, 90:10, v:v); IR (thin film, cm^{-1}): 695, 733, 1027, 1061, 1103, 1309, 1363, 1497, 2922; NMR data reported as a mixture of 1,2-*cis*:1,2-*trans* (54:46) anomers; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.51 – 7.23 (m, 34.5H), 5.01 – 4.92 (m, 3H, C*H*H Bn, C*H*H Bn, C*H*H Bn), 4.89 (d, J = 12.6 Hz, 1H, CH*H* Bn), 4.78 – 4.73 (m, 3H, CH_2 Bn, H-1$_{1,2\text{-}trans}$), 4.64 (d, J = 11.0 Hz, 5H, CH*H* Bn, CH*H* Bn, CH_2 Bn), 4.50 (d, J = 11.9 Hz, 1H, C*H*H Bn), 4.43 (d, J = 11.9 Hz, 1H, CH*H* Bn), 4.34 (d, J = 0.7 Hz, 1H, H-1$_{1,2\text{-}cis}$), 3.98 (dq, J = 9.3, 7.1 Hz, 1H, C*H*H Et$_{1,2\text{-}cis}$), 3.91 – 3.86 (m, 2.26H, H-2$_{1,2\text{-}cis}$, H-3$_{1,2\text{-}trans}$), 3.79 (dd, J = 3.2, 1.8 Hz, 1.3H, H-2$_{1,2\text{-}trans}$), 3.75 – 3.56 (m, 4.8H, H-4$_{1,2\text{-}cis}$, H-4$_{1,2\text{-}trans}$, H-5$_{1,2\text{-}trans}$, C*H*H Et$_{1,2\text{-}trans}$), 3.52 – 3.43 (m, 2H, H-3$_{1,2\text{-}cis}$, CH*H* Et$_{1,2\text{-}cis}$), 3.39 (dq, J = 9.7, 7.1 Hz, 1.26H, CH*H* Et$_{1,2\text{-}trans}$), 3.31 (dq, J = 9.2, 6.1 Hz, 1H, H-5$_{1,2\text{-}cis}$), 1.38 (d, J = 6.2 Hz, 3H, $CH_{3\text{-}1,2\text{-}cis}$), 1.33 (d, J = 6.1 Hz, 3.8H,

$CH_{3\text{-}1,2\text{-}trans}$), 1.26 (t, J = 7.0 Hz, 3H, CH_3 $Et_{1,2\text{-}cis}$), 1.14 (t, J = 7.1 Hz, 3.8H, CH_3 $Et_{1,2\text{-}trans}$); ^{13}C NMR (101 MHz, $CDCl_3$ HSQC, HMBC-Gated): δ 138.9, 138.8, 138.7, 138.6, 138.5, 138.4 ($C_{q\text{-}arom}$), 128.6, 128.5, 128.5, 128.2, 128.2, 128.2, 128.0, 127.8, 127.8, 127.7, 127.7, 127.7, 127.6, 127.6, 127.5 (CH_{arom}), 101.4 (C-$1_{1,2\text{-}cis}$), 97.8 (C-$1_{1,2\text{-}trans}$), 82.3 (C-$3_{1,2\text{-}cis}$), 80.7, 80.4, 80.3 (C-$2_{1,2\text{-}cis}$/C-$4_{1,2\text{-}cis}$/C-$4_{1,2\text{-}trans}$), 75.6 (CH_2 Bn, CH_2 Bn), 75.0 (C-$2_{1,2\text{-}trans}$), 73.9 (CH_2 Bn), 73.9 (C-$3_{1,2\text{-}trans}$), 72.9, 72.2 (CH_2 Bn), 72.0 (C-$5_{1,2\text{-}cis}$), 71.4 (CH_2 Bn), 68.0 (C-$5_{1,2\text{-}trans}$), 65.3 (CH_2 $Et_{1,2\text{-}cis}$), 62.9 (CH_2 $Et_{1,2\text{-}trans}$), 18.1 ($CH_{3\text{-}1,2\text{-}cis}$, $CH_{3\text{-}1,2\text{-}trans}$), 15.4 ($CH_3$ $Et_{1,2\text{-}cis}$), 15.1 (CH_3 $Et_{1,2\text{-}trans}$); GATED NMR (101 MHz, $CDCl_3$): δ 101.4 ($J_{H1\text{-}C1}$ = 152 Hz, 1,2-*cis*); 97.8 ($J_{H1\text{-}C1}$ = 167 Hz, 1,2-*trans*); HRMS: $[M+Na]^+$ calcd for $C_{29}H_{34}O_5$ 485.2304, found 485.2314.

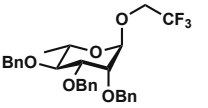


2-Fluoroethyl 2,3,4-tri-*O*-benzyl-L-rhamnopyranoside (S7). The title compound was prepared according to general procedure I. The reaction was quenched after 2 h. Flash column chromatography (97:3 → 85:15, pentane:EtOAc) afforded the title compound (44 mg, 92 µmol, 92%, colorless oil, 1,2-*cis*:1,2-*trans*; 77:23). TLC: R_f 0.42, 0.56 (pentane:EtOAc, 85:15, v:v); IR (thin film, cm^{-1}): 696, 731, 1028, 1072, 1154, 1308, 1449, 1719, 2908; Data for the major stereoisomer (1,2-*cis*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.68 – 7.21 (m, 15H, CH_{arom}), 5.00 – 4.85 (m, 4H, C*H*H Bn, CH_2 Bn), 4.79 – 4.39 (m, 6H, CH*H* Bn, CH_2 Bn, H-1, CH2CH_2F), 4.09 (dddd, J = 35.8, 12.1, 3.9, 2.4 Hz, 1H, C*H*HCH$_2$F), 3.95 (dd, J = 3.0, 0.6 Hz, 1H, H-2), 3.67 – 3.55 (m, 1H, H-4), 3.45 (dd, J = 9.4, 3.1 Hz, 1H, H-3), 3.31 (dp, J = 9.2, 6.0 Hz, 1H, H-5), 1.38 (d, J = 6.2 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 138.7, 138.5, 138.2 ($C_{q\text{-}arom}$), 131.2, 129.4, 128.6, 128.5, 128.5, 128.2, 128.2, 127.7, 124.9 (CH_{arom}), 101.6 (C-1), 83.0 (d, J = 169.3 Hz, CH_2CH_2F), 82.1 (C-3), 80.1 (C-4), 75.6, 74.1 (CH_2 Bn), 73.8 (C-2), 72.1 (C-5), 71.5 (CH_2 Bn), 68.6 (d, J = 19.6 Hz, CH_2CH$_2$F), 18.1 (CH_3); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 101.6 ($J_{H1\text{-}C1}$ = 154 Hz, 1,2-*cis*); Data for the minor stereoisomer (1,2-*trans*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.68 – 7.21 (m, 15H, CH_{arom}), 4.81 (d, J = 1.8 Hz, 1H, H-1), 3.89 (dd, J = 9.1, 3.2 Hz, 1H, H-3), 1.33 (d, J = 6.1 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 138.7, 138.6, 138.4 ($C_{q\text{-}arom}$), 128.6, 128.6, 128.2, 128.1, 128.0, 127.8, 127.8, 127.8, 127.7, 127.6, 127.6 (CH_{arom}), 98.3 (C-1), 82.6 (d, J = 169.7 Hz, CH_2CH_2F), 80.5 (C-4), 80.2 (C-3), 75.5 (CH_2 Bn), 74.9 (C-2), 73.0, 72.3 (CH_2 Bn), 68.3 (C-5), 66.4 (d, J = 19.9 Hz, CH_2CH$_2$F), 18.1 (CH_3); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 98.3 ($J_{H1\text{-}C1}$ = 170 Hz, 1,2-*trans*); HRMS: $[M+Na]^+$ calcd for $C_{29}H_{33}FO_5$ 503.2210, found 503.2216.

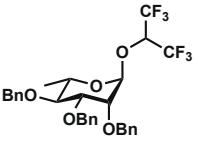


2,2-Difluoroethyl 2,3,4-tri-*O*-benzyl-L-rhamnopyranoside (S8). The title compound was prepared according to general procedure I. The reaction was quenched after 2 h. Flash column chromatography (97:3 → 85:15, pentane:EtOAc) afforded the title compound (35 mg, 70 µmol, 70%, colorless oil, 1,2-*cis*:1,2-*trans*; 30:70). TLC: R_f 0.35, 0.52 (pentane:EtOAc, 90:10, v:v); IR (thin film, cm^{-1}): 697, 736, 1028, 1068, 1146, 1363, 1454, 1729, 2891; NMR data reported as a mixture of 1,2-*cis*:1,2-*trans* (30:70) anomers; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.39 – 7.26 (m, 49.6H, CH_{arom}), 5.92 (dddd, J = 56.4, 54.7, 5.6, 2.8 Hz, 1H, $CH_2CHF_{2\text{-}1,2\text{-}cis}$), 5.81 (tdd, J = 55.4, 4.6, 3.7 Hz, 2.3H, $CH_2CHF_{2\text{-}1,2\text{-}trans}$), 4.99 – 4.90 (m, 4.3H, C*H*H $Bn_{1,2\text{-}cis}$, C*H*H $Bn_{1,2\text{-}cis}$, C*H*H $Bn_{1,2\text{-}trans}$), 4.85 (d, J = 12.5 Hz, 1H, CH*H* $Bn_{1,2\text{-}cis}$), 4.80 – 4.74 (m, 4.6H, C*H*H $Bn_{1,2\text{-}trans}$, H-$1_{1,2\text{-}trans}$), 4.70 (d, J = 12.4 Hz, 2.3H, CH*H* $Bn_{1,2\text{-}trans}$), 4.67 – 4.53 (m, 7.8H, CH*H* $Bn_{1,2\text{-}cis}$, CH*H* $Bn_{1,2\text{-}trans}$, CH_2 $Bn_{1,2\text{-}trans}$), 4.52 (d, J = 11.9 Hz, 1H, C*H*H $Bn_{1,2\text{-}cis}$), 4.46 (d, J = 11.8 Hz, 1H, CH*H* $Bn_{1,2\text{-}cis}$), 4.41 (d, J = 0.8 Hz, 1H, H-$1_{1,2\text{-}cis}$), 4.04 (dddd, J = 21.7, 11.6, 10.2, 2.8 Hz, 1H, C*H*HCHF$_{2\text{-}1,2\text{-}cis}$), 3.93 (dd, J = 3.0, 0.8 Hz, 1H, H-$2_{1,2\text{-}cis}$), 3.87 – 3.55 (m, 18H, H-$4_{1,2\text{-}cis}$, H-$2_{1,2\text{-}trans}$, H-$3_{1,2\text{-}trans}$, H-$4_{1,2\text{-}trans}$, H-$5_{1,2\text{-}trans}$, C*H*HCHF$_{2\text{-}1,2\text{-}trans}$, CH*H*CHF$_{2\text{-}1,2\text{-}trans}$), 3.45 (dd, J = 9.4, 3.0 Hz, 1H, H-$3_{1,2\text{-}cis}$), 3.45 – 3.35 (m, 1H, CH*H*CHF$_{2\text{-}1,2\text{-}cis}$), 3.32 (dq, J = 9.2, 6.1 Hz, 1H, H-$5_{1,2\text{-}cis}$), 1.38 (d, J = 6.1 Hz, 3H, $CH_{3\text{-}1,2\text{-}cis}$), 1.33 (d, J = 5.9 Hz, 6.8H, $CH_{3\text{-}1,2\text{-}trans}$); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 138.6, 138.5 ($C_{q\text{-}arom\text{-}1,2\text{-}trans}$), 138.5, 138.4 ($C_{q\text{-}arom\text{-}1,2\text{-}cis}$), 138.2 ($C_{q\text{-}arom\text{-}1,2\text{-}trans}$), 138.2 ($C_{q\text{-}arom\text{-}1,2\text{-}cis}$), 128.9, 128.6, 128.6, 128.5, 128.5, 128.3, 128.2, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7, 127.7, 127.7 (CH_{arom}), 114.4 (dd, J = 242.0, 239.8 Hz, $CH_2CHF_{2\text{-}1,2\text{-}cis}$), 114.1 (t, J = 241.2 Hz, $CH_2CHF_{2\text{-}1,2\text{-}trans}$), 101.7 (C-$1_{1,2\text{-}cis}$), 98.9 (C-$1_{1,2\text{-}trans}$), 82.0 (C-$3_{1,2\text{-}cis}$), 80.3 (C-$4_{1,2\text{-}trans}$), 80.0 (C-$4_{1,2\text{-}cis}$), 79.9 (C-$3_{1,2\text{-}trans}$), 75.6 ($CH_2$ $Bn_{1,2\text{-}cis}$), 75.6 (CH_2 $Bn_{1,2\text{-}trans}$), 74.7 (C-$2_{1,2\text{-}trans}$), 74.2 (CH_2 $Bn_{1,2\text{-}cis}$), 73.7 (C-$2_{1,2\text{-}cis}$), 73.1, 72.4 (CH_2 $Bn_{1,2\text{-}trans}$), 72.3 (C-

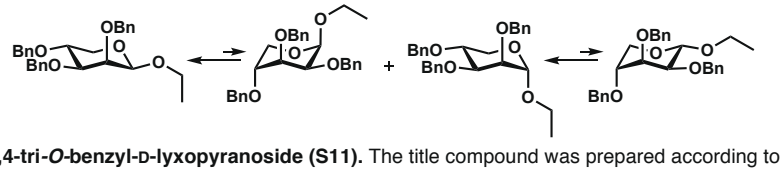
$5_{1,2\text{-}cis}$), 71.7 (CH_2 $Bn_{1,2\text{-}cis}$), 68.7 (C-$5_{1,2\text{-}trans}$),68.4 (dd, *J* = 30.6, 26.0 Hz, $CH_2CHF_{2\text{-}1,2\text{-}cis}$), 66.5 (t, *J* = 28.2 Hz, $CH_2CHF_{2\text{-}1,2\text{-}trans}$), 18.1 ($CH_{3\text{-}1,2\text{-}cis}$), 18.0 ($CH_{3\text{-}1,2\text{-}trans}$); GATED NMR (101 MHz, $CDCl_3$): δ 101.7 ($J_{H1\text{-}C1}$ = 155 Hz, 1,2-*cis*); 98.9 ($J_{H1\text{-}C1}$ = 170 Hz, 1,2-*trans*); HRMS: $[M+Na]^+$ calcd for $C_{29}H_{32}F_2O_5$ 521.2116, found 521.2126.



2,2,2-Trifluoroethyl 2,3,4-tri-*O*-benzyl-L-rhamnopyranoside (S9). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Flash column chromatography (97:3 → 85:15, pentane:EtOAc) afforded the title compound (49 mg, 95 µmol, 95%, colorless oil, 1,2-*cis*:1,2-*trans*; 8:92). TLC: R_f 0.66 (pentane:EtOAc, 90:10, v:v); IR (thin film, cm^{-1}): 696, 735, 982, 1028, 1084, 1162, 1277, 1454, 2893; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC, HMBC-Gated): δ 7.48 – 7.10 (m, 15H, CH_{arom}), 4.93 (d, *J* = 10.9 Hz, 1H, C*H*H Bn), 4.82 (d, *J* = 1.4 Hz, 1H, H-1), 4.78 (d, *J* = 12.3 Hz, 1H, C*H*H Bn), 4.69 (d, *J* = 12.5 Hz, 1H, CH*H* Bn), 4.66 – 4.60 (m, 3H, CH*H* Bn, C*H*H Bn, CH*H* Bn), 3.99 – 3.74 (m, 4H, H-2, H-3, C*H*HCF$_3$, CH*H*CF$_3$), 3.75 – 3.58 (m, 2H, H-4, H-5); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 138.5, 138.5, 138.1 ($C_{q\text{-}arom}$), 128.5, 128.5, 128.2, 128.0, 127.9, 127.9, 127.8, 127.8 (CH_{arom}), 98.8 (C-1), 80.2 (C-4), 79.8 (C-3), 75.6 (CH_2 Bn), 74.7 (C-2), 73.3, 72.5 (CH_2 Bn), 69.0 (C-5), 64.1 (q, *J* = 34.9 Hz, CH_2CF_3), 18.1 (CH_3); ^{13}C-GATED NMR (126 MHz, $CDCl_3$): δ 98.8 ($J_{H1\text{-}C1}$ = 170 Hz, 1,2-*trans*); HRMS: $[M+Na]^+$ calcd for $C_{29}H_{31}F_3O_5$ 539.2021, found 539.2021.

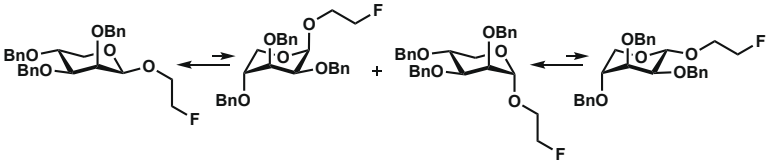


1,1,1,3,3,3-Hexafluoro-2-propyl 2,3,4-tri-*O*-benzyl-1,2-*trans*-L-rhamnopyranoside (S10). The title compound was prepared according to general procedure I. The reaction was quenched after 112 h. Flash column chromatography (100:0 → 80:20, pentane:Et_2O) afforded the title compound (27 mg, 46 µmol, 46%, white solid, 1,2-*cis*:1,2-*trans*; <2:98). TLC: R_f 0.45 (pentane:EtOAc, 95:5, v:v); $[\alpha]_D^{20}$ –20.0° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 685, 696, 966, 1073, 1100, 1146, 1196, 1220, 1287, 1366, 1449, 2917; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated, ^1H-^{19}F Decoupled): δ 7.38 – 7.26 (m, 15H, CH_{arom}), 4.94 (d, *J* = 2.1 Hz, 1H, H-1), 4.87 (d, *J* = 10.8 Hz, 1H, C*H*H Bn), 4.76 (d, *J* = 12.2 Hz, 1H, C*H*H Bn), 4.65 (dd, *J* = 11.7, 2.7 Hz, 3H, CH_2 Bn, CH*H* Bn), 4.59 (d, *J* = 10.9 Hz, 1H, CH*H* Bn), 4.38 (hept, *J* = 6.0 Hz, 1H, C*H*$(CF_3)_2$), 3.86 – 3.72 (m, 3H, H-2, H-3, H-5), 3.62 (t, *J* = 9.0 Hz, 1H, H-4), 1.30 (d, *J* = 6.1 Hz, 3H, CH_3); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 138.3, 138.3, 137.8 ($C_{q\text{-}arom}$), 129.6, 128.9, 128.6, 128.6, 128.2, 128.2, 128.1, 128.0, 127.9, 127.9, 127.7 (CH_{arom}), 100.9 (C-1), 80.0 (C-4), 79.1 (C-3), 75.3 (CH_2 Bn), 74.8 (C-2), 73.5, 72.8 (CH_2 Bn), 72.2 (p, *J* = 33.0 Hz), 70.0 (C-5), 18.0 (CH_3); ^{13}C-GATED NMR (126 MHz, $CDCl_3$): δ 100.9 ($J_{H1\text{-}C1}$ = 174 Hz, 1,2-*trans*); HRMS: $[M+Na]^+$ calcd for $C_{30}H_{30}F_6O_5$ 607.1895, found 607.1911.

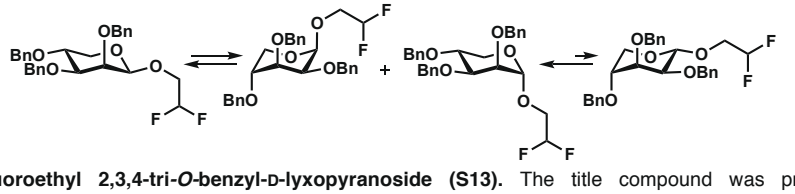


Ethyl 2,3,4-tri-*O*-benzyl-D-lyxopyranoside (S11). The title compound was prepared according to general procedure I. The reaction was quenched after 2 h. Flash column chromatography (97:3 → 85:15, pentane:EtOAc) afforded the title compound (39 mg, 87 µmol, 87%, colorless oil, 1,2-*cis*:1,2-*trans*; 53:47). TLC: R_f 0.31, 0.55 (pentane:EtOAc, 90:10, v:v); IR (thin film, cm^{-1}): 694, 732, 907, 1089, 1308, 1362, 2903; NMR data reported as a mixture of 1,2-*cis*:1,2-*trans* (53:47) anomers: ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC, HMBC-Gated): δ 7.48 – 7.25 (m, 30H, $CH_{arom\text{-}1,2\text{-}cis}$, $CH_{arom\text{-}1,2\text{-}trans}$), 4.84 (d, *J* = 12.4 Hz, 1H, C*H*H Bn), 4.79 (d, *J* = 12.4 Hz, 1H, CH*H* Bn), 4.76 – 4.67 (m, 7H, CH_2 Bn, CH_2 Bn, CH_2 Bn, H-$1_{1,2\text{-}trans}$), 4.67 – 4.52 (m, 4H, CH_2 Bn, CH_2 Bn), 4.47 (d, *J* = 1.8 Hz, 1H, H-$1_{1,2\text{-}cis}$), 4.05 (dd, *J* = 11.7, 4.4 Hz, 1H, H-

5$_{eq\text{-}1,2\text{-}cis}$), 3.98 – 3.81 (m, 5H, H-2$_{1,2\text{-}cis}$, H-3$_{1,2\text{-}cis}$, H-4$_{1,2\text{-}cis}$, H-4$_{1,2\text{-}trans}$, C*H*HCH$_3$ Et$_{1,2\text{-}trans}$), 3.80 – 3.68 (m, 3H, H-2$_{1,2\text{-}trans}$, H-5$_{1,2\text{-}trans}$, C*H*HCH$_3$ Et$_{1,2\text{-}cis}$), 3.59 – 3.46 (m, 3H, H-3$_{1,2\text{-}trans}$, H-5$_{1,2\text{-}trans}$, CH*H*CH$_3$ Et$_{1,2\text{-}trans}$), 3.42 (dq, *J* = 9.6, 7.1 Hz, 1H, CH*H*CH$_3$ Et$_{1,2\text{-}cis}$), 3.23 (dd, *J* = 11.8, 7.7 Hz, 1H, H-5$_{ax\text{-}1,2\text{-}cis}$), 1.26 (t, *J* = 7.1 Hz, 3H, CH$_3$ Et$_{1,2\text{-}cis}$), 1.17 (t, *J* = 7.1 Hz, 3H, CH$_3$ Et$_{1,2\text{-}trans}$); ^{13}C NMR (101 MHz, CDCl$_3$, HSQC, HMBC, HMBC-Gated): δ 138.9, 138.7, 138.6, 138.6, 138.5 (C$_{q\text{-}arom}$), 128.5, 128.4, 128.4, 128.4, 128.3, 128.0, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 127.6 (CH$_{arom}$), 100.5 (C-1$_{1,2\text{-}trans}$), 98.7 (C-1$_{1,2\text{-}cis}$), 79.2 (C-2$_{1,2\text{-}cis}$/C-3$_{1,2\text{-}cis}$/C-4$_{1,2\text{-}cis}$/C-4$_{1,2\text{-}trans}$), 79.1 (C-3$_{1,2\text{-}trans}$), 75.7 (C-2$_{1,2\text{-}trans}$), 75.0 (C-2$_{1,2\text{-}cis}$/C-3$_{1,2\text{-}cis}$/C-4$_{1,2\text{-}cis}$/C-4$_{1,2\text{-}trans}$), 74.9 (C-2$_{1,2\text{-}cis}$/C-3$_{1,2\text{-}cis}$/C-4$_{1,2\text{-}cis}$/C-4$_{1,2\text{-}trans}$), 74.3 (C-2$_{1,2\text{-}cis}$/C-3$_{1,2\text{-}cis}$/C-4$_{1,2\text{-}cis}$/C-4$_{1,2\text{-}trans}$), 73.4, 73.3, 73.3, 73.0, 72.8, 72.2 (CH$_2$ Bn), 64.8 (*CH*$_2$CH$_3$ Et$_{1,2\text{-}trans}$), 63.4 (*CH*$_2$CH$_3$ Et$_{1,2\text{-}cis}$), 62.7 (C-5$_{1,2\text{-}cis}$), 61.6 (C-5$_{1,2\text{-}trans}$), 15.4 (CH$_3$ Et$_{1,2\text{-}trans}$), 15.2 (CH$_3$ Et$_{1,2\text{-}cis}$); ^{13}C-GATED NMR (101 MHz, CDCl$_3$): δ 100.5 (*J*$_{H1\text{-}C1}$ = 157 Hz, 1,2-*cis*), δ 98.7 (*J*$_{H1\text{-}C1}$ = 169 Hz, 1,2-*trans*); HRMS: [M+Na]$^+$ calcd for $C_{28}H_{32}O_5$ 471.2147, found 471.2153.

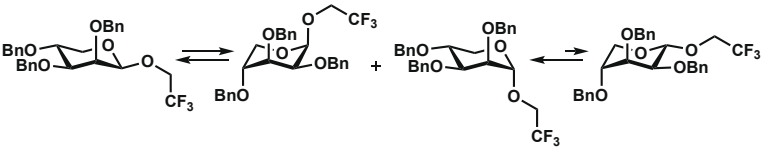


2-Fluoroethyl 2,3,4-tri-*O*-benzyl-D-lyxopyranoside (S12). The title compound was prepared according to general procedure I. The reaction was quenched after 2 h. Flash column chromatography (97:3 → 85:15, pentane:EtOAc) afforded the title compound (47 mg, 100 µmol, *quant.*, colorless oil, 1,2-*cis*:1,2-*trans*; 73:27). TLC: R$_f$ 0.26, 0.46 (pentane:EtOAc, 85:15, v:v); IR (thin film, cm^{-1}): 694, 732, 1042, 1088, 1453, 1722, 2916; ^{1}H NMR (400 MHz, CDCl$_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.71 – 7.19 (m, 15H, CH$_{arom}$), 4.85 – 4.44 (m, 8H, CH$_2$ Bn, CH$_2$ Bn, CH$_2$ Bn, H-1, CH$_2$C*H*HF, CH$_2$CH*H*F), 4.12 – 4.00 (m, 1H, H-5$_{eq}$), 4.00 – 3.69 (m, 4H, H-2, H-4, C*H*HCH$_2$F, CH*H*CH$_2$F), 3.57 (dd, *J* = 7.3, 3.1 Hz, 1H, H-3), 3.27 (dd, *J* = 11.9, 7.2 Hz, 1H, H-5$_{ax}$); ^{13}C NMR (101 MHz, CDCl$_3$, HSQC, HMBC-Gated): δ 138.6, 138.5, 138.4 (C$_{q\text{-}arom}$), 131.1, 129.4, 128.5, 128.4, 128.4, 128.3, 127.8, 127.7, 127.7, 124.9 (CH$_{arom}$), 100.6 (C-1), 83.0 (d, *J* = 169.4 Hz, CH$_2$*CH*$_2$F), 78.4 (C-3), 74.7 (C-4), 74.1 (C-2), 73.4, 72.9, 72.2 (CH$_2$ Bn), 68.1 (d, *J* = 20.0 Hz, *CH*$_2$CH$_2$F), 62.3 (C-5); ^{13}C-GATED NMR (101 MHz, CDCl$_3$): δ 100.6 (*J*$_{H1\text{-}C1}$ = 158 Hz, 1,2-*cis*); Data for the minor stereoisomer (1,2-*trans*): ^{1}H NMR (400 MHz, CDCl$_3$, HH-COSY, HSQC, HMBC-Gated): all signals overlap with 1,2-*trans* anomer peaks; ^{13}C NMR (101 MHz, CDCl$_3$, HSQC, HMBC-Gated): δ 138.7, 138.5, 138.4 (C$_{q\text{-}arom}$), 128.5, 128.4, 128.4, 128.0, 127.8, 127.7, 127.6 (CH$_{arom}$), 99.2 (C-1), 82.6 (d, *J* = 169.7 Hz, CH$_2$*CH*$_2$F), 78.9, 75.5, 74.8 (C-2/C-3/C-4), 66.8 (d, *J* = 19.9 Hz, *CH*$_2$CH$_2$F), 61.7 (C-5); ^{13}C-GATED NMR (101 MHz, CDCl$_3$): δ 99.2 (*J*$_{H1\text{-}C1}$ = 169 Hz, 1,2-*trans*); HRMS: [M+Na]$^+$ calcd for $C_{28}H_{31}FO_5$ 489.2053, found 489.2057.

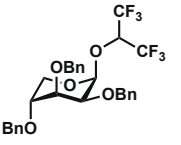


2,2-Difluoroethyl 2,3,4-tri-*O*-benzyl-D-lyxopyranoside (S13). The title compound was prepared according to general procedure I. The reaction was quenched after 2 h. Flash column chromatography (97:3 → 85:15, pentane:EtOAc) afforded the title compound (45 mg, 93 µmol, 93%, colorless oil, 1,2-*cis*:1,2-*trans*; 64:36). TLC: R$_f$ 0.40, 0.44 (pentane:EtOAc, 90:10, v:v); IR (thin film, cm^{-1}): 695, 732, 887, 1062, 1308, 1362, 1453, 1496, 2874; Data for the major stereoisomer (1,2-*cis*): ^{1}H NMR (400 MHz, CDCl$_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.42 – 7.25 (m, 15H, CH$_{arom}$), 5.94 (tdd, *J* = 55.6, 5.1, 3.4 Hz, 1H, CHF$_2$), 4.78 – 4.66 (m, 3H, C*H*H Bn, C*H*H Bn, CH*H* Bn), 4.63 (d, *J* = 12.2 Hz, 1H, C*H*H Bn), 4.60 – 4.53 (m, 3H, CH*H* Bn, CH*H* Bn, H-1), 4.05 (dd, *J* = 12.0, 3.7 Hz, 1H, H-5$_{eq}$), 3.99 – 3.86 (m, 2H, H-2, C*H*HCF$_3$), 3.85 – 3.70 (m, 2H, H-4, CH*H*CF$_3$), 3.61 (dd, *J* = 6.8, 3.2 Hz, 1H, H-3), 3.31 (dd, *J* = 12.0, 6.3 Hz, 1H, H-5$_{ax}$); ^{13}C NMR (101 MHz, CDCl$_3$, HSQC, HMBC-Gated): δ 138.6, 138.3, 138.2 (C$_{q\text{-}arom}$), 128.5, 128.4, 128.4, 128.3, 127.9, 127.7 (CH$_{arom}$), 114.5 (t, *J* = 241.0 Hz), 100.4 (C-1), 77.5 (C-3), 74.7 (C-4), 73.9 (C-2), 73.3, 72.7, 72.5 (CH$_2$ Bn), 68.1 (t, *J* = 28.6 Hz, *CH*$_2$CHF$_2$), 61.7 (C-5); ^{13}C-GATED NMR (101 MHz, CDCl$_3$): δ 100.4 (*J*$_{H1\text{-}C1}$ = 162 Hz, 1,2-*cis*); Data for the minor stereoisomer (1,2-*trans*): ^{1}H NMR (400 MHz, CDCl$_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.42 – 7.25 (m, 15H), 5.85 (tdd, *J* = 55.4, 4.8, 3.6 Hz, 1H, CHF$_2$), 3.55 (dd, *J* = 11.3, 8.3 Hz, 1H, H-5$_{ax}$); ^{13}C NMR (101 MHz, CDCl$_3$, HSQC, HMBC-Gated): δ 138.6, 138.4 (C$_{q\text{-}arom}$), 128.5, 128.5, 128.5,

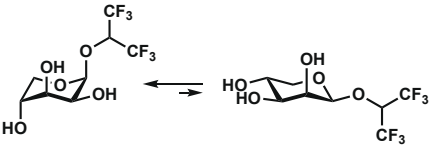
128.1, 127.9, 127.9, 127.8, 127.7, 127.7, 127.7 (CH_{arom}), 114.2 (t, J = 241.1 Hz, CHF_2), 99.8 (C-1), 78.5, 75.4, 74.6 (C-2/C-3/C-4), 73.5, 73.2, 73.0 (CH_2 Bn), 67.0 (t, J = 28.2 Hz, CH_2CHF_2), 62.1 (C-5); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 99.8 ($J_{H1\text{-}C1}$ = 170 Hz, 1,2-*trans*); HRMS: $[M+Na]^+$ calcd for $C_{28}H_{30}F_2O_5$ 507.1959, found 507.1967.



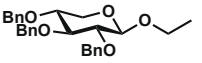
2,2,2-Trifluoroethyl 2,3,4-tri-*O*-benzyl-D-lyxopyranoside (S14). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Flash column chromatography (97:3 → 90:10, pentane:EtOAc) afforded the title compound (31 mg, 62 µmol, 62%, colorless oil, 1,2-*cis*:1,2-*trans*; 59:41). TLC: R_f 0.40, 0.57 (pentane:EtOAc, 90:10, v:v); IR (thin film, cm^{-1}): 697, 736, 986, 1084, 1161, 1278, 1362, 1454, 1497, 2893; Data for the major stereoisomer (1,2-*cis*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.43 – 7.22 (m, 15H, CH_{arom}), 4.81 – 4.58 (m, 6H, CH_2 Bn, CH_2 Bn, C*H*H Bn, H-1) , 4.55 (d, J = 12.2 Hz, 1H, CH*H* Bn), 4.18 – 4.03 (m, 2H, H-5_{eq}, C*H*HCF$_3$), 4.02 – 3.75 (m, 6H, H-2, H-4, CH*H*CF$_3$), 3.62 (dd, J = 6.9, 3.1 Hz, 1H, H-3), 3.32 (dd, J = 12.0, 6.4 Hz, 1H, H-5_{ax}); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 138.6, 138.3, 138.3 ($C_{q\text{-}arom}$), 128.5, 128.4, 128.3, 128.1, 127.9, 127.7 (CH_{arom}), 124.0 (q, J = 278.5 Hz, CF_3), 100.2 (C-1), 77.7 (C-3), 74.9 (C-4), 73.9 (C-2), 73.3, 72.7, 72.5 (CH_2 Bn), 65.6 (q, J = 34.6 Hz), 62.0 (C-5); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 100.2 ($J_{H1\text{-}C1}$ = 163 Hz, 1,2-*cis*); Data for the minor stereoisomer (1,2-*trans*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.43 – 7.22 (m, 15H, CH_{arom}), 3.54 (dd, J = 11.3, 8.5 Hz, 1H, H-5_{ax}); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 138.6, 138.4, 138.2 ($C_{q\text{-}arom}$), 128.5, 128.5, 128.5, 127.9, 127.9, 127.8, 127.8, 127.7, 127.6 (CH_{arom}), 121.1 (d, J = 278.3 Hz, CF_3), 99.7 (C-1), 78.5, 75.3, 74.5 (C-2/C-3/C-4), 73.7, 73.2, 73.1 (CH_2 Bn), 64.5 (q, J = 34.7 Hz, CH_2CF_3), 62.3 (C-5); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 99.7 ($J_{H1\text{-}C1}$ = 170 Hz, 1,2-*trans*); HRMS: $[M+Na]^+$ calcd for $C_{28}H_{29}F_3O_5$ 525.1865, found 525.1872.



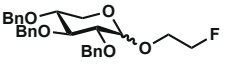
1,1,1,3,3,3-Hexafluoro-2-propyl 2,3,4-tri-*O*-benzyl-1,2-*cis*-D-lyxopyranoside (S15). The title compound was prepared according to general procedure I. The reaction was quenched after 112 h. Flash column chromatography (100:0 → 90:10, pentane:EtOAc) afforded the title compound (26 mg, 46 µmol, 46%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). TLC: R_f 0.32 (pentane:EtOAc, 95:5, v:v); $[\alpha]_D^{20}$ 11.3° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 688, 749, 1103, 1146, 1194, 1219, 1287, 1371, 1454, 2921; ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated, NOESY, ^{1}H-^{19}F Decoupled): δ 7.38 – 7.24 (m, 15H, CH_{arom}), 4.99 (d, J = 2.9 Hz, 1H, H-1), 4.82 (d, J = 11.9 Hz, 1H, C*H*H Bn), 4.75 (d, J = 11.9 Hz, 1H, C*H*H Bn), 4.62 (d, J = 11.9 Hz, 1H, CH*H* Bn), 4.59 – 4.51 (m, 4H, $CH(CF_3)_2$, CH_2 Bn, CH*H* Bn), 4.15 (dd, J = 12.2, 2.3 Hz, 1H, H-5), 3.96 (t, J = 2.7 Hz, 1H, H-2), 3.78 – 3.72 (m, 2H, H-3, H-4), 3.46 (dd, J = 12.3, 4.3 Hz, 1H, H-5); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 138.7, 138.1 ($C_{q\text{-}arom}$), 129.6, 128.9, 128.6, 128.5, 128.4, 128.0, 127.9, 127.6 (CH_{arom}), 99.9 (C-1), 75.9 (C-3), 75.3 (C-4), 73.7 (C-2), 72.8 , 72.8 (CH_2 Bn), 72.5 (C*H*$(CF_3)_2$), 72.3 (CH_2 Bn), 61.3 (C-5); ^{13}C-GATED NMR (126 MHz, $CDCl_3$): δ 99.9 ($J_{H1\text{-}C1}$ = 170 Hz, 1,2-*cis*); HRMS: $[M+Na]^+$ calcd for $C_{29}H_{28}F_6O_5$ 593.1739, found 593.1755.



1,1,1,3,3,3-Hexafluoro-2-propyl 1,2-*cis*-D-lyxopyranoside (S16). 1A (100 mg, 0.175 mmol) was dissolved in dissolved in 5 mL 9:1 MeOH/H_2O under N_2 atmosphere. Then $Pd(OH)_2$ (50 mg, 0.071 mmol) and acetic acid (10 eq, 100 µl) were added and the mixture was purged with H_2. The mixture was stirred under H_2 atmosphere for 16 h after which filtration over a Celite© Hyflo Supercel (Merck) pad and subsequent concentration afforded (30 mg, 0.175 mmol, *quant.*, colorless oil). TLC: R_f 0.20 (DCM:MeOH, 90:10, v:v); $[\alpha]_D^{20}$ –32.6° (*c* 1, MeOH); IR (thin film, cm^{-1}): 687, 1105, 1198, 1370, 1639, 3328; ^1H NMR (500 MHz, DMSO-d_6, HH-COSY, HSQC, HMBC-Gated, NOESY, ^1H-^{19}F Decoupled): δ 5.53 (hept, *J* = 6.6 Hz, 1H, $CH(CF_3)_2$), 4.79 (d, *J* = 2.7 Hz, 1H, H-1), 3.85 (dd, *J* = 11.6, 3.4 Hz, 1H, H-5_{eq}), 3.74 (t, *J* = 3.1 Hz, 1H, H-2), 3.59 (td, *J* = 6.0, 3.3 Hz, 1H, H-4), 3.46 (dd, *J* = 6.3, 3.2 Hz, 1H, H-3), 3.17 (dd, *J* = 11.6, 5.7 Hz, 1H, H-5_{ax}); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 121.8 (qd, *J* = 282.1, 281.4, 63.1 Hz, $CH(CF_3)_2$), 102.0 (C-1), 72.3 (p, *J* = 31.4 Hz, $CH(CF_3)_2$), 71.3 (C-3), 67.5 (C-4), 67.0 (C-2), 62.8 (C-5). ^{13}C-GATED NMR (126 MHz, $CDCl_3$): δ 102.0 ($J_{H1\text{-}C1}$ = 165 Hz, 1,2-*cis*).

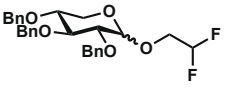


Ethyl 2,3,4-tri-*O*-benzyl-1,2-*trans*-D-xylopyranoside (S17). The title compound was prepared according to general procedure I. The reaction was quenched after 2 h. Flash column chromatography (97:3 → 85:15, pentane:EtOAc) afforded the title compound (40 mg, 89 µmol, 89%, colorless oil, 1,2-*cis*:1,2-*trans*; 15:85). TLC: R_f 0.57 (pentane:EtOAc, 90:10, v:v); $[\alpha]_D^{20}$ –19.3° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 694, 732, 997, 1070, 1358, 1444, 2894; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.39 – 7.25 (m, 15H), 4.92 (d, *J* = 10.9 Hz, 1H, C*H*H Bn), 4.86 (d, *J* = 3.6 Hz, 2H, CH_2 Bn), 4.73 (d, *J* = 11.6 Hz, 1H, C*H*H Bn), 4.72 (d, *J* = 10.9 Hz, 1H, CH*H* Bn), 4.62 (d, *J* = 11.6 Hz, 1H, CH*H* Bn), 4.34 (d, *J* = 7.6 Hz, 1H, H-1), 4.00 – 3.87 (m, 2H, H-5_{eq}, C*H*HCH$_3$ Et), 3.66 – 3.51 (m, 3H, H-3, H-4, CH*H*CH$_3$ Et), 3.36 (dd, *J* = 8.8, 7.6 Hz, 1H, H-2), 3.19 (dd, *J* = 11.6, 9.8 Hz, 1H, H-5_{ax}), 1.27 (t, *J* = 7.1 Hz, 3H, CH_3 Et); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 138.8, 138.7, 138.3 ($C_{q\text{-}arom}$), 128.6, 128.5, 128.5, 128.2, 128.1, 128.0, 127.8, 127.7 (CH_{arom}), 104.2 (C-1), 83.9 (C-4), 82.1 (C-2), 78.0 (C-3), 75.8, 75.1, 73.6 (CH_2 Bn), 65.7 (CH_2 Et), 64.0 (C-5), 15.5 (CH_3 Et); ^{13}C-GATED NMR (101 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 104.2 ($J_{H1\text{-}C1}$ = 158 Hz, 1,2-*trans*); Data for the minor stereoisomer (1,2-*cis*): ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 4.65 (d, *J* = 3.5 Hz, 1H, H-1); ^{13}C-GATED NMR (101 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 139.1, 138.5, 138.4 ($C_{q\text{-}arom}$), 96.7 (C-1), 81.6 (C-4), 79.8 (C-2), 78.3 (C-3), 75.9, 73.7, 73.5 (CH_2 Bn), 63.3 (CH_2 Et), 60.0 (C-5), 15.1 (CH_3 Et); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 104.2 ($J_{H1\text{-}C1}$ = 167 Hz, 1,2-*cis*); HRMS: $[M+Na]^+$ calcd for $C_{28}H_{32}O_5$ 471.2147, found 471.2151.

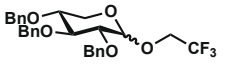


2-Fluoroethyl 2,3,4-tri-*O*-benzyl-D-xylopyranoside (S18). The title compound was prepared according to general procedure I. The reaction was quenched after 2 h. Flash column chromatography (95:5 → 80:20 pentane:EtOAc) afforded the title compound (47 mg, 100 µmol, *quant.*, colorless oil, 1,2-*cis*:1,2-*trans*; 29:71). TLC: R_f 0.46 (pentane:EtOAc, 85:15, v:v); IR (thin film, cm^{-1}): 694, 732, 738, 881, 1072, 1444, 1718, 2886; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.69 – 7.25 (m, 15H, CH_{arom}), 4.97 – 4.80 (m, 4H, CH_2 Bn, C*H*H Bn), 4.79 – 4.69 (m, 2H, CH*H* Bn, C*H*H Bn), 4.68 – 4.58 (m, 2H, CH*H* Bn, CH_2C*H*HF), 4.58 – 4.47 (m, 1H, CH_2CH*H*F), 4.39 (d, *J* = 7.6 Hz, 1H, H-1), 4.04 (dddd, *J* = 32.3, 12.1, 4.7, 2.6 Hz, 1H, C*H*HCH$_2$F), 3.93 (dd, *J* = 11.5, 5.0 Hz, 1H, H-5_{eq}), 3.89 – 3.76 (m, 1H, CH*H*CH$_2$F), 3.64 – 3.52 (m, 2H, H-3, H-4), 3.40 (dd, *J* = 8.9, 7.5 Hz, 1H, H-2), 3.21 (dd, *J* = 11.7, 9.6 Hz, 1H, H-5_{ax}); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 138.7, 138.5, 138.2 ($C_{q\text{-}arom}$), 131.2, 129.4, 128.6, 128.4, 128.1, 127.9, 124.9 (CH_{arom}), 104.4 (C-1), 83.7 (C-3), 82.7 (d, *J* = 170.3 Hz, CH_2CH_2F), 81.8 (C-2), 77.8 (C-4), 75.7, 75.1, 73.5 (CH_2 Bn), 68.89 (d, *J* = 19.9 Hz, CH_2CH_2F), 64.0 (C-5); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 104.4 ($J_{H1\text{-}C1}$ = 159 Hz, 1,2-*trans*); Data for the minor stereoisomer (1,2-*cis*): ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.69 – 7.25 (m, 15H, CH_{arom}), 3.47 (dd, *J* = 9.6, 3.6 Hz, 1H, H-2); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 139.0, 138.4, 138.3 ($C_{q\text{-}arom}$), 128.5, 128.4, 128.2, 128.1, 128.0, 127.9,

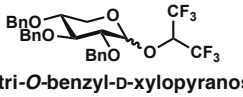
127.8, 127.7, 127.7 (CH_{arom}), 97.4 (C-1), 82.7 (d, J = 169.7 Hz, $CH_2\mathit{CH_2}F$), 81.3 (C-3), 79.7 (C-2), 78.1 (C-4), 75.9, 73.6, 73.4 (CH_2 Bn), 66.9 (d, J = 20.2 Hz, $\mathit{CH_2}CH_2F$), 60.1 (C-5); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 97.4 ($J_{H1\text{-}C1}$ = 167 Hz, 1,2-*cis*); HRMS: $[M+Na]^+$ calcd for $C_{28}H_{31}FO_5$ 489.2053, found 489.2058.



2,2-Difluoroethyl 2,3,4-tri-*O*-benzyl-D-xylopyranoside (S19). The title compound was prepared according to general procedure I. The reaction was quenched after 2 h. Flash column chromatography (97:3 → 85:15, pentane:EtOAc) afforded the title compound (43 mg, 89 µmol, 89%, colorless oil, 1,2-*cis*:1,2-*trans*; 37:63). TLC: R_f 0.42 (pentane:EtOAc, 90:10, v:v); IR (thin film, cm^{-1}): 695, 737, 1070, 1363, 1454, 1497, 1727, 2867; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.68 – 7.25 (m, 15H, CH_{arom}), 5.90 (tdd, J = 55.3, 5.0, 3.3 Hz, 1H, $CH_2C\mathit{H}F_2$), 4.98 – 4.55 (m, 12H), 4.39 (d, J = 7.5 Hz, 1H, H-1), 4.04 – 3.85 (m, 2H, H-5_{eq}, $C\mathit{H}HCHF_2$), 3.85 – 3.68 (m, 1H, $CH\mathit{H}CHF_2$), 3.68 – 3.49 (m, 2H, H-3, H-4), 3.39 (dd, J = 8.8, 7.5 Hz, 1H, H-2), 3.21 (dd, J = 11.7, 9.4 Hz, 1H, H-5_{ax}); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 138.6, 138.3, 138.1 ($C_{q\text{-}arom}$), 131.2, 129.5, 128.6, 128.5, 128.0, 124.9 (CH_{arom}), 114.2 (t, J = 241.2 Hz, $CH_2\mathit{CH}F_2$), 104.6 (C-1), 83.6 (C-3), 81.7 (C-2), 77.7 (C-4), 75.8, 75.2, 73.5 (CH_2 Bn), 68.65 (dd, J = 29.3, 27.4 Hz), 64.1 (C-5); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 104.6 ($J_{H1\text{-}C1}$ = 161 Hz, 1,2-*trans*); Data for the minor stereoisomer (1,2-*cis*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.68 – 7.25 (m, 15H, CH_{arom}), 5.95 (tt, J = 55.5, 4.3 Hz, 1H, $CH_2C\mathit{H}F_2$), 4.80 (d, J = 11.9 Hz, 1H, $C\mathit{H}$H Bn), 3.46 (dd, J = 9.6, 3.6 Hz, 1H, H-2); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 138.9, 138.3, 138.2 ($C_{q\text{-}arom}$), 128.6, 128.2, 128.1, 128.1, 128.0, 127.9, 127.9, 127.8, 127.8 (CH_{arom}), 114.3 (t, J = 241.4 Hz, $CH_2C\mathit{H}F_2$), 98.0 (C-1), 81.2 (C-3), 79.6 (C-2), 77.9 (C-4), 76.0, 73.7, 73.7 (CH_2 Bn), 67.00 (t, J = 28.9 Hz, $\mathit{CH_2}CHF_2$), 60.4 (C-5); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 98.0 ($J_{H1\text{-}C1}$ = 169 Hz, 1,2-*cis*); HRMS: $[M+Na]^+$ calcd for $C_{28}H_{30}F_2O_5$ 507.1959, found 507.1960.

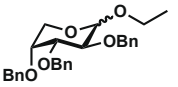


2,2,2-Trifluoroethyl 2,3,4-tri-*O*-benzyl-D-xylopyranoside (S20). The title compound was prepared according to general procedure I. The reaction was quenched after 40 h. Flash column chromatography (97:3 → 90:10, pentane:EtOAc) afforded the title compound (39 mg, 78 µmol, 78%, colorless oil, 1,2-*cis*:1,2-*trans*; 36:64). TLC: R_f 0.60 (pentane:EtOAc, 90:10, v:v); IR (thin film, cm^{-1}): 695, 734, 1028, 1072, 1161, 1276, 1358, 1454, 1497, 2872; NMR data reported as a mixture of 1,2-*cis*:1,2-*trans* (36:64) anomers: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.39 – 7.25 (m, 23.6H), 4.95 – 4.58 (m, 10.4H, CH_2 $Bn_{1,2\text{-}cis}$, CH_2 $Bn_{1,2\text{-}cis}$, CH_2 $Bn_{1,2\text{-}cis}$, H-$1_{1,2\text{-}cis}$, CH_2 $Bn_{1,2\text{-}trans}$, CH_2 $Bn_{1,2\text{-}trans}$, CH_2 $Bn_{1,2\text{-}trans}$), 4.46 (d, J = 7.4 Hz, 1H, H-$1_{1,2\text{-}trans}$), 4.14 (dq, J = 12.3, 8.7 Hz, 1H, $C\mathit{H}HCF_3$), 4.00 – 3.79 (m, 3.7H, H-$3_{1,2\text{-}cis}$, $C\mathit{H}HCF_{3\text{-}1,2\text{-}cis}$, $CH\mathit{H}CF_{3\text{-}1,2\text{-}cis}$, H-$5_{eq\text{-}1,2\text{-}trans}$, $CH\mathit{H}CF3_{\text{-}1,2\text{-}trans}$), 3.66 – 3.45 (m, 3.7H, H-$2_{1,2\text{-}cis}$, H-$4_{1,2\text{-}cis}$, H-$5_{1,2\text{-}cis}$, H-$5_{1,2\text{-}cis}$, H-$3_{1,2\text{-}trans}$, H-$4_{1,2\text{-}trans}$), 3.42 (t, J = 8.0 Hz, 1H, H-$2_{1,2\text{-}trans}$), 3.23 (dd, J = 11.7, 9.1 Hz, 1H, H-$5_{ax\text{-}1,2\text{-}trans}$); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 138.9 ($C_{q\text{-}arom\text{-}1,2\text{-}cis}$), 138.6 ($C_{q\text{-}arom\text{-}1,2\text{-}trans}$), 138.3, 138.2 ($C_{q\text{-}arom\text{-}1,2\text{-}cis}$), 138.1, 138.1 ($C_{q\text{-}arom\text{-}1,2\text{-}trans}$), 128.6, 128.6, 128.5, 128.5, 128.1, 128.1, 128.1, 128.0, 127.9, 127.9, 127.8, 127.8, 125.3, 125.2, 122.5, 122.4 (CH_{arom}), 104.3 (C-$1_{1,2\text{-}trans}$), 97.9 (C-$1_{1,2\text{-}cis}$), 83.4 (C-$3_{1,2\text{-}trans}$), 81.4 (C-$2_{1,2\text{-}trans}$), 81.0 (C-$3_{1,2\text{-}cis}$), 79.5 (C-$2_{1,2\text{-}cis}$), 77.7 (C-$4_{1,2\text{-}cis}$), 77.7 (C-$4_{1,2\text{-}trans}$), 76.0 (CH_2 $Bn_{1,2\text{-}cis}$), 75.8, 75.1 (CH_2 $Bn_{1,2\text{-}trans}$), 73.7 (CH_2 $Bn_{1,2\text{-}cis}$), 73.5 (CH_2 $Bn_{1,2\text{-}cis}$, CH_2 $Bn_{1,2\text{-}trans}$), 66.0 (q, J = 34.8 Hz, $\mathit{CH_2}CF_{3\text{-}1,2\text{-}trans}$), 64.6 (q, J = 34.8 Hz, $\mathit{CH_2}CF_{3\text{-}1,2\text{-}cis}$), 64.1 (C-$5_{1,2\text{-}trans}$), 60.6 (C-$5_{1,2\text{-}cis}$); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 104.3 ($J_{H1\text{-}C1}$ = 162 Hz, 1,2-*trans*), 97.9 ($J_{H1\text{-}C1}$ = 169 Hz, 1,2-*cis*); HRMS: $[M+Na]^+$ calcd for $C_{28}H_{29}F_3O_5$ 525.1865, found 525.1870.

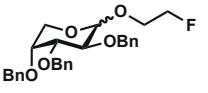


1,1,1,3,3,3-Hexafluoro-2-propyl 2,3,4-tri-*O*-benzyl-D-xylopyranoside (S21). The title compound was prepared according to general procedure I. The reaction was quenched after 112 h. Flash column chromatography (100:0 → 80:20, pentane:Et_2O) afforded the title compound (28 mg, 0.049 mmol, 49%, colorless oil, 1,2-*cis*:1,2-*trans*; 32:68). TLC: R_f 0.23, 0.38 (pentane:EtOAc, 95:5, v:v); IR (thin film, cm^{-1}): 688, 743, 898, 1028, 2073, 1194, 1220, 1286, 1369, 1454, 2916; Data for the major stereoisomer (1,2-*trans*): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated, ^{1}H-^{19}F Decoupled): δ 7.41 – 7.28 (m,

15H, CH_{arom}), 4.91 – 4.85 (m, 2H, C*H*H Bn, C*H*H Bn), 4.83 (d, *J* = 11.1 Hz, 1H, CH*H* Bn), 4.76 – 4.66 (m, 3H, C*H*H Bn, CH*H* Bn, H-1), 4.63 (d, *J* = 11.5 Hz, 1H, CH*H* Bn), 4.58 (p, *J* = 6.0 Hz, 1H, $CH(CF_3)_2$), 4.00 (dd, *J* = 11.9, 4.6 Hz, 1H, H-5_{eq}), 3.71 – 3.62 (m, 2H, H-3, H-4), 3.56 – 3.49 (m, 1H, H-2), 3.36 (dd, *J* = 11.9, 7.7 Hz, 1H, H-5_{ax}); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 138.5, 138.0, 137.8 ($C_{q\text{-}arom}$), 128.6, 128.5, 128.4, 128.0, 127.9, 127.9 (CH_{arom}), 104.1 (C-1), 82.8 (C-3), 80.7 (C-2), 77.6 (C-4), 75.5, 75.0, 73.1 (CH_2 Bn), 72.07 (p, *J* = 32.8 Hz, *C*H($CF_3)_2$), 64.1 (C-5); ^{13}C-GATED NMR (126 MHz, $CDCl_3$): δ 104.1 ($J_{H1\text{-}C1}$ = 168 Hz, 1,2-*trans*); Data for the minor stereoisomer (1,2-*cis*): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated, ^{1}H-^{19}F Decoupled): δ 7.41 – 7.28 (m, 15H), 5.06 (d, *J* = 3.7 Hz, 1H), 4.94 (d, *J* = 10.8 Hz, 1H, C*H*H Bn), 4.78 (d, *J* = 11.6 Hz, 1H, C*H*H Bn), 4.44 (hept, *J* = 5.7 Hz, 1H, $CH(CF_3)_2$),), 3.92 (dd, *J* = 9.8, 8.6 Hz, 1H, H-3); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 138.7, 138.1, 137.8 ($C_{q\text{-}arom}$), 128.9, 128.5, 128.5, 128.1, 128.1, 128.0, 127.7, 127.7 (CH_{arom}), 99.3 (C-1), 80.7 (C-3), 78.8 (C-2), 77.4 (C-4), 75.9, 73.8, 73.6 (CH_2 Bn), 61.4 (C-5); ^{13}C-GATED NMR (126 MHz, $CDCl_3$): δ 99.3 ($J_{H1\text{-}C1}$ = 171 Hz, 1,2-*cis*); HRMS: $[M+Na]^+$ calcd for $C_{29}H_{28}F_6O_5$ 593.1739, found 593.1749.

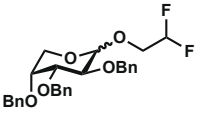


Ethyl 2,3,4-tri-*O*-benzyl-D-arabinopyranoside (S22). The title compound was prepared according to general procedure I. The reaction was quenched after 1.5 h. Flash column chromatography (97:3 → 85:15, pentane:EtOAc) afforded the title compound (45 mg, 100 µmol, *quant.*, colorless oil, 1,2-*cis*:1,2-*trans*; 18:82). TLC: R_f 0.24, 0.31 (pentane:EtOAc, 90:10, v:v); IR (thin film, cm^{-1}): 694, 732, 1045, 1087, 1444, 2920; Data for the major stereoisomer (1,2-*trans*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.51 – 7.21 (m, 15H, CH_{arom}), 4.90 (d, *J* = 10.9 Hz, 1H, C*H*H Bn), 4.80 – 4.73 (m, 2H, C*H*H Bn, CH*H* Bn), 4.70 (d, *J* = 11.0 Hz, 1H, C*H*H Bn), 4.66 – 4.63 (m, 2H, CH*H* Bn , CH*H* Bn), 4.31 (d, *J* = 7.1 Hz, 1H, H-1), 4.03 (dd, *J* = 12.7, 2.9 Hz, 1H, H-5), 3.97 (dq, *J* = 9.5, 7.0 Hz, 1H, C*H*HCH$_3$ Et), 3.80 (dd, *J* = 9.2, 7.1 Hz, 1H, H-2), 3.68 (td, *J* = 3.1, 1.3 Hz, 1H, H-4), 3.58 (dq, *J* = 9.5, 7.0 Hz, 1H, CH*H*CH$_3$ Et), 3.49 (dd, *J* = 9.2, 3.4 Hz, 1H, H-3), 3.25 (dd, *J* = 12.8, 1.3 Hz, 1H, H-5), 1.27 (t, *J* = 7.0 Hz, 3H, CH_3 Et); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 138.9, 138.6, 138.3 ($C_{q\text{-}arom}$), 128.4, 128.4, 128.2, 128.1, 127.8, 127.7, 127.7, 127.6 (CH_{arom}), 103.8 (C-1), 80.0 (C-3), 79.3 (C-2), 75.2, 72.5 (CH_2 Bn), 72.3 (C-4), 71.2 (CH_2 Bn), 65.4 (CH_2 Et), 62.9 (C-5), 15.4 (CH_3 Et); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 103.8 ($J_{H1\text{-}C1}$ = 158 Hz, 1,2-*trans*); Data for the minor stereoisomer (1,2-*cis*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): All peaks overlap with 1,2-*trans* anomer peaks; ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 128.0, 128.0, 127.6 (CH_{arom}), 97.8 (C-1), 77.4, 76.6, 74.1 (C-2/C-3/C-4), 73.6, 72.9, 71.8 (CH_2 Bn), 63.5 (CH_2 Et), 60.4 (C-5), 15.1 (CH_3 Et); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 97.8 ($J_{H1\text{-}C1}$ = 169 Hz, 1,2-*cis*); HRMS: $[M+Na]^+$ calcd for $C_{28}H_{32}O_5$ 471.2147, found 471.2160.

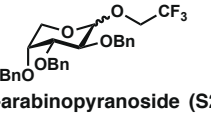


2-Fluoroethyl 2,3,4-tri-*O*-benzyl-D-arabinopyranoside (S23). The title compound was prepared according to general procedure I. The reaction was quenched after 1.5 h. Flash column chromatography (95:5 → 80:20, pentane:EtOAc) afforded the title compound (45 mg, 96 µmol, 96%, colorless oil, 1,2-*cis*:1,2-*trans*; 56:44). TLC: R_f 0.16, 0.24 (pentane:EtOAc, 85:15, v:v); IR (thin film, cm^{-1}): 694, 736, 997, 1044, 1088, 1334, 1723, 2908; NMR data reported as a mixture of 1,2-*cis*:1,2-*trans* (1.29:1) anomers: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.69 – 7.21 (m, 34.4H, CH_{arom}), 4.91 (d, *J* = 10.8 Hz, 1H, C*H*H Bn$_{1,2\text{-}trans}$), 4.88 – 4.81 (m, 2.6H, C*H*H Bn$_{1,2\text{-}cis}$, H-1$_{1,2\text{-}cis}$), 4.80 – 4.47 (m, 16.1H, CH*H* Bn$_{1,2\text{-}cis}$, CH*H* Bn$_{1,2\text{-}trans}$, CH_2 Bn$_{1,2\text{-}cis}$, CH_2 Bn$_{1,2\text{-}cis}$, CH_2C*H*$_2$F$_{1,2\text{-}cis}$, CH_2 Bn$_{1,2\text{-}trans}$, CH_2 Bn$_{1,2\text{-}trans}$, CH_2C*H*$_2$F$_{1,2\text{-}trans}$), 4.37 (d, *J* = 6.9 Hz, 1H, H-1$_{1,2\text{-}trans}$), 4.15 – 3.99 (m, 3.29H, H-2$_{1,2\text{-}cis}$, H-5$_{1,2\text{-}trans}$, C*H*HCH$_2$F$_{1,2\text{-}trans}$), 3.95 – 3.63 (m, 10.7H, H-3$_{1,2\text{-}cis}$, H-4$_{1,2\text{-}cis}$, H-5$_{1,2\text{-}cis}$, H-5$_{1,2\text{-}cis}$, C*H*HCH$_2$F$_{1,2\text{-}cis}$, CH*H*CH$_2$F$_{1,2\text{-}cis}$, H-2$_{1,2\text{-}trans}$, H-4$_{1,2\text{-}trans}$, CH*H*CH$_2$F$_{1,2\text{-}trans}$), 3.51 (dd, *J* = 9.0, 3.3 Hz, 1H, H-3$_{1,2\text{-}trans}$), 3.27 (dd, *J* = 12.6, 1.4 Hz, 1H, H-5$_{1,2\text{-}trans}$); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 138.8, 138.8, 138.7, 138.5, 138.4, 138.3 ($C_{q\text{-}arom}$), 131.2, 129.4, 128.5, 128.5, 128.4, 128.4, 128.4, 128.1, 128.1, 128.0, 127.8, 127.8, 127.8, 127.7, 127.7, 127.7, 127.6, 124.9 (CH_{arom}), 104.0 (C-1$_{1,2\text{-}trans}$), 98.5 (C-1$_{1,2\text{-}cis}$), 83.7 (CH_2*CH*$_2$F$_{1,2\text{-}cis}$), 82.0 (CH_2*CH*$_2$F$_{1,2\text{-}trans}$), 79.7 (C-3$_{1,2\text{-}trans}$), 79.0 (C-2$_{1,2\text{-}trans}$), 77.2 (C-3$_{1,2\text{-}cis}$), 76.4 (C-2$_{1,2\text{-}cis}$), 75.2 (CH_2 Bn$_{1,2\text{-}trans}$), 74.0 (C-4$_{1,2\text{-}cis}$), 73.7, 72.9 (CH_2 Bn$_{1,2\text{-}cis}$), 72.6 (CH_2 Bn$_{1,2\text{-}trans}$), 72.2 (C-4$_{1,2\text{-}trans}$), 71.9 (CH_2 Bn$_{1,2\text{-}cis}$), 71.4(CH_2 Bn$_{1,2\text{-}trans}$), 68.6 (d, *J* = 20.1 Hz, *CH*$_2$CH$_2$F$_{1,2\text{-}trans}$), 67.1 (d, *J* = 20.0 Hz, *CH*$_2$CH$_2$F$_{1,2\text{-}cis}$), 63.0 (C-5$_{1,2\text{-}trans}$), 60.5 (C-5$_{1,2\text{-}cis}$); ^{13}C-

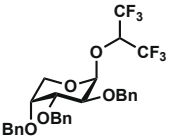
GATED NMR (101 MHz, $CDCl_3$): δ 104.0 ($J_{H1\text{-}C1}$ = 160 Hz, 1,2-*trans*), 98.5 ($J_{H1\text{-}C1}$ = 170 Hz, 1,2-*cis*); HRMS: $[M+Na]^+$ calcd for $C_{28}H_{31}FO_5$ 489.2053, found 489.2064.



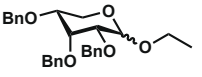
2,2-Difluoroethyl 2,3,4-tri-*O*-benzyl-D-arabinopyranoside (S24). The title compound was prepared according to general procedure I. The reaction was quenched after 1.5 h. Flash column chromatography (95:5 → 85:15, pentane:EtOAc) afforded the title compound (26 mg, 54 µmol, 54%, colorless oil, 1,2-*cis*:1,2-*trans*; 62:38). TLC: R_f 0.13, 0.25 (pentane:EtOAc, 90:10, v:v); IR (thin film, cm^{-1}): 694, 734, 903, 1046, 1349, 1453, 1723, 2920; Data for the major stereoisomer (1,2-*cis*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.70 – 7.24 (m, 15H, CH_{arom}), 6.10 – 5.77 (m, 1H, CH_2CHF_2), 4.87 – 4.81 (m, 2H, C*H*H Bn, H-1), 4.79 – 4.59 (m, 5H, CH*H* Bn, CH_2 Bn, CH_2 Bn), 4.09 – 3.92 (m, 1H, H-2), 3.87 (dd, *J* = 9.6, 3.2 Hz, 1H, H-3), 3.85 – 3.61 (m, 5H, H-4, H-5, H-5, C*H*HCHF$_2$, C*H*HCHF$_2$); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 138.7, 138.6, 138.3 ($C_{q\text{-}arom}$), 131.2, 129.5, 128.5, 128.5, 128.1, 128.0, 127.8, 127.7, 124.9 (CH_{arom}), 114.3 (t, *J* = 240.3 Hz, CH_2CHF_2), 99.1 (C-1), 77.0 (C-3), 76.2 (C-2), 73.9 (CH_2 Bn), 73.8 (C-4), 72.9, 72.0 (CH_2 Bn), 67.35 (t, *J* = 28.7 Hz, CH_2CHF_2), 60.9 (C-5); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 99.1 ($J_{H1\text{-}C1}$ = 170 Hz, 1,2-*cis*); Data for the minor stereoisomer (1,2-*trans*): ^{1}H NMR (400 MHz, Chloroform-*d*, HH-COSY, HSQC, HMBC-Gated): δ 7.70 – 7.24 (m, 15H, CH_{arom}), 4.37 (d, *J* = 6.8 Hz, 1H, H-1), 3.51 (dd, *J* = 8.9, 3.3 Hz, 1H, H-3), 3.28 (dd, *J* = 12.6, 1.6 Hz, 1H, H-5); ^{13}C NMR (101 MHz, $CDCl_3$ HSQC, HMBC-Gated): δ 138.5, 138.4, 138.2 ($C_{q\text{-}arom}$), 128.3, 128.1, 127.9, 127.9, 127.8, 127.7, 127.7 (CH_{arom}), 114.4 (dd, *J* = 241.9, 240.0 Hz, CH_2CHF_2), 104.0 (C-1), 79.5 (C-3), 78.7 (C-2), 75.2, 72.6 (CH_2 Bn), 72.1 (C-4), 71.5 (CH_2 Bn), 68.4 (dd, *J* = 30.3, 26.9 Hz, CH_2CHF_2), 63.1 (C-5); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 104.0 ($J_{H1\text{-}C1}$ = 160 Hz, 1,2-*trans*); HRMS: $[M+Na]^+$ calcd for $C_{28}H_{30}F_2O_5$ 507.1959, found 507.1958.



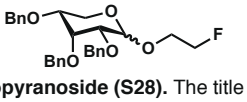
2,2,2-Trifluoroethyl 2,3,4-tri-*O*-benzyl-D-arabinopyranoside (S25). The title compound was prepared according to general procedure I. The reaction was quenched after 40 h. Flash column chromatography (97:3 → 90:10, pentane:EtOAc) afforded the title compound (45 mg, 90 µmol, 90%, colorless oil, 1,2-*cis*:1,2-*trans*; 88:12). TLC: R_f 0.19, 0.40 (pentane:EtOAc, 90:10, v:v); IR (thin film, cm^{-1}): 695, 735, 1088, 1147, 1277, 1453, 2923; Data for the major stereoisomer (1,2-*cis*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.32 (tdd, *J* = 11.8, 9.0, 6.2 Hz, 15H, CH_{arom}), 4.87 (d, *J* = 3.4 Hz, 1H, H-1), 4.83 (d, *J* = 12.0 Hz, 1H, C*H*H Bn), 4.74 (d, *J* = 11.8 Hz, 1H, C*H*H Bn), 4.70 (s, 2H, CH_2 Bn), 4.67 (d, *J* = 12.0 Hz, 1H, CH*H* Bn), 4.63 (d, *J* = 11.8 Hz, 1H, CH*H* bn), 4.03 (dd, *J* = 9.5, 3.4 Hz, 1H, H-2), 3.96 – 3.83 (m, 3H, H-3, CH_2CF_3), 3.79 (dt, *J* = 4.7, 2.2 Hz, 1H, H-4), 3.67 (m, 2H, H-5, H-5); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 138.7, 138.6, 138.2 ($C_{q\text{-}arom}$), 128.5, 128.5, 128.4, 128.0, 128.0, 127.8, 127.7, 127.7 (CH_{arom}), 125.3, 122.5, 119.8 (CF_3), 99.0 (C-1), 76.8 (C-4), 76.0 (C-2), 73.7 (C-3), 73.7, 72.9, 72.0 (CH_2 Bn), 64.9 (q, *J* = 34.7 Hz, CH_2CF_3), 61.1 (C-5); ^{13}C-GATED NMR NMR (101 MHz, $CDCl_3$): δ 99.0 ($J_{H1\text{-}C1}$ = 170 Hz, 1,2-*cis*); Data for the minor stereoisomer (1,2-*trans*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.47 – 7.24 (m, 15H, CH_{arom}), 4.44 (d, *J* = 6.6 Hz, 1H, H-1), 4.24 – 4.11 (m, 2H, CH_2CF_3), 3.52 (dd, *J* = 8.7, 3.3 Hz, 1H, H-3), 3.29 (dd, *J* = 12.5, 1.6 Hz, 1H, H-5); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 138.4, 138.3, 138.1 ($C_{q\text{-}arom}$), 128.4, 128.1, 127.9, 127.8, 127.7 (CH_{arom}), 103.5 (C-1), 79.2 (C-3), 78.4 (C-2), 72.09 (C-4), 65.7 (q, *J* = 34.7 Hz), 63.0 (C-5); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 103.5 ($J_{H1\text{-}C1}$ = 160 Hz, 1,2-*trans*); HRMS: $[M+Na]^+$ calcd for $C_{28}H_{29}F_3O_5$ 525.1865, found 525.1874.



1,1,1,3,3,3-Hexafluoro-2-propyl 2,3,4-tri-*O*-benzyl-1,2-*cis*-D-arabinopyranoside (S26). The title compound was prepared according to general procedure I. The reaction was quenched after 112 h. Flash column chromatography (100:0 → 80:20, pentane:Et_2O) afforded the title compound (8 mg, 14 µmol, 14%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). TLC: R_f 0.17 (pentane:EtOAc, 95:5, v:v); $[\alpha]_D^{20}$ -11.7° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 696, 735, 1102, 1195, 1219, 1286, 1369, 1454, 2924; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated, ^1H-^{19}F Decoupled): δ 7.41 – 7.26 (m, 15H, CH_{arom}), 5.17 (d, *J* = 3.6 Hz, 1H, H-1), 4.93 – 4.86 (m, 1H, C*H*H Bn), 4.81 – 4.67 (m, CH*H* Bn, ,CH*H* BnCH_2 Bn), 4.66 – 4.58 (m, 1H, CH*H* Bn), 4.46 (hept, *J* = 6.2 Hz, 1H, ($CH(CF_3)_2$), 4.10 (dd, *J* = 9.7, 3.6 Hz, 1H, H-2), 3.89 (dd, *J* = 9.7, 3.1 Hz, 1H, H-3), 3.86 – 3.81 (m, 1H, H-4), 3.74 (m, 2H, H-5, H-5); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 138.6, 138.3, 138.2 ($C_{q\text{-}arom}$), 128.6, 128.5, 128.0, 128.0, 127.8, 127.7 (CH_{arom}), 100.4 (C-1), 76.7 (C-3), 75.4 (C-2), 73.8 (CH_2 Bn), 73.7 (C-4), 73.0 (CH_2 Bn), 72.7, 72.5, 72.2 (*CH*$(CF_3)_2$), 72.2 (CH_2 Bn), 62.1 (C-5); ^{13}C-GATED NMR (126 MHz, $CDCl_3$): δ 100.4 ($J_{H1\text{-}C1}$ = 171 Hz, 1,2-*cis*); HRMS: $[M+Na]^+$ calcd for $C_{29}H_{28}F_6O_5$ 593.1739, found 593.1746.

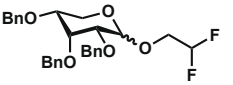


Ethyl 2,3,4-tri-*O*-benzyl-D-ribopyranoside (S27). The title compound was prepared according to general procedure I. The reaction was quenched after 1.5 h. Flash column chromatography (97:3 → 85:15, pentane:EtOAc) afforded the title compound (45 mg, 100 µmol, *quant.*, colorless oil, 1,2-*cis*:1,2-*trans*; 28:72). TLC: R_f 0.43 (pentane:EtOAc, 90:10, v:v); IR (thin film, cm^{-1}): 695, 732, 1064, 1318, 1453, 1497, 1723, 2879; Data for the major stereoisomer (1,2-*trans*): ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.49 – 7.20 (m, 15H, CH_{arom}), 4.90 – 4.77 (m, 3H, H-1, C*H*H Bn, C*H*H Bn), 4.65 (d, *J* = 12.2 Hz, 1H, CH*H* Bn), 4.61 (s, 1H, CH*H* Bn), 4.53 (m, 2H, CH_2 Bn), 4.10 – 4.04 (m, 1H, H-3), 3.89 (dq, *J* = 9.6, 7.0 Hz, 1H, C*H*HCH_3 Et), 3.87 – 3.72 (m, 2H, H-5, H-5), 3.59 (dq, *J* = 9.6, 7.1 Hz, 1H, CH*H*CH_3 Et), 3.50 – 3.40 (m, 1H, H-4), 3.25 (dd, *J* = 7.3, 2.8 Hz, 1H, H-2), 1.24 (t, *J* = 7.1 Hz, 3H, CH_3 Et); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 139.1, 138.9, 138.2 ($C_{q\text{-}arom}$), 131.2, 129.4, 128.5, 128.4, 128.3, 128.0, 127.8, 127.7, 127.6 (CH_{arom}), 100.9 (C-1), 78.4 (C-2), 75.6 (C-3), 75.3 (C-4), 74.0, 73.1, 71.5 (CH_2 Bn), 65.3 (CH_2 Et), 62.2 (C-5), 15.5 (CH_3 Et); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 100.9 ($J_{H1\text{-}C1}$ = 162 Hz, 1,2-*trans*); Data for the minor stereoisomer (1,2-*cis*): ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 4.94 (d, *J* = 12.3 Hz, 1H, C*H*H Bn), 4.75 (d, *J* = 3.8 Hz, 1H, H-1), 3.38 (t, *J* = 3.3 Hz, 1H, H-2), 1.29 (t, *J* = 7.1 Hz, 3H, CH_3 Et); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 139.6, 138.4, 138.3 ($C_{q\text{-}arom}$), 128.5, 128.5, 128.1, 127.8, 127.6, 127.1 (CH_{arom}), 96.8 (C-1), 76.3 (C-2), 73.2, 71.3, 71.0 (CH_2 Bn), 64.0 (CH_2 Et), 57.4 (C-5), 15.3 (CH_3 Et); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 96.8 ($J_{H1\text{-}C1}$ = 166 Hz, 1,2-*cis*); HRMS: $[M+Na]^+$ calcd for $C_{28}H_{32}O_5$ 471.2147, found 471.2155.

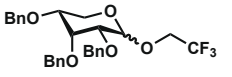


2-Fluoroethyl 2,3,4-tri-*O*-benzyl-D-ribopyranoside (S28). The title compound was prepared according to general procedure I. The reaction was quenched after 1.5 h. Flash column chromatography (95:5 → 80:20, pentane:EtOAc) afforded the title compound (47 mg, 100 µmol, *quant.*, colorless oil, 1,2-*cis*:1,2-*trans*; 39:61). TLC: R_f 0.22, 0.44 (pentane:EtOAc, 85:15, v:v); IR (thin film, cm^{-1}): 694, 734, 1066, 1444, 2883; Data for the minor stereoisomer (1,2-*trans*): ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.49 – 7.20 (m, 15H, CH_{arom}), 3.54 (ddd, *J* = 9.4, 4.7, 2.5 Hz, 1H, H-4), 3.30 (dd, *J* = 7.0, 2.8 Hz, 1H, H-2); ^{13}C NMR (101 MHz, $CDCl_3$ HSQC, HMBC-Gated): δ 139.0, 138.8, 138.2 ($C_{q\text{-}arom}$), 128.4, 128.3, 128.0, 127.6, 127.5 (CH_{arom}), 101.3 (C-1), 82.77 (d, *J* = 169.6 Hz, CH_2CH_2F), 78.1 (C-2), 75.5 (C-3), 75.1 (C-4), 73.9, 73.1, 71.4 (CH_2 Bn), 68.6 (d, *J* = 20.0 Hz, CH_2CH_2F), 62.2 (C-5); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 101.3 ($J_{H1\text{-}C1}$ = 164 Hz, 1,2-*cis*); Data for the minor stereoisomer (1,2-*cis*): ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.49 – 7.20 (m, 15H, CH_{arom}), 4.94 (d, *J* = 12.3 Hz, 1H, C*H*H Bn), 4.88 – 4.76 (m, 2H, C*H*H Bn, H-1), 4.74 – 4.45 (m, 6H, CH_2 Bn, CH_2 Bn, CH_2CH_2F), 4.16 – 4.02 (m, 2H, H-3, H-

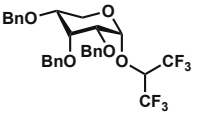
5), 4.01 – 3.69 (m, 2H, C*H*$_2$CH$_2$F), 3.50 – 3.43 (m, 2H, H-4, H-5), 3.40 (t, *J* = 3.4 Hz, 1H, H-2); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 139.5, 138.3, 138.2 ($C_{q\text{-arom}}$), 128.5, 128.5, 128.1, 127.8, 127.8, 127.6, 127.1 (CH_{arom}), 97.3 (C-1), 83.1 (d, *J* = 169.2 Hz, CH$_2$*CH$_2$*F), 76.3 (C-2), 74.7 (C-4), 73.5 (C-3), 73.3, 71.5, 71.0 (CH_2 Bn), 67.4 (d, *J* = 20.5 Hz, C*H$_2$*CH$_2$F), 57.5 (C-5); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 97.3 ($J_{H1\text{-}C1}$ = 165 Hz, 1,2-*cis*); HRMS: $[M+Na]^+$ calcd for $C_{28}H_{31}FO_5$ 489.2053, found 489.2054.



2,2-Difluoroethyl 2,3,4-tri-*O*-benzyl-D-ribopyranoside (S29). The title compound was prepared according to general procedure I. The reaction was quenched after 1.5 h. Flash column chromatography (95:5 → 80:20, pentane:EtOAc) afforded the title compound (35 mg, 72 µmol, 72%, colorless oil, 1,2-*cis*:1,2-*trans*; 50:50). TLC: R_f 0.23, 0.42 (pentane:EtOAc, 90:10, v:v); IR (thin film, cm^{-1}): 697, 735, 1064, 1389, 1454, 2877; NMR data reported as a mixture of 1,2-*cis*:1,2-*trans* (50:50) anomers: ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.49 – 7.21 (m, 30H, CH_{arom}), 5.96 (tdd, *J* = 55.7, 5.0, 3.7 Hz, 1H, CH$_2$C*H*F$_2$), 5.90 (tdd, *J* = 55.6, 4.8, 3.6 Hz, 1H, CH$_2$C*H*F$_2$), 4.92 (d, *J* = 12.2 Hz, 1H, C*H*H Bn), 4.87 – 4.74 (m, 6H, C*H*H Bn, CH*H* Bn, CH$_2$ Bn, H-1$_{1,2\text{-}cis}$, H-1$_{1,2\text{-}trans}$), 4.66 – 4.48 (m, 7H, CH*H* Bn, CH$_2$ Bn, CH$_2$ Bn, CH$_2$ Bn), 4.14 (s, 1H, H-3$_{1,2\text{-}cis}$), 4.12 – 4.02 (m, 2H, H-3$_{1,2\text{-}trans}$, H-5$_{1,2\text{-}trans}$), 3.98 – 3.67 (m, 7H, H-5$_{1,2\text{-}cis}$, H-5$_{1,2\text{-}cis}$, *CH$_2$*CHF$_2$, *CH$_2$*CHF$_2$), 3.55 – 3.44 (m, 3H, H-4$_{1,2\text{-}cis}$, H-4$_{1,2\text{-}trans}$, H-5$_{1,2\text{-}trans}$), 3.39 (t, *J* = 3.4 Hz, 1H, H-2$_{1,2\text{-}cis}$), 3.27 (dd, *J* = 7.1, 2.8 Hz, 1H, H-2$_{1,2\text{-}trans}$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 139.5, 139.0, 138.6, 138.2, 138.1, 138.1 ($C_{q\text{-arom}}$), 128.6, 128.6, 128.5, 128.5, 128.3, 128.1, 128.0, 128.0, 127.9, 127.8, 127.8, 127.8, 127.7, 127.7, 127.6, 127.6, 127.2 (CH_{arom}), 114.8 (t, *J* = 241.1 Hz, CH$_2$*CH*F$_2$), 114.3 (t, *J* = 240.9 Hz, CH$_2$*CH*F$_2$), 101.8 (C-1$_{1,2\text{-}trans}$), 97.7 (C-1$_{1,2\text{-}cis}$), 78.1 (C-2$_{1,2\text{-}trans}$), 76.3 (C-2$_{1,2\text{-}cis}$), 75.4 (C-3$_{1,2\text{-}trans}$), 75.0 (C-4$_{1,2\text{-}cis}$), 74.7 (C-4$_{1,2\text{-}trans}$), 74.1, 73.5 (CH_2 Bn), 73.4 (C-3$_{1,2\text{-}cis}$), 73.1 (CH_2 Bn), 71.6 (CH_2 Bn, CH_2 Bn), 71.1 (CH_2 Bn), 68.7 (t, *J* = 28.5 Hz, *CH$_2$*CHF$_2$), 67.8 (t, *J* = 29.0 Hz, *CH$_2$*CHF$_2$), 62.4 (C-5$_{1,2\text{-}cis}$), 57.6 (C-5$_{1,2\text{-}trans}$); GATED NMR (126 MHz, $CDCl_3$): δ 101.8 ($J_{H1\text{-}C1}$ = 167 Hz, 1,2-*trans*); 97.7 ($J_{H1\text{-}C1}$ = 168 Hz, 1,2-*cis*); HRMS: $[M+Na]^+$ calcd for $C_{28}H_{30}F_2O_5$ 507.1959, found 507.1964.

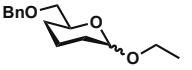


2,2,2-Trifluoroethyl 2,3,4-tri-*O*-benzyl-D-ribopyranoside (S30). The title compound was prepared according to general procedure I. The reaction was quenched after 40 h. Flash column chromatography (97:3 → 90:10, pentane:EtOAc) afforded the title compound (35 mg, 68 µmol, 68%, colorless oil, 1,2-*cis*:1,2-*trans*; 52:48). TLC: R_f 0.30, 0.57 (pentane:EtOAc, 90:10, v:v); IR (thin film, cm^{-1}): 696, 735, 1068, 1153, 1278, 1454, 2889; NMR data reported as a mixture of 1,2-*cis*:1,2-*trans* (52:48): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.47 – 7.20 (m, 29.1H, CH_{arom}), 4.95 – 4.87 (m, 2H, C*H*H Bn, H-1$_{1,2\text{-}trans}$), 4.87 – 4.76 (m, 5H, CH$_2$ Bn, CH$_2$ Bn, H-1$_{1,2\text{-}cis}$), 4.66 – 4.48 (m, 5H, CH*H* Bn, CH$_2$ Bn, CH$_2$ Bn), 4.18 – 3.97 (m, 5H, H-3$_{1,2\text{-}cis}$, H-4$_{1,2\text{-}cis}$, H-5$_{1,2\text{-}trans}$, , C*H*HCF$_3$, CH*H*CF$_3$), 3.96 – 3.74 (m, 4H, H-5$_{1,2\text{-}cis}$, H-5$_{1,2\text{-}cis}$, C*H*HCF$_3$, CH*H*CF$_3$), 3.57 – 3.44 (m, 3H, H-3$_{1,2\text{-}trans}$, H-4$_{1,2\text{-}trans}$, H-5$_{1,2\text{-}trans}$), 3.42 (t, *J* = 3.3 Hz, 1H, H-2$_{1,2\text{-}cis}$), 3.31 (dd, *J* = 7.0, 2.8 Hz, 1H, H-2$_{1,2\text{-}trans}$); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 139.4, 138.9, 138.5, 138.2, 138.1, 138.0 ($C_{q\text{-arom}}$), 128.6, 128.5, 128.4, 128.3, 128.1, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 127.6, 127.1 (CH_{arom}), 125.5, 125.1, 122.7, 122.4 (CF_3), 101.4 (C-1$_{1,2\text{-}trans}$), 97.5 (C-1$_{1,2\text{-}cis}$), 77.7 (C-2$_{1,2\text{-}trans}$), 76.4 (C-2$_{1,2\text{-}cis}$), 75.3 (C-3$_{1,2\text{-}trans}$), 74.8 (C-4$_{1,2\text{-}trans}$), 74.3 (C-3$_{1,2\text{-}cis}$), 74.0, 73.4 (CH_2 Bn), 73.4 (C-4$_{1,2\text{-}cis}$), 73.1 (CH_2 Bn) 71.6 (CH_2 Bn, CH_2 Bn), 70.9 (CH_2 Bn), 66.1 (q, *J* = 34.8 Hz, *CH$_2$*CF$_3$), 65.2 (q, *J* = 34.6 Hz, *CH$_2$*CF$_3$), 62.5 (C-5$_{1,2\text{-}cis}$), 57.9 (C-5$_{1,2\text{-}trans}$); GATED NMR (101 MHz, $CDCl_3$): δ 101.4 ($J_{H1\text{-}C1}$ = 165 Hz, 1,2-*trans*); 97.5 ($J_{H1\text{-}C1}$ = 167 Hz, 1,2-*cis*); HRMS: $[M+Na]^+$ calcd for $C_{28}H_{29}F_3O_5$ 525.1865, found 525.1876.

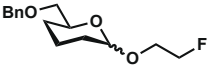


1,1,1,3,3,3-Hexafluoro-2-propyl 2,3,4-tri-*O*-benzyl-1,2-*cis*-D-ribopyranoside (S31). The title compound was prepared according to general procedure I. The reaction was quenched after 112 h. Flash column chromatography (100:0 → 80:20, pentane:Et$_2$O) afforded the title compound (14 mg, 25 µmol, 25%,

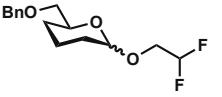
colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). TLC: R_f 0.19 (pentane:EtOAc, 95:5, v:v); $[\alpha]_D^{20}$ 67.0° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 689, 696, 733, 1071, 1103, 1193, 1218, 1287, 1370, 1454, 2917; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated, ^1H-^{19}F Decoupled): δ 7.37 – 7.20 (m, 15H, CH_{arom}), 5.08 (d, *J* = 3.9 Hz, 1H, H-1), 4.94 (d, *J* = 12.1 Hz, 1H, C*H*H Bn), 4.84 (d, *J* = 12.1 Hz, 1H, CH*H* Bn), 4.65 (d, *J* = 11.9 Hz, 1H, C*H*H Bn), 4.59 – 4.52 (m, 2H, C*H*H Bn, CH*H* Bn), 4.52 – 4.41 (m, 2H, $CH(CF_3)_2$, CH*H* Bn), 4.21 – 4.12 (bs, 1H, H-3), 4.16 (t, *J* = 10.7 Hz, 1H, H-5_{ax}), 3.54 (dd, *J* = 10.5, 4.7, 1H, H-5_{eq}), 3.48 (ddd, *J* = 10.6, 4.9, 2.5 Hz, 1H, H-4), 3.42 (dd, *J* = 4.0, 2.6 Hz, 1H, H-2); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 139.3, 138.0, 137.7 ($C_{q\text{-}arom}$), 128.5, 128.5, 128.0, 127.9, 127.9, 127.6, 127.6, 127.5, 127.0 (CH_{arom}), 98.2 (C-1), 76.4 (C-2), 74.0 (C-4), 73.4 (CH_2 Bn), 72.7 (p, *J* = 32.8 Hz, C*H*$(CF_3)_2$), 72.7 (C-3), 71.3, 70.8 (CH_2 Bn), 58.2 (C-5); ^{13}C-GATED NMR (126 MHz, $CDCl_3$): δ 98.2 ($J_{H1\text{-}C1}$ = 171 Hz, 1,2-*cis*); HRMS: $[M+Na]^+$ calcd for $C_{29}H_{28}F_6O_5$ 593.1739, found 593.1748.



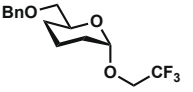
6-Benzyloxymethyl-2-ethyloxy-tetrahydropyran (S32). The title compound was prepared according to a modified general procedure I: after Tf_2O addition, the reaction mixture was stirred for 5 min after which the acceptor was added at –80 °C. The reaction was quenched after 1 h. Flash column chromatography (100:0 → 90:10, pentane:Et_2O) afforded the title compound (8 mg, 12 µmol, 12%, colorless oil, 2,6-*cis*:2,6-*trans*; 50:50). TLC: R_f 0.75 (pentane:Et_2O, 95:5, v:v); TLC: R_f 0.70 (pentane:Et_2O, 95:5, v:v); IR (thin film, cm^{-1}): 697, 736, 967, 1043, 1089, 1136, 1279, 1455, 2856, 2925; NMR data reported as a mixture of 2,6-*cis*:2,6-*trans* (52:48) anomers: ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.54 – 7.17 (m, 10H, CH_{arom}), 4.89 (s, 1H, H-$1_{2,6\text{-}trans}$), 4.64 – 4.48 (m, 4H, C*H*H $Bn_{2,6\text{-}cis}$, CH*H* $Bn_{2,6\text{-}cis}$, C*H*H $Bn_{2,6\text{-}trans}$, CH*H* $Bn_{2,6\text{-}trans}$), 4.44 (dd, *J* = 9.4, 2.2 Hz, 1H, H-$1_{2,6\text{-}cis}$), 4.02 – 3.92 (m, 2H, H-5, H-6), 3.76 (dq, *J* = 9.8, 7.1 Hz, 1H, H-6), 3.69 – 3.41 (m, 7H, H-5, H-$6_{2,6\text{-}cis}$, H-$6_{2,6\text{-}trans}$, C*H*HCH$_3$ $Et_{2,6\text{-}cis}$, CH*H*CH$_3$ $Et_{2,6\text{-}cis}$, C*H*HCH$_3$ $Et_{2,6\text{-}trans}$, CH*H*CH$_3$ $Et_{2,6\text{-}trans}$), 1.92 – 1.16 (m, 18H, H-$2_{2,6\text{-}cis}$, H-$2_{2,6\text{-}trans}$, H-$3_{2,6\text{-}cis}$, H-$3_{2,6\text{-}trans}$, H-$4_{2,6\text{-}cis}$, H-$4_{2,6\text{-}trans}$, CH$_3$ $Et_{2,6\text{-}cis}$, CH$_3$ $Et_{2,6\text{-}trans}$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC): δ 128.5, 128.5, 127.8, 127.7, 127.6 (CH_{arom}), 102.0 (C-$1_{2,6\text{-}cis}$), 97.1 (C-$1_{2,6\text{-}trans}$), 75.6 (C-5), 73.7 (CH_2 Bn), 73.6 (CH_2 Bn), 73.6 (*C*H$_2$ Et), 73.4(*C*H$_2$ Et), 68.0 (C-5), 64.2 (C-6), 62.3 (C-6), 31.0, 29.8, 27.8, 22.0, 18.8, 17.9 (C-$2_{2,6\text{-}cis}$, C-$2_{2,6\text{-}trans}$, C-$3_{2,6\text{-}cis}$, C-$3_{2,6\text{-}trans}$, C-$4_{2,6\text{-}cis}$, C-$4_{2,6\text{-}trans}$), 15.4 (*C*H$_3$ Et), 15.3 (*C*H$_3$ Et).



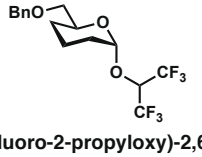
6-Benzyloxymethyl-2-(2-fluoroethyloxy)-tetrahydropyran (S33). The title compound was prepared according to a modified general procedure I: after Tf_2O addition, the reaction mixture was stirred for 5 min after which the acceptor was added at –80 °C. The reaction was quenched after 1 h. Flash column chromatography (100:0 → 90:10, pentane:Et_2O) afforded the title compound (8 mg, 12 µmol, 12%, colorless oil, 2,6-*cis*:2,6-*trans*; 48:52). TLC: R_f 0.75 (pentane:Et_2O, 95:5, v:v); TLC: R_f 0.60, 0.55 (pentane:Et_2O, 95:5, v:v); IR (thin film, cm^{-1}): 696,736, 1028, 1454, 2853, 2923; NMR data reported as a mixture of 2,6-*cis*:2,6-*trans* (48:50) anomers: ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC): δ 7.98 – 7.15 (m, 10H, $CH_{arom\text{-}2,6\text{-}cis}$, $CH_{arom\text{-}2,6\text{-}trans}$), 4.92 (d, *J* = 3.3 Hz, 1H, H-$1_{2,6\text{-}trans}$), 4.70 – 4.50 (m, 8H, C*H*H $Bn_{2,6\text{-}cis}$, C*H*H $Bn_{2,6\text{-}cis}$, C*H*H $Bn_{2,6\text{-}trans}$, C*H*H $Bn_{2,6\text{-}trans}$, C*H*HCHF$_{2\text{-}2,6\text{-}cis}$, CH*H*CHF$_{2\text{-}2,6\text{-}ciss}$, C*H*HCHF$_{2\text{-}2,6\text{-}trans}$, CH*H*CHF$_{2\text{-}2,6\text{-}trans}$), 4.49 (dd, *J* = 9.3, 2.2 Hz, 1H, H-$1_{2,6\text{-}cis}$), 4.07 (dddd, *J* = 33.8, 12.2, 4.5, 2.6 Hz, 1H, C*H*HF$_{2,6\text{-}trans}$), 4.00 – 3.85 (m, 2H, H-$5_{2,6\text{-}trans}$, C*H*HF$_{2,6\text{-}cis}$), 3.85 – 3.63 (m, 3H, H-5, CH*H*F$_{2,6\text{-}cis}$, CH*H*F$_{2,6\text{-}trans}$), 3.57 (dd, *J* = 10.1, 6.2 Hz, 1H, H-$6_{2,6\text{-}trans}$), 3.52 – 3.40 (m, 3H, H-$6_{2,6\text{-}cis}$, H-$6_{2,6\text{-}cis}$, H-$6_{2,6\text{-}trans}$), 1.95 – 1.37 (m, 12H, H-$2_{2,6\text{-}cis}$, H-$2_{2,6\text{-}cis}$, H-$2_{,6\text{-}trans}$, H-$2_{,6\text{-}trans}$, H-$3_{2,6\text{-}cis}$, H-$3_{2,6\text{-}cis}$, H-$3_{,6\text{-}trans}$, H-$3_{2,6\text{-}trans}$, H-$4_{2,6\text{-}cis}$, H-$4_{2,6\text{-}cis}$, H-$4_{,6\text{-}trans}$ H-$4_{,6\text{-}trans}$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC): δ 138.5 ($C_{q\text{-}arom}$), 138.5 ($C_{q\text{-}arom}$), 128.5, 128.4, 127.8, 127.7, 127.7, 127.6 (CH_{arom}), 102.4 (C-$1_{2,6\text{-}trans}$), 97.6 (C-$1_{2,6\text{-}cis}$), 83.8 (d, *J* = 2.0 Hz, *C*H$_2$CH$_2$F$_{2,6\text{-}trans}$), 82.4 (d, *J* = 2.0 Hz, *C*H$_2$CH$_2$F$_{2,6\text{-}cis}$), 75.6 (C-$5_{2,6\text{-}cis}$), 73.6, 73.6, 73.4 (C-$6_{2,6\text{-}cis}$, C-$6_{2,6\text{-}trans}$, CH_2 $Bn_{2,6\text{-}cis}$, CH_2 $Bn_{2,6\text{-}trans}$), 68.2 (C-$5_{2,6\text{-}trans}$), 67.7 (d, *J* = 20.0 Hz, *C*H$_2$F$_{2,6\text{-}trans}$), 66.1 (d, *J* = 19.7 Hz, *C*H$_2$F$_{2,6\text{-}cis}$), 31.1 (C-$2_{2,6\text{-}cis}$), 29.8, 29.5, 27.5, 21.7 (C-$3_{2,6\text{-}cis}$, C-$3_{2,6\text{-}trans}$, C-$4_{2,6\text{-}cis}$, C-$4_{2,6\text{-}trans}$), 17.7 (C-$2_{2,6\text{-}trans}$); HRMS: $[M+Na]^+$ calcd for $C_{15}H_{21}F_1O_3$ 291.13641, found 291.13669.



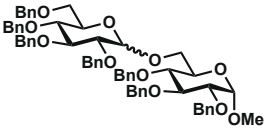
6-Benzyloxymethyl-2-(2,2-difluoroethyloxy)-tetrahydropyran (S34). The title compound was prepared according to a modified general procedure I: after Tf_2O addition, the reaction mixture was stirred for 5 min after which the acceptor was added at –80 °C. The reaction was quenched after 1 h. Flash column chromatography (100:0 → 90:10, pentane:Et_2O) afforded the title compound (8 mg, 12 µmol, 12%, colorless oil, 2,6-*cis*:2,6-*trans*; 12:88). TLC: R_f 0.70, 0.65 (pentane:Et_2O, 95:5, v:v; IR (thin film, cm^{-1}): 698, 737, 1040, 1073, 1116, 1454, 2856, 2925; Data for the major stereoisomer (1,2-*trans*): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC): δ 7.37 – 7.26 (m, 5H, CH_{arom}), 5.97 (tdd, *J* = 55.7, 4.9, 3.6 Hz, 1H, CH_2F), 4.91 (d, *J* = 3.2 Hz, 1H, H-1), 4.57 (s, 2H, CH_2 Bn), 3.95 (dddd, *J* = 11.8, 6.0, 4.3, 2.3 Hz, 1H, H-5), 3.84 (dddd, *J* = 15.5, 14.8, 11.9, 3.6 Hz, 1H, C*H*HCHF$_2$), 3.70 (tdd, *J* = 13.3, 11.9, 4.9 Hz, 1H, CH*H*CH$_2$F), 3.44 (h, *J* = 4.3 Hz, 2H, H-6, H-6), 1.91 – 1.38 (m, 6H, H-2, H-2, H-3, H-3, H-4, H-4); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC): δ 138.4 ($C_{q\text{-}arom}$), 128.5, 127.7, 127.7 (CH_{arom}), 114.7 (t, *J* = 240.6 Hz, *C*HF$_2$), 98.3 (C-1), 73.4 (C-6), 68.6 (C-5), 66.6 (t, *J* = 28.0 Hz, *C*H$_2$CH$_2$F), 29.3 (C-2), 27.3 (C-4), 17.6 (C-3); 2,6-*cis* anomer reference peaks: ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC): δ 6.09 – 5.81 (m, 1H, CH_2F), 4.47 (dd, *J* = 9.3, 2.2 Hz, 1H, H-1); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC): δ 102.8 (C-1), 75.7 (C-5), 73.6 (CH_2 Bn), 73.2 (C-6), 67.9 (dd, *J* = 29.7, 27.2 Hz, *C*H$_2$CH$_2$F), 30.8 (C-2), 27.3 (C-4), 21.6 (C-3); HRMS: [M+Na]$^+$ calcd for $C_{15}H_{20}F_2O_3$ 309.12727, found 309.12719.



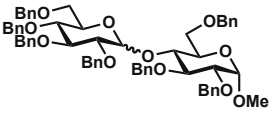
6-Benzyloxymethyl-2-(2,2,2-trifluoroethyloxy)-2,6-*trans*-tetrahydropyran (S35). The title compound was prepared according to a modified general procedure I: after Tf_2O addition, the reaction mixture was stirred for 5 min after which the acceptor was added at –80 °C. The reaction was quenched after 1 h. Flash column chromatography (100:0 → 90:10, pentane:Et_2O) afforded the title compound (8 mg, 12 µmol, 12%, colorless oil, 2,6-*cis*:2,6-*trans*; <2:98). TLC: R_f 0.85 (pentane:Et_2O, 95:5, v:v); $[\alpha]_D^{25}$ –0.4° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}); IR (thin film, cm^{-1}): 697, 736, 969, 1043, 1089, 1136, 1279, 1454, 2855, 2927; ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC, ^{1}H-^{19}F Decoupled): δ 7.37 – 7.26 (m, 5H, CH_{arom}), 4.96 (d, *J* = 3.2 Hz, 1H, H-1), 4.57 (s, 2H, C*H*H Bn, CH*H* Bn), 4.00 (dq, *J* = 12.3, 9.1 Hz, 1H, C*H*HCF$_3$), 3.96-3.81 (m, 2H, H-5, CH*H*CF$_3$), 3.45 (dd, *J* = 4.9, 3.8 Hz, 2H, H-6), 1.93 – 1.75 (m, 2H, H-2, H-3), 1.72 – 1.55 (m, 3H, H-2, H-3, H-4), 1.45 (tdd, *J* = 13.0, 11.1, 4.1 Hz, 1H, H-4); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC): δ 138.4 (Cq_{arom}), 128.5, 127.7, 127.7 (CH_{arom}), 125.4, 123.2 (CH_2CF_3), 97.9 (C-1), 73.5 (CH_2 Bn), 73.3 (C-6), 68.9 (C-5), 63.8 (q, *J* = 34.4 Hz, C-3), 29.1 (C-3), 27.3 (C-4), 17.4 (C-2); HRMS: [M+Na]$^+$ calcd for $C_{15}H_{19}F_3O_3$ 327.11785, found 309.11732.



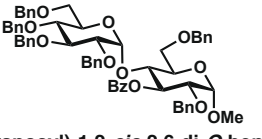
6-Benzyloxymethyl-2-(1,1,1,3,3,3-Hexafluoro-2-propyloxy)-2,6-*trans*-tetrahydropyran (S36). The title compound was prepared according to a modified general procedure I: after Tf_2O addition, the reaction mixture was stirred for 5 min after which the acceptor was added at –80 °C. The reaction was quenched after 1 h. Flash column chromatography (100:0 → 90:10, pentane:Et_2O) afforded the title compound (8 mg, 12 µmol, 12%, colorless oil, 2,6-*cis*:2,6-*trans*; <2:98). TLC: R_f 0.75 (pentane:Et_2O, 95:5, v:v); $[\alpha]_D^{25}$ –0.9° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 688, 1028, 1146, 1028, 1216, 1288, 2925; ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC, ^{1}H-^{19}F Decoupled): δ 7.37 – 7.26 (m, 5H, CH_{arom}), 5.16 (d, *J* = 3.4 Hz, 1H, H-1), 4.60 – 4.51 (m, 3H, CH(CF$_3$)$_2$, C*H*H Bn, C*H*H Bn), 4.01 (dtd, *J* = 11.6, 4.6, 2.3 Hz, 1H, H-5), 3.46 (m, 2H, H-6, H-6), 1.90 – 1.78 (m, 2H, H-2, H-3), 1.77 – 1.46 (m, 4H, H-2, H-3, H-4, H-4); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC): δ 138.3 ($C_{q\text{-}arom}$), 128.5, 127.7, 127.6 (CH_{arom}), 125.8 – 119.0 (m, CH(*C*F$_3$)$_2$), 99.4 (d, *J* = 1.6 Hz, C-1), 73.4 (CH_2 Bn), 72.9 (C-6), 71.5 (dt, *J* = 64.7, 32.4 Hz, *CH*(CF$_3$)$_2$), 69.6 (d, *J* = 1.5 Hz, C-5), 28.9 (C-3), 27.0 (C-4), 17.1(C-2); HRMS: [M+Na]$^+$ calcd for $C_{16}H_{18}F_6O_3$ 395.10523, found 395.10532.



Methyl 6-*O*-(2,3,4-*O*-benzyl-D-glucopyranosyl)-2,3,4-tri-*O*-benzyl-D-glucopyranoside (S37). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Flash column chromatography (95:5 → 80:20, pentane:EtOAc) and size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound (75 mg, 76 µmol, 79%, colorless oil, 1,2-*cis*:1,2-*trans*; 15:85). TLC: R_f 0.63 (pentane:EtOAc, 80:20, v:v); IR (thin film, cm^{-1}): 1029, 1041, 1366, 1455, 1489, 2921; Data of the major stereoisomer (1,2-*trans*): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.7 – 7.1 (m, 35H, CH_{arom}), 5.0 – 4.5 (m, 15H, H-1', C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.3 (d, *J* = 7.8 Hz, 1H, H-1), 4.2 (dd, *J* = 10.8, 2.0 Hz, 1H, H-6), 4.0 (t, *J* = 9.3 Hz, 1H, H-3'), 3.8 (ddd, *J* = 10.3, 4.9, 2.1 Hz, 1H, H-5'), 3.7 – 3.5 (m, 9H, H-2, H-3, H-4, H-2', H-4', H-6', H-6, H-6), 3.4 (dtd, *J* = 6.8, 4.8, 2.8 Hz, 1H, H-5), 3.32 (s, 3H, CH_3'); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 139.0, 138.7, 138.5, 138.5, 138.4, 138.3 ($C_{q\text{-}arom}$), 138.2, 131.2, 129.4, 128.6, 128.5, 128.5, 128.5, 128.3, 128.1, 128.1, 128.0, 128.0, 127.8, 127.7, 124.9 (CH_{arom}), 103.9 (C-1), 98.2 (C-1'), 84.9 (C-4'), 82.2 (C-2), 82.1 (C-3'), 79.9 (C-2'), 78.1 (C-4), 78.0 (C-3), 75.8, 75.8 (CH_2 Bn), 75.2 (C-5), 75.1, 75.0, 75.0, 73.6, 73.5 (CH_2 Bn), 70.0 (C-5'), 69.1 (C-6), 68.7 (C-6'), 55.3 (CH_3'); Data for the minor stereoisomer (1,2-*cis*): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.98 (signal overlaps with major stereoisomer, 1H, H-1), 4.55 (signal overlaps with major stereoisomer, 1H, H-1'); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 98.1 (C-1'), 97.4 (C-1), 55.3 (CH_3'); HRMS: $[M+Na]^+$ calcd for $C_{62}H_{66}O_{11}Na$ 1009.45028, found 1009.44947.

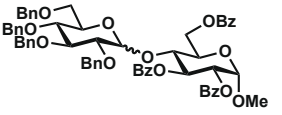


Methyl 4-*O*-(2,3,4-*O*-benzyl-D-glucopyranosyl)-2,3,6-tri-*O*-benzyl-D-glucopyranoside (S38). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Flash column chromatography (95:5 → 80:20, pentane:EtOAc) and size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound (90 mg, 91 µmol, 91%, colorless oil, 1,2-*cis*:1,2-*trans*; 42:58). TLC: R_f 0.51 (pentane:EtOAc, 80:20, v:v); IR (thin film, cm^{-1}): 1031, 1042, 1367, 1465, 1491, 2920; Data of the major stereoisomer (1,2-*trans*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.6 – 7.1 (m, 35H, CH_{arom}), 5.1 (d, *J* = 11.3 Hz, 1H, C*H*H Bn), 5.0 – 4.4 (m, 14H, H-1, H-1', C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.3 (d, *J* = 12.2 Hz, 1H, CH*H* Bn), 4.2 – 3.5 (m, 10H, H-3, H-4, H-6, H-6, H-2', H-3', H-4', H-5', H-6', H-6'), 3.4 (m, 4H, H-2, CH_3') 3.35 (ddd, *J* = 9.8, 4.7, 1.8 Hz, 1H, H-5); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 139.7, 138.9, 138.7, 138.7, 138.5, 138.4, 138.1 ($C_{q\text{-}arom}$), 128.6, 128.5, 128.5, 128.5, 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 127.9,, 127.8, 127.7, 127.6, 127.5, 127.4 (CH_{arom}), 102.6 (C-1), 98.5 (C-1'), 85.0, 82.9 (C-2), 82.2, 82.1, 80.5, 79.0, 78.2, 76.7, 75.7 (CH_2 Bn), 75.5 (CH_2 Bn), 75.3 (C-5), 75.0 (CH_2 Bn), 74.9 (CH_2 Bn), 73.8 (CH_2 Bn), 73.5 (CH_2 Bn), 70.1 (C-5'), 69.1 (C-6/C-6'), 68.0 (C-6'/C-6), 55.4 (CH_3'); Data for the minor stereoisomer (1,2-*cis*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.75 (d, *J* = 3.6 Hz, 1H, H-1), 5.08 (d, *J* = 11.6 Hz, 1H, C*H*H Bn); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 139.1, 138.7, 138.6, 138.3, 138.1, 138.0 ($C_{q\text{-}arom}$), 97.9 (C-1'), 96.8 (C-1), 79.6 (C-2), 75.7, 75.1, 74.5, 73.6, 73.5, 73.4, 73.3 (CH_2 Bn), 69.2 (C-6/C-6'), 68.3 (C-6'/C-6), 55.3 (CH_3'); HRMS: $[M+Na]^+$ calcd for $C_{62}H_{66}O_{11}Na$ 1009.45028, found 1009.44951.

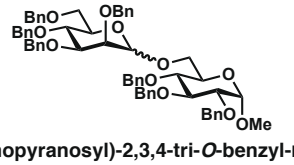


Methyl 4-*O*-(2,3,4-*O*-benzyl-D-lyxopyranosyl)-1,2-*cis*-2,6-di-*O*-benzyl-3-*O*-benzoyl-D-glucopyranoside (S39). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Flash column chromatography (95:5 → 80:20, pentane:EtOAc) and size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound (62 mg, 62 µmol, 62%, colorless oil,

1,2-*cis*:1,2-*trans*; 61:39). TLC: R_f 0.33 (pentane:EtOAc, 80:20, v:v); IR (thin film, cm^{-1}): 814, 1034, 1253, 1451, 1725, 2929; Data of the major stereoisomer (1,2-*cis*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.10 – 7.03 (m, 35H, CH_{arom}), 5.92 (t, J = 9.6 Hz, 1H, H-3'), 5.01 (d, J = 3.3 Hz, 1H, H-1), 4.85 – 4.21 (m, 7H, H-1', C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.18 – 4.00 (m, 1H, H-4'), 3.99 – 3.76 (m, 3H, H-3, H-6', H-5'), 3.75 – 3.60 (m, 4H, H-6', H-2', H-5), 3.56 – 3.12 (m, 7H, H-2, H-6, H-6, H-4, CH_3'); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 165.5 (C=O Bz), 139.0 ($C_{q\text{-}arom}$), 138.6 (CH_{arom}), 138.3 ($C_{q\text{-}arom}$), 138.2, 137.9, 132.8, 130.9, 130.0, 128.6, 128.4, 128.4, 128.4, 128.2, 128.2, 128.2, 128.1, 128.0, 127.8, 127.7 (CH_{arom}), 98.0 (C-1), 97.8 (C-1'), 81.6, 79.4 (C-2), 77.5, 77.2, 75.6 (CH_2 Bn), 74.9 (CH_2 Bn), 74.7, 73.9 (C-3'), 73.5 (CH_2 Bn), 73.4 (CH_2 Bn), 72.9 (CH_2 Bn, CH_2 Bn), 72.5 (CH_2 Bn), 71.3, 69.9, 68.6 (C-6'), 68.6 (C-6), 55.4 (CH_3'); Data for the minor stereoisomer (1,2-*trans*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.69 (t, J = 9.7 Hz, 1H, H-3'), 4.24 (d, J = 7.8 Hz, 1H, H-1); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 165.6 (C=O Bz), 138.8, 138.7, 138.6, 138.3, 137.9, 137.8 ($C_{q\text{-}arom}$), 132.6 (CH_{arom}), 131.1 ($C_{q\text{-}arom}$), 102.5 (C-1), 98.1 (C-1'), 75.6 (CH_2 Bn), 75.1 (CH_2 Bn), 73.6 (CH_2 Bn), 69.3 (C-6/C-6'), 67.7 (C-6/C-6'), 55.5 (CH_3);HRMS: $[M+Na]^+$ calcd for $C_{62}H_{64}O_{12}Na$ 1023.42955, found 1023.42900.

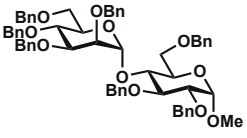


Methyl 4-*O*-(2,3,4-*O*-benzyl-D-glucopyranosyl)-2,3,6-tri-*O*-benzoyl-D-glucopyranoside (S40). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound afforded the title compound (60 mg, 58 µmol, 58%, colorless oil, 1,2-*cis*:1,2-*trans*; 88:12). TLC: R_f 0.50 (1,2-*cis*) and 0.40 (1,2-*trans*) (pentane:EtOAc, 80:20, v:v); $[\alpha]_D^{25}$ 22.5° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 751, 809, 1029, 1277, 1412, 1730, 2913; Data of the major stereoisomer (1,2-*cis*): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.15 – 7.05 (m, 35H, CH_{arom}), 6.21 (dd, J = 10.2, 8.1 Hz, 1H, H-3'), 5.27 (dd, J = 10.3, 3.6 Hz, 1H, H-2'), 5.15 (d, J = 3.6 Hz, 1H, H-1), 5.04 (d, J = 3.5 Hz, 1H, H-1), 4.90 – 4.07 (m, 11H, H-4', H-6', H-6', C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.00 – 3.91 (m, 2H, H-3, H-5'), 3.86 (dt, J = 9.9, 2.9 Hz, 1H, H-5), 3.81 – 3.49 (m, 3H, H-4, H-6, H-6), 3.45 (s, 3H, CH_3'), 3.31 (dd, J = 9.9, 3.4 Hz, 1H, H-2); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 166.3, 166.3, 165.7 (C=O Bz), 138.9, 138.6, 138.3, 138.0 ($C_{q\text{-}arom}$), 133.5, 133.4, 133.2 (CH_{arom}), 130.3, 130.2 ($C_{q\text{-}arom}$), 130.2, 130.0, 129.3, 128.7, 128.6, 128.5, 128.5, 128.5, 128.2, 128.1, 128.0, 128.0, 127.9, 127.9, 127.9, 127.9, 127.8, 127.8, 127.8, 127.7 (CH_{arom}), 99.3 (C-1), 97.0 (C-1'), 81.7 (C-3), 79.2 (C-2), 77.6 (C-4), 76.2 (C-5'), 75.8, 75.1, 73.7, 73.0 (CH_2 Bn), 72.3 (C-2'), 72.1 (C-3'), 72.0 (C-5), 69.0 (C-4'), 68.4 (C-6), 63.6 (C-6'), 55.6 (CH_3'); Data for the minor stereoisomer (1,2-*trans*): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 6.01 (dd, J = 10.2, 9.3 Hz, 1H, H-3), 5.23 (dd, J = 10.2, 3.7 Hz, 1H, H-2), 5.18 (d, J = 3.5 Hz, 1H, H-1), 5.13 (d, J = 10.0 Hz, 1H, H-1'); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 99.7 (C-1'), 99.5 (C-1), 55.7 (CH_3'); HRMS: $[M+Na]^+$ calcd for $C_{62}H_{60}O_{14}Na$ 1051.38808, found 1051.38750.

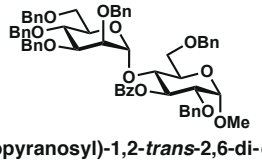


Methyl 6-*O*-(2,3,4-*O*-benzyl-D-mannopyranosyl)-2,3,4-tri-*O*-benzyl-D-glucopyranoside (S41). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Flash column chromatography (95:5 → 80:20, pentane:EtOAc) and size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound (78 mg, 79 µmol, 79%, colorless oil, 1,2-*cis*:1,2-*trans*; 77:23). TLC: R_f 0.37 (pentane:EtOAc, 80:20, v:v); IR (thin film, cm^{-1}): 710, 739, 1031, 1051, 1354, 1420, 1486, 2913; Data of the major stereoisomer (1,2-*cis*): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.48 – 7.08 (m, 35H, CH_{arom}), 5.01 (d, J = 10.9 Hz, 1H, C*H*H Bn), 4.93 (d, J = 12.5 Hz, 1H, C*H*H Bn), 4.88 (d, J = 10.8 Hz, 1H, C*H*H Bn), 4.85 – 4.41 (m, 12H, H-1', CH*H* Bn, CH*H* Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn C*H*H Bn, CH*H* Bn C*H*H Bn, CH*H* Bn C*H*H Bn, CH*H* Bn), 4.16 (dd, J = 10.5, 2.0 Hz, 1H, H-6'), 4.12 (s, 1H, H-1), 4.01 (t, J = 9.2 Hz, 1H, H-3'), 3.89 – 3.63 (m, 5H, H-3, H-4, H-6, H-6, H-5'), 3.50 (dd, J = 9.7, 3.5 Hz, 1H, H-2'), 3.48 – 3.35 (m, 4H, H-2, H-5, H-4', H-6'), 3.32 (s, 3H, CH_3'); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 139.0,

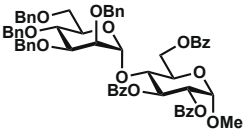
138.9, 138.6, 138.4, 138.3, 138.2 ($C_{q\text{-}arom}$), 128.6, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.1, 127.9, 127.8, 127.7, 127.7, 127.7, 127.6, 127.5 (CH_{arom}), 101.6 (C-1), 97.9 (C-1'), 82.4 (C-2), 82.3 (C-3'), 80.0 (C-2'), 77.8 (C-4'), 76.1 (C-5), 75.8, 75.2 (CH_2 Bn), 75.1 (C-4), 74.9, 73.8 (CH_2 Bn), 73.7 (C-3), 73.6, 73.5, 71.7 (CH_2 Bn), 69.9 (C-5'), 69.9 (C-6), 68.4 (C-6'), 55.2 (CH_3'); Data for the minor stereoisomer (1,2-*trans*): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.96 (d, *J* = 2.2 Hz, 1H, H-1), 4.58 (signal overlaps with major isomer, 1H, H-1'), 3.60 (td, *J* = 10.7, 1.8 Hz, 1H, H-6'), 3.30 (s, 3H, CH_3'); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 138.8, 138.8, 138.5, 138.5, 138.3, 138.3 ($C_{q\text{-}arom}$), 98.4 (C-1'), 97.9 (C-1), 75.9, 75.1, 75.1, 73.4, 72.6, 72.1 (CH_2 Bn), 69.2 (C-6), 65.9 (C-6'), 55.2 (CH_3'); HRMS: $[M+Na]^+$ calcd for $C_{62}H_{66}O_{11}Na$ 1009.45503, found 1009.44973.



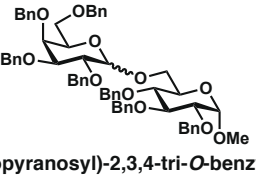
Methyl 4-*O*-(2,3,4-*O*-benzyl-D-mannopyranosyl)-1,2-*trans*-2,3,6-tri-*O*-benzyl-D-glucopyranoside (S42). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Flash column chromatography (95:5 → 80:20, pentane:EtOAc) and size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound (69 mg, 70 µmol, 70%, colorless oil, 1,2-*cis*:1,2-*trans*; <2:98). TLC: R_f 0.29 (pentane:EtOAc, 80:20, v:v); IR (thin film, cm^{-1}): 699, 731, 1042, 1089, 1467, 1499, 2910; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.38 – 7.09 (m, 35H, CH_{arom}), 5.29 (d, *J* = 2.2 Hz, 1H, H-1'), 5.08 (d, *J* = 11.7 Hz, 1H, C*H*H Bn), 4.83 (d, *J* = 10.8 Hz, 1H, C*H*H Bn), 4.72 – 4.39 (m, 11H, H-1, CH*H* Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.31 (d, *J* = 12.1 Hz, 1H, C*H*H Bn), 4.21 (d, *J* = 12.1 Hz, 1H, CH*H* Bn), 3.97 (t, *J* = 9.4 Hz, 1H, H-4'), 3.89 – 3.75 (m, 3H, H-3, H-3', H-5'), 3.75 – 3.59 (m, 6H, H-2, H-4, H-5, H-6, H-6', H-6'), 3.60 – 3.50 (m, 2H, H-2', H-6') 3.39 (s, 3H, CH_3'); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 139.0, 138.8, 138.7, 138.6, 138.5, 138.0 ($C_{q\text{-}arom}$), 128.5, 128.4, 128.4, 128.3, 128.2, 128.2, 127.9, 127.8, 127.7, 127.5, 127.5, 127.2, 127.2, 126.8 (CH_{arom}), 100.6 (C-1), 97.8 (C-1'), 81.7 (C-3'), 80.1 (C-2'), 79.9 (C-3), 77.9 (C-4), 76.4 (C-2) ,75.1, 75.1 (CH_2 Bn), 75.0 (C-4'), 73.5, 73.4, 73.3 (CH_2 Bn), 73.1 (C-5), 72.4, 72.2 (CH_2 Bn), 70.0 (C-5'), 69.5 (C-6), 69.5 (C-6'), 55.4 (CH_3'); HRMS: $[M+Na]^+$ calcd for $C_{62}H_{66}O_{11}Na$ 1009.45503, found 1009.45509.



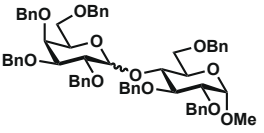
Methyl 4-*O*-(2,3,4-*O*-benzyl-D-mannopyranosyl)-1,2-*trans*-2,6-di-*O*-benzyl-3-*O*-benzoyl-D-glucopyranoside (S43). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Flash column chromatography (95:5 → 80:20, pentane:EtOAc) and size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound (77 mg, 77 µmol, 77%, colorless oil, 1,2-*cis*:1,2-*trans*; <2:98). TLC: R_f 0.37 (pentane:EtOAc, 80:20, v:v); $[\alpha]_D^{25}$ 20.2° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 813, 1021, 1254, 1446, 1726, 2912; ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.09 – 6.90 (m, 35H, CH_{arom}), 5.77 (dd, *J* = 10.0, 9.0 Hz, 1H, H-3'), 5.09 (d, *J* = 2.0 Hz, 1H, H-1), 4.81 (d, *J* = 10.9 Hz, 1H, C*H*H Bn), 4.74 (d, *J* = 3.5 Hz, 1H, H-1'), 4.62 – 4.35 (m, 9H, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.16 (d, *J* = 11.9 Hz, 1H, C*H*H Bn), 3.99 – 3.51 (m, 12H, H-2, H-3, H-4, H-5, H-6, H-6, H-2', H-4', H-5', H-6', H-6', CH*H* Bn), 3.42 (s, 3H, CH_3'); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 165.4 (C=O Bz), 138.7, 138.6, 138.4, 138.4, 138.3, 137.7 ($C_{q\text{-}arom}$), 133.5 (CH_{arom}), 130.1 ($C_{q\text{-}arom}$), 128.5, 128.4, 128.3, 128.3, 128.1, 128.1, 128.0, 128.0, 127.9, 127.9, 127.8, 127.7, 127.6, 127.6, 127.6, 127.5, 127.5, 127.5 (CH_{arom}), 100.6 (C-1), 97.6 (C-1'), 79.7 (C-3), 77.1 (C-4'), 76.9 (C-2'), 75.9 (C-2), 75.0 (CH_2 Bn), 74.5 (C-3', C-4), 73.5, 73.4 (CH_2 Bn), 73.1 (C-5), 72.8, 72.6, 71.6 (CH_2 Bn), 69.7 (C-5'), 69.5 (C-6/C-6'), 69.0 (C-6'/C-6), 55.5 (CH_3'); HRMS: $[M+Na]^+$ calcd for $C_{62}H_{64}O_{12}Na$ 1023.42955, found 1023.42900.



Methyl 4-*O*-(2,3,4-*O*-benzyl-D-mannopyranosyl)-1,2-*trans*-2,3,6-tri-*O*-benzoyl-D-glucopyranoside (S44). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Flash column chromatography (95:5 → 80:20, pentane:EtOAc) and size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound (61 mg, 59 µmol, 59%, colorless oil, 1,2-*cis*:1,2-*trans*; <2:98). TLC: R_f 0.49 (pentane:EtOAc, 80:20, v:v); $[\alpha]_D^{25}$ –80.1° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 745, 817, 1021, 1275, 1454, 1743, 2809, 2921; ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.2 – 6.9 (m, 35H, CH_{arom}), 6.1 (dd, *J* = 10.0, 8.5 Hz, 1H, H-3'), 5.2 – 5.1 (m, 3H, H-1, H-1', H-2'), 4.8 – 4.7 (m, 2H, H-6', C*H*H Bn), 4.6 – 4.4 (m, 4H, H-6', CH*H* Bn, C*H*H Bn, C*H*H Bn), 4.4 (d, *J* = 10.8 Hz, 1H, CH*H* Bn), 4.3 (d, *J* = 12.1 Hz, 1H, CH*H* Bn), 4.2 – 4.1 (m, 3H, H-4', H-5', C*H*H Bn), 4.0 (t, *J* = 9.4 Hz, 1H, H-4), 3.9 – 3.8 (m, 3H, H-3, H-5, CH*H* Bn), 3.7 (dd, *J* = 10.9, 4.0 Hz, 1H, H-6), 3.6 – 3.5 (m, 2H, H-2, H-6), 3.4 (s, 3H, CH_3'); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 166.3, 166.0, 165.6 (C=O Bz), 138.7, 138.5, 138.5, 138.4 ($C_{q\text{-}arom}$), 133.7, 133.5, 133.2 (CH_{arom}), 130.1 ($C_{q\text{-}arom}$), 130.0, 129.9 (CH_{arom}), 129.4, 129.2 ($C_{q\text{-}arom}$), 128.8, 128.6, 128.5, 128.4, 128.4, 128.3, 128.1, 128.1, 127.8, 127.6, 127.6, 127.5, 127.4, 127.2, 127.2 (CH_{arom}), 100.8 (C-1), 96.9 (C-1'), 79.6 (C-3), 76.5 (C-4'), 76.3 (C-2), 75.0 (CH_2 Bn), 74.5 (C-4), 73.5 (C-5), 73.5 (CH_2 Bn), 73.1 (C-3'), 72.8 (CH_2 Bn), 72.0 (C-2'), 71.9 (CH_2 Bn), 68.9 (C-6), 68.6 (C-5'), 63.6 (C-6'), 55.6 (CH_3'); HRMS: $[M+Na]^+$ calcd for $C_{62}H_{60}O_{14}Na$ 1051.38808, found 1051.38753.

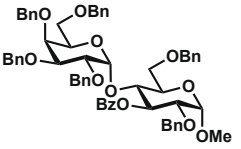


Methyl 6-*O*-(2,3,4-*O*-benzyl-D-galactopyranosyl)-2,3,4-tri-*O*-benzyl-D-glucopyranoside (S45). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Flash column chromatography (95:5 → 80:20, pentane:EtOAc) and size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound (74 mg, 75 µmol, 75%, colorless oil, 1,2-*cis*:1,2-*trans*; 30:70). TLC: R_f 0.67 (pentane:EtOAc, 80:20, v:v); IR (thin film, cm^{-1}): 721, 1047, 1367, 1464, 1481, 2921; Data of the major stereoisomer (1,2-*trans*): ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 7.68 – 7.13 (m, 35H, CH_{arom}), 4.97 – 4.33 (m, 16H, H-1', H-4'or H-4, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.30 (d, *J* = 7.7 Hz, 1H, H-1), 4.14 (dd, *J* = 10.8, 2.0 Hz, 1H, H-6/H-6'), 3.94 – 3.87 (m, 3H, H-3', H-4/H-4', H-5/H-5'), 3.88 – 3.66 (m, 2H, H-2, H-5'/H-5), 3.66 – 3.42 (m, 9H, H-3, H-2', H-6/H-6', H-6/H-6', H-6/H-6'), 3.29 (s, 3H, CH_3'); δ 139.0, 138.8, 138.8, 138.6, 138.5, 138.3, 138.0 ($C_{q\text{-}arom}$), 131.2, 129.4, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.2, 128.1, 128.1, 128.1, 128.1, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7, 127.6, 127.6, 127.6, 127.5, 124.9 (CH_{arom}), 104.3 (C-1), 98.0 (C-1'), 82.4 (C-3), 82.1 (C-3'), 80.0 (C-2'), 79.4 (C-2), 78.2 (C-4/C-4'), 75.8, 75.3, 74.9, 74.6, 73.6 (CH_2 Bn), 73.6 (C-4'/C-4), 73.5 (C-5/C-5'), 73.4 (CH_2 Bn, CH_2Bn), 73.0 (C-6/C-6'), 70.0 (C-5/C-5'), 68.7 (C-6'/C-6), 55.3 (CH_3'); Data for the minor stereoisomer (1,2-*cis*): ^1H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.99 (d, *J* = 3.6 Hz, 1H, H-1), 4.53 (d, *J* = 3.6 Hz, 1H, H-1'), 4.03 (dd, *J* = 9.3, 3.6 Hz, 1H, H-2), 3.41 (dd, *J* = 9.6, 3.5 Hz, 1H, H-2'); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 139.0, 138.8, 138.5, 138.3, 138.1 ($C_{q\text{-}arom}$), 98.0 (C-1), 98.0 (C-1'), 80.3, 76.6, 75.8, 75.1, 74.9, 73.5, 72.9, 72.6 (CH_2 Bn), 69.0 (C-6/C-6'), 66.5 (C-6'/C-6), 55.1 (CH_3'); HRMS: $[M+Na]^+$ calcd for $C_{62}H_{66}O_{11}Na$ 1009.45503, found 1009.44973.

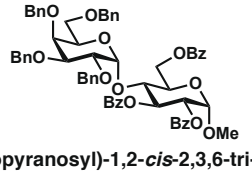


Methyl 4-*O*-(2,3,4-*O*-benzyl-D-galactopyranosyl)-2,3,6-tri-*O*-benzyl-D-glucopyranoside (S46). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h.

Flash column chromatography (95:5 → 80:20, pentane:EtOAc) and size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound (69 mg, 70 µmol, 70%, colorless oil, 1,2-*cis*:1,2-*trans*; 70:30). TLC: R_f 0.51 (pentane:EtOAc, 80:20, v:v); IR (thin film, cm^{-1}): 687, 745, 1031, 1076, 1471, 2912; Data of the major stereoisomer (1,2-*cis*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.40 – 7.09 (m, 35H, CH_{arom}), 5.76 (d, *J* = 3.9 Hz, 1H, H-1), 4.97 (d, *J* = 11.4 Hz, 1H, C*H*H Bn), 4.89 – 4.49 (m, 11H, H-1', C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.42 (d, *J* = 12.3 Hz, 1H, CH*H* Bn), 4.38 – 4.19 (m, 2H, C*H*H Bn, CH*H* Bn), 4.06 (t, *J* = 9.0 Hz, 1H, H-3'), 4.03 – 3.78 (m, 5H, H-2, H-3, H-4, H-5, H-4'), 3.78 – 3.57 (m, 2H, H-6, H-6), 3.57 – 3.40 (m, 4H, H-2', H-5', H-6', H-6'); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 139.1, 138.7, 138.7, 138.5, 138.4, 138.1 ($C_{q\text{-}arom}$), 128.5, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.0, 127.9, 127.9, 127.6, 127.5, 127.5, 126.8 (CH_{arom}), 97.9 (C-1'), 97.6 (C-1), 82.2 (C-3'), 80.3 (C-2'), 79.3 (C-3), 75.7 (C-2), 74.9 (CH_2 Bn), 74.7 (C-4'), 74.5, 73.9, 73.5, 73.5, 73.2, 72.9 (CH_2 Bn), 72.8 (C-4), 70.0 (C-5'), 69. (C-5)6, 69.5 (C-6), 68.8 (C-6'), 55.2 (CH_3'); Data for the minor stereoisomer (1,2-*trans*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): 4.57 (signal overlaps with major stereoisomer, 1H, H-1'), 4.30 (signal overlaps with major stereoisomer, 1H, H-1); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 139.6, 139.2, 139.1, 138.7, 138.6, 138.3, 138.2 ($C_{q\text{-}arom}$), 102.9 (C-1), 98.6 (C-1'), 75.6, 75.4, 74.8, 73.8, 73.3, 72.7 (CH_2 Bn), 68.3 (C-6/C-6'), 68.1 (C-6'or C-6), 55.4 (CH_3'); HRMS: $[M+Na]^+$ calcd for $C_{62}H_{66}O_{11}Na$ 1009.45503, found 1009.45511.

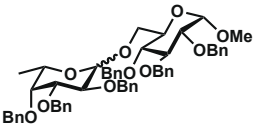


Methyl 4-*O*-(2,3,4-*O*-benzyl-D-galactopyranosyl)-1,2-*cis*-2,6-di-*O*-benzyl-3-*O*-benzoyl-D-glucopyranoside (S47). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Flash column chromatography (95:5 → 80:20, pentane:EtOAc) and size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound (70 mg, 70 µmol, 70%, colorless oil, 1,2-*cis*:1,2-*trans*; 92:8). TLC: R_f 0.55 (pentane:EtOAc, 80:20, v:v); $[\alpha]_D^{25}$ 10.2° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 814, 1042, 1271, 1451, 1728, 2921; Data of the major stereoisomer (1,2-*cis*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.13 – 7.02 (m, 35H, CH_{arom}), 5.88 (t, *J* = 9.6 Hz, 1H, H-3'), 5.05 (d, *J* = 3.2 Hz, 1H, H-1), 4.83 (d, *J* = 11.4 Hz, 1H, C*H*H Bn), 4.74 (d, *J* = 3.6 Hz, 1H, H-1'), 4.60 – 4.53 (m, 5H, C*H*H Bn, C*H*H Bn, C*H*H Bn, C*H*H Bn, C*H*H Bn), 4.47 (d, *J* = 11.4 Hz, 1H, CH*H* Bn), 4.43 – 4.28 (m, 3H, CH*H* Bn CH*H* Bn CH*H* Bn), 4.11 (t, *J* = 9.5 Hz, 1H, H-4'), 4.02 – 3.88 (m, 3H, H-5, H-6, CH*H* Bn), 3.86 (ddd, *J* = 9.9, 3.4, 1.9 Hz, 1H, H-5'), 3.83 – 3.71 (m, 3H, H-2, H-3, H-4), 3.66 (dd, *J* = 9.8, 3.4 Hz, 1H, H-2'), 3.60 (dd, *J* = 10.8, 2.0 Hz, 1H, H-6), 3.48 – 3.35 (m, 5H, H-6', H-6', CH_3'); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 165.6 (C=O Bz), 139.1, 138.7, 138.7, 138.2, 138.2, 137.9 ($C_{q\text{-}arom}$), 132.8 (CH_{arom}), 130.9 ($C_{q\text{-}arom}$), 130.0, 128.4, 128.4, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.8, 127.7, 127.6, 127.6, 127.6, 127.5, 127.4 (CH_{arom}), 98.8 (C-1), 97.8 (C-1'), 78.7 (C-3), 77.1 (C-2'), 76.1 (C-4), 75.4 (C-2), 75.2 (C-4'), 74.8 (CH_2 Bn), 73.8 (C-3'), 73.5, 73.4, 73.3, 72.9, 72.8 (CH_2 Bn), 70.4 (C-5), 70.0 (C-5'), 69.3 (C-6'), 68.7 (C-6), 55.4 (CH_3'); Data for the minor stereoisomer (1,2-*trans*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): 5.66 (t, *J* = 9.6 Hz, 1H, H-3'), 4.72 (d, *J* = 3.7 Hz, 1H, H-1'), ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 103.1 (C-1), 74.3, 73.2, 72.4, 70.7 (CH_2 Bn), 69.5 (C-6/C-6'), 67.6 (C-6'/C-6), 55.5 (CH_3'); HRMS: $[M+Na]^+$ calcd for $C_{62}H_{64}O_{12}Na$ 1023.42955, found 1023.42906.

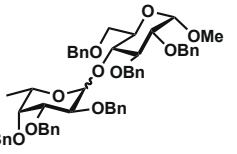


Methyl 4-*O*-(2,3,4-*O*-benzyl-D-galactopyranosyl)-1,2-*cis*-2,3,6-tri-*O*-benzoyl-D-glucopyranoside (S48). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Flash column chromatography (95:5 → 80:20, pentane:EtOAc) and size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound (68 mg, 66 µmol, 66%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). TLC: R_f 0.52 (pentane:EtOAc, 80:20, v:v); $[\alpha]_D^{25}$ 34.3° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 765, 1060, 1232, 1451, 1725, 2939; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.14 – 7.01

(m, 35H, CH_{arom}), 6.20 (dd, *J* = 10.3, 8.8 Hz, 1H, H-3'), 5.22 (dd, *J* = 10.2, 3.6 Hz, 1H, H-2'), 5.16 (d, *J* = 3.6 Hz, 1H, H-1), 5.13 (d, *J* = 3.5 Hz, 1H, H-1'), 4.85 – 4.75 (m, 2H, H-6', C*H*H Bn), 4.68 – 4.57 (m, 3H, H-6', CH_2 Bn), 4.43 (d, *J* = 11.3 Hz, 1H, CH*H* Bn), 4.36 – 4.20 (m, 4H, H-6, H-4', C*H*H Bn, C*H*H Bn), 4.15 (d, *J* = 11.8 Hz, 1H, CH*H* Bn), 4.05 (d, *J* = 12.1 Hz, 1H, CH*H* Bn), 4.00 (t, *J* = 6.5 Hz, 1H, H-4), 3.94 – 3.87 (m, 2H, H-3, H-5'), 3.82 (dd, *J* = 9.8, 3.6 Hz, 1H, H-2), 3.47 – 3.32 (m, 5H, H-5, H-6, CH_3'); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 166.2, 166.2, 165.6 (C=O Bz), 138.9, 138.6, 138.4, 138.1 ($C_{q\text{-}arom}$), 133.4, 133.2, 133.1, 130.1 (CH_{arom}), 130.0 ($C_{q\text{-}arom}$), 129.9, 129.8 (CH_{arom}), 129.2 ($C_{q\text{-}arom}$), 128.5, 128.5, 128.4, 128.3, 128.2, 127.9, 127.7, 127.7, 127.5 (CH_{arom}), 99.1 (C-1), 96.9 (C-1'), 78.8 (C-3), 75.4 (C-2), 75.1 (C-5'), 74.9 (CH_2 Bn), 74.7 (C-4'), 73.4, 73.3, 73.1 (CH_2 Bn), 72.4 (C-2'), 72.3 (C-3'), 70.7 (C-4), 68.7 (C-5), 68.6 (C-6), 63.6 (C-6'), 55.5 (CH_3'); HRMS: $[M+Na]^+$ calcd for $C_{62}H_{60}O_{14}Na$ 1051.38808, found 1051.38753.

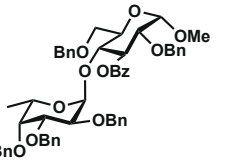


Methyl 6-*O*-(2,3,4-*O*-benzyl-D-fucopyranosyl)-2,3,4-tri-*O*-benzyl-D-glucopyranoside (S49). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Flash column chromatography (95:5 → 80:20, pentane:EtOAc) and size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound (89 mg, 90 µmol, 90%, colorless oil, 1,2-*cis*:1,2-*trans*; 45:55). TLC: R_f 0.29 (pentane:EtOAc, 80:20, v:v); IR (thin film, cm^{-1}): 732, 1028, 1375, 1451, 1499, 2922; Data of the major stereoisomer (1,2-*trans*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.50 – 7.06 (m, 30H, CH_{arom}), 5.01 – 4.93 (m, 2H, C*H*H Bn, C*H*H Bn), 4.88 – 4.52 (m, 11H, H-1', CH*H* Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.40 (d, *J* = 7.7 Hz, 1H, H-1), 4.17 (dd, *J* = 11.4, 3.9 Hz, 1H, H-6'), 4.01 – 3.93 (m, 1H, H-3'), 3.85 – 3.71 (m, 3H, H-2, H-5', H-6'), 3.71 – 3.39 (m, 5H, H-3, H-4, H-5, H-2', H-4'), 3.32 (s, 3H, CH_3'), 1.16 (d, *J* = 6.4 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 144.8, 139.1, 139.0, 138.8, 138.5, 138.4 ($C_{q\text{-}arom}$), 128.5, 128.5, 128.4, 128.3, 128.3, 128.1, 128.0, 127.8, 127.7, 127.6 (CH_{arom}), 103.9 (C-1), 98.1 (C-1'), 82.5 (C-3), 82.1 (C-3'), 80.4 (C-2'), 79.6 (C-2), 77.9 (C-4, C-4'), 75.8, 75.2, 75.2, 74.7, 73.5, 73.3 (CH_2 Bn), 70.4 (C-5), 70.2 (C-5'), 67.6 (C-6'), 55.2 (CH_3'), 17.0 (CH_3); Data for the minor stereoisomer (1,2-*cis*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.90 (d, *J* = 3.5 Hz, 1H, H-1), 4.04 (dd, *J* = 10.1, 3.5 Hz, 1H, H-2), 3.90 (q, *J* = 6.5 Hz, 1H, H-5), 3.31 (s, 3H, CH_3'), 1.10 (d, *J* = 6.5 Hz, 3H. CH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 98.1 (C-1), 98.1 (C-1'), 80.2 (C-3), 76.4 (C-2), 75.9, 75.0, 74.9, 73.4, 73.2, 73.0 (C-6), 70.2 (C-5'), 66.5 (C-6'), 66.4 (C-5), 55.2 (CH_3'), 16.7 (CH_3); HRMS: $[M+Na]^+$ calcd for $C_{55}H_{60}O_{10}Na$ 903.40842, found 903.40787.

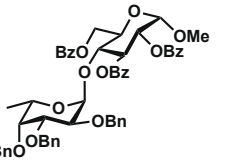


Methyl 4-*O*-(2,3,4-*O*-benzyl-D-fucopyranosyl)-2,3,6-tri-*O*-benzyl-D-glucopyranoside (S50). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Flash column chromatography (95:5 → 80:20, pentane:EtOAc) and size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound (74 mg, 75 µmol, 75%, colorless oil, 1,2-*cis*:1,2-*trans*; 90:10). TLC: R_f 0.31 (pentane:EtOAc, 80:20, v:v); IR (thin film, cm^{-1}): 694, 735, 1031, 1095, 1443, 1470, 2913; Data of the major stereoisomer (1,2-*cis*): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.49 – 7.12 (m, 30H, CH_{arom}), 5.05 (d, *J* = 10.9 Hz, 1H, C*H*H Bn), 4.99 (d, *J* = 3.7 Hz, 1H, H-1), 4.89 (d, *J* = 11.6 Hz, 1H, C*H*H Bn), 4.79 – 4.67 (m, 5H, C*H*H Bn, C*H*H Bn, CH*H* Bn, CH*H* Bn), 4.64 – 4.53 (m, 5H, C*H*H Bn, C*H*H Bn, CH*H* Bn, CH*H* Bn), 4.40 – 4.30 (m, 2H, C*H*H Bn, CH*H* Bn), 4.02 – 3.95 (m, 2H, H-2, H-5), 3.90 (ddd, *J* = 9.3, 7.2, 1.6 Hz, 1H, H-3'), 3.85 (dd, *J* = 10.3, 2.8 Hz, 1H, H-3), 3.79 (m, *J* = 7.5 Hz, 2H, H-4', H-5'), 3.70 (dd, *J* = 10.8, 3.0 Hz, 1H, H-6'), 3.64 (dd, *J* = 10.9, 1.5 Hz, 1H, H-6'), 3.57 (dd, *J* = 9.5, 3.6 Hz, 1H, H-2'), 3.36 – 3.32 (m, 4H, H-4, CH_3'), 0.66 (d, *J* = 6.4 Hz, 3H, CH_3); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 139.0, 138.9, 138.8, 138.5, 138.1, 138.1 ($C_{q\text{-}arom}$), 128.6, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.7, 127.7, 127.6, 127.6, 127.6, 127.5 (CH_{arom}), 97.9 (C-1'), 97.7 (C-1), 80.6 (C-2'), 80.3 (C-3'), 79.6 (C-3), 77.6 (C-4), 76.4 (C-2), 75.7, 74.8, 74.5 (CH_2 Bn), 73.8 (C-4'), 73.4, 73.3, 72.8 (CH_2

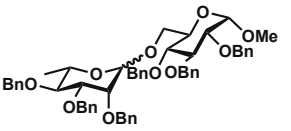
Bn), 70.4 (C-5'), 68.7 (C-6'), 66.8 (C-5), 55.1 (CH_3'), 16.4 (CH_3); HRMS: $[M+Na]^+$ calcd for $C_{55}H_{60}O_{10}Na$ 903.40842, found 903.40788.



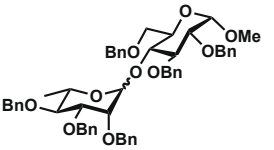
Methyl 4-*O*-(2,3,4-*O*-benzyl-D-fucopyranosyl)-1,2-*cis*-2,6-di-*O*-benzyl-3-*O*-benzoyl-D-glucopyranoside (S51). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound afforded the title compound (85 mg, 85 µmol, 85%, colorless oil, 1,2-*cis*:1,2-*trans*; 93:7). TLC: R_f 0.25 (pentane:EtOAc, 80:20, v:v); IR (thin film, cm^{-1}): 822, 1041, 1272, 1453, 1728, 2917; Data of the major stereoisomer (1,2-*cis*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.11 – 6.98 (m, 30H, CH_{arom}), 5.75 (dd, *J* = 9.9, 9.0 Hz, 1H, H-3'), 4.94 (d, *J* = 3.4 Hz, 1H, H-1), 4.82 (m, 2H, C*H*H Bn, C*H*H Bn), 4.75 – 4.63 (m, 3H, H-1', C*H*H Bn, C*HH* Bn), 4.57 – 4.45 (m, 4H, C*H*H Bn, CH*H* Bn, CH*H* Bn, CH*H* Bn), 4.40 – 4.29 (m, 2H, C*H*H Bn, CH*H* Bn), 4.01 – 3.81 (m, 5H, H-2, H-3, H-4', H-5', H-6'), 3.73 (qd, *J* = 6.4, 1.1 Hz, 2H, H-5), 3.64 (dd, *J* = 11.0, 1.9 Hz, 1H, H-6'), 3.56 (dd, *J* = 9.9, 3.5 Hz, 1H, H-2'), 3.47 (dd, *J* = 2.5, 1.4 Hz, 1H, H-4), 3.38 (s, 3H, CH_3'), 0.57 (d, *J* = 6.4 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 165.9 (C=O Bz), 138.7, 138.7, 138.5, 138.2, 137.6 ($C_{q\text{-}arom}$), 133.0 (CH_{arom}), 130.5 ($C_{q\text{-}arom}$), 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.2, 128.1, 127.9, 127.7, 127.7, 127.6, 127.6, 127.5, 127.5 (CH_{arom}), 99.5 (C-1), 97.4 (C-1'), 79.8 (C-3), 77.7 (C-4), 77.6 (C-2'), 76.1 (C-2), 75.3 (C-4'), 75.0, 74.5 (CH_2 Bn), 73.4 (C-3'), 73.3, 72.7, 72.7 (CH_2 Bn), 70.3 (C-5'), 68.3 (C-6'), 67.2 (C-5), 55.3 (CH_3'), 16.2 (C-6); Data for the minor stereoisomer (1,2-*trans*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.86 (t, *J* = 9.6 Hz, 1H, H-3'), 4.42 (d, *J* = 7.7 Hz, 1H, H-1), 3.25 (q, *J* = 6.2 Hz, 1H, H-5), 3.04 (dd, *J* = 9.7, 3.0 Hz, 1H, H-3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 103.7 (C-1), 97.6 (C-1'), 82.3 (C-2), 70.6 (C-5); HRMS: $[M+Na]^+$ calcd for $C_{55}H_{58}O_{11}Na$ 917.38768, found 917.38713.



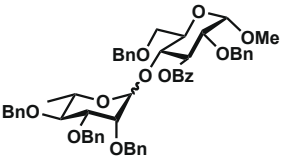
Methyl 4-*O*-(2,3,4-*O*-benzyl-D-fucopyranosyl)-1,2-*cis*-2,3,6-tri-*O*-benzoyl-D-glucopyranoside (S52). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound afforded the title compound (78 mg, 76 µmol, 76%, colorless oil, 1,2-*cis*:1,2-*trans*; >98:2). TLC: R_f 0.19 (pentane:EtOAc, 80:20, v:v); $[\alpha]_D^{25}$ 22.6° (*c* 1, $CHCl_3$); IR (thin film, cm^{-1}): 817, 1024, 1281, 1451, 1721, 2890; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.13 – 7.14 (m, 30H), 5.99 (ddd, *J* = 11.3, 9.0, 1.6 Hz, 1H, H-3'), 5.13 – 5.07 (m, 2H, H-1', H-2'), 4.97 – 4.66 (m, 10H, H-1, H-6', H-6', C*H*H Bn, C*HH* Bn, C*H*H Bn, C*HH* Bn, C*H*H Bn), 4.51 (d, *J* = 11.5 Hz, 1H, CH*H* Bn), 4.17 (ddd, *J* = 10.0, 4.5, 2.1 Hz, 1H, H-5'), 4.06 – 3.90 (m, 3H, H-2, H-3, H-4'), 3.80 (dd, *J* = 6.4, 1.4 Hz, 1H, H-5), 3.51 (dd, *J* = 2.4, 1.4 Hz, 1H, H-4), 3.39 (s, 3H, CH_3'), 0.64 (d, *J* = 6.4 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 166.2, 166.1, 166.0 (C=O Bz), 138.8, 138.6, 138.2 ($C_{q\text{-}arom}$), 133.4, 133.2, 133.1 (CH_{arom}), 130.2 ($C_{q\text{-}arom}$), 130.0 (CH_{arom}), 129.9 ($C_{q\text{-}arom}$), 129.8, 129.1 (CH_{arom}), 128.6 ($C_{q\text{-}arom}$), 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.2, 127.8, 127.6, 127.6, 127.5 (CH_{arom}), 100.7 (C-1), 96.8 (C-1'), 79.5 (C-3), 77.8 (C-4), 76.9 (C-4'), 75.8 (C-2), 75.0, 74.5, 72.8 (CH_2 Bn), 72.6 (C-2'), 71.9 (C-3'), 69.1 (C-5'), 67.8 (C-5), 63.1 (C-6'), 55.4 (CH_3), 16.1 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{55}H_{54}O_{13}$ 945.34621, found 945.34566.



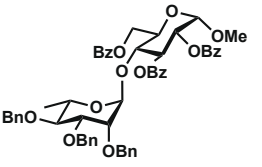
Methyl 6-*O*-(2,3,4-*O*-benzyl-D-rhamnopyranosyl)-2,3,4-tri-*O*-benzyl-D-glucopyranoside (S53). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Flash column chromatography (95:5 → 80:20, pentane:EtOAc) and size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound (90 mg, 91 µmol, 91%, colorless oil, 1,2-*cis*:1,2-*trans*; 66:34). TLC: R_f 0.20 (1,2-*cis*) and 0.50 (1,2-*trans*) (pentane:EtOAc, 80:20, v:v); IR (thin film, cm^{-1}): 731, 1031, 1033, 1366, 1451, 1489, 2850, 2912; Data of the major stereoisomer (1,2-*cis*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.49 – 7.12 (m, 30H, CH_{arom}), 5.01 – 4.91 (m, 2H, C*H*H Bn, C*H*H Bn), 4.87 (d, *J* = 11.6 Hz, 1H, CH*H* Bn), 4.85 – 4.74 (m, 2H, C*H*H Bn, C*H*H Bn), 4.75 – 4.57 (m, 6H, H-1', CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.55 – 4.40 (m, 3H, H-1, C*H*H Bn, CH*H* Bn), 4.28 (dd, *J* = 11.1, 3.1 Hz, 1H, H-6'), 4.03 – 3.90 (m, 2H, H-2, H-4'), 3.77 – 3.53 (m, 4H, H-4, H-2', H-5', H-6'), 3.52 – 3.40 (m, 2H, H-3, H-3'), 3.38 – 3.29 (m, 4H, H-5, CH_3'), 1.35 (d, *J* = 6.2 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 139.0, 138.9, 138.6, 138.5, 138.3, 138.3 ($C_{q\text{-}arom}$), 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.2, 128.2, 128.1, 128.0, 128.0, 127.9, 127.8, 127.8, 127.8, 127.7, 127.7, 127.7, 127.5 (CH_{arom}), 101.5 (C-1), 98.4 (C-1'), 82.1 (C-4), 82.0 (C-3), 80.3 (C-3'), 79.9 (C-2'), 77.9 (C-2), 75.9, 75.5, 75.3 (CH_2 Bn), 74.3 (C-4'), 74.1, 73.6 (CH_2 Bn), 72.1 (C-5), 71.4 (CH_2 Bn), 70.1 (C-5'), 67.3 (C-6'), 55.3 (CH_3'), 18.1 (CH_3); ^{13}C-GATED NMR (101 MHz, $CDCl_3$) δ 101.5 ($J_{H1\text{-}C1}$ = 154 Hz, 1,2-*cis*); Data for the minor stereoisomer (1,2-*trans*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.71 (d, *J* = 1.8 Hz, 1H, H-1), 4.52 (d, *J* = 3.5 Hz, 1H, H-1'), 4.36 (d, *J* = 11.0 Hz, 1H, C*H*H Bn), 3.26 (s, 3H, CH_3'), 1.30 (d, *J* = 6.1 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 138.8, 138.7, 138.6, 138.4, 138.2, 138.2 ($C_{q\text{-}arom}$), 98.3 (C-1), 97.9 (C-1'), 75.9, 75.6, 75.1, 73.4, 72.8, 72.4 (CH_2 Bn), 70.0 (C-5), 68.1 (C-5'), 66.1 (C-6'), 55.1 (CH_3'), 18.1 (CH_3); ^{13}C-GATED NMR (101 MHz, $CDCl_3$) δ 98.3 ($J_{H1\text{-}C1}$ = 168 Hz, 1,2-*trans*); HRMS: $[M+Na]^+$ calcd for $C_{55}H_{60}O_{10}Na$ 903.40842, found 903.40787.



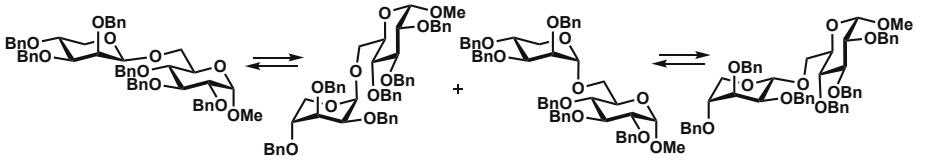
Methyl 4-*O*-(2,3,4-*O*-benzyl-D-rhamnopyranosyl)-2,3,6-tri-*O*-benzyl-D-glucopyranoside (S54). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Flash column chromatography (95:5 → 80:20, pentane:EtOAc) and size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound (83 mg, 84 µmol, 84%, colorless oil, 1,2-*cis*:1,2-*trans*; 12:88). TLC: R_f 0.55 (pentane:EtOAc, 80:20, v:v); IR (thin film, cm^{-1}): 731, 1022, 1089, 1458, 1456, 2916; Data of the major stereoisomer (1,2-*trans*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.63 – 7.04 (m, 30H, CH_{arom}), 5.04 (d, *J* = 1.9 Hz, 1H, H-1), 4.96 (d, *J* = 10.2 Hz, 1H, C*H*H Bn), 4.91 (d, *J* = 10.9 Hz, 1H, C*H*H Bn), 4.77 – 4.69 (m, 2H, C*H*H Bn, C*H*H Bn), 4.63 – 4.53 (m, 9H, H-1', CH*H* Bn, CH*H* Bn, CH*H* Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.48 (d, *J* = 12.1 Hz, 1H, C*H*H Bn), 4.41 (d, *J* = 12.1 Hz, 1H, CH*H* Bn), 3.91 (td, *J* = 9.4, 4.6 Hz, 1H, H-5), 3.86 – 3.73 (m, 2H, H-3', H-4'), 3.68 (t, *J* = 2.5 Hz, 2H, H-2), 3.63 (ddd, *J* = 9.0, 3.7, 1.7 Hz, 1H, H-5'), 3.60 – 3.48 (m, 4H, H-3, H-4, H-2', H-6'), 3.47 – 3.39 (m, 1H, H-6'), 3.35 (s, 3H, CH_3'), 1.06 (d, *J* = 6.1 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 138.9, 138.7, 138.7, 138.5, 138.1, 138.0 ($C_{q\text{-}arom}$), 128.5, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 127.6, 127.6, 127.5, 127.4 (CH_{arom}), 98.2 (C-1), 98.0 (C-1'), 80.8 (C-4), 80.6 (C-2'), 80.1 (C-3'), 79.8 (C-3), 75.6, 75.3 (CH_2 Bn), 75.2 (C-2), 75.2 (C-4'), 73.6, 73.5, 72.5, 72.2 (CH_2 Bn), 70.1 (C-5'), 69.0 (C-6'), 68.8 (C-5), 55.4 (CH_3'), 18.0 (CH_3); ^{13}C-GATED NMR (101 MHz, $CDCl_3$) δ 98.2 ($J_{H1\text{-}C1}$ = 168 Hz, 1,2-*trans*); Data for the minor stereoisomer (1,2-*cis*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.61 (signal overlaps with major stereoisomer, 1H, H-1), 4.21 (d, *J* = 11.8 Hz, 1H, C*H*H Bn), 4.16 (d, *J* = 11.7 Hz, 1H, CH*H* Bn), 3.44 (s, 3H, CH_3'); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 102.5 (C-1), 55.5 (CH_3'), 18.1 (CH_3); HRMS: $[M+Na]^+$ calcd for $C_{55}H_{60}O_{10}Na$ 903.40842, found 903.40789.



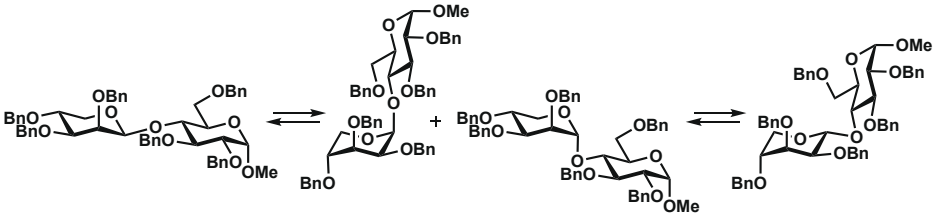
Methyl 4-*O*-(2,3,4-*O*-benzyl-D-rhamnopyranosyl)-2,6-di-*O*-benzyl-3-*O*-benzoyl-D-glucopyranoside (S55). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Flash column chromatography (95:5 → 80:20, pentane:EtOAc) and size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound (78 mg, 78 µmol, 78%, colorless oil, 1,2-*cis*:1,2-*trans*; 10:90). TLC: R_f 0.27 (pentane:EtOAc, 80:20, v:v); IR (thin film, cm^{-1}): 843, 1054, 1261, 1451, 1743, 2925; Data of the major stereoisomer (1,2-*trans*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 8.09 – 7.11 (m, 30H, CH_{arom}), 5.70 (t, *J* = 9.6 Hz, 1H, H-3'), 4.88 (d, *J* = 2.0 Hz, 1H, H-1), 4.77 (d, *J* = 11.4 Hz, 1H, C*H*H Bn), 4.70 (d, *J* = 3.5 Hz, 1H, H-1'), 4.67 – 4.40 (m, 11H, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 3.96 (t, *J* = 9.7 Hz, 1H, H-4'), 3.77 (ddd, *J* = 9.9, 3.4, 1.9 Hz, 1H, H-5'), 3.70 (dd, *J* = 9.2, 2.9 Hz, 1H, H-3), 3.61 (t, *J* = 2.4 Hz, 1H, H-2), 3.60 – 3.49 (m, 2H, H-5, H-2'), 3.49 – 3.35 (m, 6H, H-4, H-6', H-6', CH_3'); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 165.7 (C=O Bz), 139.0, 138.8, 138.6, 137.9, 137.8 ($C_{q\text{-}arom}$), 132.9 (CH_{arom}), 130.5 ($C_{q\text{-}arom}$), 130.1, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.2, 128.1, 128.1, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 127.5, 127.4 (CH_{arom}), 99.0 (C-1), 97.8 (C-1'), 80.5 (C-4), 79.6 (C-3), 77.4 (C-2'), 75.8 (C-2), 75.3 (C-4'), 74.6, 73.8, 72.8, 72.7 (CH_2 Bn), 72.6 (C-3'), 72.5 (CH_2 Bn), 69.9 (C-5'), 69.0 (C-5), 68.7 (C-6'), 55.5 (CH_3'), 17.7 (CH_3); ^{13}C-GATED NMR (101 MHz, $CDCl_3$) δ 99.0 ($J_{H1\text{-}C1}$ = 167 Hz, 1,2-*trans*); Data for the minor stereoisomer (1,2-*cis*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.81 (dd, *J* = 10.2, 8.9 Hz, 1H, H-3'), 4.41 (signa loverlaps with major stereoisomer, 1H, H-1); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 102.9 (C-1), 18.0 (CH_3); HRMS: $[M+Na]^+$ calcd for $C_{55}H_{58}O_{11}Na$ 917.38768, found 917.38713.



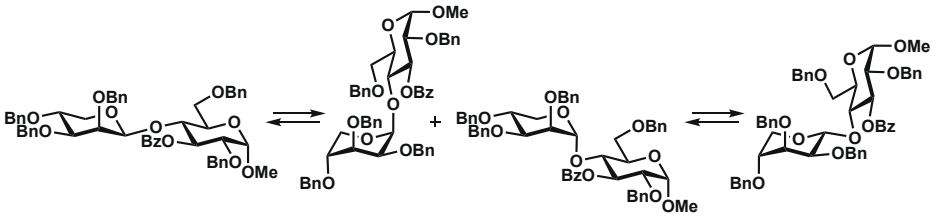
Methyl 4-*O*-(2,3,4-*O*-benzyl-D-rhamnopyranosyl)-1,2-*trans*-2,3,6-tri-*O*-benzoyl-D-glucopyranoside (S56). The title The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Flash column chromatography (95:5 → 80:20, pentane:EtOAc) and size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound (52 mg, 51 µmol, 51%, colorless oil, 1,2-*cis*:1,2-*trans*; <2:98). TLC: R_f 0.30 (pentane:EtOAc, 80:20, v:v); IR (thin film, cm^{-1}): 809, 1013, 1251, 1442, 1713, 2933; ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 8.15 – 7.16 (m, 30H, CH_{arom}), 5.94 (tt, *J* = 9.0, 1.9 Hz, 1H, H-3'), 5.12 – 5.06 (m, 2H, H-1', H-2'), 4.86 – 4.78 (m, 2H, H-1, C*H*H Bn), 4.72 – 4.46 (m, 5H, H-6', CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.20 (dd, *J* = 12.2, 4.0 Hz, 1H, H-6'), 4.07 – 3.93 (m, 2H, H-4', H-5'), 3.80 – 3.70 (m, 2H, H-2, H-3), 3.58 (dq, *J* = 9.4, 6.2 Hz, 1H, H-5), 3.48 – 3.37 (m, 4H, H-4, CH_3'), 0.81 (d, *J* = 6.1 Hz, 3H, CH_3); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 166.2, 166.1, 165.9 (C=O Bz), 138.9, 138.6, 138.3 ($C_{q\text{-}arom}$), 133.5, 133.4, 133.1, 130.0, 129.9, 129.9(CH_{arom}), 129.9, 129.8, 129.1 ($C_{q\text{-}arom}$), 128.8, 128.5, 128.5, 128.4, 128.3, 128.1, 127.9, 127.9, 127.7, 127.7, 127.5 (CH_{arom}), 99.9 (C-1), 96.9 (C-1'), 80.3 (C-4), 79.3 (C-3), 76.0 (C-4'), 75.4 (C-2), 74.9, 73.1, 72.5 (CH_2 Bn), 72.4 (C-2'), 71.1 (C-3'), 69.3 (C-5), 68.8 (C-5'), 62.7 (C-6'), 55.6 (CH_3'), 17.6 (CH_3); ^{13}C-GATED NMR (126 MHz, $CDCl_3$) δ 99.9 ($J_{H1\text{-}C1}$ = 165 Hz, 1,2-*trans*); HRMS: $[M+Na]^+$ calcd for $C_{55}H_{54}O_{13}$ 945.34621, found 945.34566.



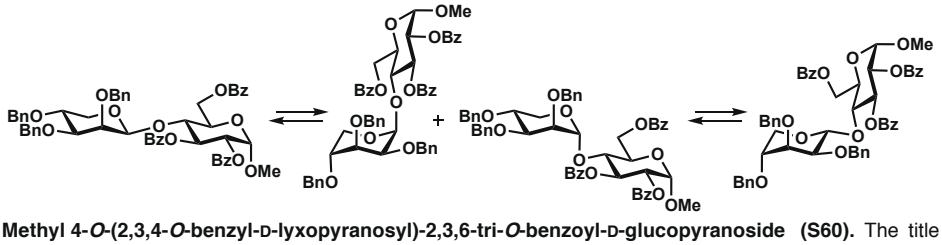
Methyl 6-*O*-(2,3,4-*O*-benzyl-D-lyxopyranosyl)-2,3,4-tri-*O*-benzyl-D-glucopyranoside (S57). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Flash column chromatography (95:5 → 70:30, pentane:EtOAc) and size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound (94 mg, 95 µmol, 95%, colorless oil, 1,2-*cis*:1,2-*trans*; 60:40). TLC: R_f 0.25 and 0.33 and (pentane:EtOAc, 80:20, v:v); IR (thin film, cm^{-1}): 730, 1031, 1045, 1367, 1451, 1491, 2922; Data of the major stereoisomer (1,2-*cis*): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.42 – 7.15 (m, 60H, CH_{arom}), 4.98 (d, *J* = 10.8 Hz, 2H, C*H*H Bn), 4.92 – 4.50 (m, 12H, H-1', CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.29 (bs, 1H, H-1), 4.10 – 3.38 (m, 10H, H-2, H-2', H-3, H-3', H-4, H-4', H-5, H-5', H-6', H-6'), 3.30 (s, 3H, CH_3'), 3.18 (dd, *J* = 11.6, 7.8 Hz, 1H, H-5); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 138.9, 138.7, 138.6, 138.5, 138.3, 138.2 ($C_{q\text{-}arom}$), 128.6, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.2, 128.1, 128.1, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7 (CH_{arom}), 100.8 (C-1), 97.9 (C-1'), 82.2 (C-3'), 82.2 (C-4'), 80.0 (C-2'), 77.7 (C-3), 75.9, 75.8, 75.1 (CH_2 Bn), 74.9 (C-2, C-4), 74.9, 73.4, 73.2 (CH_2 Bn), 69.9 (C-5'), 66.2 (C-6'), 62.9 (C-5), 55.2 (CH_3'); ^{13}C-GATED NMR (126 MHz, $CDCl_3$) δ 100.8 ($J_{H1\text{-}C1}$= 159 Hz, 1,2-*cis*); Data for the minor stereoisomer (1,2-*trans*): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 4.80 (signal overlaps with major stereoisomer, 1H, H-1) 3.31 (s, 3H, CH_3'); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 99.1 (C-1), 98.3 (C-1'), 67.9 (C-6'), 70.0 (C-5'), 62.0 (C-5), 55.1 (CH_3'); ^{13}C-GATED NMR (126 MHz, $CDCl_3$) δ 99.1 ($J_{H1\text{-}C1}$= 165 Hz, 1,2-*trans*); HRMS: $[M+Na]^+$ calcd for $C_{54}H_{58}O_{10}Na$ 889.39277, found 889.39222.



Methyl 4-*O*-(2,3,4-*O*-benzyl-D-lyxopyranosyl)-2,3,6-tri-*O*-benzyl-D-glucopyranoside (S58). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound afforded the title compound (73 mg, 0.084 mmol, 84%, colorless oil, 1,2-*cis*:1,2-*trans*; 90:10). TLC: R_f 0.30 and 0.25 (pentane:EtOAc, 80:20, v:v); IR (thin film, cm^{-1}): 695, 734, 1027, 1086, 1452, 1496, 2925; ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.39 – 7.17 (m, 30H, CH_{arom}), 4.99 (d, *J* = 10.9 Hz, 1H, C*H*H Bn), 4.92 – 4.48 (m, 7H, H-1, CH*H* Bn, CH_2 Bn, CH_2 Bn, H-3), 4.30 (s, 1H, H-1), 4.07 – 3.97 (m, 3H, H-5_{eq}, H-3', H-6'), 3.87 (td, *J* = 7.5, 4.3 Hz, 1H, H-4), 3.78 (ddd, *J* = 10.4, 5.0, 1.8 Hz, 1H, H-5'), 3.74 (dd, *J* = 3.1, 1.8 Hz, 1H, H-2), 3.56 – 3.42 (m, 4H, H-3, H-2', H-4', H-6'), 3.31 (s, 3H, OMe'), 3.19 (dd, *J* = 11.9, 7.7 Hz, 1H, H-5_{ax}); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 138.9, 138.4, 138.2 ($C_{q\text{-}arom}$), 128.5, 128.5, 128.4, 128.4, 128.4, 128.3, 128.2, 128.0, 127.9, 127.8, 127.8, 127.7, 127.6 (CH_{arom}), 100.7 (C-1), 97.9 (C-1'), 82.2 (C-3'), 80.0 (C-2'), 77.7 (C-4'), 75.0 (CH_2 Bn), 74.9 (C-4, CH_2 Bn), 75.0, 74.9, 74.9 (CH_2 Bn), 74.4 (C-2), 73.4, 73.3, 73.0, 72.3 (CH_2 Bn), 69.9 (C-5'), 67.8 (C-6'), 62.7 (C-5), 55.1 (Me'); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 100.7 ($J_{H1\text{-}C1}$ = 159 Hz, 1,2-*cis*); HRMS: $[M+NH_4]^+$ calcd for $C_{54}H_{58}O_{10}$ 884.43682, found 884.43612.

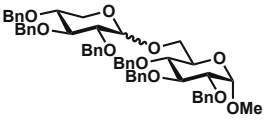


Methyl 4-*O*-(2,3,4-*O*-benzyl-D-lyxopyranosyl)-2,6-di-*O*-benzyl-3-*O*-benzoyl-D-glucopyranoside (S59). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Flash column chromatography (95:5 → 70:30, pentane:EtOAc) and size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound (74 mg, 74 µmol, 74%, colorless oil, 1,2-*cis*:1,2-*trans*; 55:45). TLC: R_f 0.26 and 0.35 and (pentane:EtOAc, 80:20, v:v); IR (thin film, cm^{-1}): 814, 1053, 1251, 1431, 1723, 2919; NMR data reported as a mixture of 1,2-*cis*:1,2-*trans* (55:45) anomers: ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated) δ 8.16 – 6.86 (m, 60H, $CH_{arom\text{-}1,2\text{-}trans}$, $CH_{arom\text{-}1,2\text{-}cis}$), 5.88 – 5.72 (m, 2H, H-$3_{1,2\text{-}trans}$', H-$3_{1,2\text{-}cis}$'), 4.98 (d, *J* = 3.0 Hz, 1H, H-$1_{1,2\text{-}trans}$), 4.75 (d, *J* = 3.4 Hz, 1H, H-1'$_{1,2\text{-}trans}$), 4.74 (d, *J* = 3.5 Hz, 1H, H-1'$_{1,2\text{-}cis}$), 4.70 – 4.62 (m, 2H, H-$1_{1,2\text{-}cis}$, C*H*H Bn), 4.62 – 4.30 (m, 17H, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.23 (d, *J* = 11.7 Hz, 1H, C*H*H $Bn_{1,2\text{-}trans}$), 4.09 – 3.49 (m, 18H, CH*H* $Bn_{1,2\text{-}trans}$, H-$2_{1,2\text{-}trans}$, H-$2_{1,2\text{-}cis}$, H-$3_{1,2\text{-}trans}$, H-$3_{1,2\text{-}cis}$, H-$4_{1,2\text{-}trans}$, H-$5_{1,2\text{-}trans}$, H-$5_{1,2\text{-}cis}$, H-2'$_{1,2\text{-}trans}$, H-2'$_{1,2\text{-}cis}$, H-4'$_{1,2\text{-}trans}$, H-4'$_{1,2\text{-}cis}$, H-5'$_{1,2\text{-}trans}$, H-5'$_{1,2\text{-}cis}$, H-$6_{1,2\text{-}trans}$, H-$6_{1,2\text{-}trans}$, H-6'$_{1,2\text{-}cis}$, H-6'$_{1,2\text{-}cis}$), 3.49 – 3.33 (m, 8H, H-$4_{1,2\text{-}cis}$, H-$5_{1,2\text{-}trans}$, CH_3'$_{1,2\text{-}trans}$, CH_3'$_{1,2\text{-}cis}$), 2.89 (dd, *J* = 12.3, 4.4 Hz, 1H, H-$5_{1,2\text{-}cis}$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 165.6 (C=O $Bz_{1,2\text{-}cis}$), 165.4 (C=O $Bz_{\text{-}1,2\text{-}trans}$), 138.9, 138.8, 138.6, 138.4, 138.3, 138.2, 138.1, 137.9, 137.7 ($C_{q\text{-}arom}$), 133.3, 132.6, 131.1, 130.2, 129.9, 129.9, 128.7, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.2, 128.2, 128.1, 128.1, 128.0, 127.8, 127.8, 127.7, 127.7, 127.6, 127.6, 127.5, 127.4, 127.3 (CH_{arom}), 100.9 (C-$1_{1,2\text{-}trans}$), 100.3 (C-$1_{1,2\text{-}cis}$), 97.8 (C-1'$_{1,2\text{-}cis}$), 97.7 (C-1'$_{1,2\text{-}trans}$), 77.5 (C-$3_{1,2\text{-}cis}$), 77.0 (C-$3_{1,2\text{-}trans}$, C-4'$_{1,2\text{-}trans}$), 76.5 (C-$2_{1,2\text{-}cis}$), 76.0 (C-4'$_{1,2\text{-}cis}$), 75.0 (C-$4_{1,2\text{-}cis}$), 74.6 (C-$2_{1,2\text{-}trans}$), 74.5 (C-3'$_{1,2\text{-}trans}$), 74.5 (C-$4_{1,2\text{-}trans}$), 73.7 (CH_2 $Bn_{1,2\text{-}cis}$), 73.4 (CH_2 $Bn_{1,2\text{-}cis}$), 73.3 (CH_2 $Bn_{1,2\text{-}trans}$), 72.9 (C-3'$_{1,2\text{-}cis}$), 72.7 (CH_2 $Bn_{1,2\text{-}trans}$, CH_2 $Bn_{1,2\text{-}cis}$, CH_2 $Bn_{1,2\text{-}cis}$), 72.4 (CH_2 $Bn_{1,2\text{-}trans}$), 72.2 (CH_2 $Bn_{1,2\text{-}cis}$), 72.1 (CH_2 $Bn_{1,2\text{-}trans}$), 71.9 (CH_2 $Bn_{1,2\text{-}trans}$), 69.9 (C-5'$_{1,2\text{-}cis}$), 69.6 (C-5'$_{1,2\text{-}trans}$), 68.7 (C-6'$_{1,2\text{-}trans}$), 68.3 (C-6'$_{1,2\text{-}cis}$), 62.5 (C-$5_{1,2\text{-}trans}$), 60.3 (C-$5_{1,2\text{-}cis}$), 55.5 (CH_3'$_{1,2\text{-}trans}$), 55.4 (CH_3'$_{1,2\text{-}cis}$); ^{13}C-GATED NMR (126 MHz, $CDCl_3$) δ 100.9 ($J_{H1\text{-}C1}$= 167 Hz, 1,2-*cis*), 100.3 ($J_{H1\text{-}C1}$= 164 Hz, 1,2-*trans*); HRMS: $[M+Na]^+$ calcd for $C_{54}H_{56}O_{11}Na$ 903.37029, found 903.37148.

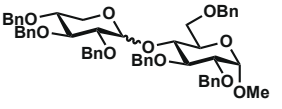


Methyl 4-*O*-(2,3,4-*O*-benzyl-D-lyxopyranosyl)-2,3,6-tri-*O*-benzoyl-D-glucopyranoside (S60). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound (61 mg, 0.067 mmol, 67%, colorless oil, 1,2-*cis*:1,2-*trans*; 61:39). TLC: R_f 0.30, 0.25 (pentane:EtOAc, 90:10, v:v); IR (thin film, cm^{-1}): 735, 1008, 1068, 1452, 1720, 2923; Data for the major stereoisomer (1,2-*trans*): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 8.17 – 6.96 (m, 30H, CH_{arom}), 6.14 – 6.05 (m, 1H, H-3'), 5.19 – 5.11 (m, 4H, H-1', H-2'), 5.01 (d, *J* = 4.4 Hz, 1H, H-1), 4.79 – 4.23 (m, 9H, H-4, H-6', H-6', C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.20 – 4.12 (m, 2H, H-4', H-5'), 3.72 – 3.61 (m, 3H, H-3, H-5), 3.60 – 3.53 (m, 2H, H-2, H-5), 3.44 (s, 3H, Me); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 166.3, 166.0, 165.6 (C=O Bz), 138.9, 138.7, 138.4, 138.3, 138.0, 138.0 ($C_{q\text{-}arom}$), 133.4, 133.3, 133.3, 133.2, 133.1, 132.8, 130.4, 130.2, 130.1, 130.0, 129.8, 129.8, 129.7, 129.6, 129.2, 129.1, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.3, 128.3, 128.1, 127.8, 127.8, 127.7, 127.7, 127.7, 127.4, 127.4, 127.3 (CH_{arom}), 101.1 (C-1), 97.0 (C-1'), 78.1 (C-3), 76.7 (C-2), 75.8 (C-4'), 73.5 (CH_2 Bn), 72.7 (C-3'), 72.5

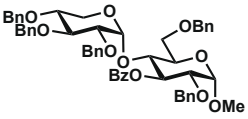
(CH_2 Bn), 72.3 (CH_2 Bn), 72.2 (C-2'), 68.6 (C-5'), 63.4 (C-6'), 62.8 (C-5), 55.6 (Me'); HRMS: $[M+NH_4]^+$ calcd for $C_{54}H_{52}O_{13}$ 926.37462, found 926.37443.



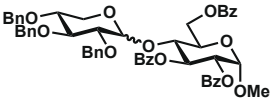
Methyl 6-*O*-(2,3,4-*O*-benzyl-D-xylopyranosyl)-2,3,4-tri-*O*-benzyl-D-glucopyranoside (S61). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Flash column chromatography (95:5 → 70:30, pentane:EtOAc) and size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound (89 mg, 90 µmol, 90%, colorless oil, 1,2-*cis*:1,2-*trans*; 38:62). TLC: R_f 0.22 and 0.31 and (pentane:EtOAc, 80:20, v:v); IR (thin film, cm^{-1}): 723, 1053, 1376, 1461, 1497, 2933; Data of the major stereoisomer (1,2-*trans*): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.41 – 7.11 (m, 30H, CH_{arom}), 5.00 – 4.55 (m, 12H, H-1', C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.50 (d, *J* = 11.1 Hz, 1H, CH*H* Bn), 4.28 (d, *J* = 7.6 Hz, 1H, H-1), 4.07 (dd, *J* = 10.8, 2.0 Hz, 1H, H-6'), 3.98 (m, 1H, H-3'), 3.90 (dd, *J* = 11.6, 5.1 Hz, 1H, H-5), 3.89 – 3.73 (m, 1H, H-5'), 3.73 – 3.47 (m, 5H, H-3, H-4, H-2', H-4', H-6'), 3.47 – 3.38 (m, 1H, H-2), 3.32 (s, 3H, CH_3'), 3.15 (dd, *J* = 11.6, 9.9 Hz, 1H, H-5); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 138.9, 138.7, 138.5, 138.4, 138.2 ($C_{q\text{-}arom}$), 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.3, 128.2, 128.1, 128.1, 128.1, 128.0, 128.0, 128.0, 127.9, 127.8, 127.8, 127.8, 127.7, 127.7, 127.7, 127.6 (CH_{arom}), 104.2 (C-1), 98.2 (C-1'), 84.1 (C-3), 82.1 (C-3'), 81.8 (C-2), 79.8 (C-2'), 77.9 (C-4), 77.9 (C-4'), 75.8, 75.8, 75.1, 73.5 (CH_2 Bn), 73.5 (CH_2 Bn, CH_2 Bn), 69.8 (C-5'), 68.3 (C-6'), 64.0 (C-5), 55.3 (CH_3'); Data for the minor stereoisomer (1,2-*cis*): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.86 (d, *J* = 3.5 Hz, 1H, H-1), 4.56 (d, *J* = 3.6 Hz, 1H, H-1'), 3.35 (s, 3H, CH_3'); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 139.0, 138.6, 138.6, 138.5, 138.3 ($C_{q\text{-}arom}$), 98.1 (C-1'), 97.4 (C-1), 75.9, 75.7, 75.1, 73.5, 72.7 (CH_2 Bn), 70.5 (C-5'), 66.2 (C-6'), 60.2 (C-5), 55.3 (CH_3'); HRMS: $[M+Na]^+$ calcd for $C_{54}H_{58}O_{10}Na$ 889.39277, found 889.39223.



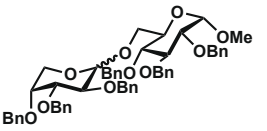
Methyl 4-*O*-(2,3,4-*O*-benzyl-D-xylopyranosyl)-2,3,6-tri-*O*-benzyl-D-glucopyranoside (S62). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Flash column chromatography (95:5 → 70:30, pentane:EtOAc) and size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound (69 mg, 70 µmol, 70%, colorless oil, 1,2-*cis*:1,2-*trans*; 60:40). TLC: R_f 0.27 (pentane:EtOAc, 80:20, v:v); IR (thin film, cm^{-1}): 685, 744, 1031, 1094, 1422, 1487, 2921; Data of the major stereoisomer (1,2-*cis*): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.50 – 7.04 (m, 30H, CH_{arom}), 5.57 (d, *J* = 3.6 Hz, 1H, H-1), 5.03 (d, *J* = 11.5 Hz, 1H, C*H*H Bn), 4.92 – 4.48 (m, 12H, H-1', CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.08 (t, *J* = 9.1 Hz, 1H, H-3'), 4.04 (t, *J* = 8.7 Hz, 1H, H-4'), 3.93 – 3.76 (m, 3H, H-4, H-5', H-6'), 3.72 (dd, *J* = 10.3, 1.8 Hz, 1H, H-6'), 3.59 (dd, *J* = 9.0, 3.4 Hz, 1H, H-2'), 3.57 – 3.44 (m, 2H, H-5, H-5), 3.42 – 3.35 (m, 5H, H-2, H-3, CH_3'); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 139.0, 138.9, 138.4, 138.3, 138.1, 138.0 ($C_{q\text{-}arom}$), 128.7, 128.6, 128.6, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.2, 128.1, 128.1, 128.0, 127.9, 127.9, 127.8, 127.5, 126.9 (CH_{arom}), 97.9 (C-1'), 96.4 (C-1), 82.1 (C-3'), 81.2 (C-3), 80.3 (C-2'), 79.2 (C-2), 78.0 (C-4), 75.7, 74.4, 73.6, 73.5, 73.4, 73.3 (CH_2 Bn), 71.9 (C-4'), 69.4 (C-5'), 69.1 (C-6'), 61.0 (C-5), 55.3 (CH_3'); Data for the minor stereoisomer (1,2-*trans*): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 4.55 (signal overlaps with major stereoisomer, 1H, H-1'), 4.34 (d, *J* = 12.0 Hz, 1H, CH*H* Bn), 4.25 (d, *J* = 7.7 Hz, 1H, H-1), 3.37 (s, 3H, CH_3'), 3.27 (dd, *J* = 9.2, 7.7 Hz, 1H, H-2), 2.95 (dd, *J* = 11.7, 10.4 Hz, 1H, H-5); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 139.0, 138.8, 138.7, 138.5, 138.0 ($C_{q\text{-}arom}$), 103.2 (C-1), 98.7 (C-1'), 82.6 (C-2), 76.0, 75.7, 75.2, 73.9, 73.4, 73.3 (CH_2 Bn), 70.2 (C-5'), 67.8 (C-6'), 63.8 (C-5), 55.5 (CH_3'); HRMS: $[M+Na]^+$ calcd for $C_{54}H_{58}O_{10}Na$ 889.39277, found 889.39220.



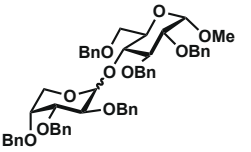
Methyl 4-*O*-(2,3,4-*O*-benzyl-D-xylopyranosyl)-1,2-*cis*-2,6-di-*O*-benzyl-3-*O*-benzoyl-1,2-*cis*-D-glucopyranoside (S63). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Flash column chromatography (95:5 → 70:30, pentane:EtOAc) and size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound (91 mg, 91 µmol, 91%, colorless oil, 1,2-*cis*:1,2-*trans*; 60:40). TLC: R_f 0.38 (pentane:EtOAc, 80:20, v:v); IR (thin film, cm^{-1}): 691, 732, 1031, 1089, 1453, 1490, 1730, 2924; Data of the major stereoisomer (1,2-*cis*): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 8.09 – 7.06 (m, 30H, CH_{arom}), 5.92 (dd, *J* = 10.0, 9.1 Hz, 1H, H-3'), 4.93 (d, *J* = 3.3 Hz, 1H, H-1), 4.77 (d, *J* = 3.5 Hz, 1H, H-1'), 4.76 – 4.49 (m, 12H, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn), 4.47 (d, *J* = 12.4 Hz, 1H, CH*H* Bn), 4.36 (d, *J* = 11.9 Hz, 1H, C*H*H Bn), 4.14 (t, *J* = 9.3 Hz, 1H, H-4'), 4.06 (d, *J* = 12.1 Hz, 1H, CH*H* Bn), 3.97 – 3.85 (m, 2H, H-5', H-6'), 3.77 (dd, *J* = 9.6, 8.7 Hz, 1H, H-3), 3.75 – 3.69 (m, 1H, H-6'), 3.69 – 3.59 (m, 2H, H-2', H-4), 3.55 (t, *J* = 10.9 Hz, 1H, H-5), 3.51 – 3.43 (m, 1H, H-5), 3.41 (s, 3H, CH_3'), 3.21 – 3.11 (m, 1H, H-2); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 165.4 (C=O Bz), 139.0, 138.8, 138.2, 138.1, 137.8 ($C_{q\text{-}arom}$), 132.9 (CH_{arom}), 130.8 ($C_{q\text{-}arom}$), 129.9, 129.8, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.1, 128.1, 128.1, 127.9, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7, 127.7, 127.6, 127.6, 127.5 (CH_{arom}), 97.8 (C-1'), 97.4 (C-1), 80.7 (C-3), 79.0 (C-2), 77.6 (C-2'), 77.2 (C-4), 75.5 (CH_2 Bn), 73.9 (C-3'), 73.8 (C-4'), 73.4, 73.4, 72.8, 72.7 (CH_2 Bn), 69.7 (C-5'), 68.6 (C-6'), 61.3 (C-5), 55.4 (CH_3'); ^{13}C-GATED NMR (126 MHz, $CDCl_3$) δ 97.4 ($J_{H1\text{-}C1}$ = 168 Hz, 1,2-*cis*); Data for the minor stereoisomer (1,2-*cis*): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 5.66 (dd, *J* = 10.0, 9.2 Hz, 1H, H-3'), 4.11 (d, *J* = 7.5 Hz, 1H, H-1), 2.77 (td, *J* = 9.4, 1.2 Hz, 1H, H-5), 3.40 (s, 3H, CH_3'); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 165.8 (C=O Bz), 138.6, 138.3, 138.0, 137.9, 131.4 ($C_{q\text{-}arom}$), 103.4 (C-1), 98.2 (C-1'), 75.3, 75.2, 73.5, 73.0, 72.9 (CH_2 Bn), 72.9 (C-3'), 69.8 (C-5'), 67.7 (C-6'), 63.1 (C-5), 55.5 (CH_3'); ^{13}C-GATED NMR (126 MHz, $CDCl_3$) δ 103.4 ($J_{H1\text{-}C1}$ = 164 Hz, 1,2-*trans*); HRMS: $[M+Na]^+$ calcd for $C_{54}H_{56}O_{11}Na$ 903.37029, found 903.37147.



Methyl 4-*O*-(2,3,4-*O*-benzyl-D-xylopyranosyl)-2,3,6-tri-*O*-benzoyl-D-glucopyranoside (S64). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Flash column chromatography (95:5 → 70:30, pentane:EtOAc) and size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound (56 mg, 54 µmol, 54%, colorless oil, 1,2-*cis*:1,2-*trans*; 60:40). TLC: R_f 0.25 (pentane:EtOAc, 80:20, v:v); IR (thin film, cm^{-1}): 811, 1037, 1265, 1454, 1725, 2912; Data of the major stereoisomer (1,2-*trans*): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 8.13 – 7.03 (m, 30H, CH_{arom}), 5.95 (dd, *J* = 10.3, 8.7 Hz, 1H, H-3'), 5.18 – 5.08 (m, 2H, H-1', H-2'), 4.90 – 4.56 (m, 15H, H-6', H-6', C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.54 – 4.43 (m, 1H, C*H*H Bn), 4.35 (d, *J* = 11.8 Hz, 1H, CH*H* Bn), 4.33 (d, *J* = 7.5 Hz, 1H, H-1), 4.09 – 3.90 (m, 2H, H-4', H-5'), 3.69 – 3.35 (m, 4H, H-3, CH_3'), 3.30 – 3.15 (m, 3H, H-2, H-4, H-5), 2.85 (m, 1H, H-5); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 166.1, 166.0, 165.9 (C=O Bz), 138.7, 138.4, 138.1 ($C_{q\text{-}arom}$), 133.4, 133.3, 132.7 (CH_{arom}), 130.7 ($C_{q\text{-}arom}$), 130.1 (CH_{arom}), 130.0 ($C_{q\text{-}arom}$), 129.8, 129.9 (CH_{arom}), 129.3 ($C_{q\text{-}arom}$), 128.6, 128.6, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.2, 128.1, 127.9, 127.9, 127.9, 127.8, 127.6 (CH_{arom}), 103.8 (C-1), 96.9 (C-1'), 83.9 (C-3), 82.1 (C-2), 77.9 (C-4), 76.5 (C-4'), 75.5, 75.5, 73.1 (CH_2 Bn), 72.0 (C-2'), 70.9 (C-3'), 68.9 (C-5'), 63.9 (C-5), 63.4 (C-6'), 55.6 (CH_3'); ^{13}C-GATED NMR (126 MHz, $CDCl_3$) δ 103.8 ($J_{H1\text{-}C1}$ = 161 Hz, 1,2-*trans*); Data for the minor stereoisomer (1,2-*cis*): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 6.20 (ddd, *J* = 10.2, 7.8, 2.1 Hz, 1H, H-3'), 5.23 (dd, *J* = 10.2, 3.6 Hz, 1H, H-2'), 4.89 (d, *J* = 3.4 Hz, 1H, H-1), 4.28 (d, *J* = 12.2 Hz, 1H, C*H*H Bn), 3.82 (t, *J* = 9.1 Hz, 1H, H-3), 3.18 (dd, *J* = 9.5, 3.5 Hz, 1H, H-2); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 166.2, 166.2, 165.6 (C=O Bz), 138.9, 138.4, 138.1, 130.1, 129.2 ($C_{q\text{-}arom}$), 98.7 (C-1), 96.9 (C-1'), 80.7 (C-3), 78.6 (C-2), 75.6, 73.4, 73.1 (CH_2 Bn), 68.7 (C-5'), 62.8 (C-6'), 61.5 (C-5), 55.6 (CH_3'); ^{13}C-GATED NMR (126 MHz, $CDCl_3$) δ 96.9 ($J_{H1\text{-}C1}$ = 169 Hz, 1,2-*cis*); HRMS: $[M+Na]^+$ calcd for $C_{54}H_{52}O_{13}Na$ 931.33056, found 931.33001.

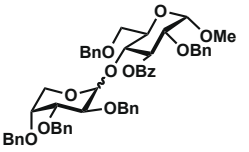


Methyl 6-*O*-(2,3,4-*O*-benzyl-D-arabinopyranosyl)-2,3,4-tri-*O*-benzyl-D-glucopyranoside (S65). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Flash column chromatography (95:5 → 80:20, pentane:EtOAc) and size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound (92 mg, 93 µmol, 93%, colorless oil, 1,2-*cis*:1,2-*trans*; 30:70). TLC: R_f 0.41 and 0.49 (pentane:EtOAc, 80:20, v:v); IR (thin film, cm^{-1}): 745, 1031, 1053, 1320, 1464, 1489, 2921; Data of the major stereoisomer (1,2-*trans*): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.47 – 7.06 (m, 30H, CH_{arom}), 5.00 – 4.55 (m, 13H, H-1', C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.41 (d, *J* = 6.6 Hz, 1H, H-1), 4.14 (dd, *J* = 11.4, 4.2 Hz, 1H, H-6'), 4.04 – 3.89 (m, 2H, H-5, H-3'), 3.81 (dd, *J* = 8.7, 6.5 Hz, 1H, H-2), 3.79 – 3.59 (m, 4H, H-4, H-4', H-5', H-6'), 3.52 (dd, *J* = 8.7, 3.4 Hz, 1H, H-3), 3.44 (dd, *J* = 9.6, 3.6 Hz, 1H, H-2'), 3.32 (s, 3H, CH_3'), 3.25 (dd, *J* = 12.6, 1.6 Hz, 1H, H-5); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 139.0, 138.9 ($C_{q\text{-}arom}$), 138.6 ($C_{q\text{-}arom}$), 138.4, 138.4 ($C_{q\text{-}arom}$), 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.1, 128.0, 128.0, 128.0, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 127.6 (CH_{arom}), 103.7 (C-1), 98.2 (C-1'), 82.2 (C-3'), 80.3 (C-2'), 79.5 (C-3), 79.0 (C-2), 77.9 (C-4'), 75.8, 75.1, 74.9, 73.5 (CH_2 Bn), 72.6 (C-4), 72.5, 71.2 (CH_2 Bn), 70.2 (C-5'), 67.7 (C-6'), 62.5 (C-5), 55.2 (CH_3') ^{13}C-GATED NMR (126 MHz, $CDCl_3$) δ 103.7 ($J_{H1\text{-}C1}$= 161 Hz, 1,2-*trans*); Data for the minor stereoisomer (1,2-*cis*): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 4.91 (d, *J* = 3.2 Hz, 1H, H-1), 4.58 (signa loverlaps with major isomer, 1H, H-1'), 3.86 (dd, *J* = 10.8, 1.6 Hz, 1H, H-6'), 3.48 (dd, *J* = 9.5, 3.6 Hz, 1H, H-2'), 3.30 (s, 3H, CH_3'); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 138.9, 138.8, 138.8, 138.6, 138.5, 138.4 ($C_{q\text{-}arom}$), 98.5 (C-1), 98.1 (C-1'), 75.9, 75.1, 73.6, 73.4, 72.5, 71.8 (CH_2 Bn), 70.1 (C-5'), 66.6 (C-6'), 60.6 (C-5), 55.2 (CH_3'); ^{13}C-GATED NMR (126 MHz, $CDCl_3$) δ 98.5 ($J_{H1\text{-}C1}$= 167 Hz, 1,2-*cis*); HRMS: $[M+Na]^+$ calcd for $C_{54}H_{58}O_{10}Na$ 889.39277, found 889.39230.

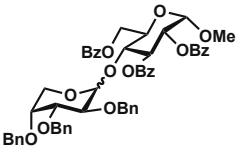


Methyl 4-*O*-(2,3,4-*O*-benzyl-D-arabinopyranosyl)-2,3,6-tri-*O*-benzyl-D-glucopyranoside (S66). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Flash column chromatography (95:5 → 80:20, pentane:EtOAc) and size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound (83 mg, 84 µmol, 84%, colorless oil, 1,2-*cis*:1,2-*trans*; 53:47). TLC: R_f 0.30 (pentane:EtOAc, 80:20, v:v); IR (thin film, cm^{-1}): 690, 741, 1020, 1043, 1330, 1476, 1491, 2909; NMR data reported as a mixture of 1,2-*cis*:1,2-*trans* (53:47) anomers: ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated) δ 7.40 – 7.13 (m, 60H, CHarom), 5.03 (d, *J* = 11.0 Hz, 1H, C*H*H Bn), 5.01 (d, *J* = 3.2 Hz, 1H, H-$1_{1,2\text{-}cis}$), 4.90 (d, *J* = 11.2 Hz, 1H, C*H*H Bn), 4.83 – 4.48 (m, 23H, H-$1_{1,2\text{-}trans}$, H-$1'_{1,2\text{-}cis}$, H-$1'_{1,2\text{-}trans}$, CH*H* Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.41 (d, *J* = 12.1 Hz, 1H, C*H*H Bn), 4.29 (d, *J* = 12.1 Hz, 1H, CH*H* Bn), 3.99 – 3.69 (m, 14H, H-$2_{1,2\text{-}cis}$, H-$2_{1,2\text{-}trans}$, H-$3_{1,2\text{-}cis}$, H-$5_{1,2\text{-}cis}$, H-$5_{1,2\text{-}trans}$, H-$3'_{1,2\text{-}cis}$, H-$3'_{1,2\text{-}trans}$, H-$4'_{1,2\text{-}cis}$, H-$4'_{1,2\text{-}trans}$, H-$5'_{1,2\text{-}cis}$, H-$5'_{1,2\text{-}trans}$, H-$6'_{1,2\text{-}cis}$, H-$6'_{1,2\text{-}trans}$, H-$6'_{1,2\text{-}trans}$), 3.62 – 3.58 (m, 2H, H-$4_{1,2\text{-}trans}$, H-$6'_{1,2\text{-}cis}$), 3.56 (dd, *J* = 9.5, 3.5 Hz, 1H, H-$2'_{1,2\text{-}cis}$), 3.52 (dd, *J* = 9.6, 3.5 Hz, 1H, H-$2'_{1,2\text{-}trans}$), 3.48 – 3.32 (m, 8H, H-$3_{1,2\text{-}trans}$, H-$4_{1,2\text{-}cis}$, $CH_3'_{1,2\text{-}cis}$, $CH_3'_{1,2\text{-}trans}$), 3.29 (dd, *J* = 12.9, 2.5 Hz, 1H, H-$5_{1,2\text{-}cis}$), 3.07 (dd, *J* = 12.8, 1.4 Hz, 1H, H-$5_{1,2\text{-}trans}$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 138.9, 138.8, 138.7, 138.6, 138.6, 138.5, 138.4, 138.2, 138.1, 138.1 ($C_{q\text{-}arom}$), 128.6, 128.5, 128.4, 128.4, 128.3, 128.3, 128.3, 128.1, 128.1, 128.1, 128.0, 128.0, 127.9, 127.8, 127.8, 127.7, 127.7, 127.7, 127.6, 127.5, 127.4 (CH_{arom}), 103.2 (C-$1_{1,2\text{-}trans}$), 98.4 (C-$1_{1,2\text{-}cis}$), 98.0 (C-$1'_{1,2\text{-}cis}$), 98.0 (C-$1'_{1,2\text{-}trans}$), 82.3 (C-$3'_{1,2\text{-}trans}$), 80.5 (C-$2'_{1,2\text{-}cis}$), 80.1 (C-$3'_{1,2\text{-}cis}$), 80.1 (C-$2'_{1,2\text{-}trans}$), 79.8 (C-$2_{1,2\text{-}cis}$), 79.6 (C-$2_{1,2\text{-}trans}$), 77.5 (C-$3_{1,2\text{-}trans}$), 76.6 (C-$3_{1,2\text{-}cis}$), 75.5, 75.4, 75.3, 74.7 (CH_2 Bn), 74.3 (C-$4'_{1,2\text{-}trans}$), 74.0 (C-$4'_{1,2\text{-}cis}$), 73.5, 73.5, 73.4 (CH_2 Bn), 73.4 (C-$4_{1,2\text{-}cis}$), 73.3 (CH_2 Bn), 72.9 (C-$4_{1,2\text{-}trans}$), 72.4, 72.1, 71.3, 71.2 (CH_2 Bn), 70.4 (C-$5'_{1,2\text{-}cis}$), 69.9 (C-$5'_{1,2\text{-}trans}$), 69.2 (C-$6'_{1,2\text{-}trans}$), 68.4 (C-$6'_{1,2\text{-}cis}$), 62.7 (C-$5_{1,2\text{-}trans}$), 60.3 (C-$5_{1,2\text{-}cis}$), 55.4

(CH3'$_{1,2\text{-}cis}$), 55.2 (CH3'$_{1,2\text{-}trans}$); ^{13}C-GATED NMR (126 MHz, $CDCl_3$) δ 103.2 ($J_{H1\text{-}C1}$= 164 Hz, 1,2-*trans*), 98.3 ($J_{H1\text{-}C1}$= 171 Hz, 1,2-*cis*); HRMS: [M+Na]$^+$ calcd for $C_{54}H_{58}O_{10}Na$ 889.39277, found 889.39241.

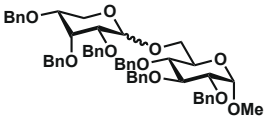


Methyl 4-*O*-(2,3,4-*O*-benzyl-D-arabinopyranosyl)-2,6-di-*O*-benzyl-3-*O*-benzoyl-D-glucopyranoside (S67). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Flash column chromatography (95:5 → 70:30, pentane:EtOAc) and size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound (79 mg, 79 µmol, 79%, colorless oil, 1,2-*cis*:1,2-*trans*; 75:25). TLC: R_f 0.21 (pentane:EtOAc, 80:20, v:v); IR (thin film, cm^{-1}): 812, 1031, 1262, 1449, 1731, 2920; Data of the major stereoisomer (1,2-*cis*): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 8.11 – 7.00 (m, 30H, CH_{arom}), 5.70 (t, *J* = 9.4 Hz, 1H, H-3'), 4.97 (d, *J* = 3.7 Hz, 1H, H-1), 4.85 (d, *J* = 11.5 Hz, 1H, C*H*H Bn), 4.72 (d, *J* = 3.4 Hz, 1H, H-1'), 4.72 – 4.44 (m, 8H, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.29 (d, *J* = 12.1 Hz, 1H, CH*H* Bn), 4.00 (dd, *J* = 11.0, 3.5 Hz, 1H, H-6'), 3.98 – 3.90 (m, 2H, H-2, H-4'), 3.89 – 3.84 (m, 1H, H-5'), 3.80 (dd, *J* = 10.2, 3.1 Hz, 1H, H-3), 3.65 – 3.56 (m, 2H, H-4, H-6'), 3.54 (dd, *J* = 9.9, 3.4 Hz, 1H, H-2'), 3.47 (dd, *J* = 12.8, 1.3 Hz, 1H, H-5), 3.39 (s, 3H, CH_3'), 3.13 (dd, *J* = 12.7, 2.2 Hz, 1H, H-5); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 166.1 (C=O Bz), 138.7, 138.6, 138.4, 138.3, 137.7 ($C_{q\text{-}arom}$), 132.9 (CH_{arom}), 130.7 ($C_{q\text{-}arom}$), 129.9, 128.4, 128.4, 128.4, 128.4, 128.2, 128.0, 128.0, 127.9, 127.9, 127.8, 127.7, 127.6, 127.6 (CH_{arom}), 100.6 (C-1), 97.5 (C-1'), 78.1 (C-3), 77.7 (C-2'), 76.7 (C-4'), 76.3 (C-2), 74.7 (CH_2 Bn), 73.3 (C-4), 73.2 (C-3'), 72.7, 72.0, 71.6 (CH_2 Bn), 70.2 (C-5'), 68.2 (C-6'), 60.6 (C-5), 55.4 (CH_3'); ^{13}C-GATED NMR (126 MHz, $CDCl_3$) δ 100.6 ($J_{H1\text{-}C1}$= 168 Hz, 1,2-*cis*); Data for the minor stereoisomer (1,2-*trans*): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 5.86 (dd, *J* = 10.1, 9.1 Hz, 1H, H-3'), 4.77 (d, *J* = 3.5 Hz, 1H, H-1'), 4.65 (d, *J* = 6.1 Hz, 1H, H-1), 4.07 (t, *J* = 9.5 Hz, 1H, H-4'), 3.43 (s, 3H, CH_3'), 3.35 (dd, *J* = 6.5, 3.3 Hz, 1H, H-3), 3.20 (dd, *J* = 11.7, 2.8 Hz, 1H, H-5); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 165.3 (C=O Bz), 138.6, 138.5, 138.5, 138.4, 137.8, 130.5 ($C_{q\text{-}arom}$), 101.7 (C-1), 97.7 (C-1'), 74.9 (C-3'), 73.9 (CH_2 Bn), 73.7 (C-4'), 73.6, 72.7, 72.0, 71.1 (CH_2 Bn), 69.6 (C-5'), 68.7 (C-6'), 60.9 (C-5), 55.5 (CH_3'); ^{13}C-GATED NMR (126 MHz, $CDCl_3$) δ 101.7 ($J_{H1\text{-}C1}$= 164 Hz, 1,2-*trans*); HRMS: [M+Na]$^+$ calcd for $C_{54}H_{56}O_{11}Na$ 903.37029, found 903.37137.

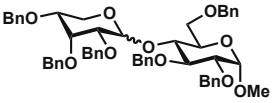


Methyl 4-*O*-(2,3,4-*O*-benzyl-D-arabinopyranosyl)-2,3,6-tri-*O*-benzoyl-D-glucopyranoside (S68). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound (53 mg, 59 µmol, 59%, colorless oil, 1,2-*cis*:1,2-*trans*; 78:22). TLC: R_f 0.30 and 0.25 (pentane:EtOAc, 80:20, v:v); IR (thin film, cm^{-1}): 736, 1026, 1271, 1452, 1720, 2923; Data for the major stereoisomer (1,2-*cis*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC, HMBC-Gated): δ 8.18 – 7.08 (m, 30H, CH_{arom}), 5.97 (dd, *J* = 10.0, 9.0 Hz, 1H, H-3'), 5.12 – 5.09 (m, 1H, H-1'), 5.06 (dd, *J* = 10.1, 3.6 Hz, 1H, H-2'), 4.96 (d, *J* = 3.6 Hz, 1H, H-1), 4.92 (dd, *J* = 12.0, 2.1 Hz, 1H, H-6'), 4.85 (d, *J* = 11.3 Hz, 1H, C*H*H Bn), 4.78 (dd, *J* = 11.9, 4.1 Hz, 1H, H-6'), 4.70 (d, *J* = 11.3 Hz, 1H, CH*H* Bn), 4.65 – 4.60 (m, 2H, CH_2 Bn), 4.54 – 4.51 (m, 2H, CH_2 Bn), 4.17 (ddd, *J* = 9.9, 4.2, 2.1 Hz, 1H, H-5'), 4.06 – 3.95 (m, 2H, H-2, H-4'), 3.85 (dd, *J* = 10.1, 3.1 Hz, 1H, H-3), 3.67 – 3.58 (m, 1H, H-4), 3.49 (dd, *J* = 12.7, 1.3 Hz, 1H, H-5), 3.39 (s, 3H, CH_3'), 3.15 (dd, *J* = 12.6, 2.3 Hz, 1H, H-5); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC, HMBC-Gated): δ 166.2, 166.2, 166.0 (C=O Bz), 138.6, 138.2, 138.1 ($C_{q\text{-}arom}$), 133.4, 133.2, 133.1 (CH_{arom}), 130.2 ($C_{q\text{-}arom}$), 130.0, 129.8, 129.7 (CH_{arom}), 129.2 ($C_{q\text{-}arom}$), 128.6, 128.6, 128.5, 128.4, 128.4, 127.9, 127.8, 127.7, 127.6 (CH_{arom}), 101.6 (C-1), 96.8 (C-1'), 78.0 (C-3), 77.9 (C-4'), 75.7 (C-2), 74.7 (CH_2 Bn), 73.5 (C-4), 72.7 (C-2'), 72.1, 71.8 (CH_2 Bn), 71.6 (C-3'), 69.0 (C-5'), 62.8 (C-6'), 61.0 (C-5), 55.4 (CH_3'); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 101.6 ($J_{H1\text{-}C1}$ = 167 Hz, 1,2-*cis*); Data for the minor stereoisomer (1,2-*trans*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC, HMBC-Gated δ 8.18 – 7.08 (m, 30H, CH_{arom}), 6.14 (ddt, *J* = 10.9, 9.0, 2.1 Hz, 1H, H-3'), 4.57 (d, *J* = 6.2 Hz,

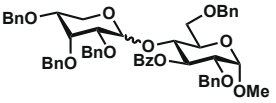
1H, H-1), 4.49 – 4.46 (m, 1H, C*H*H Bn), 4.40 (d, *J* = 12.1 Hz, 1H, CH*H* Bn), 4.33 (d, *J* = 11.5 Hz, 1H, CH*H* Bn), 3.67 – 3.58 (m, 2H, H-2, H-5), 3.44 (s, 3H, CH_3'), 3.25 (dd, *J* = 7.8, 3.2 Hz, 1H, H-5); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC, HMBC, HMBC-Gated): δ 166.3, 166.1, 165.5 (C=O Bz), 138.7, 138.5, 138.3 ($C_{q\text{-arom}}$), 133.4, 133.1, 133.0, 129.8, 128.5, 128.5, 128.3, 128.0, 128.0, 127.9 (CH_{arom}), 103.0 (C-1), 97.0 (C-1'), 78.3 (C-2), 74.4, 72.1, 70.9 (CH_2 Bn), 63.5 (C-6'), 61.6 (C-5), 55.5 (CH_3'); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 103.0 ($J_{H1\text{-}C1}$ = 163 Hz, 1,2-*trans*); HRMS: $[M+NH_4]^+$ calcd for $C_{54}H_{52}O_{13}$ 926.37462, found 926.37408.



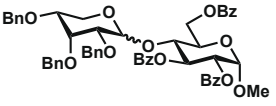
Methyl 6-*O*-(2,3,4-*O*-benzyl-D-ribopyranosyl)-2,3,4-tri-*O*-benzyl-D-glucopyranoside (S69). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Flash column chromatography (100:0 → 90:10, pentane:EtOAc) afforded the title compound (55 mg, 63 µmol, 63%, colorless oil, 1,2-*cis*:1,2-*trans*; 35:65). TLC: R_f 0.40, 0.30 (pentane:EtOAc, 80:20, v:v); IR (thin film, cm^{-1}): 733, 1027, 1043, 1364, 1452, 1496, 2923; NMR data reported as a mixture of 1,2-*cis*:1,2-*trans* (44:56) anomers: ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.47 – 7.11 (m, 55.8H, CH_{arom}), 5.01 (d, *J* = 11.5 Hz, 0.85H, C*H*H $Bn_{1,2\text{-}cis}$), 4.97 – 4.93 (m, 2H, H-$1_{1,2\text{-}trans}$, C*H*H $Bn_{1,2\text{-}trans}$), 4.83 – 4.75 (m, 1.86H, CH*H* $Bn_{1,2\text{-}cis}$, CH*H* $Bn_{1,2\text{-}trans}$), 4.72 – 4.68 (m, 1.85H, C*H*H $Bn_{1,2\text{-}cis}$, C*H*H $Bn_{1,2\text{-}trans}$), 4.64 – 4.53 (m, 4.58H, H-$1_{1,2\text{-}cis}$, H-1'$_{1,2\text{-}cis}$, , H-1'$_{1,2\text{-}trans}$, CH*H* $Bn_{1,2\text{-}cis}$, CH*H* $Bn_{1,2\text{-}trans}$), 4.53 – 4.37 (m, 2.72H, CH_2 $Bn_{1,2\text{-}cis}$, C*H*H $Bn_{1,2\text{-}trans}$,), 4.28 (d, *J* = 11.5 Hz, 1H, CH*H* $Bn_{1,2\text{-}trans}$), 4.14 (t, *J* = 2.6 Hz, 1H, H-$3_{1,2\text{-}trans}$), 4.04 (t, *J* = 9.1 Hz, 0.86H, H-4'$_{1,2\text{-}cis}$), 3.97 – 3.89 (m, 1H, H-$5_{ax\text{-}1,2\text{-}cis}$), 3.88 – 3.77 (m, 1.86H, H-6'$_{1,2\text{-}cis}$, H-6'$_{1,2\text{-}trans}$), 3.77 – 3.73 (m, 2H, H-$5_{1,2\text{-}trans}$, H-$5_{1,2\text{-}trans}$), 3.68 (dd, *J* = 10.4, 2.1 Hz, 0.86H, H-6'$_{1,2\text{-}cis}$), 3.61 (dd, *J* = 10.6, 1.9 Hz, 1H, H-6'$_{1,2\text{-}trans}$), 3.56 (dd, *J* = 9.6, 3.5 Hz, 1H, H-$3_{1,2\text{-}cis}$ or H-5'$_{1,2\text{-}cis}$), 3.53 – 3.46 (m, 1H, H-$4_{1,2\text{-}trans}$, H-2'$_{1,2\text{-}trans}$), 3.39 (s, 2,58H, CH_3'$_{1,2\text{-}cis}$), 3.36 (s, 3H, CH_3'$_{1,2\text{-}trans}$), 3.30 (dd, *J* = 11.3, 3.8 Hz, 0.86H, H-$5_{eq\text{-}1,2\text{-}cis}$), 3.22 (dd, *J* = 7.7, 2.7 Hz, 1H, H-$2_{1,2\text{-}trans}$); HRMS: $[M+Na]^+$ calcd for $C_{54}H_{58}O_{10}Na$ 889.39277, found 889.39212.



Methyl 4-*O*-(2,3,4-*O*-benzyl-D-ribopyranosyl)-2,3,6-tri-*O*-benzyl-D-glucopyranoside (S70). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Flash column chromatography (95:5 → 70:30, pentane:EtOAc) and size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound (74 mg, 75 µmol, 75%, colorless oil, 1,2-*cis*:1,2-*trans*; 40:60). TLC: R_f 0.35 (pentane:EtOAc, 80:20, v:v); IR (thin film, cm^{-1}): 698, 745, 1031, 1097, 1453, 1491, 2921; Data of the major stereoisomer (1,2-*trans*): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 7.43 – 7.10 (m, 30H, CH_{arom}), 4.98 – 4.91 (m, 2H, H-1, C*H*H Bn), 4.83 – 4.37 (m, 21H, H-1', CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.28 (d, *J* = 11.5 Hz, 1H, CH*H* Bn), 4.14 (t, *J* = 2.6 Hz, 1H, H-3), 3.98 – 3.88 (m, 1H, H-4'), 3.87 – 3.77 (m, 2H, H-3', H-6'), 3.77 – 3.72 (m, 2H, H-5, H-5), 3.71 – 3.58 (m, 2H, H-5', H-6'), 3.54 – 3.46 (m, 2H, H-4, H-2'), 3.36 (s, 3H, CH_3'), 3.22 (dd, *J* = 7.7, 2.7 Hz, 1H, H-2); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 139.2 ($C_{q\text{-arom}}$), 138.7, 138.5 ($C_{q\text{-arom}}$), 138.1 ($C_{q\text{-arom}}$, $C_{q\text{-arom}}$), 128.6, 128.6, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.2, 128.2, 128.2, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 127.6, 127.6, 127.4, 127.0 (CH_{arom}), 101.0 (C-1'), 98.6 (C-1), 80.5 (C-3'), 79.4 (C-2), 79.1 (C-2'), 77.2 (C-4'), 75.8 (CH_2 Bn), 75.7 (C-4), 75.5 (C-3), 73.8, 73.1, 73.1, 72.8, 71.4 (CH_2 Bn), 70.3 (C-5'), 68.1 (C-6'), 62.4 (C-5), 55.4 (CH_3'); ^{13}C-GATED NMR (126 MHz, $CDCl_3$) δ 101.0 ($J_{H1\text{-}C1}$= 167 Hz, 1,2-tran*s*); Data for the minor stereoisomer (1,2-*cis*): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.27 (bs, 1H, H-1), 5.01 (d, *J* = 11.5 Hz, 1H, C*H*H Bn), 4.62 (d, *J* = 3.5 Hz, 1H, H-1'), 4.04 (t, *J* = 9.2 Hz, 1H, H-3'), 3.56 (dd, *J* = 9.6, 3.5 Hz, 1H, H-2'), 3.40 (s, 3H, CH_3'), 3.30 (dd, *J* = 11.3, 3.8 Hz, 1H, H-5); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 139.1, 138.8, 138.2 ($C_{q\text{-arom}}$), 97.9 (C-1'), 82.5 (C-3'), 80.2 (C-2'), 69.6 (C-5'), 69.1 (C-6'), 55.3 (CH_3'); HRMS: $[M+Na]^+$ calcd for $C_{54}H_{58}O_{10}Na$ 889.39277, found 889.39250.



Methyl 4-*O*-(2,3,4-*O*-benzyl-D-ribopyranosyl)-2,6-di-*O*-benzyl-3-*O*-benzoyl-D-glucopyranoside (S71). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Flash column chromatography (95:5 → 70:30, pentane:EtOAc) and size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound (55 mg, 61 µmol, 61%, colorless oil, 1,2-*cis*:1,2-*trans*; 40:60). TLC: R_f 0.25 (pentane:EtOAc, 80:20, v:v); IR (thin film, cm^{-1}): 731, 803, 1235, 1261, 1451, 1730, 2923; Data of the major stereoisomer (1,2-*trans*): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC-Gated): δ 8.18 – 6.91 (m, 30H, CH_{arom}), 5.68 (dd, *J* = 10.0, 9.1 Hz, 1H, H-3'), 4.79 – 4.72 (m, 3H, H-1, C*H*H Bn, CH*H* Bn), 4.70 (d, *J* = 3.5 Hz, 1H, H-1'), 4.65 (d, *J* = 11.8 Hz, 1H, C*H*H Bn), 4.61 – 4.23 (m, 7H, CH*H* Bn, CH*H* Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 3.99 (td, *J* = 2.4, 0.9 Hz, 1H, H-3), 3.97 – 3.85 (m, 1H, H-4'), 3.86 – 3.73 (m, 2H, H-5', H-6'), 3.66 – 3.55 (m, 2H, H-2', H-6'), 3.47 (t, *J* = 10.4 Hz, 1H, H-5), 3.39 (s, 3H, CH_3'), 3.22 – 3.15 (m, 1H, H-4), 3.12 (dd, *J* = 7.5, 2.7 Hz, 1H, H-2), 2.97 (ddd, *J* = 10.9, 4.9, 1.2 Hz, 1H, H-5); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC-Gated): δ 166.0 (C=O Bz), 139.1, 138.6, 138.0, 138.0 ($C_{q\text{-}arom}$), 132.4 (CH_{arom}), 131.4 ($C_{q\text{-}arom}$), 129.9, 128.6, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.1, 128.1, 128.0, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 127.6, 127.5, 127.4, 127.3 (CH_{arom}), 101.6 (C-1), 98.1 (C-1'), 79.1 (C-2), 77.1 (C-4'), 76.8 (C-2'), 75.4 (C-3), 75.3 (C-4), 74.3, 73.5 (CH_2 Bn), 73.1 (C-3'), 72.9, 72.8, 71.3 (CH_2 Bn), 69.9 (C-5'), 68.0 (C-6'), 61.7 (C-5), 55.5 (CH_3'); ^{13}C-GATED NMR (126 MHz, $CDCl_3$) δ 101.6 ($J_{H1\text{-}C1}$ = 165 Hz, 1,2-*trans*); Data for the minor stereoisomer (1,2-*cis*): ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.95 (dd, *J* = 10.0, 9.1 Hz, 1H, H-3'), 4.97 (bs, 1H, H-1), 4.16 (t, *J* = 9.3 Hz, 1H, H-4'), 3.41 (s, 3H, CH_3'); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 165.3 (C=O Bz), 139.3, 138.4, 130.6 ($C_{q\text{-}arom}$), 97.6 (C-1'), 97.3 (C-1), 73.3, 72.7, 71.1 (CH_2 Bn), 69.5 (C-5'), 68.7 (C-6'), 55.4 (CH_3'); HRMS: $[M+Na]^+$ calcd for $C_{54}H_{56}O_{11}Na$ 903.37029, found 903.37121.



Methyl 4-*O*-(2,3,4-*O*-benzyl-D-ribopyranosyl)-2,3,6-tri-*O*-benzoyl-D-glucopyranoside (S72). The title compound was prepared according to general procedure I. The reaction was quenched after 16 h. Size-exclusion column chromatography (DCM:MeOH 1:1) afforded the title compound (61 mg, 67 µmol, 67%, colorless oil, 1,2-*cis*:1,2-*trans*; 50:50). TLC: R_f 0.35, 0.30 (pentane:EtOAc, 80:20, v:v); IR (thin film, cm^{-1}): 736, 806, 1025, 1267, 1452, 1720, 2923; Data for the 1,2-*trans* stereoisomer: ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC, HMBC-Gated): δ 8.12 – 7.02 (m, 30H, CH_{arom}), 5.98 (dd, *J* = 9.7, 9.0 Hz, 1H, H-3'), 5.17 – 5.10 (m, 2H, H-1', H-2'), 4.83 (d, *J* = 7.3 Hz, 1H, H-1), 4.81 – 4.25 (m, 8H, H-6', H-6', CH_2 Bn, CH_2 Bn, CH_2 Bn), 4.15 (dddd, *J* = 18.0, 10.1, 4.8, 2.0 Hz, 1H, H-5'), 4.06 – 3.93 (m, 1H, H-4'), 3.92 (t, *J* = 2.3 Hz, 1H, H-3), 3.44 – 3.35 (m, 4H, H-5, CH_3'), 3.22 – 3.13 (m, 2H, H-2, H-4), 3.01 (dd, *J* = 11.3, 4.4 Hz, 1H, H-5);); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC, HMBC-Gated): δ 166.0, 166.0, 165.4 (C=O Bz), 139.0, 138.2, 138.0 ($C_{q\text{-}arom}$), 133.4, 133.3, 133.1, 133.0, 132.7 (CH_{arom}), 130.5 ($C_{q\text{-}arom}$), 130.1, 130.0, 129.8, 129.7 ($C_{q\text{-}arom}$), 129.3, 129.2 ($C_{q\text{-}arom}$), 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 128.2, 128.2, 128.1, 128.0, 127.8, 127.8, 127.7, 127.7, 127.6, 127.6, 127.6, 127.5, 127.4, 127.3 ($C_{q\text{-}arom}$), 102.1 (C-1), 96.7 (C-1'), 78.8 (C-2), 78.2 (C-4'), 74.8 (C-4), 74.6 (C-3), 73.9 (CH_2 Bn), 72.6 (CH_2 Bn), 72.1 (C-2'), 71.2 (CH_2 Bn), 68.9 (C-5'), 63.0 (C-6'), 62.0 (C-5), 55.5 (CH_3); ^{13}C-GATED NMR (126 MHz, $CDCl_3$): δ 102.1 ($J_{H1\text{-}C1}$ = 164 Hz, 1,2-*trans*); Data for the 1,2-*cis* stereoisomer: ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC, HMBC-Gated): δ 8.12 – 7.02 (m, 30H, CH_{arom}), 6.23 (t, *J* = 9.3 Hz, 1H, H-3'), 5.17 – 5.10 (m, 2H, H-1', H-2'), 5.08 (br s, 1H, H-1), 4.81 – 4.25 (m, 8H, H-6', H-6', CH_2 Bn, CH_2 Bn, CH_2 Bn), 3.44 – 3.35 (m, 3H, CH_3'), 3.22 – 3.13 (m, 1H , H-2); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC, HMBC, HMBC-Gated): δ 166.2, 166.1, 166.0 ($C_{q\text{-}arom}$), 96.8 (C-1' and C-1), 75.3 (C-2), 73.9 (CH_2 Bn), 71.1 (CH_2 Bn), 63.2 (C-6'), 55.3 (CH_3'); ^{13}C-GATED NMR (126 MHz, $CDCl_3$): δ 96.8 ($J_{H1\text{-}C1}$ = 174 Hz, 1,2-*cis*); HRMS: $[M+NH_4]^+$ calcd for $C_{54}H_{52}O_{13}$ 926.37462, found 926.37411.

References

(1) Elshahawi, S. I.; Shaaban, K. A.; Kharel, M. K.; Thorson, J. S. A Comprehensive Review of Glycosylated Bacterial Natural Products. *Chem. Soc. Rev.* **2015**, *44* (21), 7591–7697.

(2) Bohé, L.; Crich, D. A Propos of Glycosyl Cations and the Mechanism of Chemical Glycosylation; the Current State of the Art. *Carbohydr. Res.* **2015**, *403*, 48–59.

(3) Satoh, H.; Hansen, H. S.; Manabe, S.; van Gunsteren, W. F.; Hünenberger, P. H. Theoretical Investigation of Solvent Effects on Glycosylation Reactions: Stereoselectivity Controlled by Preferential Conformations of the Intermediate Oxacarbenium-Counterion Complex. *J. Chem. Theory Comput.* **2010**, *6* (6), 1783–1797.

(4) Hosoya, T.; Takano, T.; Kosma, P.; Rosenau, T. Theoretical Foundation for the Presence of Oxacarbenium Ions in Chemical Glycoside Synthesis. *J. Org. Chem.* **2014**, *79* (17), 7889–7894.

(5) Hosoya, T.; Kosma, P.; Rosenau, T. Contact Ion Pairs and Solvent-Separated Ion Pairs from D-Mannopyranosyl and D-Glucopyranosyl Triflates. *Carbohydr. Res.* **2015**, *401*, 127–131.

(6) Beaver, M. G.; Woerpel, K. A. Erosion of Stereochemical Control with Increasing Nucleophilicity: *O*-Glycosylation at the Diffusion Limit. *J. Org. Chem.* **2010**, *75* (4), 1107–1118.

(7) Adero, P. O.; Amarasekara, H.; Wen, P.; Bohé, L.; Crich, D. The Experimental Evidence in Support of Glycosylation Mechanisms at the S_N1–S_N2 Interface. *Chem. Rev.* **2018**, *118* (17), 8242–8284.

(8) Shenoy, S. R.; Woerpel, K. A. Investigations into the Role of Ion Pairing in Reactions of Heteroatom-Substituted Cyclic Oxocarbenium Ions. *Org. Lett.* **2005**, *7* (6), 1157–1160.

(9) Crich, D.; Sharma, I. Is Donor–Acceptor Hydrogen Bonding Necessary for 4,6-*O*-Benzylidene-Directed β-Mannopyranosylation? Stereoselective Synthesis of β-*C*-Mannopyranosides and α-*C*-Glucopyranosides. *Org. Lett.* **2008**, *10* (21), 4731–4734.

(10) Vorm, S. van der; Hansen, T.; Overkleeft, H. S.; Marel, G. A. van der; Codée, J. D. C. The Influence of Acceptor Nucleophilicity on the Glycosylation Reaction Mechanism. *Chem. Sci.* **2017**, *8* (3), 1867–1875.

(11) Codée, J. D. C.; Litjens, R. E. J. N.; den Heeten, R.; Overkleeft, H. S.; van Boom, J. H.; van der Marel, G. A. Ph_2SO/Tf_2O: A Powerful Promotor System in Chemoselective Glycosylations Using Thioglycosides. *Org. Lett.* **2003**, *5* (9), 1519–1522.

(12) Ardèvol, A.; Rovira, C. The Molecular Mechanism of Enzymatic Glycosyl Transfer with Retention of Configuration: Evidence for a Short-Lived Oxocarbenium-Like Species. *Angew. Chem. Int. Ed.* **2011**, *50* (46), 10897–10901.

(13) Ardèvol, A.; Iglesias-Fernández, J.; Rojas-Cervellera, V.; Rovira, C. The Reaction Mechanism of Retaining Glycosyltransferases. *Biochem. Soc. Trans.* **2016**, *44* (1), 51–60.

(14) Iglesias-Fernández, J.; Hancock, S. M.; Lee, S. S.; Khan, M.; Kirkpatrick, J.; Oldham, N. J.; McAuley, K.; Fordham-Skelton, A.; Rovira, C.; Davis, B. G. A Front-Face "S_Ni Synthase" Engineered from a Retaining "Double-S_N2" Hydrolase. *Nat. Chem. Biol.* **2017**, *13* (8), 874–881.

(15) Whitfield, D. M.; Guo, J. Proton Transfer and Hydrogen Bonding in Glycosylation Reactions. *J. Carbohydr. Chem.* **2017**, *36* (2–3), 59–99.

(16) Vorm, S. van der; Hansen, T.; Hengst, J. M. A. van; S. Overkleeft, H.; Marel, G. A. van der; C. Codée, J. D. Acceptor Reactivity in Glycosylation Reactions. *Chem. Soc. Rev.* **2019**, *48* (17), 4688–4706.

(17) van der Vorm, S.; Overkleeft, H. S.; van der Marel, G. A.; Codée, J. D. C. Stereoselectivity of Conformationally Restricted Glucosazide Donors. *J. Org. Chem.* **2017**, *82* (9), 4793–4811.

(18) Demchenko, A. V.; Rousson, E.; Boons, G.-J. Stereoselective 1,2-*Cis*-Galactosylation Assisted by Remote Neighboring Group Participation and Solvent Effects. *Tet. Lett.* **1999**, *40* (36), 6523–6526.

(19) Liu, H.; Hansen, T.; Zhou, S.-Y.; Wen, G.-E.; Liu, X.-X.; Zhang, Q.-J.; Codée, J. D. C.; Schmidt, R. R.; Sun, J.-S. Dual-Participation Protecting Group Solves the Anomeric Stereocontrol Problems in Glycosylation Reactions. *Org. Lett.* **2019**, *21* (21), 8713–8717.

(20) Liu, H.; Zhou, S.-Y.; Wen, G.-E.; Liu, X.-X.; Liu, D.-Y.; Zhang, Q.-J.; Schmidt, R. R.; Sun, J.-S. The 2,2-Dimethyl-2-(*Ortho*-Nitrophenyl)Acetyl (DMNPA) Group: A Novel Protecting Group in Carbohydrate Chemistry. *Org. Lett.* **2019**, *21* (19), 8049–8052.

Glycosyl Kationen in Glycosyleringsreacties

Koolhydraten, ook wel suikers genoemd, en glycoconjugaten zijn een zeer diverse klasse van biomoleculen, die voorkomt in alle rijken van het leven. Ze zijn betrokken bij een significant aantal pathologieën, waaronder bacteriële infecties, kanker en ontstekingsziekten. Ze vervullen een onmisbare rol als structurele component, in biologische energieopslag en als signaalmoleculen. De studie naar koolhydraten en de ontwikkeling van op koolhydraat-gebaseerde medicatie (antibacteriële geneesmiddelen, antikankermiddelen en vaccines) is een enorme uitdaging omdat deze moleculen vaak in de natuur als mengsel voorkomen, wat de isolatie vanuit deze bronnen bemoeilijkt.

Synthetische chemie is één van de belangrijkste leveranciers van goed gedefinieerde en zuivere koolhydraten en glycoconjugaten. Meerdere synthetische analogen hebben hun weg gevonden naar de kliniek, waaronder het antistollingsmiddel Fondaparinux (Arixtra®) en het antivirale middel Oseltamivir (Tamiflu®). Ondanks deze successen, blijft de synthese van complexe koolhydraten en glycoconjugaten een uitzonderlijk ingewikkelde onderneming, omdat er geen algemene oplossing is voor het introduceren van de gewenste glycosidische bindingen. Een glycosidische binding verbindt simpele suikers of monosacchariden met elkaar waardoor het vormen van langere biopolymeren of polysacchariden mogelijk is.

Deze binding wordt geïntroduceerd met behulp van een glycosyleringsreactie, de centrale reactie in de synthetische koolhydraatchemie. In deze reactie reageert een acceptor molecuul (het nucleofiel, vaak een alcohol in een suiker bouwsteen) met een geactiveerde donor suiker (het elektrofiel), waardoor een glycosidische binding wordt gevormd tussen beide reactiepartners. Hierbij kan een 1,2-*cis* band, een 1,2-*trans* band of een mengsel daarvan ontstaan, terwijl slechts één van de twee glycosidische bindingen gewenst is. Het vormen van de juiste glycosidische binding (de stereochemie) is erg complex en om de koolhydraatchemie verder te brengen is meer inzicht nodig over hoe glycosidische bindingen precies tot stand komen. De studie beschreven in dit proefschrift heeft als doel om meer inzicht te krijgen in de mechanismen van de glycosyleringsreactie en de reactieve intermediairen die hierbij een rol spelen.

De bestaande kennis van het mechanisme alsmede de belangrijkste reactieve intermediairen worden in Hoofdstuk 1 beschreven. De studie in Hoofdstuk 2 is gericht op het ontwikkelen van een computationele methode om het mogelijk te maken om glycosyl kationen (ook wel oxocarbenium ionen genoemd) te bestuderen. Deze kationen zijn hoogenergetische intermediairen en worden verwacht aanwezig te zijn in de reactie, maar kunnen onder die omstandigheden lastig bestudeerd worden. Ook wordt gespeculeerd dat deze deeltjes een belangrijke rol spelen bij de stereoselectiviteit waarmee de reactieproducten gevormd worden. De ontwikkelde computationele aanpak op basis van DFT (dichtheidsfunctionaaltheorie) berekeningen maakt het mogelijk om de stabiliteit, reactiviteit en flexibiliteit van deze glycosyl kationen te onderzoeken. Vervolgens zijn meer dan 30 verschillende glycosyl kationen met verschillende substitutiepatronen geanalyseerd. Uit deze studie tezamen met de uitkomsten van bijbehorende experimentele glycosyleringsreacties bleek dat de conformatie (3D-vorm) van deze deeltjes sterk bepalend is voor de uitkomst van de reactie met een typisch S_N1-nucleofiel triethylsilane-*d* (TES-*d*). Direct bewijs voor de berekende conformationele voorkeur van deze ionen, werd verkregen door deze te genereren in een superzuur medium (HF/SbF_5). In dit medium zijn deze hoogenergetische deeltjes voor een korte tijd stabiel en kunnen spectroscopisch geanalyseerd worden. De structuren van de experimenteel gevonden glycosyl kationen kwamen goed overeen met de berekende structuren. Waar voorheen gedacht werd dat deze deeltjes, door hun intrinsiek hoge energie, vaak leiden tot de vorming van mengsels van 1,2-*cis* en 1,2-*trans* reactieproducten, werd in dit hoofdstuk bewezen dat deze kationen uiterst selectief kunnen reageren. Voor kationen afkomstig van L-fucose, L-rhamnose, D-glucose, D-mannose en D-galactose donoren, kan een zeer selectieve glycosyleringsreactie via een S_N1 mechanisme verwacht worden op basis van de berekende eigenschappen van deze deeltjes.

Hoofdstuk 3 bouwt voort op Hoofdstuk 2 en beschrijft een studie naar reacties tussen de kationen en twee verschillende typische S_N1-nucleofielen. Allyltrimethylsilane en triethylsilane-*d* bleken in de meeste glycosyleringsreacties dezelfde reactie uitkomst te geven. In parallel lieten computationele studies zien dat de meeste kationen reageerden tot het product zonder enige energiebarrière. Voor deze reacties, kan de conformationele

voorkeur van de kationen gebruikt worden om de stereoselectiviteit te begrijpen van reacties waarbij deze kationen een rol spelen. Voor een aantal glycosyl kationen bleek de reactie voor de twee acceptoren echter verschillende resultaten te geven, en hieruit kon geconcludeerd worden dat voor deze reacties de aard van de acceptor ook van belang is. Voor deze gevallen kon met behulp van computationele technieken een overgangstoestand gevonden worden voor de reactie van de kationen met de twee acceptoren. De hoogte van de energiebarrières bleken afhankelijk van het type acceptor dat werd gebruikt. Met de DFT-berekeningen konden gedetailleerde kinetische scenario's worden geschetst, waarmee de gevonden stereoselectiviteit van de reacties verklaard kon worden. Met het gebruiken van het zogenaamde activatie-spanning model was het mogelijk om op een kwantitatieve manier te kijken naar de factoren die de reactiebarrières beïnvloedden. De verschillende reactie uitkomsten, die gevonden werden voor de twee typische S_N1 acceptoren allyltrimethylsilane en triethylsilane-*d*, konden worden teruggeleid tot een wisselwerking tussen de stabiliteit van het kation, de "timing" van de overgangstoestand en de sterische hindering tussen de acceptor en het kation.

Het onderwerp van hoofdstuk 4 behelst de vorming van dioxolenium kationen uit de corresponderende glycosyl kationen door "lange-afstandsparticipatie" van ver gelegen acylgroepen. Deze lange-afstandsparticipatie heeft de potentie om de uitkomst van de glycosyleringsreactie te sturen. Het bestuderen van deze hoogenergetische dioxolenium kationen is, net als de studie van glycosyl kationen, een uitdagende exercitie. Er werd een drievoudige aanpak, bestaande uit infrarood ion spectroscopie, computationele berekeningen en model glycosyleringsreacties, gebruikt om dit effect te bestuderen. Eerst werd met DFT-berekeningen gekeken naar de relatieve stabiliteit van de glycosyl kationen en dioxolenium ionen en deze data lieten zien welke systemen vatbaar kunnen zijn voor lange-afstandsparticipatie. Om hier direct experimenteel bewijs voor te krijgen werden de kationen in de gasfase bestudeerd met behulp van infrarood ion spectroscopie. Om uiteindelijk te onderzoeken of deze deeltjes ook invloed hadden op de uitkomst van glycosyleringsreacties, werd een coherente serie modelexperimenten uitgevoerd. Tezamen bewezen deze studies dat lange-afstandsparticipatie een belangrijke rol kan spelen in het vormen van de reactieproducten. Een grote rol voor lange-afstandsparticipatie werd gevonden voor C-3 acyl mannosyl donoren en in mindere mate voor C-4 acyl galactosyl donoren. Acylgroepen aan de C-6 bleken nauwelijks deel te nemen aan lange-afstandsparticipatie. De mate van lange-afstandsparticipatie nam af in de volgende volgorde: 3-Ac-Man >> 4-Ac-Gal > 3-Ac-Glc ~ 3-Ac-Gal > 4-Ac-Glc > 4-Ac-Man ~ 6-Ac-Glc/Gal/Man.

Het onderzoek in hoofdstuk 5 implementeert de gevonden fundamentele inzichten uit de voorgaande hoofstukken, zodat de synthese van een fragment van een biologisch relevant en complex mycobacteriëel glycolipide kon worden bewerkstelligd. Dit glycolipide (LOS-IV) is opgebouwd uit bijzondere en complexe monosacchariden, zoals bijvoorbeeld caryophyllose dat een tetragesubstitueerd koolstofstereocentrum bevat. Een geïntegreerde aanpak, bestaande uit systematische model glycosyleringsreacties in combinatie met de

detectie en karakterisatie van verschillende reactieve intermediairen met behulp van lage-temperatuur NMR-spectroscopie en computationele berekeningen, werd gebruikt om reactiviteit-stereoselectiviteit relaties vast te stellen voor de complexe monosaccharide bouwstenen. Tijdens zogenoemde pre-activatie glycosyleringen van de gesynthetiseerde donoren bleek de beschermde zuurstof van de ethergroep in de C4-zijketen van caryophyllose (Car) en yersioniose (YerA), gemakkelijk aan te vallen op het geactiveerde anomere centrum, waarbij een gebrugde verbinding wordt gevormd, leidend tot onproductieve reacties. Dit gedrag kon verklaard worden aan de hand van de stabiliteit van de betrokken reactieve intermediairen, bestudeerd door middel van computationele technieken. Preventie van de nucleofiele aanval door de zuurstof in de zijketen is een voorwaarde om effectieve donoren te creëren. Door het vastleggen van de C4-zijketen door middel van een cyclische beschermgroep werd de intra-moleculaire aanval effectief verhinderd. De aldus rationeel ontworpen monosaccharide bouwstenen maakte het mogelijk om effectief en stereoselectief het LOS-IV fragment te synthetiseren, dat het meest ingewikkelde deel omvat van het natuurlijk voorkomende glycolipide.

/ Concluderend, deze thesis beschrijft het gebruik van een combinatie van computationele en experimentele technieken om zo inzicht te verkrijgen in de glycosyleringsreactie en de reactieve intermediairen die hierbij een rol spelen. Het onderzoek in deze thesis laat zien dat glycosyl kationen als reactieve intermediairen kunnen optreden, en ook voor de stereoselectieve introductie van een glycosidische binding kunnen zorgen. De fundamentele kennis gepresenteerd in dit proefschrift kan worden gebruikt om de uitkomst van glycosyleringsreacties beter te begrijpen en nieuwe glycosylerings strategieën te ontwikkelen. Dit zal toekomstige syntheses vereenvoudigen om uiteindelijk sneller en efficiënter complexe koolhydraten op te leveren om glycobiologisch onderzoek mogelijk te maken. /

| Book chapters

2. Hansen. T.; van der Vorm, S.; Tugny C.; Remmerswaal, W. A.; van Hengst, J. M. A.; van der Marel, G. A.; Codée, J. D. C. Stereoelectronic effects in glycosylation reactions. *Comprehensive Glycoscience 2nd ed.* **2020**, *Accepted.*

1. Hagen, B.; van der Vorm, S.; Hansen. T.; van der Marel, G. A.; Codée, J. D. C. Stereoselective Glycosylations – Additions to Oxocarbenium Ions. *Selective Glycosylations: Synthetic Methods and Catalysts* **2017**, Wiley & Sons, 1–28.

| Peer-reviewed journal publications

22. Vermeeren, P.‡; Hansen, T.‡; Grasser, M.; Silva, D. R.; Hamlin, T.; Bickelhaupt, F. M.; A. S_N2 versus E2 Competition for F^- and PH_2^- Revisited, *J. Org. Chem.* **2020**, *Accepted.*

21. Vermeeren, P.‡; Hansen, T.‡; Jansen, P.; Swart, M.; Hamlin, T.; Bickelhaupt, F. M.; A Unified Framework for Understanding Nucleophilicity and Protophilicity in the S_N2/E2 Competition, *Chem. Eur. J.* **2020**, *Accepted*; (*Featured on the Cover*).

20. Hansen, T.‡; Ofman, T. P.‡; Vlaming, J. G. C.‡; Gagarinov, I. A.; van Beek, J.; Goté, T. A.; Tichem, J. A.; Ruijgrok, G., Overkleeft, H. S.; Filippov, D. V.; van der Marel, G. A.; Codée, J. C. D. Reactivity-Stereoselectivity Mapping for the Assembly of *Mycobacterium Marinum* Lipooligosaccharides, *Angew. Chem. Int. Ed.* **2020**, *Accepted.*

19. Hansen, T.‡; Vermeeren, P.‡; Haim, A.; van Dorp, M. J. H.; Codée, J. D. C.; Bickelhaupt, F. M.; Hamlin, T. A. Regioselectivity of Epoxide Ring-Openings via S_N2 Reactions Under Basic and Acidic Conditions, *Eur. J. Org. Chem.* **2020**, 2020 (25), 3822–3828.

18. Hansen, T.‡; Elferink, H.‡; van Hengst, J. M. A.; Houthuijs, K.; Remmerswaal, W. A.; Kromm, A.; Berden, G.; van der Vorm, S.; Rijs, A.; Overkleeft, H. S.; Filippov, D. V.; Rutjes, F. P. J. T.; van der Marel, G. A.; Martens J.; Oomens, J.; Codeé, J. D. C.; Boltje, T. J. Characterization of Glycosyl Dioxolenium Ions and Their Role in Glycosylation Reactions. *Nat. Commun.* **2020**, 11 (1), 2664.

17. de Geus, M. A. R.‡; Maurits, E.‡; Sarris, A. J.‡; Hansen, T.; Kloet, M. S.; Kamphorst, K.; ten Hoeve, W.; Robillard, M. S.; Pannwitz, A.; Bonnet, S. A.; Codée, J. D. C.; Filippov, D. V.; Overkleeft, H. S.; van Kasteren, S. I., Fluorogenic Bifunctional *Trans*-cyclooctenes as Efficient Tools for Investigating Click-to-Release Kinetics. *Chem. Eur. J.* **2020**, 26 (1), 9900–9904.

16. Liu, H., Hansen, T.; Zhou, S.; Wen, G., Liu, X.; Zhang, Q.-J.; Codée, J. D. C.; Schmidt, R. R.; Sun, J.-S., A Dual-Participation Protecting Group Solves the Anomeric Stereocontrol Problems in Glycosylation Reactions. *Org. Lett.* **2019**, 21 (21), 8713–8717.

15. Chen, J.; Hansen, T.; Zhang, Q.-J.; Liu, D.-Y.; Sun, Y.; Yan, H.; Codée, J. D. C.; Schmidt, R. R.; Sun, J.-S. 1-Picolinyl-5-Azido Thiosialosides: Versatile Donors for the Stereoselective Construction of Sialyl Linkages. *Angew. Chem. Int. Ed.* **2019**, 58 (47), 17000–17008.

14. van der Ham, A.[‡]; Hansen, T.[‡]; Lodder, G.; Codée, J. D. C.; Hamlin, T. A.; Filippov, D. V. Computational and NMR Studies on the Complexation of Lithium Ion to 8-Crown-4. *ChemPhysChem* **2019**, 20 (16), 2103–2109.

13. Zhang, Q.-J.; Gimeno, A.; Santana, D.; Wang, Z.; Valdés-Balbin, Y.; Rodríguez-Noda, L. M.; Hansen, T.; Kong, L.; Shen, M.; Overkleeft, H. S.; Vérez-Bencomo, V.; van der Marel, G. A.; Jiménez-Barbero, J.; Chiodo, F.; Codée, J. D. C. Synthetic, Zwitterionic Sp1 Oligosaccharides Adopt a Helical Structure Crucial for Antibody Interaction. *ACS Cent. Sci.* **2019**, 5 (8), 1407–1416.

12. van der Vorm, S.; Hansen, T.; van Rijssel, E. R.; Dekkers, R.; Madern, J. M.; Overkleeft, H. S.; Filippov, D. V.; van der Marel, G. A.; Codée, J. D. C. Furanosyl Oxocarbenium Ion Conformational Energy Landscape Maps as a Tool to Study the Glycosylation Stereoselectivity of 2-Azidofuranoses, 2-Fluorofuranoses and Methyl Furanosyl Uronates. *Chem. Eur. J.* **2019**, 25 (29), 7149–7157; (*Featured on the Cover*).

11. Hansen, T.; Lebedel, L.; Remmerswaal, W. A.; van der Vorm, S.; Wander, D. P. A.; Somers, M.; Overkleeft, H. S.; Filippov, D. V.; Désiré, J.; Mingot, A.; Bleriot, Y.; van der Marel, G. A.; Thibaudeau, S.; Codeé, J. D. C. Defining the S_N1 Side of Glycosylation Reactions: Stereoselectivity of Glycopyranosyl Cations. *ACS Cent. Sci.* **2019**, 5 (5), 781–788; (*Featured on the Cover*).

10. Madern, J. M.; Hansen, T.; van Rijssel, E. R.; Kistemaker, H. A. V.; van der Vorm, S.; Overkleeft, H. S.; van der Marel, G. A.; Filippov, D. V.; Codée, J. D. C. Synthesis, Reactivity, and Stereoselectivity of 4-Thiofuranosides. *J. Org. Chem.* **2019**, 84 (3), 1218–1227.

9. van der Vorm, S.; Hansen, T.; van Hengst, J. M. A.; Overkleeft, H. S.; van der Marel, G. A.; Codée, J. D. C. Acceptor Reactivity in Glycosylation Reactions. *Chem. Soc. Rev.* **2019**, 48 (17), 4688–4706.

8. Artola, M.; Kuo, C.-L.; McMahon, S. A.; Oehler, V.; Hansen, T.; van der Lienden, M.; He, X.; van den Elst, H.; Florea, B. I.; Kermode, A. R.; van der Marel, G. A.; Gloster, T. M.; Codée, J. D. C.; Overkleeft, H. S.; Aerts, J. M. F. G. New Irreversible α-L-Iduronidase Inhibitors and Activity-Based Probes. *Chem. Eur. J.* **2018**, 24 (71), 19081–19088.

7. Sarris, A. J. C.; Hansen, T.; de Geus, M. A. R.; Maurits, E.; Doelman, W.; Overkleeft, H. S.; Codée, J. D. C.; Filippov, D. V.; van Kasteren, S. I. Fast and pH-Independent Elimination of *Trans*-Cyclooctene by Using Aminoethyl-Functionalized Tetrazines. *Chem. Eur. J.* **2018**, 24 (68), 18075–18081.

6. Schröder, S. P.; Kallemeijn, W. W.; Debets, M. F.; Hansen, T.; Sobala, L. F.; Hakki, Z.; Williams, S. J.; Beenakker, T. J. M.; Aerts, J. M. F. G.; van der Marel, G. A.; Codée, J. D. C.; Davies, G. J.; Overkleeft, H. S. Spiro-Epoxyglycosides as Activity-Based Probes for Glycoside Hydrolase Family 99 Endomannosidase/Endomannanase. *Chem. Eur. J.* **2018**, 24 (39), 9983–9992.

5. Schröder, S. P.; Wu, L.; Artola, M.; Hansen, T.; Offen, W. A.; Ferraz, M. J.; Li, K.-Y.; Aerts, J. M. F. G.; van der Marel, G. A.; Codée, J. D. C.; Davies, G. J.; Overkleeft, H. S. Gluco-1*H*-Imidazole: A New Class of Azole-Type β-Glucosidase Inhibitor. *J. Am. Chem. Soc.* **2018**, 140 (15), 5045–5048.

4. Rooden, E. J. van; Kreekel, R.; Hansen, T.; A. Janssen, A. P.; Esbroeck, A. C. M. van; den Dulk, H.; van den Berg, R. J. B. H. N.; Codée, J. D. C.; van der Stelt, M. Two-Step Activity-Based Protein Profiling of Diacylglycerol Lipase. *Org. Biomol. Chem.* **2018**, 16 (29), 5250–5253.

3. Beenakker, T. J. M.; Wander, D. P. A.; Offen, W. A.; Artola, M.; Raich, L.; Ferraz, M. J.; Li, K.-Y.; Houben, J. H. P. M.; van Rijssel, E. R.; Hansen, T.; van der Marel, G. A.; Codée, J. D. C.; Aerts, J. M. F. G.; Rovira, C.; Davies, G. J.; Overkleeft, H. S. Carba-Cyclophellitols Are Neutral Retaining-Glucosidase Inhibitors. *J. Am. Chem. Soc.* **2017**, 139 (19), 6534–6537.

2. van der Vorm, S.; Hansen, T.; Overkleeft, H. S.; van der Marel, G. A.; Codée, J. D. C. The Influence of Acceptor Nucleophilicity on the Glycosylation Reaction Mechanism. *Chem. Sci.* **2017**, 8 (3), 1867–1875.

1. Mukhopadhyay, P.; Baggelaar, M.; Erdelyi, K.; Cao, Z.; Cinar, R.; Fezza, F.; Ignatowska-Janlowska, B.; Wilkerson, J.; Gils, N. van; Hansen, T.; Ruben, M.; Soethoudt, M.; Heitman, L.; Kunos, G.; Maccarrone, M.; Lichtman, A.; Pacher, P.; van der Stelt, M. The Novel, Orally Available and Peripherally Restricted Selective Cannabinoid CB_2 Receptor Agonist LEI-101 Prevents Cisplatin-Induced Nephrotoxicity. *Br. J. Pharmacol.* **2016**, 173 (3), 446–458.

ACS Cent. Sci. **2019**, 5 (5)

Chem. Eur. J. **2019**, 25 (29)

Thomas Hansen was born in Leiden, The Netherlands, on July 30th, 1992. From 2004 until 2009, he attended the Da Vinci College in Leiden, at which secondary education diplomas, with majors in science, were obtained in 2009 (HAVO). In 2009, he started his bachelor in chemistry at the University of Applied Sciences Leiden. As part of the bachelor program, a research internship in the field of inorganic chemistry was followed, concerning the kinetics of microstructure formation between iron-oxides and dolomite, under the guidance of prof. dr. S. R. van der Laan. Another research internship in the field of organic chemistry was followed, concerning the synthesis of CB_2-selective cannabinoid receptor ligands, under the guidance of prof. dr. M. van der Stelt. In 2013, he obtained his B.A.Sc. degree from the University of Applied Sciences Leiden. Subsequently, the research M.Sc. program in chemistry was started with a specialization in chemical biology. During the program, a research internship at the bio-organic synthesis group, headed by prof. dr. H. S. Overkleeft and prof. dr. G. A. van der Marel, of the Leiden University, was pursued. The research was directed at unraveling mechanistic features of the glycosylation reaction, crucial for the assembly of synthetic oligosaccharides for biological research. His research was awarded the "AkzoNobel Graduation Award for Chemistry and Process Technology 2016" for the master thesis entitled "The relationship between the acceptor properties and stereoselectivity in glycosylations: a continuum of mechanisms" under supervision of prof. dr. J. D. C. Codée and prof. dr. G. A. van der Marel. In 2015, he obtained his M.Sc. degree (*summa cum laude*).

In November of 2015, the research described in this Ph.D. thesis was started under the supervision of prof. dr. J. D. C. Codée and prof. dr. G. A. van der Marel, in the bio-organic synthesis group. Parts of the research described in this thesis was performed at the superacid group under the supervision of prof. dr. S. Thibaudeau and prof. dr. Y. Blériot in Poitiers (France) with a Van Gogh travel grant (October 2017). During the final two years of his doctoral studies, he also joined the theoretical chemistry group under the supervision of prof. dr. F. M. Bickelhaupt and dr. T. A. Hamlin. Parts of the research described herein were presented as oral presentations at 29th International Carbohydrate Symposium (Portugal, 2018), Carbohydrate and Fluorine Symposium, (France, 2018), EUROCARB XX, (The Netherlands, 2019), and CHAINS (The Netherlands, 2019). In May 2020, he started his postdoctoral research in the theoretical chemistry group of prof. dr. F. M. Bickelhaupt and dr. T. A. Hamlin.

De laatste regels van dit proefschrift zijn natuurlijk gewijd aan alle mensen die dit mogelijk maakten. Dit was zeker niet gelukt zonder de ondersteuning en inbreng van velen, en die wil ik bij deze zeer danken!

Ten eerste wil ik graag Jeroen en Gijs bedanken voor alle begeleiding door de jaren heen! De talloze koffiemomenten en motiverende discussies zijn onmisbaar geweest. Jullie hebben me zoveel geleerd, waarbij kritisch kijken naar wetenschap centraal stond. Jeroen jouw onbreekbare positieve houding heeft mij met gemak over de finishlijn gebracht. Ook de nodige schouderklopjes en labbezoekjes van Gijs waren zeker goud waard. Eveneens was de inbreng van Hermen met zijn scherpe en doelmatige commentaren zeer waardevol.

Ik begon het Ph.D. avontuur met wat mooie glycosyl kationen die we zouden gaan bestuderen. Dit mondde uit in een mooie *ACS Central Science* publicatie, waarbij hulp uit Frankrijk essentieel was. Merci beaucoup, Ludivine, Sébastien and Yves for all the hard work and hospitality! Idem de vele computeravonden met Dima waren een mooie toevoeging aan het verhaal. Ook Wouter Driever wil ik danken voor zijn bijdrage met wat pracht moleculen, die jammer genoeg minder stabiel bleken in HF/SbF_5 dan gehoopt.

Vervolgens zijn we in parallel gestart met het bouwen van het "beest" (LOS-IV), wat uiteindelijk beschreven staat in *Angewandte Chemie*. Deze verbinding bleek een inspanning van vele kanten te vereisen, en zo zijn er een behoorlijk aantal studenten, Jacqueline, Gijs, Tim, Tessa, Joey en Jessey, die ik zeer wil bedanken voor het aangaan van deze monstrueuze uitdaging. Vooral Tim en Joey hebben een enorme bak aan synthese kunnen verzetten! Tim jouw hoeveelheid proefjes in parallel zullen weinigen kunnen evenaren en jouw passie voor scheikunde maakte elke dag, een dag vol met mooie proefjes. Nu zitten we in hetzelfde schuitje en ben je ook lekker bezig aan je Ph.D., super! Joey, jouw mentale onbreekbaarheid heeft mede geleid tot het uiteindelijke synthetische fragment, grote hulde hiervoor! Bovendien kan jij als één van de beste op bijna kiloschaal werken in een lab dat daar eigenlijk niet voor bedoeld is, en deze hobby ga jij gelukkig de komende jaren ook voortzetten in je Ph.D.!

Nadat we de glycosyl kationen met model nucleofielen redelijk begrepen, gingen we aan de slag met *O*-nucleofielen, en dit bleek toch veel moeilijker dan gedacht. Veel dank aan Wouter Remmerswaal voor zijn bijdrage aan dit project. Zelfs met alle inspanning hebben we deze puzzel nog niet geheel opgelost, maar gelukkig kan jij nog 4 jaar lang doorklussen aan deze ongelofelijke hersenbreker! Wouter jouw enthousiasme en gezellige babbel brachten geen moment stilte op het lab. Echt geen moment.

Vervolgens zijn we gestart met een project dat al lange tijd op de plank lag, onderzoek naar lange-afstands participatie. Halverwege kwamen we erachter dat ook onze vrienden in Nijmegen met dit project aan de slag waren. Eerst geteisterd door misschien wel een kaping van het project vanuit deze richting, nu gelukkig mooie samenwerkingspartners! Dit mondde uit in een prachtige *Nature Communications* publicatie, waarbij ik in het speciaal Hidde en Thomas Boltje zeer wil bedanken! Natuurlijk wil ik ook Jacob en Wouter R. bedanken voor de ondersteuning vanuit Leiden in dit project.

Het laatste onderzoek van dit proefschrift omvat nog een verdere studie naar glycosyl kationen, maar met het grootste detail, waarbij de theoretische achterban in Amsterdam onmisbaar was! Heel veel dank aan Pascal, Hans, Stephanie, Eva, Celine, Trevor, Célia en Matthias voor alle hulp en de gezellige sfeer! Eveneens veel dank aan alle mensen binnen de bio-organic synthesis groep die alle rekenhulp met open armen ontvingen, waaronder, Stefan, Thomas Beenakker, Dennis, Eva, Sybrin, Martha, Alexi, Jerre, Qingju, Alex, Elmer, Mark en Dima! Also, Jian-Song, from outside Leiden, thank you for some very fruitful collaborations! As well, many thanks to Pascal and Trevor for some very cool chemistry, which will be published soon! Also, Royji thank you for all your hard work. I know this work is going to be another awesome story!

Natuurlijk zijn er veel meer mensen die ik wil bedanken buiten de projecten, en laat ik beginnen met Fons en Karthick die talloze prachtige NMR platen voor me hebben geschoten. Hans voor alle HRMS-analyses. Stefan dank voor alles wat je me hebt geleerd door de jaren. Je was de beste begeleider die ik me kan voorstellen voor mijn voorafgaande masterproject! Berend ik heb genoten van de heerlijke CHAINS-reisjes en de gezellige middagjes koffie. En natuurlijk de heerlijke werkatmosfeer in EE4.02 met Tim, Alex, Mark, Jerre, Dennis, Coralie en Jacob! De donderdagavond borrels in het kantoor ga ik zeker missen! Evenzeer mensen buiten het lab waren een essentiële steunpilaar om zo deze jaren door te komen en zorgden voor de nodige afleiding buiten het onderzoek. Dank aan Marinda, Steven, Wyanne, Daan, Maico, Sanne, Robert, Bas, Nikki, Matthieu en Iris voor het aanhoren van alle chemische verhalen en de nodige drankjes die dit proefschrift tot stand hebben gebracht.

Rest mij mijn familie te bedanken. Ten eerste mijn ouders en broer, ook al begrepen jullie niet altijd precies wat ik deed, waren jullie altijd benieuwd en enthousiast over wat er gaande was. Jullie aanmoedig heeft me geholpen om ook in de mindere periodes gewoon door te gaan! En tot slot, Eliane, zonder jou was me dit nooit gelukt! Bedankt voor al je steun en liefde. Ik kijk uit naar de toekomst die wij samen tegemoet gaan.

Thomas

0000-0002-6291-1569