Reactivity and selectivity in glycosylation reactions

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List of abbreviations

Ac	acetyl
AIBN	2,2'-azobis(2-methyl-propionitrile)
All	allyl
APT	attached proton test
aq.	aqueous
Ar	aryl
Ara	arabinose
AraA	arabinuronic acid
AraF	2-deoxy-2-fluoro arabinose
$AraN_3$	2-azido-2-deoxy arabinose
Arom	aromatic
B	boat
B3LYP	Becke, 3-parameter, Lee-Yang-Parr
BAIB	(diacetoxyiodo)benzene
BDA	butane-2,3-diacetal
Bn	benzyl
bs	broad singlet
Bu	butyl
Bz	benzoyl
C	chair
cal	calorie
calcd	calculated
cat.	catalytic
CBz	carboxybenzyl
CEL	conformational energy landscape
CIP	contact ion pair
COSY	correlation spectroscopy
C_q	quaternary carbon atom
CSA	camphor-10-sulfonic acid
Cy	cyclohexyl
δ	chemical shift (ppm)
d	doublet
DAST	diethylaminosulfur trifluoride
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	difluorethanol
DFT	density function theory
DiPEA	diisopropylethylamine
DMAP	4-dimethylaminopyridine
DMF	dimethylformamide
DMM	dimethylmaleimide
DMSO	dimethylsulfoxide
DNPY	dinitropyridone
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
eq.	molar equivalent
Et	ethyl
E-X	electrophilic activator system
F	field-inductive parameter
f	Fukui value
FT	Fourier transform
gg	gauche-gauche
gt	gauche-trans
GATED	proton decoupling applied only during relaxation
Gal	galactose
Glc	glucose
GlcA	glucuronic acid
GlcN	glucosamine
$GlcN_3$	2-azido-2-deoxy glucose
GlcNAc	*N*-acetyl glucosamine
h	hour(s)
H	half-chair
HECADE	heteronuclear couplings from aSSCI-domain experiments with E.COSY-type cross peaks
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
IR	infrared
J	coupling constant
KIE	kinetic isotope effect
LC-MS	liquid chromatography - mass spectrometry

LG	leaving group
LTQ	linear trap quadropole
LUMO	lowest unoccupied molecular orbital
Lyx	lyxose
LyxA	lyxuronic acid
LyxF	2-deoxy-2-fluoro lyxose
$LyxN_3$	2-azido-2-deoxy lyxose
M	molar
m	multiplet
m.s.	molecular sieves
m/z	mass over charge ratio
min	minutes
Man	mannose
ManA	mannuronic acid
Me	methyl
MFE	monofluoroethanol
M.S.	molecular sieves
N	Mayr's nucleophilicity parameter
N-PSP	*N*-(phenylseleno)phthalimide
Nap	2-methylnaphthyl
NBS	*N*-bromosuccinimide
NFM	*N*-formylmorpholine
NIS	*N*-iodosuccinimide
NMR	nuclear magnetic resonance
NMP	*N*-methyl-2-pyrrolidone
NOESY	nuclear Overhauser effect spectroscopy
Nu	nucleophile
p	para
P	protection group
PCM	polarizable continuum model
PET	positron-emission tomography
PFBS-F	perfluorobutanesulfonyl fluoride
Ph	phenyl
Phth	phthaloyl
pK_a	$-\log_{10}$ (acid dissociation constant)
PMB	4-methoxybenzyl
ppm	parts per million
q	quartet
q	atomic charge
qd	quartet of doublets
r.t.	room temperature
R_f	retention factor
RDAS	reciprocal donor-acceptor selectivity
Rib	ribose
RibA	riburonic acid
RibF	2-deoxy-2-fluoro ribose
$RibN_3$	2-azido-2-deoxy ribose
RRV	relative reactivity value
s	singlet
s	chemical softness
S	skew boat
sat.	saturated
S_N1	uni-molecular nucleophilic substitution
S_N2	bi-molecular nucleophilic substitution
SSIP	solvent-separated ion pair
t	triplet
t	*tert*-
T	twist
Taz	tiazolinyl
tg	trans-gauge
TBAF	tetrabutylammonium fluoride
TBAI	tetrabutylammonium iodide
TBAT	tetrabutylammonium triphenylsilyl difluoride
TBS	*tert*-butyldimethylsilyl
TBDMS	*tert*-butyldimethylsilyl
TBDPS	*tert*-butyldiphenylsilyl
TCA	trichloroacetyl
TES	triethylsilyl
TEMPO	2,2,6,6-tetramethylpiperidine
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
Trt	trityl; triphenylmethyl
Ts	tosyl; 4-methylbenzene-1-sulfonyl
TS	transition state
td	triple doublet
tt	triple triplet
TTBP	2,4,6-tri-*tert*-butylpyrimidine
UDP	uridine diphosphate
UV	ultraviolet
VT	variable temperature
Xyl	xylose
XylA	xyluronic acid
XylF	2-deoxy-2-fluoro xylose
$XylN_3$	2-azido-2-deoxy xylose
ZPE	zero-point energy

Chapter 1

General introduction

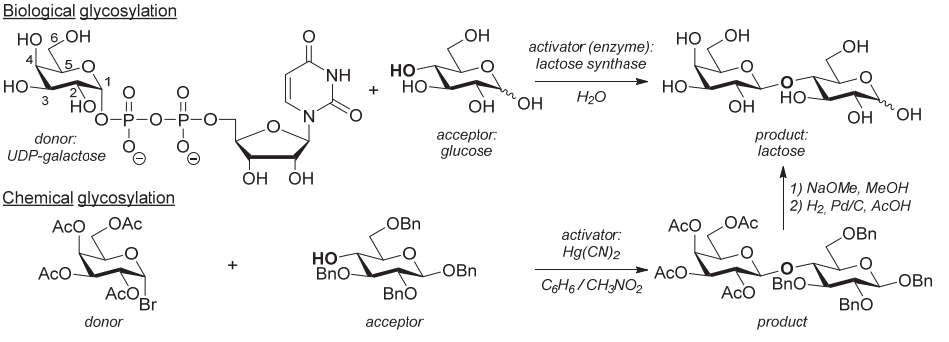
Introduction

Carbohydrates are the most diverse and abundant class of biomolecules on earth, and play important roles in all facets of life, amongst others in cell-cell recognition and activation of the immune system.[1,2] Extracting carbohydrates from natural sources, if available at all, is a tedious and expensive process owing to the complex mixture of similar compounds present. Synthetic chemistry is one of the most important suppliers of well-defined carbohydrates and glycoconjugates, in sufficient quantities and free from contaminants that may interfere with or are detrimental to the activity. However, the assembly of complex oligosaccharides remains a complex task and gaining full control over the stereoselectivity in the crucial glycosylation reaction still is a major challenge in synthetic carbohydrate chemistry. This Thesis investigates the mechanisms of the glycosylation reaction by establishing structure-reactivity-selectivity relationships.

In a glycosylation reaction, a carbohydrate donor is activated to provide an electrophilic species to react with a nucleophilic acceptor molecule (see Scheme 1), which

can be as simple and small as water, or as structurally complex and large as a protein.[3–8] In a chemical glycosylation, the glycosyl donor has protecting groups to temporarily inactivate the reactive carbohydrate alcohol groups and avoid side reactions, and a leaving group at the anomeric (C-1) position.[9,10] This leaving group can be activated by a promotor to make it sufficiently reactive to be substituted by the nucleophilic acceptor, which also bears protecting groups to mask positions where reactions must be avoided. The additional synthetic steps to construct protected building blocks and exchange or remove them can in itself be a monumental undertaking, but one that is often unavoidable due to inherent similarities between the carbohydrate alcohols.[11–15]

Scheme 1. Depiction of a glycosylation reaction: synthesis of lactose through enzymatic and chemical methods.[a]



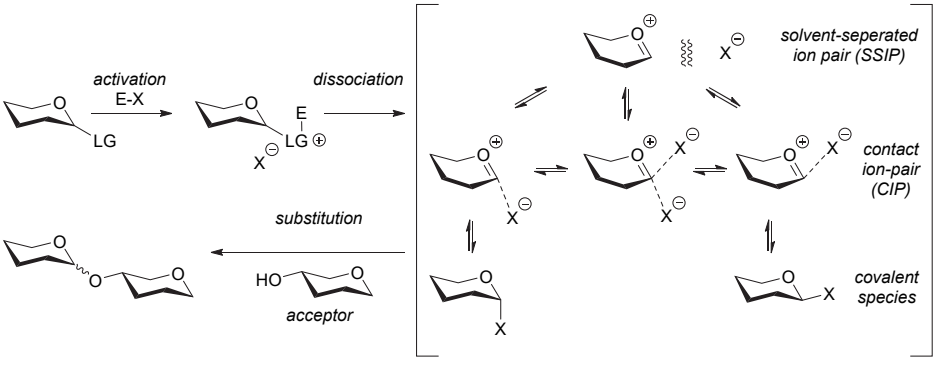
[a]UDP = uridine diphosphate. Numbers indicate the conventional labelling of glycosides. The biosynthetic pathway,[16] and conditions for enzymatic biosynthesis[17] and chemical synthesis[18] are reported in cited references.

The glycosylation reaction mechanism

There is no single general reaction mechanism to describe every chemical glycosylation reaction. For over a century, and especially the past 50 years,[19,20] many new glycosylation protocols have been developed and each of these requires different reagents and reaction conditions. The current mechanistic understanding, which was already formulated and proposed in the 1960s and 1970s,[21–24] centers on the equilibrium between a covalent glycosylating species, in which the anomeric leaving group is attached to the glycosyl donor, and the related ion pairs, in which the leaving group is dissociated from the donor (see Scheme 2). Substitution may take place on any of the intermediate states, with partially dissociated bonds, or in a geometry not generally depicted in a reaction scheme.[25] Although donors may look similar, their behavior in glycosylation reactions

may be very different. Whether a reaction is feasible is determined by many factors, not the least of which are the potential of ionization at the anomeric center, the geometry of the donor when it undergoes glycosylation, and the nucleophilicity of the acceptor.

Scheme 2. General glycosylation mechanism.[a]



[a]LG = leaving group. E-X = electrophilic activator. Donor and acceptor substituents are left out for clarification. The fate of the acceptor proton, donor leaving group and activator is ignored.

Earlier work on chemical glycosylations evolved around (modified) Koenings-Knorr reactions featuring glycosyl halides as glycosyl donors.[20,26,27] When activated and sufficiently reactive, the covalently linked leaving group can be substituted in an S_N2 substitution reaction, or isomerized to the opposite anomer followed by an S_N2 substitution. The intermediacy of the oxocarbenium ion (solvent-separated ion pair, SSIP, Scheme 2) in a glycosylation reaction was largely ignored as it was argued that the lifetime of an oxonium-type ion in water is too short even for solvent equilibration, and for the typical low polarity glycosylation solvents the ion pairs would not separate sufficiently to allow the free oxocarbenium ion to play a role as an intermediate.[28,29] Instead, exploded transition states with elongated bonds or tightly packed contact ion pairs (CIP) were deemed responsible for the interconversion of anomeric halides and some glycosylations.

Donor reactivity: electronic and conformational aspects

A large variety of anomeric leaving groups exists to date, each with its own reactivity and activation scheme.[9,19] Using them in tandem enables orthogonal glycosylation strategies.[30] Chemically similar groups may be distinguished by their reactivity, resulting in chemoselective glycosylations. The difference in reactivity is a result of the cumulative electronic properties, the position and orientation of the ring substituents.[31]

The nature of the anomeric leaving group has a large impact on the outcome of a glycosylation reaction. In general, a better leaving group, for example a glycosyl bromide *versus* a glycosyl chloride, gives a more reactive donor.[20] The higher reactivity can lead to a faster S_N2 substitution, but also a faster anomerisation reaction to provide the opposite anomer. Generally, an equatorially oriented β-anomer, lacking the stabilizing anomeric effect, is more reactive than its α-anomer, which is often the most prevalent species present. The role of the more reactive β-anomer becomes more important when poor acceptors are to be glycosylated.[22,32,33] When better leaving groups such as triflates are employed,[34] the potency to depart is high enough to cause a large degree of S_N2 substitution but also establish a fast equilibrium between various ionic species.

The reactivity of the donor is largely determined by the different protecting and functional groups present, a fact already known for over half a century.[35–37] Inductive effects from electronegative atoms and electron-withdrawing groups destabilize the developing positive charge at the anomeric center upon departure of the leaving group. Ether-type protecting groups (benzyl, methyl, etc.) are less electron-withdrawing than esters (acetyl, benzoyl, etc.) and these are consequently termed "arming" and "disarming", respectively (Figure 1D).[38–40] Removing an oxygen substituent from the carbohydrate ring (e.g. in the common deoxysugars rhamnose and fucose) increases the reactivity of the donor.[41] The configuration of the donor is important as well, with a pattern of hydrolysis reactivity following the order: α-galactose > α-mannose > α-glucose. This trend is in part related to the eclipsing interactions that develop between neighboring substituents, upon the formation of an oxocarbenium ion-type intermediate.[42] More severe torsional strain may be imposed on the system by ring-fusing the carbohydrate ring with another five- or six-membered ring, which makes the system more rigid. The isopropylidene, benzylidene and butane diacetal (BDA) are examples of such torsionally restrained systems (Figure 1A).[43,44] Trans-fused six-membered ring systems such as the benzylidene in **2** are unable to ring flip from their di-equatorial setting to a di-axial constellation: the atoms end up too far apart. Additional eclipsing interactions are developed in the secondary ring, which must now deviate from its preferred chair conformation to conform to the changing geometry associated with the transition to the oxocarbenium ion in the primary ring. These attributes come at the cost of an energy penalty and these fused-ring systems are therefore torsionally disarming. The cyclic protecting groups also severely limit the conformational space of the

oxocarbenium ion (Figure 1C), which is of critical importance to the stereoselectivity of the reaction (*vide infra*).

Besides torsionally disarming the system, cyclic diol protecting groups can also impose electronic effects. The 4,6-*O*-benzylidene system is interesting in this respect, since it fixes the C-6–O-6 dipole such that it is directed away from the anomeric center. This results in the most disarming orientation of the O-6 group: the *tg* rotamer (Figure 1B).[45–47] The relative reactivity of different donors has been investigated by the groups of Fraser-Reid, Ley, and Bols complemented by an extensive study by the group of Wong, and by now a large set of relative reactivity values (RRV) exists (Figure 1D).[38–40,48–59]

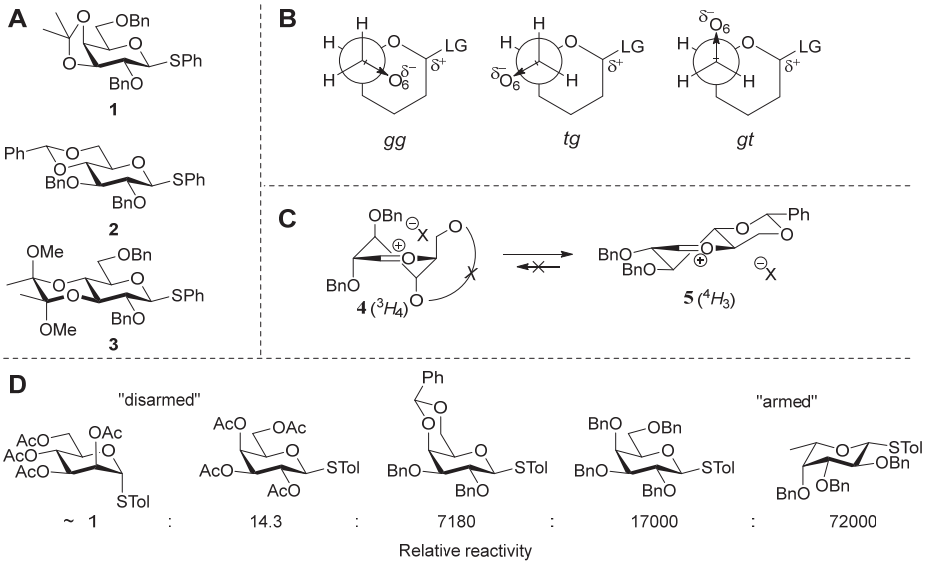


Figure 1. (A) Example structures of isopropylidene, benzylidene, and BDA cyclic protecting groups. (B) Top-view Newman projection of the C-6–C-5 bond, with *gg*-, *tg*-, *gt*-rotamers, the C-6–O-6 dipole is indicated by the small arrow, and partial charges are displayed. (C) Both oxocarbenium ion conformations available for a donor without torsional strain, only the $^4H_3$ conformation is available for benzylidene and BDA structures **2** and **3**. (D) Armed-disarmed principle with relative reactivity values obtained by the laboratory of Wong, relative to tolyl tetraacetyl-1-thio-α-D-mannopyranoside.

Glycosylation stereoselectivity

There are numerous strategies that enable the stereoselective formation of glycosylation linkages, but unfortunately these are often not generally applicable and each new glycosylation presents another challenge. Two types of products can be formed in a glycosylation reaction: 1,2-*trans*- and 1,2-*cis*-linked glycosidic bonds. For the former

type, anchimeric assistance of an acyl-type protecting group on C-2 is usually sufficient to direct stereoselectivity (Figure 2). This form of neighboring group participation is reliable, but its efficiency does depend on the other groups on the carbohydrate ring.[60–64] Double stereodifferentiation (see also next chapter) or severe steric hindrance (as is the case with 4,6-silylidene protected galactopyranosides) may thwart effective neighboring group participation.[65–67]

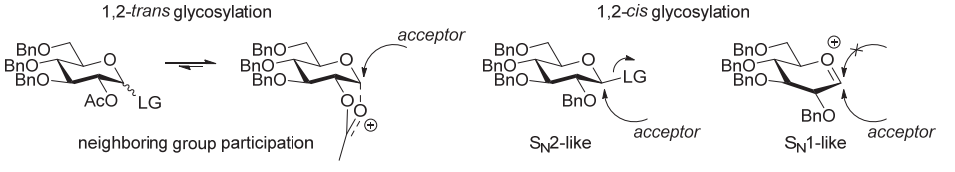


Figure 2. 1,2-*trans* and 1,2-*cis* glycosylation strategies.

1,2-*Cis*-glycosidic linkages are much more difficult to construct and can generally only be affected using a non-participating group at C-2. Several different approaches have been reported to date to install specific 1,2-*cis*-linkages, which for example make use of remote participation,[68–70] site selective delivery of the acceptor, [71,72] steric screening from one of the ring faces by a bulky group[66,67,73], or exploiting the anomeric effect during or after the glycosylation,[74–80] among others.[81–83] From a mechanistic point of view, two pathways may be followed: inverting a 1,2-*trans*-leaving group in an S_N2 reaction, or exploiting the stereoselective addition on oxocarbenium ion-type intermediates in an S_N1 reaction.

Several examples have been reported using the S_N2 directed inversion of a leaving group. For example glycosyl halides can be used. Here, α-halides are generated and an equilibrium is set up with the more reactive β-halide.[22] Substitution of the latter halide then provides the α-product. The same idea applies for other anomeric leaving groups and *in situ* formed anomeric functionalities, such as those formed in the presence of participating solvents, such as DMF, acetonitrile or diethyl ether.[84–86] Inversion reactions also happen when the nucleophile is part of a chimeric activator, as was demonstrated for carboxylic acid and phosphate acceptors on the activation and inversion of trichloroimidates.[87,88]

On the S_N1 side of the reaction continuum, oxocarbenium ions and their associated ion pairs can provide 1,2-*cis*-stereoselective glycosylations. Simple carbocations or oxocarbenium ions have long been regarded as "flat" and unselective but the recent appreciation of the effect of the rich stereochemical environment of (cyclic)

carbohydrate oxocarbenium ions has changed that perspective. The generation of an oxocarbenium ion is preceded by efficient orbital overlap of the ring oxygen's lone pair electrons and the antibonding σ*-orbital of the leaving group. For an axial leaving group the orbitals readily overlap as they have an *anti*-periplanar orientation leading directly to an oxocarbenium ion in a half-chair conformation. The opposite anomer with equatorial orientation must change its conformation first to accommodate efficient orbital overlap (which may occur with *syn*-periplanar arrangement), and will provide a skew-boat conformation.[89–92] These initially formed oxocarbenium ion conformations can be attacked immediately, with or without steric screening from its counter ion. In the absence of an acceptor, or in reactions with poor nucleophiles, the oxocarbenium ion may change to its most stable conformation, which then dictates the stereochemical outcome.

A model system to account for the stereoselectivity of cyclic oxocarbenium ions was devised by Woerpel and co-workers, which was termed the two-conformer model.[93–96] This model assumes that the most stable oxocarbenium ions will have a C-1–O-4/5 double bond and therefore a flat constellation of four atoms (C-2–C-1–O-5–C-5 in six-membered ring pyranoses and C-2–C-1–O-4–C-4 in five-membered ring furanoses). This gives rise to two low energy conformations of a five-membered ring (^3E and E_3) and eight of a six-membered ring ($^3H_4$, $^4H_3$, $^{2,5}B$, $B_{2,5}$, ^3E, E_3, ^4E, E_4) excluding the completely flat geometry. For six-membered rings the $^3H_4$ and $^4H_3$ half-chair conformations are generally energetically most favorable as these have less steric (eclipsing and 1,3-diaxial) interactions than their relatives in the boat and envelope conformations, resulting in two conformations relevant for the stereoselectivity in this model. Central to this model are two possible approaches for the nucleophile: from the top or bottom side, arbitrarily defined for the D-glycosides in the representations in Figure 3. Since furanoses have only a single out-of-plane ring atom, the type of nucleophilic attack is also referred to as inside or outside attack, relating to the concave or convex face of C-3 respectively.[97] Without considering the type of substituents on the furanose ring, two things become readily apparent. Firstly, the incoming nucleophile has eclipsing interactions with the axially orientated substituent on C-2 when performing an outside attack, and 1,3-(*pseudo*)diaxial interactions with the axially orientated substituent of C-3 for the inside attack.

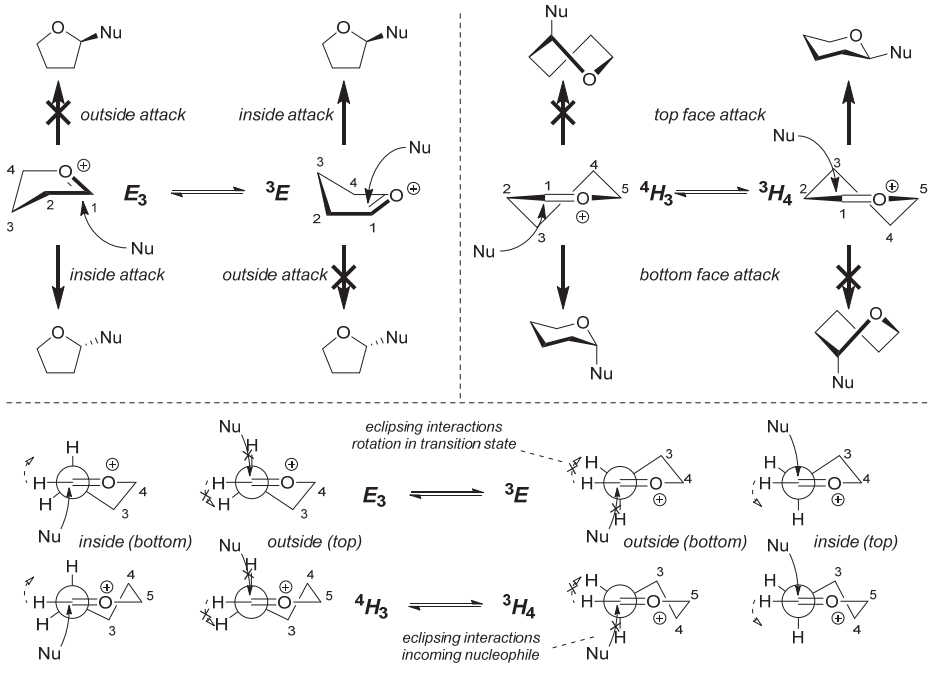


Figure 3. (top) The two-conformer model for furanoses and pyranoses. (bottom) Newman projections along the C-1–C-2 bond visualizing the movement of the nucleophile and equatorial substituents at C-1 and C-2, and consequently the eclipsing interactions that occur, indicted by crossed arrows.

Secondly, rehybridisation of the anomeric center will lead to an eclipsed C-1–C-2 situation upon outside attack, while inside attack will provide a staggered constellation. In the pyranose case, attack on the top face of the $^4H_3$ conformer will change the half-chair conformation to a skew-boat conformation with increasing eclipsing interactions between the *pseudo*-equatorial substituents on C-1 and C-2 in the transition state.[98] Attack from the top face of the alternative $^3H_4$ half chair, or bottom face of the $^4H_3$ however, will lead to a favorable chair conformation, free of eclipsing interactions, and has therefore a lower transition state energy. These arguments dictate the general rules for facial selectivity: in furanosides inside attack will be favorable where pyranosyl oxocarbenium ions will be preferentially attacked on the face that leads to a chair-like, lowest energy transition state.

Having established the face-selective preferences of oxocarbenium ions in the two-conformer model, the next goal was to qualitatively and ultimately quantitatively predict *which* conformation is preferentially formed and attacked. The group of Woerpel has made predictions based on experimental evidence and rationalization of relative (de)stabilization properties of the ring substituents. The individual substituent effects

were gauged by glycosylating allyltrimethylsilane with a series of (partially) substituted furanosides and pyranosides ("stripped-down carbohydrates").[93,94,99–102] In summary, the substituents prefer to occupy a *pseudo*-equatorial orientation to minimize steric interactions with its neighbors when the substituent is an electropositive/neutral group, such as carbon-substituent. When a substituent has an electronegative element bound to the cyclic oxocarbenium ion, which is the case for all carbohydrates, the preference for the orientation of the substituents at C-3 (for furanosides) and C-3 and C-4 (for pyranosides) changes dramatically. By placing them in a *pseudo*-axial orientation the oxygen (or another electronegative element) is brought closer in space to the oxocarbenium ion. In effect, this constellation has a more favorable dipole direction of the C–O bond and electrostatic stabilization from the lone electron pairs on oxygen towards the anomeric center. The preference for a *pseudo*-equatorial orientation of C-2 is enhanced by an electronegative substituent. The decisive effect at play here is the hyperconjugative stabilisation of the *pseudo*-axially orientated C–H or C–C bond, overlapping its σ-orbital with the p- or π^*-orbital of the oxocarbenium ion (a σ-bond of a carbon and an electronegative element is generally a very poor hyperconjugative σ-bond donor). For the C-4 position in furanosides and C-5 in pyranosides, steric and electronic effects strongly oppose each other and the rotation around the C-4–C-5 or C-5–C-6 bond also plays an important role. In general, most stabilization can be effected in the geometry that places the lone pairs on O-6 closest to the oxocarbenium ion anomeric carbon atom (*i.e.* the *gg*-rotamer, see Figure 1B).

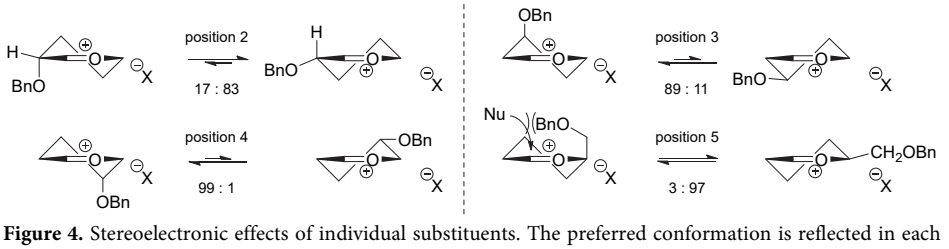


Figure 4. Stereoelectronic effects of individual substituents. The preferred conformation is reflected in each case by the isolated product ratios (given below the equilibrium arrows) of glycosylation with allyltrimethylsilane, based on the inside-attack model.

With this set of preferences Woerpel and co-workers have formulated qualitative selectivity rules, and substantial experimental evidence has corroborated these (Figure 4). In some cases, an axial-rich half-chair conformation may have interfering 1,3-diaxial interactions with the incoming nucleophile, especially with the C-5 position (See Figure 4) and when C-3 has a methyl substituent.[93,100,103] The validity of the two-conformer

model can be called into question when other conformations start to become relevant, including skew-boat and twist structures. A quantitative approach based on Density Functional Theory, predicts the favorable geometries of an oxocarbenium ion based on their relative energies, and their thermodynamic distribution can dictate the stereoselectivity behind the reaction.[104–106] The contribution of unusual conformations and their selectivity are difficult to estimate and quantum mechanical calculations from these structures have yet to give a decisive answer. Ultimately, the energy difference of the transition states leading to the different products and their pre-equilibria in a Curtin-Hammett type scenario are the deciding factors in the reaction outcome.[22,107]

Conclusions

The glycosylation reaction is not just a simple substitution reaction proceeding with either an S_N2 or S_N1 reaction profile. The buildup of positive charge at the anomeric center, a secondary carbon atom, can be sustained by the lone pairs of the ring oxygen atom, but is inductively destabilized by the oxygen ring-substituents. Overall, the intricate balance of stabilizing and destabilizing stereoelectronic effects in the system determines how well the positive charge can be accommodated during a glycosylation reaction. Depending on the nucleophilicity of the acceptor, stronger or weaker electrophilic species may be required for an effective glycosylation. Currently it is impossible to predict, up front, where on the S_N2-S_N1 reaction continuum a glycosylation will take place and deeper insight into the factors that decide this position (reactivity of the activated donor, reactivity of the acceptor, role of the solvent) are dearly needed.

Outline of this thesis

In this thesis several approaches have been undertaken to systematically investigate the glycosylation mechanism. The main focus of the content described here is the origin of the stereoselectivity observed in glycosylation reactions and the constructions of models with a qualitative predictive value. Both reaction partners, the donor and acceptor, are systematically studied. **Chapter 2** provides an overview of the current ideas and findings regarding the reactivity of the acceptor nucleophile. Although many isolated cases have been reported on the influence of the acceptor on the outcome of a glycosylation reaction, a focused study on how to exploit acceptor reactivity has not before been reported. **Chapter 3** introduces a set of fluorinated ethanol-based nucleophiles to serve as model acceptor of gradually decreasing reactivity in a set of well-established model

glycosylation reactions. With the use of this model set it is shown how the selectivity of glycosylations of three types of glycosyl donors changes upon changing acceptor nucleophilicity, as a consequence of a change in reaction mechanism. **Chapter 4** expands on Chapter 3 with a focus on how the stereoselectivitiy of glucosazide-based donors changes depending on acceptor nucleophilicity. Both the reactivity of the donor and of the acceptor have impact on the outcome of the glycosylation reaction selectivity. Whereas the donors in Chapter 4 all had a 4,6-tethering group, in **Chapter 5** a glucosazide with a 3,4-tethering group (a butane diacetal, BDA) is investigated. Although the conformational restraint imposed by the 3,4- and 4,6-tethering protecting groups is similar, it is shown that the different torsional and electronic effects of the groups have a major effect on the glycosylation results. **Chapter 6** provides a systematic approach to establish a first set of relative reactivities for carbohydrate acceptors. Two donors from Chapters 3 and 4 are used as model donors because the stereoselectivity of glycosylations of these donors was shown to strongly correlate with the reactivity of the acceptor nucleophiles. A broad and systematic set of C-4–OH acceptors, varying in benzyl and benzoyl protecting groups, as well as the nature of the C-6 functionality are examined and structure-reactivity-stereoselectivity relationships are established. **Chapter 7** describes the syntheses, of the complete set of diastereoisomeric *ribo*-, *arabino*-, *xylo*- and *lyxo*furanoside donors, modified at the C-2 and C-5 position. These are used in **Chapter 8**, to establish the effect the substituents (C-2–N_3, C-2–F, C-5–CO_2Me) have on the stereochemical outcome of the glycosylations of these donors. The putative oxocarbenium ion intermediates are studied by DFT calculations. **Chapter 9** provides a concise summary of the results of this thesis, as well as an outlook for extended investigations and new paths to take to unravel the details of the glycosylation mechanism.

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Chapter 2

Acceptor reactivity in glycosylations

Introduction

The chemical glycosylation reaction involving the union of two species to form a new glycosidic bond is dependent on a large set of variables.[1–3] The previous chapter introduced the basic concepts of reactivity and selectivity in glycosylation reactions, primarily from the perspective of the glycosyl donor. As amply illustrated by the vast amount of chemical carbohydrate literature, the donor is the reactant to which most of the attention has been directed and it is now well appreciated how the reactivity depends on the substitution pattern of the glycoside and how donor reactivity affects the outcome of a glycosylation reaction. The reactivity of the acceptor, on the other hand, is less well studied and detailed knowledge of this reaction partner may provide new mechanistic understanding and practical guidelines for glycosylation reactions. Although it was stated by Paulsen in 1982 that the nature of the acceptor is mostly *a priori* determined, differences in reactivity can influence the glycosylation outcome both in terms of stereoselectivity and isolated yield.[4] Not many studies directed at understanding and

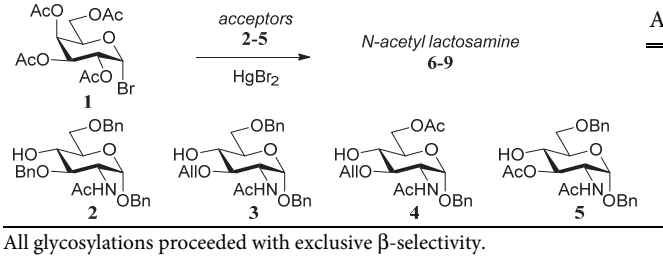
harnessing acceptor reactivity have been reported and, notwithstanding the systematic studies that have been reported and that will be described in this Chapter, the influence of the acceptor on the outcome of a glycosylation reaction is often neglected.

Numerous examples of glycosylation reactions indicate that the reactivity of the acceptor, like that of glycosyl donors, can be manipulated by changing protecting groups.[5–15] Unfortunately, most studies that report on new glycosylation methods, strategies or mechanisms, employ a rather variable set of acceptors, often chosen because of ease of availability, or used because a target oriented approach is taken. As a result the acceptors used in these studies differ greatly in steric and electronic properties, making it difficult to establish structure-reactivity relationships.[16–21] Unexpected stereoselectivities and/or poor yields, as a result of ill understood acceptor reactivity, continue to be reported,[22–26] clearly indicating the need for more systematic and deeper insight into how glycosylations are influenced by the reactivity of the glycosyl acceptor. At a time when the mechanism of glycosylation and the reactivity of the donor is understood better than ever before, the details of the mechanism and the influence of the acceptor therein will be an important pursuit to arrive at a more complete and generalized picture of glycosylation reactions.[27] This Chapter surveys the systematic approaches that have been undertaken to probe the influence of the reactivity of the acceptor on the outcome of a glycosylation reaction and describes methods to analyze and quantify acceptor reactivity.

Observations on acceptor reactivity

In two early examples by Sinaÿ in 1978[28] and Paulsen in 1981,[29] the influence of the acceptor on the glycosylation outcome was recognized. The work of Sinaÿ clearly showed how the yield of glycosylations of galactosyl bromide **1** (Table 1) varied upon changing the protecting groups on the acceptor. *N*-acetyl-glucosamine acceptors **2-5**, with an *O*-benzyl (**2**) or *O*-allyl (**3**, **4**) group at C-3 gave good yields, regardless of the nature of

Table 1. Acceptor protecting groups influencing glycosylation yield. (Sinaÿ, 1978).



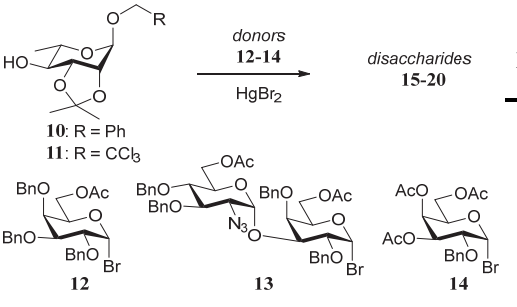
Acceptor	Product	Yield (%)
2	**6**	87
3	**7**	77
4	**8**	78
5	**9**	5

All glycosylations proceeded with exclusive β-selectivity.

the protecting group at C-6 (*O*-benzyl or *O*-acetyl). In contrast, the yield dropped to a mere 5% when the acceptor bearing an *O*-acetyl at the C-3 (**4**) was used.

Paulsen and Lockhoff examined a set of donors (**12-14**, Table 2) with two very similar rhamnosyl acceptors, differing only in the anomeric protection (*O*-benzyl in **10** *vs O*-trichloroethyl in **11**). In this set of experiments both the influence of the reactivity of the donor (**12**>**13**>**14**) and acceptor (**10**>**11**) was evident. The trichloroethyl protected rhamnosyl acceptor **11** provided relatively more of the α-linked products than the benzyl protected analogue **10**, which could be correlated to the lower reactivity of acceptor **11**. The more nucleophilic **10** can displace the α-bromide of 'armed' donor **12** to provide the β-product. Lowering the reactivity of either the donor or the acceptor hampers this direct substitution pathway and the less reactive acceptor can only substitute the more reactive β-bromide, formed by *in situ* anomerization with $HgBr_2$, giving the α-galactosyl linkage.

Table 2. Decrease in acceptor reactivity leads to increase in α-selectivity. (Paulsen and Lockhoff, 1981).

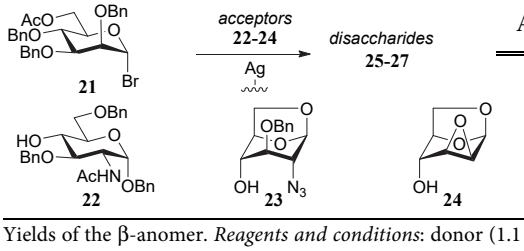


	Acceptor **10**		Acceptor **11**	
Donor	Product	α : β (yield)	Product	α : β (yield)
12	**15**	19 : 81 (75%)	**18**	81 : 19 (82%)
13	**16**	34 : 66 (66%)	**19**	100 : 0 (54%)
14	**17**	100 : 0 (81%)	**20**	100 : 0 (87%)

Yields of combined isolated anomers. *Reagents and conditions*: donor (1 eq.), acceptor (1 eq.), powdered 4Å M.S., $HgBr_2$ (0.1 eq.), DCM, room temperature (**20**), 0°C (**17**), or -20°C (**15**, **16**, **18**, **19**).

In another example by Paulsen and Lebuhn the silver-silicate promoted glycosylation of mannosyl bromide **21** with different glucose and glucosamine acceptors was investigated (Table 3). While the conformationally locked glucosamine acceptor **23**

Table 3. Conformationally restricted acceptors provide more β-product. (Paulsen and Lebuhn, 1983).



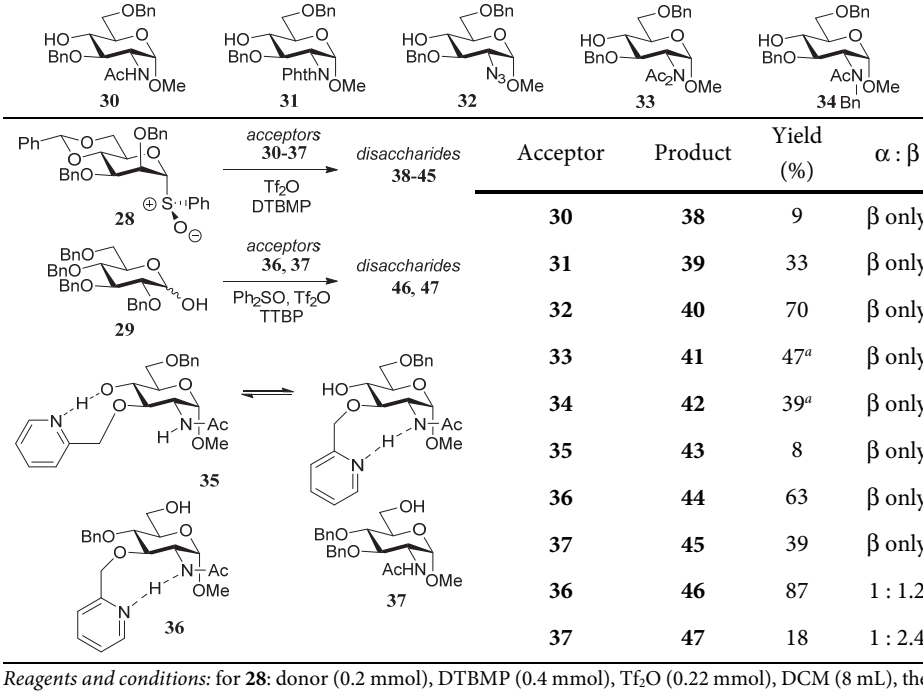
Acceptor	Product	Yield (%)	α : β
22	**25**	75	α only
23	**26**	65	1 : 6
24	**27**	63	1 : 5.5

Yields of the β-anomer. *Reagents and conditions*: donor (1.1 eq.), acceptor (1 eq.), powdered 4Å M.S., silver-silicate, DCM, room temperature (or 35°C for **25**).

and glucose acceptor **24** proved efficient acceptors for the synthesis of 1,2-*cis*-linked disaccharides **26** and **27**, likely formed through an S_N2-type displacement of the activated bromide, the use of *N*-acetyl glucosamine **22** only gave the undesired α-product.[30]

Over the years it has become clear that *N*-acetylglucosamine C-4–OH acceptors are generally very poor nucleophiles.[4] In a detailed study by Crich and co-workers, several glucosamine acceptors (**30**-**34**, Table 4) were used to investigate the underlying reasons why *N*-acetylglucosamine acceptors behave so poorly in glycosylation reactions.[31] Glucosamine acceptors bearing various *N*-protecting groups were investigated (acetyl **30**, phthalimide **31**, azide **32**, and imides **33** and **34**). Glycosylations of these acceptors with mannosyl sulfoxide **28** are reported in Table 4 and the results showed the azide to be far superior to the imides, which in turn are superior to amide **30** in terms of isolated yield. Competition experiments of **30**, **31**, and **32** by glycosylating a mixture of an equimolar amount of all three acceptors and analyzing the product mixture

Table 4. Intermolecular hydrogen-bonding is detrimental to acceptor reactivity. (Crich and Dudkin, 2001).



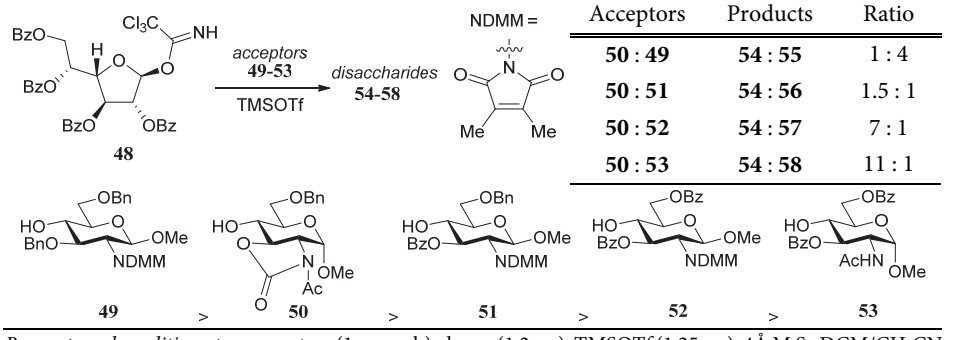
Acceptor	Product	Yield (%)	α : β
30	**38**	9	β only
31	**39**	33	β only
32	**40**	70	β only
33	**41**	47[a]	β only
34	**42**	39[a]	β only
35	**43**	8	β only
36	**44**	63	β only
37	**45**	39	β only
36	**46**	87	1 : 1.2
37	**47**	18	1 : 2.4

Reagents and conditions: for **28**: donor (0.2 mmol), DTBMP (0.4 mmol), Tf_2O (0.22 mmol), DCM (8 mL), then acceptor (0.4 mmol, 2 mL DCM), -78°C to 0°C; for **29**: donor (0.1 mmol), Ph_2SO (0.28 mmol) Tf_2O (0.15 mmol), toluene/DCM (3/1, 1 mL), -78°C to -40°C then TTBP (0.5 mmol, 0.5 mL DCM), acceptor (0.1 mmol, 1 mL DCM), -78°C to room temperature.

by HPLC, revealed a ratio of 1:3:10 (**30**:**31**:**32**) supporting the results of the individual glycosylations. An intermolecular hydrogen-bonding network from the amide (NH and C=O) was hypothesized to be at the basis of the poor reactivity of **30** and to support this, picolyl protected **35** and **36** were prepared to disrupt this network by favoring intramolecular hydrogen-bonding. Glycosylation with C-4–OH acceptor **35** was as ineffective as with benzylated acceptor **30**. To account for this result the hydrogen-bond interaction between C-4–OH and the picolyl-*N* was forwarded as destructive for the acceptor reactivity, instead of making the acceptor more reactive. The C-6–OH derivatives **36** and **37** in comparison gave the anticipated result. Intramolecular hydrogen-bonding between the picolyl and amide provided a more reactive acceptor, leading to a higher yield in the glycosylation reaction with **36**, with respect to the coupling of C-3–*O*-benzyl acceptor **37** which is incapable of forming an intramolecular hydrogen-bond. The use of glucose donor **29**, activated under dehydrative conditions, corroborated these findings, and a good yield was obtained in the condensation with acceptor **36** while the coupling of **29** and acceptor **37** proceeded with poor yield. Cyclic carbamates have also been used as a protecting group to provide appropriate glucosamine C-4–OH acceptors. The cyclic nature of the 2-*N*-3-*O*-carbamate ties back the group at C-3, rendering the C-4–OH more accessible.[32–34]

Rúveda and co-workers investigated the relative reactivities of a series of dimethylmaleimide (DMM) protected glucosamine acceptors (**49**, **51**, and **52**, Table 5) by competition experiments.[35] The reactivity of these nucleophiles was compared to that of *N*-acetyl glucosamine acceptor **53** and cyclic carbamate **50**. From these results it

Table 5. Acceptor competitions revealed the effect of protecting groups on the reaction rates. (Rúveda, 2006).



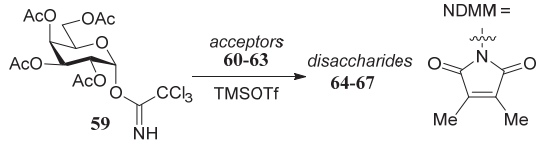
Acceptors	Products	Ratio
50 : **49**	**54** : **55**	1 : 4
50 : **51**	**54** : **56**	1.5 : 1
50 : **52**	**54** : **57**	7 : 1
50 : **53**	**54** : **58**	11 : 1

Reagents and conditions: two acceptors (1 eq. each), donor (1.2 eq.), TMSOTf (1.25 eq.), 4Å M.S., DCM/CH_3CN (29/1, 0.34 M), -30°C.

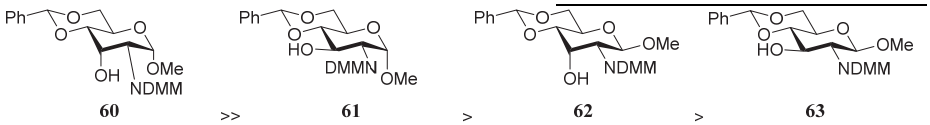
becomes clear that benzoyl groups in the acceptor have a retarding effect on the glycosylation rate, as **49** proved to be the most reactive acceptor, followed by **51** and finally **52**. Also in this study the poor reactivity of *N*-actyl glucosamine **53** is apparent.

Another set of competition experiments, comparing benzylidene allosamine and glucosamine acceptors with the DMM *N*-protecting group, was conducted by the same research group (Table 6).[36] Allosamine **60** by far outcompeted its epimeric acceptors **61** and **62**. These results show that axially orientated hydroxyl groups, as in **60** (C-3–OH), although sterically more encumbered, are not always less reactive than their equatorial counterparts.[37] In this particular series, the relative reactivity results were supported by NMR and computational studies on the possibility of hydrogen-bond formation between the C-3–OH and the maleimide C=O.

Table 6. Acceptor competitions revealed the effect of protecting groups on the reaction rates. (Rúveda, 2011).



Acceptors	Products	Ratio
60 : **61**	**64** : **65**	10 : 1
60 : **62**	**64** : **66**	13 : 1
61 : **62**	**65** : **66**	2 : 1
61 : **63**	**65** : **67**	5 : 1
62 : **63**	**66** : **67**	3 : 1

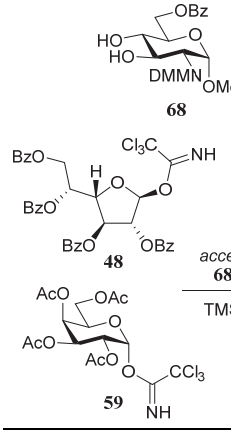


Reagents and conditions: two acceptors (1 eq. each), donor (1.1 eq.), TMSOTf (0.28 eq.), 4Å M.S., DCM, -25°C.

The influence of the C-6 protecting group on the regioselectivity of DMM protected glucosamine acceptors **68**-**70** when glycosylated with donors **48** and **57** was investigated by the group of Rúveda (Table 7).[38] The regioselectivity for the C-3-OH over the C-4–OH increased in the order of C-6–OBz > C-6–OTBDPS > C-6–OBn. The C-6–OBz in **68** makes the C-4–OH more electron poor than the C-3–OH, leading to the strong preference to glycosylate the latter alcohol (C-3/C-4, 1:0 for **48**, and 2:1 for **67**). The bulky TBDPS sterically hampers the nucleophilic attack of the C-4–OH, leading to improved C-3/C-4-regioselectivity with respect to the C-6–OBn (compare 5:1 for **70** and 3.2:1 for **69**, with donor **48**). Notably, the β-anomeric acceptors showed different regioselectivities (see also Table 16), which was again attributed to the difference in hydrogen-bonding capacity of the DMM group with the C-3-OH in the different

anomers.[39,40] The conformational change at the reducing end of an acceptor in a monosaccharide, disaccharide or oligosaccharide, has been reported to influence reactivity of the nucleophilic hydroxyl on the other side of the acceptor.[41–43]

Table 7. Stereoelectronic effects of protecting groups influence the regioselectivity of diols. (Rúveda, 2007).

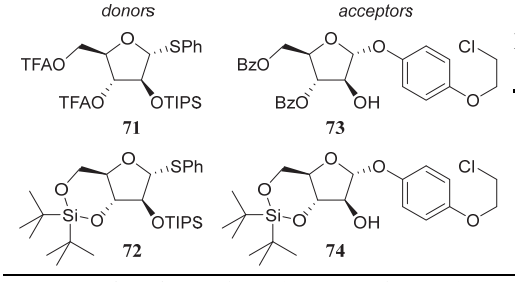


Donor	Acceptor	Yield (%)	(1→3) : (1→4)
48	**68**	68	1 : 0
48	**69**	71	3.2 : 1
48	**70**	73	5 : 1
59	**68**	91	2 : 1
59	**69**	56	1 : 1
59	**70**	50	1.6 : 1

Reagents and conditions: donor (0.11 mmol, 1.1 eq.), acceptor (0.1 mmol, 1 eq.), 4Å M.S., TMSOTf (0.21 mmol, 2.1 eq.), DCM/CH_3CN (37/1), -25°C.

The group of Konovov investigated the difference in reaction rates by observing differences in the activation temperature of the reaction (Table 8).[44] Two donors of varying reactivity (**71** and **72**) were glycosylated with acceptor **73**, bearing two electron-withdrawing benzoyl groups, and with acceptor **74** having the cyclic silylidene protecting group. The activation temperature varied from -42°C to -22°C following the order of reactivity of both the donor and acceptor.

Table 8. The impact of acceptor reactivity on the temperature of activation. (Kononov, 2014).

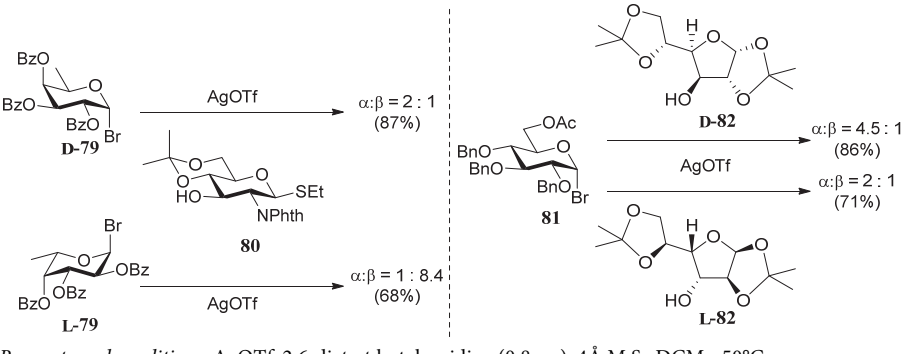


Donor	Acceptor	Product	T_{act} (°C)	Yield (%)	α : β
71	**73**	**75**	-22	66	1 : 2
71	**74**	**76**	-30	84	1 : 6.3
72	**73**	**77**	-39	92	1 : 4.5
72	**74**	**78**	-42	80	1 : 3

Reagents and conditions: donor (0.042 mmol, 1.5 eq.), acceptor (0.028 mmol, 1 eq.), powdered 4Å M.S., NIS (0.042 mmol, 1.5 eq.), AgOTf (0.003 mmol, 0.1 eq.), DCM (1 mL), -78°C to T_{act}, then to +10°C.

In the early 90's Spijker and van Boeckel were the first to introduce the concept of double stereodifferentation[45] in synthetic carbohydrate chemistry.[46] They unambiguously showed how the chirality of the coupling partners could impact the transition state of the glycosylation reaction. Carbohydrates experience different steric effects when coupled to different enantiomers of the same reaction partner. In their 1991 publication, two situations are highlighted (Scheme 1). Either two enantiomeric donors (D-fucosyl bromide **D-79** and L-fucosyl bromide **L-79**) were coupled to the same D-glucosamine acceptor **80**, or the absolute chirality of the acceptor was changed from D-diacetoneglucose **D-82** to its L-enantiomer **L-82** while keeping the donor the same (D-glucosyl bromide **81**). Remarkable results were obtained. While neighboring group participation to provide 1,2-*trans*-glycosides is generally a very powerful stereocontrolling phenomenon, the glycosylation of donor **D-79** and acceptor **80** provided an anomeric mixture (α:β, 2:1). The use of the enantiomeric donor **L-79** restored the expected *trans*-selectivtity (α:β, 1:8.4). The difference in α:β product ratio is less pronounced in the second case, in which acceptor **D-82** provides more α-product than its enantiomer **L-82**. The observed changes in stereoselectivity are clearly the result of drastically different steric interactions in the diastereoisomeric transition states.

Scheme 1. Double stereodifferentation in glycosylation reactions. (Spijker and van Boeckel, 1991).

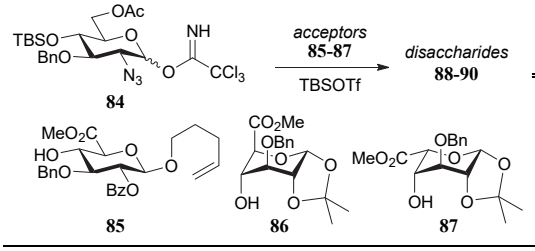


Reagents and conditions: AgOTf, 2,6-di-*tert*-butylpyridine (0.8 eq.), 4Å M.S., DCM, -50°C.

Another clear manifestation of the effect of the shape of the acceptor on the outcome of a glycosylation reaction can be observed when carbohydrate acceptors are locked in 'inverted' chair conformations. As was shown above, conformationally locking a glucose/glucosamine acceptor in a $^1C_4$ chair places the C-4–OH in a position that is well accessible leading to a better nucleophile.[30,47] It is well established in the field of heparin synthesis that glycosylations of glucosazide donors with L-idose/L-iduronic acid acceptors, generally adopting a $^1C_4$ chair conformation, proceed with excellent α-

selectivity (an important manifestation of double stereodifferentiation).[48,49] Based on this knowledge Seeberger and co-workers decided to lock D-glucuronic acid ester acceptors for heparin synthesis in a similar $^1C_4$ chair conformation (Table 9).[50,] In condensations with glucosazide donor **84** D-glucuronic acid acceptor **85** provided an anomeric mixture (**88**; α:β, 3:1) in relatively low yield. By conformationally locking the glucuronate acceptor in the inverted $^1C_4$ conformation (as in **86**), a high yield and excellent α-selectivity was obtained in the condensation with **84**. The use of L-iduronic acid acceptor **87** provided an analogous result.

Table 9. Conformational restriction leads to higher yields and α-selectivities. (Seeberger, 2002).

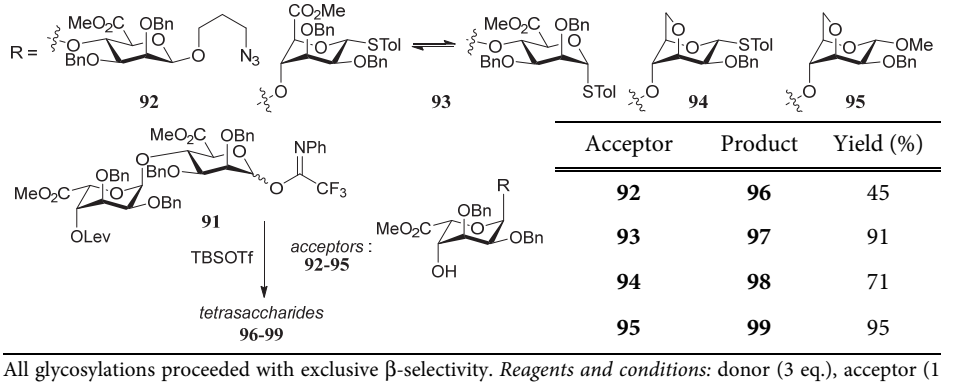


Acceptor	Product	Yield (%)	α : β
85	**88**	57	3 : 1
86	**89**	86	α only
87	**90**	91	α only

Reagents and conditions: donor (1.25 eq.), acceptor (1 eq.), TBSOTf (0.125 eq.), 4Å M.S., DCM, -78°C to room temperature, 2.5 h.

A rigid conformational lock is not always necessary to mold an acceptor in a reactive conformation, as was described by Zhang *et al.* (Table 10).[51] They showed that the conformational rigidity of disaccharide acceptor **92** hampered the glycosylation with donor **91**. Changing the reducing end of the disaccharide acceptor from a β-*O*-(azidopropyl) mannuronic acid to an α-*S*-tolyl manuronic acid (**93**), provided a more

Table 10. Conformational flexibility of acceptor **161** dramatically increased glycosylation yield. (Codée, 2015).



Acceptor	Product	Yield (%)
92	**96**	45
93	**97**	91
94	**98**	71
95	**99**	95

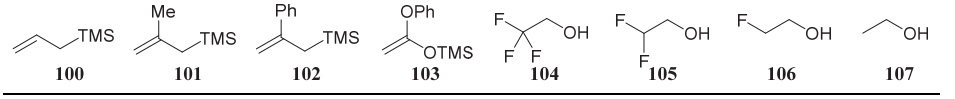
All glycosylations proceeded with exclusive β-selectivity. *Reagents and conditions:* donor (3 eq.), acceptor (1 eq.), TBSOTf (0.6 eq.), 4Å M.S., DCM, -78°C to -45°C.

flexible acceptor, as judged from the broadened resonances observed in NMR-spectroscopy. The flexible character of acceptor **93** led to greatly enhanced glycosylation productivity. The contribution of the $^1C_4$ structure in the conformational equilibrium of **93** was verified by the use of model disaccharide acceptors having a conformationally locked $^1C_4$ reducing end saccharide (either an α-*O*-methyl (**94**) or an α-*S*-tolyl (**95**)).

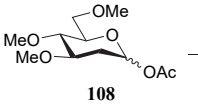
Systematic studies on acceptor reactivity

Although it is clear that the nature of the protecting groups has an influence on the glycosylation outcome it is often difficult to dissect electronic, steric and conformational effects.[52] Woerpel and co-workers have reported a systematic study relating the effect of the nucleophilicity of the acceptor on the outcome of a glycosylation reaction, using both *C*- and *O*-model nucleophiles.[53–57] Table 11 reports the results of both sets of nucleophiles, with 2-deoxyglucosyl acetate or ethanethiolate donors **108** and **109**. The trend that becomes apparent from these results is that poorer nucleophiles provide more α-product. To account for these results, it was reasoned that the poorest *C*- and *O*-nucleophiles **100** and **104**, as assessed by Mayr's nucleophilicity parameter *N*,[58–63] or the field inductive parameter *F*,[64] react with the glucosyl oxocarbenium ion that

Table 11. Model *C*- and *O*-nucleophilic acceptors in glycosylations correlating nucleophilicity to stereoselectivity. (Woerpel, 2008-2010).



100 **101** **102** **103** **104** **105** **106** **107**

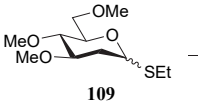


108

acceptors **93-96** → *products* **110-113**

$BF_3{\cdot}OEt_2$

Acceptor	N^a	Product	Yield (%)	α : β
100	1.8	**110**	80	89 : 11
101	4.4	**111**	79	43 : 57
102	6.2	**112**	83	61 : 39
103	8.2	**113**	83	45 : 55

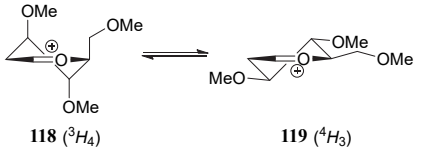


109

acceptors **97-100** → *products* **114-117**

NIS

Acceptor	F^b	Product	Yield (%)	α : β
104	0.38	**114**	80	83 : 17
105	0.29	**115**	78	67 : 33
106	0.15	**116**	69	56 : 44
107	0.0	**117**	82	51 : 49



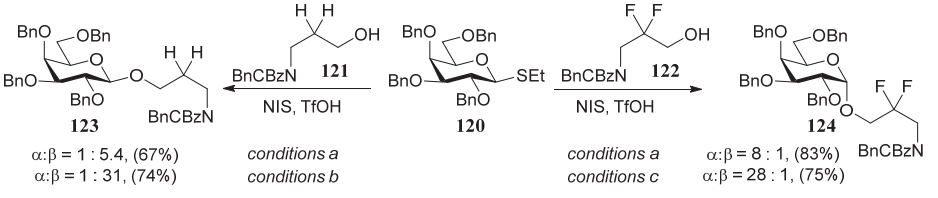
118 ($^3H_4$) **119** ($^4H_3$)

[a]Mayr's nucleophilicity parameter. [b]Field inductive parameter.[61] *Reagents and conditions for acetyl donors*: donor (1 eq.), acceptor (4 eq.), BF_3OEt_2 (1.5 eq.), DCM, -42°C to 0°C. *Reagents and conditions for thiodonors*: donor (1 eq.), acceptor (4 eq.), NIS (2 eq.), CH_3CN, 0°C.

preferentially takes up a $^4H_3$ conformation (**119**), in a stereoselective manner from the α-face. The selectivity is reduced when the nucleophilicity is increased. This erosion of stereoselectivity (from **110** to **113**, and from **114** to **117**) is caused by alternative reaction pathways becoming accessible for the stronger nucleophiles: either a non-selective S_N1 reaction in which both sides of oxocarbenium ion **119** are attacked, or an S_N2-type substitution.

In line with the results of Woerpel, a glycosylation study of linkers **121** and **122** with donor **120** by the group of Seeberger, found the more nucleophilic **121** to give high β-selectivity whereas the weaker nucleophile **122** gave mainly the α-product (Scheme 2).[65] These results can be explained by an S_N2-type substitution of the reactive primary alcohol on the intermediately formed anomeric α-triflate, where attack of the weaker difluoro acceptor requires a more reactive electrophile, either an intermediate oxocarbenium ion or the corresponding β-triflate. By tweaking the reaction temperature and solvent, nearly complete α-stereoselectivity could be obtained. A variety of different donors provided a similar reactivity-stereoselectivity trend.

Scheme 2. Linkers of varying nucleophilicity gave opposite glycosylation stereoselectivity. (Seeberger, 2016).

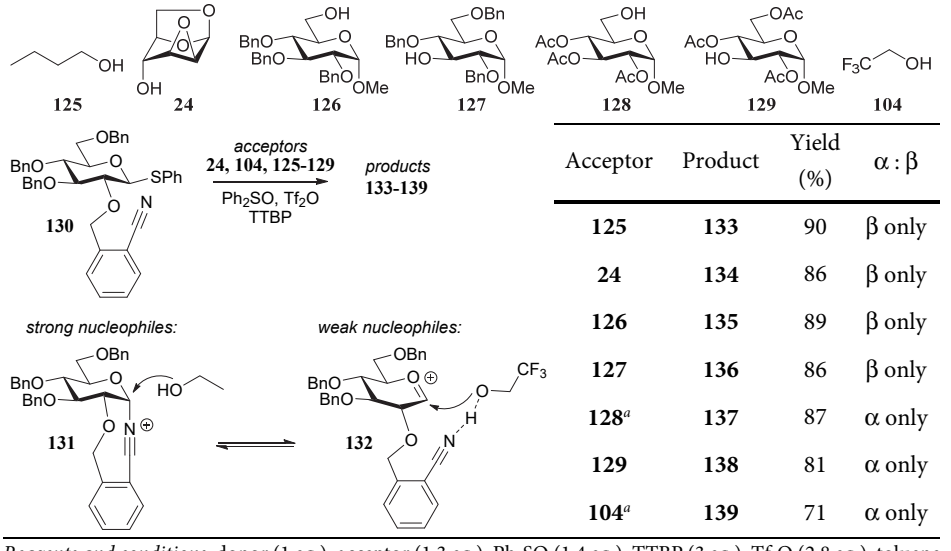


Reagents and conditions: donor (1.5 eq.), acceptor (1 eq.), NIS (1.5 eq.), TfOH (0.2 eq.); a) DCM, -20°C; b) CH_3CN -40°C; c) toluene/dioxane (3/1), room temperature.

Le Mai Hoang and Liu introduced donors equipped with a 2-cyanobenzyl group at the C-2-OH and they investigated these donors, using a preactivation glycosylation scheme, with a panel of acceptors (Table 12).[66] Next to the model acceptors *n*-butanol **125** and trifluoroethanol **104**, this study also included carbohydrate acceptors with benzyl and acetyl protection groups. It was observed that the stronger nucleophiles stereoselectively provided the β-linked product, while the use of weaker nucleophiles led to the generation of the α-linked products in a fully stereoselective manner.[67] The stronger nucleophiles **24**, **125-127** can partake in an S_N2-like substitution of the anomeric α-triflate, a closely related contact ion pair, or as suggested by the authors by a substitution of the intermediate α-nitrilium ion **131**, to provide selectively the β-product. The weaker, acetyl bearing acceptors **128** and **129** and trifluoroethanol **104** can be

directed by hydrogen-bonding with the cyano functionality on the C-2–*O*-protecting group to the α-face of the donor (as in **132**), as poorer nucleophiles are generally also stronger acids, forming hydrogen-bonds more readily. Alternatively, the weaker acceptors may also attack the oxocarbenium ion selectively on the α-diastereotopic face without coordination by the 2-cyanobenzyl group.

Table 12. Reactive acceptors give pure β-selectivity, weak acceptors pure α-selectivity. (Le Mai Hoang, 2014).

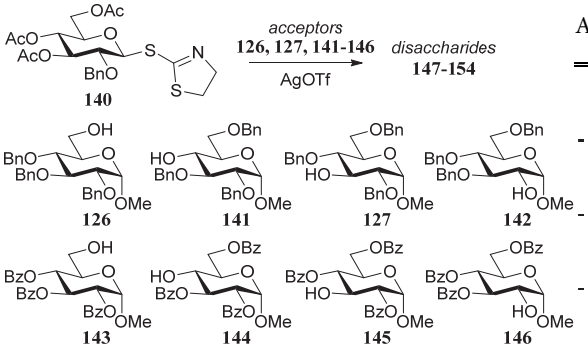


Acceptor	Product	Yield (%)	α : β
125	**133**	90	β only
24	**134**	86	β only
126	**135**	89	β only
127	**136**	86	β only
128[a]	**137**	87	α only
129	**138**	81	α only
104[a]	**139**	71	α only

Reagents and conditions: donor (1 eq.), acceptor (1.3 eq.), Ph_2SO (1.4 eq.), TTBP (3 eq.), Tf_2O (2.8 eq.), toluene -60°C. [a]Et_2O was used as solvent.

A systematic study by Demchenko revealed the effect of acyl *vs* alkyl protecting groups and the position of the free alcohol on the carbohydrate acceptors on the stereochemistry of glycosylations with STaz donor **140** (Table 13).[68] The acceptors studied, varied from tri-*O*-benzyl protected acceptors **126**, **127**, **141**, and **142** to tri-*O*-benzoyl protected acceptors **143**-**146**. While the yields of the silver triflate mediated reactions proved independent of acceptor reactivity, the stereoselectivity of the glycosylations involving the *O*-benzyl protected acceptors is generally lower than the selectivity for the same acceptors bearing *O*-benzoyl groups. The latter group consistently give higher α-selectivities. It was observed that the *O*-benzyl protected acceptors were converted faster to their respective products than their *O*-benzoyl protected counterparts.

Table 13. Differentially substituted glucose acceptors provide a trend in reaction times and stereoselectivity. (Demchenko, 2010).

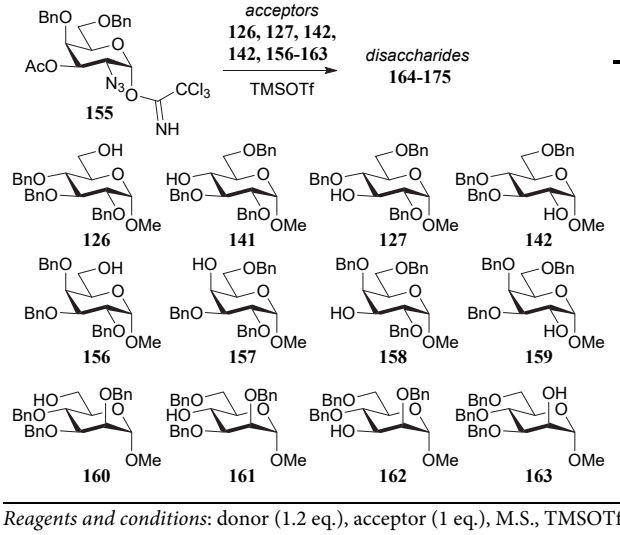


Acceptor	Product	Time (h)	Yield (%)	α : β
126	**147**	1.5	81	2.7 : 1
143	**148**	2	89	7.4 : 1
141	**149**	14	90	6.8 : 1
144	**150**	16	89	11.7 : 1
127	**151**	8	85	6.5 : 1
145	**152**	12	87	12.1 : 1
142	**153**	6	87	9.3 : 1
146	**154**	12	72	12.0 : 1

Reagents and conditions: donor (0.11 mmol, 1.1 eq.), acceptor (0.10 mmol, 1 eq.), 3Å M.S., AgOTf (0.22 mmol, 2 eq.), 1,2-dichloroethane (2 mL), room temperature.

In an extension of the work of Demchenko, Kalikanda and Li investigated the effect of different configurations of the glycosyl acceptors. In one of the few systematic studies devoted to acceptor reactivity, they studied twelve tri-*O*-benzylated acceptors, having either a *gluco*-, *galacto*-, or *manno*-configuration in glycosylations with galactosazide donor **155** (Table 14).[69] Again, it becomes clear that the most reactive alcohols react in a β-selective manner, while the least reactive nucleophiles provide α-linked products. Although the exact mechanism of these glycosylations are not clear, the

Table 14. Systematic study of the impact of configuration of the acceptor reactivity. (Kalikanda and Li, 2011).



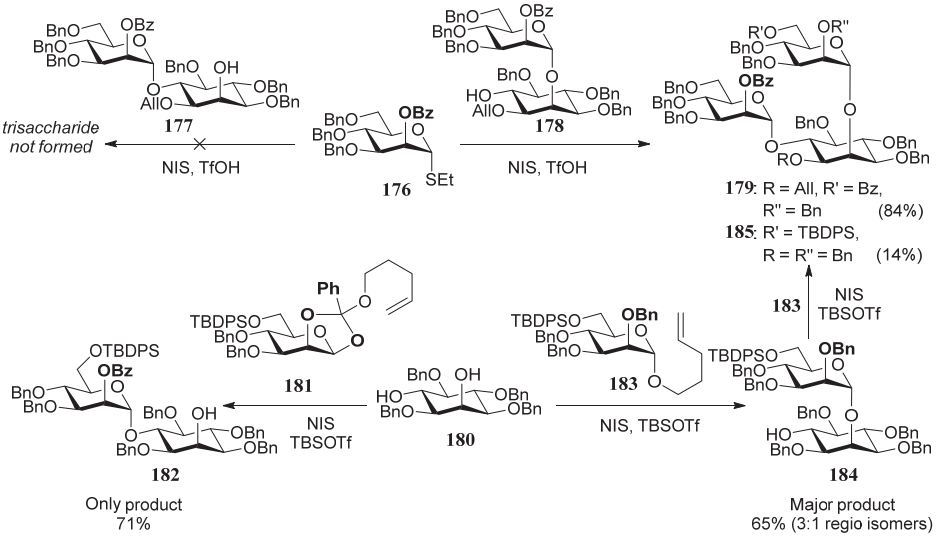
Acceptor	Product	Yield (%)	α : β
126	**164**	98	β only
141	**165**	56	1.8 : 1
127	**166**	53	1 : 3.4
142	**167**	68	α only
156	**168**	75	1 : 4
157	**169**	63	α only
158	**170**	65	3 : 1
159	**171**	90	1.3 : 1
160	**172**	90	1 : 10
161	**173**	81	1.2 : 1
162	**174**	82	1 : 4.7
163	**175**	93	α only

Reagents and conditions: donor (1.2 eq.), acceptor (1 eq.), M.S., TMSOTf (0.15 eq.), DCM (0.2 M), -78°C.

result show that in general, the primary alcohols are the most reactive and the secondary, axially orientated hydroxyls are the least reactive. Notably, the reactivity order, as assessed from the α/β-product ratio, in the glucose series matches those established in Demchenko's study described above.[68] However, the relative order of reactivity may strongly depend on the donor used and the steric interactions between donor and acceptor in the product forming transition state.

In fact, the relative reactivity of two alcohol nucleophiles can even be reversed depending on the donor system used and it has already been suggested by Paulsen that for an optimal glycosylaton outcome the reactivity of both reaction partners should be "matched".[70–73] This becomes apparent form the following striking examples. Scheme 3 shows an attempted synthesis by van Boom and co-workers of a mycobacterial phospholipid using mannosyl donor **176** and *myo*-inositol acceptor **177**.[74] Glycosylation of the C-2–OH of this acceptor proved ineffective, but the construction of the desired pseudo-trisaccharide **179** in a different order was successful. In the event, pseudo-disaccharide **178**, in which the mannosyl substituent had already been installed at the C-2–OH, could be effectively glycosylated at the inositol C-6–OH with mannosyl donor **176** to give product **179** in 84% yield.[75] Similar results were later reported by Fraser-Reid, who noted a distinct preference of donors **181** and **183** for different alcohols on diol **180**.

Scheme 3. Donor-acceptor match and mismatch, led to the formulation of reciprocal donor-acceptor selectivity. (van Boom, 1990, 1992; Fraser-Reid, 2000).



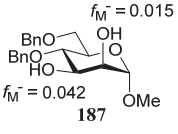
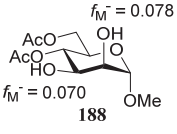
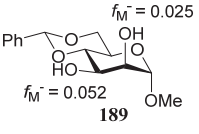
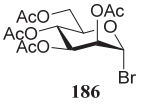
Reagents and conditions: van Boom: donor (1.1 eq.), acceptor (1 eq.), NIS (1.2 eq.), TfOH (0.24 eq.), DCE, -10°C. Fraser-Reid: donor (1.3 eq.), acceptor (1 eq.), NIS (1.3 eq.), TBSOTf (cat), DCM, room temperature.

The preference of the equatorial hydroxyl in structures **178**, **180**, and **184** to be glycosylated with a donor bearing a participating group (**176** or **181**) is evident from the results in Scheme 3. However, donor **183**, bearing a non-participating benzyl group preferentially glycosylates the axial hydroxyl.[76,77] From these observations Fraser-Reid developed the concept of reciprocal donor acceptor selectivity (RDAS), to classify reactions of diols that have different regioselective preferences towards different donors.[78–81] The RDAS concept still awaits a better mechanistic explanation but the counter-intuitive outcome of several more recent reactions have been interpreted with this phenomenon.[82–86]

Quantification of acceptor reactivity

Notwithstanding the progress that has been made in computational chemistry, only few attempts have been reported to investigate the nucleophilicity of glycosyl alcohol acceptors. The Fukui function, and its atom-condensed numerical indices provide a measure of change in electron density at the atom of interest when an electron is subtracted (or added). The Fukui indices have been reported as a measure for site selectivity of electrophilic (f^-) or nucleophilic (f^+) reactions. For the reaction of the OH-nucleophile on an electrophilic center, the index f^- can be computationally approached. Kalikanda and Li have computed Fukui f^--indices for a series of mannosyl diol acceptors (Table 15).[87] The higher value of the two computed for each diol system will indicate the regioselectivity of the reaction. Indeed, the diols **187** and **189** are completely

Table 15. Fukui values determined for mannosyl diol acceptors. (Kalikanda and Li, 2010).

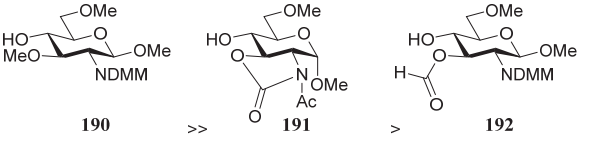
		 **187**	 **188**	 **189**
Entry	Electrophile	Ratio O3/O2	Ratio O3/O2	Ratio O3/O2
1	Ac_2O (+pyridine)	6: 1	3 : 2	1 : 0
2	 **186**	1 : 0	3 : 1	1 : 0

Thiophenyl and trichloroimidate donors also gave trisaccharide byproducts, the disaccharides were formed with the same selectivity regardless of the donor. Atom-condensed Fukui values f_m^- were based on Mulliken charges and were obtained by DFT (Q-CHEM 3.2, B3LYP/6-31+G*). *Reagents and conditions*: donor (1 eq.), acceptor (1 eq.), 3Å M.S., AgOTf (1 eq.), DCM, -30°C.

stereoselective in experimental glycosylations with donor **186** and with acetic anhydride. When the Fukui values are close to each other a loss in stereoselectivity is observed (as for **188**), the preference then found can be a result of the different steric requirements and hydrogen-bonding capabilities.[88]

The group of Rúveda and Stortz also employed Fukui functions, and discussed the chemical hardness/softness and atomic charges as indicators for the relative reactivity of a series of acceptors (**190**-**192**, Figure 1). They reached the conclusion that carbohydrate acceptors and donors are neither well described by hard-hard (atomic charges) interactions nor by soft-soft (Fukui functions) interactions.[35,39] The chemical softness (*s*) in these examples provided the best correlation with experimental results (see Table 5), with the lowest $s_{O\text{-}4}$ value in **190** corresponding to the most reactive acceptor (**49**).

Figure 1. Computation evaluation of relative acceptor reactivities. (Rúveda, 2006).

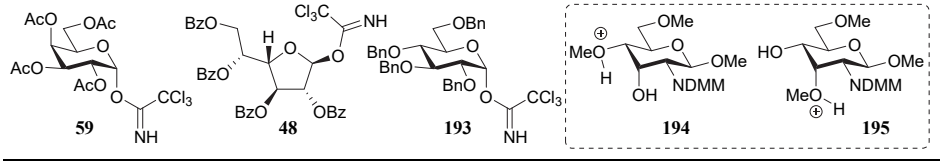


Atomic charge *q*, atom condensed Fukui value *f* and local chemical softness *s* are determined by multiple approaches, see the original publication for details.

In a different approach by the same group, the reactivity of the acceptors was assessed by calculation of the methylated regioisomeric acceptors (see examples **194** and **195**).[89] The charged structures served to mimic the glycosylation transition state and allow for the investigation of the influence of intramolecular hydrogen-bonding on the stability and geometry on the acceptor part.[90,91] Table 16 reports the experimental and computational results of a variety of diol acceptors (see also Table 7 above). Galactopyranose and -furanose donors **59** and **48** were glycosylated with glucosamine acceptors **68**, **69**, **198**, and **199**, and allosamine acceptors **196** and **197**. Experimentally, acceptors **196** and **197** gave exclusive condensation with donor **59** at the axial C-3 position rather than the equatorial C-4 position. The calculated energy difference between the isomeric cationic structures **194** and **195** and their respective α-anomers provided evidence in support of the regioselectivities observed. Applying the same technique to glucosamine acceptors **68**, **69**, **198**, and **199**, the calculated energy

differences again correlated well with the experimentally observed regioselectivity ratios, bar the glycosylation pair **59** and **198**. The computational gas-phase approach may be a shortcoming in this case, and the steric hindrance in the transition state with a carbohydrate donor will be significantly different. In benzylidene allose diols **200** and **201** the C-3-OH also proved to be the most reactive nucleophile, both experimentally and computationally. Questioning whether the computational method would allow the comparison of the reactivity of individual acceptors with a single free hydroxyl group, the authors compared the energies of formation (from the neutral hydroxyl acceptor and methyl cation) of structures **202** and **203**. The energy difference ΔΔE of 7.9 kcal·mol^{-1} between the two systems is in agreement with the observed reactivity difference (Table 6; **61**/**63**, 5:1). It appears that this relatively simple method is a promising way to estimate relative acceptor reactivities qualitatively when a higher level of theory, a larger set of acceptors, and an experimentally well-understood donor/activator system is used.

Table 16. Regioselectivity approach by glycosylations and computations. (Stortz, 2011).



Acceptor	O-3/O-4 Donor **59**	O-3/O-4 Donor **48**	O-3/O-4 Donor **193**	$E_{3\text{-O-Me}}-E_{4\text{-O-Me}}$ (kcal·mol^{-1})
196	1 : 0			-8.64
197	1 : 0			-6.93
68	2 : 1	1 : 0		-4.60
69	1 : 1	3.2 : 1		-1.85
198	1 : 13	1 : 1		-0.03
199	0 : 1	1 : 2.9		+2.15
200			2.6 : 1	-4.39
201			1.2 : 1	-2.25

Energies obtained by DFT (Jaguar 6.0, B3LYP/6-31+G**). *Reagents and conditions*: donor (1.1 eq.), acceptor (1 eq.), TMSOTf (2.1 eq.), 4Å M.S., DCM/CH_3CN (29/1, 0.34 M), -25°C.

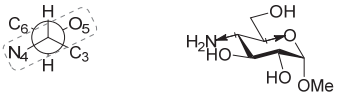
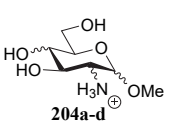


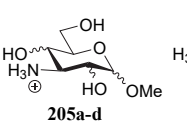
Figure 2. Anti-periplanar relationship between the ring oxygen and the C-4 substituent in methyl glucoside.

Bols and Inouye have taken a rather different approach to estimate the reactivity of different carbohydrate alcohols. They evaluated model systems in which specific hydroxyl groups were changed to amine functions.[92,93] The pK_as of their ammonium salts were determined by titration and the results are displayed in Table 17. The pK_a values indicate the 6-NH_2 group to be the most nucleophilic (towards H_3O^+). The order of reactivity in glucose found with aminoglycosides **204-207a/b**, C-6–NH_3^+ > C-3–NH_3^+ > C-2–NH_3^+ > C-4–NH_3^+, roughly corresponds with the nucleophilicity on the parent hexoses.[94–96] Using the pK_a data in Table 17, the authors established correlations between the effects of the neighboring substituent and the pK_a values of the ammonium group. It was pointed out that an anti-periplanar arrangement of the C-4–N and the C-5–O in **206a/b/d** (Figure 2), but also of C-2–N and C-1–O in **204a/b/d** led to a less basic NH_2 group.[97]

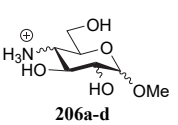
Table 17. pK_a values of aminosugars. (Inouye, 1968; Bols, 2011).



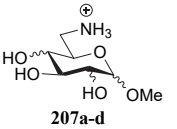
204a-d



205a-d



206a-d



207a-d

a = α-Glc
b = β-Glc
c = α-Gal
d = α-Man

Position	α-Glc	pK_a	β-Glc	pK_a	α-Gal	pK_a	α-Man	pK_a
2-NH_3^+	**204a**	7.5	**204b**	7.2	**204c**	7.9	**204d**	7.2
3-NH_3^+	**205a**	7.8	**205b**	7.6	**205c**	8.0	**205d**	8.1
4-NH_3^+	**206a**	6.8	**206b**	6.7	**206c**	7.3	**206d**	7.2
6-NH_3^+	**207a**	8.9	**207b**	8.6	**207c**	8.9	**207d**	9.0

Conclusions

The reactivity of a glycosyl acceptor is of fundamental importance to the outcome of a glycosylation reaction. The nucleophilicity of a carbohydrate alcohol is influenced by electronic aspects, through inductive effects and hydrogen-bonding, and by steric and conformational effects. The protecting groups on the acceptor play a pivotal role in shaping the acceptor reactivity. In contrast to the reactivity of glycosyl donors, for which Relative Reactivity Values have been established[98,99] to provide a numerical means to

compare their reactivity, the relative reactivity of glycosyl acceptors remains relatively poorly understood and no numerical scales are available to assess acceptor reactivity. The insightful competition experiments performed by Rúveda did provide relative acceptor reactivities based on kinetics but to be more generally useful should be significantly expanded.[38] It would also be of interest to see how relative acceptor values change with different donors. A systematic evaluation of different well established donor systems with the same set of acceptors may provide an accurate structure-reactivity-stereoselectivity map. Another approach would be to establish Kinetic Isotope Effects for donor-acceptor combinations or to perform cation-clock kinetics. Both methods have been used by the group of Crich, but only on the relatively nucleophilic and minimally intrusive *iso*-propanol.[100–104] An extention of these methods spanning a wider range of acceptors, such as the model acceptors introduced by Woerpel and the set used in Chapter 3 of this Thesis, will provide the much needed insight how the reactivity of the acceptors determines the position of the operational reaction mechanisms along the S_N2-S_N1-continuum.

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Chapter 3

The influence of acceptor nucleophilicity on the glycosylation reaction mechanism

Introduction

The connection of two carbohydrate building blocks to construct a glycosidic linkage in a glycosylation reaction is one of the most important and one of the most difficult steps in the assembly of an oligosaccharide.[1–3] The stereoselective formation of 1,2-*cis*-glycosidic linkages remains a major synthetic challenge and often requires careful tuning of reaction conditions for a profitable outcome.[4] The variation in stereochemical outcome of a chemical glycosylation reaction originates from the different mechanistic pathways that can be followed for the union of an activated donor glycoside and an acceptor. Figure 1 depicts the current understanding of the continuum of mechanisms operational during a glycosylation reaction. The activation of a donor glycoside leads to an array of reactive intermediates, formed from the donor glycoside and the activator derived counterion. α- and β-configured covalent reactive intermediates can be formed and these are in equilibrium with less stable and more reactive oxocarbenium ion based species. These can be either closely associated with the counterion providing close (or

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contact) ion pairs (CIPs), or further separated from their counterion in solvent separated ion pairs (SSIPs). These reactive intermediates can be attacked by an incoming nucleophile following a reaction mechanism with both S_N1 and S_N2 features. The covalent species are displaced in a reaction mechanism having an associative S_N2-character, while the oxocarbenium ion-like intermediates are engaged in an S_N1-like reaction. The exact position(s) on the continuum where a given glycosylation reaction

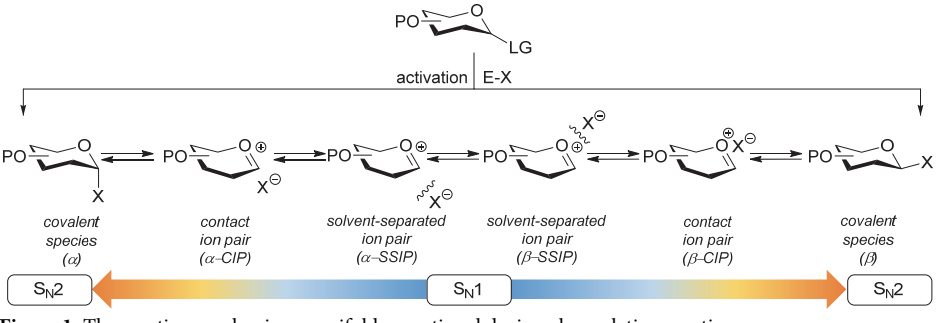


Figure 1. The reaction mechanism manifold operational during glycosylation reactions.

takes place, and hence the stereoselectivity of the process, depends critically on the reactivity of both reaction partners: the donor and the acceptor glycoside. The impact of the reactivity of the donor glycoside on the stereochemical outcome has been studied extensively, and the effect of functional and protecting groups on glycosyl donor reactivity is well documented.[5–10] In contrast, the influence of the reactivity of the nucleophile (the acceptor) on the outcome of a glycosylation reaction remains poorly understood.[11–18] This chapter presents a systematic study to determine the effect of acceptor nucleophilicity on the stereochemical course of a glycosylation reaction. It is shown how a simple "toolset" of partially fluorinated alcohols[13] can be used to dissect reaction mechanisms that are operational during a glycosylation reaction. It is revealed that the stereoselectivity of some glycosylation systems varies more with changing acceptor nucleophilicity than others, and these differences are related to changes in reaction pathways that are followed. A panel of model carbohydrate acceptors is scrutinized to place the reactivity of these building blocks in the context of the nucleophilicity scale set by the series of fluorinated ethanols.

Results and discussion

In this study the effect of acceptor nucleophilicity on the glycosylation selectivity is systematically investigated by the hand of a set of model *O*-nucleophiles, encompassing ethanol, monofluoroethanol (MFE), difluoroethanol (DFE), trifluoroethanol (TFE),

hexafluoro-*iso*-propanol (HFIP) and cyclohexanol, as well as a *C*-nucleophile, allyltrimethylsilane (allyl-TMS), and a deuterium nucleophile, deuterated triethylsilane (TES-*d*).[12,13] Next a series of carbohydrate acceptors is used to put the reactivity of these alcohols in the context of the reactivity of the ethanol model acceptors (See Figure 2B and C). Three glycosylation systems have been investigated with these acceptors: the benzylidene mannose and analogous benzylidene glucose system as well as the mannuronic acid system (See Figure 2A). These systems have been selected because they have previously been studied in depth to provide insight into the major reaction pathways that operate during glycosylation reactions of these donors (*vide infra*). Although these three glycosylation systems all selectively provide 1,2-*cis*-products, the major product-forming pathways significantly differ.

The benzylidene mannose system, introduced by Crich and co-workers for the stereoselective construction of β-mannosidic linkages, represents the best studied

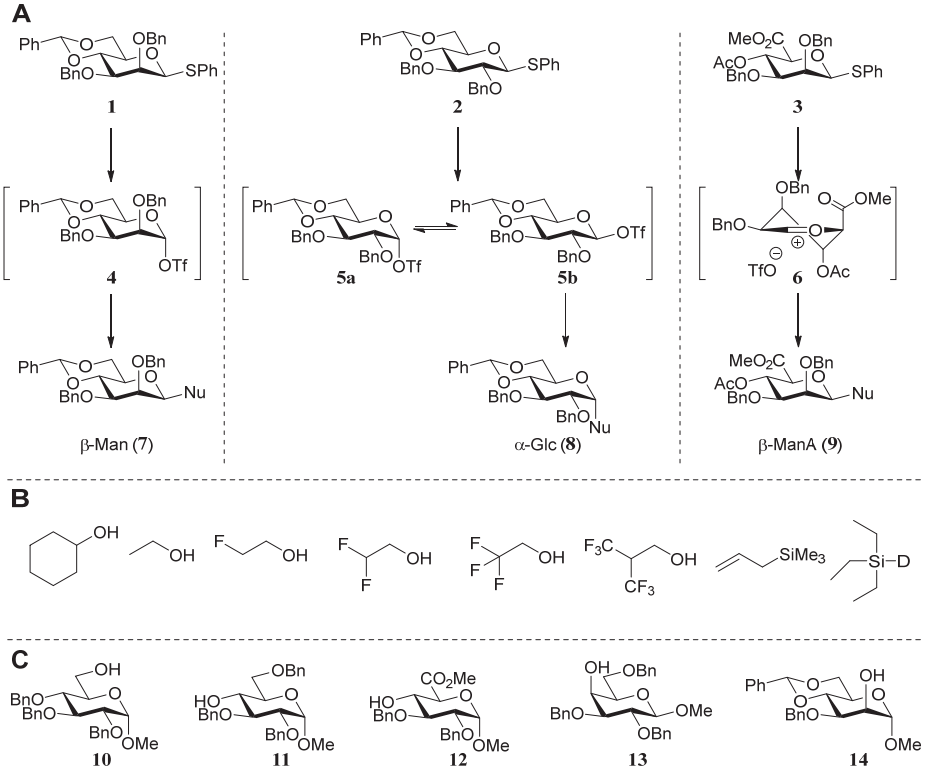


Figure 2. (A) The benzylidene mannose, benzylidene glucose and mannuronic acid glycosylation systems studied and the major glycosylation pathways of these donors. (B) Set of model nucleophiles used in this study. (C) Set of carbohydrate alcohols used.

glycosylation system to date.[19,20] It has been found that benzylidene mannose donors can be transformed into the corresponding α-anomeric triflate **4** upon activation. These triflates have been extensively characterized in variable temperature NMR studies.[21–24] A significant body of evidence has been gathered through a vast amount of glycosylation reactions[19–23,25–33], the establishment of kinetic isotope effects in combination with computational methods[34,35], and the application of cation clock methodology[36–38], to indicate that these triflates can be substituted in an S_N2-manner to provide β-mannosides. However, an alternative hypothesis to account for the β-selectivity of benzylidene mannose glycosylations has also been forwarded. This hypothesis is based on a $B_{2,5}$-oxocarbenium ion as product forming intermediate.[39–42]

The closely related benzylidene glucose system provides α-selective glycosylation reactions.[21,22,29,40,43–47] It has been proposed that this selectivity originates from an *in situ* anomerization kinetic scheme, in which the initially formed α-triflate **5α** anomerizes into its more reactive β-counterpart **5β**.[21] Substitution of this species provides the α-glucosyl products. Mechanistic studies, amongst others kinetic isotope effect and cation-clock experiments, using the reactive nucleophile *iso*-propanol have provided support for this pathway.[34,37,38]

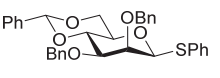
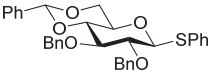
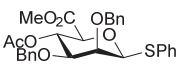
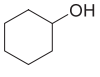
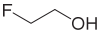
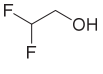
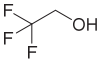
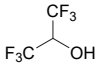
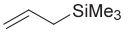
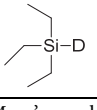
Glycosylations of mannuronic acids have been shown to proceed in a highly selective manner to provide α-mannuronic acid products. Based on the conformational behavior of the donors and the intermediate α-triflates **18α**, adopting an $^1C_4$ conformation[48,49], the high reactivity of these donors[50,51] and a large variety of glycosylation reactions, both in solution[50,52–55], and on fluorous[56] and solid supports[57], it has been postulated that the selectivity in these glycosylation reactions can be related to the intermediacy of an $^4H_3$ oxocarbenium ion-like intermediate.[53,54,58]

The experimental setup that was used in this study is based on preactivation of the thioglycoside donors **1**[59], **2**[21] and **3** using a slight excess of diphenyl sulfoxide and triflic anhydride (Ph_2SO/Tf_2O) at low temperature. This transforms all three donors into the corresponding anomeric triflates[21–24,48,60], prior to addition of the acceptor nucleophiles. The preactivation set-up generates a pool of reactive intermediates in the absence of the acceptor, thereby eliminating product forming pathways that originate from direct displacement reactions on the activated parent donor species. Table 1 summarizes the results obtained with the three donor systems and the set of model acceptors. As a measure for the reactivity of the used acceptors, Mayr's nucleophilicity parameters have been tabularized where available.[61–63] The field inductive parameters for

the -CH_3, -CH_2F, -CHF_2 and -CF_3 groups have also been shown, to indicate the gradual increase of electron-withdrawing character of these groups.[64]

From the results depicted in Table 1 it becomes immediately apparent that the stereoselectivity of the benzylidene mannose and mannuronic acid systems shows relatively little variation with changing nucleophilicity, where the stereoselectivity of the glycosylations involving the benzylidene glucose donor changes significantly depending on the reactivity of the used nucleophile. Reactive nucleophiles such as ethanol,

Table 1. Model acceptor glycosylations.

			 **1**	 **2**	 **3**
Acceptor	N^a	F^b	Product α:β (yield)[c]	Product α:β (yield)	Product α:β (yield)
	-	-	**1A** 1 : 6 (96%)	**2A** 1 : 5 (71 %)	**3A** 1 : 8 (83%)
	7.44	0.01	**1B** 1 : 5 (70 %)	**2B** 1 : 10 (68 %)	**3B** 1 : 8 (95 %)
	-	0.15	**1C** 1 : 5 (86 %)	**2C** 1 : 3 (70 %)	**3C** 1 : 6 (70 %)
	-	0.29	**1D** 1 : 5 (90 %)	**2D** 5 : 1 (70 %)	**3D** 1 : 5 (87 %)
	1.11	0.38	**1E** 1 : 4 (78 %)	**2E** > 20 : 1 (64 %)	**3E** 1 : 2.5 (85 %)
	-1.93	-	**1F** 3 : 1 (56 %)	**2F** > 20 : 1 (65 %)	**3F** 1 : 1 (52 %)
	3.58	-	**1G** < 1 : 20 (60 %)	**2G** > 20 : 1 (79 %)	**3G** < 1 : 20 (95 %)
	1.68	-	**1H** < 1 : 20 (44 %)[d]	**2H** > 20 : 1 (42 %)[d]	**3H** < 1 : 20 (40%)[d]

[a]Mayr's nucleophilicity parameters. [b]Field inductive parameters. [c]α/β-Ratios were established by NMR spectroscopy of the crude and purified reaction mixtures. [d]Both anomers of donor glycoside were also found after the glycosylation reaction. Literature yields of **1H**[40]: 57% and **2H**[40]: 56%.

cyclohexanol and MFE predominantly provide β-linked products (**2A**,[65] **2B** and **2C**), where the use of less reactive nucleophiles such as DFE, TFE, HFIP, TES-*d* and allyl-TMS leads to the preferential formation of the α-glucosyl products (**2D**-**2H**). A clear trend becomes apparent between the reactivity of the non-fluorinated and partially fluorinated ethanols and the stereoselectivity of the glucosylations involving these acceptors. The formation of the β-linked products **2A**, **2B** and **2C** can be explained to originate from an S_N2-like substitution on the intermediate α-triflate **5α** (See Figure 3). The α-products in these glucosylations (**α-2A**, **α-2B**, **α-2C**) may be formed from the corresponding β-glucosyl triflate **5β**, as postulated by Crich and co-workers and as supported by kinetic isotope effect and cation clock studies.[34,35,37,66] It is however less likely that the unreactive *O*-nucleophiles, such as TFE and HFIP, and the weak *C*- and *D*-nucleophiles, are capable of displacing the anomeric triflate **5** in an S_N2-manner. Woerpel and co-workers have previously shown that TFE requires a glycosylating agent bearing significant oxocarbenium ion character.[13] An explanation for the observed α-selectivity in the glucosylations of these nucleophiles may be found in the S_N1-like substitution on the benzylidene glucose oxocarbenium ion **15**. This ion preferentially adopts a $^4H_3/^4E$-structure, as verified by several computational studies[67,68], that is attacked in a diastereoselective fashion from the bottom face, leading *via* a chair-like transition state to the α-linked products. As the reactivity of the nucleophile diminishes, it is likely that the amount of S_N2-character in the substitution of the β-triflate **5β** gradually

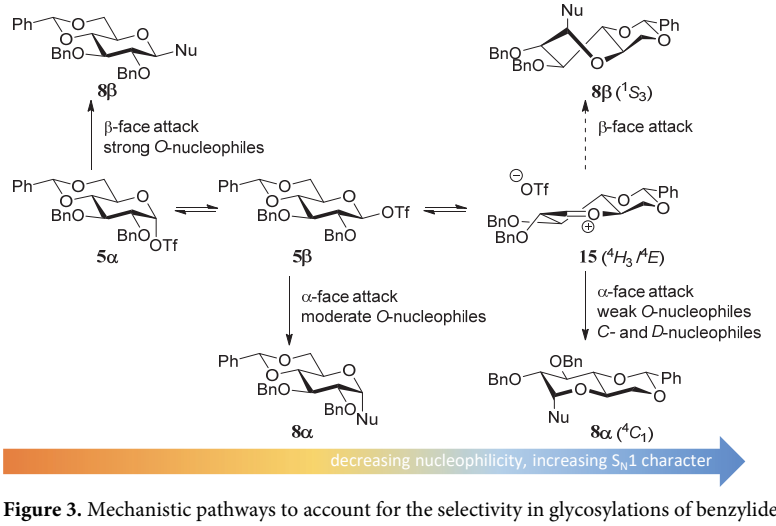


Figure 3. Mechanistic pathways to account for the selectivity in glycosylations of benzylidene glucose donors.

decreases and the amount of S_N1-character with the intermediacy of the corresponding CIP and SSIP (**15**) increases.[13] The least reactive nucleophiles require the most "naked" oxocarbenium ions, with the triflate counterions significantly, if not completely, dissociated from the carbohydrate ring.

The stereoselectivity of the benzylidene mannose system seems to be less sensitive to variation in nucleophilicity of the acceptor. Donor **1** provides β-selective glycosylations with the range of acceptors studied. There is a slight decrease in selectivity going from the reactive *O*-nucleophiles to the weak *O*-nucleophiles and the condensation of benzylidene mannose **1** with HFIP proceeds with moderate α-selectivity. The most likely explanation for the β-selectivity observed with the reactive *O*-nucleophiles is an associative S_N2-type substitution of the intermediate α-triflate **4** (See Figure 4). As discussed above, it is unlikely that unreactive acceptors such as TFE and HFIP react in an S_N2-type reaction, directly displacing the α-mannosyl triflate **4**. Formation of the β-linked products formed from the unreactive acceptors and donor **1** may be better explained with an oxocarbenium ion-like product forming intermediate. Various theoretical studies have indicated that the $B_{2,5}$-oxocarbenium ion **16** is the most stable benzylidene mannose oxocarbenium ion conformer.[67,68] This oxocarbenium ion is preferentially attacked from the convex top face, as attack from the bottom face would lead to unfavorable interactions with the *pseudo*-axial H-2 and to an eclipsed C-1–C-2 configuration upon rehybridization.[36,40,69,70]

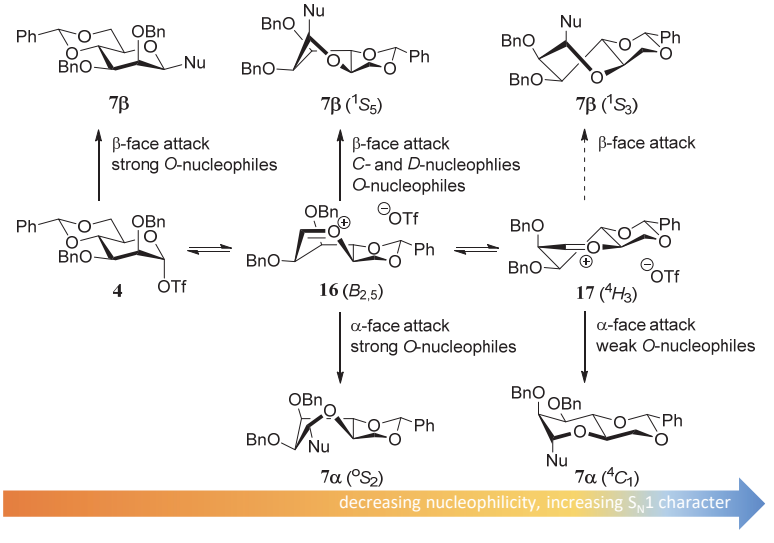


Figure 4. Mechanistic pathways to account for the selectivity in glycosylations of benzylidene mannose donors.

The α-products formed in the condensations of donors **1** likely originate from an oxocarbenium ion intermediate. Reactive *O*-nucleophiles may react with an oxocarbenium ion in a relatively indiscriminative manner leading to the formation of both α- and β-products.[11–13] Because unreactive *O*-nucleophiles are expected to react in a more diastereoselective fashion with an oxocarbenium ion, it is unlikely that the α-products derived from the weak *O*-nucleophiles, such as TFE and HFIP, originate from the $B_{2,5}$-oxocarbenium ion **16**. Instead, α-face attack on the $^4H_3$ half-chair conformer **17** may be a plausible reaction pathway to account for the α-products of the less reactive *O*-nucleophiles. In a later transition state, product development control plays a more important role, and the developing anomeric effect and the low energy chair conformation that results from the α-face attack on the $^4H_3$ half-chair **17**, make this trajectory favorable[71]. For the weak *C*- and *D*-nucleophiles, which react in a highly β-selective manner, this latter pathway does not play a major role, and these nucleophiles attack the $B_{2,5}$-oxocarbenium ion **16** selectively from the top face.[40,72]

In line with the benzylidene mannose system, the mannuronic acid donor provides β-selective condensations with all acceptors explored, except with the very unreactive *O*-nucleophile HFIP where both anomers were formed in equal amounts. Where reactions with nucleophilic *O*-nucleophiles can be expected to form from the α-triflate **18α**,[34–37] the weaker *O*-nucleophiles and allyl-TMS and TES-*d* will react preferentially with an oxocarbenium ion (Figure 5). It has been postulated that the $^3H_4$ half-chair mannuronic acid oxocarbenium ion **6** is the most stable oxocarbenium ion conformer.[51,54,55] To substantiate this hypothesis, the energy associated with a range of mannuronic acid oxocarbenium ion conformers have been calculated using DFT-calculations at the B3LYP/6-311G level.[73] From these calculations the $^3H_4$ conformer **6** appears to be significantly more stable (by > 5 kcal·mol^{-1}) than other conformers such as the alternative $^4H_3$ half-chair **19** and the $B_{2,5}$ boat conformers. The relative stability of the $^3H_4$ half-chair oxocarbenium ion can be explained by favorable interaction of the ring substituents with the electron depleted carbocation. Hyperconjugative stabilization of the C-2–H bond and through space stabilization of the *pseudo*-axial C-3, C-4 oxygen atoms and the axial C-5 carboxylate each contribute to the stability of the half-chair oxocarbenium ion.[51,54,74–76] This oxocarbenium ion is preferentially attacked from the top face to provide the β-linked products *via* a chair-like transition state. For the weaker *O*-nucleophiles, a later transition state leads to significant steric interactions with the axial substituents in the $^3H_4$ half-chair oxocarbenium **6** and a reaction pathway, involving

attack of the nucleophiles on the higher energy $^4H_3$ half-chair oxocarbenium ion **19** becomes relevant. In line with the discussion above, product development control is favorable for the formation of α-*O*-mannuronic acids.

Next, the set of carbohydrate acceptors depicted in Figure 2C was explored. The results of these condensation reactions are summarized in Table 2. Where it can be reasoned that the secondary carbohydrate acceptors **11**[77], **12**[78], **13**[77] and **14**[79] electronically resemble DFE and TFE, because of the amount of electron-withdrawing β- and/or γ- and δ-substituents, the size of the carbohydrate acceptors obviously differs significantly from the small ethanol based acceptors. The picture that emerges from Table 2 follows in broad lines the results described in Table 1 and corroborates this analysis. The benzylidene glucose donor system **2** shows most variation in stereoselectivity, where both the benzylidene mannose and mannuronic acid donors **1** and **3** provide β-selective reactions with all carbohydrate acceptors studied. The series of benzylidene glucose condensations again reveals that reactive *O*-nucleophiles can provide β-selective glycosylations, while less reactive *O*-nucleophiles give the α-linked products. The electron-withdrawing effect of the C-5 carboxylate in acceptor **12**, makes this acceptor less reactive and more α-selective than its C-5-benzyloxymethylene counterpart **11**. In line with the discussion above, formation of the β-linked products can be explained with triflate **5α** as product forming intermediate. Less reactive acceptors require a glycosylating species that is more electrophilic and react in a more dissociative substitution reaction, with a substantial

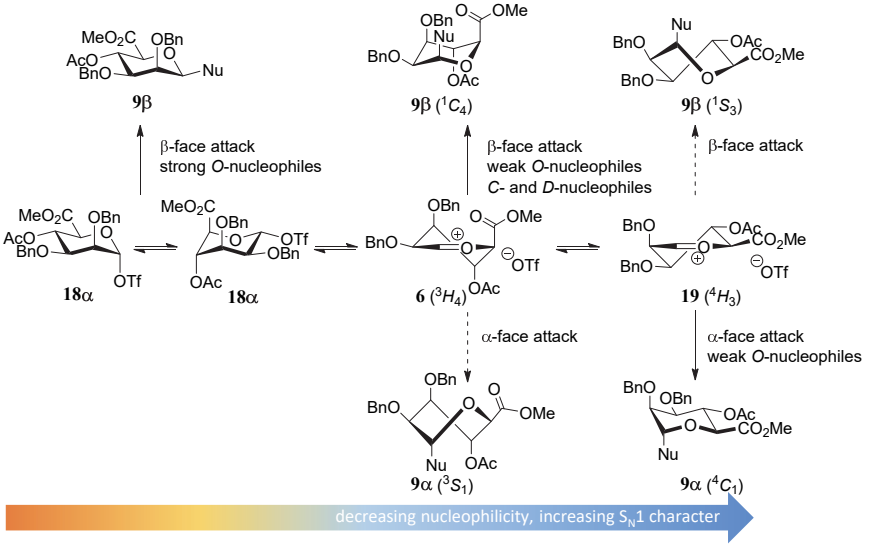
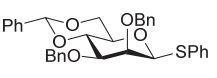
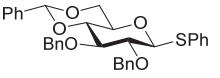
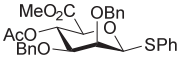
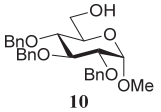
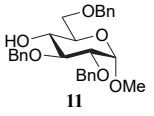
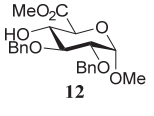
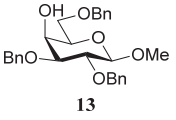
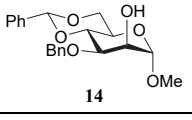


Figure 5. Mechanistic pathways to account for the selectivity in glycosylations of mannuronic acid donors.

Table 2. Glycosylation of donors **1-3** with carbohydrate acceptors **10-14**.

	 **1**	 **2**	 **3**
Acceptor	Product α:β (yield)	Product α:β (yield)	Product α:β (yield)
 **10**	**20** 1 : 10 (97 %)	**25** 1 : 3 (81 %)	**30** < 1 : 20 (71 %)
 **11**	**21** 1 : 9 (75 %)	**26** 1 : 1 (79 %)	**31** < 1 : 20 (61 %)
 **12**	**22** 1 : 10 (87 %)	**27** 5 : 1 (90 %)	**32** 1 : 10 (71 %)
 **13**	**23** < 1 : 20 (70%)	**28** > 20 : 1 (83 %)	**33** < 1 : 20 (76%)
 **14**	**24** < 1 : 20 (87 %)	**29** > 20 : 1 (80 %)	**34** 1 : 7 (80 %)

amount of oxocarbenium ion character and the glucose ring taking up a $^4H_3$-like structure (**15**).

The benzylidene mannose and mannuronic acid donors **1** and **3** provide very β-selective condensation reactions, in line with the vast amount of previously reported glycosylations of these two donors. Based on the results presented here and in previous work the following picture emerges. Reactive carbohydrate acceptors react in a reaction with significant S_N2-character, displacing the anomeric α-triflate (**4** and **18α**). Weaker nucleophiles, such as most secondary carbohydrate acceptors, will react with a species that bears more carbocation character. For the benzylidene mannose donor, this species will resemble $B_{2,5}$ boat oxocarbenium ion **16**, whereas the mannuronic acid reactive intermediate will be structurally close to $^3H_4$ oxocarbenium ion **6**. The minor α-products in these condensations likely arise from a higher energy $^4H_3$ oxocarbenium ion **19**, through a transition state that benefits from a developing anomeric effect and favorable conformational properties.

Conclusions

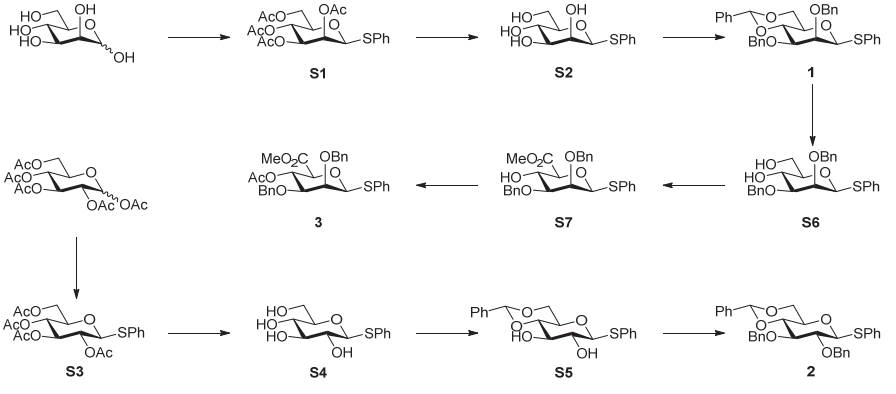
The influence of structural changes in a glycosyl donor on the outcome of a glycosylation reaction, in terms of yield and stereoselectivity, has received considerable attention over the years and many ingenious donor systems have been developed for the stereoselective construction of glycosidic bonds. The influence of the reactivity of the acceptor in glycosylation reactions, on the other hand, is less well understood. Here we have investigated in a systematic manner how the outcome of a glycosylation system can change depending on the gradually changing reactivity of the nucleophile. We have shown that a series of partially fluorinated alcohols of gradually decreasing nucleophilicity, can be used to map how the stereoselectivity of a glycosylation system varies with changing acceptor reactivity. The simple "toolset" of partially fluorinated ethanols represents a rapid and easy means to dissect S_N2-type (for ethanol) and S_N1-type (for trifluoroethanol and hexafluoro-*iso*-propanol) glycosylation reaction mechanisms.[80] It is expected that application of this set of model nucleophiles to newly developed glycosylation methodology or re-investigation of already established methods will bring detailed insight into the complex and intriguing glycosylation reaction mechanism. This will allow for more directed optimization of glycosylation reactions, taking away the trial and error component and ill-understood reaction protocols that have plagued carbohydrate chemistry for so long.

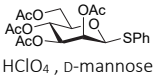
Experimental section

General procedure for Tf_2O/Ph_2SO mediated glycosylations: Donor (0.1 mmol), Ph_2SO (26 mg, 0.13 mmol, 1.3 eq.) and TTBP (62 mg, 0.25 mmol, 2.5 eq.) were coevaporated twice with dry toluene (4 Å molecular sieves) and dissolved in DCM (2 mL, 0.05 M donor). Activated 3Å molecular sieves (rods, size 1/16 in.) were added and the reaction mixture stirred for 30 min at room temperature. The solution was cooled to -78°C and Tf_2O (22 µl, 0.13 mmol, 1.3 eq.) was slowly added. The reaction mixture was allowed to warm to -60°C in approximately 45 min, followed by recooling to -78°C and addition of the acceptor (0.2 mmol, 2 eq.) in DCM (0.4 mL, 0.5 M). The reaction mixture was allowed to warm to -40°C in approximately 60 min and stirred for an additional 0-18 h depending on the acceptor. The reaction was quenched with Et_3N (0.1 mL, 0.72 mmol, 7.2 eq.) at -40°C and diluted with DCM. The solution was transferred to a separatory funnel and water was added, the layers were separated and the water phase extracted once more with DCM. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by silica gel flash column chromatography and when needed, sephadex™ LH-20 size exclusion chromatography yielded the glycosylation product as a mixture of anomers.

General computational procedure: Density functional theory (DFT) *ab initio* calculations were performed with the B3LYP model. Conformations were generated from a conformer distribution search option included in the Spartan 04 program[82] in the gas phase at the 6-31G* basis set level. All generated geometries were further optimized with Gaussian 03[83] at the 6-311G** level, their zero-point energy (ZPE) corrections calculated and further optimized with incorporated polarizable continuum model (PCM) to correct for solvation in dichloromethane.

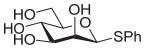
Preparation of donors **1**, **2**, and **3**.



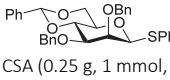


Phenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-mannopyranoside (S1). To a mixture of HBr (33 wt% in AcOH, 35 mL, 200 mmol, 1 eq.) and Ac_2O (93 mL, 1020 mmol, 5.1 eq.) and 10 drops of 70% aq. $HClO_4$, D-mannose (36.0 g, 200 mmol) was added portion wise at 0 °C. After 20 minutes an additional amount of HBr (33 wt% in AcOH, 70 mL, 400 mmol, 2 eq.) was added. After stirring for 16 h at r.t. the reaction mixture was concentrated *in vacuo* at 30 °C. The resulting black oil was co-evaporated with toluene until neutral pH was reached and was used in the following step without further purification. To a solution of the crude product in DMF (400 mL), thiophenol (21.5 mL, 210 mmol, 1.05 eq.) was added. The reaction mixture was cooled to 0 °C and NaH (60% dispersion in mineral oil, 8.4 g, 210 mmol, 1.05 eq.) was added portion wise. After 2 h stirring at r.t. the reaction was quenched by the addition of aq. HCl (1 M). To the resulting black suspension, 4 L of water was added and extracted 10 times with Et_2O. The combined organic layers were washed with water, dried with $MgSO_4$ and concentrated *in vacuo*. Flash column chromatography (9/1 to 7/3 pentane/EtOAc) afforded the title compound as an orange oil (57.3 g, 130 mmol, 65%). R_f: 0.70 (1/1 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[84,85] $[\alpha]_D^{26}$ = -44.4° (*c* = 0.5, $CHCl_3$); IR (neat): 1047, 1213, 1368, 1742; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.56 – 7.47 (m, 2H, CH_{arom} SPh), 7.34 – 7.30 (m, 3H, CH_{arom} SPh), 5.66 (dd, 1H, *J* = 3.5, 0.8 Hz, H-2), 5.28 (t, 1H, *J* = 10.0 Hz, H-4), 5.07 (dd, 1H, *J* = 10.1, 3.5 Hz, H-3), 4.94 (d, 1H, *J* = 1.0 Hz, H-1), 4.29 (dd, 1H, *J* = 12.2, 6.5 Hz, H-6), 4.17 (dd, 1H, *J* = 12.2, 2.4 Hz, H-6), 3.72 (ddd, 1H, *J* = 10.0, 6.4, 2.5 Hz, H-5), 2.20 (s, 3H, CH_3 OAc), 2.09 (s, 3H, CH_3 OAc), 2.04 (s, 3H, CH_3 OAc), 1.98 (s, 3H CH_3, OAc); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC): δ 170.5, 170.1, 167.0, 169.6

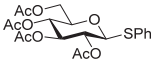
(C=O Ac), 133.2 (C_q SPh), 131.9, 129.1, 128.1 (CH_{arom} SPh), 85.5 (C-1), 76.4 (C-5), 71.8 (C-3), 70.6 (C-2), 65.8 (C-4), 62.8 (C-6), 20.7, 20.7, 20.6, 20.6 (CH_3 Ac); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 85.5 ($J_{C1,H1}$ = 153 Hz, C-1 β); HRMS: $[M+Na]^+$ calcd for $C_{20}H_{24}O_9SNa$ 463.10332, found 463.10305.



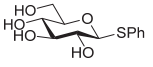
Phenyl 1-thio-β-D-mannopyranoside (S2). To a solution of **S1** (24.9 g, 56.5 mmol) in MeOH (280 mL), NaOMe (0.31 g, 5.7 mmol, 0.1 eq.) was added. The reaction mixture was stirred for 16 h. Amberlite IR120 H^+ was added until pH 6 was reached and the mixture was filtered and concentrated *in vacuo*. This afforded the title compound (15.3 g, 56.4 mmol, 99%) as a white foam. R_f: 0.20 (9/1 DCM/MeOH). Spectroscopic data were in accord with those previously reported.[86,87] IR (neat, cm^{-1}): 880, 1085, 1636, 2974, 3312; ^{1}H NMR (400 MHz, MeOD, HH-COSY, HSQC): δ 7.53 – 7.46 (m, 2H, CH_{arom} SPh), 7.34 – 7.17 (m, 3H, CH_{arom} SPh), 5.00 (s, 1H, H-1), 4.05 (dd, 1H, *J* = 3.4, 1.0 Hz, H-2), 3.88 (dd, 1H, *J* = 11.9, 2.4 Hz, H-6), 3.73 (dd, 1H, *J* = 12.1, 5.7 Hz, H-6), 3.63 (t, 1H, *J* = 9.5 Hz, H-4), 3.51 (dd, 1H, *J* = 9.5, 3.4 Hz, H-3), 3.29 (m, 1H, *J* = 5.8 Hz, H-5); ^{13}C-APT NMR (101 MHz, MeOD, HSQC): δ 131.0, 130.0, 127.7 (CH_{arom} SPh), 88.8 (C-1), 82.4 (C-5), 76.2 (C-3), 74.3 (C-2), 68.3 (C-4), 62.9 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{12}H_{16}O_5SNa$ 295.06107, found 295.06107.



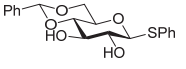
Phenyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-mannopyranoside (1). To a solution of **S2** (1.36 g, 5 mmol) in DMF (50 mL), benzaldehyde dimethyl acetal (3.0 mL, 20 mmol, 4 eq.) and CSA (0.25 g, 1 mmol, 0.2 eq.) were added. After the solution was stirred for 16 h, benzyl bromide (2.4 mL, 20 mmol, 4 eq.) and NaH (60% dispersion in mineral oil, 0.48 g, 20 mmol, 4 eq.) were added at 0 °C. The suspension was allowed to warm up until r.t. and stirred for an additional 2 h. The reaction mixture was quenched with MeOH, followed by the addition of DCM (250 mL) and ice water (500 mL). The water layer was extracted once with DCM and the combined organic layers were washed with water and brine. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Flash column chromatography (1/0 to 9/1 pentane/EtOAc) and subsequent recrystallization from EtOAc and pentane afforded the title compound as a white solid (1.38 g, 2.56 mmol, 51% over 2 steps). R_f: 0.27 (9/1 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[59] IR (neat): 733, 1026, 1069, 1452, 2864; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC): δ 7.64 – 7.14 (m, 20H, CH_{arom}), 5.64 (s, 1H, C*H*Ph), 5.12 (d, 1H, *J* = 11.1 Hz, C*H*H Bn), 4.89 (d, 1H, *J* = 12.3 Hz, CH*H* Bn), 4.86 (d, 1H, *J* = 11.1 Hz, C*H*H Bn), 4.85 (d, 1H, *J* = 1.3 Hz, H-1), 4.74 (d, 1H, *J* = 12.3 Hz, CH*H* Bn), 4.36 – 4.26 (m, 2H, H-4, H-6), 4.18 (dd, 1H, *J* = 3.1, 1.3 Hz, H-2), 3.95 (t, 1H, *J* = 10.3 Hz, H-6), 3.74 (dd, 1H, *J* = 9.8, 3.1 Hz, H-3), 3.42 (td, 1H, *J* = 9.7, 4.9 Hz, H-5); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC, HMBC): δ 138.1, 137.6, 135.1 (C_q), 131.2, 129.1, 129.1, 128.8, 128.6, 128.4, 127.9, 127.9, 127.8, 127.6, 126.2 (CH_{arom}), 101.6 (CHPh), 89.2 (C-1), 79.9 (C-3), 79.1 (C-2), 78.8 (C-4), 76.0, 73.3 (CH_2 Bn), 71.8 (C-5), 68.6 (C-6); ^{13}C-GATED NMR (101 MHz, $CDCl_3$) δ 89.2 ($J_{C1,H1}$ = 152 Hz, C-1 β); HRMS: $[M+NH_4]^+$ calcd for $C_{33}H_{36}NO_5S$ 558.23087, found 558.23071.



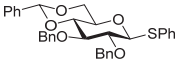
Phenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (S3). To a 140°C solution of NaOAc (8.2 g, 100 mmol, 0.5 eq) in Ac_2O (190 mL, 2 mol, 10 eq.) D-glucose (36 g, 200 mmol, 1 eq.) was added portionwise and the reaction mixture was refluxed for an additional 15 min. The solution was cooled to r.t. and poured over crushed ice. The product was filtered, taken up in DCM, concentrated *in vacuo* and recrystallized from hot EtOH (750 mL) to give the pentaacetate as a white solid (69.4 g, 178 mmol, 89%). Spectroscopic data were in accord with those previously reported.[88,89] Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 5.72 (d, 1H, *J* = 8.3 Hz, H-1), 5.26 (t, 1H, *J* = 9.4 Hz, H-3), 5.19 – 5.08 (m, 2H, H-2, H-4), 4.30 (dd, 1H, *J* = 12.7, 3.8 Hz, H-6), 4.15 – 4.08 (m, 1H, H-6), 3.88 – 3.81 (m, 1H, H-5), 2.12 (s, 3H, CH_3 OAc), 2.09 (s, 3H, CH_3 OAc), 2.04 (s, 6H, 2xCH_3 OAc), 2.02 (s, 3H, CH_3 OAc); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 170.7, 170.2, 169.5, 169.4, 169.1 (C_q OAc), 91.8 (C-1), 72.9, 72.8 (C-3, C-5), 70.3, 67.9 (C-2, C-4), 61.6 (C-6), 21.0, 20.8, 20.7 (CH_3 OAc).D-glucose pentaacetate (20 g, 51 mmol) was dissolved in DCM (100 mL) and cooled to 0°C. Thiophenol (7.8 mL, 76.5 mmol, 1.5 eq.) was added followed by addition of boron trifluoride diethyl etherate (10.9 mL, 76.5 mmol, 1.5 eq.) and the mixture was refluxed overnight. Sat. aq. $NaHCO_3$ (300 mL) and Et_2O (100 mL) were added and the mixture was extracted three times with Et_2O. The organic layer was washed with brine, dried with $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by crystallization from EtOAc/hexane (1/10) to obtain the title compound as a white solid. (16.8 g, 38.2 mmol, 75%). Spectroscopic data were in accord with those previously reported.[77,90–92] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.50 (dd, 2H, *J* = 6.6, 3.0 Hz, CH_{arom}), 7.34 – 7.28 (m, 3H, CH_{arom}), 5.24 (t, 1H, *J* = 9.3 Hz, H-3), 5.04 (t, 1H, *J* = 9.8 Hz, H-4), 4.97 (t, 1H, *J* = 9.6 Hz, H-2), 4.75 (d, 1H, *J* = 10.0 Hz, H-1), 4.23 (dd, 1H, *J* = 12.3, 5.1 Hz, H-6), 4.17 (dd, 1H, *J* = 12.3, 2.5 Hz, H-6), 3.76 (ddd, 1H, *J* = 10.0, 5.1, 2.5 Hz, H-5), 2.07 (s, 3H, CH_3 OAc), 2.06 (s, 3H, CH_3 OAc), 2.01 (s, 3H, CH_3 OAc), 1.98 (s, 3H, CH_3 OAc); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 170.2, 169.8, 169.2, 169.0 (C=O Ac), 132.8 (CH_{arom}), 131.5 (C_q), 128.8, 128.2 (CH_{arom}), 85.3 (C-1), 75.5 (C-5), 73.8 (C-3), 69.8 (C-2), 68.1 (C-4), 61.9 (C-6), 20.5, 20.5, 20.4, 20.4 (CH_3 Ac).



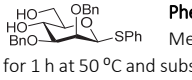
Phenyl 1-thio-β-D-glucopyranoside (S4). To a solution of **S3** (16.3 g, 37.0 mmol) in MeOH (200 mL) was added Na(s) (89 mg, 3.7 mmol, 0.1 eq) and the reaction was stirred for 18 h at r.t. The reaction mixture was neutralized with Amberlite H^+, filtered and Celite® was added to the filtrate and the mixture concentrated *in vacuo*. The residue was purified by flash column chromatography (1% to 12% EtOH in EtOAc) to obtain a white solid (8.6 g, 31.6 mmol, 85%). Spectroscopic data were in accord with those previously reported.[93] ^{1}H NMR (MeOD, 400 MHz, HH-COSY, HSQC): δ 7.61 – 7.54 (m, 2H, CH_{arom}), 7.33 – 7.24 (m, 3H, CH_{arom}), 4.60 (d, 1H, *J* = 9.8 Hz, H-1), 3.87 (dd, 1H, *J* = 12.1, 1.8 Hz, H-6), 3.67 (dd, 1H, *J* = 12.2, 5.2 Hz, H-6), 3.39 (t, 1H, *J* = 8.5 Hz, H-3), 3.35 – 3.26 (m, 2H, H-4, H-5), 3.22 (dd, 1H, *J* = 9.8, 8.6 Hz, H-2); ^{13}C-APT NMR (MeOD, 101 MHz, HSQC): δ 135.3 (C_q), 132.7, 129.9, 128.3 (CH_{arom}), 89.4 (C-1), 82.0 (C-4), 79.7 (C-3), 73.7 (C-2), 71.3 (C-5), 62.8 (C-6).



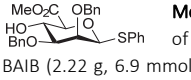
Phenyl 4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (S5). To a solution of **S4** (12.81 g, 47 mmol) and *p*-TsOH·H_2O (100 mg, 0.5 mmol, 0.01 eq.) in DMF (25 mL) and CH_3CN (100 mL) was added benzaldehyde dimethyl acetal (9.9 mL, 65.8 mmol, 1.4 eq.). The reaction was heated to 50°C at 250 mbar for 5 hours and subsequently quenched with Et_3N (2 mL) and diluted with EtOAc (250 mL). The solution was washed with H_2O (2x 100 mL) and brine (100 mL). The organic layer was dried ($MgSO_4$) and concentrated *in vacuo*. Precipitation from EtOAc/petroleum ether formed a waxy material (12.0 g, 33.3 mmol) and the remaining mother liquors were purified by column chromatography (3/1 to 1/3 pentane/EtOAc) to give another batch of product (3.86 g, 10.7 mmol). Total yield 15.9 g, 44 mmol, 94%. R_f: 0.50 (1/2 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[90–92] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.59 – 7.51 (m, 2H, CH_{arom}), 7.51 – 7.44 (m, 2H, CH_{arom}), 7.40 – 7.31 (m, 6H, CH_{arom}), 5.54 (s, 1H, C*H*Ph), 4.64 (d, 1H, *J* = 9.8 Hz, H-1), 4.39 (dd, 1H, *J* = 10.5, 4.4 Hz, H-6), 3.91 – 3.74 (m, 2H, H-4, H-6), 3.59 – 3.43 (m, 3H, H-2, H-3, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 137.0 (C_q), 133.2 (CH_{arom}), 131.4 (C_q), 129.5, 129.3, 128.7, 128.5, 126.4 (CH_{arom}), 102.1 (CHPh), 88.8 (C-1), 80.4 (C-3), 74.7 (C-4), 72.7 (C-2), 70.7 (C-5), 68.7 (C-6).



Phenyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (2). Diol **S5** (7.21 g, 20 mmol) was dissolved in DMF (100 mL) and cooled to 0°C. Benzyl bromide (5.75 mL, 48 mmol, 2.4 eq.) and NaH (60% dispersion in mineral oil, 2.4 g, 60 mmol, 3 eq.) were added and the reaction mixture was allowed to stir overnight. MeOH was added to quench the reaction followed by H_2O (500 mL) and EtOAc (300 mL). The organic layer was washed with brine and dried with MgSO4. After concentration of the organic layer under reduced pressure, the crude product was crystallized from EtOAc (50 mL) and hexane (100 mL) to obtain the title compound as a white solid (9.49 g, 17.4 mmol, 86%). Spectroscopic data were in accord with those previously reported.[21,90–92] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.56 – 7.51 (m, 2H, CH_{arom}), 7.51 – 7.46 (m, 2H, CH_{arom}), 7.42 – 7.26 (m, 16H, CH_{arom}), 5.59 (s, 1H, C*H*Ph), 4.94 (d, 1H, *J* = 11.1 Hz, C*H*H Bn), 4.86 (d, 1H, *J* = 10.2 Hz, C*H*H Bn), 4.81 (d, 1H, *J* = 10.3 Hz, CH*H* Bn), 4.80 – 4.73 (m, 2H, CH*H* Bn, H-1), 4.39 (dd, 1H, *J* = 10.5, 5.0 Hz, H-6), 3.84 (dd, 1H, *J* = 9.3, 8.3 Hz, H-3), 3.80 (t, 1H, *J* = 10.3 Hz, H-6), 3.71 (t, 1H, *J* = 9.3 Hz, H-4), 3.56 – 3.42 (m, 2H, H-2, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.4, 138.1, 137.4, 133.2 ($C_{q\text{-}arom}$), 132.5, 129.1, 129.1, 128.5, 128.5, 128.4, 128.3, 128.2, 128.0, 128.0, 127.9, 126.1 (CH_{arom}), 101.3 (CHPh), 88.4 (C-1), 83.1 (C-3), 81.6 (C-4), 80.6 (C-2), 76.0, 75.5 (CH_2 Bn), 70.4 (C-5), 68.8 (C-6); HRMS: $[M+H]^+$ calcd for $C_{33}H_{33}O_5S$ 541.20432, found 541.20392.

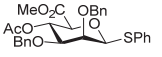


Phenyl 2,3-di-*O*-benzyl-1-thio-β-D-mannopyranoside (S6). To a solution of **1** (1.62 g, 3 mmol) in MeOH (30 mL), *p*-TsOH·H_2O (60 mg, 0.3 mmol, 0.1 eq.) was added. The suspension was stirred for 1 h at 50 °C and subsequently quenched with Et_3N. After concentration *in vacuo* the resulting product was purified by flash column chromatography (9/1 to 1/1 pentane/EtOAc) to yield the title compound as a colourless foam (1.26 g, 2.78 mmol, 93%). R_f: 0.10 (4/1 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[51] $[\alpha]_D^{26}$ = -62.4° (*c* = 0.5, $CHCl_3$); IR (neat): 734, 1026, 1119, 1454, 924, 3391; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.54 – 7.19 (m, 15H, CH_{arom}), 4.97 (d, 1H, *J* = 11.3 Hz, C*H*H Bn), 4.85 (s, 1H, H-1), 4.85 (d, 1H, *J* = 11.3 Hz, CH*H* Bn), 4.75 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.53 (d, 1H, *J* = 11.7 Hz, CH*H* Bn), 4.20 (d, 1H, *J* = 2.1 Hz, H-2), 4.05 (td, 1H, *J* = 9.5, 2.3 Hz, H-4), 3.93 (ddd, 1H, *J* = 11.0, 7.2, 3.6 Hz, H-6), 3.82 (dt, 1H, *J* = 12.1, 6.3 Hz, H-6), 3.46 (dd, 1H, *J* = 9.5, 2.8 Hz, H-3), 3.38 (ddd, 1H, *J* = 9.5, 6.0, 3.6 Hz, H-5), 2.33 (s, 1H, 4-OH), 2.14 (t, 1H, *J* = 6.4 Hz, 6-OH); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC): δ 138.0, 137.6, 135.1 (C_q), 130.7, 129.2, 128.8, 128.5, 128.4, 128.3, 127.9, 127.9, 127.5 (CH_{arom}), 87.9 (C-1), 83.6 (C-3), 80.1 (C-5), 76.7 (C-2), 75.3, 72.3 (CH_2 Bn), 67.5 (C-4), 63.1 (C-6); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 87.9 (*J* = 152 Hz, C-1 β); HRMS: $[M+Na]^+$ calcd for $C_{26}H_{28}O_5SNa$ 475.15497, found 475.15430.



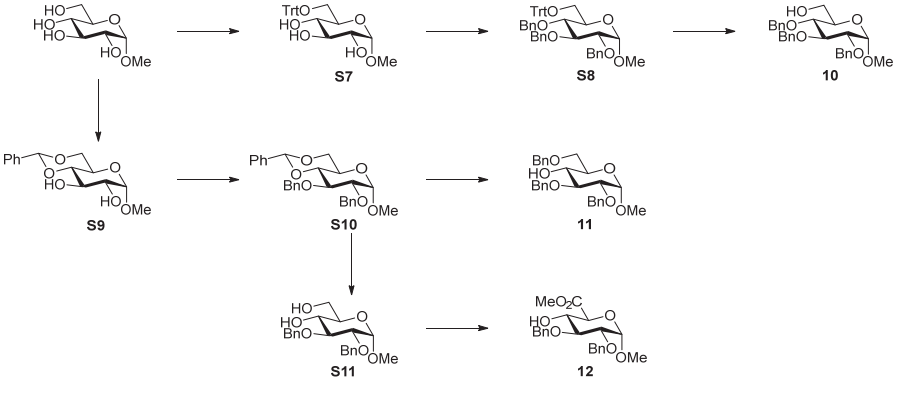
Methyl (phenyl 2,3-di-*O*-benzyl-1-thio-β-D-mannopyranosyl uronate) (S7). To a two phase system of **S6** (1.25 g, 2.76 mmol) in DCM (10 mL) and H_2O (5 mL), TEMPO (86 mg, 0.55 mmol, 0.2 eq.), BAIB (2.22 g, 6.9 mmol, 2.5 eq.) and AcOH (50 µL) were added. The reaction mixture was stirred for 6 h and was

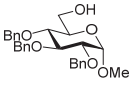
quenched with sat. aq. $Na_2S_2O_3$. The resulting suspension was concentrated under reduced pressure and co-evaporated three times with toluene. The formed solid was dissolved in DMF (15 mL), K_2CO_3 (1.14 g, 8.28 mmol, 3 eq.) and methyl iodide (0.52 mL, 8.28 mmol, 3 eq.) were added. The suspension was stirred for 16 h at r.t. and followed by the addition of H_2O (150 mL). The aqueous layer was extracted three times with Et_2O and subsequently washed with sat. aq. $NaHCO_3$ and brine. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Flash column chromatography (1/0 to 3/1 pentane/EtOAc) followed by recrystallization in EtOAc and pentane afforded the title compound as a white solid (0.48 g, 1.75 mmol, 63% over 2 steps). R_f: 0.70 (1/1 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[51] $[\alpha]_D^{26}$ = -72,0° (*c* = 0.5, $CHCl_3$); IR (neat): 696, 735, 1026, 1064, 1123, 1429, 1454, 1744, 2855, 2924, 3462; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.51 – 7.25 (m, 20H, CH_{arom}), 5.02 (d, 1H, *J* = 11.4 Hz, C*H*H Bn), 4.86 (d, 1H, *J* = 11.3 Hz, CH*H* Bn), 4.79 – 4.74 (m, 3H, C*H*H Bn, CH*H* Bn, H-1), 4.41 (td, 1H, *J* = 9.5, 2.1 Hz, H-4), 4.12 (dd, 1H, *J* = 3.0, 1.0 Hz, H-2), 3.84 – 3.77 (m, 4H, H-5, CH_3 CO_2Me), 3.50 (dd, 1H, *J* = 9.5, 2.9 Hz, H-3), 3.11 (d, 1H, *J* = 2.3 Hz, 4-OH); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC): δ 138.0, 135.1 (C_q), 131.3, 129.1, 128.7, 128.6, 128.3, 128.1, 127.9, 127.9, 127.6 (CH_{arom}), 89.0 (C-1), 82.4 (C-3), 78.3 (C-5), 77.0 (C-2), 75.4, 73.1 (CH_2 Bn), 68.6 (C-4), 52.9 (CH_3 CO_2Me); ^{13}C- GATED NMR (101 MHz, $CDCl_3$): δ 89.0 ($J_{C1,H1}$ = 154 Hz, C-1 β). HRMS: $[M+H]^+$ calcd for $C_{27}H_{29}O_6S$ 481,16794, found 481,16812.



Methyl (phenyl 4-*O*-acetyl-2,3-di-*O*-benzyl-thio-β-D-mannopyranosyl uronate) (3). To a suspension of **S7** (1.20 g, 2.5 mmol) in pyridine (3.0 mL, 37.5 mmol, 15 eq.), Ac_2O (0.30 mL, 3.1 mmol, 1.25 eq.) was added. After stirring for 16 h at r.t., the reaction mixture was quenched with H_2O (25 mL). To the quenched reaction mixture, EtOAc was added and the layers were separated. The water layer was extracted for an additional 2 times with EtOAc. The combined organic layers were washed with sat. aq. $NaHCO_3$ and brine. The resulting organic layer was dried over $MgSO_4$, filtered and concentrated under reduced pressure. Flash column chromatography (9/1 to 7/3 pentane/EtOAc) afforded the title compound as a white solid (1.2 g, 2.3 mmol, 92%). R_f: 0.42 (7/3 pentane/EtOAc). $[\alpha]_D^{26}$ = -84.0° (*c* = 0.5, $CHCl_3$); IR (neat): 733, 1024, 1053, 1089, 1746, 2870; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.50 – 7.23 (m, 15H, CH_{arom}), 5.61 (t, 1H, *J* = 9.6 Hz, H-4), 5.03 (d, 1H, *J* = 11.6 Hz, C*H*H Bn), 4.85 (d, 1H, *J* = 11.6 Hz, CH*H* Bn), 4.78 (d, 1H, *J* = 1.1 Hz, H-1), 4.67 (d, 1H, *J* = 12.2 Hz, C*H*H Bn), 4.57 (d, 1H, *J* = 12.2 Hz, CH*H* Bn), 4.15 (dd, 1H, *J* = 2.8, 1.0 Hz, H-2), 3.88 (d, 1H, *J* = 9.6 Hz, H-5), 3.74 (s, 3H, CH_3 CO_2Me), 3.61 (dd, 1H, *J* = 9.7, 2.9 Hz, H-3), 2.01 (s, 3H, CH_3 OAc); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC): δ 169.7, 167.8 (C=O CO_2Me, Ac), 137.9, 137.7, 135.1 (C_q), 131.3, 129.1, 128.7, 128.6, 128.3, 128.1, 127.9, 127.7, 127.7 (CH_{arom}), 88.7 (C-1), 80.4 (C-3), 77.3 (C-5), 76.4 (C-2), 75.1, 72.6 (CH_2 Bn), 68.9 (C-4), 52.8 (CH_3 CO_2Me), 21.0 (CH_3 Ac); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 88.7 ($J_{C1,H1}$ = 152 Hz, C-1 β); HRMS: $[M+NH_4]^+$ calcd for $C_{29}H_{34}NO_7S$ 540.20505, found 540.20515.

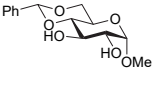
Preparation of acceptors **10**, **11**, and **12**.



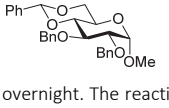


Methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (10). To a solution of methyl-α-D-glucopyranoside (1.94 g, 10 mmol, 1 eq.) in DMF (50 mL), trityl chloride (3.1 g, 11 mmol, 1.1 eq.), Et_3N (2.1 mL, 15 mmol, 1.5 eq.) and DMAP (0.12 g, 1 mmol, 0.1 eq.) were added. After stirring for 6 h at 60 °C the reaction was cooled to 0 °C and followed by the addition of benzyl bromide (4.8 mL, 40 mmol, 4 eq.), NaH (2 g, 50 mmol, 5 eq.). The suspension was stirred for 16 h at r.t. and subsequently quenched with MeOH. The reaction mixture was concentrated under reduced pressure and the remaining oil was transferred to a separation funnel. Et_2O and H_2O were added and the layers were separated. The water layer was extracted three more times

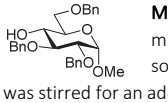
with Et_2O. The combined organic layers were washed with water, sat. aq. $NaHCO_3$ and brine. The resulting organic layer was dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product **S8** was suspended in MeOH (100 mL) followed by the addition of *p*-TsOH·H_2O (0.19 g, 1 mmol, 0.1 eq.). After stirring for 1 h at 50 °C the reaction mixture was quenched with sat. aq. $NaHCO_3$ and concentrated *in vacuo*. Flash column chromatography (1/0 to 7/3 pentane/EtOAc) afforded the title compound as a waxy solid (3.6 g, 7.7 mmol, 78% over 3 steps). Spectroscopic data were in accord with those previously reported.[77,94] R_f: 0.57 (7/3 pentane/EtOAc). IR (neat): 880, 1043, 1086, 1381, 1636, 2893, 2974, 3312; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.42 – 7.24 (m, 15H, CH_{arom}), 4.99 (d, 1H, *J* = 10.8 Hz, C*H*H Bn), 4.92 – 4.77 (m, 3H, C*H*H Bn, CH*H* Bn, C*H*H Bn), 4.72 – 4.60 (m, 2H, CH*H* Bn, CH*H* Bn), 4.56 (d, 1H, *J* = 3.5 Hz, H-1), 4.01 (t, 1H, *J* = 9.3 Hz, H-4), 3.82 – 3.73 (m, 1H, H-6), 3.73 – 3.61 (m, 2H, H-6, H-5), 3.58 – 3.45 (m, 2H, H-6, H-2, H-3), 3.37 (s, 3H, CH_3 OMe), 1.61 (dd, 1H, *J* = 7.3, 5.4 Hz, 6-OH); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC, HMBC): δ 138.8, 138.2 (C_q), 128.6, 128.6, 128.6, 128.3, 128.2, 128.1, 128.1, 128.0, 127.8 (CH_{arom}), 98.3 (C-1), 82.1 (C-4), 80.0 (C-2), 77.4 (C-3), 75.9, 75.2, 73.6 (CH_2 Bn), 70.7 (C-5), 62.0 (C-6), 55.3 (CH_3 OMe); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 98.3 ($J_{C1,H1}$ = 164 Hz, C-1 α); HRMS: $[M+Na]^+$ calcd for $C_{28}H_{32}O_6Na$ 487.20911, found 487.20851.



Methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (S9). To a solution of methyl α-D-glucopyranoside (38.8 g, 200 mmol) in acetonitrile (800 mL) was added $PhCH(OMe)_2$ (36 mL, 240 mmol, 1.2 eq.) and *p*-TsOH·H_2O (3.8 g, 20 mmol, 0.1 eq.). The solution was stirred overnight at ambient temperature followed by concentration *in vacuo* (60°C, 600 mbar, 1.5 h) to a quarter of its original volume. The reaction mixture was treated with Et_3N (3 mL), diluted with EtOAc (500 mL) and subsequently washed with H_2O (2x 150 mL), sat. aq. $NaHCO_3$ (50 mL) and brine (2x 100 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated in vacuo. The resulting crude residue was crystalized from EtOAc/petroleum ether to give the title product in two crops (49.2 g, 174 mmol, 87%, white solid). Spectroscopic data were in accord with those previously reported.[77,95] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.51 – 7.45 (m, 2H, CH_{arom}), 7.36 (dd, 3H, *J* = 5.1, 2.0 Hz, CH_{arom}), 5.51 (s, 1H, C*H*Ph), 4.75 (d, 1H, *J* = 3.8 Hz, H-1), 4.28 (dd, 1H, *J* = 9.6, 4.3 Hz, H-6), 3.91 (t, 1H, *J* = 9.2 Hz, H-3), 3.84 – 3.68 (m, 2H, H-5, H-6), 3.60 (dd, 1H, *J* = 9.2, 3.9 Hz, H-2), 3.47 (t, 1H, *J* = 9.3 Hz, H-4), 3.43 (s, 3H, CH_3 OMe), 2.87 (bs, 2H, OH); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 137.2 (C_q), 129.4, 128.4, 126.4 (CH_{arom}), 102.0 (CHPh), 99.9 (C-1), 81.1 (C-4), 72.9 (C-2), 71.7 (C-3), 69.0 (C-6), 62.5 (C-5), 55.7 (OMe).

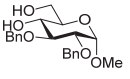


Methyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (S10). Benzyl bromide (10.5 mL, 88 mmol, 2.2 eq.) and sodium hydride (60% dispersion, 4.16 g, 104 mmol, 2.6 eq.) were added to a 0°C solution of diol **S9** (11.29 g, 40 mmol) in DMF (200 mL) and the solution was stirred overnight. The reaction mixture was quenched by slow addition of MeOH, diluted with EtOAc (500 mL) and washed with H_2O (200 mL) and brine (200 mL). The organic layer was dried with $MgSO_4$, filtered and concentrated *in vacuo*. The solid residue was recrystallization from EtOAc/pentane to yield the title compound as a white solid (16.0 g, 34.6 mmol, 87%). R_f: 0.57 (4/1 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[21,77] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.52 – 7.46 (m, 2H, CH_{arom}), 7.41 – 7.25 (m, 13H, CH_{arom}), 5.55 (s, 1H, C*H*Ph), 4.92 (d, 1H, *J* = 11.3 Hz, C*H*H Bn), 4.85 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.84 (d, 1H, *J* = 11.3 Hz, CH*H* Bn), 4.70 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.59 (d, 1H, *J* = 3.7 Hz, H-1), 4.26 (dd, 1H, *J* = 10.1, 4.7 Hz H-6), 4.05 (t, 1H, *J* = 9.3 Hz, H-3), 3.83 (td, 1H, *J* = 9.9, 4.7 Hz, H-5), 3.70 (t, 1H, *J* = 10.2 Hz, H-6), 3.60 (t, 1H, *J* = 9.4 Hz, H-4), 3.56 (dd, 1H, *J* = 9.3, 3.7 Hz, H-2), 3.40 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.8, 138.3, 137.5 (C_q), 129.0, 128.6, 128.4, 128.3, 128.2, 128.1, 128.0, 127.7, 126.1 (CH_{arom}), 101.4 (CHPh), 99.3 (C-1), 82.2 (C-4), 79.3 (C-2), 78.7 (C-3), 75.5, 73.9 (CH_2 Bn), 69.2 (C-6), 62.4 (C-5), 55.5 (OMe).

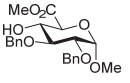


Methyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (11). Fully protected compound **S10** (3.24 g, 7.0 mmol) was dissolved in THF (100 mL) and $NaCNBH_3$ (4.0 g, 63 mmol, 9 eq.) was added. To this solution 4.0 M HCl in 1,4-dioxane (18 mL, 72 mmol, 10.3 eq.) was slowly added and the reaction was stirred for an additional hour. Ice cold H_2O (300 mL) was added and the mixture extracted with DCM (2x 120 mL). The combined organic layers were washed with sat. aq. $NaHCO_3$ (100 mL) and brine (100 mL), dried with $MgSO_4$ and concentrated *in vacuo*. Flash column chromatography (6/1 to 4/1 pentane/EtOAc,) gave the title compound as a colorless oil (2.7 g, 5.85 mmol, 87%). R_f: 0.37 (4/1 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[77] IR (neat): 695, 732, 1027, 1047, 1453, 2910, 3477; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.41 – 7.23 (m, 15H, CH_{arom}), 4.99 (d, 1H, *J* = 11.4 Hz, C*H*H Bn), 4.75 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.73 (d, 1H, *J* = 11.4 Hz, CH*H* Bn), 4.68 – 4.60 (m, 2H, CH*H* Bn, H-1), 4.57 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.52 (d, 1H, *J* = 12.2 Hz, CH*H* Bn), 3.78 (dd, 1H, *J* = 9.6, 8.8 Hz, H-3), 3.74 – 3.63 (m, 3H, H-5, H-6, H-6), 3.59 (t, 1H, *J* = 9.2 Hz, H-4), 3.52 (dd, 1H, *J* = 9.6, 3.5 Hz, H-2), 3.37 (s, 3H, CH_3 OMe), 2.44 (bs, 1H, 4-OH); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.8, 138.1, 138.0 (C_q), 128.6, 128.5, 128.4, 128.1, 128.0, 128.0, 127.8, 127.6, 127.6 (CH_{arom}), 98.2 (C-1), 81.5 (C-3), 79.6 (C-2), 75.4, 73.6, 73.1

(CH_2 Bn), 70.7 (C-4), 69.9 (C-5), 69.5 (C-6), 55.2 (OMe); HRMS: $[M+NH_4]^+$ calcd for $C_{28}H_{36}NO_6$ 482.25371, found 482.25357.

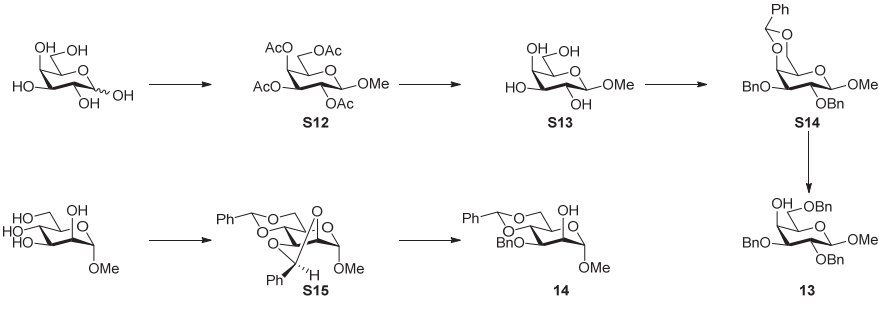


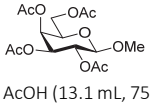
Methyl 2,3-di-*O*-benzyl-α-D-glucopyranoside (S11). Fully protected **S10** (9.25 g, 20 mmol) and *p*-TsOH·H_2O (380 mg, 2 mmol, 0.1 eq.) were added to MeOH (100 mL) and heated at 60°C for 15 min after all solids were dissolved and TLC analysis showed full conversion to a lower running spot. The reaction mixture was quenched with Et_3N (1 mL) and concentrated *in vacuo*. The crude product was purified by flash column chromatography (8/1 to 3/2 pentane/acetone) to give the tile compound as a white solid (7.4 g, 19.8 mmol, 99%) as a white solid. R_f: 0.33 (2/1 pentane/acetone). Spectroscopic data were in accord with those previously reported.[77,96] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.37 – 7.26 (m, 10H, CH_{arom}), 5.00 (d, 1H, *J* = 11.4 Hz, C*H*H Bn), 4.75 (d, 1H, *J* = 12.2 Hz, C*H*H Bn), 4.71 (d, 1H, *J* = 11.5 Hz, CH*H* Bn), 4.64 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.59 (d, 1H, *J* = 3.5 Hz, H-1), 3.78 (dd, 1H, *J* = 9.6, 8.6 Hz, H-3), 3.78 – 3.69 (m, 2H, H-6), 3.61 – 3.56 (m, 1H, H-5), 3.51 (dd, 1H, *J* = 9.8, 8.6 Hz, H-4), 3.48 (dd, 1H, *J* = 9.5, 3.5 Hz, H-2), 3.36 (s, 3H, CH_3 OMe), 2.46 (bs, 2H, OH); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.8, 138.1 ($C_{q\text{-}arom}$), 128.7, 128.6, 128.2, 128.1, 128.0, 127.9 (CH_{arom}), 98.2 (C-1), 81.4 (C-3), 79.9 (C-2), 75.5, 73.2 (CH_2 Bn), 70.8 (C-5), 70.3 (C-4), 62.3 (C-6), 55.3 (OMe).



Methyl (methyl 2,3-di-*O*-benzyl-α-D-glucopyranosyl uronate) (12). To a solution of diol **S11** (6.95 g, 18.6 mmol) in DCM (70 mL) and AcOH (0.1 mL) was added BAIB (14.95 g, 46.4 mmol, 2.5 eq.), TEMPO (580 mg, 3.7 mmol, 0.2 eq.) and H_2O (30 mL). The solution was stirred vigorously for 2.5 hours at room temperature, quenched by the addition of $Na_2S_2O_3$ (10% aq.) and this suspension stirred for 15 min. The mixture was extracted two times with EtOAc and the combined organic fractions were dried ($MgSO_4$), filtered, concentrated *in vacuo* and coevaporated with toluene once. The crude carboxylic acid was dissolved in DMF (75 mL) and cooled to 0°C. K_2CO_3 (7.7 g, 55.7 mmol, 3 eq.) and MeI (3.5 mL, 55.7 mmol, 3 eq.) were added and the reaction mixture stirred overnight. H_2O was added and the reaction mixture was extracted twice with EtOAc. The combined organic layers where dried ($MgSO_4$), filtered and concentrated in vacuo. Purification by flash column chromatography (1/0 to 9/1 toluene/acetone) followed by recrystallization from DCM/EtOAc/petroleum ether (1/1/23) gave the title product as white needles (3.84 g, 9.54 mmol, 52%, 2 steps). Spectroscopic data were in accord with those previously reported.[78] $[\alpha]_D^{23}$ = +19.0° (c=1.0, $CHCl_3$), lit.: $[\alpha]_D^{30}$ = +17.9° (c=0.5, $CHCl_3$)[78] ; IR: 700, 738, 1040, 1061, 1738, 2918, 3532; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.39 – 7.26 (m, 10H, CH_{arom}), 4.92 (d, 1H, *J* = 11.3 Hz, C*H*H Bn), 4.81 (d, 1H, *J* = 11.4 Hz, CH*H* Bn), 4.79 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.67 – 4.62 (m, 2H, CH*H* Bn, H-1), 4.15 (d, 1H, *J* = 8.9 Hz, H-5), 3.87 – 3.76 (m, 5H, H-3, H-4, CH_3 CO_2Me), 3.53 (dd, 1H, *J* = 8.9, 3.4 Hz, H-2), 3.42 (s, 3H, CH_3 OMe), 2.89 (bs, 1H, 4-OH); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 170.8 (C=O CO_2Me), 138.7, 138.0 ($C_{q\text{-}arom}$), 128.6, 128.3, 128.1, 128.0, 127.9 (CH_{arom}), 98.8 (C-1), 80.5 (C-3), 78.6 (C-2), 75.6, 73.7 (CH_2 Bn), 71.9 (C-4), 70.6 (C-5), 56.0 (OMe), 52.8 (CO_2Me); HRMS: $[M+Na]^+$ calcd for $C_{22}H_{26}O_7Na$ 425.15707, found 425.15649.

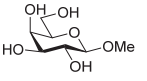
Preparation of acceptors **13** and **14**.



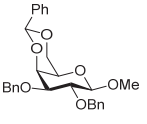


Methyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside (S12). Following the procedure of Kartha *et al.*[97] D-galactose (4.5 g, 25 mmol) was portionwise added to a mixture of 70% aq. $HClO_4$ (cat., 5 drops) and Ac_2O (14.2 mL, 150 mmol, 6 eq.). After stirring overnight a 33 wt% solution of HBr in AcOH (13.1 mL, 75 mmol, 3 eq.) was added and the reaction stirred at r.t. for 5 h. Solvents were evaporated by a water aspirator and the crude product was dissolved in EtOAc and washed with cold sat.aq. $NaHCO_3$ and brine. The organic phase was dried (Na_2SO_4) and concentrated *in vacuo*. The crude bromide was dissolved in MeOH (100 mL) and cooled to 0°C. Iodine (3.17 g, 12.5 mmol, 0.5 eq.) was added and the reaction was stirred for 2 h. The reaction mixture was

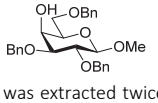
quenched by sat. aq. $Na_2S_2O_3$ and extracted with Et_2O twice. The organic layer was washed with sat. aq. $NaHCO_3$ and brine, dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Flash column chromatography (8/1 to 1/1 pentane/EtOAc) gave the methyl galactoside as an anomerically pure yellow oil (4.31 g, 11.9 mmol, 48% over three steps). Spectroscopic data were in accord with those previously reported.[98,99] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 5.40 (dd, 1H, *J* = 3.4, 1.2 Hz, H-4), 5.20 (dd, 1H, *J* = 10.5, 7.9 Hz, H-2), 5.03 (dd, 1H, *J* = 10.5, 3.4 Hz, H-3), 4.42 (d, 1H, *J* = 7.9 Hz, H-1), 4.25 – 4.11 (m, 2H, H-6), 3.93 (td, 1H, *J* = 6.7, 1.2 Hz, H-5), 3.52 (s, 3H, CH_3 OMe), 2.16 (s, 3H, CH_3 Ac), 2.07 (s, 3H, CH_3 Ac), 2.06 (s, 3H, CH_3 Ac), 1.99 (s, 3H, CH_3 Ac); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 170.4, 170.2, 170.1, 169.5 (C=O Ac), 102.0 (C-1), 71.0 (C-3), 70.6 (C-5), 68.8 (C-2), 67.1 (C-4), 61.3 (C-6), 57.0 (OMe), 20.8, 20.7, 20.7, 20.6 (CH_3 Ac).



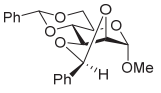
Methyl β-D-galactopyranoside (S13). Acetylated **S12** (4.31 g, 11.9 mmol) was dissolved in MeOH (50 mL) and NaOMe (325 mg, 6.0 mmol, 0.5 eq.) was added. After 30 min Amberlite H^+ was added until neutral pH was achieved and the resin was subsequently filtered off. The solution was concentrated *in vacuo* to give the crude tetra-ol. Spectroscopic data were in accord with those previously reported.[100] ^{1}H NMR (D_2O, 400 MHz, HSQC): δ 4.79 (bs, 4H, OH), 4.30 (d, 1H, *J* = 7.9 Hz, H-1), 3.90 (d, 1H, *J* = 3.5 Hz, H-4), 3.81 – 3.73 (m, 2H, H-6), 3.75 – 3.64 (m, 1H, H-5), 3.63 (dd, 1H, *J* = 9.9, 3.5 Hz, H-3), 3.55 (s, 3H, CH_3 OMe), 3.48 (dd, 1H, *J* = 9.9, 7.9 Hz, H-2); ^{13}C NMR (D_2O, 101 MHz, HSQC): δ 103.8 (C-1), 75.2 (C-5), 72.8 (C-3), 70.8 (C-2), 68.7 (C-4), 61.0 (C-6), 57.2 (OMe).



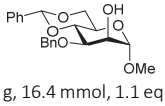
Methyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-galactopyranoside (S14). Crude **S13** (1.94 g, 10 mmol), benzaldehyde dimethyl acetal (0.30 mL, 20 mmol, 2 eq.) and *p*-TsOH·H_2O (475 mg, 2,5 mmol, 0.25 eq.) were dissolved in CH_3CN (50 mL) and DMF (15 mL) and the poorly soluble reaction mixture was stirred at 60°C, 350 mbar for 3 h. Et_3N (0.8 mL) was added and the reaction mixture was portioned between EtOAc and H_2O. The organic layer did not contain observable product, therefore the water layer was evaporated to give the crude product. Column chromatography (1:0 to 9/1 DCM/MeOH) gave the benzylidene protected galactoside as a waxy solid (1.73 g, 6.1 mmol, 61%). Spectroscopic data were in accord with those previously reported.[77,95,101] ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.55 – 7.46 (m, 2H), 7.40 – 7.34 (m, 3H), 5.55 (s, 1H), 4.36 (dd, 1H, *J* = 12.5, 1.5 Hz), 4.24 – 4.20 (m, 2H), 4.12 – 4.07 (m, 1H), 3.79 – 3.67 (m, 2H), 3.59 (d, 3H, *J* = 0.7 Hz), 3.49 (t, 1H, *J* = 1.6 Hz).The crude methyl 4,6-*O*-benzylidene-β-D-galactopyranoside was coevaporated with dry toluene twice before being dissolved in DMF (30 mL). Benzyl bromide (3.2 mL, 18.4 mmol, 3 eq.) and NaH (60% dispersion in mineral oil, 736 mg, 18.4 mmol, 3 eq.) were added and the reaction mixture was stirred overnight. H_2O was added and the mixture was extracted with EtOAc twice. The organic layer was washed with brine twice and dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude product was purified by flash column chromatography (8/1 to 3/1 pentane/EtOAc) to afford the benzylated product (2.11 g, 4.56 mmol, 75%). R_f: 0.63 (3/2 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[77] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.59 – 7.53 (m, 2H, CH_{arom}), 7.42 – 7.26 (m, 13H, CH_{arom}), 5.50 (s, 1H, C*H*Ph), 4.91 (d, 1H, *J* = 10.9 Hz, C*H*H Bn), 4.81 – 4.71 (m, 3H, CH*H* Bn, CH_2 Bn), 4.36 – 4.27 (m, 2H, H-1, H-6), 4.11 (dd, 1H, *J* = 3.7, 1.1 Hz, H-4), 4.02 (dd, 1H, *J* = 12.3, 1.8 Hz, H-6), 3.84 (dd, 1H, *J* = 9.7, 7.7 Hz, H-2), 3.60 – 3.53 (m, 4H, H-3, CH_3 OMe), 3.32 (d, 1H, *J* = 1.3 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 139.0, 138.5, 137.9 (C_q), 129.1, 128.5, 128.4, 128.2, 128.2, 127.9, 127.8, 127.6, 126.7 (CH_{arom}), 104.8 (C-1), 101.5 (CHPh), 79.3 (C-3), 78.6 (C-2), 75.4 (CH_2 Bn), 74.1 (C-4), 72.1 (CH_2 Bn), 69.4 (C-6), 66.5 (C-5), 57.2 (OMe).



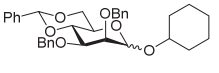
Methyl 2,3,6-tri-*O*-benzyl-β-D-galactopyranoside (13). To a solution of **S16** (2.10 g, 4.54 mmol) and $NaCNBH_3$ (1.7 g, 27.2 mmol, 6 eq.) in THF (60 mL), 4.0 M HCl in 1,4-dioxane (9 mL, 36 mmol, 7.9 eq.) was added. The reaction mixture was stirred for 1 h and then H_2O was added. The solution was extracted twice with DCM and the organic layer was washed with brine, dried with $MgSO_4$ en concentrated *in vacuo*. Flash column chromatography (9/1 to 1/1 pentane/EtOAc) provided the free alcohol as an oil (1.56 g, 3.36 mmol, 74%). R_f: 0.74 (3/2 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[77,102,103] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.41 – 7.21 (m, 15H, CH_{arom}), 4.88 (d, 1H, *J* = 11.1 Hz, C*H*H Bn), 4.71 (d, 1H, *J* = 11.0 Hz, CH*H* Bn), 4.67 (s, 2H, CH_2 Bn), 4.56 (s, 2H, CH_2 Bn), 4.26 (d, 1H, *J* = 7.7 Hz, H-1), 3.98 (d, 1H, *J* = 3.4 Hz, H-4)), 3.79 (dd, 1H, *J* = 9.9, 5.9 Hz, H-6), 3.72 (dd, 1H, *J* = 9.9, 6.0 Hz, H-6), 3.64 (dd, 1H, *J* = 9.4, 7.7 Hz, H-2), 3.59 – 3.50 (m, 4H, H-5, CH3 OMe), 3.46 (dd, 1H, *J* = 9.4, 3.4 Hz, H-3), 2.70 (s, 1H, 4-OH); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.6, 137.9, 137.8 (C_q), 128.4, 128.3, 128.0, 127.8, 127.8, 127.7, 127.7, 127.5 (CH_{arom}), 104.7 (C-1), 80.5 (C-3), 79.0 (C-2), 75.1, 73.6 (CH_2 Bn), 73.1 (C-5), 72.3 (CH_2 Bn), 69.2 (C-6), 66.8 (C-4), 56.9 (OMe); HRMS: $[M+Na]^+$ calcd for $C_{28}H_{33}O_6Na$ 487.20911, found 487.20848.



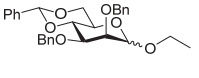
Methyl 2,3-*exo*;4,6-di-*O*-benzylidene-α-D-mannopyranoside (S15). To a solution of methyl α-D-mannoside (19.4 g, 100 mmol) in CH_3CN (120 mL) was added benzylidene dimethyl acetal (36 mL, 240 mmol, 2.4 eq.) and *p*-TsOH·H_2O (475 mg, 2.5 mmol, 0.025 eq.). The reaction mixture was stirred at 60°C and 500 mbar for 3 h and the volume was reduced by half. Sat. aq. $NaHCO_3$ was added to quench the reaction and the precipitate collected and washed with cold H_2O. The solids were recrystallized from EtOH/EtOAc to obtain two crops of white needles (total yield: 29.6 g, 80 mmol, 80% exo only). Spectroscopic data were in accord with those previously reported.[104] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.55 – 7.51 (m, 2H, CH_{arom}), 7.48 – 7.44 (m, 2H, CH_{arom}), 7.41 – 7.34 (m, 6H, CH_{arom}), 6.30 (s, 1H, C*H*$Ph_{2,3\ exo}$), 5.64 (s, 1H, C*H*$Ph_{4,6}$), 5.02 (s, 1H, H-1), 4.63 (dd, 1H, *J* = 7.8, 5.4 Hz, H-3), 4.40 – 4.32 (m, 1H, H-6), 4.14 (d, 1H, *J* = 5.4 Hz, H-2), 3.93 – 3.88 (m, 1H, H-4), 3.88 – 3.81 (m, 2H, H-5, H-6), 3.41 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.7, 137.3 (C_q), 129.3, 128.5, 128.4, 126.4, 126.2 (CH_{arom}), 103.1 ($CHPh_{2,3\ exo}$), 102.2 ($CHPh_{4,6}$), 99.0 (C-1), 77.6 (C-4), 75.7 (C-3), 75.4 (C-2), 69.1 (C-6), 60.5 (C-5), 55.4 (OMe).



Methyl 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (14). Compound **S15** (5.56 g, 15 mmol) was dissolved in 100 mL DCM and 150 mL Et_2O. A solution of $LiAlH_4$ (2.4 M in THF, 8 mL, 19.2 mmol, 1.3 eq.) was added to the reaction mixture at 0°C followed by addition of $AlCl_3$ (2.2 g, 16.4 mmol, 1.1 eq.). The reaction mixture was allowed to stir for 3 h at r.t. before being quenched by careful addition of EtOAc and H_2O. The mixture was extracted with EtOAc and the organic phase was washed with brine, dried $MgSO_4$ and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (6/1 to 1/1 pentane/EtOAc) gave the title compound as a colorless oil (5.37 g, 14.4 mmol, 96%). R_f: 0.38 (2/1 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[32,79,104] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.53 – 7.47 (m, 2H, CH_{arom}), 7.41 – 7.27 (m, 8H, CH_{arom}), 5.60 (s, 1H, C*H*Ph), 4.84 (d, 1H, *J* = 11.9 Hz, C*H*H Bn), 4.73 (d, 1H, *J* = 1.4 Hz, H-1), 4.69 (d, 1H, *J* = 11.9 Hz, CH*H* Bn), 4.27 (dd, 1H, *J* = 9.4, 4.0 Hz, H-6), 4.09 (t, 1H, *J* = 9.2 Hz, H-4), 4.01 (dt, 1H, *J* = 3.3, 1.6 Hz, H-2), 3.93 – 3.75 (m, 3H, H-3, H-5, H-5), 3.35 (s, 3H, CH_3 OMe), 2.82 (d, 1H, *J* = 1.7 Hz, 2-OH); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.1, 137.7 (C_q), 129.0, 128.6, 128.3, 128.0, 127.9, 126.2 (CH_{arom}), 101.7 (CHPh), 101.2 (C-1), 78.9 (C-4), 75.7 (C-3), 73.1 (CH_2 Bn), 69.9 (C-2), 69.0 (C-6), 63.3 (C-5), 55.0 (OMe); HRMS: $[M+Na]^+$ calcd for C21H24O6Na 395.14651, found 395.14638.

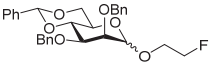


Cyclohexyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-mannopyranoside (1A). Donor **1** and cyclohexanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated and purified by flash column chromatography (1/0 to 9/1 pentane/EtOAc) to yield glycosylation product **1A** (50.9 mg, 51 µmol, 96%, α:β = 1:5). R_f: 0.43 (9/1 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[105,106] IR (neat): 694, 733, 964, 1026, 1047, 1084, 1361, 1452, 2857, 2857, 2930; Data for the β-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.55 – 7.23 (m, 15H, CH_{arom}), 5.61 (s, 1H, C*H*Ph), 5.02 (d, 1H, *J* = 12.5 Hz, C*H*H Bn), 4.91 (d, 1H, *J* = 12.5 Hz, CH*H* Bn), 4.67 (d, 1H, *J* = 12.5 Hz, C*H*H Bn), 4.58 (s, 1H, H-1), 4.58 (d, 1H, *J* = 12.5 Hz, CH*H* Bn), 4.30 (dd, 1H, *J* = 10.4, 4.9 Hz, H-6), 4.22 (t, 1H, *J* = 9.6 Hz, H-4), 3.94 (t, 1H, *J* = 10.3 Hz, H-6), 3.87 (d, 1H, *J* = 3.0 Hz, H-2), 3.70 (dt, 1H, *J* = 8.6, 4.7 Hz, CH Cy), 3.58 (dd, 1H, *J* = 9.9, 3.1 Hz, H-3), 3.31 (td, 1H, *J* = 9.9, 4.9 Hz, H-5), 2.06 – 0.99 (m, 10H, CH_2 Cy); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC): δ 138.68, 138.54, 137.79 (C_q), 129.05, 128.92, 128.85, 128.49, 128.40, 128.28, 128.22, 128.19, 127.84, 127.68, 127.62, 127.60, 127.58, 127.53, 126.18, 126.14, 125.21 (CH_{arom}), 101.48 (CHPh), 100.12 (C-1), 78.76 (C-4), 78.25 (C-3), 76.84 (CH Cy), 76.31 (C-2), 74.71 (CH_2 Bn), 72.39 (CH_2 Bn), 68.82 (C-6), 67.68 (C-5), 33.48, 31.57, 25.78, 23.87, 23.72 (CH_2 Cy); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): 100.1 ($J_{C1,H1}$ = 154 Hz, C-1 β); Diagnostic peaks α-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.64 (s, 0.20H, C*H*Ph), 4.89 – 4.79 (m, 0.60H, C*H*H Bn, CH*H* Bn, C-1), 4.71 (d, 0.20H, *J* = 12.3 Hz, CH*H* Bn), 4.00 (dd, 0.20H, *J* = 10.0, 3.2 Hz, H-2), 3.78 (dd, 0.20H, *J* = 3.1, 1.6 Hz, H-3), 3.54 – 3.49 (m, 0.20H, CH Cy); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC): δ 97.41 (C-1), 64.36 (C-5), 33.38, 31.31, 25.69, 25.25, 24.11 (CH_2 Cy); HRMS: $[M+Na]^+$ calcd for $C_{33}H_{38}O_6Na$ 553.25606, found 553.25531.

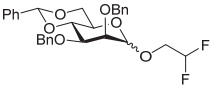


Ethyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-mannopyranoside (1B). Donor **1** and ethanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations and purified by flash column chromatography (1/0 to 9/1 pentane/EtOAc) to yield glycosylation product **1B** (33.5 mg, 70 µmol, 70%, α:β = 1:5). R_f: 0.43 (9/1 pentane/EtOAc). IR (neat): 696, 734, 893, 912, 968, 1004, 1049, 1088, 1373, 1452, 2866, 2926; Data for the β-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.53 – 7.28 (m, 15H, CH_{arom}), 5.62 (s, 1H, C*H*Ph), 4.99 (d, 1H, *J* = 12.4 Hz, C*H*H Bn), 4.89 (d, 1H, *J* = 12.4 Hz, CH*H* Bn), 4.68 (d, 1H, *J* = 12.6 Hz, C*H*H Bn), 4.58 (d, 1H, *J* = 12.5 Hz, CH*H* Bn), 4.46 (s, 1H, H-1), 4.31 (dd, 1H, *J* = 10.4, 4.9 Hz, H-6), 4.21 (t, 1H, *J* = 9.6 Hz, H-4), 4.02 – 3.89 (m, 3H, C*H*HCH_3 Et, H-2, H-6), 3.58 (dd, 1H, *J* = 9.9, 3.1 Hz, H-3), 3.56 – 3.47 (m, 1H, CH*H*CH_3 Et), 3.36 – 3.28 (m, 1H, H-5), 1.27 (t, 3H, *J* = 7.0 Hz, CH_3 Et); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC): δ 138.6, 138.5,

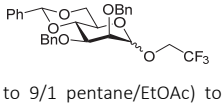
137.8 (C_q), 123.0, 128.9, 128.4, 128.3, 128.2, 127.7, 127.7, 127.6, 126.2, (CH_{arom}) 102.2 (C-1), 101.5 (CHPh), 78.8 (C-4), 78.0 (C-3), 75.9 (C-2), 74.8 (CH_2 Bn), 72.5 (CH_2 Bn), 68.8 (C-6), 67.7 (C-5), 65.7 (CH_2 Et), 15.3 (CH_3 Et); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 102.2 ($J_{C1,H1}$ = 153 Hz, C-1 β); Diagnostic peaks α-anomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.65 (s, 0.20H), 4.86 – 4.81 (m, 0.40H, C*H*H Bn, CH*H* Bn), 4.80 (d, 0.20H, *J* = 1.5 Hz, H-1), 4.74 (d, 0.20H, *J* = 12.3 Hz, C*H*H Bn), 3.74 – 3.66 (m, 0.20H, CH*H*CH_3), 3.46 – 3.39 (m, 0.20H, CH*H*CH_3 Et); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC): δ 128.9, 128.5, 128.4, 128.3, 128.2, 127.9, 127.6, 126.2 (C_q), 101.6 (CHPh), 99.3 (C-1), 79.4 (C-3), 76.5 (C-4), 76.4 (C-2), 73.7 (CH_2 Bn), 73.3 (CH_2 Bn), 69.3 (C-6), 64.3 (C-5) 63.3 (CH_2 Et), 15.1 (CH_3 Et); HRMS: $[M+Na]^+$ calcd for $C_{29}H_{32}O_6Na$ 499.20911, found 499.20846.



2-Fluoroethyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-mannopyranoside (1C). Donor **1** and 2-fluoroethanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated and purified by flash column chromatography (1/0 to 4/1 pentane/EtOAc) to yield glycosylation product **1C** (42.7 mg, 86 µmol, 86%, α:β = 1:5). R_f: 0.18 (9/1 pentane/EtOAc). IR (neat): 696, 738, 802, 887, 1025, 1043, 1066, 1086, 1261, 1371, 1454, 2870; Data for the β-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.66 – 7.32 (m, 15H, CH_{arom}), 5.62 (s, 1H, C*H*Ph), 4.99 (d, 1H, *J* = 12.3 Hz, C*H*H Bn), 4.89 (d, 1H, *J* = 12.3 Hz, CH*H* Bn), 4.70 – 4.51 (m, 5H, C*H*H Bn, CH*H* Bn, H-1, CH_2*CH*HF, CH_2CH*H*F), 4.30 (dd, 1H, *J* = 10.4, 4.8 Hz, H-6), 4.22 (t, 1H, *J* = 9.6 Hz, H-4), 4.08 (ddt, 1H, *J* = 35.7, 12.2, 3.0 Hz, C*H*HCH_2F), 3.98 (d, 1H, *J* = 2.9 Hz, H-2), 3.92 (t, 1H, *J* = 10.3 Hz, H-6), 3.80 (dtd, 1H, *J* = 22.6, 11.9, 7.8, 2.4 Hz, CH*H*CH_2F), 3.59 (dd, 1H, *J* = 9.9, 3.1 Hz, H-3), 3.33 (td, 1H, *J* = 9.7, 4.9 Hz, H-5); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC): δ 138.4, 138.4, 137.6 (C_q), 131.2, 129.4, 129.0, 128.8, 128.4, 128.3, 128.2, 127.7, 127.7, 126.2, 124.9 (CH_{arom}), 102.3 (C-1), 101.5 (CHPh), 82.8 (d, *J* = 169.74 Hz, CH_2F), 78.6 (C-4), 77.8 (C-3), 75.7 (C-2), 75.0 (CH_2 Bn), 72.5 (CH_2 Bn), 69.0 (d, *J* = 19.7 Hz, *C*$H_2$$CH_2$F), 67.7 (C-6). ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 102.3 ($J_{C1,H1}$ = 156 Hz, C-1 β); Diagnostic peaks α-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.62 (s, 0.20H, C*H*Ph), 4.93 – 4.80 (m, 0.60H, C*H*H Bn, CH*H* Bn, H-1); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC): δ 99.7 (C-1), 82.5 (d, *J* = 170 Hz, CH_2F), 79.2 (C-4), 76.5 (C-3), 76.4 (C-2), 73.8 (CH_2 Bn), 73.3 (CH_2 Bn), 68.9 (C-6), 66.7 (d, *J* = 19.9 Hz, *C*$H_2$$CH_2$F), 64.4 (C-5); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 99.7 ($J_{C1,H1}$ = 170 Hz, C-1 α); HRMS: $[M+Na]^+$ calcd for $C_{29}H_{31}FO_6Na$ 517.19969, found 517.19888.

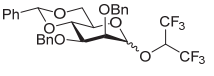


2,2-Difluoroethyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-mannopyranoside (1D). Donor **1** and 2,2-difluoroethanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations and purified by flash column chromatography (1/0 to 4/1 pentane/EtOAc) to yield glycosylation product **1D** (46.1 mg, 90 µmol, 90%, α:β = 1:5). R_f: 0.50 (9/1 pentane/EtOAc). IR (neat): 694, 744, 795, 1026, 1094, 1261, 1369, 1454, 2868; Data for the β-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.68 – 7.27 (m, 15H, CH_{arom}), 5.90 (dddd, 1H, *J* = 54.8, 5.1, 2.8, 1.5 Hz, CHF_2) 5.62 (s, 1H, C*H*Ph), 4.94 (d, 1H, *J* = 12.2 Hz, C*H*H Bn), 4.86 (d, 1H, *J* = 12.2 Hz, CH*H* Bn), 4.70 (d, 1H, *J* = 12.5 Hz, C*H*H Bn), 4.60 (d, 1H, *J* = 12.4 Hz, CH*H* Bn), 4.51 (s, 1H. H-1), 4.31 (dd, 1H, *J* = 10.4, 4.9 Hz, H-6), 4.22 (t, 1H, *J* = 9.6 Hz, H-4), 4.05 (dtd, 1H, *J* = 20.7, 11.1, 2.9 Hz, C*H*HCHF_2), 3.98 – 3.88 (m, 2H, H-2, H-6), 3.82 – 3.65 (m, 1H, CH*H*CHF_2), 3.59 (dd, 1H, *J* = 9.9, 3.1 Hz, H-3), 3.33 (td, 1H, *J* = 9.7, 4.8 Hz, H-5); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC): δ 138.3, 138.2, 137.5 (C_q), 128.8, 128.5, 128.3, 127.7, 126.2 (C_{arom}), 115.4 (t, *J* = 241.9, CHF_2), 102.3 (C-1), 101.6 (CHPh), 78.6 (C-4), 77.8 (C-3), 75.5 (C-2), 75.1 (CH_2 Bn), 72.6 (CH_2 Bn), 68.5 (t, *J* = 33.0 Hz, *C*$H_2$$CHF_2$), 68.5 (C-6), 67.8 (C-5); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): 102.3 ($J_{C1,H1}$ = 156 Hz, C-1 β); Diagnostic peaks α-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.98 (dt, 0.03 H, *J* = 5.7, 4.1 Hz, CHF_2), 5.84 (dt, 0.10H, *J* = 5.9, 4.1 Hz, CHF_2), 5.70 (dt, 0.03H, *J* = 6.1, 4.1 Hz, CHF_2), 4.84 (m, 0.34H, C-1, C*H*H Bn), 4.72 (d, 0.17H, *J* = 12.1 Hz, CH*H* Bn), 4.66 (d, 0.17H, *J* = 12.2 Hz, C*H*H Bn); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC): δ 115.4 (t, *J* = 240.10, CHF_2), 101.6 (CHPh), 100.1 (C-1), 79.0 (C-4), 76.3 (C-3), 76.2 (C-2), 73.9 (CH_2 Bn), 73.4 (CH_2 Bn), 68.5 (C-6), 64.8 (C-5); HRMS: $[M+Na]^+$ calcd for $C_{29}H_{30}F_2O_6Na$ 535.19027, found 535.18950.

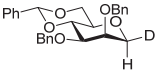


2,2,2-Trifluoroethyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-mannopyranoside (1E). Donor **1** and 2,2,2-trifluoroethanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations and purified by flash column chromatography (1/0 to 9/1 pentane/EtOAc) to yield glycosylation product **1E** (41.7 mg, 79 µmol, 79%, α:β = 1:3.4). R_f: 0.60 (9/1 pentane/EtOAc). IR (neat): 696, 737, 1028, 1057, 1085, 1161, 1277, 1454, 2870; Data for the β-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.50 – 7.28 (m, 15H, CH_{arom}) 5.62 (s, 1H, C*H*Ph), 4.96 (d, 1H, *J* = 12.2 Hz, C*H*H Bn), 4.87 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.69 (d, 1H, *J* = 12.5 Hz, C*H*H Bn), 4.59 (d, 1H, *J* = 12.5 Hz, CH*H* Bn), 4.57 (s, 1H, H-1), 4.31 (dd, 1H, *J* = 10.4, 4.9 Hz, C-6), 4.28 – 4.17 (m, 2H, C-4, C*H*HCF_3), 4.01 – 3.86 (m, 3H, H-2, H-6, CH*H*CF_3), 3.59 (dd, 1H, *J* = 9.9, 3.1 Hz, H-3), 3.34 (td, 1H, *J* = 9.8, 4.9 Hz, H-5); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC): δ 138.2, 138.0, 137.5 (C_q), 129.1, 128.9, 128.5, 128.3, 127.9, 127.8, 127.7, 126.2 (C_{arom}), 123.7 (q, *J* = 277.6 Hz, CF_3) 101.9 (C-1), 101.6 (CHPh),

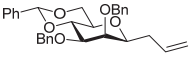
78.4 (C-4), 77.7 (C-3), 77.5 (C-2), 75.1 (CH_2 Bn), 75.0 (CH_2 Bn), 72.6 (C-6), 68.4 (C-5), 66.2 (q, *J* = 34.9 Hz, CH_2CF_3); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): 101.9 ($J_{C1,H1}$ = 157 Hz, C-1 β); Diagnostic peaks α-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.64 (s, 0.29H, C*H*Ph), 4.88 – 4.82 (m, 0.87H, C*H*H Bn, CH*H* Bn, H-1), 4.73 – 4.64 (m, 0.58H, C*H*H Bn, CH*H* Bn); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC): δ 101.6 (CHPh), 100.1 (C-1), 78.9 (C-4), 76.2 (C-3), 76.0 (C-2), 74.1 (CH_2 Bn), 73.5 (CH_2 Bn), 68.7 (C-6), 65.0 (C-5); HRMS: $[M+Na]^+$ calcd for $C_{29}H_{29}F_3O_6Na$ 553.18084, found 553.18021.



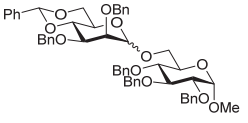
1,1,1,3,3,3-Hexafluoro-2-propyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-mannopyranoside (1F). Donor **1** and 1,1,1,3,3,3-hexafluoro-2-propanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 120 hours at -40°C) and purified by flash column chromatography (1/0 to 9/1 pentane/EtOAc) to yield glycosylation product **1F** (33.6 mg, 34 µmol, 56%, α:β = 3.3:1). R_f: 0.81 (8/2 pentane/EtOAc). IR (neat): 694, 898, 977, 1058, 1091, 1195, 1217, 1287, 136, 2924; Data for the α-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.54 – 7.27 (m, 15H, CH_{arom}), 5.64 (s, 1H, C*H*Ph), 4.95 (s, 1H, H-1), 4.86 (d, 1H, *J* = 5.5 Hz, C*H*H Bn), 4.82 (d, 1H, *J* = 8.9 Hz, CH*H* Bn), 4.69 (d, 1H, *J* = 2.8 Hz, C*H*H Bn), 4.65 (d, 1H, *J* = 7.7 Hz, CH*H* Bn), 4.38 – 4.19 (m, 3H, H-3, H-6, $CH(CF_3)_2$), 3.92 (d, 1H, *J* = 4.9 Hz, H-4), 3.89 – 3.83 (m, 2H, H-6, H-5); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC): δ 138.5, 137.5, 137.4 (C_q), 129.1, 128.7, 128.5, 128.4, 128.3, 127.8, 127.7, 126.1 (CH_{arom}), 121.6 (q, *J* = 282.7 Hz, CF_3), 101.8 (C-1), 101.6 (CHPh), 78.4 (C-3), 76.1 (C-4), 75.5 (C-2), 74.3 (CH_2 Bn), 73.8 (CH_2 Bn), 72.4 (hept, *J* = 32.7 Hz, $CH(CF_3)_2$), 72.1 (CH_2 Bn), 68.3 (C-6), 65.8 (C-5);^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 101.8 ($J_{C1,H1}$ = 175 Hz, C-1 α); Diagnostic peaks β-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC): δ 5.61 (s, 0.30H, C*H*Ph), 4.82 (d, 0.60H, *J* = 11.9 Hz, C*H*H Bn), 4.79 (s, 0.30H, H-1,), 4.69 (d, 0.30H, *J* = 12.9 Hz, CH*H* Bn), 4.02 (d, 0.30H, *J* = 2.9 Hz, H-2), 3.61 (dd, 0.30H, *J* = 9.9, 3.1 Hz, H-3), 3.36 (td, 0.30H, *J* = 9.9, 4.9 Hz, H-5); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC, HMBC): δ 101.3 (C-1), 72.6 (C-6), 68.2 (C-5); ^{13}C HMBC-GATED NMR (101 MHz, $CDCl_3$): δ 101.3 ($J_{C1,H1}$ = 159 Hz, C-1 β); HRMS: $[M+Na]^+$ calcd for $C_{30}H_{28}F_6O_6Na$ 621.16823, found 621.16790.



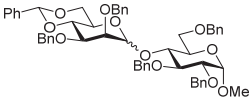
1-[^{2}H]-1,5-anhydro-2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannitol (1G). Donor **1** and triethylsilane-D were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 24 hours at -40°C) and purified by flash column chromatography (19/1 to 3/1 pentane/Et_2O) to yield glycosylation product **42** (25.8 mg, 60 µmol, 60%, α:β = <1:20). R_f: 0.2 (4/1 pentane/Et_2O). Spectroscopic data of the non-dueterated mannitol were in accord with those previously reported.[107] $[\alpha]_D^{22}$ = -27.2° (*c* = 0.5, $CHCl_3$); IR (neat): 694, 733, 1092, 1119, 1452, 2349, 2866; Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.54 – 7.48 (m, 2H, CH_{arom}), 7.44 – 7.26 (m, 13H, CH_{arom}), 5.65 (s, 1H, C*H*Ph), 4.82 (d, 1H, *J* = 12.6 Hz, C*H*H Bn), 4.81 (d, 1H, *J* = 12.5 Hz, C*H*H Bn), 4.76 (d, 1H, *J* = 12.5 Hz, CH*H* Bn), 4.68 (d, 1H, *J* = 12.4 Hz, CH*H* Bn), 4.28 (dd, 1H, *J* = 11.2, 4.1 Hz, H-6), 4.25 (t, 1H, *J* = 10.1 Hz, H-4), 3.85 (t, 1H, *J* = 10.3 Hz, H-6), 3.79 (d, 1H, *J* = 3.3 Hz, H-2), 3.68 (dd, 1H, *J* = 9.8, 3.3 Hz, H-3), 3.42 (s, 1H, H-1), 3.34 (td, 1H, *J* = 9.7, 4.9 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.6, 138.3, 137.8 (C_q), 128.9, 128.5, 128.4, 128.3, 128.2, 127.9, 127.7, 127.7, 126.1 (CH_{arom}), 101.5 (CHPh), 79.4 (C-4), 78.6 (C-3), 74.4 (C-2), 72.7 (CH_2 Bn), 72.5 (C-5), 72.4 (CH_2 Bn), 68.8 (t, *J* = 22 Hz, C-1), 68.7 (C-6); ^{2}H NMR ($CHCl_3$, 77 MHz): δ 4.08 (D-1); HRMS: $[M+H]^+$ calcd for $C_{27}H_{28}DO_5$ 434.20723, found 434.20691.



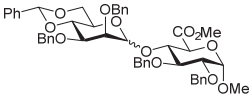
Allyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-1-deoxy-β-D-mannopyranose (1H). Donor **1** and allyl trimethylsilane were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 96 hours at -40°C) and purified by flash column chromatography (1/0 to 9/1 pentane/EtOAc) to yield glycosylation product **1H** (20.7 mg, 44 µmol, 44%, α:β = <1:20). R_f: 0.80 (9/1 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[72] $[\alpha]_D^{26}$ = -19.6° (*c* = 0.5, $CHCl_3$); IR (neat): 696, 1028, 1097, 1454, 2860, 2924; Data for the β-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, NOESY): δ 7.52 – 7.26 (m, 15H, CH_{arom}), 5.76 – 5.59 (m, 1H, C*H*CH_2 allyl), 5.64 (s, 1H, C*H*Ph), 5.11 – 4.98 (m, 3H, C*H*H Bn, CHCH_2 allyl), 4.92 (d, 1H, *J* = 12.3 Hz, C*H*H Bn), 4.76 (d, 1H, *J* = 12.3 Hz, CH*H* Bn), 4.69 (d, 1H, *J* = 11.4 Hz, CH*H* Bn), 4.35 – 4.16 (m, 2H, H-4, H-6), 3.84 (t, 1H, *J* = 10.3 Hz, H-6), 3.80 (d, 1H, *J* = 2.2 Hz, H-2), 3.73 (dd, 1H, *J* = 9.8, 2.9 Hz, H-3), 3.45 (t, 1H, *J* = 6.8 Hz, H-1), 3.38 (td, 1H, *J* = 9.8, 4.9 Hz, H-5), 2.46 (dt, 1H, *J* = 13.5, 6.7 Hz, C*H*HCH allylic), 2.25 (dt, 1H, *J* = 14.3, 7.2 Hz, CH*H*CH allylic); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC, HMBC): δ 138.8, 138.6, 137.9 (C_q), 134.4 (*CH*CH_2 allyl), 128.9, 128.6, 128.5, 128.4, 128.3, 127.8, 127.7, 127.7, 126.2 (CH_{arom}), 117.6 (CHCH_2 allyl), 101.5 (CHPh), 80.9 (C-3), 79.8 (C-1), 79.7 (C-4), 76.6 (C-2), 75.1 (CH_2 Bn), 73.3 (CH_2 Bn), 72.1 (C-5), 68.8 (C-6), 35.6 (CH_2CH allylic); HRMS: $[M+H]^+$ calcd for $C_{30}H_{33}O_5$ 473.23225, found 473.23219.



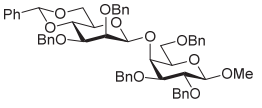
Methyl 6-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-mannopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (20). Donor **1** and acceptor **10** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 16 hours at -40°C) and purified by flash column chromatography (9/1 to 7/3 pentane/EtOAc) to yield glycosylation product **20** (86.6mg, 97 µmol, 97%, α:β = 1:10). R_f: 0.67 (7/3 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[105,108,109] $[\alpha]_D^{26}$ +5.2° (*c* = 1, $CHCl_3$, 546 nm), $[\alpha]_D^{26}$ 0.0° (*c* = 1, $CHCl_3$, 589 nm), (lit:[108] $[\alpha]_D^{20}$ = -1.7° (*c* = 1.8, $CHCl_3$), lit:[105] $[\alpha]_D^{27}$ = -5.8° (*c* = 0.94, $CHCl_3$)); IR (neat): 731, 1026, 1049, 1084, 1452, 2872; Data for the β-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.58 – 7.05 (m, 30H, CH_{arom}), 5.59 (s, 1H, C*H*Ph), 5.03 (d, 1H, *J* = 10.9 Hz, C*H*H Bn), 4.92 (d, 1H, *J* = 12.3 Hz, C*H*H Bn), 4.86 – 4.76 (m, 4H, C*H*H Bn, C*H*H Bn, CH*H* Bn, CH*H* Bn), 4.72 (d, 1H, *J* = 12.5 Hz, C*H*H Bn), 4.67 (d, 1H, *J* = 12.2 Hz, CH*H* Bn), 4.61 (d, 1H, *J* = 12.6 Hz, CH*H* Bn), 4.58 (d, 1H, *J* = 3.5 Hz, H-1), 4.50 (d, 1H, *J* = 11.6 Hz, CH*H* Bn), 4.25 (dd, 1H, *J* = 10.4, 4.8 Hz, H-6'), 4.18 (t, 1H, *J* = 9.6 Hz, H-4'), 4.08 (m, 2H, H-1', H-6), 4.02 (t, 1H, *J* = 9.3 Hz, H-4), 3.91 (t, 1H, *J* = 10.3 Hz, H-6'), 3.80 – 3.72 (m, 1H, H-2), 3.69 (d, 1H, *J* = 2.9 Hz, H-2'), 3.47 (m, 4H, H-3, H-3', H-5, H-6), 3.33 (s, 3H, CH_3 OMe), 3.22 (td, 1H, *J* = 9.8, 4.8 Hz, H-5'); ^{13}C-APT NMR (101 MHz, $CDCl_3$): δ 138.9, 138.5, 138.5, 138.5, 138.1, 137.7 (C_q), 129.0, 128.7, 128.6, 128.5, 128.5, 128.5, 128.3, 128.3, 128.2, 128.1, 128.1, 127.8, 127.8, 127.7, 126.1 (CH_{arom}), 102.1 (H-1'), 101.5 (CHPh), 97.9 (C-1), 82.3 (C-4), 79.9 (C-3), 78.8 (C-4), 77.9 (C-3'), 76.8 (C-5), 75.8 (CH_2 Bn), 75.7 (C-2'), 74.8 (CH_2 Bn), 74.6 (CH_2 Bn), 73.5 (CH_2 Bn), 72.6 (CH_2 Bn), 69.7 (C-2), 68.7 (C-6'), 68.3 (C-6), 67.7 (C-5'), 55.2 (CH_3 OMe); HRMS: $[M+Na]^+$ calcd for $C_{55}H_{58}O_{11}Na$ 917.38713, found 917.38729.



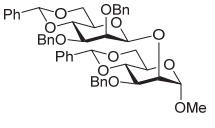
Methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-mannopyranosyl)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (21). Donor **1** and acceptor **11** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 16 hours at -40°C) and purified by flash column chromatography (9/1 to 7/3 pentane/EtOAc) to yield glycosylation product **21** (67.4 mg, 75 µmol, 75%, α:β = 1:9). R_f: 0.67 (7/3 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[105,108–110] $[\alpha]_D^{26}$ –15.8° (*c* = 1, $CHCl_3$), (lit:[110] $[\alpha]_D^{25}$ = –15.5° (*c* = 0.8, $CHCl_3$)); IR (neat): 735, 1028, 1083, 1452, 2862; Data for the β-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.46 – 7.21 (m, 25H, CH_{arom}), 5.51 (s, 1H, C*H*Ph), 5.05 (d, 1H, *J* = 10.6 Hz, C*H*H Bn), 4.84 – 4.70 (m, 5H, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, C*H*H Bn), 4.70 – 4.52 (m, 4H, CH*H* Bn, CH*H* Bn, C*H*H Bn, H-1), 4.36 (s, 1H, H-1'), 4.28 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.12 – 4.01 (m, 2H, H-4', H-6), 3.94 – 3.81 (m, 2H, H-3, H-4), 3.63 (d, 1H, *J* = 2.9 Hz, H-2'), 3.62 – 3.47 (m, 4H, H-5, H-2, H-6, H-6', H-6'), 3.47, 3.40 (s, 3H, CH_3 OMe), 3.32 (dd, 1H, *J* = 9.8, 3.0 Hz, H-3'), 3.05 (td, 1H, *J* = 9.7, 4.8 Hz, H-5'); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC): δ 139.5, 138.8, 138.7, 138.4, 137.8, 137.6 (C_q), 128.9, 128.7, 128.6, 128.5, 128.5, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.6, 127.6, 127.4, 127.3, 126.2 (CH_{arom}), 101.7 (C-1'), 101.4 (CHPh), 98.5 (C-1), 80.4 (C-4), 79.1 (C-2), 78.8 (C-4'), 78.4 (C-3'), 77.8 (C-3), 77.1 (C-2), 75.4 (CH_2 Bn), 75.1 (CH_2 Bn), 73.8 (CH_2 Bn), 73.7 (CH_2 Bn), 72.6 (CH_2 Bn), 69.7 (C-5), 68.7 (C-6), 68.4 (C-6'), 67.4 (C-5), 55.5 (CH_3 OMe); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): 101.7 ($J_{C1,H1}$ = 156 Hz, C-1 β); Diagnostic peaks α-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.60 (s, 0.11H, C*H*Ph), 5.30 (d, 0.11H, *J* = 1.3 Hz, C-1'); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC): δ 101.5 (C-1'), 101.4 (CHPh); HRMS: $[M+Na]^+$ calcd for $C_{55}H_{58}O_{11}Na$ 917.38713, found 917.38706.



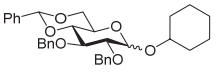
Methyl (methyl [4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-mannopyranosyl]-2,3-di-*O*-benzyl-α-D-glucopyranosyl uronate) (22). Donor **1** and acceptor **12** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 48 hours at -40°C) and purified by flash column chromatography (9/1 to 7/3 pentane/EtOAc) to yield glycosylation product **22** (72.8 mg, 87 µmol, 87%, α:β = 1:10). R_f: 0.65 (7/3 pentane/EtOAc); $[\alpha]_D^{26}$ = -19.2° (*c* = 1, $CHCl_3$); IR (neat): 735, 1045, 1084, 1454, 1748, 2866; Data for the β-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.55 – 7.24 (m, 25H, CH_{arom}), 5.54 (s, 1H, C*H*Ph), 5.06 (d, 1H, *J* = 10.6 Hz, C*H*H Bn), 4.88 – 4.71 (m, 5H, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*HBn, C*H*H Bn), 4.67 – 4.53 (m, 4H, CH*H* Bn, CH*H* Bn, H-1), 4.45 (s, 1H, H-1), 4.17 – 4.01 (m, 3H, H-4, H-4', H-6'), 3.95 – 3.85 (m, 2H, H-3, H-5), 3.82 – 3.75 (m, 1H, H-2'), 3.65 – 3.55 (m, 4H, H-6', CH_3 CO_2Me), 3.55 – 3.47 (m, 2H, H-2, H-3'), 3.44 (s, 3H, CH_3 OMe), 3.19 (td, 1H, *J* = 9.6, 4.8 Hz, H-5'); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC): δ 170.2 (C=O CO_2Me), 139.2, 138.7, 138.5, 138.1, 137.7 (C_q), 128.6, 128.5, 128.4, 128.3, 128.2, 128.2, 128.1, 127.7, 127.7, 127.6, 127.4, 126.2 (CH_{arom}), 102.5 (H-1'), 101.5 (CHPh), 98.9 (C-1), 80.2 (C-3/C-5), 79.8 (C-3/C-5), 78.7 (C-4'), 78.5 (H-2, H-3'), 77.9 (C-2'), 77.2 (CH_2 Bn), 75.6 (CH_2 Bn), 75.2 (CH_2 Bn), 74.0 (CH_2 Bn), 72.7 (CH_2 Bn), 69.7 (C-6), 68.6 (C-6'), 67.7 (C-5'), 56.0 (CH_3 CO_2Me) , 52.5 (CH_3 OMe); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 102.5 ($J_{C1,H1}$ = 157 Hz, C-1 β); Diagnostic peaks α-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.58 (s, 0.10H, C*H*Ph), 5.27 (s, 0.10H, H-1'), 4.98 (d, 0.10H, *J* = 11.4 Hz, C*H*H Bn), 4.31 (d, 0.10H, *J* = 11.9 Hz, CH*H* Bn); ^{13}C-APT NMR (101 MHz, $CDCl_3$): δ 101.54 (CHPh), 100.45 (C-1'), 98.63 (C-1); HRMS: $[M+Na]^+$ calcd for $C_{49}H_{52}O_{12}Na$ 855.33510, found 855.33507.



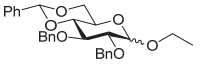
Methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-mannopyranosyl)-2,3,6-tri-*O*-benzyl-β-D-galactopyranoside (23). Donor **1** and acceptor **13** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 16 hours at -40°C) and purified by flash column chromatography (9/1 to 7/3 pentane/EtOAc) to yield glycosylation product **23** (62.7 mg, 70 µmol, 70%, α:β = <1:20). R_f: 0.80 (7/3 pentane/EtOAc); $[\alpha]_D^{26}$ = -26.8° (*c* = 1, $CHCl_3$); IR (neat): 737, 1072, 1454, 2866; Data for the β-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.46 – 7.14 (m, 30H, CH_{arom}), 5.59 (s, 1H, C*H*Ph), 4.96 (d, 1H, *J* = 12.4 Hz, C*H*H Bn), 4.91 (d, 1H, *J* = 11.0 Hz, C*H*H Bn), 4.86 (d, 1H, *J* = 12.4 Hz, CH*H* Bn), 4.79 (s, 1H, H-1'), 4.78 (d, 1H, *J* = 11.6 Hz, C*H*H Bn), 4.68 (d, 1H, *J* = 11.0 Hz, CH*H* Bn), 4.62 – 4.47 (m, 5H, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.31 (d, 1H, *J* = 7.7 Hz, H-1), 4.21 – 4.09 (m, 3H, H-4', H-6'), 4.01 (d, 1H, *J* = 3.0 Hz, H-2'), 3.90 – 3.81 (m, 2H, H-6, H-6'), 3.72 (dd, 1H, *J* = 9.8, 5.7 Hz, H-6), 3.67 (dd, 1H, *J* = 9.6, 7.7 Hz, H-2), 3.63 – 3.55 (m, 4H, H-5, CH_3 OMe), 3.52 (dd, 1H, *J* = 9.6, 3.0 Hz, H-3), 3.40 (dd, 1H, *J* = 9.9, 3.1 Hz, H-3'), 3.18 (td, 1H, *J* = 9.8, 4.9 Hz, H-5); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC): δ 138.9, 138.8, 138.5, 138.4, 138.2, 137.6 (C_q), 129.0, 128.7, 128.7, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 128.0, 127.8, 127.7, 127.6, 127.6, 127.5, 126.1 (CH_{arom}), 105.1 (C-1), 102.6 (C-1'), 101.4 (CHPh), 81.8 (H-3), 79.5 (H-2), 78.5 (C-3'), 78.5 (C-4'), 75.4 (C-2'), 75.1 (CH_2 Bn), 74.7 (CH_2 Bn), 73.7 (CH_2 Bn), 73.6 (H-5), 73.6 (CH_2 Bn), 73.3 (C-4), 72.2(CH_2 Bn), 69.5 (C-6), 68.7 (C-6'), 67.8 (C-5), 57.2 (CH_3 OMe); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 102.6 ($J_{C1,H1}$ = 159 Hz, C-1 β); HRMS: $[M+Na]^+$ calcd for $C_{55}H_{58}O_{11}Na$ 917.38713, found 917.38696.



Methyl 2-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-mannopyranosyl)-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (24). Donor **1** and acceptor **14** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 16 hours at -40°C) and purified by flash column chromatography (9/1 to 7/3 pentane/EtOAc) to yield glycosylation product **24** (70.2 mg, 87 µmol, 87%, α:β = <1:20). R_f: 0.68 (7/3 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[108–111] $[\alpha]_D^{26}$ –44.4° (*c* = 1, $CHCl_3$); (lit:[110] $[\alpha]_D^{25}$ = –44.2° (*c* = 4.2, $CHCl_3$), lit:[111] $[\alpha]_D^{20}$ = –44.8° (*c* = 3.9, $CHCl_3$)); IR (neat): 733, 1002, 1028, 1055, 1083, 1452, 2862; Data for the β-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.53 – 7.16 (m, 25H, CH_{arom}), 5.60 (s, 1H, C*H*Ph), 5.51 (s, 1H, C*H*Ph), 5.06 (d, 1H, *J* = 12.3 Hz, C*H*H Bn), 4.97 (d, 1H, *J* = 12.3 Hz, CH*H* Bn), 4.81 – 4.56 (m, 6H, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, H-1, H-1'), 4.30 – 4.18 (m, 4H, H-2, H-4´, H-6, H-6'), 4.10 (t, 1H, *J* = 9.2 Hz, H-4), 3.98 (d, 1H, *J* = 2.8 Hz, H-2'), 3.94 (dd, 1H, *J* = 10.0, 3.2 Hz, H-3) 3.88 (t, 1H, *J* = 10.3 Hz, H-6'), 3.78 (m, 2H, H-5, H-6), 3.59 (dd, 1H, *J* = 9.9, 3.0 Hz, H-3'), 3.46 – 3.21 (m, 4H, H-5', CH_3 OMe); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC): δ δ 139.0, 138.7, 138.5, 137.7, 137.7 (C_q), 129.0, 128.7, 128.4, 128.3, 128.3, 128.2, 127.7, 127.6, 127.6, 127.4, 126.2, 126.2 (CH_{arom}), 101.7 (CHPh), 101.5 (CHPh), 101.0 (C-1'), 99.6 (C-1), 78.8 (C-4), 78.6 (H-4'), 77.8 (C-3'), 76.1 (C-2'), 75.3 (H-2), 74.7 (H-3), 74.2 (CH_2 Bn), 72.4 (CH_2 Bn), 71.5 (CH_2 Bn), 69.1 (C-6), 68.7 (C-6'), 67.9 (C-5'), 64.2 (C-5), 55.1 (CH_3 OMe); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 101.0 ($J_{C1,H1}$ = 154 Hz, C-1' β); HRMS: $[M+Na]^+$ calcd for $C_{48}H_{50}O_{11}Na$ 825.32453, found 825.32425.

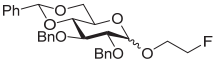


Cyclohexyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene- α/β-D-glucopyranoside (2A). Donor **2** and cyclohexanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations and purified by flash column chromatography (1/0 to 0/1 pentane/toluene to 6% EtOAc in toluene) to yield glycosylation product **2A** (37.8 mg, 71 µmol, 71%, α:β = 1:5). R_f: 0.22 (toluene). Spectroscopic data were in accord with those previously reported.[65] IR (neat): 696, 735, 746, 997, 1028, 1049, 1072, 1366, 1452, 1497, 2857, 2930; Data for the β-anomer:^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.51 – 7.46 (m, 2H, CH_{arom}), 7.41 – 7.24 (m, 13H, CH_{arom}), 5.56 (s, 1H, C*H*Ph), 4.94 (d, 1H, *J* = 10.8 Hz, C*H*H Bn), 4.90 (d, 1H, *J* = 11.1 Hz, C*H*H Bn), 4.79 (d, 1H, *J* = 11.5 Hz, CH*H* Bn), 4.76 (d, 1H, *J* = 10.9 Hz, CH*H* Bn), 4.62 (d, 1H, *J* = 7.7 Hz, H-1), 4.33 (dd, 1H, *J* = 10.5, 5.0 Hz, H-6), 3.79 (t, 1H, *J* = 10.3 Hz, H-6), 3.76 – 3.65 (m, 3H, C*H* Cy, H-3, H-4), 3.46 (t, 1H, *J* = 8.1 Hz, H-2), 3.39 (td, 1H, *J* = 9.5, 5.0 Hz, H-5), 2.00 – 1.91 (m, 2H, CH_2 Cy), 1.82 – 1.72 (m, 2H, CH_2 Cy), 1.59 – 1.18 (m, 6H, CH_2 Cy); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.7, 138.6, 137.5 (C_q), 129.0, 128.4, 128.4, 128.3, 128.3, 128.1, 127.8, 127.7, 126.1 (CH_{arom}), 102.5 (C-1), 101.2 (CHPh), 82.3 (C-2), 81.6, 81.2 (C-3, C-4), 78.3 (CH Cy), 75.5, 75.2 (CH_2 Bn), 69.0 (C-6), 66.1 (C-5), 33.9, 32.1, 25.7, 24.2, 24.1 (CH_2 Cy); Diagnostic peaks α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 4.69 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.26 (dd, 1H, *J* = 10.2, 4.9 Hz, H-6), 4.07 (t, 1H, *J* = 9.3 Hz, H-3), 3.96 (td, 1H, *J* = 10.0, 4.9 Hz, H-5), 3.61 (t, 1H, *J* = 9.4 Hz, H-4), 3.58 – 3.50 (m, 2H, CH Cy, H-2); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 101.3 (CHPh), 96.1 (C-1), 82.5 (C-4), 79.5 (C-2) 78.8 (C-3), 76.1 (CH Cy), 75.4, 73.4 (CH_2 Bn), 69.2 (C-6), 62.6 (C-5); HRMS: $[M+H]^+$ calcd for $C_{33}H_{39}O_6$ 531.27412, found 531.27400.

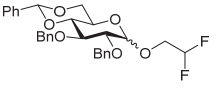


Ethyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranoside (2B). Donor **2** and ethanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations and

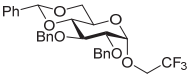
purified by flash column chromatography (1/1 to 0/1 pentane/toluene to 6% EtOAc in toluene) to yield glycosylation product **2B** (32.2 mg, 68 µmol, 68%, α:β = 1:10). R_f: 0.43 (6% EtOAc in toluene). IR (neat): 692, 743, 1006, 1028, 1183, 1364, 1453, 2872; Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.52 – 7.46 (m, 2H, CH_{arom}), 7.41 – 7.24 (m, 13H, CH_{arom}), 5.56 (s, 1H, C*H*Ph), 4.93 – 4.88 (m, 2H, 2xC*H*H Bn), 4.83 – 4.74 (m, 2H, 2xCH*H* Bn), 4.51 (d, 1H, *J* = 7.7 Hz, H-1), 4.34 (dd, 1H, *J* = 10.5, 5.0 Hz, H-6), 3.97 (dq, 1H, *J* = 9.6, 7.1 Hz, C*H*H Et), 3.79 (t, 1H, *J* = 9.5 Hz, H-6), 3.76 – 3.63 (m, 3H, H-3, H-4, CH*H* Et), 3.46 (t, 1H, *J* = 8.1 Hz, H-2), 3.40 (ddd, 1H, *J* = 10.0, 9.0, 5.0 Hz, H-5), 1.29 (t, 3H, *J* = 7.0 Hz, CH_3 Et); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.7, 138.6, 137.5 (C_q), 129.0, 128.5, 128.4, 128.4, 128.2, 128.1, 127.8, 127.7, 126.1 (CH_{arom}), 104.1 (C-1), 101.3 (CHPh), 82.3 (C-2), 81.7 (C-4), 81.0 (C-3), 75.5, 75.2 (CH_2 Bn), 69.0 (C-6), 66.2 (CH_2 Et), 66.2 (C-5), 15.5 (CH_3 Et); Diagnostic peaks α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 5.55 (s, 1H, C*H*Ph), 4.92 (d, 1H, *J* = 11.2 Hz, C*H*H Bn), 4.86 – 4.83 (m, 2H, C*H*H Bn, CH*H* Bn), 4.73 (d, 1H, *J* = 3.8 Hz, H-1), 4.68 (d, 1H, *J* = 12.2 Hz, CH*H* Bn), 4.25 (dd, 1H, *J* = 10.2, 4.8 Hz, H-6), 4.06 (t, 1H, *J* = 9.3 Hz, H-3), 3.88 (td, 1H, *J* = 10.0, 4.8 Hz, H-5), 3.63 – 3.60 (m, 1H, H-4), 3.59 – 3.52 (m, 2H, H-2, CH*H* Et); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 101.3 (CHPh), 97.9 (C-1), 82.4 (C-4), 79.5 (C-2), 78.8 (C-3), 73.7 (CH_2 Bn), 69.2 (C-6), 63.8 (CH_2 Et), 62.5 (C-5); HRMS: $[M+H]^+$ calcd for $C_{29}H_{33}O_6$ 477.22717, found 477.22699.



2-Fluoroethoxyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranoside (2C). Donor **2** and 2-fluoroethanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations and purified by flash column chromatography (1/1 to 0/1 pentane/toluene to 6% EtOAc in toluene) to yield glycosylation product **2C** (34.7 mg, 70 µmol, 70%, α:β = 1:3). R_f: 0.30 and 0.34 (4% EtOAc in toluene). IR (neat): 695, 744, 1000, 1028, 1072, 1085, 1177, 1452, 2868. Reported as a 0.33 : 1.00 mixture of anomers: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.52 – 7.44 (m, 2.66H, CH_{arom}), 7.42 – 7.24 (m, 17.29H, CH_{arom}), 5.56 (s, 1H, C*H*Ph$_\beta$), 5.55 (s, 0.33H, C*H*Ph$_\alpha$), 4.92 (dd, 2.33H, *J* = 11.1, 3.4 Hz, 2xC*H*H Bn$_\beta$, C*H*H Bn$_\alpha$), 4.87 – 4.73 (m, 2.99H, 2xCH*H* Bn$_\beta$, CH*H* Bn$_\alpha$, C*H*H Bn$_\alpha$, H-1$_\alpha$), 4.72 – 4.60 (m, 1.66H, CH*H* Bn$_\alpha$, C*H*H-CH_2F_α, C*H*H-CH_2F_β), 4.59 – 4.49 (m, 2.33H, CH*H*-CH_2F_α, CH*H*-CH_2F_β, H-1$_\beta$), 4.34 (dd, 1H, *J* = 10.5, 5.0 Hz, H-6$_\beta$), 4.26 (dd, 0.33H, *J* = 10.2, 4.9 Hz, H-6$_\alpha$), 4.13 (ddd, 0.50H, *J* = 12.1, 4.7, 2.6 Hz, C*H*HF$_\beta$), 4.10 – 4.02 (m, 0.83H, C*H*HF$_\beta$, H-3$_\alpha$), 3.94 – 3.66 (m, 5.32H, CH*H*F$_\beta$, C*H*$_2$F$_\alpha$, H-3$_\beta$, H-4$_\beta$, H-5$_\alpha$, H-6$_\alpha$, H-6$_\beta$), 3.61 (t, 0.33H, *J* = 9.4 Hz, H-4$_\alpha$), 3.58 (dd, 0.33H, *J* = 9.3, 3.8 Hz, H-2$_\alpha$), 3.50 (t, 1H, *J* = 8.1 Hz, H-2$_\beta$), 3.41 (ddd, 1H, *J* = 10.0, 9.0, 5.0 Hz, H-5$_\beta$); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.9, 138.6, 138.4, 138.3, 137.5, 137.4 (C_q), 129.1, 129.0, 128.6, 128.5, 128.4, 128.4, 128.3, 128.2, 128.1, 128.1, 128.0, 127.7, 126.1 (CH_{arom}), 104.4 (C-1$_\beta$, 101.4 (CHPh$_\alpha$), 101.3 (CHPh$_\beta$), 98.4 (C-1$_\alpha$), 82.7 (d, *J* = 170.2 Hz, CH_2F_α), 82.6 (d, *J* = 170.2 Hz, CH_2F_β), 82.2 (C-4$_\alpha$), 82.1 (C-2$_\beta$), 81.5 (C-4$_\beta$), 80.9 (C-3$_\beta$), 79.4 (C-2$_\alpha$), 78.6 (C-3$_\alpha$), 75.5 (CH_2 Bn$_{\alpha,\beta}$), 75.2 (CH_2 Bn$_\beta$), 73.7 (CH_2 Bn$_\alpha$), 69.4 (d, *J* = 20.0 Hz, *CH*$_2$-CH_2F_β), 69.1 (C-6$_\alpha$), 68.8 (C-6), 67.3 (d, *J* = 20.2 Hz, *CH*$_2$-CH_2F_α), 66.2 (C-5$_\beta$), 62.6 (C-5$_\alpha$); HRMS: $[M+H]^+$ calcd for $C_{29}H_{32}FO_6$ 495.21774, found 495.21745.

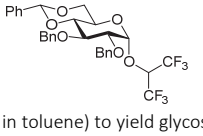


2,2-Difluoroethyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranoside (2D). Donor **2** and 2,2-difluoroethanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations and purified by flash column chromatography (1/1 to 0/1 pentane/toluene to 6% EtOAc in toluene) to yield glycosylation product **2D** (36 mg, 70 µmol, 70%, α:β = 5:1). R_f: 0.32 and 0.36 (4% EtOAc in toluene). IR (neat): 696, 747, 996, 1028, 1071, 1086, 1369, 1453, 2865. Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.48 (m, 2H, CH_{arom}), 7.41 – 7.26 (m, 13H, CH_{arom}), 5.95 (tt, 1H, *J* = 55.4, 4.2 Hz, C*H*F$_2$), 5.55 (s, 1H, C*H*Ph), 4.92 (d, 1H, *J* = 11.3 Hz, C*H*H Bn), 4.84 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.83 (d, 1H, *J* = 11.4 Hz, CH*H* Bn), 4.75 (d, 1H, *J* = 3.9 Hz, H-1), 4.66 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.25 (dd, 1H, *J* = 10.2, 4.8 Hz, H-6), 4.03 (t, 1H, *J* = 9.3 Hz, H-3), 3.90 – 3.65 (m, 4H, *CH*$_2$-CHF_2, H-5, H-6), 3.62 (t, 1H, *J* = 9.4 Hz, H-4), 3.58 (dd, 1H, *J* = 9.3, 3.8 Hz, H-2); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.8, 138.2, 137.4 (C_q), 129.1, 128.6, 128.4, 128.4, 128.2, 128.1, 128.1, 127.7, 126.1 (CH_{arom}), 114.2 (t, *J* = 241.5 Hz, CHF_2), 101.4 (CHPh), 98.9 (C-1), 82.0 (C-4), 79.3 (C-2), 78.4 (C-3), 75.5, 74.0 (CH_2 Bn), 69.0 (C-6), 67.4 (t, *J* = 28.8 Hz, *CH*$_2$-CHF_2), 63.0 (C-5); Diagnostic peaks β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 5.90 (tdd, 1H, *J* = 55.4, 5.0, 3.4 Hz, C*H*F$_2$), 5.56 (s, 1H, C*H*Ph), 4.54 (d, 1H, *J* = 7.6 Hz, H-1), 4.34 (dd, 1H, *J* = 10.5, 5.0 Hz, H-6), 3.48 (t, 1H, *J* = 8.1 Hz, H-2), 3.41 (td, 1H, *J* = 9.6, 5.0 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 104.5 (C-1), 101.3 (CHPh), 81.9 (c-2), 81.4, 80.8 (C-3, C-4), 75.6, 75.3 (CH_2 Bn), 68.7 (C-6), 66.3 (C-5); HRMS: $[M+H]^+$ calcd for $C_{29}H_{31}F_2O_6$ 513.20832, found 513.20808.

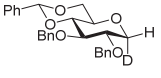


2,2,2-Trifluoroethyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (2E). Donor **2** and 2,2,2-trifluoroethanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations and purified by flash column chromatography (1/1 to 0/1 pentane/toluene to 6% EtOAc in toluene) to yield glycosylation product **2E** (33.7 mg, 64 µmol, 64%, α:β = >20:1). R_f: 0.45 (4% EtOAc in toluene). $[\alpha]_D^{23}$ = +7.0° (*c* = 0.67, DCM); IR (neat): 697, 747, 1001, 1029, 1077, 1161, 1279, 1373, 1454, 2864; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.51 – 7.46 (m, 2H, CH_{arom}), 7.41 –

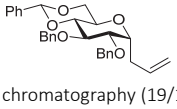
7.26 (m, 13H, CH_{arom}), 5.55 (s, 1H, C*H*Ph), 4.92 (d, 1H, *J* = 11.2 Hz, C*H*H Bn), 4.84 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.83 (d, 1H, *J* = 11.3 Hz, CH*H* Bn), 4.80 (d, 1H, *J* = 3.9 Hz, H-1), 4.67 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.25 (dd, 1H, *J* = 10.2, 4.8 Hz, H-6), 4.05 (t, 1H, *J* = 9.3 Hz, H-3), 3.92 (q, 2H, *J* = 8.7 Hz, CH_2-CF_3), 3.85 (td, 1H, *J* = 9.9, 4.8 Hz, H-5), 3.70 (t, 1H, *J* = 10.3 Hz, H-6), 3.63 (t, 1H, *J* = 9.4 Hz, H-4), 3.59 (dd, 1H, *J* = 9.3, 3.8 Hz, H-2); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.8, 138.2, 137.4 (C_q), 129.1, 128.6, 128.4, 128.4, 128.2, 128.1, 128.1, 127.8, 126.2 (CH_{arom}), 123.8 (q, *J* = 278.6 Hz, CF_3), 101.4 (CHPh), 99.0 (C-1), 81.9 (C-4), 79.2 (C-2), 78.3 (C-3), 75.5, 73.9 (CH_2 Bn), 68.9 (C-6), 65.2 (q, *J* = 35.0 Hz, CH_2-CF_3), 63.3 (C-5); Diagnostic peaks β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 5.56 (s, 1H, C*H*Ph), 4.73 (d, 1H, *J* = 10.7 Hz, CH*H* Bn), 4.60 (d, 1H, *J* = 7.7 Hz, H-1), 4.34 (dd, 1H, *J* = 10.5, 5.0 Hz, H-6), 3.51 (t, 1H, *J* = 8.0 Hz), 3.41 (td, 1H, *J* = 9.6, 5.2 Hz, H-5); HRMS: $[M+H]^+$ calcd for $C_{29}H_{30}F_3O_6$ 531.19890, found 531.19857.



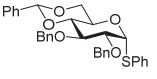
1,1,1,3,3,3-Hexafluoro-2-propyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (2F). Donor **2** and 1,1,1,3,3,3-hexafluoroisopropanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 144 hours at -40°C) and purified by flash column chromatography (1/1 to 0/1 pentane/toluene to 10% EtOAc in toluene) to yield glycosylation product **2F** (39 mg, 65 µmol, 65%, α:β = >20:1). R_f: 0.31 (4/1 pentane/Et_2O). $[\alpha]_D^{25}$ = -40.9° (*c* = 0.68, $CHCl_3$); IR (neat): 689, 746, 997, 1086, 1196, 1219, 1368, 1454, 2868; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.51 – 7.47 (m, 2H, CH_{arom}), 7.40 – 7.27 (m, 13H, CH_{arom}), 5.55 (s, 1H, C*H*Ph), 5.07 (d, 1H, *J* = 4.0 Hz, H-1), 4.93 (d, 1H, *J* = 11.1 Hz, C*H*H Bn), 4.83 (d, 1H, *J* = 11.1 Hz, CH*H* Bn), 4.79 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.73 (d, 1H, *J* = 11.7 Hz, CH*H* Bn), 4.41 (hept, 1H, *J* = 5.9 Hz, CH HFIP), 4.24 (dd, 1H, *J* = 10.2, 5.0 Hz, H-6), 4.06 (t, 1H, *J* = 9.4 Hz, H-3), 3.94 (td, 1H, *J* = 10.0, 4.9 Hz, H-5), 3.70 (t, 1H, *J* = 10.2 Hz, H-6), 3.75 – 3.60 (m, 2H, H-2, H-4); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.6, 137.7, 137.2 (C_q), 129.2, 128.6, 128.5, 128.4, 128.2, 128.1, 127.8, 126.1 (CH_{arom}), 121.7 (q, *J* = 285 Hz, CF_3), 121.2 (q, *J* = 285 Hz, CF_3), 101.4 (CHPh), 100.4 (C-1), 81.5 (C-4), 78.3, 78.3 (C-2, C-3), 75.6, 74.1 (CH_2 Bn), 73.4 (hept, *J* = 32.9 Hz, CH HFIP), 68.5 (C-6), 64.0 (C-5); ^{13}C-HMBC NMR ($CDCl_3$, 101 MHz): $^3J(H_{HFIP}$-C1) observed; HRMS: $[2M-2(CF_3)_2CHO+H_2O+NH_4]^+$ calcd for $(C_{27}H_{27}O_5)_2O$ 896.40044, found 896.40115; LC-MS: Rt = 10.09, no conclusive mass. TLC-MS: $[M+Na]^+$ calcd for $C_{30}H_{28}F_6O_6Na$ 621.17 found 621.2, and $[M+H_2O$-benzaldehyde$+Na]^+$ calcd for $C_{23}H_{24}F_6O_6Na$ 533.14 found 533.0.



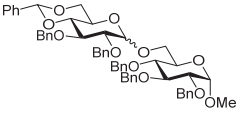
1-[^{2}H]-1,5-anhydro-2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucitol (2G). Donor **2** and triethylsilane-D were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 144 hours at -40°C) and purified by flash column chromatography (19/1 to 4/1 Et_2O/pentane) to yield glycosylation product **2G** (34 mg, 79 µmol, 79%, α:β = >20:1). R_f: 0.38 (4/1 pentane/Et_2O). Spectroscopic data of the non-dueterated glucitol were in accord with those previously reported.[112] $[\alpha]_D^{23}$ = +5.4° (*c* = 0.78, $CHCl_3$); IR (neat): 696, 748, 1009, 1028, 1088, 1368, 1454, 2868; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.51 – 7.48 (m, 2H, CH_{arom}), 7.41 – 7.34 (m, 5H, CH_{arom}), 7.34 – 7.26 (m, 7H, CH_{arom}), 5.55 (s, 1H, C*H*Ph), 4.96 (d, 1H, *J* = 11.4 Hz, C*H*H Bn), 4.83 (d, 1H, *J* = 11.6 Hz, CH*H* Bn), 4.80 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.66 (d, 1H, *J* = 11.6 Hz, CH*H* Bn), 4.31 (dd, 1H, *J* = 10.4, 5.0 Hz, H-6), 3.98 (d, 1H, *J* = 5.6 Hz, H-1), 3.75 (t, 1H, *J* = 8.8 Hz, H-3), 3.70 – 3.63 (m, 2H, H-2, H-6), 3.61 (t, 1H, *J* = 9.2 Hz, H-4), 3.36 (ddd, 1H, *J* = 10.1, 9.2, 5.0 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.8, 138.3, 137.5 (C_q), 129.0, 128.6, 128.4, 128.4, 128.1, 128.0, 128.0, 127.7, 126.1 (CH_{arom}), 101.3 (CHPh), 82.5 (C-3), 82.2 (C-4), 77.7 (C-2, 75.1, 74.0 (CH_2 Bn), 71.4 (C-5), 69.0 (C-6), 68.7 (t, $J_{C1,D1}$ = 22.3 Hz); ^{2}H NMR ($CHCl_3$, 61 MHz): 3.34 (s, 1D, D-1); HRMS: $[M+H]^+$ calcd for $C_{27}H_{28}DO_5S$ 434.20723, found 434.20714.



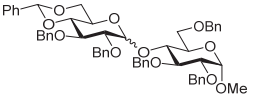
Allyl 2,3-di-*O*-benzyl-1-deoxy-4,6-*O*-benzylidene-α-D-glucopyranoside (2H). Donor **2** and allyl trimethylsilane were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 16 hours at -40°C) and purified by flash column chromatography (19/1 to 9/1 pentane/EtOAc) to yield glycosylation product **2H** (20 mg, 42 µmol, 42%, α:β = >1:20). Contaminated with a 1-OTMS glycoside by-product. α-Thio glycoside **2α** was formed as a by-product. R_f: 0.60 (9/1 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[40,72] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HH-NOESY, HSQC): δ 7.53 – 7.47 (m, 2H, CH_{arom}), 7.42 – 7.27 (m, 13H, CH_{arom}), 5.77 (ddt, 1H, *J* = 17.1, 10.2, 6.9 Hz, C*H* allyl), 5.57 (s, 1H, C*H*Ph), 5.18 – 5.05 (m, 2H, CH_2 allyl), 4.93 (d, 1H, *J* = 11.4 Hz, C*H*H Bn), 4.81 (d, 1H, *J* = 11.4 Hz, CH*H* Bn), 4.78 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.64 (d, 1H, *J* = 11.7 Hz, CH*H* Bn), 4.27 – 4.21 (m, 1H, H-6), 4.08 (td, 1H, *J* = 7.7, 5.7 Hz, H-1), 3.92 – 3.85 (m, 1H, H-3), 3.76 (dd, 1H, *J* = 8.6, 5.7 Hz, H-2), 3.69 – 3.63 (m, 3H, H-4, H-5, H-6), 2.57 – 2.51 (m, 2H, CH_2 allylic); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 138.7, 138.3, 137.5 ($C_{q\text{-}arom}$), 134.4 (CH allyl), 129.0, 128.6, 128.5, 128.4, 128.1, 128.0, 127.9, 127.8, 126.1 (CH_{arom}), 117.4 (CH_2 allyl), 101.3 (CHPh), 82.9 (C-4), 79.5 (C-2), 78.9 (C-3), 75.0 (C-1), 75.0, 73.7 (CH_2 Bn), 69.6 (C-6), 63.5 (C-5), 30.8 (CH_2 allylic); HRMS: $[M+H]^+$ calcd for $C_{30}H_{33}O_5$ 473.23225, found 473.23228.



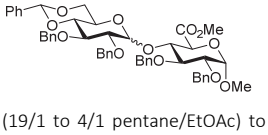
Phenyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-1-thio-α-D-glucopyranoside (2α). R_f: 0.38 (4/1 pentane/Et_2O). Spectroscopic data were in accord with those previously reported.[21] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.53 – 7.44 (m, 4H, CH_{arom}), 7.43 – 7.36 (m, 7H, CH_{arom}), 7.36 – 7.27 (m, 9H, CH_{arom}), 5.59 (d, 1H, *J* = 5.5 Hz, H-1), 5.57 (s, 1H, C*H*Ph), 4.92 (d, 1H, *J* = 11.3 Hz, CH*H* Bn), 4.86 (d, 1H, *J* = 11.3 Hz, CH*H* Bn), 4.81 (d, 1H, *J* = 11.8 Hz, C*H*H Bn), 4.76 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.39 (td, 1H, *J* = 9.9, 4.9 Hz, H-5), 4.19 (dd, 1H, *J* = 10.3, 5.0 Hz, H-6), 3.98 (t, 1H, *J* = 9.2 Hz, H-3), 3.90 (dd, 1H, *J* = 9.3, 5.5 Hz, H-2), 3.71 (t, *J* = 10.3 Hz, H-6), 3.66 (t, *J* = 9.3 Hz, H-4); HRMS: $[M+NH_4]^+$ calcd for $C_{33}H_{36}NO_5$ 558.23087, found 558.23075.



Methyl 6-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (25). Donor **2** and acceptor **10** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 16 hours at -40°C) and purified by flash column chromatography (9/1 to 3/1 pentane/EtOAc) to yield glycosylation product **25** (72.1 mg, 81 µmol, 81%, α:β = 1:2.7). R_f: 0.83 (6/4 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[108] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 7.51 – 7.44 (m, 2H, CH_{arom}), 7.41 – 7.12 (m, 28H, CH_{arom}), 5.54 (s, 1H, C*H*Ph), 4.97 (d, 1H, *J* = 10.8 Hz, C*H*H Bn), 4.93 – 4.88 (m, 2H, 2xC*H*H Bn), 4.84 – 4.76 (m, 4H, 3xCH*H* Bn, C*H*H Bn), 4.73 – 4.63 (m, 2H, C*H*H Bn, CH*H* Bn), 4.61 (d, 1H, *J* = 3.6 Hz, H-1), 4.49 (d, 1H, *J* = 11.2 Hz, CH*H* Bn), 4.44 (d, 1H, *J* = 7.7 Hz, H-1'), 4.31 (dd, 1H, *J* = 10.5, 5.0 Hz, H-6'), 4.11 (dd, 1H, *J* = 10.7, 2.0 Hz, H-6), 3.99 (t, *J* = 9.3 Hz, 1H, H-3), 3.82 – 3.65 (m, 5H, H-3', H-4', H-5, H-6, H-6'), 3.56 – 3.48 (m, 3H, H-2, H-2', H-4), 3.40 – 3.34 (m, 1H, H-5'), 3.33 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 138.9, 138.5, 138.4, 138.3, 138.2, 137.4 (C_q), 128.6, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 128.1, 128.1, 128.1, 128.0, 128.0, 128.0, 127.7, 127.7, 127.7, 127.7, 127.6, 126.1 (CH_{arom}), 104.2 (C-1'), 101.2 (CHPh), 98.2 (C-1), 82.1 (C-3), 81.9 (C-2'), 81.5, 81.2 (C-3', C-4'), 79.8 (C-2), 77.9 (C-4), 75.8, 75.5, 75.2, 75.0, 73.5 (CH_2 Bn), 69.8 (C-5), 68.8 (C-6, C-6'), 66.2 (C-5'), 55.3 (OMe); Diagnostic peaks α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.53 (s, 0.33H), 4.57 (d, 0.33H, *J* = 3.6 Hz), 4.20 (dd, 0.33H, *J* = 10.1, 4.8 Hz), 3.89 (td, 0.33H, *J* = 10.0, 4.8 Hz), 3.43 (dd, 0.33H, *J* = 9.6, 3.6 Hz), 3.34 (s, 1H); ^{13}C-APT NMR ($CDCl_3$, 101 MHz): δ 138.9, 138.8, 138.5, 138.3, 137.6, 129.0-126.2, 101.4, 98.3, 98.1, 82.3, 82.2, 80.2, 79.4, 78.0, 77.8, 75.8, 75.1, 75.1, 73.5, 73.0, 70.5, 69.2, 66.4, 62.6, 55.3; HRMS: $[M+Na]^+$ calcd for $C_{55}H_{58}O_{11}Na$ 917.38713, found 917.38678.

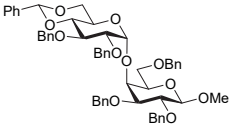


Methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranosyl)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (26). Donor **2** and acceptor **11** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 16 hours at -40°C) and purified by flash column chromatography (19/1 to 4/1 pentane/EtOAc) to yield glycosylation product **26** (71 mg, 79 µmol, 79%, α:β = 1:1). R_f: 0.54 (4/1 pentane/EtOAc). Spectroscopic data were in accord with those previously reported for the α-anomer.[108] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 7.52 – 7.45 (m, 4H, CH_{arom}), 7.44 – 7.18 (m, 56H, CH_{arom}), 5.75 (d, 1H, *J* = 3.8 Hz, H-1'$_\alpha$), 5.52 (s, 1H, C*H*Ph$_\alpha$), 5.49 (s, 1H, C*H*Ph$_\beta$), 5.04 (d, 1H, *J* = 11.7 Hz, C*H*H Bn$_\alpha$), 4.95 – 4.87 (m, 3H, 3xC*H*H Bn), 4.84 – 4.51 (m, 17H, 6xC*H*H Bn, 9xCH*H* Bn, H-1, H-1$_\beta$), 4.36 (d, 1H, *J* = 7.8 Hz, H-1'$_\beta$), 4.30 (d, 1H, *J* = 12.0 Hz, CH*H* Bn$_\beta$), 4.19 (dd, 1H, *J* = 10.5, 5.0 Hz, H-6'$_\beta$), 4.15 – 4.09 (m, 3H, H-3$_\alpha$, H-4$_\alpha$, H-6'$_\alpha$), 3.99 (t, 1H, *J* = 9.3 Hz, H-3'$_\alpha$), 3.94 (t, 1H, *J* = 9.4 Hz, H-4$_\beta$), 3.90 – 3.78 (m, 5H, H-2$_\beta$, H-5$_\alpha$, H-5$_\alpha$', H-6$_\alpha$, H-6$_\beta$), 3.69 – 3.41 (m, 11H, H-2$_\alpha$, H-2'$_\alpha$, H-3$_\beta$, H-3'$_\beta$, H-4'$_\alpha$, H-4'$_\beta$, H-5$_\beta$, H-6$_\alpha$, H-6$_\beta$, H-6'$_\alpha$, H-6'$_\beta$), 3.40 – 3.31 (m, 7H, CH_3 OMe, CH_3 OMe$_\beta$, H-2'$_\beta$), 3.10 (td, 1H, *J* = 9.5, 4.9 Hz, H-5'$_\beta$); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 139.4, 139.0, 138.7, 138.6, 138.5, 138.4, 138.2, 138.0, 137.9, 137.9, 137.6, 137.5 (C_q), 129.0, 128.9, 128.6, 128.5, 128.5, 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, 127.7, 127.7, 127.5, 127.5, 127.4, 127.3, 126.8, 126.1, 126.1 (CH_{arom}), 102.9 (C-1'$_\beta$), 101.2 (CHPh), 98.5, 97.8 (C-1$_\alpha$, C-1$_\beta$), 97.2 (C-1'$_\alpha$), 82.7 (C-2'$_\beta$), 82.4 (C-4'$_\alpha$), 82.2 (C-3$_\alpha$), 81.8 (C-4'$_\beta$), 81.0 (C-3'$_\beta$), 80.3 (C-2$_\beta$), 80.3, 78.9 (C-2$_\alpha$, C-3'$_\alpha$), 78.8 (C-2'$_\alpha$, C-3$_\beta$), 76.9 (C-4$_\beta$), 75.6, 75.5, 75.4, 75.0, 74.4, 73.9, 73.7, 73.4, 73.4 (CH_2 Bn), 71.6 (C-4$_\alpha$), 70.0 (C-5$_\beta$), 69.4 (C-5$_\alpha$), 69.0, 68.9, 68.8 (C-6$_\alpha$, C-6'$_\alpha$, C-6'$_\beta$), 67.7 (C-6$_\beta$), 65.8 (C-5'$_\beta$), 63.4 (C-5'$_\alpha$), 55.5 (OMe$_\beta$), 55.3 (OMe$_\alpha$); HRMS: $[M+NH_4]^+$ calcd for $C_{55}H_{62}O_{11}N$ 912.43174, found 912.43282.

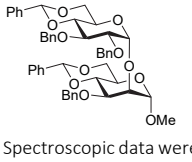


Methyl (methyl 4-*O*-[2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranosyl]-2,3,6-tri-*O*-benzyl-α-D-glucopyranosyl uronate) (27). Donor **2** and acceptor **12** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 24 hours at -40°C) and purified by flash column chromatography (19/1 to 4/1 pentane/EtOAc) to yield glycosylation product **27** (75.2 mg, 90 µmol, 90%, α:β = 5:1). R_f: 0.77 (7/3 pentane/EtOAc). IR (neat): 694, 732, 912, 988, 1026, 1043, 1074, 1086, 1358, 1454, 1749, 28866, 2932; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 7.48 – 7.43 (m, 2H, CH_{arom}), 7.40 – 7.16 (m, 23H, CH_{arom}), 5.51 (s, 1H, C*H*Ph), 5.44 (d, 1H, *J* = 3.8 Hz, H-1'), 4.95 – 4.86 (m, 3H, CH_2 Bn, C*H*H Bn), 4.78 (d, 1H, *J* = 11.2 Hz,

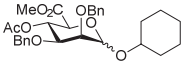
CH*H* Bn), 4.71 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.67 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.59 – 4.53 (m, 3H, 2xCH*H* Bn, H-1), 4.28 (dd, 1H, *J* = 6.5, 3.8 Hz, H-6'), 4.25 (d, 1H, *J* = 9.5 Hz, H-5), 4.11 (t, 1H, *J* = 9.1 Hz, H-4), 4.05 (t, 1H, *J* = 8.9 Hz, H-3), 3.98 (t, 1H, *J* = 9.1 Hz, H-3'), 3.76 (s, 3H, CH_3 CO_2Me), 3.64 (t, 1H, *J* = 10.0 Hz, H-6'), 3.61 – 3.54 (m, 3H, H-2, H-4', H-5'), 3.48 (dd, 1H, *J* = 5.6, 3.9 Hz, H-2'), 3.40 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 170.1 (C=O CO_2Me), 139.0, 138.6, 138.0, 137.8, 137.6 (C_q), 129.0, 128.6, 128.4, 128.4, 128.3, 128.3, 128.3, 128.2, 128.1, 128.1, 127.8, 127.7, 127.7, 127.3, 127.0, 126.1 (CH_{arom}), 101.3 (CHPh), 98.6 (C-1), 98.4 (C-1'), 82.0 (C-4'), 80.8 (C-3), 79.2 (C-2), 78.7 (C-2'), 78.4 (C-3'), 76.1 (C-4), 75.3, 75.0, 73.7, 73.7 (CH_2 Bn), 70.3 (C-5), 68.6 (C-6'), 63.1 (C-5'), 55.8 (CH_3 OMe), 52.9 (CH_3 CO_2Me); ^{13}C-HMBC NMR ($CDCl_3$, 101 MHz): δ 98.4 ($J_{C1',H1'}$ = 174 Hz, C-1' α); Diagnostic peaks β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.47 (s, 0.18H, CHPh), 4.62 (d, 0.18H, *J* = 12.1 Hz), 3.87 (dd, 0.18H, *J* = 9.6, 8.4 Hz), 3.50 (s, 0.54H, CH_3 CO_2Me), 3.44 (s, 0.54H, CH_3 OMe), 3.38 – 3.28 (m, 0.36H, H-2', H-5'); ^{13}C-APT NMR ($CDCl_3$, 101 MHz): δ 170.1, 139.2, 138.6, 138.2, 137.4, 129.0, 128.5, 128.3, 128.1, 127.7, 127.5, 126.1, 102.9 (C-1'), 101.2 (CHPh), 99.0 (C-1), 82.3, 81.8, 81.3, 79.6, 78.5, 78.2, 75.6, 75.5, 75.2, 73.9, 70.0, 68.8, 65.9, 55.9, 52.7; ^{13}C-HMBC NMR ($CDCl_3$, 101 MHz): δ 102.9 ($J_{C1',H1'}$ = 164 Hz, C-1' β); HRMS: $[M+Na]^+$ calcd for $C_{49}H_{52}O_{12}Na$ 855.33510, found 855.33496.



Methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranosyl)-2,3,6-tri-*O*-benzyl-β-D-galactopyranoside (28). Donor **2** and acceptor **13** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 16 hours at -40°C) and purified by flash column chromatography (19/1 to 4/1 pentane/EtOAc) to yield glycosylation product **28** (74 mg, 83 μmol, 83%, α:β = >20:1). R_f: 0.50 (4/1 pentane/EtOAc). $[\alpha]_D^{23}$ = +38.4° (*c* = 1.0, $CHCl_3$); IR (neat): 696, 735, 997, 1028, 1072, 1366, 1452, 1497, 2859, 2922; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 7.49 (dd, 2H, *J* = 7.9, 1.8 Hz, CH_{arom}), 7.42 – 7.16 (m, 28H, CH_{arom}), 5.50 (s, 1H, C*H*Ph), 4.98 (d, *J* = 3.7 Hz, H-1'), 4.97 (d, *J* = 11.0 Hz, C*H*H Bn), 4.93 – 4.87 (m, 2H, 2xC*H*H Bn), 4.85 – 4.74 (m, 3H, 2xCH*H* Bn, C*H*H Bn), 4.72 – 4.63 (m, 2H, 2xCH*H* Bn), 4.31 – 4.22 (m, 4H, CH_2 Bn, H-1, H-5'), 4.18 (t, 1H, *J* = 9.4 Hz, H-3'), 4.06 – 3.97 (m, 2H, H-4, H-6), 3.84 (dd, 1H, *J* = 10.1, 4.9 Hz, H-6'), 3.72 (dd, 1H, *J* = 10.0, 7.6 Hz, H-2), 3.63 – 3.45 (m, 8H, CH_3 OMe, H-2', H-4', H-5, H-6, H-6'), 3.42 (dd, 1H, *J* = 10.0, 2.9 Hz, H-3); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 138.9, 138.7, 138.6, 138.4, 138.2, 137.8 (C_q), 128.9, 128.5, 128.4, 128.4, 128.3, 128.3, 128.1, 128.0, 127.8, 127.7, 127.6, 126.2 (CH_{arom}), 105.1 (C-1), 101.2 (CHPh), 100.7 (C-1'), 83.0 (C-4'), 80.6 (C-3), 79.7 (C-2'), 78.9 (C-2, C-3'), 75.9 (C-4), 75.3, 75.2, 74.0 (CH_2 Bn), 73.5 (C-5), 73.2, 72.8 (CH_2 Bn), 69.1 (C-6'), 68.0 (C-6), 63.0 (C-5'), 57.2 (OMe); ^{13}C-HMBC NMR ($CDCl_3$, 101 MHz): δ 105.1 ($J_{C1',H1'}$ = 159 Hz, C-1 β), 100.7 ($J_{C1',H1'}$ = 170 Hz, C-1' α); HRMS: $[M+NH_4]^+$ calcd for $C_{55}H_{62}O_{11}N$ 912.43174, found 912.43266.

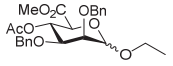


Methyl 2-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranosyl)-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (29). Donor **2** and acceptor **14** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 16 hours at -40°C) and purified by flash column chromatography (19/1 to 4/1 pentane/EtOAc) to yield glycosylation product **29** (64.3 mg, 80 μmol, 80%, α:β = >20:1). R_f: 0.27 (8/1 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[108] IR (neat): 696, 748, 999, 1028, 1074, 1088, 1369, 1454, 1498, 2864, 2911; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 7.49 (ddd, 4H, *J* = 8.9, 5.8, 1.9 Hz, CH_{arom}), 7.44 – 7.35 (m, 8H, CH_{arom}), 7.35 – 7.24 (m, 10H, CH_{arom}), 7.17 (dp, 3H, *J* = 4.4, 1.6 Hz, CH_{arom}), 5.60 (d, 1H, *J* = 3.9 Hz, H-1'), 5.57 (s, 1H, CHPh'), 5.43 (s, 1H, CHPh), 4.95 – 4.85 (m, 3H, C*H*H Bn, CH_2 Bn), 4.78 (d, 1H, *J* = 11.2 Hz, C*H*H Bn), 4.72 (d, 1H, *J* = 11.7 Hz, CH*H* Bn), 4.71 (d, 1H, *J* = 1.7 Hz, H-1), 4.47 (d, 1H, *J* = 11.1 Hz, CH*H* Bn), 4.33 – 4.26 (m, 2H, H-4, H-6'), 4.24 – 4.18 (m, 2H, H-2, H-6), 4.08 (t, 1H, *J* = 9.3 Hz, H-3'), 4.02 (dd, 1H, *J* = 9.9, 2.9 Hz, H-3), 3.93 – 3.70 (m, 4H, H-5, H-5', H-6, H-6'), 3.63 (t, 1H, *J* = 9.4 Hz, H-4'), 3.56 (dd, 1H, *J* = 9.3, 3.9 Hz, H-2'), 3.36 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 139.1, 138.6, 138.5, 137.9, 137.5 (C_q), 129.1, 129.0, 128.5, 128.4, 128.3, 128.3, 128.3, 128.0, 127.9, 127.9, 127.8, 127.6, 127.6, 126.1, 126.1 (CH_{arom}), 101.3, 101.3, 101.2 (CHPh, C-1'), 98.0 (C-1), 82.1 (C-4'), 79.4 (C-2'), 79.3 (C-4), 77.9 (C-3'), 76.9 (C-3), 75.3 (CH_2 Bn), 74.4 (C-2), 74.0, 71.9 (CH_2 Bn), 69.1 (C-6'), 68.8 (C-6), 64.4 (C-5), 63.0 (C-5'), 54.9 (OMe); ^{13}C-HMBC NMR ($CDCl_3$, 101 MHz): δ 101.3 ($J_{C1',H1'}$ = 168 Hz, C-1' α), 98.0 ($J_{C1',H1'}$ = 170 Hz, C-1' α); HRMS: $[M+NH_4]^+$ calcd for $C_{48}H_{54}NO_{11}$ 820.36914, found 820.36958.

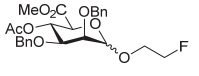


Methyl (cyclohexyl 4-*O*-acetyl-2,3-di-*O*-benzyl-α/β-D-mannopyranosyl uronate) (3A). Donor **3** and cyclohexanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 16 hours at -40°C) and purified by flash column chromatography (9/1 to 4/1 pentane/EtOAc) to yield glycosylation product **3A** (42.5 mg, 83 μmol, 83%, α:β = 1:8.3). R_f: 0.46 (7/3 pentane/EtOAc). IR (neat): 1026, 1047, 1105, 1238, 1368, 1452, 1740, 1751, 2855, 2930; Data for the β-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.48 – 7.18 (m, 10H, CH_{arom}), 5.50 (t, 1H, *J* = 9.7 Hz, H-4), 5.00 (d, 1H, *J* = 12.8 Hz, C*H*H Bn), 4.88 (d, 1H, *J* = 12.8 Hz, CH*H* Bn), 4.54 (s, 1H, H-1), 4.46 (d, 1H, *J* = 12.4 Hz, C*H*H Bn), 4.31

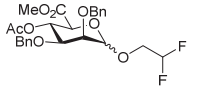
(d, 1H, *J* = 12.4 Hz, CH*H* Bn), 3.84 (d, 1H, *J* = 2.8 Hz, H-2), 3.82 (d, 1H, *J* = 9.7 Hz, H-5), 3.73 (s, 3H, CH_3 CO_2Me), 3.73 – 3.65 (m, 1H, CH Cy), 3.46 (dd, 1H, *J* = 9.8, 2.9 Hz, H-2), 2.02 (s, 3H, CH_3 OAc), 1.99 – 1.21 (m, 15H, CH_2 Cy); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC): δ 169.7, 168.3 (C=O CO_2Me, Ac), 138.6, 138.0 (C_q), 128.7, 128.5, 128.2, 127.8, 127.5, 127.5 (CH_{arom}), 99.5 (C-1), 78.7 (C-3), 77.0 (CH Cy), 74.0 (C-5), 73.9 (CH_2 Bn), 73.4 (C-2), 71.4 (CH_2 Bn), 69.1 (C-4), 52.7 (CH_3 CO_2Me), 33.4, 31.4, 25.8, 23.9 (CH_2 Cy), 21.0 (CH_3 Ac); Diagnostic peaks α-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.50 (t, 0.12H, *J* = 9.7 Hz, H-4), 5.24 (d, 0.12H, *J* = 3.3 Hz, H-1), 4.78 (d, 0.12H, *J* = 12.0 Hz, C*H*H Bn), 4.68 (d, 0.12H, *J* = 12.4 Hz, CH*H* Bn); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC): δ 69.7 (C-1); HRMS: $[M+NH_4]^+$ calcd for $C_{29}H_{40}NO_8$ 530.27484, found 530.27495.



Methyl (ethyl 4-*O*-acetyl-2,3-di-*O*-benzyl-α/β-D-mannopyranosyl uronate) (3B). Donor **3** and ethanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 16 hours at -40°C) and purified by flash column chromatography (9/1 to 4/1 pentane/EtOAc) to yield glycosylation product **3B** (43.4 mg, 95 µmol, 95%, α:β = 1:8.3). R_f: 0.36 (7/3 pentane/EtOAc). IR (neat): 735, 1026, 1047, 1103, 1229, 1369, 1454, 1744, 2924; Data for the β-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.68 – 7.15 (m, 10H, CH_{arom}), 5.51 (t, 1H, *J* = 9.5 Hz, H-4), 4.96 (d, 1H, *J* = 12.6 Hz, C*H*HBn), 4.84 (d, 1H, *J* = 12.6 Hz, CH*H* Bn), 4.48 (d, 1H, *J* = 12.4 Hz, C*H*H Bn), 4.43 (s, 1H, H-1), 4.33 (d, 1H, *J* = 12.4 Hz, CH*H* Bn), 4.02 (dq, 1H, *J* = 9.2, 7.1 Hz, C*H*HCH$_3$ Et), 3.88 (d, 1H, *J* = 2.8 Hz, H-2), 3.84 (d, 1H, *J* = 9.5 Hz, H-5), 3.73 (s, 3H, CH_3 CO_2Me), 3.54 – 3.44 (m, 2H, H-3, CH*H*CH$_3$ Et, H-3), 2.02 (s, 3H, CH_3 OAc), 1.27 (t, 3H, *J* = 7.0 Hz, CH_3 Et); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC): δ 169.7, 168.2 (C=O CO_2Me, Ac), 138.5, 137.9 (C_q), 129.4, 128.6, 1285, 128.2, 124.9 (CH_{arom}), 101.5 (C-1), 78.2 (C-3), 73.9 (CH_2 Bn), 73.9 (C-5), 73.1 (C-2), 71.4 (CH_2 Bn), 69.1 (C-4), 65.9 (CH_2 Et), 52.7 (CH_3 CO_2Me), 21.0 (CH_3 Ac), 15.2 (CH_3 Et); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 101.5 ($J_{C1,H1}$ = 160 Hz, C-1 β); Diagnostic peaks α-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.51 (t, 0.12H, H-4), 5.13 (d, 0.12H, *J* = 4.3 Hz, H-1), 4.78 (d, 0.12H, *J* = 12.4 Hz, C*H*H Bn), 4.68 (d, 0.12H, *J* = 12.3 Hz, CH*H* Bn), 3.67 (s, 0.36H, CH_3 CO_2Me). ^{13}C-APT NMR (101 MHz, $CDCl_3$) δ 98.4 (C-1), 77.4 (C-3), 74.6 (C-5), 73.2 (CH_2 Bn), 72.5 (CH_2 Bn), 69.5 (CH_2 Et), 52.6 (CH_3 CO_2Me); HRMS: $[M+Na]^+$ calcd for $C_{25}H_{30}O_8Na$ 481.18329, found 481.18250.

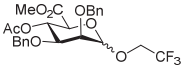


Methyl (2-fluoroethyl 4-*O*-acetyl-2,3-di-*O*-benzyl-α/β-D-mannopyranosyl uronate) (3C). Donor **3** and 2-fluoroethanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 16 hours at -40°C) and purified by flash column chromatography (9/1 to 7/3 pentane/EtOAc) to yield glycosylation product **3C** (33.2 mg, 70 µmol, 70%, α:β = 1:5). R_f: 0.18 (7/3 pentane/EtOAc). IR (neat): 1045, 1103, 1231, 1369, 1454, 1746, 2895, 2924; Data for the β-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.69 – 7.18 (m, 10H, CH_{arom}), 5.52 (t, 1H, *J* = 9.3 Hz, H-4), 4.95 (d, 1H, *J* = 12.5 Hz, C*H*H Bn), 4.83 (d, 1H, *J* = 12.5 Hz, CH*H* Bn), 4.76 – 4.94 (m, 2H, CH_2F), 4.54 (s, 1H, H-1), 4.49 (d, 1H, *J* = 12.4 Hz, C*H*H Bn), 4.34 (d, 1H, *J* = 12.4 Hz, CH*H* Bn) 4.13 (dddd, 1H, *J* = 37.0, 12.2, 3.3, 2.2 Hz, C*H*HCH$_2$F), 3.95 (d, 1H, *J* = 2.6 Hz, H-2), 3.86 (d, 1H, *J* = 9.2 Hz, H-5), 3.84 – 3.74 (m, 1H, CH*H*CH$_2$F), 3.72 (s, 3H, CH_3 CO_2Me), 3.49 (dd, 1H, *J* = 9.4, 2.9 Hz, H-3), 2.10 – 1.94 (s, 3H, CH_3 OAc); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC): δ 169.7, 168.1 (C=O CO_2Me, Ac), 138.3, 137.81 (C_q), 131.2, 129.46, 128.6, 128.5, 128.4, 128.3, 128.0, 127.9, 127.7, 127.7, 127.6, 124.9 (CH_{arom}), 101.6 (C-1), 82.96 (d, *J* = 169.5 Hz, CH_2F), 77.9 (C-3), 74.5 (CH_2 Bn), 74.1 (C-5), 73.8 (C-2), 72.9 (CH_2 Bn), 69.01 (d, *J* = 19.5 Hz, *C*H$_2$CH$_2$F), 68.9 (C-4), 52.8 (CH_3 CO_2Me), 21.0 (CH_3 Ac). ^{13}C-GATED NMR (101 MHz, $CDCl_3$) δ 101.6 ($J_{C1,H1}$ = 156 Hz, C-1); Diagnostic peaks α-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.52 (t, 0.20H, *J* = 9.3 Hz, H-4), 5.19 (d, 0.20H, *J* = 4.7 Hz, H-1), 3.66 (s, 0.60H, CH_3 CO_2Me), 2.04 (s, 0.6H, CH_3 OAc); ^{13}C-APT NMR (101 MHz, $CDCl_3$): δ 98.9 (C-1); HRMS: $[M+Na]^+$ calcd for $C_{25}H_{29}FO_8Na$ 499.17387, found 499.17297.

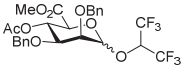


Methyl (2,2-difluoroethyl 4-*O*-acetyl-2,3-di-*O*-benzyl-α/β-D-mannopyranosyl uronate) (3D). Donor **3** and 2,2-difluoroethanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 16 hours at -40°C) and purified by flash column chromatography (9/1 to 7/3 pentane/EtOAc) to yield glycosylation product **3D** (43.1 mg, 87 µmol, 87%, α:β = 1:4.2). R_f: 0.51 (7/3 pentane/EtOAc). IR (neat): 737, 1026, 1051, 1078, 1232, 1439, 1454, 1741, 2870, 2924; Data for the β-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.57 – 7.12 (m, 10H, CH_{arom}), 5.94 (dddd, 1H, *J* = 56.7, 54.4, 5.7, 2.5 Hz, CH_2CHF_2), 5.54 (t, 1H, *J* = 8.9 Hz, H-4), 4.89 (d, 1H, *J* = 12.4 Hz, C*H*H Bn), 4.78 (d, 1H, *J* = 12.4 Hz, C*H*H Bn), 4.56 (s, 1H, H-1), 4.53 (d, 1H, *J* = 12.3 Hz, C*H*H Bn), 4.38 (d, 1H, *J* = 12.4 Hz, C*H*H Bn), 4.19 – 4.04 (m, 1H, C*H*HCHF$_2$), 3.92 (d, 1H, *J* = 2.1 Hz, H-2), 3.89 (d, 1H, *J* = 8.7 Hz, H-5), 3.80 – 3.67 (m, 1H, C*H*HCHF$_2$), 3.70 (s, 3H, CH_3 CO_2Me), 3.52 (dd, 1H, *J* = 9.0, 2.9 Hz, H-3), 2.03 (s, 3H, CH_3 OAc); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC):δ 169.7, 167.9 (C=O CO_2Me, Ac), 138.1, 137.8 (C_q), 131.2, 129.5, 128.5, 128.3, 127.9, 127.8, 127.6, 124.9 (CH_{arom}), 114.3 (dd, *J* = 242.2, 239.7 Hz, CHF_2), 101.3 (C-1), 77.4 (C-3), 74.0 (CH_2 Bn), 73.6 (C-5), 72.8 (C-2), 71.7 (CH_2 Bn), 69.0 (C-4) 68.5 (dd, *J* = 31.2, 25.6 Hz, *C*H$_2$CHF$_2$), 52.8 (CH_3 CO_2Me), 21.0 (CH_3 Ac); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 101.3

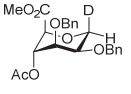
($J_{C1,H1}$ = 160 Hz, C-1 β); Diagnostic peaks α-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.52 (t, 0.24H, *J* = 11.2 Hz, H-4), 5.23 (d, 0.24H, *J* = 5.6 Hz, H-1), 3.64 (s, 0.72H, CH_3 CO_2Me); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC):δ 99.31 (C-1), 75.45 (C-3), 74.47 (C-2), 73.41 (CH_2 Bn), 69.46 (C-4), 52.61 (CH_3 CO_2Me); HRMS: $[M+NH_4]^+$ calcd for $C_{25}H_{32}F_2NO_8$ 512.20905, found 512.20889.



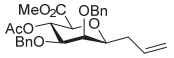
Methyl (2,2,2-trifluoroethyl 4-*O*-acetyl-2,3-di-*O*-benzyl-α/β-D-mannopyranosyl uronate) (3E). Donor **3** and 2,2,2-trifluoroethanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 24 hours at -40°C) and purified by flash column chromatography (9/1 to 7/3 pentane/EtOAc) to yield glycosylation product **3E** (43.7 mg, 85 μmol, 85%, α:β = 1:2.6). R_f: 0.60 (9/1 pentane/EtOAc). IR (neat): 741, 1058, 1161, 1234, 1280, 1371, 1443, 1748, 2854, 2924; Data for the β-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.83 – 6.86 (m, 10H, CH_{arom}), 5.55 (t, 1H, *J* = 8.6 Hz, H-4), 4.90 (d, 1H, *J* = 12.3 Hz, C*H*H Bn), 4.78 (d, 1H, *J* = 12.4 Hz, CH*H* Bn), 4.65 (s, 1H, H-1), 4.54 (d, 1H, *J* = 12.3 Hz, C*H*H Bn), 4.37 (d, 1H, *J* = 12.3 Hz, CH*H* Bn), 4.35 – 4.23 (m, 1H, C*H*HCF_3), 3.98 – 3.94 (m, 2H, CH*H*CF_3, H-2), 3.92 (d, 1H, *J* = 8.3 Hz, H-5), 3.69 (s, 3H, CH_3 CO_2Me), 3.54 (dd, 1H, *J* = 8.8, 2.8 Hz, H-3), 2.03 (s, 3H, CH_3 OAc); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC): δ 169.7, 167.8 (C=O CO_2Me, Ac), 137.9, 137.8 (C_q), 131.2, 129.5, 129.5, 128.5, 128.5, 128.3, 128.0, 127.9, 127.8, 127.5 (CH_{arom}), 123.8 (q, *J* = 278.7 Hz, CF_3), 100.8 (C-1), 77.1 (C-3), 73.8 (CH_2 Bn), 73.6 (C-5), 72.4 (C-2), 71.7 (CH_2 Bn), 69.0 (C-4), 66.1 (q, *J* = 34.8 Hz, CH_2CF_3), 52.8 (CH_3 CO_2Me), 21.0 (CH_3 Ac); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 100.8 ($J_{C1,H1}$ = 160 Hz, C-1 β); Diagnostic peaks α-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.51 (t, 0.38H, *J* = 5.5 Hz, H-4), 5.27 (d, 0.38H, *J* = 5.6 Hz, H-1), 4.23 – 4.12 (m, 0.38H, C*H*HCF_2), 3.86 (dd, 0.38H, *J* = 6.2, 3.0 Hz, H-3); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC): δ 99.1 (C-1), 75.4 (C-3), 74.3 (C-2), 73.5 (CH_2 Bn), 72.9 (CH_2 Bn), 69.4 (C-4), 52.6 (CH_3 CO_2Me), 21.0 (CH_3 Ac); ^{13}C-GATED NMR (101 MHz, $CDCl_3$) δ 99.1 ($J_{C1,H1}$ = 172 Hz, C-1 α); HRMS: $[M+Na]^+$ calcd for $C_{25}H_{27}F_3O_8Na$ 535.15502, found 535.15415.



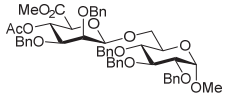
Methyl (1,1,1,3,3,3-hexafluoro-2-propyl 4-*O*-acetyl-2,3-di-*O*-benzyl-α/β-D-mannopyranosyl uronate) (3F). Donor **3** and 1,1,1,3,3,3-hexafluoro-2-propanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 240 hours at -40°C) and purified by flash column chromatography (9/1 to 4/1 pentane/EtOAc) to yield glycosylation product **3F** (30.1 mg, 52 μmol, 52%, α:β = 1:1). R_f: 0.85 (α), 0.75 (β) (7/3 pentane/EtOAc). IR (neat): 1105, 1371, 1454, 1751, 2872, 2924; Data for the β-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.72 – 7.13 (m, 10H, CH_{arom}), 5.55 (t, 1H, *J* = 9.5 Hz, H-4), 4.92 (d, 1H, *J* = 12.3 Hz, C*H*H Bn), 4.78 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.74 (s, 1H, H-1), 4.51 (d, 1H, *J* = 12.3 Hz, C*H*H Bn), 4.72 – 4.56 (m, 1H, $CH(CF_3)_2$) 4.36 (d, 1H, *J* = 12.7 Hz, CH*H* Bn), 3.99 (d, 1H, *J* = 2.5 Hz, H-2), 3.87 (d, 1H, *J* = 9.4 Hz, H-5), 3.73 (s, 3H, CH_3 CO_2Me), 3.50 (dd, 1H, *J* = 9.6, 2.8 Hz, H-3), 2.02 (s, 3H, CH_3 OAc); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC): δ 169.6, 167.3 (C=O CO_2Me, Ac), 137.8, 137.5 (C_q), 128.6, 128.5, 128.4, 128.0, 128.0, 127.8, 127.6, (CH_{arom}), 120.8 (q, *J* = 281.0 Hz, CF_3), 100.3 (C-1), 78.0 (C-3), 74.3 (CH_2 Bn), 73.9 (C-5), 72.8 (C-2), 72.4 (CH_2 Bn), 71.8 (hept, *J* = 33.0 Hz, $CH(CF_3)_2$), 68.5 (C-4), 53.0 (CH_3 CO_2Me), 20.9 (CH_3 Ac); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 100.3 ($J_{C1,H1}$ = 165 Hz, C-1 β); Diagnostic peaks α-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.49 (t, 0.90H, *J* = 5.6 Hz, H-4), 5.39 (d, 0.90H, *J* = 5.5 Hz, H-1), 4.72 – 4.56 (m, 4.5H, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn, $CH(CF_3)_2$), 4.37 – 4.35 (m, 0.90H, H-5), 3.84 (dd, 0.90H, *J* = 6.0, 2.9 Hz, H-3), 3.68 (dd, 0.90H, *J* = 5.5, 2.8 Hz, H-2). ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC):δ 169.9, 168.3 (C=O CO_2Me, Ac), 137.8, 137.65 (C_q), 128.6, 128.5, 128.4, 128.0, 128.0, 127.9, 127.8, 127.6 (CH_{arom}), 100.0 (C-1), 75.4 (C-3), 74.3 (CH_2 Bn), 74.3 (C-2), 73.7 (C-2), 73.17 (d, *J* = 32.8 Hz, $CH(CF_3)_2$), 72.7 (C-5), 69.3 (C-4), 52.7 (CH_3 CO_2Me), 21.0 (CH_3 Ac); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 100.0 ($J_{C1,H1}$ = 175 Hz, C-1 α); HRMS: $[M+NH_4]^+$ calcd for $C_{26}H_{30}F_6NO_8$ 598.18707, found 598.18711.



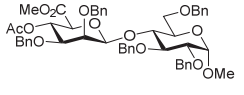
Methyl (4-*O*-acetyl-2,3-di-*O*-benzyl-1-deoxy-β-deuterio-D-mannopyranosyl uronate) (3G). Donor **3** and triethylsilane-D were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 240 hours at -40°C) and purified by flash column chromatography (9/1 to 7/3 pentane/EtOAc) to yield glycosylation product **3G** (39.6 mg, 95 μmol, 95%, α:β = <1:20). R_f: 0.45 (7/3 pentane/EtOAc). $[\alpha]_D^{26}$ = -34.4° (*c* = 0.5, $CHCl_3$); IR (neat): 698, 736, 1051, 1136, 1228, 1371, 1454, 1745, 2872, 2924; Data for the β-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, NOESY) δ 7.39 – 7.17 (m, 10H, CH_{arom}), 5.60 (dd, 1H, *J* = 4.9, 3.5 Hz, H-4), 4.63 (s, 2H, CH_2 Bn), 4.53 (s, 2H, CH_2 Bn), 4.19 (d, 1H, *J* = 3.2 Hz, H-5), 3.81 (m, 2H, H-2, H-3), 3.68 (d, 1H, *J* = 3.9 Hz, H-1), 3.61 (s, 3H, CH_3 CO_2Me), 2.06 (s, 3H, CH_3 OAc); ^{2}H NMR (61 MHz, $CHCl_3$) δ 4.73 (D-1); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC, HMBC): δ 169.9, 168.9 (C=O CO_2Me, Ac), 138.1, 137.8 (C_q), 131.2, 129.4, 128.6, 128.5, 128.4, 127.9, 127.8, 127.8, 127.8, 124.9 (CH_{arom}), 73.8 (C-5), 73.4 (C-3), 72.3 (CH_2 Bn), 71.4 (C-2), 71.3 (CH_2 Bn), 70.0 (C-4), 62.4 (C-1), 52.4 (CH_3 CO_2Me), 21.1 (CH_3 Ac). HRMS: $[M+Na]^+$ calcd for $C_{23}H_{25}DO_7Na$ 438.16335, found 438.16264.



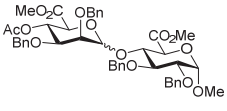
Methyl (allyl 4-*O*-acetyl-2,3-di-*O*-benzyl-1-deoxy-β-D-mannopyranosyl uronate) (3H). Donor **3** and allyl trimethylsilane were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 96 hours at -40°C) and purified by flash column chromatography (9/1 to 7/3 pentane/EtOAc) to yield glycosylation product **3H** (18.3 mg, 40 µmol, 40%, α:β = <1:20). R_f: 0.25 (8/2 pentane/EtOAc). $[\alpha]_D^{20}$ = -38.8° (*c* = 1, $CHCl_3$); IR (neat): 696, 735, 1026, 1055, 1114, 1228, 1368, 1746, 2855, 2924; Data for the β-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, NOESY): δ 7.36 – 7.20 (m, 10H, CH_{arom}), 5.71 – 5.58 (m, 1H, C*H*CH_2 allyl), 5.53 (t, 1H, *J* = 9.8 Hz, H-4), 5.07 – 4.95 (m, 1H, CHC*H*$_2$ allyl), 5.01 (d, 1H, *J* = 11.5 Hz, C*H*H Bn), 4.72 (d, 1H, *J* = 12.2 Hz, C*H*H Bn), 4.66 (d, 1H, *J* = 11.6 Hz, CH*H* Bn), 4.61 (d, 1H, *J* = 12.2 Hz, CH*H* Bn), 3.83 (d, 1H, *J* = 9.9 Hz, H-5), 3.79 (d, 1H, *J* = 2.3 Hz, H-2), 3.71 (s, 3H, CH_3 CO_2Me), 3.60 (dd, 1H, *J* = 9.9, 2.7 Hz, H-3), 3.36 (t, 1H, *J* = 7.1 Hz, H-1), 2.56 – 2.48 (m, 1H, C*H*HCH allylic), 2.40 – 2.26 (m, 1H, CH*H*CH), 2.01 (s, 3H, CH_3 OAc); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC, HMBC): δ 169.9, 168.5 (C=O CO_2Me, Ac), 138.3, 138.0 (C_q), 134.0 (*C*HCH_2 allyl), 131.3, 131.2, 129.4, 129.1, 128.6, 128.6, 128.6, 128.5, 128.4, 128.3, 128.1, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 127.6, 124.9 (CH_{arom}), 117.9 (CH*C*H_2 allyl), 88.6 (H-3), 79.1 (H-1), 77.6 (C-5), 74.5 (CH_2 Bn), 73.7 (C-2), 72.6 (CH_2 Bn), 69.5 (C-4), 52.7 (CH_3 CO_2Me), 35.4 (*C*H_2CH allyl), 21.0 (CH_3 Ac); HRMS: $[M+NH_4]^+$ calcd for $C_{26}H_{34}NO_7$ 472.23298, found 472.23294.



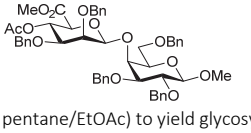
Methyl 6-*O*-(methyl [4-*O*-acetyl-2,3-di-*O*-benzyl-β-D-mannopyranosyl uronate])-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (30). Donor **3** and acceptor **10** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 16 hours at -40°C) and purified by flash column chromatography (9/1 to 7/3 pentane/EtOAc) to yield glycosylation product **30** (57.5 mg, 66 µmol, 66%, α:β = <1:20). R_f: 0.54 (7/3 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[113] $[\alpha]_D^{26}$ = -11,6° (*c* = 1, $CHCl_3$), (lit:[113] $[\alpha]_D^{22}$ = -11.0° (*c* = 0.6, $CHCl_3$)). IR (neat): 733, 906, 1028, 1055, 1101, 1242, 1361, 1452, 1748, 2908; Data for the β-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC): δ 7.40 – 7.19 (m, 25H, CH_{arom}), 5.48 (t, 1H, *J* = 9.6 Hz, H-4'), 5.02 (d, 1H, *J* = 10.9 Hz, C*H*H Bn), 4.91 (d, 1H, *J* = 12.6 Hz, C*H*H Bn), 4.83 (d, 1H, *J* = 10.9 Hz, CH*H* Bn), 4.82 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.80 – 4.71 (m, 3H, CH*H* Bn, CH*H* Bn, C*H*H Bn), 4.67 (d, 1H, *J* = 12.2 Hz, CH*H* Bn), 4.57 (d, 1H, *J* = 3.5 Hz, H-1), 4.50 (d, 1H, *J* = 4.4 Hz, CH*H* Bn), 4.47 (d, 1H, *J* = 5.3 Hz, C*H*H Bn), 4.36 (d, 1H, *J* = 12.4 Hz, CH*H* Bn), 4.16 – 4.09 (m, 2H, H-6, H-1'), 4.01 (t, 1H, *J* = 9.2 Hz, H-3), 3.79 (dq, 1H, *J* = 7.3, 2.8, 1.7 Hz, H-5), 3.74 (d, 1H, *J* = 9.5 Hz, H-5'), 3.72 – 3.66 (m, 4H, CH_3 CO_2Me, H-2'), 3.50 (dd, 1H, *J* = 9.7, 3.5 Hz, H-2), 3.45 – 3.34 (m, 3H, H-4, H-6, H-3'), 3.31 (s, 3H, CH_3 OMe), 2.02 (s, 3H, CH_3 OAc); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC, HMBC): δ 169.7, 168.1 (C=O CO_2Me, Ac), 138.9, 138.4, 138.1, 137.8 (C_q), 128.6, 128.5, 128.5, 128.5, 128.3, 128.3, 128.2, 128.1, 128.1, 127.9, 127.8, 127.8, 127.6, 127.6 (CH_{arom}), 101.7 (C-1'), 97.9 (C-1), 82.2 (H-3), 79.9 (H-2), 78.3 (H-3'), 77.7 (H-4), 75.9 (CH_2 Bn), 74.9 (CH_2 Bn), 73.8 (C-5'), 73.7 (CH_2 Bn), 73.5 (CH_2 Bn), 72.9 (C-2'), 71.6 (CH_2 Bn), 69.8 (C-5), 69.0 (C-4'), 68.8 (C-6), 55.2 (CH_3 OMe), 52.7 (CH_3 CO_2Me), 21.0 (CH_3 Ac); ^{13}C-GATED NMR (101 MHz, $CDCl_3$) δ 101.7 ($J_{C1,H1}$ = 155 Hz, C-1' β); HRMS: $[M+Na]^+$ calcd for $C_{51}H_{56}O_{13}Na$ 899.36131, found 899.36111.



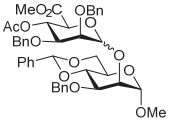
Methyl 4-*O*-(methyl [4-*O*-acetyl-2,3-di-*O*-benzyl-β-D-mannopyranosyl uronate])-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (31). Donor **3** and acceptor **11** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 16 hours at -40°C) and purified by flash column chromatography (9/1 to 7/3 pentane/EtOAc) to yield glycosylation product **31** (53.1 mg, 61 µmol, 61%, α:β = <1:20). R_f: 0.65 (7/3 pentane/EtOAc); $[\alpha]_D^{26}$ = -30.2° (*c* = 1, $CHCl_3$). IR (neat): 733, 1026, 1096, 1366, 1454, 1746, 2920; Data for the β-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC): δ 7.39 – 7.19 (m, 25H, CH_{arom}), 5.41 (t, 1H, *J* = 9.7 Hz, H-4'), 5.17 (d, 1H, *J* = 11.3 Hz, C*H*H Bn), 4.78 – 4.72 (m, 4H, CH*H* Bn, C*H*H Bn, CH*H* Bn, C*H*H Bn), 4.64 – 4.56 (m, 3H, CH*H* Bn, C*H*H Bn, H-1), 4.44 (d, 1H, *J* = 12.3 Hz, CH*H* Bn), 4.40 (s, 1H, H-1'), 4.36 (d, 1H, *J* = 12.3 Hz, C*H*H Bn), 4.28 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 3.89 (m, 2H, H-3, H-5), 3.68 – 3.63 (m, 1H,), 3.62 (d, 1H, *J* = 2.7 Hz, H-2'), 3.57 (d, 1H, *J* = 9.7 Hz, H-5'), 3.55 – 3.45 (m, 5H, H-2, CH_3 CO_2Me, C-6), 3.38 (s, 3H, CH_3 OMe), 3.18 (dd, 1H, *J* = 9.7, 2.8 Hz, H-3'), 2.01 (s, 3H, CH_3 OAc); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC, HMBC): δ 169.7, 167.9 (C=O CO_2Me, Ac), 139.6, 138.5, 138.3, 138.1, 137.9 (C_q), 128.7, 128.5, 128.5, 128.2, 128.2, 128.2, 128.2, 128.1, 128.0, 127.9, 127.9, 127.8, 127.5, 127.4, 127.1 (CH_{arom}), 101.1 (C-1'), 98.4 (C-1), 80.4 (C-3), 79.3 (H-2), 78.8 (C-3'), 78.2 (C-5), 75.4 (CH_2 Bn), 74.6 (C-2'), 74.2 (C-5'), 73.7 (CH_2 Bn), 73.7 (CH_2 Bn), 73.6 (CH_2 Bn), 71.8 (CH_2 Bn), 69.5 (H-4), 69.0 (C-4'), 68.7 (C-6), 55.4 (CH_3 OMe), 52.5 (CH_3 CO_2Me), 20.9 (CH_3 Ac); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 101.1 ($J_{C1,H1}$ = 158 Hz, C-1' β); HRMS: $[M+Na]^+$ calcd for $C_{51}H_{56}O_{13}Na$ 899.36131, found 899.36094.



Methyl (methyl 4-*O*-[methyl (4-*O*-acetyl-2,3-di-*O*-benzyl-α/β-D-mannopyranosyl uronate)]-2,3-di-*O*-benzyl-α-D-glucopyranosyl uronate) (32). Donor **3** and acceptor **12** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 48 hours at -40°C) and purified by flash column chromatography (9/1 to 7/3 pentane/EtOAc) to yield glycosylation product **32** (58.0 mg, 71 µmol, 71%, α:β = 1:10). R_f: 0.38 (7/3 pentane/EtOAc); $[\alpha]_D^{26}$ = -31.2° (*c* = 1, $CHCl_3$). IR (neat): 733, 1026, 1043, 1229, 1454, 1744, 2855, 2926; Data for the β-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC): δ 7.42 – 7.23 (m, 20H, CH_{arom}), 5.44 (t, 1H, *J* = 9.8 Hz, H-4'), 5.19 (d, 1H, *J* = 11.3 Hz, C*H*H Bn), 4.88 – 4.69 (m, 4H, C*H*H Bn, CH*H* Bn, C*H*H Bn, CH*H* Bn), 4.62 – 4.38 (m, 5H, CH*H* Bn, C*H*H Bn, C*H*H Bn, H-1', H-1), 4.08 (d, 1H, *J* = 9.3 Hz, H-5), 3.96 – 3.85 (m, 2H, H-3, H-4), 3.76 (d, 1H, *J* = 2.7 Hz, H-2'), 3.70 (d, 1H, *J* = 9.7 Hz, H-5'), 3.59 (s, 3H, CH_3 CO_2Me), 3.53 – 3.46 (m, 4H, CH_3 CO_2Me, H-2), 3.46 – 3.37 (m, 4H, CH_3 OMe, H-3'), 2.00 (s, 3H, CH_3 OAc); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC, HMBC): δ 170.2, 169.8, 167.8 (C=O CO_2Me, Ac), 139.4, 138.6, 138.1, 137.9 (C_q), 128.6, 128.5, 128.5, 128.5, 128.4, 128.3, 128.3, 128.2, 128.2, 128.1, 127.9, 127.8, 127.7, 127.6, 127.5, 127.2 (CH_{arom}), 102.3 (C-1'), 98.9 (C-1), 80.7 (C-4), 80.0 (C-3), 78.6 (C-2), 78.4 (C-3'), 75.7 (CH_2 Bn), 74.7 (C-2'), 74.5 (CH_2 Bn), 73.9 (CH_2 Bn, C-5'), 71.8 (CH_2 Bn), 69.6 (C-5), 69.0 (C-4'), 56.0 (CH_3 OMe), 52.6 (CH_3 CO_2Me), 52.5 (CH_3 CO_2Me), 20.9 (CH_3 Ac); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 102.3 ($J_{C1,H1}$ = 154 Hz, C-1' β); Diagnostic peaks α-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): 5.44 (m, 0.20H, H-1', H-4'), 2.00 (s, 0.30H, CH_3 OAc); HRMS: $[M+Na]^+$ calcd for $C_{45}H_{50}O_{14}Na$ 837.30928, found 837.30903.



Methyl 4-*O*-(methyl [4-*O*-acetyl-2,3-di-*O*-benzyl-β-D-mannopyranosyl uronate])-2,3,6-tri-*O*-benzyl-β-D-galactopyranoside (33). Donor **3** and acceptor **13** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 16 hours at -40°C) and purified by flash column chromatography (9/1 to 7/3 pentane/EtOAc) to yield glycosylation product **33** (66.8 mg, 76 µmol, 76%, α:β = <1:20). R_f: 0.39 (7/3 pentane/EtOAc); $[\alpha]_D^{26}$ = -31.6° (*c* = 1, $CHCl_3$). IR (neat): 735, 1026, 1051 1231, 1748, 2870; Data for the β-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC): δ 7.35 – 7.22 (m, 25H, CH_{arom}), 5.45 (t, 1H, *J* = 9.8 Hz, H-4'), 4.95 (d, 1H, *J* = 12.7 Hz, C*H*H Bn), , 4.93 (d, 1H, *J* = 10.9 Hz, CH*H* Bn), 4.85 (d, 1H, *J* = 12.7 Hz, CH*H* Bn), 4.78 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.75 (s, 1H, H-1'), 4.67 (d, 1H, *J* = 11.0 Hz, CH*H* Bn), 4.60 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.58 (d, 1H, *J* = 11.7 Hz, CH*H* Bn), 4.51 (d, 1H, *J* = 11.7 Hz, CH*H* Bn), 4.43 (d, 1H, *J* = 12.3 Hz, C*H*H Bn), 4.30 (d, 1H, *J* = 7.6 Hz, H-1), 4.22 (d, 1H, *J* = 12.3 Hz, CH*H* Bn), 4.15 (d, 1H, *J* = 2.5 Hz, H-2), 3.95 (d, 1H, *J* = 2.8 Hz, H-2'), 3.90 (dd, 1H, *J* = 9.7, 6.3 Hz, H-6), 3.74 (dd, 1H, *J* = 9.6, 5.7 Hz, H-6), 3.70 – 3.63 (m, 2H, H-5, H-5'), 3.63 – 3.56 (m, 7H, H-4, CH_3 OMe, CH_3 CO_2Me), 3.56 – 3.50 (m, 1H, H-3), 3.24 (dd, 1H, *J* = 9.8, 2.9 Hz, H-3'), 1.99 (s, 3H, CH_3 OAc); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC, HMBC): δ 169.8, 168.1 (C=O CO_2Me, Ac), 138.8, 138.7, 138.3, 138.0 (C_q), 128.7, 128.6, 128.5, 128.3, 128.2, 128.0, 127.9, 127.8, 127.8, 127.7, 127.5, 127.5 (CH_{arom}), 105.1 (C-1), 101.9 (C-1'), 81.8 (C-3), 79.6 (C-5), 79.0 (C-3'), 75.1 (CH_2 Bn), 73.9 (C-5), 73.8 (CH_2 Bn), 73.6 (CH_2 Bn), 73.6 (C-4), 73.2 (C-2), 72.5 (C-2'), 71.3 (CH_2 Bn), 69.4 (C-6), 68.9 (C-4'),57.2 (CH_3 CO_2Me), 52.6 (CH_3 OMe), 20.9 (CH_3 Ac); HRMS: $[M+Na]^+$ calcd for $C_{51}H_{56}O_{13}Na$ 899.36131, found 899.36109.



Methyl 2-*O*-(methyl [4-*O*-acetyl-2,3-di-*O*-benzyl-α/β-D-mannopyranosyl uronate])-3-*O*-benzyl-4,6-bezylidene-α-D-mannopyranoside (34). Donor **3** and acceptor **14** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 16 hours at -40°C) and purified by flash column chromatography (9/1 to 7/3 pentane/EtOAc) to yield glycosylation product **34** (60.4 mg, 77 µmol, 77%, α:β = 1:7.1). R_f: .34 (7/3 pentane/EtOAc); $[\alpha]_D^{26}$ = -48.6° (*c* = 1, $CHCl_3$). IR (neat): 735, 1026, 1053, 1230, 1369, 1454, 1748, 2868, 2924; Data for the β-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC): δ 7.51 – 7.22 (m, 15H, CH_{arom}), 5.60 – 5.53 (m, 2H, H-4', C*H*Ph), 5.02 (d, 1H, *J* = 12.5 Hz, C*H*H Bn), 4.93 (d, 1H, *J* = 12.5 Hz, CH*H* Bn), 4.83 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.72 (d, 1H, *J* = 1.1 Hz, H-1), 4.64 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.62 (s, 1H, H-1'), 4.50 (d, 1H, *J* = 12.4 Hz, C*H*H Bn), 4.36 – 4.31 (m, 2H, CH*H* Bn, H-2), 4.29 – 4.24 (m, 1H, H-6), 4.15 – 4.07 (m, 1H, H-4), 4.01 – 3.91 (m, 2H, H-2', H-3), 3.85 (d, 1H, *J* = 9.7 Hz, H-5'), 3.82 – 3.75 (m, 2H, H-5, H-6), 3.63 (s, 3H, CH_3 CO_2Me), 3.48 (dd, 1H, *J* = 9.7, 2.9 Hz, H-3'), 3.35 (s, 3H, CH_3 OMe), 2.03 (s, 3H, CH_3 OAc); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC, HMBC): δ 169.7, 167.9 (C=O CO_2Me, Ac), 138.8, 138.5, 137.8, 137.7 (C_q), 129.0, 128.7, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 127.9, 127.9, 127.8, 127.8, 127.7, 127.6, 127.5, 127.4, 126.3, 126.2 (C_{arom}), 101.8 (CHPh), 99.8 (C-1'), 99.2 (C-1), 78.5 (C-4), 78.2 (C-3), 74.0 (C-5'), 73.9 (H-2), 73.9 (H-3), 73.9 (CH_2 Bn), 73.0 (H-2'), 71.3 (CH_2 Bn), 71.0 (CH_2 Bn), 69.0 (C-6), 68.8 (C-4'), 64.1 (H-5), 55.1 (CH_3 OMe), 52.7 (CH_3 CO_2Me), 21.0 (CH_3 Ac); ^{13}C-GATED NMR (101 MHz, $CDCl_3$): δ 99.8 ($J_{C1,H1}$ = 154 Hz, C-1' β); Diagnostic peaks α-anomer: ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, HMBC): 5.59 (s, 0.14H, C*H*Ph), 5.50 (t, 0.14H, *J* = 7.5 Hz, H-4'), 5.45 (d, 0.14H, *J* = 4.0 Hz, H-1'), 3.66 (s, 0.42H, CH_3 CO_2Me), 3.35 (s, 0.42H, CH_3 OMe), 2.03 (s, 0.42H, CH_3 OAc); ^{13}C-APT NMR (101 MHz, $CDCl_3$, HSQC, HMBC): δ 100.3 (C-1'), 69.5 (C-4'); HRMS: $[M+NH_4]^+$ calcd for $C_{44}H_{52}NO_{13}$ 802.34332, found 802.34387.

Footnotes and references

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Chapter 4

Stereoselectivity of conformationally restricted glucosazide donors

Introduction

Glucosamine is a key constituent in numerous important oligosaccharides and glycoconjugates, where it can be either α- or β-linked.[1–5] Whereas the former type of linkage can be reliably installed through the use of neighboring-group participation of an C-2-amide- or carbamate based protecting group, the latter type continues to present a synthetic challenge.[6–8] A thorough understanding of the glycosylation mechanism and the influence of both reaction partners and reaction conditions on glycosylation stereoselectivity is needed to enable reliable and predictable glycosylation reactions. The in-depth research conducted on conformationally restricted benzylidene mannose and glucose donors has provided important insight into the glycosylation mechanisms of this type of 1,2-*cis*-selective donor.[9–17] To construct 1,2-*cis*-linkages of glucosamine donors, the C-2-amino group is most commonly masked as the nonparticipating azide.[18,19] Notably, benzylidene glucosazides have not been systematically investigated with respect to the stereoselectivity of glycosylations in which they are employed. The extrapolation

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of the stereoselectivity of benzylidene glucose donors to their glucosazide counterparts suggests that benzylidene or analogously protected glucosazides might represent an attractive class of 1,2-*cis*-selective glucosamine donor synthons.[20,21]

In Chapter 3 a comprehensive set of partially fluorinated ethanols, of gradually decreasing nucleophilicity, that can be used to map how the stereoselectivity of a given glycosylation system is dependent on the nucleophilicity of the acceptor, was introduced.[22] The stereoselectivity of the benzylidene glucose donor system proved to be greatly affected by the reactivity of the nucleophile.[23–27] In light of the demand for 1,2-*cis*-selective glucosaminylations but also with the aim in mind of furthering the understanding of the stereoelectronic effects exerted by the azido group, this chapter sets out to systematically evaluate a series of glucosazide donors in a set of glycosylation reactions involving the toolset of partially fluorinated ethanols and a selection of carbohydrate acceptors. As is described here, changes in the structure and reactivity of the donor can be effectively mapped using the panel of model acceptors, and a clear reactivity-selectivity relationship for the stereoselectivity of the glycosylations, emerges for all donors studied. Differences among the donors and the stereochemical variation in the glycosylation outcome can be explained on the basis of competition experiments and the characterization of the reactive intermediates involved.

Results and discussion

The set of (partially) fluorinated ethanol acceptors that was employed in Chapter 3, to relate the glycosylation stereoselectivity to the acceptor nucleophilicity is depicted in Figure 1 (compounds **6-11**). Glycosylating these acceptors with benzylidene mannose, benzylidene glucose, and mannuronic acid donors, as well as fucosazide donors bearing various protecting groups, established the dependence of the stereoselectivity of the

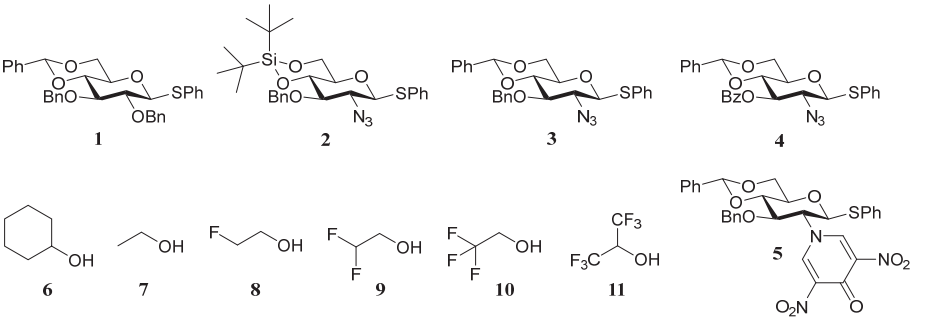


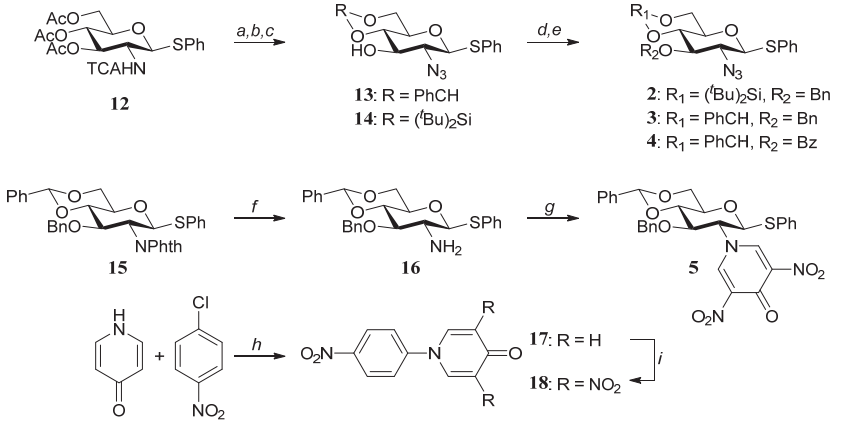
Figure 1. Glucose-configured donors **1-5** and model acceptors **6-11** used in this study.

glycosylations with these donors on the nucleophilicity of the acceptor.[22,28] For benzylidene protected glucose donor **1**, the gradual decrease in acceptor nucleophilicity going from ethanol, monofluoroethanol (MFE), difluoroethanol (DFE), trifluoroethanol (TFE), and hexafluoro-*iso*-propanol (HFIP) led to a gradual shift of the stereoselecivity from high β-selectivity to exclusive α-selectivity (See Table 3 below). Here, the results from investigating the set of conformationally restricted glucosamine donors depicted in Figure 1 (**1**-**5**) is presented. Variation in the structure of these donors is found in the cyclic protecting groups (benzylidene *vs* silylidene), in the functionality at the C-3–OH (benzyl *vs* benzoyl), and in the nature of the C-2–*N*-protecting group (azide *vs* the dinitropyridone [DNPY] group). The DNPY is introduced here as a nonparticipating *N*-protecting group.[29,30] The reactivity and selectivity of the set of glucosamine donors are related to the corresponding properties of well-studied benzylidene glucose donor **1**.[9,22]

Synthesis

Benzylidene-protected glucosazide donors **3**[31] and **4**[32] with an *O*-benzyl and an *O*-benzoyl, respectively, at C-3, as well as silylidene-protected donor **2**, were prepared from common building block **12**[33] as depicted in Scheme 1. Hydrolysis of all acetyl esters and the trichloroacetamide was followed by a diazotransfer to install the desired C-2-azide.[34]

Scheme 1. Preparation of donors **2**-**5**.



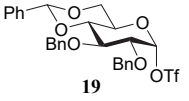
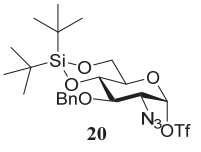
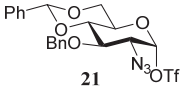
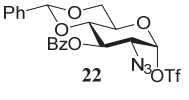
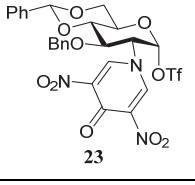
Reagents and conditions: (a) *i.* K_2CO_3, EtOH, H_2O; *ii.* $CuSO_4 \cdot 5H_2O$, imidazole-1-sulfonyl azide hydrochloride[34]; (b) di-*tert*-butylsilyl bis(trifluoromethanesulfonate), pyridine, **14**: 71% (three steps); (c) $PhCH(OMe)_2$, *p*-$TsOH \cdot H_2O$, **13**: 78% (three steps); (d) BnBr, NaH, DMF, **2**: 80%, **3**: 89%; (e) BzCl, DMAP, pyridine, DCM, 90%; (f) ethylenediamine, EtOH, 88%; (g) **18**, AcOH/pyridine (1/16, v/v), 98%; (h) K_2CO_3, NMP, 85%; (i) HNO_3, H_2SO_4, 60%.

Subsequent introduction of the di-*tert*-butylsilylidene (DTBS) and the benzylidene acetal gave intermediates **13**[31] and **14**, respectively. Benzylation of **14** and **13** and benzoylation of **13** gave the target donor compounds **2**, **3**, and **4**, respectively. Donor **5** was prepared in two steps from thioglucoside **15**[35] by exchange of the phthaloyl group for the DNPY functionality. To this end, compound **15** was treated with ethylenediamine to give amine **16**, wich was treated with DNPY reagent **18**[30,36] to furnish the target donor.

Observation of anomeric triflates

With these five donors in hand, the formation of potential covalent reactive intermediates was investigated by low-temperature NMR studies.[37] The donors were treated with the diphenyl sulfoxide/triflic anhydride (Ph_2SO/Tf_2O)[38] combination of reagents in deuterated dichloromethane. Figure 3 shows the results of these studies and Table 1 summarizes the anomeric chemical shifts of the observed triflates and the temperatures at which decomposition starts (T_{decomp}). Activation of reference donor **1** led

Table 1. Anomeric triflates observed.

Entry	Triflate	^{1}H δ (ppm)	$^3J_{H1\text{-}H2}$[a] (Hz)	^{13}C δ (ppm)	T_{decomp} (°C)
1	 **19**	6.09	3.4	106.1	-20
2	 **20**	6.00	3.4	104.8	-30
3	 **21**	6.07	3.5	105.0	-20
4	 **22**	6.23	3.5	104.5	-10
5	 **23**	6.06	n/a	102.2	-40

[a]values determined at -40°C

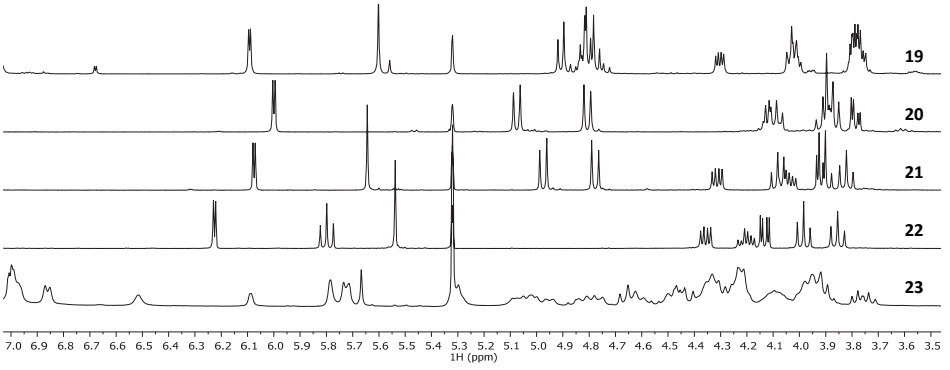
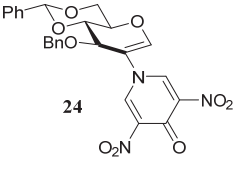


Figure 3. ^{1}H-NMR spectra at -40°C of activated donors **1**-**5** showing their respective anomeric triflates **19**-**23**.

to the formation of two species: In addition to the anomeric triflate **19**,[9] the oxosulfonium triflate **19α*** (6.68 ppm, 3.6 Hz) was also formed, as was confirmed by the activation of a sample containing additional Ph_2SO. Donors **2** and **3** were cleanly converted to their anomeric α-triflates **20** and **21** respectively, by treatment at -80°C with the activation couple. Activation of donor **4** proceeded more slowly, and an increase of the temperature from -80°C to -35°C was required for complete activation. Donor **5** proved difficult to study by low-temperature NMR spectroscopy because of significant line broadening in the resonance sets for both the donor and the products formed upon activation. Complete activation of the thioglycoside could only be achieved at -40°C, but at this temperature, decomposition of the reactive intermediates also set in. Two anomeric signals can be discriminated in the spectrum of the activated DNPY donor **5** (Figure 3), and these were tentatively assigned as the intermediate triflate (6.06 ppm) and oxosulfonium triflate (6.54 ppm). Unfortunately, complete characterization was hampered by the severe line broadening.[39] The reactive intermediates formed all decomposed to give the glucal product **24** (Figure 2). The formation of the glucal double bond is relatively fast, as the proton at C-2 is readily eliminated to provide the enol ether double bond that is conjugated to the DNPY aromatic ring.



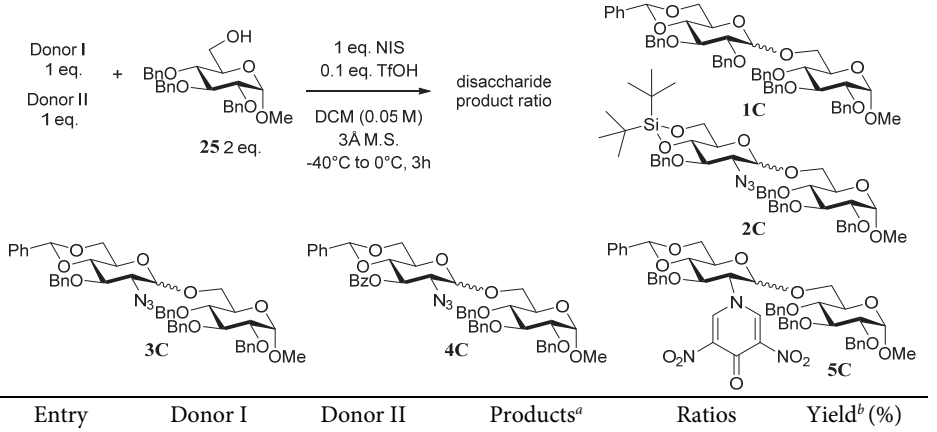
24

Figure 2. Structure of DNPY glucal **24**, cleanly forms as a decomposition product of activated donor **5**.

Competitive glycosylations and relative reactivities.

To investigate the reactivities of donors **1-5**, a series of competitive glycosylations were performed between the different thioglycosides.[40–44] In these competition experiments, an *in situ* activation protocol was used, employing *N*-iodosuccinimide (NIS)/ trifluoromethanesulfonic acid (TfOH) as activator and 2,3,4-tri-*O*-benzyl-α-*O*-methyl glucose (**25**) as the acceptor, as is commonly done to determine the reactivities of thioglycoside donors.[45,46] It should be noted, however, that the reactivity of the thiophenyl donor does not directly compare with the reactivity of an intermediate triflate in the glycosylation, although it does provide an indication of the relative disarming or arming nature of the protecting groups present on the different donors. It is apparent from Table 2 that the azide has a profound effect on the reactivity of donor **3**, as it is completely outcompeted by the C-2-*O*-benzyl donor **1**.[46] Silylidene donor **2** is more reactive than donor **3**, and the disaccharide products derived from donor **2** and **3** are

Table 2. Competitive donor activations.



Entry	Donor I	Donor II	Products[a]	Ratios	Yield[b] (%)
1	**1**	**2**	**1C/2C**	14 : 1	65
2	**1**	**3**	**1C/3C**	1 : 0	80
3	**2**	**3**	**2C/3C**	6 : 1	37
4	**3**	**4**	**3C/4C**	1.6 : 1	39
5[c]	**4**	**5**	**4C/5C**	1 : 0	64

[a]Determined by ^{1}H-NMR of the isolated disaccharide. [b]The disaccharide fraction was quantified after isolation by size-exclusion chromatography and related to the limiting amount of NIS (see experimental section). [c]The combined donor concentration for entry 5 was 0.1 M, triflic acid was added at -20°C and the reaction mixture was heated to +15°C overnight, and then the reaction was quenched (Et_3N).

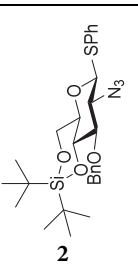
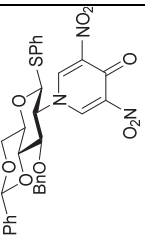
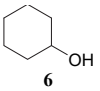
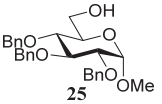
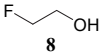
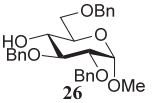
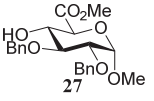
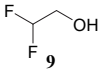
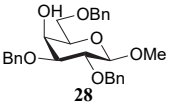
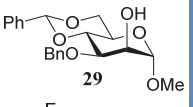
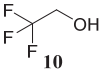
formed in a 6:1 ratio. C-3-*O*-Benzyl donor **3** in turn outcompetes benzoylated donor **4** slightly, as a result of the electron-withdrawing nature of the benzoate, giving a 1.6:1 ratio of the addition products **3C** and **4C**.[47–49] DNPY-protected donor **5** is the least reactive of the set of donors, as it did not provide any disaccharide product in the competition experiment with donor **4**.

Glycosylations

With the reactivities of these five donors established, the series of glycosylations with model acceptors **6**-**11** and carbohydrate acceptors **25**-**29**[50–52] was undertaken using the Ph_2SO/Tf_2O preactivation procedure. Table 3 list all glycosylations ordered by acceptor and donor reactivity. A clear relation between acceptor nucleophilicity and stereochemical outcome of the glycosylation reactions of all studied glucosamine donors was observed, in line with the results previously obtained with donor **1**. Upon comparison of the outcomes of the coupling reactions of glucosazide **3** with the results obtained with C-2-*O*-benzyl donor **1**, it becomes apparent that the latter donor reacts with higher α-selectivity. Donor **2**, bearing the DTBS group, overall provides slightly more of the α-linked products than its benzylidene counterpart **3**. The stereoselectivity of the condensations of donor **4**, bearing an additional electron-withdrawing protecting group (*i.e.,* the C-3-*O*-benzoyl), is very similar to the stereoselectivity observed with C-3-*O*-benzyl donor **3**. Finally, donor **5**, carrying the strongly electron-withdrawing DNPY group, is the most β-selective of the series of donors listed in Table 3.[53]

The selectivities of glycosylations with carbohydrate acceptors were also found to vary in a nucleophilicity-dependent fashion. The primary perbenzylated acceptor **25** reacts similarly to ethanol **7** to give primarily the β-linked products for all glucosamine donors studied. Secondary carbohydrate acceptors that were less nucleophilic showed variations in selectivity with the proportion of α-product increasing with decreasing acceptor reactivity. In line with the results from Chapter 3, the nucleophilicities of the secondary equatorial carbohydrate alcohols fall somewhere between the reactivities of MFE and DFE, with the reactivities of the axial hydroxyls approaching the reactivity of TFE. The differences in the reactivities of the donors are reflected in the stereoselectivities of both the glycosylations that involve the model acceptors and the glycosylations with the carbohydrate acceptors. A recurring trend is apparent for all acceptors, with the most reactive donor **1** providing most α-linked product and the least reactive donor **5** giving least α-linked product.

Table 3. Glycosylations of donors **1-5** with model acceptors **6-11** and carbohydrate acceptors **25-29.**

	Acceptor	 **1**	 **2**	 **3**	 **4**	 **5**
		Product[a] α:β (yield)[b]	Product α:β (yield)	Product α:β (yield)	Product α:β (yield)	Product α:β (yield)
A	 **7**	**1A** 1 : 10 (68 %)	**2A** < 1 : 20 (65 %)	**3A** < 1 : 20 (83 %)	**4A** < 1 : 20 (86 %)	**5A** < 1 : 20 (59 %)
B	 **6**	**1B** 1 : 5.1 (71 %)	**2B** < 1 : 20 (77 %)	**3B** < 1 : 20 (93 %)	**4B** < 1 : 20 (91 %)	**5B** < 1 : 20 (63 %)
C	 **25**	**1C** 1 : 2.7 (81 %)	**2C** 1 : 14 (92 %)	**3C** < 1 : 20 (89 %)	**4C** 1 : 14 (79 %)	**5C** < 1 : 20 (57 %)
D	 **8**	**1D** 1 : 2.8 (70 %)	**2D** 1 : 5 (79 %)	**3D** 1 : 6.7 (90 %)	**4D** 1 : 6.5 (83 %)	**5D** < 1 : 20 (43 %)
E	 **26**	**1E** 1 : 1 (79 %)	**2E** 1 : 3 (81 %)	**3E** 1 : 7 (88 %)	**4E** 1 : 6 (71 %)	**5E** 1 : 20 (55 %)
F	 **27**	**1F** 5 : 1 (90 %)	**2F** 3.3 : 1 (84 %)	**3F** 1.1 : 1 (93 %)	**4F** 1 : 1.4 (59 %)	**5F** 1 : 3.6 (30 %)
G	 **9**	**1G** 5 : 1 (70 %)	**2G** 2.7 : 1 (76 %)	**3G** 2.9 : 1 (64 %)	**4G** 2.7 : 1 (84 %)	**5G** 1 : 1 (59 %)
H	 **28**	**1H** > 20 : 1 (83 %)	**2H** 7 : 1 (52 %)	**3H** 9 : 1 (75 %)	**4H** 4 : 1 (51 %)	**5H** < 1 : 20 (52 %)
I	 **29**	**1I** > 20 : 1 (80 %)	**2I** > 20 : 1 (85 %)	**3I** 9 : 1 (74 %)	**4I** 5 : 1 (73 %)	**5I** 1 : 1.3 (53 %)
J	 **10**	**1J** > 20 : 1 (64 %)	**2J** > 20 : 1 (82 %)	**3J** > 20 : 1 (94 %)	**4J** > 20 : 1 (86 %)	**5J** 4 : 1 (58 %)
K	 **11**	**1K** > 20 : 1 (65 %)	**2K** > 20 : 1 (34 %)	**3K** > 20 : 1 (53 %)	-[c]	32% **24**

[a]Glycosylation results of donor **1**, are also reported in Chapter 2 of this thesis. [b]Ratio and yield of isolated product after column chromatography, anomers were not separated. [c]Only hydrolysed donor was found.

Mechanistic discussion

Two major trends become apparent from the table of glycosylations. First, with decreasing acceptor nucleophilicity the α/β ratio increases. Second, decreasing donor reactivity corresponds to a decrease in the α/β ratio. These trends also emerged in Chapter 3 and the work on fucosazide donors.[22,28] The reactive intermediates that can play a role in the glycosylations of the conformationally restricted glucosamine donors and the reaction trajectories of the incoming nucleophiles are presented in Figure 4. Previous studies by the group of Crich have indicated that substitutions on the benzylidene glucosyl triflate **19** proceed in an S_N2-like manner. In these mechanistic studies, which involved the determination of kinetic isotope effects and cation-clock methodology, isopropanol was used as an acceptor.[12,14] In the kinetic scenario that was proposed the relatively stable α-triflate (observed by low-temperature NMR spectroscopy) is in equilibrium with its more reactive β-counterpart. In both species, the triflate can be displaced by alcohols if they are nucleophilic enough. The higher β-selectivity that is seen for the glucosazide and DNPY-glucosamine donors in comparison to donor **1** can be explained by the stronger electron-withdrawing effect of the azide with respect to the benzyl ether. This leads to a more stable covalent α-triflate and favors an associative displacement mechanism. A similar effect has been observed by the group of Crich in glycosylations of the analogous 2-deoxy-2-fluoro benzylidene glucosides.[54] The DNPY group is even more electron withdrawing, leading to a further increase in β-selectivity through associative displacement. However, an S_N2-like reaction pathway is

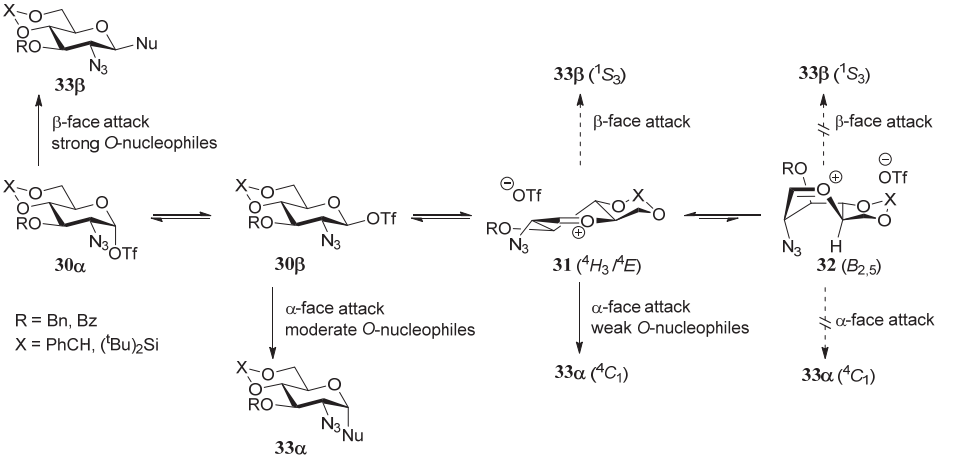


Figure 4. Reactive intermediates and reaction pathways for the 4,6-tethered glucosazide donors.

less likely for the weaker nucleophiles, such as TFE and HFIP. The high α-selectivity for these acceptors can be explained perhaps more precisely by considering the involvement of more electrophilic intermediates such as the glycosyl oxocarbenium ion. The benzylidene and silylidene protecting groups restrict the conformational space that the donor pyranosides can adopt and the intermediate oxocarbenium ion likely adopt a $^4E/^4H_3$–like conformation.[55,56] Nucleophiles attack this envelope/half-chair conformer preferentially from the bottom face to lead to the α-linked products through a chair-like transition state.[57] The more reactive donors more readily dissociate to form an oxocarbenium ion, and this accounts for the increased α-selectivity for these donors. Donor **2**, bearing the silylidene group is the most reactive of the studied glucosamine donors. It also is slightly more flexible than the benzylidene restricted donors, and these two factors allow the activated donor to more readily form a flattened oxocarbenium ion-like intermediate. Consequently, it is the most α-selective of the studied glucosamine donors. Finally, it is notable that the C-3-*O*-benzoyl protected glucosazide **4** reacts in a slightly more β-selective fashion than its C-3-*O*-benzyl counterpart **3**. In light of the discussion above, this makes sense, as the electron-withdrawing benzoyl stabilizes the anomeric α-triflate. It contrasts, however, with the behavior of acyl groups at the C-3 position of benzylidene mannosyl donors. The 1,2-*cis*-selectivity generally observed for these donors can be completely changed to selectively give the α-linked products by installing a C-3-acyl group in the donor.[58,59] The difference between the benzylidene mannose and benzylidene glucose series can be found in the different geometries that the oxocarbenium ions adopts. For the benzylidene mannose system, a $B_{2,5}$-like structure is one of the lower-energy oxocarbenium ion conformers.[12,55,56] In this constellation, the C-3-benzoate can fold over to the electron-depleted anomeric center to provide stabilization, without a major skeletal rearrangement. For the benzylidene glucose, on the other hand, a $B_{2,5}$-like structure such as **32** is significantly less favorable because this puts the C-2-azide in a flagpole position. Given the selectivities observed for this donor, influences arising from this boat conformation do not play a significant role here.

Conclusions

A set of model acceptors of gradually changing nucleophilicity has been used to investigate how the stereochemistry of glycosylations involving 4,6-tethered glucosamine donors relates to the nucleophilicity of the acceptor. The set of acceptors was complemented by a suite of carbohydrate alcohols to translate the results obtained with

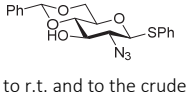
the model acceptors to a more relevant glycosylation setting. Four glucosamine donors were probed that differed in the type of tether spanning the C-4 and C-6-alcohols, the nature of the protecting group at the C-3-OH, and the amino functionality at C-2. Similarly to the previously described benzylidene glucose donor **1**, the stereoselectivity of the studied glucosamine donors show a strong correlation to the nucleophilicity of the acceptor, with strong nucleophiles providing completely β-selective condensations and weak nucleophiles selectively leading to the formation of the α-linked products. Benzylidene glucosazide donors are less α-selective than their C-2-*O*-benzyl congeners, because of the increased electron-withdrawing power of the azide, which retards the formation of an oxocarbenium ion species and favors a more associative mechanistic pathway. This chapter also introduced a novel protecting group for the C-2-amino group: the dinitropyridone functionality.[29,30,36] Although this group is easily installed and removed from the C-2-amine, its strongly electron-withdrawing character limits its use. In the 4,6-benzylidene glucosamine donor studied here it disarms the donor glycoside to the extent that it turns into a suboptimal glycosyl donor. A major incentive for the reported study was the good to excellent α-selectivity that has previously been reported for benzylidene glucose donor **1**. Unfortunately, installation of a 4,6-benzylidene on the analogous glucosazide donors does not provide a reliable donor to affect 1,2-*cis*-selective glycosylations. Only with relatively poor nucleophiles are useful stereoselectivities obtained. Changing the benzylidene for a silylidene group, however, turns the donor into a more reactive glycosylating agent showing improved α-selectivity. This donor, attractive because of its fully orthogonal protecting group scheme, might find application in the future assembly of oligosaccharides featuring α-glucosamines. Finally, it is prudent to note that this study provides another illustration of the application of the toolset of partially fluorinated ethanols to efficiently map the reactivity-selectivity relationship of a class of donor glycosides. Implementation of this methodology to investigate novel donor systems will broaden the insight into the different mechanistic pathways at play during glycosylations and eventually generate a complete picture how to tune both reaction partners to achieve stereoselective glycosylation reactions in a predictable manner.

Experimental section

General procedure for Tf_2O/Ph_2SO mediated glycosylations: Donor (0.1 mmol), Ph_2SO (26 mg, 0.13 mmol, 1.3 eq.) and TTBP[60] (62 mg, 0.25 mmol, 2.5 eq.) were coevaporated twice with dry toluene and dissolved in dry DCM (2 mL, 0.05 M donor). Activated 3Å molecular sieves (rods, size 1/16 in.) were added, and the reaction mixture stirred for 1 h at room temperature under a nitrogen atmosphere. The solution was cooled to -78°C and Tf_2O (22 µl, 0.13 mmol, 1.3 eq.) was added. The reaction mixture was allowed to warm to -60°C (donor **1**, **2**, **3**), -45°C (donor **5**), -35°C (donor **4**), followed by recooling to -78°C and addition of the acceptor (0.2 mmol, 2 eq.) in DCM (0.4 mL, 0.5 M). The reaction mixture was allowed to warm to -40°C in approximately 90 min and stirred for an additional 0-18 h depending on the acceptor. The reaction was quenched with Et_3N (0.1 mL, 0.72 mmol, 5.5 eq.) at -40 °C and diluted with DCM. The solution was transferred to a separatory funnel and water was added, the layers were separated and the water phase extracted once more with DCM. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by silica gel flash column chromatography and when needed, sephadex™ LH-20 size exclusion chromatography yielded the glycosylation product as a mixture of anomers.

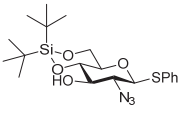
General procedure for the NIS/TfOH mediated competition experiments: Donor I (0.1 mmol, 1 eq.), donor II (0.1 mmol, 1 eq.) and acceptor **25** (0.2 mmol, 2 eq.) were together coevaporated with dry toluene (2x). Dry DCM (4 mL, donor concentration 0.05 M), a Teflon stirring bar and 3Å activated molecular sieves (rods, size 1/16 in.) were added and the mixture was stirred under a nitrogen atmosphere for 1 h at room temperature. The mixture was cooled to -40°C and NIS (0.1 mmol, 1 eq.) was added. TfOH (50 µL of a freshly prepared 0.2 M stock solution in dry DCM, 0.1 eq.) was added and the mixture was allowed to warm to 0°C in 3 hours. Et_3N (0.1 mL) was added and the mixture was diluted with EtOAc, washed with sat. aq. NaS_2O_3 and brine, dried over Na_2SO_4 and concentrated *in vacuo*. Size exclusion chromatography (Sephadex LH-20, 1/1 DCM/MeOH) enabled isolation of the disaccharide products and the monosaccharide rests, which were both analysed with NMR spectroscopy. The yield of the disaccharide fraction was determined. For the competition between donors **4** and **5**, a 0.1 M concentration, and a starting temperature of -20°C was used, which was allowed to warm to +15°C in 18h.

General procedure for the low temperature NMR experiments: A mixture of donor (30 µmol) and Ph_2SO (39 µmol) was coevaporated with dry toluene twice (for the activation of donor 1 also TTBP (75 µmol) was added). Under a nitrogen atmosphere, CD_2Cl_2 (0.6 mL) was added and the mixture transferred to a nitrogen flushed NMR tube and closed with a NMR tube septum. The NMR magnet was cooled to -80°C, locked and shimmed and the sample was measure prior to activation. In a long narrow cold bath (EtOH, -85°C) the sample was treated with Tf_2O (39 µmol), shaken thrice and cooled again after every shake. The cold sample was wiped dry and quickly inserted back in the cold magnet. The first ^1H NMR spectrum was immediately recorded. The sample was then reshimmed and spectra were recorded in 10°C intervals with at least 5 min equilibration time for every temperature.

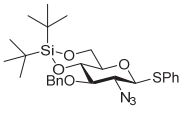


Phenyl 2-azido-4,6-*O*-benzylidene-2-deoxy-1-thio-β-D-glucopyranoside (13). To a suspension of thioglycoside **12**[33] (27.14 g, 50 mmol, 1 eq.) in EtOH (200 mL) was added K_2CO_3 (41.5 g, 300 mmol, 6 eq), and 20 mL H_2O and the mixture was refluxed overnight. The flask was cooled to r.t. and to the crude free amine[61] was added the diazo transfer reagent imidazole-1-sulfonyl azide hydrochloride[34] (13.10 g, 62.5 mmol, 1.25 eq.) in 3 equal portions followed by a catalytic amount of $CuSO_4 \cdot 5\ H_2O$ (125 mg, 0.5 mmol, 0.01 eq.). After stirring for 5 hours, the solution was filtered and reduced to 1/4 of its volume *in vacuo*. H_2O (150 mL) and 1 M aq. HCl (150 mL) were added to obtain an acidic (pH ≈ 3) solution which was extracted with EtOAc (3x 120 mL). The combined organic layers were washed with sat. aq. $NaHCO_3$ (150 mL) and brine (150 mL), dried with $MgSO_4$ and concentrated *in vacuo* to obtain crude azide; phenyl 2-azido-2-deoxy-1-thio-β-D-glucopyranoside.[62] The crude azide (≤50 mmol) was coevaporated with toluene twice and subsequently dissolved in DMF (50 mL) and MeCN (200 mL) to which benzaldehyde dimethyl acetal (15 mL, 100 mmol, 2 eq.) and *p*-$TsOH \cdot H_2O$ (950 mg, 5 mmol, 0.1 eq.) were added. The reaction mixture was heated at 60°C overnight, followed by an additional 5 hours of heating at 60°C under reduced pressure (300 mbar) to reduce the volume to 1/3. The reaction was quench by the addition of triethylamine (1 mL), and diluted with EtOAc (350 mL), washed with H_2O (2x 100 mL), sat. aq. $NaHCO_3$ (1x 100 mL), and brine (1x 100 mL). The organic layer was dried ($MgSO_4$) and concentrated *in vacuo.* The crude mixture was purified by percipitation from hot EtOAc (100 mL) / heptane (300 mL) by adding petroleum ether (500 mL) while stirring and slowly cooling to 0°C to obtain the title compound as a white powder (11.38 g, 29.5 mmol, 59%). The mother liquors were purified by flash column chromatography (8/1 to 4/1 pentane/EtOAc) to obtain an additional batch of white solid product (3.8 g, 9.6 mmol, total yield = 39.1 mmol, 78%, 3 steps). A purified sample could be recrystallized from either hot MeOH or EtOAc/petroleum ether to obtain white cotton like needles. R_f: 0.50 (6/1 pentane/EtOAc). Spectroscopic

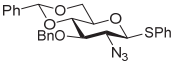
data were in accord with those previously reported.[31] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.64 – 7.52 (m, 2H, CH_{arom}), 7.50 – 7.43 (m, 2H, CH_{arom}), 7.42 – 7.32 (m, 6H, CH_{arom}), 5.53 (s, 1H, C*H*Ph), 4.54 (d, 1H, *J* = 10.1 Hz, H-1), 4.38 (dd, 1H, *J* = 10.5, 4.6 Hz, H-6), 3.85 – 3.70 (m, 2H, H-3, H-6), 3.52 – 3.40 (m, 2H, H-4, H-5), 3.35 (dd, 1H, *J* = 10.2, 9.0 Hz, H-6), 2.75 (bs, 1H, 3-OH); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 136.8 (C_q CHPh), 133.8 (CH_{arom}), 130.9 (C_q SPh), 129.6, 129.3, 128.8, 128.5, 126.4 (CH_{arom}), 102.1 (CHPh), 86.9 (C-1), 80.3 (C-4), 74.2 (C-3), 70.4 (C-5), 68.5 (C-6), 65.2 (C-2); HRMS: $[M+H]^+$ calcd for $C_{19}H_{20}N_3O_4S$ 386.11690, found 386.11708.



Phenyl 2-azido-2-deoxy-4,6-*O*-di-*tert*-butylsilylidene-1-thio-β-D-glucopyranoside (14). Crude triol phenyl 2-azido-2-deoxy-1-thio-β-D-glucopyranoside (synthesized as described for compound **13**) (≤10 mmol) was dissolved in pyridine (15 mL) and cooled to 0°C. Di-*tert*-butylsilyl bis(trifluoromethanesulfonate) (3.6 mL, 11 mmol, 1.1 eq.) was slowly added and the reaction was stirred for 1 h before being quenched with MeOH. The reaction mixture was diluted with 200 mL Et_2O and washed with 1M aq. HCl (3x 60 mL), sat. aq. $NaHCO_3$ (60 mL), and brine (60 mL). The organic layer was dried with Na_2SO_4, filtered and concentrated in vacuo. Purification by flash column chromatography (1-10% Et_2O/pentane) afforded the silylidene protected title compound as a colorless oil (3.10 g, 7.1 mmol, 71% over three steps). R_f: 0.18 (19/1 pentane/Et_2O). $[\alpha]_D^{23}$ = -42.6° (*c* = 1.0, $CHCl_3$); IR (neat): 652, 733, 824, 1072, 1092, 1155, 1277, 1474, 2112, 2859, 2884, 2934, 2963, 3449; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC) δ 7.57 – 7.51 (m, 2H, CHarom), 7.36 – 7.31 (m, 3H, CHarom), 4.49 (d, 1H, *J* = 10.2 Hz, H-1), 4.21 (dd, 1H, *J* = 10.2, 5.1 Hz, H-6), 3.89 (t, 1H, *J* = 10.2 Hz, H-6), 3.64 (t, 1H, *J* = 9.1 Hz, H-4), 3.56 (td, 1H, *J* = 9.0, 1.2 Hz, H-3), 3.40 (ddd, 1H, *J* = 10.1, 9.3, 5.1 Hz, H-5), 3.31 (dd, 1H, *J* = 10.2, 9.1 Hz, H-2), 2.92 (d, 1H, *J* = 1.6 Hz, 3-OH), 1.04 (s, 9H, CH_3 ^{t}Bu), 0.97 (s, 9H, CH_3 ^{t}Bu); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 133.7 (CH_{arom}), 131.2 (C_q), 129.2, 128.7 (CH_{arom}), 86.8 (C-1), 77.4 (C-3), 76.6 (C-4), 74.4 (C-5), 66.0 (C-6), 64.4 (C-2), 27.5, 27.0 (CH_3 ^{t}Bu), 22.8, 20.0 (C_q ^{t}Bu); HRMS: $[M-N_2+H]^+$ calcd for $C_{20}H_{32}NO_4SSi$ 410.18213, found 410.18220.

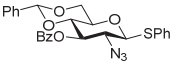


Phenyl 2-azido-3-*O*-benzyl-2-deoxy-4,6-*O*-di-*tert*-butylsilylidene-1-thio-β-D-glucopyranoside (2). Compound **14** (1.4 g, 3.2 mmol) was dissolved in DMF (15 mL) and cooled to 0°C. Benzyl bromide (421 µL, 3.52 mmol, 1.1 eq.) and NaH (60% dispersion in mineral oil, 166 mg, 4.16 mmol, 1.3 eq.) were added and the reaction was stirred for 2 h at 0°C and 1 h at r.t. The reaction mixture was quenched with MeOH and H_2O (100 mL) was added. The water phase was extracted three times with 30 mL Et_2O and the combined organic layers were washed with brine (2x), dried with Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (1%-8% Et_2O/pentane) yielded compound **2** as a colorless oil (1.35 g, 2.56 mmol, 80%). Additional impurities as observed by ^{1}H NMR originating from the previous crude steps could be removed by size exclusion chromatography (Sephadex™ LH-20, 1/1 DCM/MeOH). R_f: 0.51 (19/1 pentane/Et_2O). $[\alpha]_D^{23}$ = -85.0° (*c* = 1.0, $CHCl_3$); IR (neat): 654, 694, 746, 766, 826, 1059, 1078, 1099, 1159, 1474, 2110, 2859, 2884, 2934, 2963; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.55 – 7.48 (m, 2H, CHarom), 7.43 – 7.37 (m, 2H, CHarom), 7.36 – 7.27 (m, 6H, CHarom), 4.99 (d, 1H, *J* = 10.7 Hz, C*H*H Bn), 4.81 (d, 1H, *J* = 10.7 Hz, CH*H* Bn), 4.41 (d, 1H, *J* = 10.2 Hz, H-1), 4.21 (dd, 1H, *J* = 10.3, 5.1 Hz, H-6), 3.90 (t, 1H, *J* = 10.2 Hz, H-6), 3.87 (dd, 1H, *J* = 9.5, 8.7 Hz, H-4), 3.48 – 3.38 (m, 2H, H-3, H-5), 3.28 (dd, 1H, *J* = 10.2, 9.2 Hz, H-2), 1.07 (s, 9H, CH_3 ^{t}Bu), 1.01 (s, 9H, CH_3 ^{t}Bu); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 137.9 (C_q Bn), 133.9 (CH_{arom}), 130.9 (C_q SPh), 129.1, 128.7, 128.5, 128.5, 128.1 (CH_{arom}), 86.4 (C-1), 84.2 (C-3), 77.8 (C-4), 75.7 (CH_2 Bn), 74.7 (C-5), 66.2 (C-6), 64.2 (C-2), 27.5, 27.1 (CH_3 ^{t}Bu), 22.7, 20.0 (CH_3 ^{t}Bu); HRMS: $[M+H]^+$ calcd for $C_{27}H_{38}N_3O_4SSi$ 528.23468, found 528.23451. and $[M-N_2+H]^+$ calcd for $C_{27}H_{38}NO_4SSi$ 500.22853, found 500.22839.

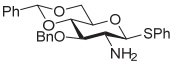


Phenyl 2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-1-thio-β-D-glucopyranoside (3). Compound **13** (4.36 g, 11.3 mmol) was coevaporated once with dry toluene and then dissolved in DMF (50 mL) and cooled to 0°C. Benzyl bromide (1.9 mL, 15.8 mmol, 1.4 eq.) and NaH (60% dispersion in mineral oil, 900 mg, 22.6 mmol, 2 eq.) were added in succession and the reaction mixture was stirred at r.t. for 4.5 h. MeOH (5 mL) was slowly added and the reaction mixture was diluted with EtOAc (150 mL) and washed with H_2O (2x 60 mL) and brine (50 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude product was purified by crystallization (10 mL hot EtOAc, addition of 100 mL petroleum ether) to yield the title compound as a white cotton like solid (4.79 g, 10.1 mmol, 89%). R_f: 0.71 (8/1 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[31] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.56 (ddt, 2H, *J* = 5.0, 3.4, 1.5 Hz, CH_{arom}), 7.47 (dd, 2H, *J* = 7.5, 2.3 Hz, CH_{arom}), 7.42 – 7.26 (m, 11H, CH_{arom}), 5.57 (s, 1H, C*H*Ph), 4.91 (d, 1H, *J* = 10.9 Hz, C*H*H Bn), 4.78 (d, 1H, *J* = 10.9 Hz, CH*H* Bn), 4.49 (d, 1H, *J* = 10.2 Hz, H-1), 4.39 (dd, 1H, *J* = 10.6, 5.0 Hz, H-6), 3.79 (t, 1H, *J* = 10.3 Hz, H-6), 3.71 – 3.59 (m, 2H, H-3, H-4), 3.52 – 3.42 (m, 1H, H-5), 3.41 – 3.32 (m, 1H, H-2); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 137.6, 137.1 (C_q), 134.0 (CH_{arom}), 130.6 (C_q SPh), 129.2,

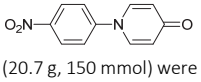
129.2, 128.8, 128.5, 128.4, 128.4, 128.1, 126.0 (CH_{arom}), 101.3 (CHPh), 86.5 (C-1), 81.3, 81.0 (C-3, C-4), 75.3 (CH_2 Bn), 70.5 (C-5), 68.5 (C-6), 64.6 (C-2); HRMS: $[M+H]^+$ calcd for $C_{26}H_{26}N_3O_4S$ 476.16385, found 476.16375.



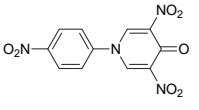
Phenyl 2-azido-3-*O*-benzoyl-4,6-*O*-benzylidene-2-deoxy-1-thio-β-D-glucopyranoside (4). To a 0°C solution of compound **13** (1.34 g, 3.48 mmol) in DCM (17 mL) and pyridine (1.4 mL, 34.8 mmol, 5 eq.) was added benzoyl chloride (0.61 mL, 5.22 mmol, 1.5 eq.) and DMAP (42 mg, 0.35 mmol, 0.1 eq.). The reaction mixture was allowed to stir overnight after which H_2O and DCM were added. The organic layer was separated and washed with sat. aq. $NaHCO_3$ and brine. The organic layer was dried with $MgSO_4$ and concentrated *in vacuo*. Flash column chromatography (19/1 to 8/1 pentane/EtOAc) afforded the title compound as a white solid (1.54 g, 3.15 mmol, 90%). The product could be recrystallized from EtOAc and petroleum ether to obtain a fluffy white solid. R_f: 0.53 (8/1 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[63] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.05 (d, 2H, *J* = 7.3 Hz, CH_{arom}), 7.59 (dd, 2H, *J* = 6.5, 3.1 Hz, CH_{arom}), 7.53 (t, 1H, *J* = 7.4 Hz, CH_{arom}), 7.44 – 7.33 (m, 7H, CH_{arom}), 7.29 – 7.23 (m, 3H, CH_{arom}), 5.52 (t, 1H, *J* = 9.6 Hz, H-3), 5.46 (s, 1H, C*H*Ph), 4.69 (d, 1H, *J* = 10.1 Hz, H-1), 4.38 (dd, 1H, *J* = 10.5, 4.9 Hz, H-6), 3.79 (t, 1H, *J* = 10.2 Hz, H-6), 3.71 (t, 1H, *J* = 9.5 Hz, H-4), 3.62 – 3.53 (m, 2H, H-2, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 165.3 (C=O Bz), 136.7 (C_q), 133.7, 133.4 (CH_{arom}), 130.8 (C_q), 129.9, 129.3 (CH_{arom}), 129.2 (C_q), 129.1, 128.8, 128.5, 128.2, 126.1 (CH_{arom}), 101.3 (CHPh), 87.1 (C-1), 78.4 (C-4), 73.5 (C-3), 70.7 (C-5), 68.3 (C-6), 63.9 (C-2); HRMS: $[M+H]^+$ calcd for $C_{26}H_{24}N_3O_5S$ 490.14312, found 490.14305.



Phenyl 2-amino-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-1-thio-β-D-glucopyranoside (16). Fully protected glycoside **15**[35] (9.11 g, 15.7 mmol) was dissolved in 160 ml EtOH and heated to reflux upon which ethylene diamine (52 mL, 785 mmol, 50 eq.) was added in three portions and reflux was maintained overnight. The reaction mixture was concentrated under reduced pressure and mixed with toluene (100 mL) and 45 g of silica gel, and the mixture evaporated to dryness. Column chromatography (8/2 to 2/1 pentane/EtOAc) gave the free amine as a white solid (6.19 g, 13.76 mmol, 88%) which could be recrystallized in EtOAc/petroleum ether. R_f: 0.40 (2/1 pentane/EtOAc). m.p. 136.1-137.5 °C. $[\alpha]_D^{20}$ = -33.5° (*c* = 0.57, $CHCl_3$); IR (thin film): 698, 748, 1026, 1069, 1123, 1371, 1452, 1583, 2870, 3030, 3059; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.56 – 7.44 (m, 4H, CH_{arom}), 7.42 – 7.24 (m, 11H, CH_{arom}), 5.59 (s, 1H, C*H*Ph), 4.99 (d, 1H, *J* = 11.3 Hz, C*H*H Bn), 4.68 (d, 1H, *J* = 11.2 Hz, CH*H* Bn), 4.58 (d, 1H, *J* = 9.9 Hz, H-1), 4.38 (dd, 1H, *J* = 10.5, 5.0 Hz, H-6), 3.81 (t, 1H, *J* = 10.3 Hz, H-6), 3.72 (t, 1H, *J* = 9.2 Hz, H-4), 3.59 (t, 1H, *J* = 9.0 Hz, H-3), 3.52 (td, 1H, *J* = 9.7, 4.9 Hz, H-5), 2.91 (t, 1H, *J* = 9.4 Hz, H-2), 1.75 (bs, 2H, NH_2); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.2, 137.4 (C_q), 133.0 (CH_{arom}), 131.8 (C_q SPh), 129.1, 128.6, 128.4, 128.3, 128.3, 128.0, 126.0 (CH_{arom}), 101.3 (CHPh), 89.6 (C-1), 82.2, 82.2 (C-3, C-4), 75.1 (CH_2 Bn), 70.7 (C-5), 68.8 (C-6), 55.5 (C-2); HRMS: $[M+H]^+$ calcd for $C_{26}H_{28}NO_4S$ 450.17336, found 450.17238.

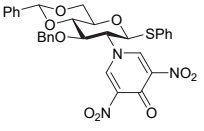


1-(4-nitrophenyl)-4-pyridone (17). Following the procedure of You and Twieg[64] 4-hydroxypyridine (14.3 g, 150 mmol), 4-chloronitrobenzene (22.9 g, 145 mmol) and K_2CO_3 (20.7 g, 150 mmol) were suspended in *N*-methyl-2-pyrrolidone (110 mL) and heated at 150°C for 2 h. The hot solution was then poured directly onto ice and allowed to precipitate until all the ice had melted. The suspension was then filtered and washed four times with cold H_2O. The resulting solid was dried under vacuum at 100°C until dry. Yield: 26.6 g, 123 mmol, 85%. IR (neat): 606, 692, 741, 752, 843, 1015, 1111, 1198, 1285, 1339, 1495, 1514, 1582, 1638, 3071; ^{1}H NMR (DMSO, 400 MHz, HH-COSY, HSQC): δ 8.38 (d, 2H, *J* = 9.1 Hz), 8.14 (d, 2H, *J* = 7.8 Hz), 7.86 (d, 2H, *J* = 9.1 Hz), 6.29 (d, 2H, *J* = 7.8 Hz); ^{13}C-APT NMR (DMSO, 101 MHz, HSQC): δ 177.6, 147.1, 145.9, 139.2, 125.3, 123.2, 118.3; HRMS: $[M+H]^+$ calcd for $C_{11}H_9N_2O_3$ 217.06077, found 217.06074.

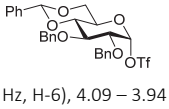


3,5-dinitro-1-(4-nitrophenyl)-4-pyridone (18). Modification of the procedure from Matsumura *et al.*[30], an ice cooled three-neck flask equipped with a condenser was charged with 120 mL H_2SO_4 (30% SO_3) followed by the slow addition of 120 mL fuming 99% HNO_3. To the cold mixture pyridone **17** (21.6 g, 100 mmol) was added in small portions. When addition was complete the mixture was slowly brought to 130°C and stirred for 40 h. The cooled down mixture was then poured over ice, stirred for 3 h, filtered, and washed three times with cold water. Yield: 18.4 g, 60 mmol, 60%. Purity (NMR): 90%. Tetra-nitro (3,5-dinitro-1-(2,4-dinitrophenyl)-4-pyridone ^{1}H NMR (DMSO, 400 MHz): δ 9.42 (s, 2H), 9.05 (d, 1H, *J* = 2.6 Hz), 8.87 (dd, 1H, *J* = 8.8, 2.6 Hz), 8.32 (d, 1H, *J* = 8.7 Hz)) and di-nitro (3-nitro-1-(4-nitrophenyl)-4-pyridone ^{1}H NMR (DMSO, 400 MHz): δ 9.18 (d, 1H, *J* = 2.5 Hz), 8.43 (d, 2H, *J* = 9.0 Hz), 8.26 (dd, 1H, *J* = 7.8, 2.5 Hz), 7.99 (d, 2H, *J* = 9.1 Hz), 6.68 (d, 1H, *J* = 7.9 Hz)) impurities are present (ratios vary slightly upon repetition). IR (neat): 717, 768, 789, 853, 910, 1141, 1261, 1306, 1350, 1449, 1514, 1591, 1672, 3076; ^{1}H NMR (DMSO, 400 MHz): δ 9.38 (s,

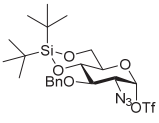
1H), 8.47 (d, 1H, *J* = 9.0 Hz), 8.05 (d, 1H, *J* = 9.1 Hz); ^{13}C-APT NMR (DMSO, 101 MHz): δ 159.3, 147.6, 145.5, 142.1, 141.6, 125.7, 125.1; HRMS: $[M+H]^+$ calcd for $C_{11}H_7N_4O_7$ 307.03093, found 307.03123.



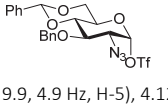
Phenyl 2-(3,5-dinitro-4-pyridone)-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-1-thio-β-D-glucopyranoside (5). Free amine **16** (3.6 g, 8 mmol) and reagent **18** (2.7 g, 8.8 mmol, 1.1 eq.) were dissolved in pyridine (48 mL) and AcOH (4 mL) and left to stir for 30 min. The mixture was diluted with EtOAc and washed with 1M aq. HCl (5x) and once with sat.aq. $NaHCO_3$. The organic layer was dried ($MgSO_4$), filtered and concentrated under reduced pressure. Column chromatography: DCM until all the nitroanaline had been removed, then 1% to 5% acetone in DCM. Yield 4.84 g, 7.8 mmol (98%) as a yellow solid. R_f: 0.21 (DCM), $[\alpha]_D^{20}$ = 10.5° (*c* = 0.5, $CHCl_3$); IR (thin film): 604, 696, 746, 989, 1055, 1094, 1211, 1300, 1329, 1516, 1674, 2856, 2926, 3034, 3059; ^{1}H NMR (Acetone-d_6, 400 MHz, HH-COSY, HSQC): δ 8.74 (s, 2H, CH pyridone), 7.63 – 7.54 (m, 2H, CH_{arom}), 7.51 – 7.39 (m, 5H, CH_{arom}), 7.39 – 7.31 (m, 3H, CH_{arom}), 7.21 – 7.14 (m, 3H, CH_{arom}), 7.14 – 7.07 (m, 2H, CH_{arom}), 5.84 (s, 1H, C*H*Ph), 5.73 (d, 1H, *J* = 10.4 Hz, H-1), 4.84 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.62 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.55 – 4.47 (m, 1H, H-3), 4.44 – 4.39 (m, 1H, H-6), 4.39 (t, 1H, *J* = 8.9 Hz, H-2), 4.06 – 3.91 (m, 3H, H-4, H-5, H-6); ^{13}C-APT NMR (Acetone-d_6, 101 MHz, HSQC): δ 159.9 (C=O pyridone), 143.1 (C_q NO_2), 138.5, 137.8 (C_q), 133.4 (CH_{arom}), 131.7 (C_q SPh), 130.3, 129.7, 129.5, 129.2, 129.0, 129.0, 127.0 (CH_{arom}), 102.0 (CHPh), 85.9 (C-1), 83.0 (C-4), 77.0 (C-3), 74.7 (CH_2 Bn), 71.6 (C-2), 70.9 (C-5), 68.8 (C-6); HRMS: $[M+H]^+$ calcd for $C_{31}H_{28}N_3O_9S$ 618.15408 found 618.15375.



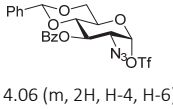
Trifluoromethanesulfonyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (19).[9] ^{1}H NMR (CD_2Cl_2, *T* = 213 K, 400 MHz, HH-COSY, HSQC): δ 6.08 (d, 1H, *J* = 3.5 Hz, H-1), 5.59 (s, 1H, C*H*Ph), 4.89 (d, 1H, *J* = 11.0 Hz, C*H*H Bn), 4.85 – 4.69 (m, 3H, CH*H* Bn, CH_2 Bn), 4.29 (dd, 1H, *J* = 10.3, 4.8 Hz, H-6), 4.09 – 3.94 (m, 2H, H-3, H-5), 3.86 – 3.70 (m, 3H, H-2, H-4, H-6); ^{13}C-APT NMR (CD_2Cl_2, *T* = 213 K, 101 MHz, HSQC): δ 106.1 (C-1), 100.8 (CHPh), 79.6 (C-4), 77.0 (C-3), 76.3 (C-2), 75.0, 74.1 (CH_2 Bn), 67.4 (C-6), 65.8 (C-5).



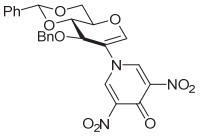
Trifluoromethanesulfonyl 2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside (20). ^{1}H NMR (CD_2Cl_2, *T* = 243 K, 400 MHz, HH-COSY, HSQC): δ 6.08 (d, 1H, *J* = 3.5 Hz, H-1), 5.64 (s, 1H, C*H*Ph), 4.98 (d, 1H, *J* = 10.6 Hz, C*H*H Bn), 4.78 (d, 1H, *J* = 10.6 Hz, CH*H* Bn), 4.32 (dd, 1H, *J* = 10.4, 4.9 Hz, H-6), 4.11 – 4.00 (m, 2H, H-3, H-5), 3.94 – 3.86 (m, 2H, H-2, H-4), 3.82 (t, 1H, *J* = 10.3 Hz, H-6); ^{13}C-APT NMR (CD_2Cl_2, *T* = 243 K, 101 MHz, HSQC): δ 137.2, 136.7 (C_q), 130.5, 128.4, 128.4, 125.9 (CH_{arom}), 105.0 (C-1), 101.3 (CHPh), 80.6 (C-4), 76.4 (C-3), 75.3 (CH_2 Bn), 67.6 (C-6), 66.2 (C-5), 61.4 (C-2).



Trifluoromethanesulfonyl 2-azido-3-*O*-benzoyl-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside (21). ^{1}H NMR (CD_2Cl_2, *T* = 243 K , 400 MHz, HH-COSY, HSQC): δ 6.23 (d, 1H, *J* = 3.5 Hz, H-1), 5.80 (t, 1H, *J* = 10.0 Hz, H-3), 5.54 (s, 1H, C*H*Ph), 4.36 (dd, 1H, *J* = 10.4, 4.9 Hz, H-6), 4.21 (td, 1H, *J* = 9.9, 4.9 Hz, H-5), 4.12 (dd, 1H, *J* = 10.2, 3.5 Hz, H-2), 3.98 (t, 1H, *J* = 9.8 Hz, H-4), 3.86 (t, 1H, *J* = 10.3 Hz, H-6); ^{13}C-APT NMR (CD_2Cl_2, *T* = 243 K, 101 MHz, HSQC): δ 104.5 (C-1), 101.8 (CHPh), 77.5 (C-4), 69.3 (C-3), 67.6 (C-6), 66.4 (C-5), 60.9 (C-2).

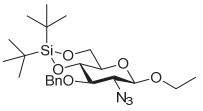


Trifluoromethanesulfonyl 2-azido-3-*O*-benzyl-2-deoxy-4,6-*O*-di-*tert*-butylsilylidene-α-D-glucopyranoside (22). ^{1}H NMR (CD_2Cl_2, *T* = 233 K, 400 MHz, HH-COSY, HSQC, HMBC): δ 6.00 (d, 1H, *J* = 3.4 Hz, H-1), 5.08 (d, 1H, *J* = 10.1 Hz, C*H*H Bn), 4.81 (d, 1H, *J* = 10.2 Hz, CH*H* Bn), 4.15 – 4.06 (m, 2H, H-4, H-6), 3.95 – 3.84 (m, 3H, H-3, H-5, H-6), 3.79 (dd, 1H, *J* = 10.1, 3.4 Hz, H-2), 1.07 (s, 9H, CH_3 ^{t}Bu), 1.00 (s, 9H, CH_3 ^{t}Bu); ^{13}C-APT NMR (CD_2Cl_2, *T* = 233 K, 101 MHz, HSQC, HMBC): δ 118.9 (q, *J* = 317.6 Hz, CF_3), 104.8 (C-1), 78.8 (C-3), 76.9 (C-4), 75.7 (CH_2 Bn), 70.0 (C-5), 65.3 (C-6), 60.6 (C-2), 27.0, 26.4 (CH_3 ^{t}Bu), 22.5, 19.7 (C_q ^{t}Bu); ^{13}C-HMBC NMR (CD_2Cl_2, 101 MHz): δ 104.8 ($J_{C1\text{-}H1}$ = 187 Hz, C-1).

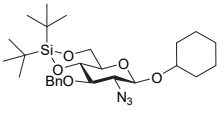


3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-(3,5-dinitro-4-pyridone)-D-glucal (24). Off-white solid. R_f: 0.20 (7/3 pentane/EtOAc). $[\alpha]_D^{23}$ = +85.9° (*c* = 0.32, DCM); IR (thin film): 698, 720, 753, 1007, 1059, 1095, 1192, 1247, 1304, 1351, 1516, 1679, 2880, 2924, 3072; ^{1}H NMR (Acetone-d_6, 500 MHz, HH-COSY, HSQC): δ 8.72 (s, 2H, CH pyridone), 7.62 – 7.53 (m, 2H, CH_{arom}), 7.49 – 7.37 (m, 4H, CH_{arom}, H-1), 7.29 – 7.14 (m, 5H, CH_{arom}), 5.88 (s, 1H, C*H*Ph), 4.93 – 4.88 (m, 2H, C*H*H Bn, H-3), 4.68 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.46 (dd, 1H, *J* = 10.5, 5.2 Hz, H-6), 4.37 (dd, 1H, *J* = 10.4, 6.9 Hz, H-4), 4.30 (td, 1H, *J* = 10.2, 5.1 Hz, H-5), 4.03 (t, 1H, *J* = 10.3 Hz, H-6); ^{13}C-APT NMR (Acetone-d_6, 101 MHz, HSQC): δ 160.0 (C=O pyridone), 149.3 (C-1), 144.7 (CH pyridone), 142.8 (C_q NO_2), 138.4 (C_q Bn, Ph), 129.8, 129.2,

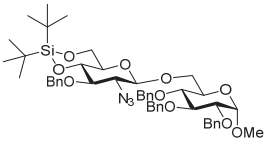
129.1, 129.0, 128.8, 127.0 (CH_{arom}), 122.1 (C-2), 101.9 (CHPh), 80.2 (C-4), 74.7 (CH_2 Bn), 74.6 (C-3), 70.7 (C-5), 68.2 (C-6); HRMS: $[M+H]^+$ calcd for $C_{25}H_{22}N_3O_9$ 508.13506, found 508.13465.



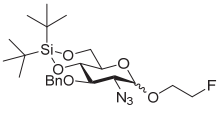
Ethyl 2-azido-3-*O*-benzyl-2-deoxy-4,6-*O*-di-*tert*-butylsilylidene-β-D-glucopyranoside (2A). Donor **2** and ethanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations and purified by flash column chromatography (0% to 5% Et_2O in pentane) to yield glycosylation product **2A** (30 mg, 65 µmol, 65%, α:β = <1:20) as a colorless oil. R_f: 0.35 (5% Et_2O in pentane). $[\alpha]_D^{23}$ = -69.6° (*c* = 0.5, $CHCl_3$); IR (neat): 652, 768, 827, 962, 1082, 1161, 1474, 2112, 2859, 2932; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.46 – 7.40 (m, 2H, CH_{arom}), 7.39 – 7.27 (m, 3H, CH_{arom}), 4.99 (d, 1H, *J* = 11.0 Hz, C*H*H Bn), 4.81 (d, 1H, *J* = 10.9 Hz, CH*H* Bn), 4.31 (dd, 1H, *J* = 7.7, 1.7 Hz, H-1), 4.16 (dd, 1H, *J* = 10.3, 5.0 Hz, H-6), 3.98 – 3.87 (m, 3H, C*H*H-CH_3 Et, H-4, H-6), 3.61 (dq, 1H, *J* = 9.5, 7.1 Hz, CH*H*-CH_3 Et), 3.41 – 3.28 (m, 3H, H-2, H-3, H-5), 1.26 (t, 3H, *J* = 7.1 Hz, CH_3 Et), 1.08 (s, 9H, CH_3 ^{t}Bu), 1.01 (s, 9H, CH_3 ^{t}Bu); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.3 (C_q), 128.5, 128.4, 128.0 (CH_{arom}), 102.1 (C-1), 82.4 (C-3), 78.1 (C-4), 75.4 (CH_2 Bn), 70.5 (C-5), 66.4 (C-6), 66.1 (CH_2 Et), 65.6 (C-2), 27.6, 27.2 (CH_3 ^{t}Bu), 22.8, 20.1 (C_q ^{t}Bu), 15.2 (CH_3 Et); HRMS: $[M-N_2+H]^+$ calcd for $C_{23}H_{38}NO_5Si$ 436.25138, found 436.25132.



Cyclohexyl 2-azido-3-*O*-benzyl-2-deoxy-4,6-*O*-di-*tert*-butylsilylidene-β-D-glucopyranoside (2B). Donor **2** and cyclohexanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations and purified by flash column chromatography (4/1 to 0/1 pentane/toluene) to yield glycosylation product **2B** (40 mg, 77 µmol, 77%, α:β = <1 : 20) as a colorless oil. R_f: 0.43 (5% Et_2O in pentane). $[\alpha]_D^{20}$ = -44.3° (*c* = 1.0, $CHCl_3$); IR (thin film): 696, 768, 827, 961, 1080, 1163, 1364, 2112, 2859, 2934; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.45 – 7.40 (m, 2H, CH_{arom}), 7.38 – 7.27 (m, 3H, CH_{arom}), 4.97 (d, 1H, *J* = 11.1 Hz, C*H*H Bn), 4.81 (d, 1H, *J* = 11.1 Hz, CH*H* Bn), 4.42 (d, 1H, *J* = 7.8 Hz, H-1), 4.15 (dd, 1H, *J* = 10.3, 5.0 Hz, H-6), 3.99 – 3.89 (m, 2H, H-3, H-6), 3.64 (tt, 2H, *J* = 9.2, 3.8 Hz, CH Cy), 3.40 – 3.24 (m, 3H, H-2, H-4, H-5), 1.96 – 1.83 (m, 2H, CH_2 Cy), 1.80 – 1.71 (m, 2H, CH_2 Cy), 1.55 – 1.48 (m, 1H, CH_2 Cy), 1.47 – 1.37 (m, 2H, CH_2 Cy), 1.34 – 1.20 (m, 3H, CH_2 Cy), 1.08 (s, 9H, ^{t}Bu), 1.01 (s, 9H, ^{t}Bu); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.4 (C_q), 128.5, 128.3, 127.9 (CH_{arom}), 100.7 (C-1), 82.3 (C-4), 78.3 (CH Cy), 78.0 (C-3), 75.4 (CH_2 Bn), 70.5 (C-5), 66.4 (C-6), 65.8 (C-2), 33.6, 31.7 (CH_2 Cy), 27.6, 27.2 (CH_3 ^{t}Bu), 25.6 (CH_2 Cy), 24.1, 23.9 (Cq ^{t}Bu), 22.8, 20.1 (CH_2 Cy); HRMS: $[M-N_2+H]^+$ calcd for $C_{27}H_{44}NO_5Si$ 490.29833, found 490.29811.

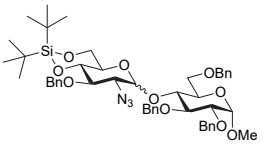


Methyl 6-*O*-(2-azido-3-*O*-benzyl-2-deoxy-4,6-*O*-di-*tert*-butylsilylidene-α/β-D-glucopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (2C). Donor **2** and acceptor **25** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 18 hours at -40°C) and purified by flash column chromatography (1/0 to 9/1 pentane/EtOAc) to yield glycosylation product **2C** (81 mg, 92 µmol, 92%, α:β = 1:14) as a white solid. R_f: 0.42 (4/1 pentane/EtOAc). $[\alpha]_D^{23}$ = -18.6° (*c* = 1.0, $CHCl_3$); IR (thin film): 654, 969, 735, 827, 962, 1028, 1070, 1161, 1362, 1454, 2112, 2859, 2931; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 7.45 – 7.39 (m, 2H, CH_{arom}), 7.38 – 7.25 (m, 18H, CH_{arom}), 4.99 (d, 1H, *J* = 11.0 Hz, C*H*H Bn), 4.98 (d, 1H, *J* = 10.9 Hz, C*H*H Bn), 4.94 (d, 1H, *J* = 11.1 Hz, C*H*H Bn), 4.85 – 4.76 (m, 3H, C*H*H Bn, 2xCH*H* Bn), 4.66 (d, 1H, *J* = 11.1 Hz, CH*H* Bn), 4.64 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.60 (d, 1H, *J* = 3.6 Hz, H-1), 4.17 (d, 1H, *J* = 7.9 Hz, H-1'), 4.15 – 4.10 (m, 1H, H-6'), 4.05 – 3.96 (m, 2H, H-3, H-6), 3.96 – 3.87 (m, 2H, H-4', H-6'), 3.76 (ddd, 1H, *J* = 9.9, 4.2, 1.7 Hz, H-5), 3.70 (dd, 1H, *J* = 10.7, 4.2 Hz, H-6), 3.59 (t, 1H, *J* = 9.5 Hz, H-4), 3.54 (dd, 1H, *J* = 9.6, 3.5 Hz, H-2), 3.40 (dd, 1H, *J* = 9.7, 7.9 Hz, H-2'), 3.37 – 3.26 (m, 5H, CH_3 Ome, H-3', H-5'), 1.07 (s, 9H, CH_3 ^{t}Bu), 1.01 (s, 9H, CH_3 ^{t}Bu); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 138.9, 138.6, 138.2, 138.1 (C_q), 128.6, 128.5, 128.5, 128.4, 128.3, 128.1, 128.0, 128.0, 127.9, 127.8, 127.7 (CH_{arom}), 102.2 (C-1'), 98.3 (C-1), 82.5 (C-3'), 82.2 (C-3), 79.9 (C-2), 77.9 (C-4'), 77.7 (C-4), 75.9, 75.4, 75.0, 73.6 (CH_2 Bn), 70.6 (C-5'), 69.7 (C-5), 68.6 (C-6), 66.3 (C-6'), 65.6 (C-2'), 55.3 (OMe), 27.5, 27.1 (CH_3 ^{t}Bu), 22.8, 20.1 (C_q ^{t}Bu); Diagnostic peaks α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.87 (d, 1H, *J* = 3.6 Hz, H-1'), 4.52 (d, 1H, *J* = 3.4 Hz, H-1); ^{13}C-APT NMR ($CDCl_3$, 101 MHz): δ 98.1, 98.0, 68.3; HRMS: $[M+NH_4]^+$ calcd for $C_{49}H_{67}N_4O_{10}Si$ 899.46210, found 899.46246.

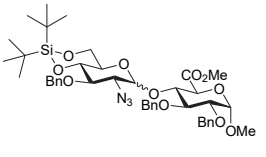


2-Fluoroethyl 2-azido-3-*O*-benzyl-2-deoxy-4,6-*O*-di-*tert*-butylsilylidene-α/β-D-glucopyranoside (2D). Donor **2** and 2-fluoroethanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations and purified by flash column chromatography (1/0 to 0/1 pentane/toluene to 2% Et_2O in toluene) to yield glycosylation product **2D** (37.8 mg, 79 µmol, 79%, α:β = 1:5.5) as a colorless oil. R_f: 0.20

(toluene). Reported as a 1.00 : 0.18 mixture of anomers: IR (neat): 654, 768, 827, 962, 1080, 1161, 1472, 2112, 2859, 2932; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.45 – 7.40 (m, 2.36H, CH_{arom}), 7.39 – 7.27 (m, 3.54H, CH_{arom}), 5.06 (d, 0.18H, *J* = 10.7 Hz, C*H*H Bnα), 4.99 (d, 1H, *J* = 10.9 Hz, C*H*H Bnβ), 4.86 (d, 0.18H, *J* = 3.6 Hz, H-1α), 4.82 (d, 0.18H, *J* = 10.6 Hz, CH*H* Bnα), 4.82 (d, 1H, *J* = 10.9 Hz, CH*H* Bnβ), 4.71 – 4.61 (m, 1.18H, C*H*HFα, C*H*HFβ), 4.58 – 4.47 (m, 1.18H, CH*H*Fα, CH*H*Fβ), 4.37 (d, 1H, *J* = 7.6 Hz, H-1β), 4.17 (dd, 1H, *J* = 10.3, 5.1 Hz, H-6β), 4.12 – 3.78 (m, 5.26H, C*H*$_2$-$CH_2F_α$, C*H*$_2$-$CH_2F_β$, H-3α, H-4α, H-4β, H-5α, H-6α, H-6α, H-6β), 3.44 – 3.29 (m, 3.18H, H-2α, H-2β, H-3β, H-5β), 1.09 (s, 1.62H, CH_3 ^{t}Buα), 1.08 (s, 9H, CH_3 ^{t}Buβ), 1.03 (s, 1.62H CH_3 ^{t}Buα), 1.01 (s, 9H, CH_3 ^{t}Buβ); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.3 ($C_{q,α}$), 138.2 ($C_{q,β}$), 128.6 (CH_{arom} Bnα), 128.5 (CH_{arom} Bnβ), 128.5 (CH_{arom} Bnα), 128.4 (CH_{arom} Bnβ), 128.0 (CH_{arom} Bnα,β), 102.4 (C-1β), 98.3 (C-1α), 82.7 (d, *J* = 170.0 Hz, $CH_2F_β$), 82.4 (d, *J* = 170.6 Hz, $CH_2F_α$), 82.3 (C-3β), 79.3, 79.0 (C-3α, C-4α), 78.0 (C-4β), 75.6 (CH_2 Bnα), 75.5 (CH_2 Bnβ), 70.6 (C-5β), 69.0 (d, *J* = 20.3 Hz, *CH*$_2$-$CH_2F_β$), 67.3 (d, *J* = 20.1 Hz, *CH*$_2$-$CH_2F_α$), 66.8 (C-5α), 66.7 (C-6α), 66.3 (C-6β), 65.5 (C-2β), 62.5 (C-2α), 27.5, 27.1 (CH_3 ^{t}Buα,β), 23.1 (C_q ^{t}Buα), 22.8 (C_q ^{t}Buβ), 20.1 (C_q ^{t}Buα), 20.1 (C_q ^{t}Buβ); HRMS: $[M-N_2+H]^+$ calcd for $C_{23}H_{37}FNO_5Si$ 454.24195, found 454.24188.

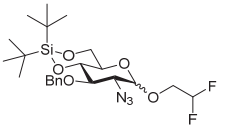


Methyl 4-*O*-(2-azido-3-*O*-benzyl-2-deoxy-4,6-*O*-di-*tert*-butylsilylidene-α/β-D-glucopyranosyl)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (2E). Donor **2** and acceptor **26** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 18 hours at -40°C) and purified by flash column chromatography (1/0 to 9/1 pentane/EtOAc) to yield glycosylation product **2E** (72 mg, 82 μmol, 82%, α:β = 1:3) as a colorless oil. R_f: 0.23 and 0.41 (9/1 pentane/EtOAc). IR (thin film): 654, 696, 735, 768, 827, 962, 1090, 1159, 1271, 1362, 1454, 2110, 2859, 2932; Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 7.44 – 7.39 (m, 2H, CH_{arom}), 7.39 – 7.21 (m, 18H, CH_{arom}), 4.98 (d, 1H, *J* = 10.8 Hz, C*H*H Bn), 4.83 – 4.74 (m, 4H, CH*H* Bn, CH_2 Bn, CH*H* Bn), 4.68 (d, 1H, *J* = 11.9 Hz, C*H*H Bn), 4.62 (d, 1H, *J* = 12.2 Hz, CH*H* Bn) 4.59 (d, 1H, *J* = 3.6 Hz, H-1), 4.44 (d, 1H, *J* = 11.9 Hz, CH*H* Bn), 4.23 (d, 1H, *J* = 8.0 Hz, H-1'), 3.97 (dd, 1H, *J* = 10.6, 3.0 Hz, H-6), 3.94 – 3.73 (m, 5H, H-3, H-4, H-4', H-5, H-6'), 3.71 – 3.66 (m, 1H, H-6), 3.55 – 3.47 (m, 2H, H-2, H-6'), 3.38 (s, 3H, CH_3 OMe), 3.27 – 3.21 (m, 1H, H-2'), 3.20 – 3.14 (m, 1H, H-3'), 3.06 (td, 1H, *J* = 9.9, 5.1 Hz, H-5'), 1.06 (s, 9H, CH_3 ^{t}Bu), 0.97 (s, 9H, CH_3 ^{t}Bu); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 139.4, 138.4, 138.1, 137.9 (C_q), 128.5, 128.5, 128.5, 128.4, 128.4, 128.2, 128.1, 128.0, 128.0, 127.9, 127.4, 127.3 (CH_{arom}), 101.0 (C-1'), 98.4 (C-1), 82.6 (C-3'), 80.2 (C-3), 79.2 (C-2), 78.1 (C-4'), 77.0 (C-4), 75.3, 75.3, 73.6, 73.6 (CH_2 Bn), 70.2 (C-5'), 69.7 (C-5), 68.3 (C-6), 66.2 (C-6'), 66.1 (C-2'), 55.4 (OMe), 27.6, 27.1 (CH_3 ^{t}Bu), 22.7, 20.0 (C_q tBu); Diagnostic peaks α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.67 (d, 1H, *J* = 4.0 Hz, H-1), 5.11 (d, 1H, *J* = 10.6 Hz, C*H*H Bn), 5.06 (d, 1H, *J* = 10.6 Hz, C*H*H Bn), 4.87 (d, 1H, *J* = 10.6 Hz, CH*H* Bn), 4.79 (d, 1H, *J* = 10.6 Hz, CH*H* Bn), 4.75 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.09 (t, 1H, *J* = 9.0 Hz, H-3), 3.56 (dd, 1H, *J* = 9.6, 3.5 Hz, H-2), 3.38 (s, CH_3 OMe), 3.21 (dd, 1H, J = 10.2, 4.0 Hz, H-2'), 1.06 (s, 9H, CH_3 ^{t}Bu), 1.04 (s, 9H, CH_3 ^{t}Bu); ^{13}C-APT NMR ($CDCl_3$, 101 MHz): δ 138.8, 138.3, 138.2, 138.0, 128.6, 128.4, 128.3, 128.1, 128.0, 128.0, 128.0, 127.9, 127.7, 127.6, 127.4, 127.3, 97.9, 97.7 (C-1, C-1'), 82.1 (C-3), 80.6 (C-2), 79.1, 79.0, 75.6, 75.1, 73.7, 73.4, 69.6, 69.2, 67.5, 66.5, 62.3 (C-2'), 55.4, 27.6, 27.2, 22.8, 20.1; HRMS: $[M+NH_4]^+$ calcd for $C_{49}H_{67}N_4O_{10}Si$ 899.46210, found 899.46246.

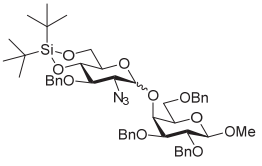


Methyl (methyl 4-*O*-[2-azido-3-*O*-benzyl-2-deoxy-4,6-*O*-di-*tert*-butylsilylidene-α/β-D-glucopyranosyl]-2,3-di-*O*-benzyl-α-D-glucopyranosyl uronate) (2F). Donor **2** and acceptor **27** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 18 hours at -40°C) and purified by flash column chromatography (1/0 to 9/1 pentane/EtOAc) to yield glycosylation product **2F** (69 mg, 84 μmol, 84%, α:β = 3.3:1) as a white solid. R_f: 0.36 and 0.39 (9/1 pentane/EtOAc). IR (thin film): 654, 696, 735, 827, 1042, 1144, 1387, 1751, 2108, 2859, 2934; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 7.43 – 7.38 (m, 2H, CH_{arom}), 7.37 – 7.25 (m, 13H, CH_{arom}), 5.45 (d, 1H, *J* = 4.1 Hz, H-1'), 5.07 – 5.02 (m, 2H, 2xC*H*H Bn), 4.90 (d, 1H, *J* = 10.6 Hz, CH*H* Bn), 4.84 – 4.78 (m, 1H, CH*H* Bn), 4.75 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.59 (d, 1H, *J* = 12.2 Hz, CH*H* Bn), 4.57 (d, 1H, *J* = 3.5 Hz, H-1), 4.21 – 4.17 (m, 1H, H-5), 4.09 – 4.01 (m, 3H, H-3, H-4, H-6'), 3.91 – 3.85 (m, 1H, H-4'), 3.83 – 3.73 (m, 5H, CH_3 CO_2Me, H-3', H-6'), 3.62 (td, 1H, *J* = 10.1, 5.0 Hz, H-5'), 3.58 – 3.53 (m, 1H, H-2), 3.41 (s, 3H, CH_3 OMe), 3.23 (dd, 1H, *J* = 10.2, 4.1 Hz, H-2'), 1.07 (s, 9H, CH_3 ^{t}Bu), 1.05 (s, 9H, CH_3 ^{t}Bu); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 169.2 (C=O CO_2Me), 138.7, 138.2, 137.8 (C_q), 128.7, 128.5, 128.5, 128.5, 128.3, 128.2, 128.0, 127.7, 127.6 (CH_{arom}), 98.5, 98.4 (C-1, C-1'), 81.0 (C-3), 79.9 (C-2), 79.0, 79.0 (C-3', C-4'), 76.2 (C-4), 75.5, 75.4, 73.6 (CH_2 Bn), 70.2 (C-5), 67.0 (C-5'), 66.4 (C-6'), 62.4 (C-2'), 55.9 (OMe), 52.9 (CO_2Me), 27.6, 27.2 (CH_3 ^{t}Bu), 22.9, 20.0 (C_q ^{t}Bu); Diagnostic peaks β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.98 (d, 1H, *J* = 10.9 Hz, C*H*H Bn), 4.39 (d, 1H, *J* = 7.7 Hz, H-1'), 4.02 – 3.96 (m, 1H), 3.82 (s, 3H, CH_3 CO_2Me), 3.52 (dd, 1H, *J* = 9.5, 3.6 Hz, H-2), 1.05 (s, 9H, CH_3 ^{t}Bu), 0.97 (s, 9H, CH_3, ^{t}Bu); ^{13}C-APT NMR ($CDCl_3$, 101 MHz): δ 170.2, 139.1, 138.1, 138.1, 128.6, 128.5, 128.4, 128.3, 128.3, 128.1, 128.0, 127.5, 127.3, 101.9 (C-1'), 98.9 (C-1), 82.5, 79.6,

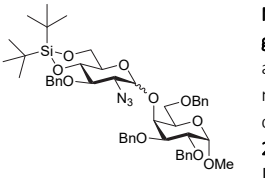
79.4, 78.8, 78.0, 75.4, 73.9, 70.4, 69.9, 66.1, 55.9, 52.8, 27.5, 27.1, 22.8, 20.0; HRMS: $[M+NH_4]^+$ calcd for $C_{43}H_{61}N_4O_{11}Si$ 837.41006, found 837.41042.



2,2-Difluoroethyl 2-azido-3-*O*-benzyl-2-deoxy-4,6-*O*-di-*tert*-butylsilylidene-α/β-D-glucopyranoside (2G). Donor **2** and 2,2-difluoroethanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations and purified by flash column chromatography (1/0 to 0/1 pentane/toluene to 2% Et_2O in toluene) to yield glycosylation product **2G** (38.1 mg, 76 µmol, 76%, α:β = 2.7:1) in two fractions (24.3 mg α only, 13.8 mg α:β = 0.3:1) as white solids. R_f: 0.43 β, 0.31 α (toluene). IR (neat): 654, 766, 826, 1070, 1474, 2108, 2860, 2934; Data for the α-anomer: $[\alpha]_D^{23}$ = +35.6° (*c* = 0.86, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.45 – 7.40 (m, 2H, CH_{arom}), 7.39 – 7.27 (m, 3H, CH_{arom}), 5.95 (tt, 1H, *J* = 55.2, 4.1 Hz, C*H*F_2), 5.06 (d, 1H, *J* = 10.6 Hz, C*H*H Bn), 4.85 (d, 1H, *J* = 3.6 Hz, H-1), 4.82 (d, 1H, *J* = 10.7 Hz, CH*H* Bn), 4.13 – 4.08 (m, 1H, H-6), 3.98 – 3.92 (m, 1H, H-3/4), 3.92 – 3.72 (m, 5H, C*H*$_2$-CHF_2, H-3/4, H-5, H-6), 3.35 (dd, 1H, *J* = 10.1, 3.6 Hz, H-2), 1.09 (s, 9H, CH_3 ^{t}Bu), 1.03 (s, 9H, CH_3 ^{t}Bu); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.1 (C_q), 128.6, 128.5, 128.1 (CH_{arom}), 113.8 (t, *J* = 241.6 Hz, CHF_2), 98.7 (C-1), 79.0, 78.9 (C-3, C-4), 75.7 (CH_2 Bn), 67.3 (t, *J* = 28.6 Hz, *C*H$_2$-CHF_2), 67.1 (C-5), 66.6 (C-6), 62.4 (C-2), 27.5, 27.1 (CH_3 ^{t}Bu), 22.8, 20.1 (C_q ^{t}Bu); Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.44 – 7.39 (m, 2H, CH_{arom}), 7.38 – 7.29 (m, 3H, CH_{arom}), 5.92 (tdd, 1H, *J* = 55.3, 5.1, 3.4 Hz, C*H*F_2), 4.99 (d, 1H, *J* = 10.9 Hz, C*H*H Bn), 4.81 (d, 1H, *J* = 11.0 Hz, CH*H* Bn), 4.35 (s, 1H, *J* = 7.7 Hz, H-1), 4.17 (dd, 1H, *J* = 10.3, 5.0 Hz, H-6), 4.02 – 3.74 (m, 4H, C*H*$_2$-CHF_2, H-4, H-6), 3.42 – 3.30 (m, 3H, H-2, H-3, H-5), 1.09 (s, 9H, CH_3 ^{t}Bu), 1.01 (s, 9H, CH_3, ^{t}Bu); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.1 (C_q), 128.5, 128.4, 128.1 (CH_{arom}), 114.1 (t, *J* = 241.4 Hz, CHF_2), 102.5 (C-1), 82.2 (C-3), 77.9 (C-4), 75.5 (CH_2 Bn), 70.7 (C-5), 68.8 (dd, *J* = 29.3, 28.8 Hz, *C*H$_2$-CHF_2), 66.2 (C-6), 65.4 (C-2), 27.5, 27.1 (CH_3 ^{t}Bu), 22.8, 20.1 (C_q ^{t}Bu); HRMS: $[M-N_2+H]^+$ calcd for $C_{23}H_{36}F_2NO_5Si$ 472.23253, found 472.23239.

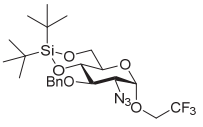


Methyl 4-*O*-(2-azido-3-*O*-benzyl-2-deoxy-4,6-*O*-di-*tert*-butylsilylidene-α/β-D-glucopyranosyl)-2,3,6-tri-*O*-benzyl-β-D-galactopyranoside (2H). Donor **2** and acceptor **28** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 18 hours at -40°C) and purified by flash column chromatography (1/0 to 9/1 pentane/EtOAc) to yield glycosylation product **2H** (46 mg, 52 µmol, 52%, α:β = 7:1) as a colorless oil. R_f: 0.33 and 0.51 (9/1 pentane/EtOAc). IR (thin film): 652, 696, 735, 826, 1001, 1036, 1206, 1364, 1454, 2108, 2859, 2932; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 7.46 – 7.41 (m, 2H, CH_{arom}), 7.41 – 7.23 (m, 18H, CH_{arom}), 5.10 (d, 1H, *J* = 10.3 Hz, C*H*H Bn), 4.89 – 4.81 (m, 3H, CH*H* Bn, 2xC*H*H Bn), 4.79 (d, 1H, *J* = 3.7 Hz, H-1'), 4.72 (d, 1H, *J* = 10.6 Hz, CH*H* Bn), 4.68 (d, 1H, *J* = 13.0 Hz, CH*H* Bn), 4.58 – 4.44 (m, 3H, CH_2 Bn, H-5'), 4.23 (d, 1H, *J* = 7.6 Hz, H-1), 4.07 – 3.99 (m, 2H, H-4, H-6), 3.99 – 3.88 (m, 3H, H-3', H-4', H-6'), 3.76 (t, 1H, *J* = 10.1 Hz, H-6'), 3.67 – 3.58 (m, 2H, H-2, H-6), 3.56 (s, 3H, CH_3 OMe), 3.48 (dd, 1H, *J* = 8.9, 5.5 Hz, H-5), 3.38 (dd, 1H, *J* = 10.0, 2.9 Hz, H-3), 3.33 (dd, 1H, *J* = 9.7, 3.7 Hz, H-2'), 1.06 (s, 9H, CH_3 ^{t}Bu), 1.02 (s, 9H, CH_3 ^{t}Bu); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 138.8, 138.4, 138.2, 137.7 (C_q), 128.6, 128.6, 128.5, 128.5, 128.5, 128.3, 128.2, 127.9, 127.8 (CH_{arom}), 105.1 (C-1), 99.2 (C-1'), 79.9, 79.9 (C-2, C-3'), 79.6, 79.4 (C-3, C-4'), 75.7, 75.6 (CH_2 Bn), 75.0 (C-4), 73.6 (CH_2 Bn), 72.9 (C-5), 72.6 (CH_2 Bn), 67.1, 67.0 (C-6, C-6'), 66.9 (C-5'), 63.2 (C-2'), 57.5 (OMe), 27.5, 27.3 (CH_3 ^{t}Bu), 22.7, 20.2 (C_q ^{t}Bu); Diagnostic peaks β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.94 (d, 0.14H, *J* = 11.1 Hz, C*H*H Bn), 4.27 (d, 0.14H, *J* = 7.7 Hz, H-1), 3.22 – 3.16 (m, 0.28H), 3.20 – 3.09 (m, 2H); ^{13}C-APT NMR ($CDCl_3$, 101 MHz): δ 105.1 (C-1), 102.0 (C-1'), 82.3, 78.0, 75.4, 75.3, 73.7, 73.7, 73.5, 73.4, 70.4, 69.6, 66.4, 65.6, 57.3, 27.6, 27.2, 22.8, 20.1; HRMS: $[M+NH_4]^+$ calcd for $C_{49}H_{67}N_4O_{10}Si$ 899.46210, found 899.46243.

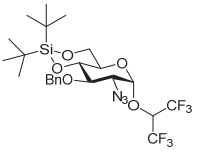


Methyl 2-*O*-(2-azido-3-*O*-benzyl-2-deoxy-4,6-*O*-di-*tert*-butylsilylidene-α-D-glucopyranosyl)-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (2I). Donor **2** and acceptor **29** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 18 hours at -40°C) and purified by flash column chromatography (1/0 to 9/1 pentane/EtOAc) to yield glycosylation product **2I** (67 mg, 85 µmol, 85%, α:β = > 20:1) as a white solid. R_f: 0.54 (9/1 pentane/EtOAc). $[\alpha]_D^{20}$ = +44.3° (*c* = 1.34, $CHCl_3$); IR (thin film): 696, 827, 937, 1040, 1088, 1130, 1364, 2108, 2859, 2957; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 7.54 – 7.47 (m, 2H, CH_{arom}), 7.46 – 7.41 (m, 2H, CH_{arom}), 7.41 – 7.22 (m, 11H, CH_{arom}), 5.65 (s, 1H, C*H*Ph), 5.23 (d, 1H, *J* = 3.6 Hz, H-1'), 5.09 (d, 1H, *J* = 10.6 Hz, C*H*H Bn), 4.89 – 4.82 (m, 2H, CH*H* Bn, C*H*H Bn), 4.74 – 4.65 (m, 2H, C*H*H Bn, H-1), 4.31 – 4.21 (m, 2H, H-4, H-6), 4.11 – 3.92 (m, 5H, H-2, H-3, H-3', H-4', H-6'), 3.92 – 3.76 (m, 4H, H-5, H-5', H-6, H-6'), 3.36 (s, 3H, CH_3 OMe), 3.27 (dd, 1H, *J* = 10.0, 3.7 Hz, H-2'), 1.09 (s, 9H), 1.05 (s, 9H); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ

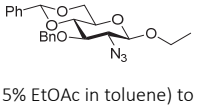
138.6, 138.4, 137.7 (C_q), 129.0, 128.5, 128.5, 128.4, 128.3, 128.3, 128.0, 127.6, 127.5, 127.4, 126.2, 126.1 (CH_{arom}), 101.7 (CHPh), 101.0 (C-1), 99.4 (C-1'), 79.3 (C-4), 79.1, 78.9 (C-3', C-4'), 76.0, 75.6 (C-2, C-3), 75.6, 73.0 (CH_2 Bn), 69.0 (C-6), 67.2 (C-5'), 66.6 (C-6'), 64.1 (C-5), 62.6 (C-2'), 55.2 (CH_3 OMe), 27.5, 27.2 (CH_3 ^{t}Bu), 22.8, 20.2 (C_q ^{t}Bu); Diagnostic peaks β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.60 (s, 1H, C*H*Ph), 4.98 (d, 1H, *J* = 11.3 Hz, C*H*H Bn), 4.39 (d, 1H, *J* = 8.2 Hz, H-1'), 3.57 – 3.48 (m, 1H); ^{13}C-APT NMR ($CDCl_3$, 101 MHz): δ 101.6, 99.6, 81.8, 78.5, 77.8, 76.4, 75.2, 74.4, 72.3, 70.9, 65.7, 55.1, 27.5, 27.1; HRMS: $[M+NH_4]^+$ calcd for $C_{42}H_{59}N_4O_{10}Si$ 807.39950, found 807.39931.



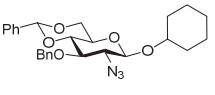
2,2,2-Trifluoroethyl 2-azido-3-*O*-benzyl-2-deoxy-4,6-*O*-di-*tert*-butylsilylidene-α-D-glucopyranoside (2J). Donor **2** and 2,2,2-trifluoroethanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 30 min at -40°C) and purified by flash column chromatography (1/0 to 0/1 pentane/toluene to 2% Et_2O in toluene) to yield glycosylation product **2J** (42.4 mg, 82 µmol, 82%, α:β = >20:1) as a colorless oil. R_f: 0.36 (toluene). $[\alpha]_D^{23}$ = +32.6° (*c* = 1.0, $CHCl_3$); IR (neat): 654, 766, 826, 1036, 1082, 1159, 1279, 1472, 2108, 2859, 2930; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.45 – 7.39 (m, 2H, CH_{arom}), 7.38 – 7.27 (m, 3H, CH_{arom}), 5.07 (d, 1H, *J* = 10.6 Hz, C*H*H Bn), 4.88 (d, 1H, *J* = 3.6 Hz, H-1), 4.82 (d, 1H, *J* = 10.6 Hz, CH*H* Bn), 4.14 – 4.07 (m, 1H, H-6), 4.03 – 3.93 (m, 3H, C*H*$_2$-CF_3, H-4), 3.92 – 3.80 (m, 3H, H-3, H-5, H-6), 3.36 (dd, 1H, *J* = 10.0, 3.6 Hz, H-2), 1.09 (s, 9H, CH_3 ^{t}Bu), 1.03 (s, 9H, CH_3 ^{t}Bu); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.1 (C_q), 128.6, 128.5, 128.1 (CH_{arom}), δ 123.5 (q, *J* = 278.4 Hz, CF3), 98.8 (C-1), 78.9 (C-3), 78.8 (C-4), 75.7 (CH_2 Bn), 67.4 (C-5), 66.5 (C-6), 65.2 (q, *J* = 35.4 Hz, *CH*$_2$-CF_3), 62.2 (C-2), 27.5, 27.1 (CH_3 ^{t}Bu), 22.8, 20.1 (C_q ^{t}Bu); HRMS: $[M-N_2+H]^+$ calcd for $C_{23}H_{35}F_3NO_5Si$ 490.22311, found 490.22292.



1,1,1,3,3,3-Hexafluoro-2-propyl 2-azido-3-*O*-benzyl-2-deoxy-4,6-*O*-di-*tert*-butylsilylidene-α-D-glucopyranoside (2K). Donor **2** and 1,1,1,3,3,3-hexafluoro-2-propanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 72 hours at -40°C) and purified by flash column chromatography (4/1 to 0/1 pentane/toluene) to yield glycosylation product **2K** (20 mg, 34 µmol, 34%, α:β = >20:1) as a white solid. R_f: 0.38 (9/1 pentane/Et_2O). $[\alpha]_D^{20}$ = +31.2° (*c* = 0.50, $CHCl_3$); IR (thin film): 689, 827, 1030, 1098, 1221, 1288, 1368, 2112, 2860, 2934; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC, NOESY): δ 7.45 – 7.28 (m, 5H, CH_{arom}), 5.12 – 5.04 (m, 2H, C*H*H Bn, H-1), 4.83 (d, 1H, *J* = 10.5 Hz, CH*H* Bn), 4.40 (hept, 1H, *J* = 5.7 Hz, C*H* HFIP), 4.09 (dd, 1H, *J* = 9.4, 4.0 Hz, H-6), 4.03 – 3.91 (m, 2H, H-4, H-5), 3.91 – 3.83 (m, 2H, H-3, H-6), 3.42 (dd, 1H, *J* = 10.2, 3.8 Hz, H-2), 1.08 (s, 9H, CH_3 ^{t}Bu), 1.03 (s, 9H, CH_3 ^{t}Bu); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 138.0 (C_q), 128.6, 128.5, 128.2 (CH_{arom}), 100.4 (C-1), 78.7 (C-3), 78.4 (C-4), 75.8 (CH_2 Bn), 73.3 (p, *J* = 33.2 Hz), 68.1 (C-5), 66.1 (C-6), 61.9 (C-2), 27.5, 27.0 (CH_3 ^{t}Bu), 22.8, 20.1 (C_q ^{t}Bu); HRMS: $[M-N_2+H]^+$ calcd for $C_{24}H_{34}F_6NO_5Si$ 558.21050, found 558.21009.

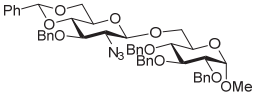


Ethyl 2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (3A). Donor **3** and ethanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations and purified by flash column chromatography (1/0 to 0/1 hexane/toluene to 5% EtOAc in toluene) to yield glycosylation product **3A** (34.3 mg, 83 µmol, 83%, α:β = <1:20) as a white solid. R_f: 0.58 (9/1 toluene/EtOAc). $[\alpha]_D^{23}$ = -79.6° (*c* = 0.69, $CHCl_3$); IR (neat): 692, 993, 1098, 1186, 1267, 1365, 1452, 2111, 2878, 2979; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.50 – 7.46 (m, 2H, CH_{arom}), 7.41 – 7.28 (m, 8H, CH_{arom}), 5.57 (s, 1H, C*H*Ph), 4.91 (d, 1H, *J* = 11.2 Hz, C*H*H Bn), 4.79 (d, 1H, *J* = 11.3 Hz, CH*H* Bn), 4.37 (d, 1H, *J* = 8.2 Hz, H-1), 4.34 (dd, 1H, *J* = 10.6, 5.0 Hz, H-6), 3.96 (dq, 1H, *J* = 9.7, 7.1 Hz, C*H*H Et), 3.80 (t, 1H, *J* = 10.3 Hz, H-6), 3.70 (t, 1H, *J* = 9.0 Hz, H-4), 3.66 (dq, 1H, *J* = 9.7, 7.2 Hz, CH*H* Et), 3.54 (t, 1H, *J* = 9.3 Hz, H-3), 3.44 (dd, 1H, *J* = 9.5, 8.0 Hz, H-2), 3.39 (td, 2H, *J* = 9.8, 5.0 Hz, H-5), 1.29 (t, 3H, *J* = 7.1 Hz, CH_3 Et); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.0, 137.2 (C_q), 129.2, 128.5, 128.4, 128.3, 128.0, 126.1 (CH_{arom}), 102.5 (C-1), 101.4 (CHPh), 81.7 (C-4), 79.1 (C-3), 75.0 (CH_2 Bn), 68.7 (C-6), 66.3 (CH_2 Et), 66.3, 66.2 (C-2, C-5), 15.2 (CH_3 Et); ^{13}C-HMBC-GATED NMR ($CDCl_3$, 101 MHz): δ 102.5 ($J_{C1,H1}$ = 161 Hz, C-1); HRMS: $[M+NH_4]^+$ calcd for $C_{22}H_{29}N_4O_5$ 429.21325, found 429.21321.

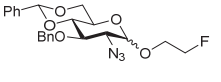


Cyclohexyl 2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (3B). Donor **3** and cyclohexanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations and purified by flash column chromatography (1/1 to 0/1 hexane/toluene to 5% EtOAc in toluene) to yield glycosylation product **3B** (43 mg, 93 µmol, 93%, α:β = <1:20) as a white solid. R_f: 0.23 (toluene). $[\alpha]_D^{23}$ = -60.5° (*c* = 0.86, DCM); IR (neat): 696, 748, 998, 1092, 1275, 1365, 1452, 2108, 2858, 2933; Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.50 – 7.44 (m, 2H, CH_{arom}), 7.42 – 7.27 (m, 8H, CH_{arom}), 5.56 (s, 1H, C*H*Ph), 4.90 (d, 1H, *J* = 11.4 Hz, C*H*H Bn), 4.79 (d, 1H, *J*

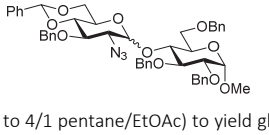
= 11.4 Hz, CH*H* Bn), 4.47 (d, 1H, *J* = 7.8 Hz, H-1), 4.32 (dd, 1H, *J* = 10.5, 5.0 Hz, H-6), 3.79 (t, 1H, *J* = 10.3 Hz, H-6), 3.74 – 3.64 (m, 2H, H-4, CH Cyc), 3.50 (t, 1H, *J* = 9.2 Hz, H-3), 3.44 (dd, 1H, *J* = 9.6, 7.8 Hz, H-2), 3.36 (td, 1H, *J* = 9.7, 5.0 Hz, H-5), 1.99 – 1.87 (m, 2H, CH_2 Cyc), 1.82 – 1.72 (m, 2H, *J* = 15.2, 4.4 Hz, CH_2 Cyc), 1.56 – 1.37 (m, 3H, CH_2 Cyc), 1.36 – 1.20 (m, 3H, CH_2 Cyc); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.0, 137.3 (C_q), 129.1, 128.5, 128.4, 128.3, 127.9, 126.1 (CH_{arom}), 101.4 (CHPh), 101.0 (C-1), 81.6 (C-4), 79.0 (C-3), 78.5 (CH Cyc), 75.0 (CH_2 Bn), 68.8 (C-6), 66.5 (C-2), 66.3 (C-5), 33.6, 31.8, 25.6, 24.1, 23.9 (CH_2 Cyc); Diagnostic peaks α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.59 (s, 0.04H, C*H*Ph), 5.03 (d, 0.04H, *J* = 3.7 Hz, H-1), 4.12 (t, 0.04H, *J* = 9.5 Hz, H-3), 4.00 (td, 0.04H, *J* = 9.9, 4.8 Hz, H-5), 3.28 (dd, 0.04H, *J* = 10.0, 3.7 Hz, H-2); ^{13}C-APT NMR ($CDCl_3$, 101 MHz): δ 101.4 (CHPh), 97.1 (C-1), 76.0 (C-3), 63.8 (C-2), 62.9 (C-5); HRMS: $[M+NH_4]^+$ calcd for $C_{26}H_{35}N_4O_5$ 483.26020 found 483.25991.



Methyl 6-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (3C). Donor **3** and acceptor **25** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 18 h at -40°C) and purified by flash column chromatography (19/1 to 4/1 pentane/EtOAc) to yield glycosylation product **3C** (73.7 mg, 89 µmol, 89%, α:β = <1:20) as a white solid. R_f: 0.42 (4/1 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[38] $[\alpha]_D^{23}$ = -32.2° (*c* = 1.0, $CHCl_3$); IR (neat): 696, 737, 999, 1028, 1070, 1090, 1277, 1362, 1497, 2108, 2876, 2926; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 7.47 (dd, 2H, *J* = 7.3, 2.5 Hz, CH_{arom}), 7.42 – 7.25 (m, 23H, CH_{arom}), 5.55 (s, 1H, C*H*Ph), 4.99 (d, 1H, *J* = 10.9 Hz, C*H*H 3-OBn), 4.95 (d, 1H, *J* = 11.2 Hz, C*H*H 4-OBn), 4.91 (d, 1H, *J* = 11.2 Hz, C*H*H 3'-OBn), 4.85 – 4.76 (m, 3H, CH*H* 3-OBn, C*H*H 2-OBn, CH*H* 3'-OBn), 4.70 – 4.63 (m, 2H, CH*H* 4-OBn, CH*H* 2-OBn), 4.61 (d, 1H, *J* = 3.6 Hz, H-1), 4.30 (dd, 1H, *J* = 10.5, 5.0 Hz, H-6'), 4.23 (d, 1H, *J* = 7.9 Hz, H-1'), 4.07 (d, 1H, *J* = 8.9 Hz, H-6), 4.00 (t, 1H, *J* = 9.3 Hz, H-3), 3.81 – 3.72 (m, 3H, H-5, H-6, H-6'), 3.69 (t, 1H, *J* = 9.1 Hz, H-4'), 3.60 (t, 1H, *J* = 9.3 Hz, H-4), 3.59 – 3.46 (m, 3H, H-2, H-2', H-3'), 3.37 (s, 3H, CH_3 OMe), 3.36 – 3.29 (m, 1H, H-5'); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 138.8, 138.5, 138.2, 137.8, 137.2 (C_q), 129.2, 128.6, 128.5, 128.5, 128.4, 128.3, 128.3, 128.1, 128.1, 128.0, 127.9, 127.9, 127.7, 126.1 (CH_{arom}), 102.4 (C-1'), 101.4 (CHPh), 98.4 (C-1), 82.2 (C-3), 81.5 (C-4'), 79.8 (C-2), 79.3 (C-3'), 77.6 (C-4), 75.9 (CH_2 3-OBn), 75.0, 75.0 (CH_2 3'-OBn, 4-OBn), 73.6 (CH_2 2-OBn), 69.6 (C-5), 68.7, 68.6 (C-6, C-6'), 66.3 (C-5'), 66.1 (C-2'), 55.4 (OMe); HRMS: $[M+NH_4]^+$ calcd for $C_{48}H_{55}N_4O_{10}$ 847.39127, found 847.39224.

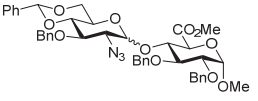


2-Fluoroethyl 2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranoside (3D). Donor **3** and 2-fluoroethanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations and purified by flash column chromatography (1/0 to 0/1 pentane/toluene to 5% EtOAc in toluene) to yield glycosylation product **3D** (38.5 mg, 90 µmol, 90%, α:β = 1:6.7) as a white solid. R_f: 0.40 (19/1 toluene/EtOAc). IR (neat): 696, 748, 996, 1028, 1072, 1091, 1174, 1276, 1368, 1454, 2108, 2873, 2917; Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.50 – 7.46 (m, 2H, CH_{arom}), 7.41 – 7.36 (m, 5H, CH_{arom}), 7.36 – 7.25 (m, 3H, CH_{arom}), 5.57 (s, 1H, C*H*Ph), 4.91 (d, 1H, *J* = 11.2 Hz, C*H*H Bn), 4.79 (d, 1H, *J* = 11.3 Hz, CH*H* Bn), 4.69 – 4.64 (m, 1H, C*H*HF), 4.55 (dt, 1H, *J* = 4.6, 2.9 Hz, CH*H*F), 4.42 (d, 1H, *J* = 7.9 Hz, H-1), 4.34 (dd, 1H, *J* = 10.5, 5.0 Hz, H-6), 4.11 (ddd, 0.5H, *J* = 12.2, 4.8, 2.9 Hz, *CH*H-CFH_2), 4.03 (ddd, 0.5H, *J* = 12.2, 4.7, 3.0 Hz, *CH*H-CFH_2), 3.92 (ddd, 0.5H, *J* = 12.2, 5.9, 3.2 Hz, CH*H*-CFH_2), 3.86 (ddd, 0.5H, *J* = 12.2, 6.0, 3.3 Hz, CH*H*-CFH_2), 3.80 (t, 1H, *J* = 10.3 Hz, H-6), 3.71 (t, 1H, *J* = 9.2 Hz, H-4), 3.56 (t, 1H, *J* = 9.2 Hz, H-3), 3.48 (dd, 1H, *J* = 9.5, 7.9 Hz, H-2), 3.39 (td, 1H, *J* = 9.7, 4.9 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 137.8, 137.1 (C_q), 129.2, 128.5, 128.4, 128.3, 128.0, 126.1 (CH_{arom}), 102.7 (C-1), 101.4 (CHPh), 82.6 (d, *J* = 170.1 Hz, CFH_2), 81.5 (C-4), 79.0 (C-3), 75.1 (CH_2 Bn), 69.3 (d, *J* = 20.1 Hz, CH_2-CFH_2), 68.6 (C-6), 66.3 (C-5), 66.1 (C-2); ^{13}C-HMBC-GATED NMR ($CDCl_3$, 101 MHz): δ 102.7 ($J_{C1,H1}$ = 162 Hz, C-1); Diagnostic peaks α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 5.58 (s, 0.15H, C*H*Ph), 4.96 (d, 0.15H, *J* = 10.9 Hz, C*H*H Bn), 4.95 (d, 0.15H, *J* = 3.7 Hz, H-1), 4.81 (d, 0.15H, *J* = 11.0 Hz, CH*H* Bn), 4.29 (dd, 0.15H, *J* = 10.2, 4.9 Hz, H-6); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 101.5 (CHPh), 98.8 (C-1), 82.8 (C-4), 76.2 (C-3), 75.2 (CH_2 Bn), 68.9 (C-6), 63.0, 62.9 (C-2, C-5); ^{13}C-HMBC-GATED NMR ($CDCl_3$, 101 MHz): δ 98.8 ($J_{C1,H1}$ = 172 Hz, C-1); HRMS: $[M+NH_4]^+$ calcd for $C_{22}H_{28}FN_4O_5$ 447.20382 found 447.20355.

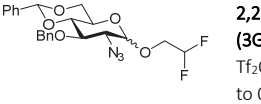


Methyl 4-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranosyl)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (3E). Donor **3** and acceptor **26** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 18 h at -40°C) and purified by flash column chromatography (19/1 to 4/1 pentane/EtOAc) to yield glycosylation product **3E** (73.3 mg, 88 µmol, 88%, α:β = 1:7) as a white solid. R_f: 0.51 α, 0.43 β (4/1 pentane/EtOAc). IR (neat): 696, 737, 1049, 1092, 1362, 1454, 2110, 2868; Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, TOCSY): δ 7.68 – 7.60 (m, 2H, CH_{arom}), 7.52 – 7.18 (m, 23H, CH_{arom}), 5.47 (s, 1H, C*H*Ph), 4.89 (d, 1H, *J* = 11.2 Hz, C*H*H Bn), 4.87 (d, 1H, *J* = 10.9 Hz, C*H*H Bn), 4.81 (d, 1H, *J* = 10.9 Hz, CH*H* Bn), 4.78

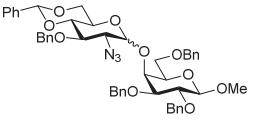
(d, 1H, *J* = 12.2 Hz, C*H*H Bn), 4.75 (d, 1H, *J* = 11.2 Hz, CH*H* Bn), 4.71 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.63 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.60 (d, 1H, *J* = 3.7 Hz, H-1), 4.41 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.19 (d, 1H, *J* = 7.6 Hz, H-1′), 4.11 (dd, 1H, *J* = 10.6, 5.0 Hz, H-6′), 4.00 – 3.90 (m, 2H, H-4, H-6), 3.85 (t, 1H, *J* = 9.3 Hz, H-3), 3.75 (dt, 1H, *J* = 9.8, 2.4 Hz, H-5), 3.69 (dd, 1H, *J* = 10.8, 1.9 Hz, H-6), 3.56 (t, 1H, *J* = 9.0 Hz, H-4′), 3.51 (dd, 1H, *J* = 9.5, 3.7 Hz, H-2), 3.45 – 3.38 (m, 4H, H-6′, CH_3 OMe), 3.36 – 3.27 (m, 2H, H-2′, H-3′), 3.00 (td, 1H, *J* = 9.8, 5.0 Hz, H-5′); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 139.3, 138.3, 137.8, 137.8, 137.3 (C_q), 131.1, 129.4, 128.6, 128.4, 128.3, 128.2, 128.2, 128.1, 128.1, 127.9, 127.9, 127.6, 126.0, 124.8 (CH_{arom}), 101.3, 101.2 (CHPh, C-1′), 98.4 (C-1), 81.7 (C-4′), 80.1 (C-3), 79.2 (C-3′), 79.0 (C-2), 76.9 (C-4), 75.4, 74.7, 73.6, 73.5 (CH_2 Bn), 69.7 (C-5), 68.6 (C-6′), 68.0 (C-6), 66.6 (C-2′), 65.8 (C-5′), 55.4 (OMe); Diagnostic peaks α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.71 (d, 1H, *J* = 4.0 Hz, H-1′), 5.53 (s, 1H, C*H*Ph), 5.11 (d, 1H, *J* = 10.7 Hz, C*H*H Bn), 4.95 (d, 1H, *J* = 10.9 Hz, C*H*H Bn); ^{13}C-APT NMR ($CDCl_3$, 101 MHz): δ 98.1, 97.8, 82.7, 82.1, 80.5, 76.2, 75.1, 73.3, 73.0, 69.4, 69.1, 68.7, 63.4, 62.9; HRMS: $[M+Na]^+$ calcd for $C_{48}H_{51}N_3O_{10}Na$ 852.34667, found 852.34668.



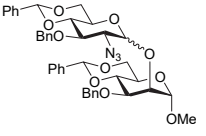
Methyl (Methyl 4-*O*-[2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranosyl]-2,3-di-*O*-benzyl-α-D-glucopyranosyl uronate) (3F). Donor **3** and acceptor **27** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 18 h at -40°C) and purified by flash column chromatography (19/1 to 4/1 pentane/EtOAc) to yield glycosylation product **3F** (71.8 mg, 93 µmol, 93%, α:β = 1.1:1) as a white solid. R_f: 0.54 (4/1 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[21] IR (neat): 696, 735, 914, 989, 1028, 1045, 1090, 1267, 1369, 1454, 1749, 2108, 2870, 2916; Reported as a 1 : 1 mixture of anomers: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 7.48 – 7.41 (m, 4H, CH_{arom}), 7.41 – 7.24 (m, 36H, CH_{arom}), 5.53 (s, 1H, C*H*Phα), 5.51 (d, 1H, *J* = 3.9 Hz, H-1′α), 5.47 (s, 1H, C*H*Phβ), 5.04 (d, 1H, *J* = 10.5 Hz, C*H*H Bn), 4.94 (d, 1H, *J* = 11.0 Hz, C*H*H Bn), 4.91 – 4.82 (m, 4H, 2xCH*H* Bn, 2xC*H*H Bn), 4.81 – 4.72 (m, 4H, 2xCH*H* Bn, 2xC*H*H Bn), 4.64 – 4.58 (m, 2H, 2xCH*H* Bn), 4.57 (d, 2H, *J* = 3.5 Hz, H-1$_{α,β}$), 4.43 (d, 1H, *J* = 8.1 Hz, H-1′β), 4.26 (dd, 1H, *J* = 10.3, 4.8 Hz, H-6′α), 4.24 – 4.19 (m, 2H, H-5α, H-5β), 4.09 – 3.99 (m, 4H, H-3β, H-4α, H-4β, H-6′β), 3.97 (t, 1H, *J* = 9.5 Hz, H-3′α), 3.89 (t, 1H, *J* = 9.2 Hz, H-3α), 3.82 (s, 3H, CH_3 CO_2Me), 3.81 (s, 3H, CH_3 CO_2Me), 3.72 – 3.56 (m, 4H, H-2β, H-4′α, H-4′β, H-6′α), 3.56 – 3.46 (m, 3H, H-2α, H-3′β, H-5′α), 3.46 – 3.38 (m, 7H, 2xCH_3 OMe, H-6′β), 3.36 – 3.29 (m, 2H, H-2′α, H-2′β), 3.26 (td, 1H, *J* = 9.7, 5.0 Hz, H-5′β); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 170.0, 170.0 (C=O CO_2Me), 139.1, 138.5, 138.0, 137.9, 137.9, 137.8, 137.4, 137.2 (C_q), 129.2, 129.1, 128.7, 128.6, 128.5, 128.5, 128.4, 128.3, 128.3, 128.3, 128.3, 128.2, 128.1, 128.0, 128.0, 127.8, 127.7, 127.5, 127.4, 126.1, 126.1 (CH_{arom}), 102.3 (C-1′β), 101.4 (CHPhβ), 101.3 (CHPhα), 98.9, 98.6 (C-1α, C-1β), 98.5 (C-1′α), 82.4 (C-4′α), 81.6 (C-4′β), 81.1 (C-3β), 79.6 (C-2β, C-4β), 79.5 (C-3α), 79.4 (C-3′β), 78.7 (C-2α), 76.3 (C-3′α), 75.6 (CH_2 Bn), 75.5 (C-4α), 75.1, 75.0, 73.9, 73.7 (CH_2 Bn), 70.0, 69.9 (C-5α, C-5β), 68.5, 68.5 (C-6α, C-6β), 66.7 (C-2′β), 66.2 (C-5′β), 63.0 (C-5′α), 62.8 (C-2′α), 55.9, 55.9 (OMe), 53.0, 52.8 (CO_2Me); HRMS: $[M+NH_4]^+$ calcd for $C_{42}H_{49}N_4O_{11}$ 785.33923, found 785.34007.



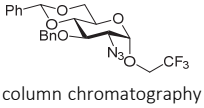
2,2-Difluoroethyl 2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranoside (3G). Donor **3** and 2,2-difluoroethanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations and purified by flash column chromatography (1/0 to 0/1 pentane/toluene to 5% EtOAc in toluene) to yield glycosylation product **3G** (28.8 mg, 64 µmol, 64%, α:β = 2.9:1) as a white solid. R_f: 0.15 and 0.18 (toluene). IR (neat): 698, 747, 998, 1070, 1093, 1372, 1454, 2109, 2867, 2934; Reported as a 1 : 0.35 mixture of anomers: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.52 – 7.45 (m, 2.70H, CH_{arom}), 7.43 – 7.26 (m, 10.80H, CH_{arom}), 5.95 (tt, 1H, *J* = 55.2, 4.2 Hz, CF_2*H*α), 5.94 (tt, 0.35H, *J* = 55.3, 3.8 Hz, CF_2*H*β), 5.58 (s, 1H, C*H*Phα), 5.57 (s, 0.35H, C*H*Phβ), 4.96 (d, 1H, *J* = 10.9 Hz, C*H*H Bnα), 4.93 (d, 1H, *J* = 3.9 Hz, H-1α), 4.92 (d, 0.35H, *J* = 11.3 Hz, C*H*H Bnβ), 4.80 (d, 1H, *J* = 11.0 Hz, CH*H* Bnα), 4.79 (d, 0.35H, *J* = 11.3 Hz, CH*H* Bnβ), 4.40 (d, 0.35H, *J* = 7.9 Hz, H-1β), 4.34 (dd, 0.35H, *J* = 10.5, 5.0 Hz, H-6β), 4.29 (dd, 1H, *J* = 10.2, 4.8 Hz, H-6α), 4.08 (t, 1H, *J* = 9.5 Hz, H-3α), 4.02 – 3.67 (m, 6.4H, H-4α, H-4β, H-5α, H-6α, H-6β, *CH*$_2$-CF_2Hα, *CH*$_2$-CF_2Hβ), 3.56 (t, 0.35H, *J* = 9.2 Hz, H-3β), 3.50 – 3.35 (m, 1.70H, H-2α, H-2β, H-5β); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 137.8, 137.8, 137.1, 137.1 (C_q), 129.4, 129.3, 129.1, 128.6, 128.5, 128.5, 128.4, 128.1, 126.1 (CH_{arom}), 114.0 (t, *J* = 241.5 Hz, $CF_2H_β$), 113.8 (t, *J* = 241.6 Hz, $CF_2H_α$), 102.8 (C-1β), 101.6 (CHPhα), 101.5 (CHPhβ), 99.3 (C-1α), 82.6 (C-4α), 81.4 (C-4β), 78.9 (C-3β), 76.0 (C-3α), 75.3 (CH_2 Bnα), 75.1 (CH_2 Bn), 69.0 (t, *J* = 29.0 Hz, *CH*$_2$-CF_2Hβ), 68.8 (C-6), 68.5 (C-6), 67.5 (t, *J* = 28.7 Hz, *CH*$_2$-CF_2Hα), 66.4 (C-5β), 66.0 (C-2β), 63.3 (C-5α), 62.9 (C-2α); HRMS: $[M+H]^+$ calcd for $C_{22}H_{24}F_2N_3O_5$ 448.16785, found 448.16761.



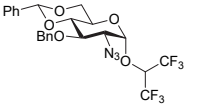
Methyl 4-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranosyl)-2,3,6-tri-*O*-benzyl-β-D-galactopyranoside (3H). Donor **3** and acceptor **28** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 18 h at -40°C) and purified by flash column chromatography (19/1 to 4/1 pentane/EtOAc) to yield glycosylation product **3H** (62.2 mg, 75 µmol, 75%, α:β = 9:1) as a white solid. R_f: 0.52 (4/1 pentane/EtOAc). IR (neat): 696, 735, 995, 1030, 1072, 1090, 1368, 1454, 1497, 2106, 2862, 2920; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 7.50 – 7.46 (m, 2H, CH_{arom}), 7.42 – 7.25 (m, 23H, CH_{arom}), 5.51 (s, 1H, C*H*Ph), 4.98 (d, 1H, *J* = 10.7 Hz, C*H*H 3'-OBn), 4.90 (d, 1H, *J* = 11.0 Hz, C*H*H 2-OBn), 4.88 (d, 1H, *J* = 3.7 Hz, H-1'), 4.84 – 4.76 (m, 3H, CH*H* 2-OBn, CH*H* 3'-OBn, CH*H* 3-OBn), 4.69 (d, 1H, *J* = 12.4 Hz, CH*H* 3-OBn), 4.59 – 4.51 (m, 2H, CH_2 6-OBn), 4.30 (td, 1H, *J* = 10.1, 4.9 Hz, H-5'), 4.25 (d, 1H, *J* = 7.6 Hz, H-1), 4.14 – 4.07 (m, 2H, H-3', H-4), 4.03 (t, 1H, *J* = 8.9 Hz, H-6), 3.80 (dd, 1H, *J* = 10.2, 4.9 Hz, H-6'), 3.70 – 3.60 (m, 3H, H-2, H-4', H-6), 3.55 (s, 3H, CH_3 OMe), 3.54 – 3.48 (m, 2H, H-5, H-6'), 3.44 – 3.36 (m, 2H, H-2', H-3); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 138.7, 138.3, 138.1, 137.7, 137.6 (C_q), 129.0, 128.6, 128.5, 128.5, 128.4, 128.3, 128.3, 128.3, 128.2, 128.0, 127.7, 127.6, 126.1 (CH_{arom}), 105.3 (C-1), 101.2 (CHPh), 99.4 (C-1'), 83.1 (C-4'), 80.1 (C-3), 78.9 (C-2), 77.0 (C-3'), 75.3 (CH_2 3'-OBn), 75.1 (CH_2 2-OBn), 74.7 (C-4), 73.6 (CH_2 6-OBn), 73.0 (CH_2 3-OBn), 72.9 (C-5), 68.9 (C-6'), 67.1 (C-6), 63.8 (C-2'), 62.9 (C-5'), 57.4 (OMe); Diagnostic peaks β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.54 (s, 1H, C*H*Ph), 3.92 (dd, 1H, *J* = 9.7, 7.7 Hz, H-2), 3.76 – 3.71 (m, 1H, H-6), 3.22 (td, 1H, *J* = 9.7, 4.8 Hz, H-5'); ^{13}C-APT NMR ($CDCl_3$, 101 MHz): δ 105.1 (C-1), 102.6 (C-1'), 101.4, 81.5, 81.3, 79.5, 79.0, 74.0, 73.4, 69.4, 68.6, 66.3, 66.0, 57.4; HRMS: $[M+NH_4]^+$ calcd for $C_{48}H_{55}N_4O_{10}$ 847.39127, found 847.39206.



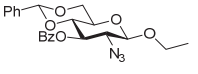
Methyl 2-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranosyl)-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (3I). Donor **3** and acceptor **29** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 18 h at -40°C) and purified by flash column chromatography (19/1 to 4/1 pentane/EtOAc) to yield glycosylation product **3I** (54.7 mg, 74 µmol, 74%, α:β = 9:1) as a white solid. R_f: 0.74 (7/2 pentane/EtOAc). IR (neat): 696, 746, 997, 1036, 1074, 1090, 1128, 1371, 1454, 2106, 2862, 2922; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 7.54 – 7.47 (m, 4H, CH_{arom}), 7.44 – 7.25 (m, 16H, CH_{arom}), 5.66 (s, 1H, C*H*Ph), 5.60 (s, 1H, C*H*Ph'), 5.39 (d, 1H, *J* = 3.7 Hz, H-1'), 5.00 (d, 1H, *J* = 11.0 Hz, C*H*H Bn), 4.90 (d, 1H, *J* = 12.2 Hz, C*H*H Bn), 4.84 (d, 1H, *J* = 10.9 Hz, CH*H* Bn), 4.73 – 4.66 (m, 2H, H-1, CH*H* Bn), 4.34 – 4.24 (m, 3H, H-4, H-6, H-6'), 4.17 (dd, 1H, *J* = 10.2, 9.0 Hz, H-3'), 4.09 (dd, 1H, *J* = 3.1, 1.7 Hz, H-2), 4.00 (dd, 1H, *J* = 9.9, 3.1 Hz, H-3), 3.95 – 3.86 (m, 2H, H-5', H-6), 3.83 – 3.70 (m, 3H, H-4', H-5, H-6'), 3.36 (s, 3H, CH_3 OMe), 3.32 (dd, 1H, *J* = 10.2, 3.8 Hz, H-2'); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 138.7, 138.0, 137.7, 137.2 (C_q), 129.2, 129.0, 128.6, 128.5, 128.4, 128.3, 128.2, 128.0, 127.6, 127.4, 126.2, 126.0 (CH_{arom}), 101.7 (CHPh), 101.5 (CHPh'), 101.0 (C-1), 99.8 (C-1'), 82.9 (C-4'), 79.4 (C-4), 75.9 (C-3), 75.6 (C-3'), 75.5 (C-2), 75.3, 73.3 (CH_2 Bn), 69.0, 68.9 (C-6, C-6'), 64.1 (C-5), 63.3 (C-5'), 63.0 (C-2'), 55.0 (OMe); Diagnostic peaks β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.43 (d, 0.1H, *J* = 8.0 Hz, H-1'), 3.62 (dd, 0.1H, *J* = 9.6, 8.0 Hz, H-2'), 3.51 (t, 0.1H, *J* = 9.3 Hz, H-4); ^{13}C-APT NMR ($CDCl_3$, 101 MHz): δ 102.0 (C-1'), 78.5 (C-4), 66.4 (C-2'); HRMS: $[M+NH_4]^+$ calcd for $C_{41}H_{47}N_4O_{10}$ 755.32867, found 755.32921.



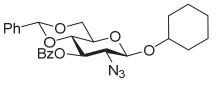
2,2,2-Trifluoroethyl 2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside (3J). Donor **3** and 2,2,2-trifluoroethanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 1 h at -40°C) and purified by flash column chromatography (1/0 to 0/1 pentane/toluene to 5% EtOAc in toluene) to yield glycosylation product **3J** (44 mg, 94 µmol, 94%, α:β = >20:1) as a colorless oil. R_f: 0.24 (toluene). $[\alpha]_D^{23}$ = +25.9° (*c* = 0.88, DCM); IR (neat): 697, 747, 1001, 1034, 1090, 1165, 1279, 1373, 2108, 2865, 2934; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.51 – 7.48 (m, 2H, CH_{arom}), 7.42 – 7.28 (m, 8H, CH_{arom}), 5.58 (s, 1H, C*H*Ph), 4.99 – 4.94 (m, 2H, C*H*H Bn, H-1), 4.80 (d, 1H, *J* = 10.9 Hz, CH*H* Bn), 4.29 (dd, 1H, *J* = 10.2, 4.8 Hz, H-6), 4.10 (dd, 1H, *J* = 10.0, 9.0 Hz, H-3), 3.98 (qd, 2H, *J* = 8.5, 3.1 Hz, C*H*$_2$-CF_3), 3.91 (td, 1H, *J* = 9.9, 4.8 Hz, H-5), 3.79 – 3.70 (m, 2H, H-4, H-6), 3.43 (dd, 1H, *J* = 10.0, 3.7 Hz, H-2); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 137.8, 137.1 (C_q), 129.3, 128.6, 128.5, 128.3, 128.1, 126.1 (CH_{arom}), 123.5 (q, *J* = 278.5 Hz), 101.6 (CHPh), 99.4 (C-1), 82.5 (C-4), 75.9 (C-3), 75.3 (CH_2 Bn), 68.7 (C-6), 65.4 (q, *J* = 35.4 Hz), 63.5 (C-5), 62.7 (C-2); ^{13}C-HMBC-GATED NMR ($CDCl_3$, 101 MHz): δ 102.5 ($J_{C1,H1}$ = 173 Hz, C-1); Diagnostic peaks β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.44 (d, 0.03H, *J* = 7.9 Hz, H-1), 4.34 (dd, 0.03H, *J* = 10.8, 5.3 Hz, H-6), 3.56 (t, 0.03H, *J* = 9.2 Hz), 3.48 (dd, 0.03H, *J* = 10.0, 7.9 Hz, H-2); ^{13}C-HMBC-GATED NMR ($CDCl_3$, 101 MHz): δ 102.4 (J_{C-H} = 150 Hz, C-1); HRMS: $[M+NH_4]^+$ calcd for $C_{22}H_{26}F_3N_4O_5$ 483.18498 found 483.18463.



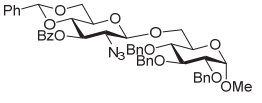
1,1,1,3,3,3-Hexafluoro-2-propyl 2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside (3K). Donor **3** and 1,1,1,3,3,3-hexafluoroisopropanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 72 h at -40°C) and purified by flash column chromatography (1/0 to 9/1 pentane/EtOAc) to yield glycosylation product **3K** (28.1 mg, 53 µmol, 53%, α:β = >20:1) as a colorless oil. $[\alpha]_D^{23}$ = +25.8° (*c* = 0.5, $CHCl_3$); IR (neat): 689, 748, 999, 1092, 1196, 1219, 1287, 1368, 2108, 2868, 2928; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.54 – 7.45 (m, 2H, CH_{arom}), 7.44 – 7.27 (m, 8H, CH_{arom}), 5.59 (s, 1H, C*H*Ph), 5.13 (d, 1H, *J* = 3.9 Hz, H-1), 4.99 (d, 1H, *J* = 10.8 Hz, C*H*H Bn), 4.82 (d, 1H, *J* = 10.8 Hz, CH*H* Bn), 4.40 (hept, 1H, *J* = 5.9 Hz, CH HFIP), 4.26 (dd, 1H, *J* = 10.3, 4.9 Hz, H-6), 4.10 (dd, 1H, *J* = 10.0, 9.1 Hz, H-3), 3.98 (td, 1H, *J* = 10.0, 4.9 Hz, H-5), 3.80 – 3.73 (m, 2H, H-4, H-6), 3.51 (dd, 1H, *J* = 10.1, 3.9 Hz, H-2); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 137.6, 136.9 (C_q), 129.3, 128.6, 128.5, 128.4, 128.2, 126.1 (CH_{arom}), 120.9 (q, *J* = 283 Hz, CF_3), 101.6 (CHPh), 101.0 (C-1), 82.1 (C-4), 75.9 (C-3), 75.5 (CH_2 Bn), 74.0, 73.7 (hept, *J* = 32.8 Hz, CH HFIP), 68.3 (C-6), 64.2 (C-5), 62.5 (C-2); HRMS: $[M+H]^+$ calcd for $C_{23}H_{21}F_6N_3O_5$ 534.14582, found 534.14569.



Ethyl 2-azido-3-*O*-benzoyl-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (4A). Donor **4** and ethanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations and purified by flash column chromatography (1/1/0 to 0/1/0 to 0/19/1 pentane/toluene/EtOAc) to yield glycosylation product **4A** (36 mg, 85 µmol, 85%, α:β = <1:20) as a white solid. R_f: 0.44 (19/1 toluene/EtOAc). $[\alpha]_D^{23}$ = -53.7° (*c* = 1.04, DCM); IR (thin film): 709, 1001, 1026, 1070, 1094, 1180, 1263, 1375, 1726, 2110, 2872; Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.11 – 8.05 (m, 2H, CH_{arom}), 7.60 – 7.55 (m, 1H, CH_{arom}), 7.48 – 7.43 (m, 2H, CH_{arom}), 7.40 – 7.35 (m, 2H, CH_{arom}), 7.32 – 7.27 (m, 3H, CH_{arom}), 5.50 (s, 1H, C*H*Ph), 5.40 (t, 1H, *J* = 9.8 Hz, H-3), 4.59 (d, 1H, *J* = 7.9 Hz, H-1), 4.38 (dd, 1H, *J* = 10.6, 5.0 Hz, H-6), 4.02 (dq, 1H, *J* = 9.5, 7.1 Hz, C*H*H Et), 3.83 (t, 1H, *J* = 10.3 Hz, H-6), 3.80 – 3.67 (m, 2H, H-4, CH*H* Et), 3.64 (dd, 1H, *J* = 10.0, 7.9 Hz, H-2), 3.56 (td, 1H, *J* = 9.7, 5.0 Hz, H-5), 1.32 (t, 3H, *J* = 7.1 Hz, CH_3 Et); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 165.5 (C=O Bz), 136.9 (C_q), 133.4, 130.1 (CH_{arom}), 129.7 (C_q), 129.2, 128.6, 128.3, 126.2 (CH_{arom}), 102.8 (C-1), 101.6 (CHPh), 79.0 (C-4), 71.8 (C-3), 68.7 (C-6), 66.6, 66.6 (C-5, CH_2 Et), 65.0 (C-2), 15.2 (CH_3 Et); Diagnostic peaks α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 5.88 (t, 0.03H, *J* = 9.9 Hz, H-3), 5.53 (s, 0.03H, C*H*Ph), 5.06 (d, 0.03H, *J* = 3.6 Hz, H-1), 4.32 (dd, 0.03H, *J* = 10.4, 4.9 Hz, H-6), 3.32 (dd, 0.03H, *J* = 10.3, 3.6 Hz, H-2); HRMS: $[M+NH_4]^+$ calcd for $C_{22}H_{27}N_4O_6$ 443.19251 found 443.19234.

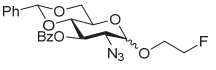


Cyclohexyl 2-azido-3-*O*-benozyl-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (4B). Donor **4** and cyclohexanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations and purified by flash column chromatography (1/1/0 to 0/1/0 to 0/19/1 pentane/toluene/EtOAc) to yield glycosylation product **4B** (43.6 mg, 91 µmol, 91%, α:β = <1:20) as a white solid. R_f: 0.18 (toluene). $[\alpha]_D^{23}$ = -41.2° (*c* = 0.87, DCM); IR (thin film): 613, 708, 999, 1096, 1263, 1730, 2110, 2859, 2934; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.11 – 8.05 (m, 2H, CH_{arom}), 7.61 – 7.54 (m, 1H, CH_{arom}), 7.49 – 7.42 (m, 2H, CH_{arom}), 7.41 – 7.35 (m, 2H, CH_{arom}), 7.31 – 7.27 (m, 3H, CH_{arom}), 5.50 (s, 1H, C*H*Ph), 5.38 (t, 1H, *J* = 9.9 Hz, H-3), 4.70 (d, 1H, *J* = 7.9 Hz, H-1), 4.37 (dd, 1H, *J* = 10.6, 5.0 Hz, H-6), 3.89 – 3.71 (m, 3H, H-4, H-6, C*H*O Cyc), 3.64 (dd, 1H, *J* = 10.1, 7.9 Hz, H-2), 3.55 (td, 1H, *J* = 9.8, 5.0 Hz, H-5), 2.04 – 1.90 (m, 2H, 2xC*H*H Cyc), 1.85 – 1.73 (m, 2H, 2xC*H*H Cyc), 1.58 – 1.40 (m, 3H, C*H*H Cyc, 2xCH*H* Cyc), 1.39 – 1.20 (m, 3H, 3xCH*H* Cyc); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 165.5 (C=O Bz), 136.9 (C_q), 133.4, 130.0 (CH_{arom}), 129.7 (C_q), 129.2, 128.5, 128.3, 126.2 (CH_{arom}), 101.6 (CHPh), 101.2 (C-1), 79.0 (C-4), 78.8 (CH Cyc), 71.8 (C-3), 68.7 (C-6), 66.6 (C-5), 65.2 (C-2), 33.7, 31.7, 25.6, 24.1, 23.9 (CH_2 Cyc); HRMS: $[M+NH_4]^+$ calcd for $C_{26}H_{33}N_4O_6$ 497.23946 found 497.23932.

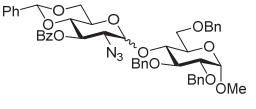


Methyl 6-*O*-(2-azido-3-*O*-benzoyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (4C). Donor **4** and acceptor **25** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 18 h at -40°C) and purified by flash column chromatography (19/1 to 3/1 pentane/EtOAc) to yield glycosylation product **4C** (67 mg, 79 µmol, 79%, α:β = 1:14) as a white solid. R_f: 0.24 (4/1 pentane/EtOAc). $[\alpha]_D^{20}$ = -17.5° (*c* = 1.34, $CHCl_3$); IR (thin film): 696, 748, 1002, 1028, 1068, 1092, 1263, 1313, 1369, 1452, 1730, 2110, 2872, 2918; Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 8.09 – 8.04 (m, 2H, CH_{arom}), 7.60 – 7.53 (m, 1H, CH_{arom}), 7.48 – 7.41 (m, 2H, CH_{arom}), 7.40 – 7.24 (m, 20H, CH_{arom}), 5.47 (s, 1H, C*H*Ph), 5.42 (t, 1H, *J* = 9.8 Hz, H-3'), 5.00 (d, 1H, *J* = 10.9 Hz, C*H*H Bn), 4.95 (d, 1H, *J* = 11.1 Hz, C*H*H Bn), 4.84 (d, 1H, *J* = 11.0 Hz, CH*H* Bn), 4.80 (d, 1H, *J* = 12.2 Hz, C*H*H Bn), 4.68 – 4.63 (m, 2H, 2xCH*H* Bn), 4.61 (d, 1H, *J* = 3.5 Hz, H-1), 4.43 (d, 1H, *J* = 8.0 Hz, H-1'), 4.33 (dd, 1H, *J* = 10.5, 5.0 Hz, H-6'), 4.12 (d, 1H, *J* = 9.1 Hz, H-6), 4.02 (t, 1H, *J* = 9.3 Hz, H-3), 3.84 – 3.72 (m, 4H, H-4', H-5, H-6, H-6'), 3.69 (dd, 1H, *J* = 9.9, 8.0 Hz, H-2'), 3.57 (t, 1H, *J* = 9.2

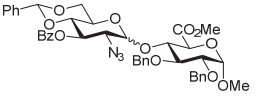
Hz, H-4), 3.54 (dd, 1H, *J* = 9.7, 3.6 Hz, H-2), 3.49 (td, 1H, *J* = 9.8, 5.0 Hz, H-5'), 3.39 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 165.4 (C=O), 138.7, 138.3, 138.2, 136.7 (CH_{arom}), 133.5, 130.0 (CH_{arom}), 129.4 (C_q Bz), 129.1, 128.6, 128.6, 128.5, 128.5, 128.3, 128.3, 128.1, 128.0, 128.0, 127.9, 127.9, 127.7, 126.1 (CH_{arom}), 102.6 (C-1'), 101.5 (CHPh), 98.3 (C-1), 82.1 (C-3), 79.8 (C-2), 78.7 (C-4'), 77.7 (C-4), 75.8, 75.0, 73.6 (CH_2 Bn), 71.9 (C-3'), 69.7 (C-5), 68.9 (C-6), 68.5 (C-6'), 66.6 (C-5'), 65.2 (C-2'), 55.4 (CH_3 OMe); Diagnostic peaks α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.79 (t, 0.07H, *J* = 9.9 Hz, H-3'), 5.50 (s, 0.07H, C*H*Ph), 5.08 (d, 0.07H, *J* = 3.5 Hz, H-1'), 4.24 (dd, 0.07H, *J* = 10.3, 4.8 Hz, H-6'), 3.41 (s, 0.21H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz): δ 101.7 (CHPh), 99.3 (C-1'), 98.1 (C-1), 82.1, 80.0, 79.7, 77.6, 75.8, 75.2, 70.0, 69.4, 67.0, 62.8, 62.1, 55.4; HRMS: $[M+NH_4]^+$ calcd for $C_{48}H_{53}N_4O_{11}$ 861.37053, found 861.37064.



2-Fluoroethyl 2-azido-3-*O*-benzoyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranoside (4D). Donor **4** and 2-fluoroethanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations and purified by flash column chromatography (1/1/0 to 0/1/0 to 0/16/1 pentane/toluene/EtOAc) to yield glycosylation product **4D** (36.6 mg, 83 µmol, 83%, α:β = 1:6.5) as a white solid. R_f: 0.41 (19/1 toluene/EtOAc). IR (thin film): 700, 748, 879, 1001, 1026, 1070, 1093, 1179, 1261, 1722, 2108, 2868; Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.10 – 8.05 (m, 2H, CH_{arom}), 7.61 – 7.54 (m, 1H, CH_{arom}), 7.49 – 7.43 (m, 2H, CH_{arom}), 7.41 – 7.36 (m, 2H, CH_{arom}), 7.33 – 7.27 (m, 3H, CH_{arom}), 5.50 (s, 1H, C*H*Ph), 5.41 (t, 1H, *J* = 9.8 Hz, H-3), 4.69 (ddt, 1H, *J* = 4.6, 3.2, 1.8 Hz, C*H*-CH_2F), 4.65 (d, 1H, *J* = 7.9 Hz, H-1), 4.58 (ddt, 1H, *J* = 4.5, 3.3, 1.8 Hz, CH*H*-CH_2F), 4.38 (dd, 1H, *J* = 10.5, 4.9 Hz, H-6), 4.14 (dddd, 1H, *J* = 30.3, 11.9, 4.6, 3.1 Hz, C*H*HF), 3.95 (dddd, 1H, *J* = 27.1, 12.1, 5.5, 3.4 Hz, CH*H*F), 3.83 (t, 1H, *J* = 10.3 Hz, H-6), 3.79 (t, 1H, *J* = 9.5 Hz, H-4), 3.69 (dd, 1H, *J* = 10.0, 7.9 Hz, H-2), 3.57 (td, 1H, *J* = 9.7, 5.0 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 165.4 (C=O), 136.8 (C_q Ph), 133.5, 130.0 (CH_{arom}), 129.5 (C_q Bz), 129.2, 128.6, 128.5, 128.3, 126.3, 126.2 (CH_{arom}), 103.0 (C-1), 101.6 (CHPh), 82.5 (d, *J* = 170.5 Hz, *C*H_2F), 78.8 (C-4), 71.7 (C-3), 69.5 (d, *J* = 20.2 Hz, *C*H_2-CH_2F), 68.5 (C-6), 66.7 (C-5), 64.9 (C-2); Diagnostic peaks α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.89 (t, 0.17H, *J* = 9.9 Hz, H-3), 5.53 (s, 0.17H, C*H*Ph), 5.12 (d, 0.17H, *J* = 3.6 Hz, H-1), 4.33 (dd, 0.17H, *J* = 10.4, 5.0 Hz, H-6), 3.38 (dd, 0.17H, *J* = 10.4, 3.6 Hz, H-2); ^{13}C-APT NMR ($CDCl_3$, 101 MHz): δ 101.8, 99.5 (C-1), 82.4 (d, *J* = 170.8 Hz), 79.6, 68.9, 67.8 (d, *J* = 20.2 Hz), 63.1, 61.8; HRMS: $[M+NH_4]^+$ calcd for $C_{22}H_{26}FN_4O_6$ 461.18309 found 461.18292.

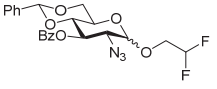


Methyl 4-*O*-(2-azido-3-*O*-benzoyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranosyl)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (4E). Donor **4** and acceptor **26** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 18 h at -40°C) and purified by flash column chromatography (19/1 to 4/1 pentane/EtOAc) to yield glycosylation product **4E** (60 mg, 71 µmol, 71%, α:β = 1:6) as a white solid. R_f: 0.67 (4/1 pentane/EtOAc). IR (thin film): 696, 733, 914, 999, 1026, 1045, 1090, 1177, 1263, 1314, 1366, 1452, 1730, 2108, 2866, 2899; Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 8.10 – 8.04 (m, 2H, CH_{arom}), 7.61 – 7.53 (m, 1H, CH_{arom}), 7.49 – 7.24 (m, 22H, CH_{arom}), 5.40 (s, 1H, C*H*Ph), 5.19 (t, 1H, *J* = 9.8 Hz, H-3'), 4.90 (d, 1H, *J* = 10.8 Hz, C*H*H Bn), 4.83 (d, 1H, *J* = 10.8 Hz, CH*H* Bn), 4.81 – 4.73 (m, 2H, 2xC*H*H Bn), 4.67 – 4.60 (m, 2H, CH*H* Bn, H-1), 4.42 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.31 (d, 1H, *J* = 8.0 Hz, H-1'), 4.17 (dd, 1H, *J* = 10.6, 5.0 Hz, H-6'), 4.08 – 3.98 (t, 1H, *J* = 9.4 Hz, H-4), 3.96 (dd, 1H, *J* = 10.8, 2.4 Hz, H-6), 3.86 (t, 1H, *J* = 9.3 Hz, H-3), 3.79 – 3.74 (m, 1H, H-5), 3.71 (dd, 1H, *J* = 10.7, 1.7 Hz, H-6), 3.61 (t, 1H, *J* = 9.5 Hz, H-4'), 3.54 (dd, 1H, *J* = 9.6, 3.7 Hz, H-2), 3.52 – 3.45 (m, 2H, H-2', H-6'), 3.39 (s, 3H, CH_3 OMe), 3.08 (td, 1H, *J* = 9.7, 5.0 Hz, H-5'); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 165.3 (C=O), 139.3, 138.3, 137.6, 136.9 (C_q), 133.4, 129.9 (CH_{arom}), 128.9 (C_q Bz), 128.6, 128.5, 128.5, 128.3, 128.3, 128.2, 127.9, 127.8, 126.2 (CH_{arom}), 101.5, 101.4 (CHPh, C-1'), 98.4 (C-1), 80.1 (C-3), 79.1 (C-2), 78.9 (C-4'), 76.8 (C-4), 75.6, 73.7, 73.6 (CH_2 Bn), 72.0 (C-3'), 69.7 (C-5), 68.6 (C-6'), 67.8 (C-6), 66.1 (C-5'), 65.6 (C-2'), 55.5 (OMe); Diagnostic peaks α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.91 (d, 0.17H, *J* = 3.9 Hz, H-1'), 5.80 (t, 0.17H, *J* = 10.0 Hz, H-3'), 5.47 (s, 0.17H, C*H*Ph), 5.15 (d, 0.17H, *J* = 10.7 Hz, C*H*H Bn), 4.74 (d, 0.17H, *J* = 12.0 Hz, C*H*H Bn), 4.09 (t, 0.17H, *J* = 9.2 Hz), 3.29 (dd, 0.17H, *J* = 10.5, 3.9 Hz, H-2'); ^{13}C-APT NMR ($CDCl_3$, 101 MHz): δ 165.6, 138.6, 138.1, 137.9, 137.0, 133.4, 130.0, 129.6, 129.0, 128.6, 128.6, 128.5, 128.4, 128.2, 128.1, 127.6, 127.6, 127.4, 101.6 (CHPh), 98.6 (C-1'), 97.7 (C-1), 82.1, 80.7, 79.5, 75.0, 73.6, 73.3, 72.8, 69.5, 69.3, 68.9, 68.7, 63.7, 61.9, 55.5; HRMS: $[M+NH_4]^+$ calcd for $C_{48}H_{53}N_4O_{11}$ 861.37053, found 861.37081.

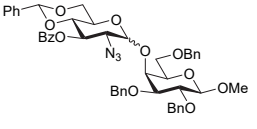


Methyl (Methyl 4-*O*-[2-azido-3-*O*-benzoyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranosyl]-2,3-di-*O*-benzyl-α-D-glucopyranosyl uronate) (4F). Donor **4** and acceptor **27** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 18 h at -40°C) and purified by flash column chromatography (19/1 to 4/1 pentane/EtOAc) to yield glycosylation product **4F** (46 mg, 59 µmol, 59%, α:β = 1:1.4) as

a white solid. R_f: 0.56 (4/1 pentane/EtOAc). IR (thin film): 698, 750, 991, 1026, 1047, 1092, 1178, 1263, 1452, 1730, 2110, 2868, 2938; Reported as a 0.7 : 1 mixture of anomers: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 8.09 – 8.03 (m, 3.4H, CH_{arom}), 7.61 – 7.52 (m, 1.7H, CH_{arom}), 7.49 – 7.25 (m, 28.9H, CH_{arom}), 5.76 (dd, 0.7H, *J* = 9.5, 10.3 Hz, H-3'$_\alpha$), 5.70 (d, 0.7H, *J* = 3.9 Hz, H-1'$_\alpha$), 5.47 (s, 0.7H, C*H*Ph$_\alpha$), 5.41 (s, 1H, C*H*Ph$_\beta$), 5.36 (t, 1H, *J* = 9.8 Hz, H-3'$_\beta$), 5.10 (d, 0.7H, *J* = 10.6 Hz, C*H*H Bn$_\alpha$), 4.93 (d, 1H, *J* = 10.9 Hz, C*H*H Bn$_\beta$), 4.87 (d, 1H, *J* = 10.9 Hz, CH*H* Bn$_\beta$), 4.83 (d, 0.7H, *J* = 10.6 Hz, CH*H* Bn$_\alpha$), 4.79 (d, 1H, *J* = 13.6 Hz, C*H*H Bn$_\beta$), 4.76 (d, 0.7H, *J* = 13.6 Hz, C*H*H Bn$_\alpha$), 4.66 – 4.62 (m, 2H, CH*H* Bn$_\beta$, H-1'$_\beta$), 4.61 – 4.58 (m, 2.4H, CH*H* Bn$_\alpha$, H-1$_\alpha$, H-1$_\beta$), 4.31 (dd, 0.7H, *J* = 10.0, 4.6 Hz, H-6'$_\alpha$), 4.28 (d, 0.7H, *J* = 9.7 Hz, H-5$_\alpha$), 4.23 (d, 1H, *J* = 9.9 Hz, H-5$_\beta$), 4.19 – 4.06 (m, 3.4H, H-3$_\alpha$, H-4$_\alpha$, H-4$_\beta$, H-6'$_\beta$), 3.91 (t, 1H, *J* = 9.2 Hz, H-3), 3.85 (s, 2.1H, CH_3 CO_2Me_α), 3.83 (s, 3H, CH_3 CO_2Me_β), 3.79 – 3.59 (m, 3.8H, H-2$_\alpha$, H-4'$_\alpha$, H-4'$_\beta$, H-5'$_\alpha$, H-6'$_\alpha$), 3.59 – 3.44 (m, 4H, H-2$_\beta$, H-2'$_\beta$, H-5'$_\beta$, H-6'$_\beta$), 3.43 (s, 3H, CH_3 OMe$_\beta$), 3.42 (s, 2.1H, CH_3 OMe$_\alpha$), 3.31 (dd, 1H, *J* = 10.4, 3.9 Hz, H-2'$_\alpha$); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 170.2, 169.9 (C=O CO_2Me), 165.5, 165.3 (C=O Bz), 139.1, 138.4, 138.0, 137.7, 137.0, 136.8 (C_q Bn, CHPh), 133.4, 133.4, 130.0, 130.0 (CH_{arom}), 129.5, 129.5 (C_q Bz), 129.1, 129.1, 128.7, 128.6, 128.5, 128.5, 128.5, 128.3, 128.3, 128.2, 128.1, 127.8, 127.7, 127.6, 127.5, 126.2, 126.2 (CH_{arom}), 102.3 (C-1'$_\beta$), 101.7 (CHPh$_\alpha$), 101.5 (CHPh$_\beta$), 99.0 (C-1'$_\alpha$), 98.8 (C-1$_\beta$), 98.5 (C-1$_\alpha$), 81.1 (C-3$_\alpha$), 79.9 (C-2$_\alpha$), 79.5, 79.5 (C-3$_\beta$, C-4$_\beta$), 79.2 (C-4'$_\alpha$), 78.9, 78.7 (C-2$_\beta$, C-4'$_\beta$), 75.7, 75.4 (CH_2 Bn), 75.2 (C-4$_\alpha$), 73.9, 73.6 (CH_2 Bn), 71.9 (C-3'$_\beta$), 69.8, 69.8 (C-5$_\alpha$, C-5$_\beta$), 69.6 (C-3'$_\alpha$), 68.5, 68.4 (C-6'$_\alpha$, C-6'$_\beta$), 66.5 (C-5'$_\beta$), 65.6 (C-2'$_\beta$), 63.2 (C-5'$_\alpha$), 61.7 (C-2'$_\alpha$), 56.0, 56.0 (CH_3 OMe), 53.1, 53.0 (CH_3 CO_2Me); HRMS: $[M+NH_4]^+$ calcd for $C_{42}H_{47}N_4O_{12}$ 799.31850, found 799.31869.

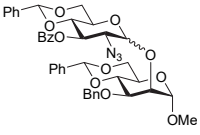


2,2-Difluoroethyl 2-azido-3-*O*-benzoyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranoside (4G). Donor **4** and 2,2-difluoroethanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations and purified by flash column chromatography (1/1/0 to 0/1/0 to 0/19/1 pentane/toluene/EtOAc) to yield glycosylation product **4G** (38.6 mg, 84 μmol, 84%, α:β = 2.7:1) as a white solid. R_f: 0.49 (19/1 toluene/EtOAc). IR (thin film): 709, 997, 1026, 1069, 1094, 1265, 1726, 2108, 2870; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.11 – 8.05 (m, 2H, CH_{arom}), 7.63 – 7.53 (m, 1H, CH_{arom}), 7.50 – 7.36 (m, 4H, CH_{arom}), 7.34 – 7.27 (m, 3H, CH_{arom}), 6.02 (tt, 1H, *J* = 55.1, 4.2 Hz, C*H*F_2), 5.91 – 5.81 (m, 1H, H-3), 5.53 (s, 1H, C*H*Ph), 5.11 (d, 1H, *J* = 3.6 Hz, H-1), 4.33 (dd, 1H, *J* = 10.4, 4.9 Hz, H-6), 4.07 (ddd, 1H, *J* = 14.8, 6.4, 3.7 Hz, H-5), 3.99 – 3.77 (m, 4H, H-4, H-6), 3.42 (dd, 1H, *J* = 10.4, 3.6 Hz, H-2); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 165.5 (C=O Bz), 136.8 (C_q), 133.5, 130.1 (CH_{arom}), 129.5 (C_q Bz), 128.5, 128.3, 126.2 (CH_{arom}), 113.7 (t, *J* = 241.7 Hz, CHF_2), 101.8 (CHPh), 99.8 (C-1), 79.4 (C-4), 69.3 (C-3), 68.7 (C-6), 67.6 (t, *J* = 29.0 Hz, *C*H_2-CHF_2), 63.5 (C-5), 61.8 (C-2); Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.97 (tdd, 0.37H, *J* = 55.2, 4.8, 3.5 Hz, C*H*F_2), 5.51 (s, 0.37H, C*H*Ph), 5.42 (t, 0.37H, *J* = 9.8 Hz, H-3), 4.63 (d, 0.37H, *J* = 7.9 Hz, H-1), 4.38 (dd, 0.37H, *J* = 10.5, 5.0 Hz, H-6), 4.12 – 3.99 (m, 0.37H, C*H*H-CHF_2), 3.98 – 3.76 (m, 1.11H, CH*H*-CHF_2, H-4, H-6), 3.69 (dd, 0.37H, *J* = 10.0, 7.9 Hz, H-2), 3.58 (td, 0.37H, *J* = 9.8, 5.0 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz): δ 165.4, 136.7, 133.5, 130.0, 129.4, 129.2, 128.6, 126.2, 113.8 (t, *J* = 241.5 Hz), 103.1, 101.7, 78.7 (C-4), 71.5 (C-3), 69.1 (t, *J* = 29.0 Hz, *C*H_2-CHF_2), 68.4 (C-6), 66.8 (C-5), 64.9 (C-2); HRMS: $[M+H]^+$ calcd for $C_{22}H_{22}F_2N_3O_6$ 462.14712, found 462.14699.

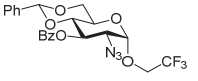


Methyl 4-*O*-(2-azido-3-*O*-benzoyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranosyl)-2,3,6-tri-*O*-benzyl-β-D-galactopyranoside (4H). Donor **4** and acceptor **28** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 18 h at -40°C) and purified by flash column chromatography (19/1 to 4/1 pentane/EtOAc) to yield glycosylation product **4H** (43 mg, 52 μmol, 52%, α:β = 4:1) as a white solid. R_f: 0.36 (4/1 pentane/EtOAc). IR (thin film): 698, 737, 997, 1072, 1094, 1265, 1452, 1730, 2106, 2862, 2930; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 8.12 – 8.05 (m, 2H, CH_{arom}), 7.57 (t, 1H, *J* = 7.4 Hz, CH_{arom}), 7.45 (t, 2H, *J* = 7.7 Hz, CH_{arom}), 7.42 – 7.20 (m, 20H, CH_{arom}), 5.85 (t, 1H, *J* = 9.9 Hz, H-3'), 5.44 (s, 1H, C*H*Ph), 5.07 (d, 1H, *J* = 3.9 Hz, H-1'), 4.93 (d, 1H, *J* = 11.0 Hz, C*H*H Bn), 4.84 (d, 1H, *J* = 10.9 Hz, CH*H* Bn), 4.79 (d, 1H, *J* = 12.4 Hz, C*H*H Bn), 4.74 (d, 1H, *J* = 12.4 Hz, CH*H* Bn), 4.55 (s, 2H, CH_2 Bn), 4.46 (td, 1H, *J* = 9.9, 4.9 Hz, H-5'), 4.26 (d, 1H, *J* = 7.6 Hz, H-1), 4.17 (d, 1H, *J* = 3.1 Hz, H-4), 3.93 (t, 1H, *J* = 9.1 Hz, H-6), 3.85 (dd, 1H, *J* = 10.2, 5.0 Hz, H-6'), 3.81 – 3.70 (m, 2H, H-2, H-4'), 3.64 (dd, 2H, *J* = 9.1, 5.4 Hz, H-6), 3.57 – 3.50 (m, 5H, CH_3 OMe, H-5, H-6'), 3.47 (dd, 1H, *J* = 10.4, 3.9 Hz, H-2'), 3.42 (dd, 1H, *J* = 10.0, 3.0 Hz, H-3); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 165.3 (C=O Bz), 138.7, 138.3, 137.6, 137.2 (C_q), 133.3, 130.0 (CH_{arom}), 129.8 (C_q), 128.9, 128.7, 128.6, 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 128.2, 128.2, 128.1, 127.9, 127.7, 127.6, 127.6, 126.3, 126.2 (CH_{arom}), 105.2 (C-1), 101.4 (CHPh), 99.4 (C-1'), 80.0 (C-4'), 79.8 (C-3), 79.0 (C-2), 75.2 (CH_2 Bn), 74.4 (C-4), 73.6, 73.2 (CH_2 Bn), 72.6 (C-5), 70.2 (C-3'), 68.8 (C-6'), 67.1 (C-6), 62.8, 62.7 (C-2', C-5'), 57.0 (OMe); Diagnostic peaks β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.47 (s, 0.25H, C*H*Ph), 5.34 (t, 0.25H, *J* = 9.8 Hz, H-3'), 4.30 (d, 0.25H, *J* = 7.7 Hz, H-1'), 4.09 (d, 0.25H, *J* =

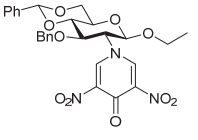
2.7 Hz, H-4); ^{13}C-APT NMR ($CDCl_3$, 101 MHz): δ 105.1 (C-1), 102.7 (C-1'), 101.5 (CHPh), 81.2, 79.6, 78.9, 75.3, 74.6, 73.9, 73.6, 73.3, 71.7, 69.4, 68.5, 66.2, 65.0, 57.3; HRMS: $[M+NH_4]^+$ calcd for $C_{48}H_{53}N_4O_{11}$ 861.37053, found 861.37067.



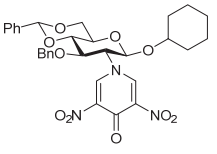
Methyl 2-*O*-(2-azido-3-*O*-benzoyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranosyl)-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (4I). Donor **4** and acceptor **29** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 18 h at -40°C) and purified by flash column chromatography (19/1 to 3/1 pentane/EtOAc) to yield glycosylation product **4I** (55 mg, 73 µmol, 73%, α:β = 5:1) as a white solid. R_f: 0.36 (4/1 pentane/EtOAc). IR (thin film): 671, 750, 1037, 1092, 1265, 1373, 1730, 2108, 2913; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 8.15 – 8.04 (m, 2H, CH_{arom}), 7.59 – 7.53 (m, 1H, CH_{arom}), 7.53 – 7.25 (m, 17H, CH_{arom}), 5.92 (dd, 1H, *J* = 10.4, 9.5 Hz, H-3'), 5.67 (s, 1H, C*H*Ph), 5.54 (s, 1H, C*H*Ph'), 5.51 (d, 1H, *J* = 3.8 Hz, H-1'), 4.94 (d, 1H, *J* = 12.2 Hz, C*H*H Bn), 4.73 (d, 1H, *J* = 1.5 Hz, H-1), 4.69 (d, 1H, *J* = 12.2 Hz, CH*H* Bn), 4.39 (t, 1H, *J* = 9.7 Hz, H-4), 4.32 (dd, 1H, *J* = 10.4, 4.9 Hz, H-6'), 4.27 (dd, 1H, *J* = 10.3, 4.7 Hz, H-6), 4.14 (dd, 1H, *J* = 3.1, 1.6 Hz, H-2), 4.06 – 3.99 (m, 2H, H-3, H-5'), 3.95 (t, 1H, *J* = 10.3 Hz, H-6), 3.86 – 3.77 (m, 3H, H-4', H-5, H-6'), 3.38 – 3.33 (m, 4H, CH_3 OMe, H-2'); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 165.5 (C=O Bz), 138.8, 137.7, 136.8 (C_q), 133.4, 130.1 (CH_{arom}), 129.6 (C_q), 129.2, 128.9, 128.5, 128.4, 128.3, 128.3, 128.3, 128.3, 127.6, 127.6, 127.4, 126.2, 126.2, 126.2, 126.1 (CH_{arom}), 101.7, 101.6 (CHPh), 100.9 (C-1), 100.1 (C-1'), 79.7 (C-4'), 79.5 (C-4), 75.9, 75.9 (C-2, C-3), 73.6 (CH_2 Bn), 69.2 (C-3'), 68.9 (C-6), 68.8 (C-6'), 64.1 (C-5), 63.3 (C-5'), 61.9 (C-2'), 54.9 (OMe); Diagnostic peaks β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.60 (s, 0.2H, C*H*Ph), 5.50 (s, 0.2H, C*H*Ph), 5.40 (t, 0.2H, *J* = 9.8 Hz, H-3'), 4.87 (d, 0.2H, *J* = 1.4 Hz, H-1), 4.80 (d, 0.2H, *J* = 12.3 Hz, C*H*H Bn), 3.57 (td, 0.2H, *J* = 9.9, 4.3 Hz), 3.40 (s, 0.6H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz): δ 101.8 (C-1'), 100.0 (CHPh), 99.4 (C-1), 78.7, 78.5, 76.4, 74.4, 72.4, 71.5, 68.9, 68.5, 66.9, 65.1, 64.2, 55.2; HRMS: $[M+NH_4]^+$ calcd for $C_{41}H_{45}N_4O_{11}$ 769.30793, found 769.30780.



2,2,2-Trifluoroethyl 2-azido-3-*O*-benzoyl-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside (4J). Donor **4** and 2,2,2-trifluoroethanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 30 min at -40°C) and purified by flash column chromatography (19/1 to 17/3 pentane/EtOAc) to yield glycosylation product **4J** (41 mg, 86 µmol, 86%, α:β = >20:1) as a white solid. R_f: 0.15 (toluene). $[\alpha]_D^{20}$ = +78.9° (*c* = 1.03, $CHCl_3$); IR (thin film): 702, 989, 1085, 1177, 1275, 1717, 2112, 2864; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.13 – 8.03 (m, 2H, CH_{arom}), 7.60 – 7.53 (m, 1H, CH_{arom}), 7.48 – 7.38 (m, 4H, CH_{arom}), 7.33 – 7.28 (m, 3H, CH_{arom}), 5.87 (t, 1H, *J* = 10.0 Hz, H-3), 5.53 (s, 1H, C*H*Ph), 5.14 (d, 1H, *J* = 3.6 Hz, H-1), 4.33 (dd, 1H, *J* = 10.4, 4.9 Hz, H-6), 4.14 – 3.97 (m, 4H, CH_2CF_3, H-5), 3.84 (t, 1H, *J* = 9.5 Hz, H-4), 3.80 (t, 1H, *J* = 10.3 Hz, H-6), 3.44 (dd, 1H, *J* = 10.4, 3.6 Hz, H-2); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 165.5 (C=O), 136.7 (C_q), 133.5, 130.0 (CH_{arom}), 129.5 (C_q Bz), 129.2, 128.5, 127.6, 126.2 (CH_{arom}), 123.42 (q, *J* = 278.6 Hz), 101.8 (CHPh), 99.9 (C-1), 79.3 (C-4), 69.1 (C-3), 68.6 (C-6), 65.41 (q, *J* = 35.6 Hz), 63.7 (C-5), 61.6 (C-2); HRMS: $[M+NH_4]^+$ calcd for $C_{22}H_{24}F_3N_4O_6$ 497.16425 found 497.16425.

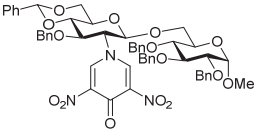


Ethyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-(3,5-dinitro-4-pyridone)-β-D-glucopyranoside (5A). Donor **5** and ethanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 1 hour at -40°C) and purified by flash column chromatography (19/1 to 8/2 pentane/EtOAc) to yield glycosylation product **5A** (32 mg, 59 µmol, 59%, α:β = <1:20) as a yellow solid alongside donor 5 (14 mg). R_f: 0.60 (7/3 pentane/EtOAc). $[\alpha]_D^{23}$ = +156.9° (*c* = 0.64, $CHCl_3$); IR (thin film): 698, 998, 1093, 1213, 1303, 1330, 1516, 1679, 2930; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.58 (s, 2H, CH pyridone), 7.56 (dd, 2H, *J* = 7.4, 2.2 Hz, CH_{arom}), 7.45 – 7.38 (m, 3H, CH_{arom}), 7.06 – 6.97 (m, 5H, CH_{arom}), 5.66 (s, 1H, C*H*Ph), 5.32 (d, 1H, *J* = 8.3 Hz, H-1), 4.70 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.57 (dd, 1H, *J* = 10.2, 8.7 Hz, H-3), 4.53 (d, 1H, *J* = 11.6 Hz, CH*H* Bn), 4.43 (dd, 1H, *J* = 10.3, 4.6 Hz, H-6), 3.99 – 3.81 (m, 4H, C*H*H Et, H-4, H-5, H-6), 3.72 (dd, 1H, *J* = 10.3, 8.3 Hz, H-2), 3.60 (dq, 1H, *J* = 9.9, 7.1 Hz, CH*H* Et), 1.08 (t, 3H, *J* = 7.1 Hz, CH_3 Et); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 160.6 (C=O pyridone), 141.7 (C_q NO_2 pyridone), 141.4 (CH pyridone), 137.1, 136.6 (C_q), 129.4, 128.9, 128.7, 128.5, 128.5, 126.3 (CH_{arom}), 101.9 (CHPh), 99.3 (C-1), 82.8 (C-4), 75.4 (C-3), 74.9 (CH_2 Bn), 73.8 (C-2), 68.7 (C-6), 66.5 (CH_2 Et), 65.7 (C-5), 15.1 (CH_3 Et); HRMS: $[M+H]^+$ calcd for $C_{27}H_{28}N_3O_{10}$ 554.17692, found 554.17642.

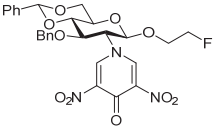


Cyclohexyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-(3,5-dinitro-4-pyridone)-β-D-glucopyranoside (5B). Donor **5** and cyclohexanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 1 hour at -40°C) and purified by flash column chromatography (19/1 to 8/2 pentane/EtOAc) to yield 51 mg of glycosylation product **5B** as an inseperable mixture with donor 5 (13 mg 5, 38 mg

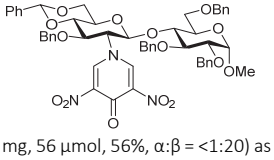
5B, 63 µmol, 63%, α:β = <1:20) as a yellow solid. R_f: 0.75 (7/3 pentane/EtOAc). R_f: 0.55 (7/3 pentane/EtOAc); IR: (thin film): 697, 718, 749, 789, 910, 997, 1092, 1212, 1302, 1330, 1516, 1623, 1674, 2931; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.60 (s, 2H, CH pyridone), 7.56 (d, 2H, *J* = 4.7 Hz, CH_{arom}), 7.48 – 7.33 (m, 3H, CH_{arom}), 7.10 – 6.96 (m, 5H, CH_{arom}), 5.65 (s, 1H, C*H*Ph), 5.41 (d, 1H, *J* = 8.2 Hz, H-1), 4.71 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.66 – 4.50 (m, 2H, CH*H* Bn, H-3), 4.44 (dd, 1H, *J* = 10.6, 5.2 Hz, H-6), 3.98 – 3.80 (m, 3H, H-4, H-5, H-6), 3.79 – 3.61 (m, 2H, C*H* Cy, H-2), 1.91 – 1.77 (m, 1H, CH_2 Cy), 1.71 – 1.54 (m, 2H, CH_2 Cy), 1.54 – 1.45 (m, 1H, CH_2 Cy), 1.43 – 0.96 (m, 6H, CH_2 Cy); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 160.5 (C=O pyridone), 141.6 (C_q NO_2 pyridone), 141.4 (CH pyridone), 137.1, 136.7 (C_q), 128.8, 128.6, 128.4, 126.3 (CH_{arom}), 101.9 (CHPh), 98.1 (C-1), 82.7 (C-4), 78.8 (CH Cy), 75.6 (C-3), 74.8 (CH_2 Bn), 74.0 (C-2), 68.8 (C-6), 65.7 (C-5), 33.3, 31.7, 25.3, 23.9, 23.6 (CH_2 Cy); HRMS: $[M+H]^+$ calcd for $C_{31}H_{34}N_3O_{10}$ 608.22387, found 608.22352.



Methyl 6-*O*-(3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-(3,5-dinitro-4-pyridone)-β-D-glucopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (5C). Donor **5** and acceptor **25** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 18 hours at -40°C) and purified by flash column chromatography (9/1 to 7/3 pentane/EtOAc) to yield glycosylation product **5C** (55 mg, 54 µmol, 54%, α:β = <1:20) as a yellow solid. R_f: 0.45 (7/3 pentane/EtOAc). $[\alpha]_D^{20}$ = +90.5° (*c* = 0.92, $CHCl_3$); IR (thin film): 698, 1001, 1069, 1094, 1213, 1331, 1454, 1522, 1678, 2868; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 8.19 (s, 2H, CH pyridone), 7.54 (dd, 2H, *J* = 7.6, 2.1 Hz, CH_{arom}), 7.45 – 7.38 (m, 3H, CH_{arom}), 7.34 – 7.22 (m, 13H, CH_{arom}), 7.20 – 7.12 (m, 5H, CH_{arom}), 7.04 (dd, 2H, *J* = 6.6, 2.9 Hz, CH_{arom}), 5.66 (s, 1H, C*H*Ph), 4.92 (d, 1H, *J* = 11.0 Hz, C*H*H Bn), 4.85 (d, 1H, *J* = 8.3 Hz, H-1'), 4.83 – 4.66 (m, 2H, 2xC*H*H Bn), 4.72 (d, 1H, *J* = 10.9 Hz, CH*H* Bn), 4.69 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.60 (d, 1H, *J* = 12.2 Hz, CH*H* Bn), 4.60 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.46 (d, 1H, *J* = 3.4 Hz, H-1), 4.39 (dd, 1H, *J* = 10.6, 5.0 Hz, H-6'), 4.34 (d, 1H, *J* = 11.3 Hz, CH*H* Bn), 4.10 (t, 1H, *J* = 7.9 Hz, H-3'), 4.01 (dd, 1H, *J* = 10.8, 1.8 Hz, H-6), 3.91 (t, 1H, *J* = 9.2 Hz, H-3), 3.89 – 3.82 (m, 2H, H-4', H-6), 3.77 – 3.69 (m, 2H, H-2', H-5), 3.65 (td, 1H, *J* = 9.7, 5.0 Hz, H-5'), 3.52 (dd, 1H, *J* = 10.8, 7.1 Hz, H-6), 3.39 (dd, 1H, *J* = 9.6, 3.5 Hz, H-2), 3.21 (s, 3H, CH_3 OMe), 3.13 (dd, 1H, *J* = 9.9, 8.9 Hz, H-4); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 159.4 (C=O pyridone), 141.7 (C_q NO_2 pyridone), 140.2 (CH pyridone), 138.6, 138.0, 138.0, 136.7, 135.8 (C_q), 129.5, 129.1, 129.0, 128.6, 128.5, 128.5, 128.5, 128.2, 128.1, 128.0, 128.0, 127.9, 127.7, 127.6, 126.1 (CH_{arom}), 101.8 (CHPh), 100.1 (C-1'), 97.9 (C-1), 82.3 (C-4'), 81.6 (C-3), 79.8 (C-2), 78.2 (C-4), 75.7, 74.8, 74.3, (CH_2 Bn), 74.0 (C-3'), 73.3 (CH_2 Bn), 72.7 (C-2'), 70.4 (C-6), 69.3 (C-5), 68.4 (C-6'), 66.1 (C-5'), 55.1 (OMe); ^{13}C-HMBC-GATED NMR ($CDCl_3$, 101 MHz): δ 100.1 (*J* = 163 Hz, C-1'); HRMS: $[M+H]^+$ calcd for $C_{53}H_{54}N_3O_{15}$ 972.35494, found 972.35546.

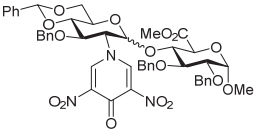


2-Fluoroethyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-(3,5-dinitro-4-pyridone)-β-D-glucopyranoside (5D). Donor **5** and 2-fluoroethanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 1 hour at -40°C) and purified by flash column chromatography (19/1 to 8/2 pentane/EtOAc) to yield glycosylation product **5D** (24 mg, 43 µmol, 43%, α:β = <1:20) as a yellow solid alongside donor 5 (15.6 mg). R_f: 0.42 (3/2 pentane/EtOAc). $[\alpha]_D^{23}$ = +142.9° (*c* = 0.48, $CHCl_3$); IR (thin film): 698, 752, 1070, 1096, 1213, 1304, 1331, 1518, 1680, 2870, 3064; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.58 (s, 2H, CH pyridone), 7.63 – 7.49 (m, 2H, CH_{arom}), 7.47 – 7.36 (m, 3H, CH_{arom}), 7.09 – 6.96 (m, 5H, CH_{arom}), 5.66 (s, 1H, C*H*Ph), 5.46 (d, 1H, *J* = 8.3 Hz, H-1), 4.71 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.57 (dd, 1H, *J* = 10.3, 8.7 Hz, H-3), 4.53 (d, 1H, *J* = 11.7 Hz, CH*H* Bn), 4.48 – 4.42 (m, 2H, C*H*HF, H-6), 4.33 (t, 1H, *J* = 4.1 Hz, CH*H*F), 4.09 – 3.81 (m, 5H, C*H*$_2$-CH_2F, H-4, H-5, H-6), 3.77 (dd, 1H, *J* = 10.3, 8.4 Hz, H-2); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 160.6 (C=O pyridone), 141.5, 141.5 (C_q NO_2, CH pyridone), 137.0, 136.6 (C_q), 129.4, 129.0, 128.7, 128.6, 128.5, 126.3 (CH_{arom}), 101.9 (CHPh), 99.8 (C-1), 82.7 (C-4), 82.5 (d, *J* = 169.4 Hz, CH_2F), 75.3 (C-3), 74.9 (CH_2 Bn), 73.6 (C-2), 69.5 (d, *J* = 19.5 Hz, *C*H_2-CH_2F), 68.6 (C-6), 65.8 (C-5); HRMS: $[M+H]^+$ calcd for $C_{27}H_{27}FN_3O_{10}$ 572.16760, found 572.16705.

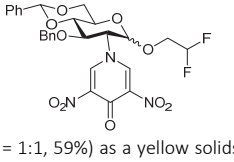


Methyl 4-*O*-(3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-(3,5-dinitro-4-pyridone)-β-D-glucopyranosyl)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (5E). Donor **5** and acceptor **26** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 18 hours at -40°C) and purified by flash column chromatography (9/1 to 7/3 pentane/EtOAc) to yield glycosylation product **5E** (54 mg, 56 µmol, 56%, α:β = <1:20) as a yellow solid. R_f: 0.37 (7/3 pentane/EtOAc). $[\alpha]_D^{23}$ = +83.3° (*c* = 0.84, $CHCl_3$); IR (thin film): 696, 734, 997, 1028, 1039, 1092, 1209, 1302, 1327, 1454, 1522, 1682, 2862, 2900, 3030, 3065; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC, HMBC, NOESY): δ 7.74 (s, 2H, CH pyridone), 7.57 – 7.53 (m, 2H, CH_{arom}), 7.49 – 7.38 (m, 8H, CH_{arom}), 7.36 – 7.25 (m, 13H, CH_{arom}), 7.04 – 7.00 (m, 2H, CH_{arom}), 5.57 (s, 1H, C*H*Ph), 4.90 (d, 1H, *J* = 11.7 Hz, C*H*H

Bn), 4.77 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.74 (d, 1H, *J* = 12.3 Hz, C*H*H Bn), 4.69 (d, 1H, *J* = 11.7 Hz, CH*H* Bn), 4.66 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.63 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.56 (d, 1H, *J* = 12.3 Hz, CH*H* Bn), 4.54 (d, 1H, *J* = 3.6 Hz, H-1), 4.35 (d, 1H, *J* = 8.2 Hz, H-1'), 4.27 – 4.20 (m, 2H, CH*H* Bn, H-6'), 3.92 (t, 1H, *J* = 9.5 Hz, H-4), 3.70 (t, 1H, *J* = 9.3 Hz, H-3), 3.67 (t, 1H, *J* = 9.0 Hz, H-4'), 3.58 (t, 1H, *J* = 10.4 Hz, H-6'), 3.53 – 3.45 (m, 2H, H-2, H-3'), 3.43 (dd, 1H, *J* = 11.4, 1.5 Hz, H-6), 3.40 – 3.34 (m, 1H, H-5), 3.31 (s, 2H, CH_3 OMe), 3.18 (dd, 1H, *J* = 10.5, 8.3 Hz, H-2'), 3.04 (dd, 1H, *J* = 11.3, 2.6 Hz, H-6), 2.92 (td, 1H, *J* = 9.8, 5.1 Hz, H-5'); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC, HMBC): δ 159.3 (C=O pyridone), 141.8 (C_q NO_2 pyridone), 139.6 (CH pyridone), 139.4, 138.1, 137.8, 136.8, 135.7 (C_q), 129.6, 129.3, 129.2, 129.0, 128.9, 128.6, 128.6, 128.5, 128.4, 128.1, 128.1, 127.8, 126.1 (CH_{arom}), 101.8 (CHPh), 98.1 (C-1), 97.6 (C-1'), 82.4 (C-4'), 79.7 (C-2), 79.2 (C-3), 75.3 (CH_2 Bn), 74.4 (C-4), 73.9, 73.6, 73.5 (CH_2 Bn), 73.0 (C-3'), 72.5 (C-2'), 69.2 (C-5), 68.4 (C-6'), 68.1 (C-6), 65.6 (C-5'), 55.7 (OMe); HRMS: $[M+H]^+$ calcd for $C_{53}H_{54}N_3O_{15}$ 972.35494, found 972.35519.

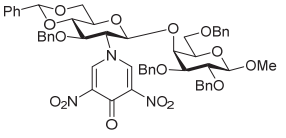


Methyl (Methyl 4-*O*-[3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-(3,5-dinitro-4-pyridone)-α/β-D-glucopyranosyl]-2,3-di-*O*-benzyl-α-D-glucopyranosyl uronate) (5F). Donor **5** and acceptor **27** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 18 hours at -40°C) and purified by flash column chromatography (9/1 to 7/3 pentane/EtOAc) to yield glycosylation product **5F** (27 mg, 30 µmol, 30%, α:β = 1:3.6) as a yellow solid. R_f: 0.51 (7/3 pentane/EtOAc). IR (thin film): 648, 698, 733, 789, 910, 995, 1090, 1171, 1209, 1302, 1331, 1454, 1520, 1678, 1744, 2932; Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC, HMBC): δ 8.06 (s, 2H, CH pyridone), 7.50 (dd, 2H, *J* = 7.3, 2.0 Hz, CH_{arom}), 7.45 – 7.35 (m, 6H, CH_{arom}), 7.33 – 7.18 (m, 9H, CH_{arom}), 7.03 (dd, 2H, *J* = 6.9, 2.2 Hz, CH_{arom}), 6.96 (dd, 1H, *J* = 14.5, 6.9 Hz, CH_{arom}), 5.55 (s, 1H, C*H*Ph), 5.17 (d, 1H, *J* = 8.2 Hz, H-1'), 4.92 (d, 1H, *J* = 11.3 Hz, C*H*H Bn), 4.82 – 4.72 (m, 3H, CH*H* Bn, 2xC*H*H Bn), 4.61 – 4.55 (m, 2H, 2xCH*H* Bn), 4.51 (d, 1H, *J* = 3.3 Hz, H-1), 4.14 (dd, 1H, *J* = 10.6, 4.8 Hz, H-6'), 3.97 – 3.88 (m, 2H, H-3', H-4), 3.83 (d, 1H, *J* = 9.7 Hz, H-5), 3.82 – 3.73 (m, 2H, H-3, H-4'), 3.54 – 3.43 (m, 6H, CH_3 CO_2Me, H-2, H-2', H-5'), 3.42 – 3.36 (m, 4H, CH_3 OMe, H-6'); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC, HMBC): δ 170.0 (C=O CO_2Me), 159.5 (C=O pyridone), 141.5 (C_q NO_2 pyridone), 140.4 (CH pyridone), 139.1, 137.8, 136.7, 135.7 (C_q), 129.5, 129.2, 129.2, 129.1, 129.0, 128.9, 128.7, 128.7, 128.6, 128.5, 128.4, 128.2, 128.2, 127.7, 127.7, 126.1, 126.0, 125.7 (CH_{arom}), 101.7 (C*H*Ph), 98.8 (C-1'), 98.3 (C-1), 82.3 (C-4'), 79.1 (C-3), 78.8 (C-2), 77.8 (C-4), 75.5, 74.2 (CH_2 Bn), 74.0 (C-3'), 73.7 (CH_2 Bn), 72.9 (C-2'), 68.8 (C-5), 68.2 (C-6'), 65.9 (C-5'), 56.1 (OMe), 52.9 (CO_2Me); ^{13}C-HMBC-GATED NMR ($CDCl_3$, 101 MHz): δ 98.8 (*J* = 167 Hz, C-1'); Diagnostic peaks α-anomer: ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 5.74 (d, 0.28H, *J* = 3.9 Hz, H-1'), 5.61 (s, 0.28H, C*H*Ph), 5.03 (d, 0.28H, *J* = 12.7 Hz, C*H*H Bn), 4.70 (d, 0.28H, *J* = 12.3 Hz), 4.62 (d, 0.28H, *J* = 12.2 Hz, C*H*H Bn), 4.46 (d, 0.28H, *J* = 12.3 Hz, CH*H* Bn), 4.37 (dd, 0.28H, *J* = 10.5, 4.9 Hz, H-6'), 4.29 (d, 0.28H, *J* = 9.9 Hz, H-5), 4.08 (t, 0.28H, *J* = 9.4 Hz), 3.69 (dd, 0.28H, *J* = 10.6, 3.9 Hz, H-2'); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 169.7, 159.2, 141.2, 101.8 (CHPh), 96.8 (C-1'), 82.6, 80.7, 79.8, 74.5, 74.4, 73.1, 72.2, 69.6, 69.5, 68.1, 63.0, 56.1, 53.3; ^{13}C-HMBC-GATED NMR ($CDCl_3$, 101 MHz): δ 96.8 (*J* = 181 Hz, C-1'); HRMS: $[M+H]^+$ calcd for $C_{47}H_{48}N_3O_{16}$ 910.30291, found 910.30315.

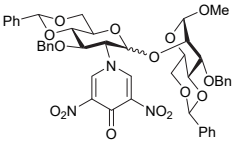


2,2-Difluoroethyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-(3,5-dinitro-4-pyridone)-α/β-D-glucopyranoside (5G). Donor **5** and 2,2-difluoroethanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 1 hour at -40°C) and purified by flash column chromatography (19/1 to 8/2 pentane/EtOAc) to yield glycosylation product **5G** (17.3 mg, 29 µmol α anomer, 17.8 mg 30 µmol β anomer. α:β = 1:1, 59%) as a yellow solids alongside donor 5 (11 mg). R_f: 0.12 and 0.30 (7/3 pentane/EtOAc). IR (thin film): 698, 997, 1069, 1094, 1211, 1300, 1339, 1520, 1684, 2922; Data for the α-anomer: ^{1}H NMR (Acetone-d_6, 400 MHz, HH-COSY, HSQC): δ 8.91 (s, 2H, CH pyridone), 7.61 – 7.53 (m, 2H, CH_{arom}), 7.48 – 7.37 (m, 3H, CH_{arom}), 7.25 – 7.10 (m, 5H, CH_{arom}), 6.16 (tt, 1H, *J* = 55.0, 3.7 Hz, C*H*F_2), 5.83 (s, 1H, C*H*Ph), 5.56 (d, 1H, *J* = 3.7 Hz, H-1), 4.91 (d, 1H, *J* = 11.9 Hz, C*H*H Bn), 4.79 (dd, 1H, *J* = 10.7, 3.7 Hz, H-2), 4.71 – 4.62 (m, 2H, CH*H* Bn, H-3), 4.37 (dd, 1H, *J* = 10.1, 4.9 Hz, H-6), 4.18 – 4.06 (m, 2H, C*H*H-CHF_2, H-5), 4.03 (dd, 1H, *J* = 9.6, 8.6 Hz, H-4), 3.96 – 3.83 (m, 2H, CH*H*-CHF_2, H-6); ^{13}C-APT NMR (Acetone-d_6, 101 MHz, HSQC): δ 160.0 (C=O pyridone), 142.9 (C_q NO_2 pyridone), 142.6 (CH pyridone), 138.6, 138.5 (C_q), 129.8, 129.2, 129.0, 129.0, 128.9, 127.0 (CH_{arom}), 115.0 (t, *J* = 239.2 Hz, CHF_2), 102.1 (CHPh), 98.8 (C-1), 83.5 (C-4), 75.0 (CH_2 Bn), 74.7 (C-3), 69.9 (C-2), 68.9 (C-6), 67.93 (t, *J* = 27.3 Hz, *C*H_2-CHF_2), 63.9 (C-5); Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.67 (s, 2H, CH pyridone), 7.60 – 7.52 (m, 2H, CH_{arom}), 7.46 – 7.37 (m, 3H, CH_{arom}), 7.03 – 6.93 (m, 5H, CH_{arom}), 5.75 (tt, 1H, *J* = 54.9, 3.9 Hz, C*H*F_2), 5.65 (s, 1H, C*H*Ph), 5.59 (d, 1H, *J* = 8.3 Hz, H-1), 4.76 – 4.64 (m, 2H, C*H*H Bn, H-3), 4.50 (d, 1H, *J* = 11.6 Hz, CH*H* Bn), 4.45 (dd, 1H, *J* = 10.4, 4.9 Hz, H-6), 4.05 (td, 1H, *J* = 9.7, 5.0 Hz, H-5), 4.00 – 3.80 (m, 4H, *C*H_2-CHF_2, H-4, H-6), 3.77 (dd, 1H, *J* = 10.3, 8.4 Hz, H-2); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 160.9 (C=O pyridone), 141.7 (C_q NO_2 pyridone), 141.5 (CH pyridone), 137.0, 136.7 (C_q), 129.4, 128.8, 128.6, 128.5, 128.4, 126.4 (CH_{arom}), 113.4 (t, *J* = 241.5 Hz, 102.0 (CHPh), 99.9 (C-1), 82.6 (C-4), 75.5 (C-

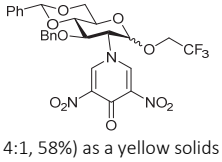
3), 75.1 (CH_2 Bn), 73.7 (C-2), 68.9 (t, *J* = 27.8 Hz, *C*H_2-CHF_2), 68.6 (C-6), 65.8 (C-5); HRMS: $[M+H]^+$ calcd for $C_{27}H_{26}F_2N_3O_{10}$ 590.15808, found 590.15741.



Methyl 4-*O*-(3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-(3,5-dinitro-4-pyridone)-β-D-glucopyranosyl)-2,3,6-tri-*O*-benzyl-β-D-galactopyranoside (5H). Donor **5** and acceptor **28** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 18 hours at -40°C) and purified by flash column chromatography (9/1 to 7/3 pentane/EtOAc) to yield glycosylation product **5H** (51 mg, 52 µmol, 52%, α:β = <1:20) as a yellow solid. R_f: 0.49 (7/3 pentane/EtOAc). $[\alpha]_D^{20}$ = +35.5° (*c* = 0.85, $CHCl_3$); IR (thin film): 698, 750, 999, 1072, 1094, 1213, 1454, 1522, 1682, 2868; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 8.20 (s, 2H, CH pyridone), 7.55 – 7.49 (m, 2H, CH_{arom}), 7.47 – 7.40 (m, 3H, CH_{arom}), 7.40 – 7.15 (m, 18H, CH_{arom}), 7.07 – 7.00 (m, 2H, CH_{arom}), 5.63 (s, 1H, C*H*Ph), 5.03 (d, 1H, *J* = 8.3 Hz, H-1'), 4.80 (d, 1H, *J* = 12.2 Hz, C*H*H Bn), 4.64 (d, 1H, *J* = 10.4 Hz, C*H*H Bn), 4.61 (d, 1H, *J* = 12.3 Hz, C*H*H Bn), 4.57 (d, 1H, *J* = 12.2 Hz, CH*H* Bn), 4.50 (s, 2H, CH_2 Bn), 4.47 (d, 1H, *J* = 12.3 Hz, CH*H* Bn), 4.29 (d, 1H, *J* = 10.4 Hz, CH*H* Bn), 4.20 (dd, 1H, *J* = 10.5, 5.0 Hz, H-6'), 4.13 (d, 1H, *J* = 7.6 Hz, H-1), 3.91 (d, 1H, *J* = 2.6 Hz, H-4), 3.88 – 3.78 (m, 2H, H-3', H-4'), 3.74 (t, 1H, *J* = 10.3 Hz, H-6'), 3.70 (dd, 1H, *J* = 9.9, 8.4 Hz, H-2'), 3.66 – 3.52 (m, 2H, H-6, H-6), 3.46 (s, 4H, CH_3 OMe, H-5), 3.41 – 3.33 (m, 2H, H-3, H-5'), 2.93 (dd, 1H, *J* = 9.6, 7.6 Hz, H-2); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 159.4 (C_q pyridone), 141.6 (C_q NO_2 pyridone), 140.5 (CH pyridone), 138.2, 138.0, 137.6, 136.6, 135.6 (C_q), 129.6, 129.3, 129.1, 129.1, 128.9, 128.7, 128.6, 128.6, 128.4, 128.4, 128.1, 128.0, 127.7, 127.5, 126.1 (CH_{arom}), 104.8 (C-1), 101.8 (CHPh), 99.6 (C-1'), 82.3 (C-4'), 80.2, 80.2 (C-2, C-3), 75.4 (CH_2 Bn), 74.6 (C-4), 74.5, 74.4 (CH_2 Bn), 74.2 (C-3'), 73.5 (CH_2 Bn), 72.5 (C-5), 72.3 (C-2'), 68.6 (C-6), 68.2 (C-6'), 66.2 (C-5'), 57.3 (OMe); ^{13}C-HMBC-GATED NMR ($CDCl_3$, 101 MHz): δ 104.8 (*J* = 159 Hz, C-1), 99.6 (*J* = 165 Hz, C-1'); HRMS: $[M+H]^+$ calcd for $C_{53}H_{54}N_3O_{15}$ 972.35494, found 972.35542.



Methyl 2-*O*-(3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-(3,5-dinitro-4-pyridone)-α/β-D-glucopyranosyl)-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (5I). Donor **5** and acceptor **29** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 18 hours at -40°C) and purified by flash column chromatography (9/1 to 7/3 pentane/EtOAc) to yield glycosylation product **5I** (47 mg, 53 µmol, 53%, α:β = 1:1.3) as a yellow solid. R_f: 0.34 and 0.49 (7/3 pentane/EtOAc). IR: (thin film): 646, 696, 731, 789, 908, 997, 1090, 1123, 1211, 1302, 1333, 1454, 1518, 1624, 1674, 2910; Reported as a 0.8 : 1 mixture of anomers. ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 8.48 (s, 2H, pyridone$_\beta$), 8.33 (s, 1.6H, pyridone$_\alpha$), 7.58 – 7.26 (m, 22.8H, CH_{arom}), 7.23 – 7.01 (m, 11.8H, CH_{arom}), 6.99 – 6.94 (m, 1.6H, CH_{arom}), 5.67 (s, 1.8H, C*H*Ph'$_\alpha$, C*H*Ph'$_\beta$), 5.62 (s, 0.8H, C*H*Ph$_\alpha$), 5.53 (s, 1H, C*H*Ph$_\beta$), 5.27 (d, 0.8H, *J* = 3.9 Hz, H-1'$_\alpha$), 5.24 (d, 1H, *J* = 8.3 Hz, H-1'$_\beta$), 4.84 (d, 1H, *J* = 12.1 Hz, C*H*H Bn$_\beta$), 4.79 (d, 0.8H, *J* = 12.2 Hz, C*H*H Bn$_\alpha$), 4.75 (d, 1H, *J* = 12.1 Hz, C*H*H Bn$_\beta$), 4.70 (d, 1H, *J* = 12.2 Hz, CH*H* Bn$_\beta$), 4.67 (d, 0.8H, *J* = 1.1 Hz, H-1$_\alpha$), 4.64 (d, 1H, *J* = 12.1 Hz, CH*H* Bn$_\beta$), 4.57 (d, 0.8H, *J* = 12.2 Hz, CH*H* Bn$_\alpha$), 4.52 (d, 0.8H, *J* = 11.1 Hz, CH*H* Bn$_\alpha$), 4.50 (dd, 1H, *J* = 10.3, 8.2 Hz, H-3'$_\beta$), 4.46 – 4.41 (m, 1H, H-6'$_\beta$), 4.33 (d, 0.8H, *J* = 11.1 Hz, CH*H* Bn$_\alpha$), 4.34 – 4.26 (m, 1.6H, H-6$_\alpha$, H-6'$_\alpha$), 4.22 – 4.15 (m, 2.8H, H-1$_\beta$, H-2$_\beta$, H-3'$_\alpha$), 4.10 – 3.96 (m, 4.4H, H-2$_\alpha$, H-2'$_\alpha$, H-2'$_\beta$, H-5'$_\alpha$, H-6$_\beta$), 3.95 – 3.83 (m, 8.2H, H-3$_\alpha$, H-3$_\beta$, H-4$_\beta$, H-4'$_\alpha$, H-4'$_\beta$, H-5'$_\beta$, H-6$_\alpha$, H-6'$_\alpha$, H-6'$_\beta$), 3.81 – 3.74 (m, 1.6H, H-4$_\alpha$, H-5$_\alpha$), 3.61 (dq, 1H, *J* = 9.0, 4.5 Hz, H-5$_\beta$), 3.50 (t, 1H, *J* = 10.3 Hz, H-6$_\beta$), 3.38 (s, 2.4H, CH_3 OMe$_\alpha$), 3.15 (s, 3H, CH_3 OMe$_\beta$); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 159.9, 159.7 (C=O pyridone), 142.1 (CH pyridone$_\alpha$), 141.7 (C_q NO_2 pyridone), 140.9 (CH pyridone$_\beta$), 140.8 (C_q NO_2 pyridone), 138.2, 137.6, 137.4, 137.4, 136.8, 136.6, 136.5, 136.0 (C_q), 129.6, 129.4, 129.1, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 128.4, 128.3, 128.3, 127.8, 127.8, 127.6, 126.2, 126.1, 126.1 (CH_{arom}), 101.9, 101.8 (CHPh'$_{\alpha,\beta}$), 101.6, 101.6 (CHPh$_{\alpha,\beta}$), 100.7 (C-1$_\alpha$), 99.8 (C-1'$_\alpha$), 99.2 (C-1$_\beta$), 98.8 (C-1'$_\beta$), 83.1 (C-4'$_\alpha$), 82.4 (C-4'$_\beta$), 79.6 (C-4$_\alpha$), 79.1 (C-2$_\alpha$), 78.5 (C-4$_\beta$), 76.1 (C-2$_\beta$), 75.0 (C-3$_\alpha$), 74.5, 74.5, 74.3 (CH_2 Bn), 74.2 (C-3$_\beta$, C-3'$_\beta$), 72.9 (C-2'$_\beta$), 72.7 (CH_2 Bn), 72.5 (C-3'$_\alpha$), 69.9 (C-2'$_\alpha$), 68.5, 68.5, 68.4 (C-6$_{\alpha,\beta}$, C-6'$_{\alpha,\beta}$), 66.1 (C-5'$_\beta$), 63.7 (C-5$_\beta$), 63.3 (C-5$_\alpha$), 63.1 (C-5'$_\alpha$), 55.1, 55.1 (OMe); ^{13}C-HMBC-GATED NMR ($CDCl_3$, 101 MHz): δ 99.8 (*J* = 176 Hz, C-1'$_\alpha$), 98.8 (*J* = 164 Hz, C-1'$_\beta$); HRMS: $[M+H]^+$ calcd for $C_{46}H_{46}N_3O_{15}$ 880.29234, found 880.29252.



2,2,2-Trifluoroethyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-(3,5-dinitro-4-pyridone)-α/β-D-glucopyranoside (5J). Donor **5** and 2,2,2-trifluoroethanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 1 hour at -40°C) and purified by flash column chromatography (19/1 to 8/2 pentane/EtOAc) to yield glycosylation product **5J** (28 mg, 46 µmol α anomer and 7 mg, 12 µmol β anomer. α:β = 4:1, 58%) as a yellow solids alongside glucal 24 (4 mg) and donor 5 (13 mg). R_f: 0.15 and 0.67 (7/3 pentane/EtOAc). IR (thin film): 698, 754, 1001, 1071, 1096, 1169, 1215, 1279, 1304, 1331, 1520, 1680, 2855, 2924, 3065; Data for the α-

anomer: ^{1}H NMR (Acetone-d_6, 400 MHz, HH-COSY, HSQC): δ 8.92 (s, 2H, CH pyridone), 7.60 – 7.54 (m, 2H, CH_{arom}), 7.47 – 7.37 (m, 3H, CH_{arom}), 7.24 – 7.13 (m, 5H, CH_{arom}), 5.84 (s, 1H, C*H*Ph), 5.65 (d, 1H, *J* = 3.7 Hz, H-1), 4.92 (d, 1H, *J* = 11.8 Hz, C*H*H Bn), 4.84 (dd, 1H, *J* = 10.7, 3.7 Hz, H-2), 4.73 (dd, 1H, *J* = 10.7, 8.4 Hz, H-3), 4.70 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.51 – 4.38 (m, 1H, C*H*H-CF_3), 4.38 (dd, 1H, *J* = 10.1, 4.7 Hz, H-6), 4.30 – 4.17 (m, 1H, CH*H*-CF_3), 4.12 (dd, 1H, *J* = 9.8, 4.7 Hz, H-5), 4.09 – 4.02 (m, 1H, H-4), 3.93 (t, 1H, *J* = 10.0 Hz, H-6); ^{13}C-APT NMR (Acetone-d_6, 101 MHz, HSQC): δ 160.0 (C=O pyridone), 142.9 (C_q NO_2 pyridone), 142.6 (CH pyridone), 138.6, 138.5 (C_q), 129.8, 129.2, 129.0, 129.0, 128.9, 127.0 (CH_{arom}), 124.72 (q, *J* = 277.4 Hz, CF_3), 102.1 (CHPh), 98.8 (C-1), 83.4 (C-4), 75.1 (CH_2 Bn), 74.6 (C-3), 69.8 (C-2), 68.8 (C-6), 65.84 (q, *J* = 35.0 Hz, CH_2-CF_3), 64.1 (C-5); Diagnostic peaks β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.61 (s, 2H, CH pyridone), 7.56 (dd, 2H, *J* = 6.6, 2.9 Hz, CH_{arom}), 7.41 (dd, 3H, *J* = 5.0, 1.7 Hz, CH_{arom}), 7.00 (s, 5H, CH_{arom}), 5.66 (s, 1H, C*H*Ph), 5.58 (d, 1H, *J* = 8.3 Hz, H-1), 4.75 – 4.62 (m, 2H, C*H*H Bn, H-3), 4.52 (d, 1H, *J* = 11.7 Hz, CH*H* Bn), 4.46 (dd, 1H, *J* = 10.5, 4.8 Hz, H-6), 4.17 – 3.99 (m, 3H, CH_2-CF_3, H-5), 3.91 – 3.82 (m, 2H, H-4, H-6), 3.78 (dd, 1H, *J* = 10.0, 8.5 Hz, H-2); HRMS: $[M+H]^+$ calcd for $C_{27}H_{25}F_3N_3O_{10}$ 608.14865, found 608.14825.

Footnotes and references

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Chapter 5

The stereoselectivity of 3,4-tethered glucosazide donors

Introduction

Both α- and β-linked glucosamine residues are widespread in naturally occurring carbohydrates.[1–5] While β-glucosamine linkages can be reliably installed using anchimeric assistance of a participating *N*-protecting group, the installation of the α-glucosamine bond commonly hinges on the use of a non-participating *N*-protecting group, where the azide is most commonly employed.[6–8] In chapters 3 and 4, a set of fluorinated model acceptors was introduced to investigate how the stereoselectivity of glycosylations of 4,6-tethered glucosazide donors relates to acceptor nucleophilicity. This approach revealed that the combination of a reactive donor glycoside and a weak nucleophile led to α-selective glycosylation reactions. In the current chapter, the stereoselectivity of glycosylations of a 3,4-tethered glucosazide donor is studied in relation to the nucleophilicity of the acceptor. The reactivity of the donor is assessed using Variable-Temperature NMR (VT-NMR) and competition experiments, followed by a series of glycosylations. The set of partially fluorinated model acceptors and a panel

of carbohydrate acceptors, introduced in the previous chapters, are used to map reactivity-stereoselectivity relationships to provide a basis for α-glucosaminylation reactions. [9–12]

Results and discussion

In an extension of the glucosazide donors described in the previous chapter, the butane diacetal (BDA)[13–15] protected glucosazide donor **1** is glycosylated with the range of acceptors depicted in Figure 1 to investigate how the stereoselectivity of glycosylations of donor **1** depends on the reactivity of these acceptors. Benzylidene glucose donor **2** and benzylidene glucosazide donor **3** serve as a direct comparison for the reactivity and selectivity of donor **1**. The 3,4-*O*-BDA protecting group locks the donor in a *trans*-decalin constellation, conformationally disarming the system, as is also the case for the 4,6-*O*-benzylidene in donors **2** and **3**. Severe conformational changes are prohibited, and the number of possible glycosylation reaction itineraries restricted.[16–18] The difference in electronic properties between the BDA group and the benzylidene acetal can be found in the rotational freedom of the C-6-substituent. In donor **1** the C-6–O-6 bond is not retained in its most electron withdrawing *tg*-conformation, as in donor **2** and **3** (Figure 1C).[18–20] The BDA protected donor **1** is therefore expected to be more reactive than benzylidene glucosazide donor **3**. This has previously been demonstrated in the *manno*-series by Crich and co-workers, who reported highly α-selective mannosylations with BDA-protected mannosyl donors. They related this to the higher reactivity of the BDA donor over the benzylidene donor and therefore a shift in the glycosylation reaction mechanism continuum from the β-selective S_N2-side for the latter donor to the α-selective S_N1-side for the former donor.[21] In contrast, glycosylations of the related 3,4-*O*-BDA-glucosyl donors proceeded with β-selectivity, which they interpreted to arise from an S_N2-type reaction on the relatively stable α-triflate. Collapse into the α-selective oxocarbeniun ion intermediate was prevented by the steric hindrance of the BDA-OMe group with the large C-2-OBn group (See Figure 3).[22] It may be hypothesized that the smaller 2-azido group in donor **1** does not experience this unfavorable steric effect allowing for the easier formation of the oxocarbenium intermediate. On the other hand, Chapter 4 has revealed the azide to promote S_N2-type reactions as a result of its electron withdrawing nature.

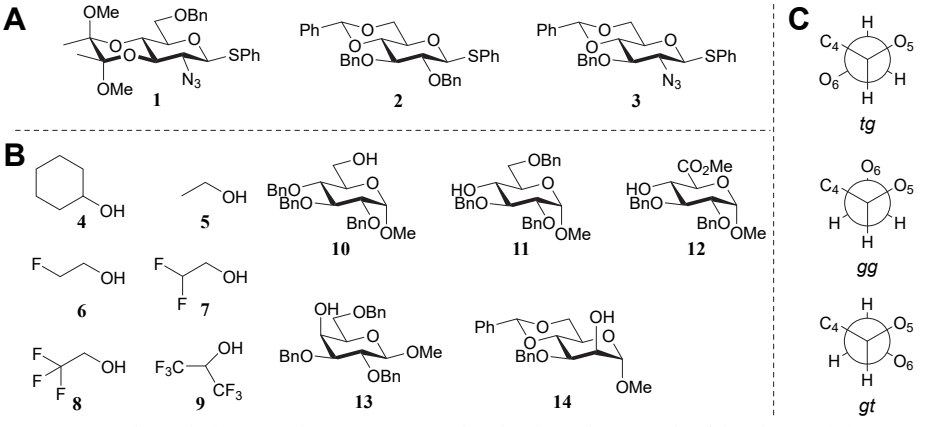
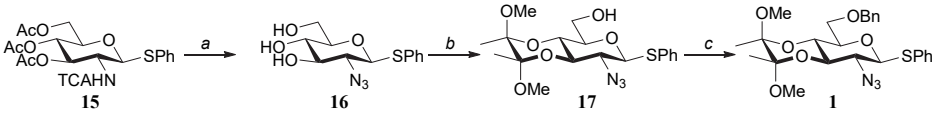


Figure 1. (A) Glycoside donors and (B) acceptors used in the glycosylation study of this chapter. (C) Newman projections of the three staggered rotamer conformations along the C-5–C-6 bond.

Donor **1** is synthesized from acetylated thioglycoside **15** (Scheme 1), by alkaline hydrolysis of the TCA and acetyl groups followed by diazotransfer to give the crude glucosazide **16**. Installation of the BDA and benzyl groups gave donor **1** in good overall yield.

Scheme 1. Synthesis of BDA-donor **1**.



Reagents and conditions: (a) *i*. K_2CO_3, EtOH, H_2O; *ii*. $CuSO_4 \cdot 5H_2O$, imidazole-1-sulfonyl azide hydrochloride[23]; (b) 2,3-butadione, trimethyl orthoformate, CSA, MeOH, 64% (three steps); (c) BnBr, NaH, DMF, 85%.

The activation of donor **1** was studied by VT-NMR.[24] To this end donor **1** was treated with Ph_2SO/Tf_2O in the presence of TTBP in deuterated DCM.[25] Figure 2A displays the spectra of the reaction mixture at a range of temperatures. Interestingly, various species are generated upon activation, the two most predominant of which were assigned as the α-anomeric triflate **18** (labelled ◊, ^{1}H δ = 6.09 ppm, $J_{H\text{-}1\text{–}H\text{-}2}$ = 3.3 Hz, ^{13}C δ = 105.8 ppm) and β-oxosulfonium triflate (labelled *, ^{1}H δ = 5.56 ppm, $J_{H\text{-}1\text{–}H\text{-}2}$ = 7.6 Hz, ^{13}C δ = 103.8 ppm) in a 3:1 ratio. Using either an equimolar amount or an excess of Ph_2SO (5 equivalents), the reaction mixture could be enriched in triflate **18** or

oxosulfonium triflate **19** (Figure 2B depicts the ^{19}F-NMR spectrum of the activation mixture using an excess Ph_2SO, showing full consumption of the anomeric triflate). When the sample (with 1.3 equivalents Ph_2SO) was heated to -50°C the signal of the β-oxosulfonium triflate disappeared irreversibly. Decomposition of the anomeric triflate started around -20°C, similar to the triflates reported in Chapter 4, and no specific product could be identified. The immediate formation of the β-oxosulfonium triflate, and the complete conversion of the anomeric triflate to this species when an excess of Ph_2SO is used, hints at the relatively high reactivity of the donor, in line with the observation made for the two most reactive donors in Chapter 4.

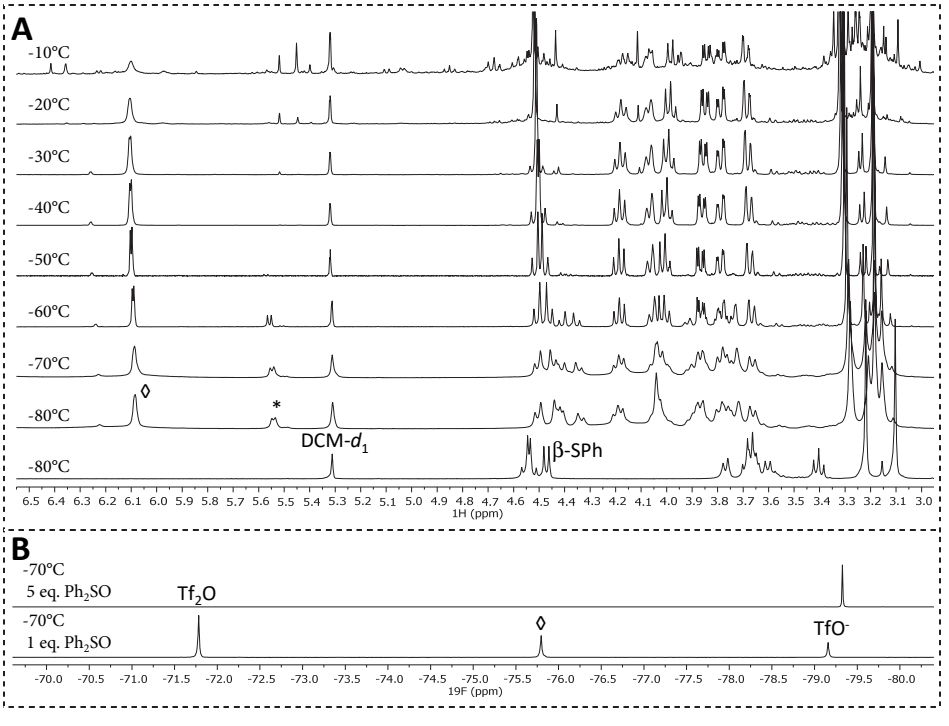
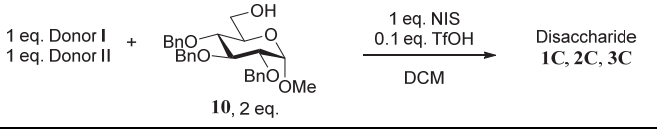


Figure 2. NMR activation study of donor **1**. (A) 1.3 eq. Ph_2SO, 1.3 eq. Tf_2O. The behavior of triflate **18** (◊) and oxosulfonium triflate **19** (*) between -80°C -10°C. (B) ^{19}F-NMR showing triflate **18** (◊) and its absence when 5 eq. Ph_2SO is added.

The relative reactivity of the BDA protected glucosazide versus its benzylidene counterpart was evaluated in a set of competition experiments (Table 1). The thioglycosides and acceptor **10** were mixed and made to compete for a limiting amount of NIS. This experiment revealed the BDA donor **1** to be six times more reactive than donor **3** towards NIS and, somewhat surprisingly given the stronger electron withdrawing capacity of the azide, two times more reactive than **2**. Apparently the combined disarming effect of the azide and BDA group, previously found to be semi-disarming,[26,27] is smaller than the disarming effect of the benzylidene group in donor **2**.

Table 1: Activation competition experiments between donors **1**, **2**, and **3**.

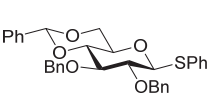
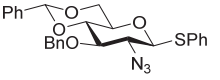
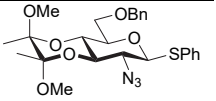
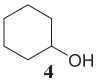
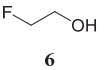
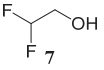
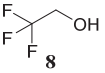
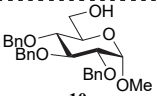
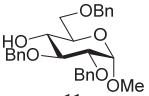
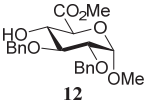
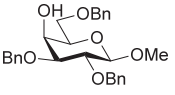
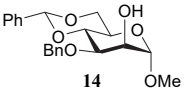


Entry	Donor I	Donor II	Solvent (M)	Product[a] I : II	Recovered donor[a] I : II	Yield[a] %	α : β
1	**1**	**2**	0.1 M DCM	**1C/2C** 2 : 1	1 : 1.4	75%	**1C**; 1 : 6 **2C**; 1 : 1
2	**1**	**3**	0.1 M DCM	**1C/3C** 6 : 1	1 : 10	99%	**1C**; 1 : 6 **3C**; 1 : 3
3	**2**	**3**	0.05 M DCM[b]	**2C/3C** 1 : 0	0 : 1	80%	**1C**; 1.5 : 1

[a]Isolated ratios after size-exclusion chromatography, and yield of the disaccharide fraction. [b]Reference relative reactivity between **2** and **3** (Chapter 4); selectivity increases with dilution.

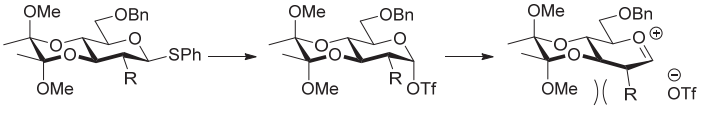
Next, the BDA glucosazide donor **1** was glycosylated with the set of fluorinated model nucleophiles and a selection of carbohydrate acceptors. The results of the glycosylations are listed in Table 2 and compared with the glycosylation results of donors **2** and **3**. The reactions were carried out by preactivating the donor from -78°C to -50°C to remove the contribution of the oxosulfonium triflate on the stereoselectivity of the reaction. Despite the high reactivity observed in the competition and activation experiments, indicating that oxocarbenium ion character readily develops at the anomeric center, the reactions of donor **1** are very β-selective. It is not surprising to find the strong nucleophiles cyclohexanol **4**, ethanol **5** and carbohydrate acceptor **10** to react with full β-selectivity, but the other acceptors, especially trifluoroethanol **8** and axially orientated nucleophiles **13** and **14**, react with unexpected low α-selectivity.

Table 2. Glycosylations of donors **1**-**3** with model acceptors **4**-**9** and carbohydrate acceptors **10**-**14**. Ordered by their overall β- to α-selectivity.

		 **2**	 **3**	 **1**
	Acceptor	Product[a] α:β (yield)[b]	Product α:β (yield)	Product α:β (yield)
A	 **4**	**2A** 71 % 1 : 5.1	**3A** 93 % < 1 : 20	**1A** 87 % < 1 : 20
B	 **5**	**2B** 68 % 1 : 10	**3B** 83 % < 1 : 20	**1B** 90 % < 1 : 20
C	 **6**	**2C** 70 % 1 : 2.8	**3C** 90 % 1 : 6.7	**1C** 97 % 1 : 20
D	 **7**	**2D** 70 % 5 : 1	**3D** 64 % 2.9 : 1	**1D** 84 % 1 : 3.5
E	 **8**	**2E** 64 % > 20 : 1	**3E** 94 % > 20 : 1	**1E** 87 % 2.5 : 1
F	 **9**	**2F** 65 % > 20 : 1	**3F** 53 % > 20 : 1	**1F**[c] 18% > 20 : 1
G	 **10**	**2G** 81 % 1 : 2.7	**3G** 89 % < 1 : 20	**1G** 86 % < 1 : 20
H	 **11**	**2H** 79 % 1 : 1	**3H** 88 % 1 : 7	**1H** 93 % 1 : 15
I	 **12**	**2I** 90 % 5 : 1	**3I** 93 % 1.1 : 1	**1I** 83 % 1.5 : 1
J	 **13**	**2J** 83 % > 20 : 1	**3J** 75 % 9 : 1	**1J** 86 % 1 : 1.8
K	 **14**	**2K** 80 % > 20 : 1	**3K** 74 % 9 : 1	**1K** 93 % 1 : 1.7

[a]Glycosylation results of donors **2** and **3**, are also reported in Chapter 3 and 4 of this thesis, respectively. [b]Ratio and yield of isolated product after column chromatography, anomers were not separated. [c]α,β-Trehalose **24** (neotrehalose) was also isolated as a single anomer in 25% yield.

The high β-selectivity for donor **1** under preactivation conditions is also apparent when compared with the previously reported C-2–OBn analogue.[22] Condensation (See Figure 3) of donor **20** and acceptor **11** provided an anomeric mixture (α/β, 1:4), whereas glycosylation of **1** and **11** led to a much higher β-selectivity (**1H**; α/β, 1:15). This observation is consistent with the scenario drawn in Chapter 4: the 2-azido group promotes an S_N2 pathway (via triflate **18**) due to additional electron-withdrawing from the anomeric center. Although the high β-selectivity appears contradictory to the high reactivity of the donor, it may also be that the BDA glucosazide oxocarbenium ion **22** (as part of a close ion pair) takes up a conformation favoring attack from the β-side.



1: R = N_3
20: R = OBn

18: R = N_3
21: R = OBn

22: R = N_3
23: R = OBn

Figure 3. Reactive species at play in the glycosylation reactions of donors **1** and **20**.

Conclusions

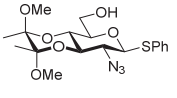
Condensations of butane diacetal (BDA) protected glucosazide donor **1** have been studied using the set of fluorinated model acceptors introduced in Chapters 3 and 4. The BDA protecting group in combination with the 2-azido functionality is highly β-directing in glycosylations without the need for a C-2 participating group. Despite the high β-selectivity, the model acceptors show the anticipated trend of reactivity of the acceptor versus glycosylation stereoselectivity, with less reactive acceptors providing more α-products as was established in Chapters 3 and 4, to provide yet another example of the importance of the reactivity of the acceptor in a glycosylation reaction. The exact underlying mechanism that causes the high β-selectivity has yet to be fully elucidated, but based on precedent, the high β-selective for donor **1** may arise from an S_N2-like substitution of the anomeric α-triflate. How this exactly relates to the high reactivity of the donor remains to be established.

Experimental section

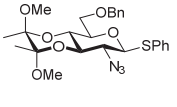
General procedure for Tf_2O/Ph_2SO mediated glycosylations: Donor (0.1 mmol), Ph_2SO (26 mg, 0.13 mmol, 1.3 eq.) and TTBP[29] (62 mg, 0.25 mmol, 2.5 eq.) were coevaporated twice with dry toluene and dissolved in dry DCM (2 mL, 0.05 M donor). Activated 3Å molecular sieves (rods, size 1/16 in.) were added, and the reaction mixture stirred for 1 h at room temperature under a nitrogen atmosphere. The solution was cooled to -78°C and Tf_2O (22 µl, 0.13 mmol, 1.3 eq.) was added. The reaction mixture was allowed to warm to -50°C followed by recooling to -78°C and addition of the acceptor (0.2 mmol, 2 eq.) in DCM (0.4 mL, 0.5 M). The reaction mixture was allowed to warm to -40°C in approximately 90 min and stirred for an additional 0-18 h depending on the acceptor. The reaction was quenched with Et_3N (0.1 mL, 0.72 mmol, 5.5 eq.) at -40 °C and diluted with DCM. The solution was transferred to a separatory funnel and water was added, the layers were separated and the water phase extracted once more with DCM. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by silica gel flash column chromatography and when needed, sephadex™ LH-20 size exclusion chromatography yielded the glycosylation product as a mixture of anomers.

General procedure for the NIS/TfOH mediated competition experiments: Donor I (0.1 mmol, 1 eq.), donor II (0.1 mmol, 1 eq.) and acceptor **25** (0.2 mmol, 2 eq.) were together coevaporated with dry toluene (2x). Dry DCM (4 mL, donor concentration 0.1 M), a Teflon stirring bar and 3Å activated molecular sieves (rods, size 1/16 in.) were added and the mixture was stirred under a nitrogen atmosphere for 1 h at room temperature. The mixture was cooled to -40°C and NIS (0.1 mmol, 1 eq.) was added. TfOH (50 µL of a freshly prepared 0.2 M stock solution in dry DCM, 0.1 eq.) was added and the mixture was allowed to warm to 0°C in 3 hours. Et_3N (0.1 mL) was added and the mixture was diluted with EtOAc, washed with sat. aq. NaS_2O_3 and brine, dried over Na_2SO_4 and concentrated *in vacuo*. Size exclusion chromatography (Sephadex LH-20, 1/1 DCM/MeOH) enabled isolation of the disaccharide products and the monosaccharide rests, which were both analysed with NMR spectroscopy. The yield of the disaccharide fraction was determined.

General procedure for the low temperature NMR experiments: A mixture of donor (30 µmol) and Ph_2SO (39 µmol) was coevaporated with dry toluene twice (for the activation of donor 1 also TTBP (75 µmol) was added). Under a nitrogen atmosphere, CD_2Cl_2 (0.6 mL) was added and the mixture transferred to a nitrogen flushed NMR tube and closed with a NMR tube septum. The NMR magnet was cooled to -80°C, locked and shimmed and the sample was measure prior to activation. In a long narrow cold bath (EtOH, -85°C) the sample was treated with Tf_2O (39 µmol), shaken thrice and cooled again after every shake. The cold sample was wiped dry and quickly inserted back in the cold magnet. The first ^1H NMR spectrum was immediately recorded. The sample was then reshimmed and spectra were recorded in 10°C intervals with at least 5 min equilibration time for every temperature.

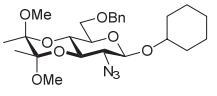


Phenyl 2-azido-2-deoxy-3,4-O-(2,3-dimethoxybutane-2,3-diyl)-1-thio-β-D-glucopyranoside (17). To a solution of crude triol **16** (synthesized as described in Chapter 4) (≤15 mmol) in dry MeOH (100 mL) was added butadione (2.0 mL, 22.5 mmol, 1.5 eq.), trimethyl orthoformate (9.8 mL, 90 mmol, 6 eq.) and CSA (523 mg, 2.25 mmol, 0.15 eq.) and the solution was refluxed overnight. Et_3N was added (1 mL) and the volatiles were removed in vacuo. Crystallization from EtOAc/petroleum ether yielded the tiles compound as a white solid (3.94 g, 9.56 mmol, 64% over three steps). Spectroscopic data were in accord with those previously reported.[30] ^1H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.62 – 7.54 (m, 2H, CH_{arom}), 7.41 – 7.34 (m, 3H, CH_{arom}), 4.47 (d, 1H, *J* = 9.9 Hz, H-1), 3.91 (ddd, 1H, *J* = 12.0, 5.6, 2.6 Hz, H-6), 3.81 – 3.70 (m, 2H, H-3, H-6), 3.66 (t, 1H, *J* = 9.7 Hz, H-4), 3.55 (ddd, 1H, *J* = 9.6, 4.5, 2.7 Hz, H-5), 3.43 (t, 1H, *J* = 9.8 Hz, H-2), 3.35 (s, 3H, CH_3 OMe), 3.27 (s, 3H, CH_3 OMe), 2.02 (dd, 1H, *J* = 7.6, 5.9 Hz, 6-OH), 1.35 (s, 3H, CH_3 Me), 1.31 (s, 3H, CH_3 Me); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 133.9 (CH_{arom}), 130.7 (C_q SPh), 129.3, 128.9 (CH_{arom}), 100.3, 99.9 (C_q BDA), 86.2 (C-1), 78.2 (C-5), 73.1 (C-3), 65.7 (C-4), 61.5 (C-2), 61.4 (C-6), 48.3, 48.2 (OMe), 17.7, 17.6 (Me).

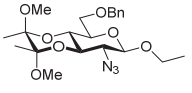


Phenyl 2-azido-6-*O*-benzyl-2-deoxy-3,4-O-(2,3-dimethoxybutane-2,3-diyl)-1-thio-β-D-glucopyranoside (1). Compound **17** was dissolved in DMF (45 mL) and cooled to 0°C. NaH (60% dispersion in mineral oil, 540 mg, 13.5 mmol, 1.5 eq.) and BnBr (1.4 mL, 11.7 mmol, 1.3 eq.) were added and the mixture was stirred at r.t. until complete conversion was observed (TLC). Excess NaH was quenched with MeOH and the solution was reduced in volume under reduced pressure. H_2O was added to the residue and extracted with Et_2O twice and DCM once. Combined organic layers were washed with H_2O and brine, dried with MgSO4, filtered and concentrated in vacuo. Flash column chromatography (1/0 to 9/1 pentane/EtOAc) and subsequently recrystallized (EtOAc, excess petroleum ether) gave the title compound as a white

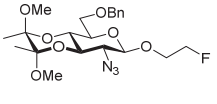
solid in two batches (total yield 3.84 g, 7.66 mmol, 85%). R_f: 0.25 (19/1 pentane/EtOAc). m.p.: 146-149°C.). $[\alpha]_D^{20}$ = +72.2° (*c* = 1.0, $CHCl_3$); IR (thin film): 689, 735, 752, 851, 885, 960, 1032, 1107, 1128, 1265, 1275, 1366, 1375, 1437, 1452, 2110, 2868; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.63 – 7.57 (m, 2H, CH_{arom}), 7.36 – 7.27 (m, 5H, CH_{arom}), 7.26 – 7.21 (m, 3H, CH_{arom}), 4.63 (d, 1H, *J* = 11.9 Hz, C*H*H Bn), 4.56 (d, 1H, *J* = 11.9 Hz, CH*H* Bn), 4.41 (d, 1H, *J* = 9.8 Hz, H-1), 3.83 – 3.68 (m, 4H, H-3, H-4, H-6, H-6), 3.66 – 3.60 (m, 1H, H-5), 3.41 (t, 1H, *J* = 9.8 Hz, H-2), 3.32 (s, 3H, CH_3 OMe), 3.17 (s, 3H, CH_3 OMe), 1.32 (s, 3H, CH_3 Me), 1.27 (s, 3H, CH_3 Me); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.5 (C_q Bn), 134.2 (CH_{arom}), 130.8 (C_q SPh), 129.2, 128.7, 128.4, 127.6, 127.5 (CH_{arom}), 100.3, 99.9 (C_q BDA), 86.1 (C-1), 78.1 (C-5), 73.6 (CH_2 Bn), 73.3 (C-3), 68.3 (C-6), 65.7 (C-4), 61.4 (C-2), 48.3, 48.2 (OMe), 17.8, 17.7 (Me); HRMS: $[M+NH_4]^+$ calcd for $C_{25}H_{35}N_3O_6S$ 519.22718, found 519.22695.



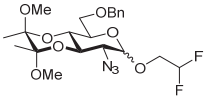
Cyclohexyl 2-azido-6-*O*-benzyl-2-deoxy-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-β-D-**glucopyranoside (1A).** Donor **1** and cyclohexanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 18 hours at -40°C) and purified by flash column chromatography (1/0 to 9/1 pentane/EtOAc) to yield glycosylation product **1A** (43 mg, 87 µmol, 87%, α:β = <1:20). R_f: 0.6 (9/1 pentane/EtOAc). $[\alpha]_D^{20}$ = +98.6° (*c* = 1.08, $CHCl_3$); IR (thin film): 698, 849, 891, 959, 1047, 1121, 1368, 1452, 2108, 2932; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.35 – 7.26 (m, 5H, CH_{arom}), 4.61 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.57 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.41 (d, 1H, *J* = 7.7 Hz, H-1), 3.76 (dd, 1H, *J* = 11.0, 1.6 Hz, H-6), 3.74 – 3.63 (m, 3H, *CH* Cy, H-4, H-6), 3.61 – 3.51 (m, 2H, H-3, H-5), 3.43 (dd, 1H, *J* = 10.4, 7.7 Hz, H-2), 3.30 (s, 3H, CH_3 OMe), 3.18 (s, 3H, CH_3 OMe), 2.02 – 1.87 (m, 2H, CH_2 Cy), 1.82 – 1.71 (m, 2H, CH_2 Cy), 1.58 – 1.37 (m, 3H, CH_2 Cy), 1.33 (s, 3H, CH_3 Me), 1.31 – 1.19 (m, 6H, CH_3 Me, CH_2 Cy); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.4 (C_q), 128.4, 127.6, 127.6 (CH_{arom}), 101.2 (C-1), 100.0, 99.8 (C_q BDA), 78.3 (CH Cy), 74.0 (C-5), 73.6 (CH_2 Bn), 70.9 (C-3), 68.4 (C-6), 66.5 (C-4), 63.0 (C-2), 48.1, 48.1 (CH_3 OMe), 33.7, 31.8, 25.6, 24.1, 24.0 (CH_2 Cy), 17.7, 17.7 (CH_3 Me); HRMS: $[M+NH_4]^+$ calcd for $C_{25}H_{41}N_4O_7$ 509.29698, found 509.29668.



Ethyl 2-azido-6-*O*-benzyl-2-deoxy-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-β-D-glucopyranoside (1B). Donor **1** and ethanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 30 min at -40°C) and purified by flash column chromatography (1/0 to 9/1 pentane/EtOAc) to yield glycosylation product **1B** (39.7 mg, 90 µmol, 90%, α:β = <1:20). R_f: 0.48 (9/1 pentane/EtOAc). $[\alpha]_D^{20}$ = +105.2° (*c* = 0.85, $CHCl_3$); IR (thin film): 698, 849, 1047, 1115, 1375, 2108, 2927; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.39 – 7.24 (m, 5H, CH_{arom}), 4.61 (d, 1H, *J* = 12.2 Hz, C*H*H Bn), 4.57 (d, 1H, *J* = 12.2 Hz, CH*H* Bn), 4.31 (d, 1H, *J* = 7.7 Hz, H-1), 3.98 (dq, 1H, *J* = 9.5, 7.1 Hz, C*H*H Et), 3.76 (dd, 1H, *J* = 10.9, 1.7 Hz, H-6), 3.71 – 3.64 (m, 2H, H-5, H-6), 3.64 – 3.55 (m, 3H, H-3, H-4, CH*H* Et), 3.46 (dd, 1H, *J* = 10.5, 7.7 Hz, H-2), 3.31 (s, 3H, CH_3 OMe BDA), 3.18 (s, 3H, CH_3 OMe BDA), 1.34 (s, 3H, CH_3 Me BDA), 1.28 (t, 4H, *J* = 7.1 Hz, CH_3 Et), 1.27 (s, 3H, CH_3 Me BDA); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.2 (C_q), 128.4, 127.6 (CH_{arom}), 102.4 (C-1), 100.1, 99.8 (C_q BDA), 74.0 (C-3/C-4), 73.6 (CH_2 Bn), 71.0 (C-3/C-4), 68.3 (C-6), 66.3 (C-5), 66.0 (CH_2 Et), 62.6 (C-2), 48.2, 48.1 (OMe BDA), 17.7, 17.7 (Me BDA), 15.2 (CH_3 Et); HRMS: $[M+NH_4]^+$ calcd for $C_{21}H_{35}N_4O_7$ 455.25003, found 455.24975.

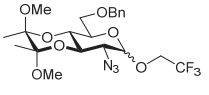


2-Fluoroethyl 2-azido-6-*O*-benzyl-2-deoxy-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-β-D-glucopyranoside (1C). Donor **1** and 2-fluoroethanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 30 min at -40°C) and purified by flash column chromatography (1/0 to 9/1 pentane/EtOAc) to yield glycosylation product **1C** (44 mg, 97 µmol, 97%, α:β = 1:20). R_f: 0.30 (9/1 pentane/EtOAc). $[\alpha]_D^{20}$ = +96.4° (*c* = 1.10, $CHCl_3$); IR (thin film): 698, 881, 1049, 1113, 1375, 1454, 2110, 2949; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.35 – 7.27 (m, 5H, CH_{arom}), 4.71 – 4.62 (m, 1H, C*H*HF), 4.62 – 4.52 (m, 3H, CH*H*F, CH_2 Bn), 4.36 (d, 1H, *J* = 7.7 Hz, H-1), 4.08 (dddd, 1H, *J* = 31.8, 12.2, 4.7, 2.6 Hz, *CH*H-CH_2F), 3.88 (dddd, 2H, *J* = 25.2, 12.1, 6.8, 2.7 Hz, CH*H*-CH_2F), 3.76 (dd, 1H, *J* = 11.0, 1.7 Hz, H-6), 3.72 (t, 1H, *J* = 10.0 Hz, H-4), 3.68 (dd, 1H, *J* = 11.0, 5.3 Hz, H-6), 3.65 – 3.56 (m, 2H, H-3, H-5), 3.50 (dd, 1H, *J* = 10.5, 7.7 Hz, H-2), 3.31 (s, 3H, CH_3 OMe), 3.19 (s, 3H, CH_3 OMe), 1.34 (s, 3H, CH_3 Me), 1.28 (s, 3H, CH_3 Me); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 138.2 (C_q), 128.4, 127.7, 127.6 (CH_{arom}), 102.7 (C-1), 100.1, 99.8 (C_q BDA), 82.7 (d, *J* = 169.9 Hz, *C*H_2F), 74.1 (C-5), 73.6 (CH_2 Bn), 71.0 (C-3), 69.0 (d, *J* = 20.3 Hz, *C*H_2-CH_2F), 68.2 (C-6), 66.2 (C-4), 62.6 (C-2), 48.2, 48.2 (OMe), 17.7, 17.7 (Me); HRMS: $[M+NH_4]^+$ calcd for $C_{21}H_{34}FN_4O_7$ 473.24060, found 473.24041.

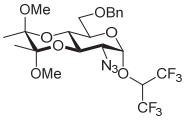


2,2-Difluoroethyl 2-azido-6-*O*-benzyl-2-deoxy-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-α/β-D-glucopyranoside (1D). Donor **1** and 2,2-difluoroethanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 30 min at -

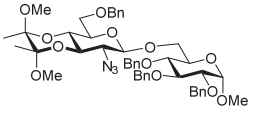
40°C) and purified by flash column chromatography (1/0 to 9/1 pentane/EtOAc) to yield glycosylation product **1D** (40 mg, 84 µmol, 84%, α:β = 1:3.5). R_f: 0.60 (9/1 pentane/EtOAc). IR (thin film): 698, 735, 849, 883, 1030, 1107, 1265, 1373, 1454, 2108, 2926; Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.38 – 7.27 (m, 5H, CH_{arom}), 6.10 – 5.82 (m, 1H, C*H*F_2), 4.62 – 4.54 (m, 2H, CH_2 Bn), 4.34 (d, 1H, *J* = 7.7 Hz, H-1), 4.05 – 3.93 (m, 1H, C*H*H-CHF_2), 3.90 – 3.78 (m, 1H, CH*H*-CHF_2,), 3.77 – 3.65 (m, 3H, H-4, H-6, H-6), 3.64 – 3.56 (m, 2H, H-3, H-5), 3.49 (dd, 1H, *J* = 10.5, 7.7 Hz, H-2), 3.30 (s, 3H, CH_3 OMe), 3.19 (s, 3H, CH_3 OMe), 1.34 (s, 3H, CH_3 Me), 1.28 (s, 3H, CH_3 Me); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 138.1 (C_q), 128.5, 127.8, 127.6 (CH_{arom}), 114.2 (dd, *J* = 241.8, 240.8 Hz, CHF_2), 102.9 (C-1), 100.1, 99.9 (C_q BDA), 74.2 (C-5), 73.7 (CH_2 Bn), 70.9 (C-3), 68.8 (dd, *J* = 30.3, 28.1 Hz, *C*H_2-CHF_2), 68.1 (C-6), 66.0 (C-4), 62.6 (C-2), 48.2, 48.2 (OMe), 17.7, 17.7 (Me); Diagnostic peaks α-anomer: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 4.97 (d, 0.3H, *J* = 3.6 Hz, H-1), 4.25 (dd, 0.3H, *J* = 10.8, 9.7 Hz, H-3), 3.39 (dd, 0.3H, *J* = 10.9, 3.6 Hz, H-2), 3.37 (s, 0.9H, CH_3 OMe), 1.35 (s, 0.9H, CH_3 Me), 1.30 (s, 0.9H, CH_3 Me); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 137.9, 128.4, 127.7, 127.6, 113.8 (t, *J* = 241.5 Hz), 100.2, 100.1 (C_q BDA), 99.4 (C-1), 73.7 (CH_2 Bn), 70.0 (C-5), 67.7 (C-6), 67.6 (t, *J* = 29.0 Hz, *C*H_2-CHF_2), 67.4 (C-3), 66.3 (C-4), 60.0 (C-2), 48.6, 17.9, 17.8; HRMS: $[M+NH_4]^+$ calcd for $C_{21}H_{33}F_2N_4O_7$ 491.23118, found 491.23061.



2,2,2-trifluoroethyl 2-azido-6-*O*-benzyl-2-deoxy-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-α/β-D-glucopyranoside (1E). Donor **1** and 2,2,2-trifluoroethanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 30 min at -40°C) and purified by flash column chromatography (1/0 to 9/1 pentane/EtOAc) to yield glycosylation product **1E** (43 mg, 87 µmol, 87%, α:β = 2.5:1). R_f: 0.35 9/1 (pentane/EtOAc). IR (thin film): 673, 737, 851, 885, 972, 1030, 1111, 1279, 1377, 2108, 2949; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 7.38 – 7.24 (m, 5H, CH_{arom}), 5.01 (d, 1H, *J* = 3.6 Hz, H-1), 4.60 – 4.55 (m, 2H, CH_2 Bn), 4.28 (dd, 1H, *J* = 10.9, 9.5 Hz, H-3), 4.01 – 3.91 (m, 3H, C*H*$_2$$CF_3$, H-5), 3.89 – 3.82 (m, 1H, H-4), 3.78 – 3.66 (m, 2H, H-6, H-6), 3.41 – 3.35 (m, 4H, CH_3 OMe, H-2), 3.19 (s, 3H, CH_3 OMe), 1.35 (s, 3H, CH_3 Me), 1.30 (s, 3H, CH_3 Me); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 137.9 (C_q), 128.4, 127.8, 127.6 (CH_{arom}), 123.5 (q, *J* = 278.4 Hz, CF_3), 100.2, 100.1 (C_q BDA), 99.3 (C-1), 73.7 (CH_2 Bn), 70.3 (C-5), 67.6 (C-6), 67.2 (C-3), 66.2 (C-4), 65.1 (q, *J* = 35.3 Hz, *C*$H_2$$CF_3$), 59.8 (C-2), 48.6, 48.2 (OMe), 17.8, 17.8 (Me); Diagnostic peaks β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.38 (d, 0.38H, *J* = 7.6 Hz, H-1), 4.16 (dq, 0.38H, *J* = 12.5, 8.7 Hz, C*H*H-CF_3), 3.65 – 3.56 (m, 2H, H-3, H-5), 3.50 (dd, 0.38H, *J* = 10.5, 7.6 Hz, H-2), 3.30 (s, 1.14H), 1.34 (s, 1.14H), 1.28 (s, 1.14H); ^{13}C-APT NMR ($CDCl_3$, 101 MHz): δ 102.4 (C-1), 100.2, 99.9, 74.4, 70.7, 68.0, 66.5, 66.0 (q, *J* = 35.1 Hz), 62.6, 48.2, 48.2, 17.7, 17.6; HRMS: $[M+NH_4]^+$ calcd for $C_{21}H_{32}F_3N_4O_7$ 509.22176, found 509.22116.

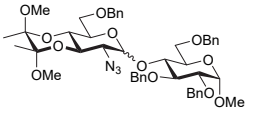


1,1,1,3,3,3-Hexafluoro-2-propyl 2-azido-6-*O*-benzyl-2-deoxy-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-α-D-glucopyranoside (1F). Donor **1** and hexafluoro-*iso*-propanol were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 120 hours at -40°C) and purified by flash column chromatography (1/0 to 9/1 pentane/EtOAc) to yield glycosylation product **1F** (10 mg, 18 µmol, 18%, α:β = >20:1). R_f: 0.7 (9/1 pentane/EtOAc). $[\alpha]_D^{23}$ = +182.1° (*c* = 0.52, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 7.36 – 7.28 (m, 5H, CH_{arom}), 5.17 (d, 1H, *J* = 3.9 Hz, H-1), 4.58 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.54 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.44 (hept, 1H, *J* = 5.8 Hz, C*H* HFIP), 4.23 (dd, 1H, *J* = 11.1, 9.6 Hz, H-3), 4.02 (ddd, 1H, *J* = 10.0, 3.5, 2.0 Hz, H-5), 3.92 (t, 1H, *J* = 9.9 Hz, H-4), 3.78 (dd, 1H, *J* = 11.2, 3.5 Hz, H-6), 3.64 (dd, 1H, *J* = 11.1, 2.0 Hz, H-6), 3.46 (dd, 1H, *J* = 11.0, 3.9 Hz, H-2), 3.38 (s, 3H, CH_3 OMe), 3.20 (s, 3H, CH_3 OMe), 1.36 (s, 3H, CH_3 Me), 1.31 (s, 3H, CH_3 Me); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 137.8 (C_q Bn), 128.5, 127.8, 127.6 (CH_{arom} Bn), 101.1 (C-1), 100.3, 100.2 (C_q BDA), 73.8 (CH_2 Bn), 73.3 (CH HFIP), 71.3 (C-5), 67.2 (C-6), 66.9 (C-3), 65.9 (C-4), 59.8 (C-2), 48.8, 48.3 (OMe), 17.8, 17.8 (Me); HRMS: $[M+NH_4]^+$ calcd for $C_{22}H_{31}F_6N_4O_7$ 577.20914, found 577.20899.

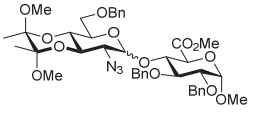


Methyl 6-*O*-(2-azido-6-*O*-benzyl-2-deoxy-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-β-D-glucopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (1G). Donor **1** and acceptor **10** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 18 hours at -40°C) and purified by flash column chromatography (19/1 to 3/1 pentane/EtOAc) to yield glycosylation product **1G** (74 mg, 86 µmol, 86%, α:β = <1:20). R_f: 0.41 (4/1 pentane/EtOAc). $[\alpha]_D^{20}$ = +54.9° (*c* = 1.85, $CHCl_3$); IR (thin film): 696, 735, 849, 962, 1107, 1134, 1369, 1454, 2108, 2907; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 7.38 – 7.24 (m, 20H, CH_{arom}), 4.98 (d, 1H, *J* = 10.9 Hz, C*H*H Bn), 4.92 (d, 1H, *J* = 11.1 Hz, C*H*H Bn), 4.84 – 4.76 (m, 2H, CH*H* Bn, C*H*H Bn), 4.66 (d, 1H, *J* = 11.0 Hz, CH*H* Bn), 4.65 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.62 (d, 1H, *J* = 3.5 Hz, H-1), 4.58 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.53 (d, 1H, *J* = 12.2 Hz, CH*H* Bn), 4.20 (d, 1H, *J* = 7.7 Hz, H-1'), 4.12 (dd, 1H, *J* = 10.9, 1.6 Hz, H-6), 4.00 (t, 1H, *J* = 9.3 Hz, H-3), 3.83 – 3.77 (m, 1H, H-5), 3.76 – 3.63 (m, 4H, H-4', H-6, H-6', H-6'), 3.63 – 3.52 (m, 4H, H-2, H-3',

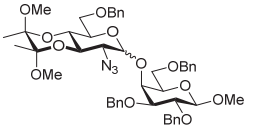
H-4, H-5'), 3.50 (dd, 1H, *J* = 10.3, 7.7 Hz, H-2'), 3.38 (s, 3H, CH_3 OMe), 3.30 (s, 3H, CH_3 OMe BDA), 3.16 (s, 3H, CH_3 OMe BDA), 1.33 (s, 3H, CH_3 Me), 1.26 (s, 3H, CH_3 Me); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 138.8, 138.5, 138.3, 138.2 (C_q), 128.5, 128.5, 128.5, 128.4, 128.2, 128.2, 128.1, 128.0, 127.8, 127.8, 127.6, 127.6, 127.5 (CH_{arom}), 102.7 (C-1'), 100.1, 99.8 (C_q BDA), 98.2 (C-1), 82.2 (C-3), 79.9 (C-2), 77.7 (C-4), 75.8, 74.9 (CH_2 Bn), 74.3 (C-5), 73.6, 73.5 (CH_2 Bn), 71.3 (C-3'), 69.8 (C-5), 68.6 (C-6), 68.3 (C-6'), 66.2 (C-4'), 62.8 (C-2'), 55.3 (CH_3 OMe), 48.1, 48.1 (CH_3 OMe BDA), 17.7, 17.6 (CH_3 Me BDA); HRMS: $[M+NH_4]^+$ calcd for $C_{47}H_{61}N_4O_{12}$ 873.42805, found 873.42812.



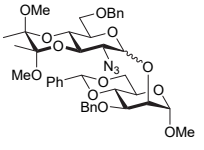
Methyl 4-*O*-(2-azido-6-*O*-benzyl-2-deoxy-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-α/β-D-glucopyranosyl)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (1H). Donor **1** and acceptor **11** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 18 hours at -40°C) and purified by flash column chromatography (19/1 to 4/1 pentane/EtOAc) to yield glycosylation product **1H** (80 mg, 93 µmol, 93%, α:β = 1:15). R_f: 0.51 (4/1 pentane/EtOAc). IR (thin film): 696, 737, 1045, 1109, 1134, 1368, 1454, 1497, 2108, 2900; Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 7.37 – 7.19 (m, 20H, CH_{arom}), 5.00 (d, 1H, *J* = 11.4 Hz, C*H*H Bn), 4.80 (d, 1H, *J* = 11.4 Hz, CH*H* Bn), 4.74 (d, 1H, *J* = 12.2 Hz, C*H*H Bn), 4.62 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.58 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.57 (d, 1H, *J* = 3.8 Hz, H-1), 4.52 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.48 (d, 1H, *J* = 12.4 Hz, C*H*H Bn), 4.35 (d, 1H, *J* = 7.8 Hz, H-1'), 4.33 (d, 1H, *J* = 12.2 Hz, CH*H* Bn), 4.00 – 3.94 (m, 1H, H-4), 3.91 (t, 1H, *J* = 9.1 Hz, H-3), 3.87 (dd, 1H, *J* = 10.8, 3.3 Hz, H-6), 3.81 – 3.76 (m, 1H, H-5), 3.71 (dd, 1H, *J* = 10.8, 1.6 Hz, H-6), 3.68 (t, 1H, *J* = 9.6 Hz, H-4'), 3.63 (dd, 1H, *J* = 11.1, 1.4 Hz, H-6'), 3.55 (t, 1H, *J* = 10.0 Hz, H-3'), 3.48 – 3.35 (m, 7H, CH_3 OMe, H-2, H-2', H-5', H-6'), 3.32 (s, 3H, CH_3 OMe BDA), 3.17 (s, 3H, CH_3 OMe BDA), 1.33 (s, 3H, CH_3 Me BDA), 1.26 (s, 3H, CH_3 Me BDA); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 139.5, 138.6, 138.3, 137.9 (C_q), 128.6, 128.5, 128.4, 128.4, 128.3, 128.2, 128.2, 128.1, 127.8, 127.8, 127.8, 127.8, 127.6, 127.5, 127.4, 127.3, 127.1 (CH_{arom}), 101.3 (C-1'), 100.1, 99.8 (C_q BDA), 98.4 (C-1), 80.3 (C-3), 79.1 (C-2), 76.7 (C-4), 75.4 (CH_2 Bn), 74.3 (C-5'), 73.7, 73.5 (CH_2 Bn), 71.6 (C-3'), 69.8 (C-5), 68.4 (C-6), 68.1 (C-6'), 66.2 (C-4'), 63.5 (C-2'), 55.3 (OMe), 48.2, 48.1 (OMe BDA), 17.7, 17.6 (Me BDA); Diagnostic peaks α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.72 (d, 0.1H, *J* = 4.1 Hz, H-1'), 5.09 (d, 0.1H, *J* = 10.5 Hz, C*H*H Bn), 4.84 (d, 0.1H, *J* = 10.5 Hz, CH*H* Bn), 4.17 – 4.11 (m, 0.1H), 4.06 (d, 0.1H, *J* = 9.1 Hz); ^{13}C-APT NMR ($CDCl_3$, 101 MHz): δ 100.0 (C_q BDA), 98.6 (C-1'), 97.7 (C-1), 82.0, 80.6, 75.1, 74.2, 73.3, 70.2, 60.0, 55.4, 48.6; HRMS: $[M+NH_4]^+$ calcd for $C_{47}H_{61}N_4O_{12}$ 873.42805, found 873.42783.



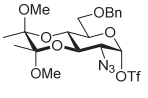
Methyl (Methyl 4-*O*-[2-azido-6-*O*-benzyl-2-deoxy-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-α/β-D-glucopyranosyl]-2,3-di-*O*-benzyl-α-D-glucopyranosyl uronate) (1I). Donor **1** and acceptor **12** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 18 hours at -40°C) and purified by flash column chromatography (19/1 to 4/1 pentane/EtOAc) to yield glycosylation product **1I** (66 mg, 83 µmol, 83%, α:β = 1.5:1). R_f: 0.44 and 0.47 (4/1 pentane/EtOAc). IR (thin film): 698, 735, 1043, 1107, 1454, 1749, 2108, 2949; Reported as a 1 : 0.7 mixture of anomers: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 7.34 – 7.21 (m, 31H), 5.58 (d, 1H, *J* = 3.8 Hz, H-1'$_\alpha$), 5.05 – 4.98 (m, 1.7H, C*H*H Bn $_\alpha$, C*H*H Bn$_\beta$), 4.85 (d, 1H, *J* = 10.5 Hz, CH*H* Bn$_\alpha$), 4.82 – 4.71 (m, 2.4H, C*H*H Bn$_\alpha$, CH*H* Bn$_\beta$, C*H*H Bn$_\beta$), 4.62 – 4.53 (m, 4.4H, C*H*H Bn$_\alpha$, CH*H* Bn$_\alpha$ CH*H* Bn$_\beta$, H-1$_\alpha$, H-1$_\beta$), 4.50 (d, 1H, *J* = 12.0 Hz, CH*H* Bn$_\alpha$), 4.43 (d, 0.7H, *J* = 12.2 Hz, C*H*H Bn$_\beta$), 4.38 (d, 0.7H, *J* = 7.8 Hz, H-1'$_\beta$), 4.34 (d, 0.7H, *J* = 12.1 Hz, CH*H* Bn$_\beta$), 4.23 (d, 0.7H, *J* = 9.8 Hz, H-5$_\beta$), 4.18 (d, 1H, *J* = 9.4 Hz, H-5$_\alpha$), 4.13 (dd, 1H, *J* = 10.9, 9.7 Hz, H-3'$_\alpha$), 4.08 – 4.00 (m, 2.7H, H-3$_\alpha$, H-4$_\alpha$, H-4$_\beta$), 3.93 (t, 0.7H, *J* = 9.1 Hz, H-3$_\beta$), 3.83 (t, 1H, *J* = 10.0 Hz, H-4'$_\alpha$), 3.81 (s, 2.1H, CH_3 CO_2Me_β), 3.73 – 3.67 (m, 4.7H, CH_3 CO_2Me_α, H-4'$_\beta$, H-6'$_\alpha$), 3.61 – 3.44 (m, 6.5H, H-2$_\alpha$, H-2$_\beta$, H-3'$_\beta$, H-5'$_\alpha$, H-5'$_\beta$, H-6'$_\alpha$, H-6'$_\beta$, H-6'$_\beta$), 3.41 – 3.36 (m, 5.8H, CH_3 OMe$_\alpha$, CH_3 OMe$_\beta$, H-2'$_\beta$), 3.35 (s, 3H, CH_3 OMe BDA$_\alpha$), 3.30 – 3.26 (m, 3.1H, CH_3 OMe BDA$_\beta$, H-2'), 3.16 (s, 2.1H, CH_3 OMe BDA$_\beta$), 3.15 (s, 3H, CH_3 OMe BDA$_\alpha$), 1.32 (s, 5.1H, CH_3 Me BDA$_\alpha$, CH_3 Me BDA$_\beta$), 1.25 (s, 2.1H, CH_3 Me BDA$_\beta$), 1.23 (s, 3H, CH_3 Me BDA$_\alpha$); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 170.1, 169.9 (C=O), 139.3, 138.5, 138.4, 138.1, 138.1, 137.8 (C_q), 128.6, 128.5, 128.5, 128.4, 128.3, 128.3, 128.2, 128.2, 128.0, 128.0, 128.0, 127.8, 127.7, 127.7, 127.6, 127.6, 127.6, 127.5, 127.4, 127.4, 127.2 (CH_{arom}), 102.1 (C-1'$_\beta$), 100.1, 99.8, 99.8 (C_q BDA), 98.9 (C-1$_\beta$), 98.6 (C-1$_\alpha$), 98.3 (C-1'$_\alpha$), 81.3 (C-3$_\alpha$), 79.8 (C-3$_\beta$), 79.6 (C-2$_\alpha$), 79.0 (C-4$_\beta$), 78.6 (C-2$_\beta$), 75.5, 75.4 (CH_2 Bn), 74.9 (C-4$_\alpha$), 74.4 (C-5'$_\beta$), 73.9, 73.8, 73.7, 73.5 (CH_2 Bn), 71.3 (C-3'$_\beta$), 70.1 (C-5$_\alpha$), 70.0 (C-5'$_\alpha$), 69.9 (C-5$_\beta$), 68.0 (C-6'$_\beta$), 67.4 (C-3'$_\alpha$), 67.3 (C-6'$_\alpha$), 66.0 (C-4'$_\beta$), 65.8 (C-4'$_\alpha$), 63.4 (C-2'$_\alpha$), 60.1 (C-2'$_\beta$), 55.9, 55.8 (OMe), 52.7, 52.7 (CO_2 Me), 48.4, 48.2, 48.1, 48.1 (OMe BDA), 17.9, 17.7, 17.7, 17.6 (Me BDA); HRMS: $[M+NH_4]^+$ calcd for $C_{41}H_{55}N_4O_{13}$ 811.37601, found 811.37610.



Methyl 4-*O*-(2-azido-6-*O*-benzyl-2-deoxy-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-α/β-D-glucopyranosyl)-2,3,6-tri-*O*-benzyl-β-D-galactopyranoside (1J). Donor **1** and acceptor **13** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 18 hours at -40°C) and purified by flash column chromatography (19/1 to 4/1 pentane/EtOAc) to yield glycosylation product **1J** (74 mg, 86 µmol, 86%, α:β = 1:1.7). R_f: 0.48 and 0.54 (4/1 pentane/EtOAc). IR (thin film): 696, 737, 1034, 1109, 1368, 1454, 2108, 2930; Reported as a 1 : 1.5 mixture of anomers: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 7.42 – 7.19 (m, 50H, CH_{arom}), 4.99 (d, 1H, *J* = 3.9 Hz, H-1'$_α$), 4.90 (d, 1H, *J* = 10.9 Hz, C*H*H Bn$_α$), 4.90 – 4.83 (m, 3H, 2xC*H*H Bn$_β$), 4.79 (d, 1H, *J* = 10.9 Hz, CH*H* Bn$_α$), 4.75 – 4.71 (m, 4H, CH*H* Bn$_β$, C*H*H Bn$_α$, H-1'$_β$), 4.66 (d, 1.5H, *J* = 12.2 Hz, CH*H* Bn$_β$), 4.62 (d, 1H, *J* = 12.5 Hz, CH*H* Bn$_α$), 4.53 (s, 2H, CH_2 Bn$_α$), 4.49 (s, 3H, CH_2 Bn$_β$), 4.48 – 4.40 (m, 4H, CH_2 Bn$_β$, C*H*H Bn$_α$), 4.32 (d, 1H, *J* = 12.2 Hz, CH*H* Bn$_α$), 4.28 (d, 1.5H, *J* = 7.8 Hz, H-1$_β$), 4.27 – 4.21 (m, 2H, H-3'$_α$, H-5'$_α$), 4.23 (d, 1H, *J* = 7.6 Hz, H-1$_α$), 4.14 (d, 1H, *J* = 3.0 Hz, H-4$_α$), 4.09 (d, 1.5H, *J* = 2.6 Hz, H-4$_β$), 3.98 – 3.87 (m, 3.5H, H-2$_β$, H-4'$_α$, H-6$_α$), 3.82 (dd, 1.5H, *J* = 10.5, 4.7 Hz, H-6'$_β$), 3.75 – 3.55 (m, 14H, CH_3 OMe$_β$, H-2$_α$, H-4'$_β$, H-5'$_β$, H-6'$_β$, H-6$_α$, H-6$_β$, H-6$_β$), 3.54 – 3.40 (m, 11H, CH_3 OMe$_α$, H-2'$_β$, H-3$_β$, H-3'$_β$, H-5$_α$, H-5$_β$, H-6'$_α$), 3.40 – 3.33 (m, 5H, CH_3 OMe BDA$_α$, H-2'$_α$, H-3$_α$), 3.31 (s, 4.5H, CH_3 OMe BDA$_β$), 3.18 – 3.10 (m, 8.5H, CH_3 OMe BDA$_{α,β}$, H-6'$_α$), 1.34 (s, 3H, CH_3 Me BDA$_α$), 1.34 (s, 4.5H, CH_3 Me BDA$_β$), 1.29 (s, 3H, CH_3 Me BDA$_α$), 1.27 (s, 4.5H, CH_3 Me BDA$_β$); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 138.9, 138.8, 138.6, 138.5, 138.5, 138.3, 138.2, 137.6 (C_q), 128.6, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.2, 128.1, 127.6, 127.6, 127.6, 127.6, 127.5, 127.5, 127.5, 127.5, 127.3, 127.2 (CH_{arom}), 105.3 (C-1$_α$), 105.1 (C-1$_β$), 102.5 (C-1'$_β$), 100.1, 100.0, 99.9, 99.8 (C_q BDA), 99.4 (C-1'$_α$), 81.3 (C-3$_β$), 80.2 (C-3$_α$), 79.5 (C-2$_β$) , 79.0 (C-2$_α$), 75.2, 75.0 (CH_2 Bn), 74.1 (C-4$_α$), 73.9 (C-5'$_β$), 73.9 (C-5$_β$), 73.7 (CH_2 Bn), 73.6 (C-4$_β$), 73.6, 73.6, 73.5, 73.4 (CH_2 Bn), 73.0 (C-5$_α$), 72.9 (CH_2 Bn), 70.7 (C-3'$_β$), 70.3 (C-6'$_β$), 69.5 (C-5'$_α$), 68.5 (C-6$_β$), 68.0 (C-3'$_α$), 67.2, 67.1 (C-6$_α$, C-6'$_α$), 66.2 (C-4'$_β$), 66.0 (C-4'$_α$), 62.7 (C-2'$_β$), 60.9 (C-2'$_α$), 57.3, 57.2 (OMe), 48.7, 48.2, 48.1, 48.1 (OMe BDA), 17.9, 17.9, 17.7, 17.7 (Me BDA); HRMS: $[M+NH_4]^+$ calcd for $C_{47}H_{61}N_4O_{12}$ 873.42805, found 873.42801.

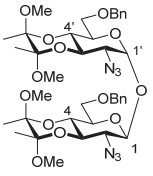


Methyl 2-*O*-(2-azido-6-*O*-benzyl-2-deoxy-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-α/β-D-glucopyranosyl)-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (1K). Donor **1** and acceptor **14** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (for an additional 18 hours at -40°C) and purified by flash column chromatography (19/1 to 4/1 pentane/EtOAc) to yield glycosylation product **1K** (71 mg, 93 µmol, 93%, α:β = 1:1.7). R_f: 0.45 (4/1 pentane/EtOAc).IR (thin film): 698, 1038, 1109, 1126, 1375, 1454, 2110, 2912; Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 7.52 – 7.47 (m, 2H, CH_{arom}), 7.40 – 7.32 (m, 3H, CH_{arom}), 7.30 – 7.19 (m, 10H, CH_{arom}), 5.60 (s, 1H, C*H*Ph), 4.86 – 4.78 (m, 2H, C*H*H Bn, H-1), 4.64 (d, 1H, *J* = 12.5 Hz, CH*H* Bn), 4.54 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.49 (d, 1H, *J* = 11.9 Hz, CH*H* Bn), 4.41 (d, 1H, *J* = 7.3 Hz, H-1'), 4.29 (dd, 1H, *J* = 3.3, 1.5 Hz, H-2), 4.24 (dd, 1H, *J* = 10.0, 4.6 Hz, H-6), 4.16 (t, 1H, *J* = 9.7 Hz, H-4), 3.93 (dd, 1H, *J* = 10.1, 3.4 Hz, H-3), 3.86 (t, 1H, *J* = 10.2 Hz, H-6), 3.82 – 3.61 (m, 6H, H-2', H-4', H-5, H-5', H-6', H-6'), 3.57 (dd, 1H, *J* = 10.8, 7.9 Hz, H-3'), 3.37 (s, 3H, CH_3 OMe), 3.30 (s, 3H, CH_3 OMe BDA), 3.18 (s, 3H, CH_3 OMe BDA), 1.34 (s, 3H, CH_3 Me BDA), 1.28 (s, 3H, CH_3 Me BDA); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 138.5, 138.1, 137.8 (C_q), 128.4, 128.3, 128.2, 127.8, 127.6, 127.4, 127.3, 126.2, 126.2 (CH_{arom}), 101.6 (CHPh), 101.4 (C-1'), 100.0, 99.8 (C_q BDA), 99.3 (C-1), 78.1 (C-4), 74.7 (C-2), 74.4 (C-5'), 73.8 (CH_2 Bn), 73.7 (C-3), 71.0 (CH_2 Bn), 70.5 (C-3'), 68.9, 68.8 (C-6, C-6'), 66.4 (C-4'), 64.2 (C-5), 63.0 (C-2'), 55.0 (OMe), 48.1 (OMe BDA), 17.7, 17.7 (Me BDA); Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 7.51 – 7.43 (m, 2H, CH_{arom}), 7.40 – 7.23 (m, 13H, CH_{arom}), 5.62 (s, 1H, C*H*Ph), 5.35 (d, 1H, *J* = 3.8 Hz, H-1'), 4.88 (d, 1H, *J* = 12.4 Hz, C*H*H Bn), 4.75 (d, 1H, *J* = 1.3 Hz, H-1), 4.69 (d, 1H, *J* = 12.4 Hz, CH*H* Bn), 4.57 (s, 2H, CH_2 Bn), 4.32 (dd, 1H, *J* = 10.9, 9.6 Hz, H-3'), 4.30 – 4.22 (m, 2H, H-4, H-6), 4.10 (dd, 1H, *J* = 3.0, 1.7 Hz, H-2), 4.03 (ddd, *J* = 10.2, 5.0, 1.7 Hz, 1H, H-5'), 3.96 (dd, 1H, *J* = 9.9, 3.1 Hz, H-3), 3.85 (t, 1H, *J* = 10.2 Hz, H-6), 3.80 – 3.66 (m, 4H, H-4', H-5, H-6', H-6'), 3.42 (s, 3H, CH_3 OMe BDA), 3.25 – 3.17 (m, 7H, CH_3 OMe BDA, CH_3 OMe, H-2'), 1.36 (s, 3H, CH_3 Me BDA), 1.32 (s, 3H, CH_3 Me BDA); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 138.8, 138.0, 137.8 (C_q), 128.9, 128.8, 128.3, 128.2, 127.7, 127.7, 127.6, 127.4, 126.2 (CH_{arom}), 101.6 (CHPh), 100.9 (C-1), 100.2 (C-1'), 100.1, 100.0 (C_q BDA), 79.5 (C-4), 76.1 (C-2), 75.5 (C-3), 73.7, 73.1 (CH_2 Bn), 70.0 (C-5'), 69.0 (C-6), 68.2 (C-6'), 66.9 (C-4'), 66.5 (C-3'), 63.9 (C-5), 60.1 (C-2'), 54.8 (OMe), 48.7, 48.2 (OMe BDA), 17.9, 17.8 (Me BDA); HRMS: $[M+NH_4]^+$ calcd for $C_{40}H_{53}N_4O_{12}$ 781.36545, found 781.36550.



Trifluoromethanesulfonyl 2-azido-6-*O*-benzyl-2-deoxy-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-α-D-glucopyranoside (18). ^{1}H NMR (CD_2Cl_2, *T* = 243 K, 500 MHz, HH-COSY, HSQC): δ 6.10 (d, 1H, *J* = 3.3 Hz, H-1), 4.52 (d, 1H, *J* = 11.5 Hz, C*H*H Bn), 4.48 (d, 1H, *J* = 11.3 Hz, CH*H* Bn), 4.19 (t, 1H, *J* = 10.2 Hz, H-3), 4.07 (d, 1H, *J* = 10.4 Hz, H-5), 4.01 (t, 1H, *J* = 9.9 Hz, H-4), 3.87 (dd, 1H, *J* = 10.8, 3.5 Hz, H-2), 3.79 (dd, 1H, *J* = 11.1, 2.3 Hz, H-6), 3.67 (d, 1H, *J* = 11.1 Hz, H-6), 3.30 (s, 3H, CH_3 OMe), 3.19 (s, 3H, CH_3 OMe),

1.30 (s, 3H, CH_3 Me), 1.25 (s, 3H, CH_3 Me); ^{13}C-APT NMR (CD_2Cl2, 126 MHz, HSQC): δ 105.8 (C-1), 99.8, 99.6 (C_q BDA), 73.2 (C-5), 72.9 (CH_2 Bn), 67.5 (C-3), 65.9 (C-6), 63.6 (C-4), 58.6 (C-2), 48.3, 48.1 (OMe), 17.3, 17.2 (Me).



1-(2-azido-6-*O*-benzyl-2-deoxy-3,4-*O*-[2,3-dimethoxybutane-2,3-diyl]-α-D-glucopyranosyl)-2-azido-6-*O*-benzyl-2-deoxy-3,4-*O*-[2,3-dimethoxybutane-2,3-diyl]-β-D-glucopyranoside (24). IR (thin film): 698, 737, 883, 1032, 1107, 1134, 1263, 1279, 1375, 1454, 2108, 2926, 2947, 2994;^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.36 – 7.21 (m, 10H, CH_{arom}), 5.20 (d, 1H, *J* = 3.6 Hz, H-1'), 4.53 – 4.46 (m, 2H, CH_2 Bn), 4.44 – 4.38 (m, 2H, C*H*H Bn, H-1), 4.35 – 4.28 (m, 2H, CH*H* Bn, H-3'), 4.23 (dt, 1H, *J* = 10.7, 2.4 Hz, H-5'), 3.93 (t, 1H, *J* = 10.0 Hz, H-4'), 3.74 – 3.52 (m, 8H, H-2, H-3, H-4, H-5, 2xH-6, 2xH-6'), 3.39 (dd, 1H, *J* = 7.3, 3.5 Hz, H-2'), 3.37 (s, 3H, CH_3 OMe), 3.32 (s, 3H, CH_3 OMe), 3.21 (s, 3H, CH_3 OMe), 3.16 (s, 3H, CH_3 OMe), 1.35 (s, 3H, CH_3 Me), 1.34 (s, 3H, CH_3 Me), 1.29 (s, 3H, CH_3 Me), 1.28 (s, 3H, CH_3 Me); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.3, 138.2 (C_q Bn), 128.5, 128.3, 127.7, 127.6 (CH_{arom}), 102.0 (C-1), 100.3, 100.2, 100.0, 99.9 (C_q BDA), 99.8 (C-1'), 74.4 (C-5), 73.6, 73.5 (CH_2 Bn), 71.6 (C-3), 70.6 (C-5'), 68.3 (C-6), 67.5 (C-3'), 67.4 (C-6'), 66.0 (C-4'), 65.9 (C-4), 63.3 (C-2), 60.1 (C-2'), 48.7, 48.2, 48.2, 48.2 (OMe), 17.9, 17.8, 17.8, 17.7 (Me); HRMS: $[M+NH_4]^+$ calcd for $C_{38}H_{56}N_6O_{13}$ 818.39306, found 818.39310.

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Chapter 6

Mapping glycosylation stereoselectivity by acceptor reactivity tuning

Introduction

The union of two carbohydrates to generate larger oligosaccharides is arguably one of the most important reactions in glycochemistry.[1–4] Although the glycosylation reaction has been actively studied for more than half a century, many aspects that affect this reaction, both in terms of yield and stereoselectivity, remain enigmatic.[5–10] The reactivity of the carbohydrate building blocks is one of the most important determinants that influence the outcome of a glycosylation reaction.[11,12] The reactivity of donor glycosides has been very well documented: the relative reactivity value (RRV) of hundreds of thioglycosides has been established and hundreds of anomeric triflates and other covalent reactive species, key reactive intermediates formed *in situ* during the reaction, have been characterized.[13–18] The reactivity of acceptor glycosides is less well understood and systematic studies investigating this important reaction parameter are extremely scarce.[19–24] At the same time, it is common practice to change protecting groups on the acceptor building block to influence the yield or change the stereoselectivity of a

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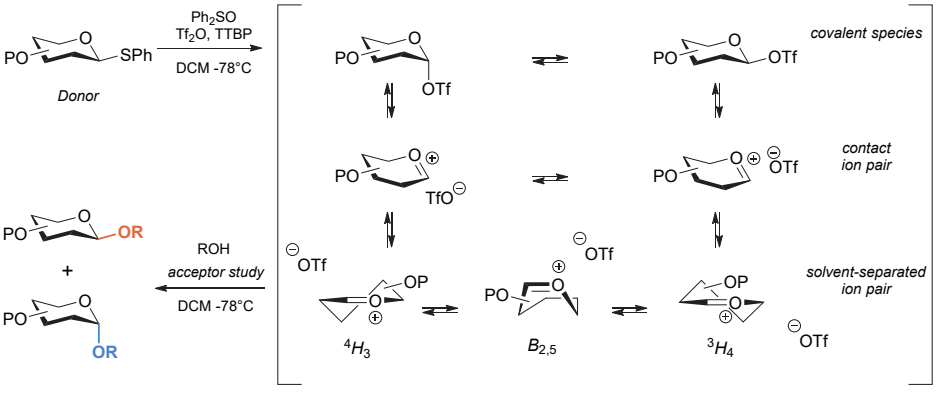
glycosylation reaction.[25–28] Often this is done in a time consuming, trial-and-error manner as well defined guidelines how to tune the reactivity of an acceptor and how this effects the glycosylation reaction are absent.[29–31]

In Chapters 3 and 4 of this thesis the profound influence acceptor nucleophilicity has on the stereoselectivity of glycosylation reactions with 4,6-*O*-benzylidene protected glucose and glucosamine donors was demonstrated.[32,33] In these studies a panel of partially fluorinated ethanols (ethanol, mono-, di- and trifluoroethanol) was used to reveal a donor's stereoselectivity dependency on acceptor nucleophilicity and described the change in the underlying continuum of mechanisms (Scheme 1).[21,34,35] An intimate relation between model acceptor reactivity and glycosylation stereoselectivity was evident. Whereas some donors are highly sensitive towards acceptor reactivity, other donors are more reluctant to changes in stereochemical outcome. They all have in common that eventually the poorest of *O*-nucleophiles lead them to converge to α-selectivity. These results have been explained by stereoelectronic properties of both the donor and acceptor molecules. In a general sense, the strongest acceptors are able to substitute an anomeric leaving group (α-triflate) in an S_N2-like substitution reaction. Somewhat weaker acceptors preferentially react with the more reactive β-triflate, and upon reducing acceptor reactivity further the mechanism shifts towards the S_N1-side of the reactivity spectrum as increasingly stronger electrophiles are required.

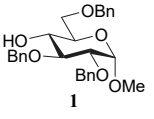
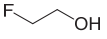
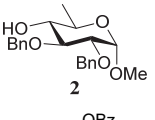
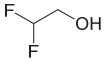
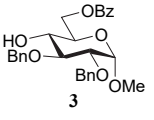
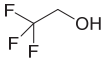
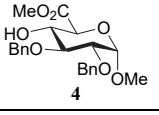
Scheme 1. General glycosylation mechanism, with distinct oxocarbenium ion conformations for the solvent-separated ion pairs. P = protecting group.



Results and discussion

Among the various donors evaluated in Chapters 3-5, the benzylidene glucose (**A**) and glucosazide donors (**B**) were identified to be the most susceptible to acceptor reactivity, based on the stereochemical results of the fluorinated ethanol model system and a few carbohydrate acceptors (See Table 1). An extension of the set of carbohydrate acceptors was envisioned, bearing protecting groups differing in electron-withdrawing properties to closely follow the trend set by the model nucleophiles, determined by the stereoselectivities in glycosylations with donors **A** and **B**. Simultaneously, the variety of acceptors can provide an accurate scale of relative acceptor reactivities to which any desired acceptor can be set against and reveal its potential stereoselectivity in glycosylation.

Table 1. Glycosylations of donor **A** and **B** with fluorinated model acceptors and carbohydrate acceptors **1**-**4**.

	 **A**	 **B**		 **A**	 **B**
Acceptor	Product[a] α:β (yield)	Product α:β (yield)	Acceptor	Product α:β (yield)	Product α:β (yield)
	1 : 10 (68%)	<1 : 20 (83%)	 **1**	**1A** 1 : 1 (82%)	**1B** 1 : 7 (88%)
	1 : 2.8 (70%)	1 : 6.7 (90%)	 **2**	**2A** 2 : 1 (85%)	**2B** 1 : 5 (69%)
	5 : 1 (70%)	2.9 : 1 (64%)	 **3**	**3A** 4 : 1 (92%)	**3B** 1 : 1.1 (67%)
	>20 : 1 (64%)	>20 : 1 (94%)	 **4**	**4A** 5 : 1 (90%)	**4B** 1.1 : 1 (93%)

[a]Ratios and yields of the isolated product after SiO_2 and LH-20 size-exclusion chromatography, anomers were not separated. Ratios were determined by integration of representative signals for each anomer in the mixture of anomers.

To keep steric and other structural effects to a minimum for comparison throughout the scope of acceptors, the primary focus was laid on a diverse set of C-4–OH glucoside acceptors (Figure 1, **1**-**20**). The other alcohol functions are protected as either *O*-benzyl or *O*-benzoyl groups, and in addition to these two groups, the primary alcohol is also either reduced or oxidized to give C-6-deoxy and C-6–CO_2Me species respectively to provide for a difference in electron-withdrawing properties. The glycosylation method used throughout this study is based on preactivation of donors **A** and **B** in DCM with the Ph_2SO/Tf_2O activation couple in the presence of hindered weak base TTBP at -80°C[36,37], followed by addition of a solution of the acceptor. Applying this protocol, the generation of an equilibrium of reactive species (Scheme 1) is ensured, enabling the rationalization of the stereoselectivity in terms of the set of reactive species, and furthermore avoids competitive alternative pathways present in the *in situ* activation scenarios (direct substitution of the activation thioglycoside, its ion pair or the first formed oxocarbenium ion conformer contribute to an increased complexity of the reaction mechanism).

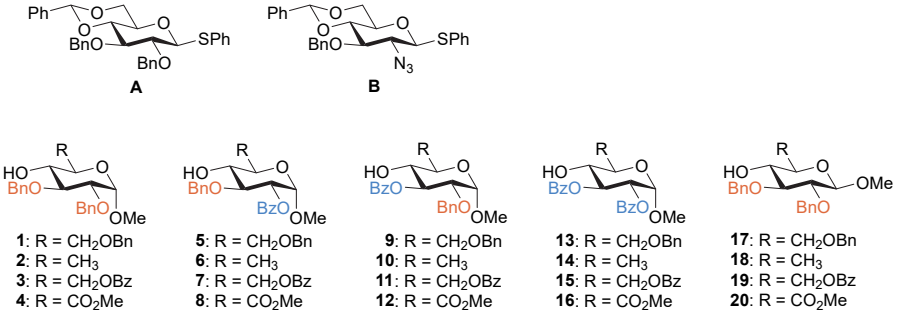
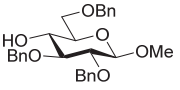
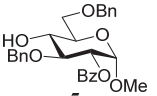
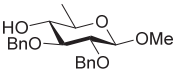
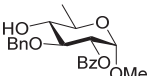
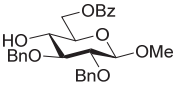
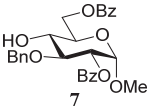
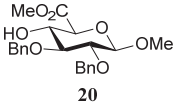
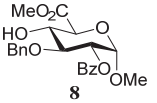
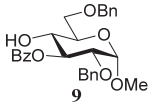
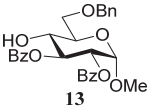
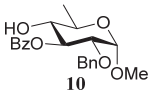
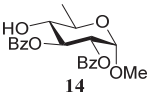
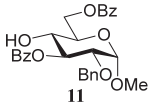
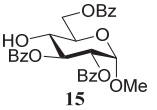
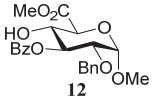
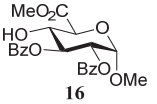
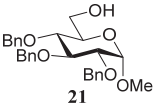
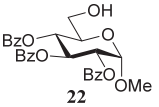


Figure 1. Donors and gluco C-4–OH acceptors used in this chapter.

In Table 1 results previously obtained with the fluorinated model alcohols are directly compared with glycosylation results of 2,3-di-*O*-benzyl acceptors **1**-**4**. A clear transition from β- to α-selectivity, following the electron-withdrawing tendency of the protecting group at the C-6 position, arises. The uronic acid having its electron-withdrawing carbonyl function closer to the acceptor's nucleophilic center than the 6-*O*-benzoyl has, is more α-directing than the latter, which in turn gives higher α-selectivity than the 6-*O*-benzyl. Changing the configuration of the remote anomeric position of the acceptor to a β-glucoside (**17**-**20**), or protecting the C-2 position with a benzoyl (**5**-**8**) rather than a benzyl has no apparent effect on the glycosylation stereoselectivities (Table 2).[38–41] However, the C-3 position has a dramatic effect on the stereoselectivity; complete

Table 2. Glycosylations of donor **A** and **B** with β-acceptors **17**-**20** and α-acceptors bearing a benzoyl on C-2 (**5**-**8**), C-3 (**9**-**12**), or both (**13**-**16**).

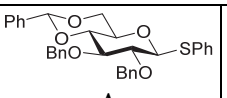
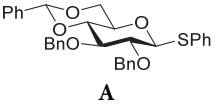
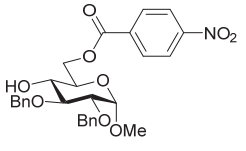
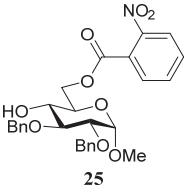
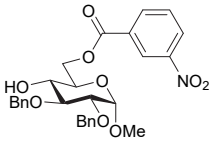
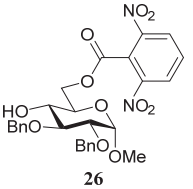
	 **A**	 **B**		 **A**	 **B**
Acceptor	Product α:β (yield)	Product α:β (yield)	Acceptor	Product α:β (yield)	Product α:β (yield)
 **17**	**17A** 1 : 1 (79%)	**17B** 1 : 7 (80%)	 **5**	**5A** 1 : 1.1 (81%)	**5B** 1 : 6 (88%)
 **18**	**18A** 1.1 : 1 (87%)	**18B** 1 : 5.6 (86%)	 **6**	**6A** 1.1 : 1 (86%)	**6B** 1 : 5 (88%)
 **19**	**19A** 3.3 : 1 (73%)	**19B** 1 : 1.2 (70%)	 **7**	**7A** 3.5 : 1 (88%)	**7B** 1.3 : 1 (87%)
 **20**	**20A** 5 : 1 (83%)	**20B** 1.2 : 1 (85%)	 **8**	**8A** 4.8 : 1 (96%)	**8B** 1.2 : 1 (82%)
 **9**	**9A** >20 : 1 (95%)	**9B** 6.7 : 1 (77%)	 **13**	**13A** >20 : 1 (90%)	**13B** 10 : 1 (93%)
 **10**	**10A** >20 : 1 (93%)	**10B** 14 : 1 (81%)	 **14**	**14A** >20 : 1 (83%)	**14B** >20 : 1 (96%)
 **11**	**11A** >20 : 1 (95%)	**11B** >20 : 1 (85%)	 **15**	**15A** >20 : 1 (91%)	**15B** >20 : 1 (69%)
 **12**	**12A** >20 : 1 (86%)	**12B** >20 : 1 (93%)	 **16**	**16A** >20 : 1 (84%)	**16B** >20 : 1 (99%)
 **21**	**21A** 1 : 2.7 (90%)	**21B** <1 : 20 (93%)	 **22**	**22A** 3 : 1 (86%)	**22B** 1 : 1.5 (95%)

α-selectivity is found only by changing the C-3–OBn group to a C-3–OBz group (Table 2, **9**-**12**). Even the more β-selective donor **B** reacts with high to complete α-selectivity with the C-3–OBz acceptors (**9**-**16**). Only exchanging the two C–H bonds for a C=O bond, by replacing a benzyl ether for a benzoyl ester, a marked change in stereoselectivity is achieved. This effect is most pronounced at the nearby C-3 position, whereas position C-6 offers slight fine-tuning of the acceptor reactivity, and position C-2 has only a negligible influence. [42]

The concept of reactivity tuning of the acceptors works consistently well for C-4–OH *gluco*-configured acceptors. The more reactive primary acceptors **21** and **22** (Table 2) showed similar behavior and upon benzoylation significantly more α-product is obtained, however the C-6 nucleophilic position remains too reactive to give complete α-selectivity.

To examine the extent of influence the protecting group on the C-6 position exerts, more electronegative elements were introduced on the benzoyl aromatic ring (Table 3, **23**-**26**).[43] A series of mono-nitrobenzoyl esters were found to marginally increase α-selectivity, but acceptor **26** bearing a 2,6-dinitrobenzoyl group enhanced α-selectivity even more than the uronic acid acceptor **4**.[44]

Table 3. Glycosylations of donor **A** and **B** with acceptor **23**-**26** bearing electron-withdrawing C-6 benzoates.

	 **A**		 **A**
Acceptor	Product α:β (yield)	Acceptor	Product α:β (yield)
 **23**	**23A** 3 : 1 (92%)	 **25**	**25A** 3.5 : 1 (83%)
 **24**	**24A** 3.3 : 1 (49%)	 **26**	**26A** 5.6 : 1 (83%)

Conclusions

The translation from a set of fluorinated model nucleophiles providing a reactivity-selectivity glycosylation picture, to a selection of carbohydrate acceptors occurs without difficulty. These carbohydrate acceptors can be tuned in reactivity just like donors have been in the past by manipulation of their protecting groups, and their reactivity exploited in obtaining stereoselectivity in glycosylations. Everyday protecting- and functional groups were successfully used to moderate the reactivity of the glycosyl acceptors. The most electron-withdrawing groups turned the acceptor into a poor nucleophile and steered the glycosyation utilizing these acceptors to the α-product. The concept of acceptor reactivity tuning holds for all the example acceptors displayed in this chapter. By using this panel of reference acceptors and the two model donors, any other relevant acceptor can have its reactivity compared with the current set of acceptors and appropriately adjusted for the desired reactivity and functional group pattern.

Experimental section

General experimental procedures:

A: reductive opening benzylidene acetal. The benzylidene protected compound (1 eq.) was coevaporated with dry toluene (2x) and dissolved at r.t. in dry THF (0.07 M). $NaCNBH_3$ (5 eq.) was added followed by drop-wise addition of a 4 M HCl solution in 1,4-dioxane (5.2 eq. pH<4). After stirring for an additional hour, the reaction was quenched by the addition of ice water (40 mL/mmol) and extracted with DCM (2x 15 mL/mmol). The combined organic layers were washed with sat.aq. $NaHCO_3$ and sat.aq. NaCl. The organic fraction was dried ($MgSO_4$), filtered, concentrated *in vacuo*, and purified by column chromatography (pentane/EtOAc mixtures).

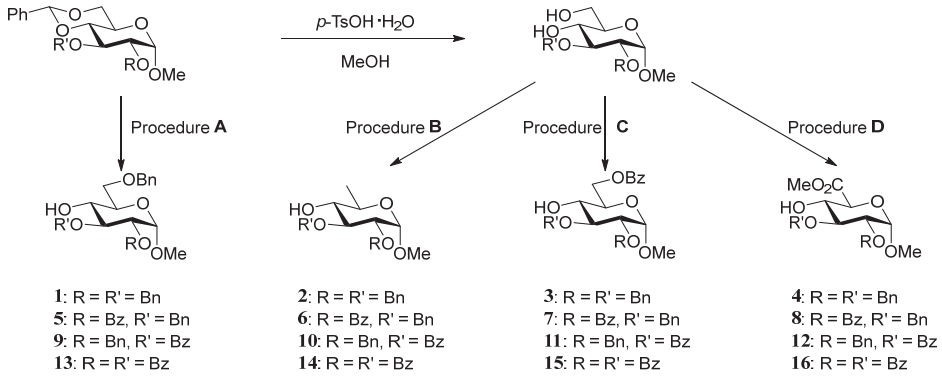
B: iodination-deoxygenation. To a 0°C solution of the diol (1 eq.) in pyridine (0.2 M) was added *p*-TsCl (1.5 eq.) and the reaction stirred until completion (TLC, 3-14 h). MeOH was added (1 mL/mmol), and the reaction mixture diluted with Et_2O (15 mL/mmol). The organic layer was washed with 5 M aq. HCl (3x), H_2O, sat.aq. $NaHCO_3$, and sat.aq. NaCl. The organic fraction was dried ($MgSO_4$), filtered and concentrated in vacuo. The crude compound was dissolved in butanone (0.2 M) and NaI (2 eq.) was added. The reaction mixture was heated for 3h at 80°C after which it was diluted with EtOAc and washed with 10% aq. $Na_2S_2O_3$ and H_2O. The organic fraction was dried ($MgSO_4$), filtered, concentrated *in vacuo*, and purified by column chromatography (pentane/EtOAc mixtures). The intermediate iodo compound (1 eq.) was coevaporated with dry toluene and dissolved in toluene (0.07 M) under a nitrogen atmosphere. AIBN (0.05 eq.) and Bu_3SnH (2 eq.) were added and the reaction refluxed (120°C) for 3-7 h. The cooled solution was diluted with EtOAc and washed with H_2O and sat.aq. NaCl. The organic fraction was dried ($MgSO_4$), filtered, concentrated *in vacuo*, and purified by column chromatography (pentane/EtOAc mixtures).

C: regioselective benzoylation. To a 0°C solution of the diol (1 eq.) in DCM (0.35 M) was added pyridine (5 eq.) followed by a solution of benzoyl chloride (1.05 eq.) in DCM (1.6 M), slowly added over 15 min. After stirring overnight, the reaction mixture was diluted with DCM, washed with 1 M HCl (2x), H_2O and sat.aq. $NaHCO_3$. The organic fraction was dried ($MgSO_4$), filtered, concentrated *in vacuo*, and purified by column chromatography (pentane/EtOAc mixtures).

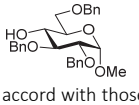
D: regioselective oxidation. To a 0°C solution of the diol (1 eq.) in DCM/H_2O (5/1, v/v, 0.20 M) was added (diacetoxy)iodobenzene (2.5 eq.) and TEMPO (0.2 eq.). The mixture was vigorously stirred for 2-5 h, and quenched by the addition of 10% aq. $Na_2S_2O_3$. The reaction mixture was extracted twice with DCM. The water layer was acidified (pH 1) with 1 M aq. HCl and extracted once with DCM. The combined organic layers were washed with H_2O, then dried ($MgSO_4$), filtered, and concentrated *in vacuo.* The crude carboxylic acid was coevaporated twice with dry toluene and dissolved in DMF (0.35 M). MeI (2 eq.) and K_2CO_3 (2 eq.) were added and stirred for 3 h. The reaction was quenched with AcOH (3 eq.), and diluted with H_2O. The mixture was extracted thrice with EtOAc, and the combined organic layers were washed with H_2O and sat.aq. NaCl. The organic fraction was dried ($MgSO_4$), filtered, concentrated *in vacuo*, and purified by column chromatography (pentane/EtOAc mixtures).

E: Tf_2O/Ph_2SO mediated pre-activation glycosylation. Donor (0.1 mmol), Ph_2SO (26 mg, 0.13 mmol, 1.3 equiv), and tri-*tert*-butylpyrimidine (TTBP) (62 mg, 0.25 mmol, 2.5 equiv) were coevaporated twice with dry toluene and dissolved in dry DCM (2 mL, 0.05 M donor). Activated 3 Å molecular sieves (rods, 1 /16 in. in size) were added, and the reaction mixture was stirred for 1 h at room temperature under a nitrogen atmosphere. The solution was cooled to −78 °C, and Tf_2O (22 μL, 0.13 mmol, 1.3 equiv) was added. The reaction mixture was allowed to warm to −60 °C and then recooled to −78 °C, after which the acceptor (0.2 mmol, 2 equiv) in DCM (0.4 mL, 0.5 M) was added. The reaction mixture was allowed to warm to −40 °C in approximately 90 min and stirred overnight at that temperature. The reaction was quenched with Et_3N (0.1 mL, 0.72 mmol, 5.5 equiv) at −40 °C, and the mixture was diluted with DCM. The solution was transferred to a separatory funnel, water was added, the layers were separated, and the water phase was extracted once more with DCM. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by silica gel flash column chromatography and sephadex LH-20 size-exclusion chromatography yielded the glycosylation product as a mixture of anomers.

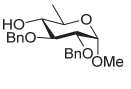
Scheme S1: Synthesis of all C-4–OH acceptors.[a,b]



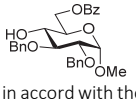
[a]Acceptors **17**-**20** follow the same four procedures from the corresponding β-methyl glycoside, acceptors **23**-**25** follow procedure C with the appropriate nitrobenzoyl chloride. [b]Acceptor **2** was made via an alternative route.



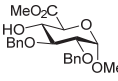
Methyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (1). Methyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside[32] (4.67 g, 10 mmol) was converted to the title compound **1** following general procedure **A**. Yield: 3.5 g, 7.5 mmol, 75%. R_f 0.20 (9/1 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[32] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.40 – 7.24 (m, 15H, CH_{arom}), 5.00 (d, 1H, *J* = 11.4 Hz, C*H*H Bn), 4.77 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.73 (d, 1H, *J* = 11.4 Hz, CH*H* Bn), 4.66 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.63 (s, 1H, H-1), 4.59 (d, 1H, *J* = 12.2 Hz, C*H*H Bn), 4.54 (d, 1H, *J* = 12.2 Hz, CH*H* Bn), 3.78 (t, 1H, *J* = 9.1 Hz, H-3), 3.74 – 3.64 (m, 3H, H-5, H-6), 3.60 (td, 1H, *J* = 9.1, 2.3 Hz, H-4), 3.53 (dd, 1H, *J* = 9.5, 3.5 Hz, H-2), 3.38 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.9, 138.2 (C_q), 128.7, 128.6, 128.6, 128.5, 128.3, 128.3, 128.1, 128.1, 128.0, 127.8, 127.8 (CH_{arom}), 98.3 (C-1), 81.6 (C-3), 79.7 (C-2), 75.6, 73.7, 73.3 (CH_2 Bn), 70.9 (C-4), 70.0 (C-5), 69.6 (C-6), 55.4 (OMe).



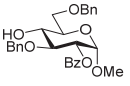
Methyl 2,3-di-*O*-benzyl-6-deoxy-α-D-glucopyranoside (2). Methyl 2,3-di-*O*-benzyl-α-D-glucopyranoside[32] (581 mg, 1.5 mmol) and *p*-TsCl (343 mg, 1.8 mmol, 1.2 eq.) were dissolved in pyridine (3 mL) and stirred overnight. The reaction mixture was poured in 1 M aq. HCl and extracted twice with Et_2O. The organic layers were washed with 1 M aq. HCl, H_2O, and sat.aq. NaCl, then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The crude was coevaporated twice with dry toluene and 12 mL Et_2O was added, followed by LiAlH4 (1 mL, 4 M in Et_2O, 2.6 eq.) and refluxed for 4 h. The reaction was quenched by addition of EtOAc and 1 M aq. HCl. The reaction mixture was washed with 1 M aq. HCl, H_2O and sat.aq. NaCl. The organic layer was dried ($MgSO_4$), filtered, and concentrated in vacuo. Purificiation by column chromatography (5% to 30% EtOAc in pentane) gave the title compound **2** as an oil. (430 mg, 1.2 mmol, 80%). R_f 0.32 (3/1 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[45] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.42 – 7.23 (m, 10H, CH_{arom}), 5.03 (d, 1H, *J* = 11.5 Hz, C*H*H Bn), 4.76 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.72 – 4.63 (m, 2H, 2xCH*H* Bn), 4.56 (d, 1H, *J* = 3.5 Hz, H-1), 3.73 (t, 1H, *J* = 9.2 Hz, H-3), 3.69 – 3.54 (m, 1H, H-5), 3.55 – 3.48 (m, 1H, H-2), 3.37 (s, 3H, CH_3 OMe), 3.15 (t, 1H, *J* = 9.2 Hz, H-4), 2.19 (d, 1H, *J* = 18.3 Hz, 4-OH), 1.23 (d, 3H, *J* = 6.2 Hz, H-6); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.8, 138.1 (C_q), 128.8, 128.6, 128.2, 128.1, 128.1, 128.1 (CH_{arom}), 98.1 (C-1), 81.4 (C-3), 80.2 (C-2), 75.4 (CH_2 Bn), 75.4 (C-4), 73.1 (CH_2 Bn) , 66.9 (C-5), 55.2 (OMe), 17.8 (C-6).



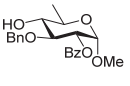
Methyl 2,3-di-*O*-benzyl-6-*O*-benzoyl-α-D-glucopyranoside (3). Methyl 2,3-di-*O*-benzyl-α-D-glucopyranoside[32] (3.37 g, 9 mmol) was converted to the title compound **3** following general procedure **C**. Yield: 3.94 g, 8.24 mmol, 92%. R_f 0.18 (4/1 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[45] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.03 (d, 2H, *J* = 7.6 Hz, CH_{arom}), 7.59 – 7.26 (m, 13H, CH_{arom}), 5.01 (dd, 1H, *J* = 11.3, 2.1 Hz, C*H*H Bn), 4.83 – 4.72 (m, 2H, CH*H* Bn, C*H*H Bn), 4.70 – 4.54 (m, 3H, H-1, CH*H* Bn, H-6), 4.51 (d, 1H, *J* = 11.7 Hz, H-6), 3.91 – 3.79 (m, 2H, H-5, H-3), 3.60 – 3.49 (m, 2H, H-4, H-2), 3.40 (s, 3H, CH_3 OMe), 2.64 (s, 1H, 4-OH); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 166.9 (C=O), 138.7, 138.1 (C_q), 133.3, 129.8, 128.8, 128.6, 128.5, 128.2, 128.2, 128.1, 128.1 (CH_{arom}), 98.3 (C-1), 81.3 (C-3), 79.8 (C-2), 75.8, 73.3 (CH_2 Bn), 70.2 (C-4), 69.6 (C-5), 63.8 (C-6), 55.4 (OMe).



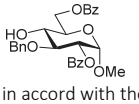
Methyl (methyl 2,3-di-*O*-benzyl-α-D-glucopyranosyl uronate) (4). Methyl 2,3-di-*O*-benzyl-α-D-glucopyranoside[32] (6.95 g, 18.6 mmol) was converted to the title compound **4** following general procedure **D**. Yield: 3.84 g, 9.54 mmol, 52%. Spectroscopic data were in accord with those previously reported.[32] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.39 – 7.26 (m, 10H, CH_{arom}), 4.92 (d, 1H, *J* = 11.3 Hz, C*H*H Bn), 4.81 (d, 1H, *J* = 11.4 Hz, CH*H* Bn), 4.79 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.67 – 4.62 (m, 2H, CH*H* Bn, H-1), 4.15 (d, 1H, *J* = 8.9 Hz, H-5), 3.87 – 3.76 (m, 5H, H-3, H-4, CH_3 CO_2Me), 3.53 (dd, 1H, J = 8.9, 3.4 Hz, H-2), 3.42 (s, 3H, CH_3 OMe), 2.89 (bs, 1H, 4-OH); ^{13}C-APT NMR (CDCl3, 101 MHz, HSQC): δ 170.8 (C=O CO_2Me), 138.7, 138.0 (C_q), 128.6, 128.3, 128.1, 128.0, 127.9 (CH_{arom}), 98.8 (C-1), 80.5 (C-3), 78.6 (C-2), 75.6, 73.7 (CH_2 Bn), 71.9 (C-4), 70.6 (C-5), 56.0 (OMe), 52.8 (CO_2Me); HRMS: $[M+Na]^+$ calcd for $C_{22}H_{26}O_7Na$ 425.15707, found 425.15649.



Methyl 2-*O*-benzoyl-3,6-di-*O*-benzyl-α-D-glucopyranoside (5). Methyl 2-*O*-benzoyl-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside[46] (3.36 g, 7 mmol) was converted to the title compound **5** following general procedure **A**. Yield: 3.07 g, 6.42 mmol, 92%. R_f 0.38 (4/1 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[47] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.12 – 8.03 (m, 2H, CH_{arom}), 7.62 – 7.15 (m, 13H, CH_{arom}), 5.09 (dd, 1H, *J* = 9.7, 3.6 Hz, H-2), 5.05 (d, 1H, *J* = 3.7 Hz, H-1), 4.86 (d, 1H, *J* = 11.4 Hz, C*H*H Bn), 4.74 (d, 1H, *J* = 11.4 Hz, CH*H* Bn), 4.64 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.58 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.02 (dd, 1H, *J* = 9.7, 8.2 Hz, H-3), 3.86 – 3.71 (m, 4H, H-5, H-6, H-4, H-6), 3.38 (s, 3H, CH_3 OMe), 2.62 (d, 1H, *J* = 2.4 Hz, 4-OH); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 166.0 (C=O), 138.4, 138.0 (C_q), 133.5, 133.4, 129.9 (CH_{arom}), 129.8 (C_q), 128.6, 128.6, 128.5, 128.0, 128.0, 127.8, 127.8, 127.1 (CH_{arom}), 97.4 (C-1), 79.8 (C-3), 75.3 (CH_2 Bn), 74.0 (C-2), 73.8 (CH_2 Bn), 71.6 (C-5), 69.9 (C-4), 69.8 (C-6), 55.4 (OMe).

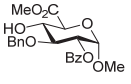


Methyl 2-*O*-benzoyl-3-*O*-benzyl-6-deoxy-α-D-glucopyranoside (6). Methyl 2-*O*-benzoyl-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside[46] (5.56 g, 17.96 mmol, 1 eq.) was dissolved in 100 ml MeOH and *p*-TsOH·H_2O (0.35 g) was added. The reaction mixture was stirred at 50°C for 3 h, after which it was quenched by addition of Et_3N (0.25 ml) and concentrated *in vacuo*. The crude product was purified by column chromatography (2:1 to 4:6 pentane/EtOAc) to yield Methyl 2-*O*-benzoyl-3-*O*-benzyl-α-D-glucopyranoside as a white solid (5.98 g, 15.39 mmol, 86%). R_f 0.26 (4/6 pentane/EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.13 – 8.04 (m, 2H, CH_{arom}), 7.63 – 7.56 (m, 1H, CH_{arom}), 7.51 – 7.42 (m, 2H, CH_{arom}), 7.31 – 7.19 (m, 5H, CH_{arom}), 5.08 – 5.01 (m, 2H, H-1, H-2), 4.88 (dd, 1H, *J* = 11.4, 1.0 Hz, C*H*H Bn), 4.70 (dd, 1H, *J* = 11.4, 0.9 Hz, CH*H* Bn), 4.07 – 4.00 (m, 1H, H-3), 3.91 – 3.78 (m, 2H, H-6, H-6), 3.77 – 3.67 (m, 2H, H-4, H-5), 3.38 (s, 3H, CH_3 OMe), 2.13 (d, 1H, *J* = 10.0 Hz, 4-OH); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 166.1 (C=O), 138.3 (C_q), 133.5, 130.0 (CH_{arom}), 129.7 (C_q), 128.7, 128.7, 128.1, 128.0 (CH_{arom}), 97.5 (C-1), 79.9 (C-3), 75.4 (CH_2 Bn), 74.2 (C-2), 70.9 (C-4), 70.7 (C-5), 62.5 (C-6), 55.5 (OMe). HRMS: $[M+Na]^+$ calcd for $C_{21}H_{24}O_7Na$ 411.1414, found 411.1421. Methyl 2-*O*-benzoyl-3-*O*-benzyl-α-D-glucopyranoside (3.01 g, 7.75 mmol) was converted to the 6-iodo intermediate following general procedure **B**. Yield: 3.21 g, 6.43 mmol, 83%. R_f 0.64 (3/1 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[48] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY): δ 8.13 – 8.06 (m, 2H, CH_{arom}), 7.64 – 7.26 (m, 8H, CH_{arom}), 5.12 – 5.03 (m, 2H, H-2, H-1), 4.88 (d, 1H, *J* = 11.4 Hz, C*H*H Bn), 4.65 (d, 1H, *J* = 11.4 Hz, CH*H* Bn), 4.02 (dd, 1H, *J* = 9.6, 8.1 Hz, H-3), 3.59 (dd, 1H, *J* = 10.6, 2.1 Hz, H-6), 3.56 – 3.52 (m, 1H, H-5), 3.52 – 3.46 (m, 1H, H-4), 3.44 (s, 3H, CH_3 OMe), 3.34 (dd, 1H, *J* = 10.5, 6.4 Hz, H-6), 2.33 (d, 1H, *J* = 2.5 Hz, 4-OH). Subsequent deoxygenation gave the title compound **6**. Yield: 2.03 g, 5.45 mmol, 85%. $[\alpha]_D^{20}$ = +112.3° (*c* = 0.90, $CHCl_3$); IR (thin film): 712, 1027, 1051, 1108, 1271, 1452, 1721, 2933, 3486; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.13 – 8.06 (m, 2H, CH_{arom}), 7.62 – 7.55 (m, 1H, CH_{arom}), 7.50 – 7.42 (m, 2H, CH_{arom}), 7.29 – 7.24 (m, 5H, CH_{arom}), 5.08 (dd, 1H, *J* = 9.9, 3.7 Hz, H-2), 4.98 (d, 1H, *J* = 3.7 Hz, H-1), 4.87 (d, 1H, *J* = 11.4 Hz, C*H*H Bn), 4.68 (d, 1H, *J* = 11.4 Hz, CH*H* Bn), 3.97 (dd, 1H, *J* = 9.9, 8.9 Hz, H-3), 3.76 (dq, 1H, *J* = 9.6, 6.2 Hz, H-5), 3.37 (s, 3H, CH_3 OMe), 3.33 (dd, 1H, *J* = 9.2, 2.7 Hz, H-4), 2.32 (d, 1H, *J* = 2.8 Hz, 4-OH), 1.32 (d, 3H, *J* = 6.2 Hz, H-6); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 166.0 (C=O), 138.3 (C_q), 133.4, 129.9 (CH_{arom}), 129.8 (C_q), 128.7, 128.6, 128.1, 128.1 (CH_{arom}), 97.3 (C-1), 80.0 (C-3), 75.6 (C-4), 75.3 (CH_2 Bn), 74.6 (C-2), 67.0 (C-5), 55.3 (OMe), 17.7 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{21}H_{24}O_6Na$ 395.1465, found 395.1472.

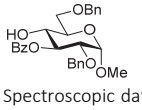


Methyl 2,6-di-*O*-benzoyl-3-*O*-benzyl-α-D-glucopyranoside (7). Methyl 2-*O*-benzoyl-3-*O*-benzyl-α-D-glucopyranoside (0.93 g, 2.4 mmol) was converted to the title compound **7** following general procedure **C**. Yield: 1.25 g, 2.4 mmol, 100%. R_f 0.25 (4/1 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[45] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.13 – 8.01 (m, 4H, CH_{arom}), 7.62 – 7.17 (m, 11H, CH_{arom}), 5.11 – 5.04 (m, 2H, H-1, H-2), 4.87 (d, 1H, *J* = 11.3 Hz, C*H*H Bn), 4.78 – 4.70 (m, 2H, CH*H* Bn, H-6), 4.54 (dd, 1H, *J* = 12.1, 2.2 Hz, H-6), 4.07 (t, 1H, *J* = 9.0 Hz, H-3), 3.97 (ddd, 1H, *J* = 10.0, 4.5, 2.1 Hz, H-5), 3.70 (t, 1H, *J* = 9.4 Hz, H-4), 3.40 (s, 3H, CH_3 OMe), 2.83 (s, 1H, 4-OH); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 167.1, 166.0

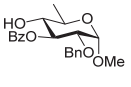
(C=O), 138.2 (C_q), 133.5, 133.4, 130.0, 129.9, 129.8 (CH_{arom}), 129.7 (C_q), 128.7, 128.6, 128.1, 128.1 (CH_{arom}), 97.5 (C-1), 79.6 (C-3), 75.6 (CH_2 Bn), 74.0 (C-2), 70.4 (C-4), 69.7 (C-5), 63.6 (C-6), 55.5 (OMe).



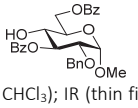
Methyl (methyl 2-*O*-benzoyl-3-*O*-benzyl-α-D-glucopyranosyl uronate) (8). Methyl 2-*O*-benzoyl-3-*O*-benzyl-α-D-glucopyranoside (1.55 g, 4 mmol) was converted to the title compound **8** following general procedure **D**. Yield: 1.01 g, 2.4 mmol, 61%. $[\alpha]_D^{20}$ = +137.4° (*c* = 0.95, $CHCl_3$); IR (thin film): 711, 1028, 1046, 1105, 1270, 1452, 1723, 1749, 2937, 3508; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.08 – 8.02 (m, 2H, CH_{arom}), 7.62 – 7.18 (m, 9H, CH_{arom}), 5.14 (d, 1H, *J* = 3.6 Hz, H-1), 5.08 (dd, 1H, *J* = 9.6, 3.6 Hz, H-2), 4.84 (s, 2H, CH_2 Bn), 4.24 (d, 1H, *J* = 9.6 Hz, H-5), 4.05 (dd, 1H, *J* = 9.7, 8.6 Hz, H-3), 3.98 (td, 1H, *J* = 9.2, 1.9 Hz, H-4), 3.86 (s, 3H, CH_3 CO_2Me), 3.43 (s, 3H, CH_3 OMe), 3.03 (s, 1H, 4-OH); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 170.8 (C=O CO_2Me), 166.0 (C=O OBz), 138.3 (C_q), 133.5, 130.0 (CH_{arom}), 129.6 (C_q), 128.6, 128.6, 128.1, 127.9 (CH_{arom}), 97.8 (C-1), 78.6 (C-3), 75.4 (CH_2 Bn), 73.1 (C-2), 72.4 (C-4), 70.2 (C-5), 56.0 (OMe), 53.0 (CO_2Me); HRMS: $[M+Na]^+$ calcd for $C_{22}H_{24}O_8Na$ 439.1363, found 439.1374.



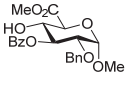
Methyl 3-*O*-benzoyl-2,6-di-*O*-benzyl-α-D-glucopyranoside (9). Methyl 3-*O*-benzoyl-2-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside[47] (3.34 g, 7 mmol) was converted to the title compound **9** following general procedure **A**. Yield: 2.11 g, 4.40 mmol, 63%. R_f 0.20 (4/1 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[47] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.07 – 8.00 (m, 2H, CH_{arom}), 7.64 – 7.21 (m, 13H, CH_{arom}), 5.50 (ddd, 1H, *J* = 9.9, 7.5, 1.3 Hz, H-3), 4.75 (d, 1H, *J* = 3.5 Hz, H-1), 4.69 – 4.52 (m, 4H, 2xCH_2 Bn), 3.86 – 3.66 (m, 5H, H-2, H-4, H-5, H-6, H-6), 3.42 (s, 3H, CH_3 OMe), 3.01 – 2.91 (m, 1H, 4-OH); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 167.7 (C=O), 138.0, 137.8 ($_{cq}$), 133.4, 130.1, 129.8, 128.5, 128.5, 128.1, 128.1, 127.8, 127.8 (CH_{arom}), 98.0 (C-1), 76.6 (C-2), 76.4 (C-3), 73.8 (CH_2 Bn), 73.1 (CH_2 Bn), 70.5 (C-4), 70.5 (C-5), 69.3 (C-6), 55.5 (OMe).



Methyl 2-*O*-benzyl-3-*O*-benzoyl-6-deoxy-α-D-glucopyranoside (10). Methyl 3-*O*-benzoyl-2-*O*-benzyl-α-D-glucopyranoside[49] (3.63 g, 9.34 mmol) was converted to the 6-iodo intermediate following general procedure **B**. Yield: 3.89 g, 7.80 mmol, 84%). ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.06 – 7.99 (m, 2H, CH_{arom}), 7.65 – 7.23 (m, 8H, CH_{arom}), 5.47 (dd, 1H, *J* = 9.8, 8.5 Hz, H-3), 4.75 (d, 1H, *J* = 3.6 Hz, H-1), 4.69 (d, 1H, *J* = 12.4 Hz, C*H*H Bn), 4.63 (d, 1H, *J* = 12.4 Hz, CH*H* Bn), 3.69 (dd, 1H, *J* = 9.8, 3.6 Hz, H-6), 3.61 (dd, 1H, *J* = 10.7, 2.3 Hz, H-2), 3.57 – 3.52 (m, 1H, H-5), 3.52 – 3.48 (m, 1H, H-4), 3.48 (s, 3H, CH_3 OMe), 3.34 (dd, 1H, *J* = 10.6, 6.4 Hz, H-6), 3.19 (dq, 1H, *J* = 5.0, 1.6 Hz, 4-OH); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 168.1 (C=O), 137.7, 133.7(C_q), 130.1, 128.6, 128.1 (CH_{arom}), 97.9 (C-1), 76.7 (C-2), 76.1 (C-3), 74.0 (C-4), 73.2 (CH_2 Bn), 70.5 (C-5), 60.5 (C-6), 55.8 (OMe), 7.0 (C-6). Subsequent deoxygenation gave the title compound **10**. Yield: 1.08 g, 2.90 mmol, 37%. $[\alpha]_D^{20}$ = +93.3° (*c* = 1.0, $CHCl_3$); IR (thin film): 710, 748, 988, 1053, 1103, 1269, 1369, 1450, 1720, 2909, 3460; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.06 – 7.99 (m, 2H, CH_{arom}), 7.64 – 7.22 (m, 8H, CH_{arom}), 5.43 (t, 1H, *J* = 9.5 Hz, H-3), 4.71 – 4.61 (m, 3H, CH_2 Bn, H-1), 3.77 (dq, 1H, *J* = 9.5, 6.2 Hz, H-5), 3.68 (dd, 1H, *J* = 9.8, 3.6 Hz, H-2), 3.42 (s, 3H, CH_3 OMe), 3.34 (td, 1H, *J* = 9.3, 5.3 Hz, H-4), 2.82 (d, 1H, *J* = 5.3 Hz, 4-OH), 1.31 (d, 3H, *J* = 6.2 Hz, H-6); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 168.1 (C=O), 137.8, 133.5 (C_q), 130.1 (CH_{arom}), 129.8 (C_q), 128.6, 128.1, 128.1 (CH_{arom}), 97.8 (C-1), 76.9 (C-2), 76.7 (C-3), 75.7 (C-4), 73.1 (CH_2 Bn), 67.6 (C-5), 55.4 (OMe), 17.7 (C-6); HRMS: $[M+NH_4]^+$ calcd for $C_{21}H_{28}NO_6$ 390.19111, found 390.19132.

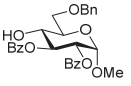


Methyl 2-*O*-benzyl-3,6-di-*O*-benzoyl-α-D-glucopyranoside (11). Methyl 3-*O*-benzoyl-2-*O*-benzyl-α-D-glucopyranoside[49] (1.36 g, 3.5 mmol) was converted to the title compound **11** following general procedure **C**. Yield: 1.47 g, 3.0 mmol, 85%. R_f 0.28 (4/1 pentane/EtOAc). $[\alpha]_D^{20}$ = +78.4° (*c* = 1.13, $CHCl_3$); IR (thin film): 709, 1051, 1070, 1097, 1107, 1275, 1452, 1724, 1749, 2945, 3493; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.08 – 8.02 (m, 4H, CH_{arom}), 7.65 – 7.54 (m, 2H, CH_{arom}), 7.49 – 7.41 (m, 4H, CH_{arom}), 7.30 – 7.22 (m, 5H, CH_{arom}), 5.54 (t, 1H, *J* = 9.5 Hz, H-3), 4.76 (d, 1H, *J* = 3.5 Hz, H-6), 4.73 – 4.63 (m, 3H, C*H*H Bn, H-1, H-6), 4.63 – 4.54 (m, 1H, CH*H* Bn), 4.02 (ddd, 1H, *J* = 10.0, 5.1, 2.3 Hz, H-5), 3.73 – 3.61 (m, 2H, H-2, H-4), 3.44 (s, 3H, CH_3 OMe), 3.35 – 3.20 (m, 1H, 4-OH); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 167.8, 166.9 (C=O), 137.8 (C_q), 133.5, 130.1, 129.9 (CH_{arom}), 129.7 (C_q), 128.6, 128.6, 128.5, 128.1, 128.1 (CH_{arom}), 97.9 (C-1), 76.7 (C-2), 76.1 (C-3), 73.2 (CH_2 Bn), 70.2 (C-4), 70.1 (C-5), 63.8 (C-6), 55.5 (OMe); HRMS: $[M+Na]^+$ calcd for $C_{28}H_{28}O_8Na$ 515.1676, found 515.1680.

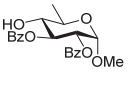


Methyl (methyl 2-*O*-benzyl-3-*O*-benzoyl-α-D-glucopyranosyl uronate) (12). Methyl 3-*O*-benzoyl-2-*O*-benzyl-α-D-glucopyranoside[49] (2.14 g, 5.5 mmol) was converted to the title compound **12** following general procedure **D**. Yield: 1.70 g, 4.08 mmol, 74%. $[\alpha]_D^{20}$ = +65.6° (*c* = 1.0, $CHCl_3$); IR (thin film): 714, 748, 910, 1049, 1111, 1200, 1269, 1450, 1724, 2932, 3472; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): 8.07 –

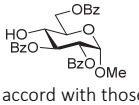
8.00 (m, 2H, CH_{arom}), 7.62 – 7.56 (m, 1H, CH_{arom}), 7.50 – 7.41 (m, 2H, CH_{arom}), 7.28 – 7.22 (m, 5H, CH_{arom}), 5.58 (t, 1H, *J* = 9.3 Hz, H-3), 4.79 (d, 1H, *J* = 3.4 Hz, H-1), 4.67 (d, 1H, *J* = 12.4 Hz, C*H*H Bn), 4.61 (d, 1H, *J* = 12.4 Hz, CH*H* Bn), 4.28 (d, 1H, *J* = 9.5 Hz, H-5), 3.96 (td, 1H, *J* = 9.4, 2.7 Hz, H-4), 3.80 (s, 3H, CH_3 CO_2Me), 3.70 (dd, 1H, *J* = 9.6, 3.4 Hz, H-2), 3.47 (s, 3H, CH_3 OMe), 3.28 (d, 1H, *J* = 4.3 Hz, 4-OH); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 170.4 (C=O CO_2Me), 166.8 (C=O OBz), 137.6 (C_q), 133.4, 130.0 (CH_{arom}), 129.7(C_q), 129.5, 128.6, 128.5, 128.2 (CH_{arom}), 98.4 (C-1), 76.0 (C-2), 74.3 (C-3), 73.3 (CH_2 Bn), 71.0 (C-4), 70.9 (C-5), 56.1 (OMe), 52.9 (CO_2Me); HRMS: $[M+NH_4]^+$ calcd for $C_{21}H_{28}NO_6$ 479.20643, found 479.20618.



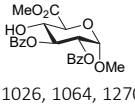
Methyl 2,3-di-*O*-benzoyl-6-*O*-benzyl-α-D-glucopyranoside (13). Methyl 2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-α-D-glucopyranoside[50] (4.68 g, 9.54 mmol) was converted to the title compound **13** following general procedure **A**. Yield: 3.74 g, 7.62 mmol, 80%. R_f 0.30 (4/1 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[51] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.02 – 7.94 (m, 4H, CH_{arom}), 7.55 – 7.27 (m, 11H, CH_{arom}), 5.74 (dd, 1H, *J* = 10.1, 8.4 Hz, H-3), 5.26 (dd, 1H, *J* = 10.2, 3.7 Hz, H-2), 5.13 (d, 1H, *J* = 3.7 Hz, H-1), 4.67 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.61 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.03 – 3.91 (m, 2H, H-5, H-4), 3.86 (dd, 1H, *J* = 10.4, 3.9 Hz, H-6), 3.81 (dd, 1H, *J* = 10.4, 3.4 Hz, H-6), 3.43 (s, 3H, CH_3 OMe), 3.02 (d, 1H, *J* = 3.5 Hz, 4-OH); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 167.5, 166.1 (C=O), 137.0 (Cq), 133.5, 133.1, 130.0 (CH_{arom}), 129.9, 129.2 (C_q), 128.6, 128.4, 128.3, 126.3 (CH_{arom}), 97.2 (C-1), 74.3 (C-3), 73.9 (CH_2 Bn), 71.6 (C-2), 70.8 (C-4), 70.3 (C-5), 69.6 (C-6), 55.6 (OMe).



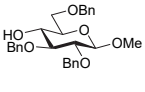
Methyl 2,3-di-*O*-benzoyl-6-deoxy-α-D-glucopyranoside (14). Methyl 2,3-di-*O*-benzoyl-α-D-glucopyranoside[50] (1.49 g, 3.7 mmol) was converted to the 6-iodo intermediate following general procedure **B**. Yield: 1.38 g, 2.7 mmol, 73%. ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.01 – 7.93 (m, 4H, CH_{arom}), 7.55 – 7.48 (m, 2H, CH_{arom}), 7.41 – 7.34 (m, 4H, CH_{arom}), 5.69 (dd, 1H, *J* = 10.1, 8.7 Hz, H-3), 5.29 (dd, 1H, *J* = 10.1, 3.7 Hz, H-2), 5.12 (d, 1H, *J* = 3.7 Hz, H-1), 3.76 – 3.63 (m, 3H, H-4, H-5, H-6), 3.49 (s, 3H, CH_3 OMe), 3.46 – 3.41 (m, 1H, H-6), 3.29 – 3.12 (m, 1H, 4-OH); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 168.0, 166.0 (C=O), 133.8, 133.6, 130.0, 130.0 (CH_{arom}), 129.2, 129.0 (C_q), 128.6, 128.6 (CH_{arom}), 97.2 (C-1), 74.4 (C-3), 73.9 (C-4), 71.3 (C-2), 70.6 (C-5), 55.8 (OMe), 6.5 (C-6). Subsequent deoxygenation gave the title compound **14**. Yield: 0.43 g, 1.12 mmol, 41%. Spectroscopic data were in accord with those previously reported.[52] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.02 – 7.93 (m, 4H, CH_{arom}), 7.56 – 7.47 (m, 2H, CH_{arom}), 7.42 – 7.32 (m, 4H, CH_{arom}), 5.65 (dd, 1H, *J* = 10.2, 9.2 Hz, H-3), 5.27 (dd, 1H, *J* = 10.1, 3.7 Hz, H-2), 5.05 (d, 1H, *J* = 3.6 Hz, H-1), 3.89 (dq, 1H, *J* = 9.5, 6.2 Hz, H-5), 3.55 (td, 1H, *J* = 9.3, 5.0 Hz, H-4), 3.43 (s, 3H, CH_3 OMe), 2.84 (d, 1H, *J* = 5.1 Hz, 4-OH), 1.40 (d, 3H, *J* = 6.2 Hz, CH_3-6); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 167.9, 166.1 (C=O), 133.6, 133.5, 130.0 (CH_{arom}), 130.0, 129.3 (Cq), 128.6, 128.5 (CH_{arom}), 97.1 (C-1), 75.4 (C-4), 74.8 (C-3), 71.7 (C-2), 67.7 (C-5), 55.4 (OMe), 17.6 (C-6).



Methyl 2,3,6-tri-*O*-benzoyl-α-D-glucopyranoside (15). Methyl 2,3-di-*O*-benzoyl-α-D-glucopyranoside[50] (2.84 g, 7 mmol) was converted to the title compound **15** following general procedure **C**. Yield: 2.3 g, 4.5 mmol, 66%. R_f 0.27 (4/1 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[53] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 – 8.05 (m, 2H, CH_{arom}), 8.03 – 7.93 (m, 4H, CH_{arom}), 7.64 – 7.12 (m, 9H, CH_{arom}), 5.79 (dd, 1H, *J* = 10.1, 9.2 Hz, H-3), 5.27 (dd, 1H, *J* = 10.2, 3.6 Hz, H-2), 5.14 (d, 1H, *J* = 3.6 Hz, H-1), 4.81 (dd, 1H, *J* = 12.1, 4.5 Hz, H-6), 4.63 (dd, 1H, *J* = 12.2, 2.3 Hz, H-6), 4.12 (ddd, 1H, *J* = 9.9, 4.5, 2.2 Hz, H-5), 3.88 (t, 1H, *J* = 9.6 Hz, H-4), 3.46 (s, 3H, CH_3 OMe), 3.39 (s, 1H, 4-OH). ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 167.5, 167.1, 166.1 (C=O), 133.6, 133.5, 133.5, 130.0, 130.0 (CH_{arom}), 129.7, 129.3, 129.2 (C_q), 128.6, 128.6, 128.5 (CH_{arom}), 97.2 (C-1), 74.0 (C-3), 71.4 (C-2), 70.2 (C-5), 69.8 (C-4), 63.6 (C-6), 55.6 (OMe).

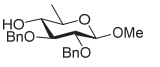


Methyl (methyl 2,3-di-*O*-benzoyl-α-D-glucopyranosyl uronate) (16). Methyl 2,3-di-*O*-benzoyl-α-D-glucopyranoside[50] (0.72 g, 1.8 mmol) was converted to the title compound **16** following general procedure **D**. Yield: 0.57 g, 1.49 mmol, 83%. $[\alpha]_D^{20}$ = +111.4° (*c* = 0.83, $CHCl_3$); IR (thin film): 710, 1026, 1064, 1270, 1452, 1701, 1719, 2895, 3486; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.03 – 7.92 (m, 4H, CH_{arom}), 7.55 – 7.30 (m, 6H, CH_{arom}), 5.85 (ddd, 1H, *J* = 11.2, 9.1, 1.7 Hz, H-3), 5.27 – 5.20 (m, 2H, H-1 H-2), 4.37 (d, 1H, *J* = 9.8 Hz, H-5), 4.16 (td, 1H, *J* = 9.6, 3.5 Hz, H-4), 3.88 (s, 3H, CH_3 CO_2Me), 3.49 (s, 3H, CH_3 OMe), 3.34 (d, 1H, *J* = 3.7 Hz, 4-OH). ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 170.4 (C=O CO_2Me), 166.7, 166.0 (C=O Bz), 133.6, 133.5, 130.0, 130.0 (CH_{arom}), 129.4, 129.1 (C_q), 128.6, 128.5 (CH_{arom}), 97.6 (C-1), 72.4 (C-3), 71.2 (C-2), 70.9 (C-4), 70.4 (C-5), 56.1 (OMe), 53.1 (CO_2Me); HRMS: $[M+Na]^+$ calcd for $C_{22}H_{22}O_9Na$ 453.1156, found 453.1165.

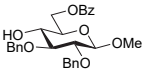


Methyl 2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (17). Methyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranoside[54] (0.69 g, 1.5 mmol) was converted to the title compound **17** following

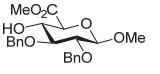
general procedure **A**. Yield: 0.45 g, 0.96 mmol, 64%. Spectroscopic data were in accord with those previously reported.[54] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.39 – 7.22 (m, 15H, CH_{arom}), 4.94 – 4.90 (m, 2H, 2xC*H*H Bn), 4.73 – 4.69 (m, 2H, 2xCH*H* Bn), 4.63 – 4.53 (m, 2H, CH_2 Bn), 4.33 (d, 1H, *J* = 7.4 Hz, H-1), 3.77 (dd, 1H, *J* = 10.4, 3.8 Hz, H-6), 3.70 (dd, 1H, *J* = 10.4, 5.3 Hz, H-6), 3.63 – 3.58 (m, 1H, H-5), 3.57 (s, 3H, CH_3 OMe), 3.50 – 3.37 (m, 3H, H-3, H-4, H-2), 2.55 (d, 1H, *J* = 2.1 Hz, 4-OH); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.7, 138.6, 138.0 (C_q), 128.7, 128.5, 128.5, 128.1, 128.1, 128.0, 127.8, 127.8, 127.8 (CH_{arom}), 104.9 (C-1), 84.1 (C-3), 81.9 (C-2), 75.4 (CH_2 Bn), 74.8(CH_2 Bn), 74.1 (C-4), 73.8 (CH_2 Bn), 71.6 (C-5), 70.4 (C-6), 57.3 (OMe).



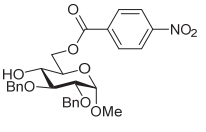
Methyl 2,3-di-*O*-benzyl-6-deoxy-β-D-glucopyranoside (18). Methyl 2,3-di-*O*-benzyl-β-D-glucopyranoside[54] (1.18 g, 3.15 mmol) was converted to the 6-iodo intermediate[55] following general procedure **B**. Yield: 1.03 g, 2.12 mmol, 67%. ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.44 – 7.18 (m, 10H, CH_{arom}), 5.01 – 4.89 (m, 2H, 2xC*H*H Bn), 4.73 – 4.58 (m, 2H, 2xCH*H* Bn), 4.38 – 4.34 (m, 1H, H-1), 3.61 (s, 3H, CH_3 OMe), 3.56 (dd, 1H, *J* = 10.6, 2.4 Hz, H-6), 3.46 – 3.41 (m, 2H, H-3, H-4), 3.37 – 3.30 (m, 1H, H-5), 3.25 (dd, 1H, *J* = 10.6, 7.8 Hz, H-2), 3.16 (ddd, 1H, *J* = 9.1, 7.8, 2.4 Hz, H-6), 2.18 (d, 1H, *J* = 2.4 Hz, OH). Subsequent deoxygenation gave the title compound **18**. Yield: 0.43 g, 1.21 mmol, 57%. $[\alpha]_D^{20}$ = -21.2° (*c* = 1.0, $CHCl_3$); IR (thin film): 698, 737, 988, 1065, 1146, 1354, 1454, 2905, 3345; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.54 – 7.03 (m, 10H, CH_{arom}), 5.00 – 4.91 (m, 2H, 2xC*H*H Bn), 4.74 – 4.61 (m, 2H, 2xCH*H* Bn), 4.33 – 4.27 (m, 1H, H-1), 3.57 (s, 3H, CH_3 OMe), 3.45 – 3.27 (m, 3H, H-3, H-2, H-5), 3.21 (ddt, 1H, *J* = 9.0, 6.7, 2.2 Hz, H-4), 1.31 (d, 3H, *J* = 6.1 Hz, CH_3 6); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.6 (C_q), 128.8, 128.5, 128.3, 128.1, 127.8 (CH_{arom}), 104.8 (C-1), 84.0 (C-2), 82.4 (C-3), 75.3 (CH_2 Bn), 75.0 (C-4), 74.7 (CH_2 Bn), 71.3 (C-5), 57.2 (OMe), 17.8 (C-6); HRMS: $[M+Na]^+$ calcd for $C_{21}H_{26}O_5Na$ 381.1672, found 381.1677.



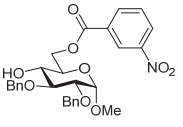
Methyl 2,3-di-*O*-benzyl-6-*O*-benzoyl-β-D-glucopyranoside (19). Methyl 2,3-di-*O*-benzyl-β-D-glucopyranoside[54] (0.56 g, 1.5 mmol) was converted to the title compound **19** following general procedure **C**. Yield: 0.70 g, 1.47 mmol, 98%. Spectroscopic data were in accord with those previously reported.[56] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.08 – 8.01 (m, 2H, CH_{arom}), 7.60 – 7.23 (m, 13H, CH_{arom}), 4.99 – 4.89 (m, 2H, 2xC*H*H Bn), 4.77 – 4.67 (m, 2H, 2xCH*H* Bn), 4.67 – 4.53 (m, 2H, H-6), 4.37 (d, 1H, *J* = 7.5 Hz, H-1), 3.62 – 3.53 (m, 5H, H-4, CH_3 OMe, H-5), 3.50 (td, 1H, *J* = 8.1, 7.2, 1.3 Hz, H-2), 3.42 (dd, 1H, *J* = 8.9, 7.5 Hz, H-3), 2.64 (s, 1H, OH); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 167.0 (C=O) 138.5, 133.3 (C_q), 130.0, 129.9 (CH_{arom}), 128.8 (C_q), 128.5, 128.5, 128.3, 128.2, 128.1, 127.9 (CH_{arom}), 105.0 (C-1), 83.8 (C-2), 81.9 (C-3), 75.6, 74.8 (CH_2 Bn), 73.7 (C-4), 70.1 (C-5), 63.9 (C-6), 57.3 (OMe).



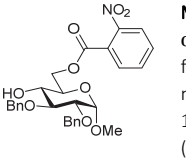
Methyl (methyl 2,3-di-*O*-benzoyl-β-D-glucopyranosyl uronate) (20). Methyl 2,3-di-*O*-benzyl-β-D-glucopyranoside[54] (745 mg, 2.0 mmol) was converted to the title compound **20** following general procedure **D**. Yield: 689 g, 1.71 mmol, 85%. Spectroscopic data were in accord with those previously reported.[57] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.37 – 7.21 (m, 10H, CH_{arom}), 4.92 – 4.84 (m, 2H, 2xC*H*H Bn), 4.80 (d, 1H, *J* = 11.3 Hz, CH*H* Bn), 4.68 (d, 1H, *J* = 11.1 Hz, CH*H* Bn), 4.34 (d, 1H, *J* = 7.5 Hz, H-1), 3.87 – 3.79 (m, 2H, H-3, H-4), 3.76 (s, 3H, CH3 CO_2Me), 3.55 (s, 3H, CH_3 OMe), 3.50 (ddd, 1H, *J* = 8.6, 6.7, 1.6 Hz, H-5), 3.42 (dd, 1H, *J* = 9.1, 7.5 Hz, H-2), 3.09 (s, 1H, 4-OH); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 169.7 (C=O CO_2Me), 138.4, 138.3 (C_q), 128.4, 128.3, 128.0, 127.9, 127.7, 127.7 (CH_{arom}), 104.9 (C-1), 83.0 (C-5), 81.1 (C-2), 75.3, 74.7 (CH_2 Bn), 74.3, 71.7 (C-3, C-4), 57.4 (OMe), 52.7 (CO_2Me).



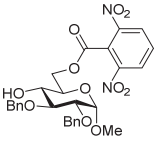
Methyl 2,3-di-*O*-benzyl-6-O-(4-nitrobenzoyl)-α-D-glucopyranoside (23). Methyl 2,3-di-*O*-benzyl-α-D-glucopyranoside[32] (374 mg, 1.0 mmol, 1 eq.) was converted to the title compound **23** following general procedure **C** (4-nitrobenzoyl chloride; 195 μL, 1.05 mmol, 1.05 eq.). Yield: 460 mg, 0.88 mmol, 88%. $[\alpha]_D^{20}$ = +28.3° (*c* = 0.6, $CHCl_3$); IR (thin film): 698, 719, 739, 1057, 1103, 1277, 1346, 1454, 1528, 1607, 1726, 2912, 3505; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 8.30 – 8.26 (m, 2H, CH_{arom} pNO_2Bz), 8.21 – 8.17 (m, 2H, CH_{arom} pNO_2Bz), 7.39 – 7.30 (m, 10H, CH_{arom} Bn), 5.04 (d, 1H, *J* = 11.3 Hz, C*H*H Bn), 4.79 (d, 1H, *J* = 12.2 Hz, C*H*H Bn), 4.73 (d, 1H, *J* = 11.3 Hz, CH*H* Bn), 4.68 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.64 (d, 1H, *J* = 3.5 Hz, H-1), 4.63 – 4.56 (m, 2H, H-6, H-6), 3.90 (ddd, 1H, *J* = 10.0, 4.6, 2.7 Hz, H-5), 3.83 (t, 1H, *J* = 9.2 Hz, H-3), 3.54 (dd, 1H, *J* = 9.5, 3.6 Hz, H-2), 3.52 (ddd, 1H, *J* = 10.0, 8.9, 2.7 Hz, H-4), 3.40 (s, 3H, CH_3 OMe), 2.43 (d, 1H, *J* = 2.8 Hz, 4-OH); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 164.8 (C=O), 150.8 (C_q NO_2), 138.6, 138.0, 135.3 (C_q), 131.0, 128.9, 128.7, 128.3, 128.2, 123.7 (CH_{arom}), 98.3 (C-1), 81.3 (C-3), 79.8 (C-2), 75.8, 73.3 (CH_2 Bn), 70.1 (C-4), 69.3 (C-5), 64.7 (C-6), 55.5 (OMe); HRMS: $[M+Na]^+$ calcd for $C_{28}H_{29}NO_9Na$ 546.1740, found 546.1748.



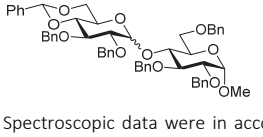
Methyl 2,3-di-*O*-benzyl-6-O-(3-nitrobenzoyl)-α-D-glucopyranoside (24). Methyl 2,3-di-*O*-benzyl-α-D-glucopyranoside[32] (300 mg, 0.8 mmol, 1 eq.) was converted to the title compound **24** following general procedure **C** (3-nitrobenzoyl chloride; 227 mg, 1.7 mmol, 1.6 eq.). Yield: 375 mg, 0.72 mmol, 90% (included 5% fully protected glycoside). $[\alpha]_D^{20}$ = +22.2° (*c* = 0.67, $CHCl_3$); IR (thin film): 698, 718, 741, 1059, 1121, 1261, 1294, 1350, 1454, 1533, 1616, 1728, 2920, 3520; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 8.83 (ddd, 1H, *J* = 2.2, 1.6, 0.4 Hz, CH_{arom} NO_2Bz), 8.39 (ddd, 1H, *J* = 8.2, 2.3, 1.1 Hz, CH_{arom} NO_2Bz), 8.33 (ddd, 1H, *J* = 7.7, 1.6, 1.2 Hz, CH_{arom} NO_2Bz), 7.62 (td, 1H, *J* = 8.0, 0.4 Hz, CH_{arom} NO_2Bz), 7.40 – 7.27 (m, 10H, CH_{arom} Bn), 5.02 (d, 1H, *J* = 11.4 Hz, C*H*H Bn), 4.78 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.74 (d, 1H, *J* = 11.4 Hz, CH*H* Bn), 4.67 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.65 (d, 1H, *J* = 3.6 Hz, H-1), 4.61 – 4.58 (m, 2H, H-6, H-6), 3.91 (dt, 1H, *J* = 10.0, 3.9 Hz, H-5), 3.86 – 3.80 (m, 1H, H-3), 3.55 (dd, 1H, *J* = 9.5, 3.6 Hz, H-2), 3.53 – 3.48 (m, 1H, H-4), 3.42 (s, 3H, CH_3 OMe), 2.59 (d, 1H, *J* = 2.7 Hz, 4-OH); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 164.6 (C=O), 148.3 (C_q NO_2), 138.6, 138.0 (C_q Bn), 135.4 (CH_{arom}), 131.7 (C_q Bz), 129.7, 128.7, 128.6, 128.2, 128.2, 128.1, 128.1, 128.1, 128.1, 127.6, 124.7 (CH_{arom}), 98.2 (C-1), 81.2 (C-3), 79.8 (C-2), 75.6, 73.3 (CH_2 Bn), 70.2 (C-4), 69.3 (C-5), 64.8 (C-6), 55.4 (OMe); HRMS: $[M+Na]^+$ calcd for $C_{28}H_{29}NO_9Na$ 546.1740, found 546.1752.



Methyl 2,3-di-*O*-benzyl-6-O-(2-nitrobenzoyl)-α-D-glucopyranoside (25). Methyl 2,3-di-*O*-benzyl-α-D-glucopyranoside[32] (374 mg, 1.0 mmol, 1 eq.) was converted to the title compound **25** following general procedure **C** (2-nitrobenzoyl chloride; 140 µL, 1.05 mmol, 1.05 eq.). Yield: 450 mg, 0.86 mmol, 86%. $[\alpha]_D^{20}$ = +15.8° (*c* = 0.6, $CHCl_3$); IR (thin film): 698, 737, 1059, 1117, 1257, 1292, 1350, 1533, 1734, 2907, 3503; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.85 – 7.81 (m, 1H, CH_{arom} NO_2Bz), 7.74 – 7.70 (m, 1H, CH_{arom} NO_2Bz), 7.64 – 7.55 (m, 2H, CH_{arom} NO_2Bz), 7.39 – 7.25 (m, 10H, CH_{arom} Bn), 4.99 (d, 1H, *J* = 11.4 Hz, C*H*H Bn), 4.78 – 4.73 (m, 2H, CH*H* Bn, C*H*H Bn), 4.64 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.62 (d, 1H, *J* = 3.5 Hz, H-1), 4.54 (d, 2H, *J* = 3.7 Hz, H-6, H-6), 3.86 – 3.78 (m, 2H, H-3, H-5), 3.51 (dd, 1H, *J* = 9.6, 3.5 Hz, H-2), 3.52 – 3.42 (m, 1H, H-4), 3.36 (s, 3H, CH_3 OMe), 2.65 (bs, 1H, 4-OH); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 165.3 (C=O), 148.3 (C_q-NO_2), 138.6, 137.9 (C_q Bn), 132.8, 132.0, 130.0, 128.6, 128.4, 128.0, 128.0, 127.9, 127.8 (CH_{arom}), 127.1 (C_q Bz), 123.8 (CH_{arom}), 98.1 (C-1), 81.1 (C-3), 79.5 (C-2), 75.4, 73.2 (CH_2 Bn), 69.9 (C-4), 69.0 (C-5), 65.3 (C-6), 55.4 (OMe); HRMS: $[M+Na]^+$ calcd for $C_{28}H_{29}NO_9Na$ 546.1740, found 546.1755.

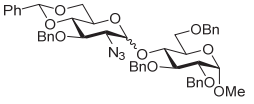


Methyl 2,3-di-*O*-benzyl-6-O-(2,6-dinitrobenzoyl)-α-D-glucopyranoside (26). Methyl 2,3-di-*O*-benzyl-α-D-glucopyranoside[32] (145 mg, 0.39 mmol, 1 eq.) was dissolved in 1.5 mL DCM and cooled to 0°C. To this solution was added 2,6-dinitrobenzoic acid (synthesized by $K_2Cr_2O_7/H_2SO_4$ oxidation of 2,6-dinitrotoluene)[58] (123 mg, 0.58 mmol, 1.5 eq.), Ph_3P (202 mg, 0.77 mmol, 2 eq.), and DEAD (~40% in toluene, ~0.8 mmol, 2 eq.). The reaction was stirred at room temperature for 2 days. The reaction mixture was diluted with H_2O and extracted with DCM twice. The combined organic layers were washed with sat. aq. $NaHCO_3$, and brine, then dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Flash column chromatography (8/2 to 7/3 pentane/EtOAc) and size-exclusion chromatography (Sephadex LH-20, 1/1 MeOH/DCM) provide the title compound as a yellow oil. Yield: 165 mg, 0.29 mmol, 74%. $[\alpha]_D^{20}$ = +22.5° (*c* = 1.25, $CHCl_3$); IR (thin film): 698, 714, 743, 918, 1057, 1279, 1454, 1582, 1748, 2920, 3493; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 8.46 (d, 2H, *J* = 8.3 Hz, CH_{arom} NO_2Bz), 7.79 (t, 1H, *J* = 8.3 Hz, CH_{arom} NO_2Bz), 7.39 – 7.26 (m, 10H, CH_{arom} Bn), 5.00 (d, 1H, *J* = 11.4 Hz, C*H*H Bn), 4.79 (dd, 1H, *J* = 11.9, 4.8 Hz, H-6), 4.77 – 4.73 (m, 2H, C*H*H Bn, CH*H* Bn), 4.66 – 4.60 (m, 3H, CH*H* Bn, H-1, H-6), 3.89 (ddd, 1H, *J* = 10.0, 4.8, 2.1 Hz, H-5), 3.86 – 3.76 (m, 1H, H-3), 3.57 – 3.50 (m, 1H, H-4), 3.49 (dd, 1H, *J* = 9.6, 3.5 Hz, H-2), 3.37 (s, 3H, CH_3 OMe), 2.51 (d, 1H, *J* = 3.3 Hz, 4-OH); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 162.6 (C=O), 146.8 (C_q NO_2), 138.7, 138.0 (C_q Bn), 131.2, 129.8, 128.7, 128.5, 128.1, 128.1, 128.0, 128.0 (CH_{arom}), 125.6 (C_q Bz), 98.3 (C-1), 81.3 (C-3), 79.6 (C-2), 75.6, 73.2 (CH_2 Bn), 69.8 (C-4), 69.0 (C-5), 66.2 (C-6), 55.6 (OMe); HRMS: $[M+Na]^+$ calcd for $C_{28}H_{28}N_2O_{11}Na$ 591.1591, found 591.1602.

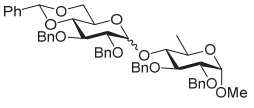


Methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranosyl)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (1A). Donor **A** and acceptor **1** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **1A** (73 mg, 82 µmol, 82%, α:β = 1:1) as a white solid. R_f: 0.55 (4/1 pentane/EtOAc); Spectroscopic data were in accord with those previously reported.[32] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 7.52 – 7.45 (m, 4H, CH_{arom}), 7.44 – 7.18 (m, 56H, CH_{arom}), 5.75 (d, 1H, J = 3.8 Hz, H-1'$_\alpha$), 5.52 (s, 1H, C*H*Ph$_\alpha$), 5.49 (s, 1H, C*H*Ph$_\beta$), 5.04 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.95 – 4.87 (m, 3H, 3xC*H*H Bn), 4.84 – 4.51 (m, 17H, 4xC*H*H Bn, 5xCH_2 Bn CH*H* Bn, H-1$_\alpha$, H-1$_\beta$), 4.36 (d, 1H, *J* = 7.8 Hz, H-1'$_\beta$), 4.30 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.19 (dd, 1H, *J* = 10.5, 5.0 Hz, H-6'$_\beta$), 4.15 – 4.09 (m, 3H, H-3$_\alpha$, H-4$_\alpha$, H-6'$_\alpha$), 3.99 (t, 1H, *J* = 9.3 Hz, H-3'$_\alpha$), 3.94 (t, 1H, *J* = 9.4 Hz, H-4$_\beta$), 3.90 –

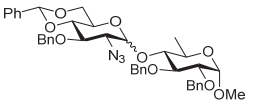
3.78 (m, 5H, H-2$_\beta$, H-5$_\alpha$, H-5'$_\alpha$, H-6$_\alpha$, H-6$_\beta$), 3.69 – 3.41 (m, 11H, H-2$_\alpha$, H-2'$_\alpha$, H-3$_\beta$, H-3'$_\beta$, H-4'$_\alpha$, H-4'$_\beta$, H-5$_\beta$, H-6$_\alpha$, H-6$_\beta$, H-6'$_\alpha$, H-6'$_\beta$), 3.40 – 3.31 (m, 7H, CH$_3$ OMe$_\alpha$, CH$_3$ OMe$_\beta$, H-2'$_\beta$), 3.10 (td, 1H, *J* = 9.5, 4.9 Hz, H-5'$_\beta$); ^{13}C-APT NMR (CDCl$_3$, 101 MHz, HSQC, HMBC): δ 139.4, 139.0, 138.7, 138.6, 138.5, 138.4, 138.2, 138.0, 137.9, 137.9, 137.6, 137.5 (C$_q$), 129.0, 128.9, 128.6, 128.5, 128.5, 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, 127.7, 127.7, 127.5, 127.5, 127.4, 127.3, 126.8, 126.1, 126.1 (CH$_{arom}$), 102.9 (C-1'$_\beta$), 101.2 (CHPh$_{\alpha,\beta}$), 98.5, 97.8 (C-1$_\alpha$, C-1$_\beta$), 97.2 (C-1'$_\alpha$), 82.7 (C-2'$_\beta$), 82.4 (C-4'$_\alpha$), 82.2 (C-3$_\alpha$), 81.8 (C-4'$_\beta$), 81.0 (C-3'$_\beta$), 80.3 (C-2$_\beta$), 80.3, 78.9 (C-2$_\alpha$, C-3'$_\alpha$), 78.8 (C-2'$_\alpha$, C-3$_\beta$), 76.9 (C-4$_\beta$), 75.6, 75.5, 75.4, 75.0, 74.4, 73.9, 73.7, 73.4, 73.4 (CH$_2$ Bn), 71.6 (C-4$_\alpha$), 70.0 (C-5$_\beta$), 69.4 (C-5$_\alpha$), 69.0, 68.9, 68.8 (C-6$_\alpha$, C-6'$_\alpha$, C-6'$_\beta$), 67.7 (C-6$_\beta$), 65.8 (C-5'$_\beta$), 63.4 (C-5'$_\alpha$), 55.5 (OMe$_\beta$), 55.3 (OMe$_\alpha$); HRMS: [M+NH$_4$]$^+$ calcd for $C_{55}H_{62}O_{11}N$ 912.43174, found 912.43282.



Methyl 4-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranosyl)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (1B). Donor **B** and acceptor **1** were condensed using the general procedure for Tf$_2$O/Ph$_2$SO mediated glycosylations (E) yielding product **1B** (mg, 88 µmol, 88% , α:β = 1:7) as a white solid. R$_f$ 0.51 α, 0.43 β (4:1 pentane/ EtOAc). Spectroscopic data were in accord with those previously reported.[11] IR (thin film): 696, 737, 1049, 1092, 1362, 1454, 2110, 2868. Data for the β-anomer: ^{1}H NMR (CDCl$_3$, 400 MHz, HH-COSY, HSQC, TOCSY): δ 7.68−7.60 (m, 2H, CH$_{arom}$), 7.52−7.18 (m, 23H, CH$_{arom}$), 5.47 (s, 1H, C*H*Ph), 4.89 (d, 1H, *J* = 11.2 Hz, C*H*H Bn), 4.87 (d, 1H, *J* = 10.9 Hz, C*H*H Bn), 4.81 (d, 1H, *J* = 10.9 Hz, CH*H* Bn), 4.78 (d, 1H, *J* = 12.2 Hz, C*H*H Bn), 4.75 (d, 1H, *J* = 11.2 Hz, CH*H* Bn), 4.71 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.63 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.60 (d, 1H, *J* = 3.7 Hz, H-1), 4.41 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.19 (d, 1H, *J* = 7.6 Hz, H-1'), 4.11 (dd, 1H, *J* = 10.6, 5.0 Hz, H-6'), 4.00 – 3.90 (m, 2H, H-4, H-6), 3.85 (t, 1H, *J* = 9.3 Hz, H-3), 3.75 (dt, 1H, *J* = 9.8, 2.4 Hz, H-5), 3.69 (dd, 1H, *J* = 10.8, 1.9 Hz, H- 6), 3.56 (t, 1H, *J* = 9.0 Hz, H-4'), 3.51 (dd, 1H, *J* = 9.5, 3.7 Hz, H-2), 3.45−3.38 (m, 4H, H-6', CH$_3$ OMe), 3.36−3.27 (m, 2H, H-2', H-3'), 3.00 (td, 1H, *J* = 9.8, 5.0 Hz, H-5'). ^{13}C-APT NMR (CDCl$_3$, 101 MHz, HSQC): δ 139.3, 138.3, 137.8, 137.8, 137.3 (C$_q$), 131.1, 129.4, 128.6, 128.4, 128.3, 128.2, 128.2, 128.1, 128.1, 127.9, 127.9, 127.6, 126.0, 124.8 (CH$_{arom}$), 101.3, 101.2 (*CH*Ph, C-1'), 98.4 (C-1), 81.7 (C-4'), 80.1 (C-3), 79.2 (C-3'), 79.0 (C-2), 76.9 (C-4), 75.4, 74.7, 73.6, 73.5 (CH$_2$ Bn), 69.7 (C-5), 68.6 (C-6'), 68.0 (C-6), 66.6 (C-2'), 65.8 (C-5'), 55.4 (OMe). Diagnostic peaks for the α-anomer: ^{1}H NMR (CDCl$_3$, 400 MHz): δ 5.71 (d, 1H, J = 4.0 Hz, H-1'), 5.53 (s, 1H, C*H*Ph), 5.11 (d, 1H, J = 10.7 Hz, C*H*H Bn), 4.95 (d, 1H, J = 10.9 Hz, C*H*H Bn). ^{13}C-APT NMR (CDCl$_3$, 101 MHz): δ 98.1, 97.8, 82.7, 82.1, 80.5, 76.2, 75.1, 73.3, 73.0, 69.4, 69.1, 68.7, 63.4, 62.9; HRMS: [M+Na]$^+$ calcd for $C_{48}H_{51}N_3O_{10}Na$ 852.34667, found 852.34668.

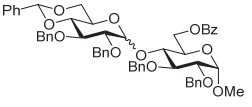


Methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranosyl)-2,3-di-*O*-benzyl-6-deoxy-α-D-glucopyranoside (2A). Donor **A** and acceptor **2** were condensed using the general procedure for Tf$_2$O/Ph$_2$SO mediated glycosylations (E) yielding product **2A** (67 mg, 85 µmol, 85%, α:β = 2:1) as a colorless oil. R$_f$: 0.50 (4/1 pentane/EtOAc); IR (thin film): 698, 737, 910, 995, 1029, 1049, 1088, 1369, 1454, 2870, 3032; Data reported for a 2:1 mixture of anomers. ^{1}H NMR (CDCl$_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 7.65 – 6.84 (m, 37.5H, CH$_{arom}$), 5.76 (d, 1H, *J* = 4.1 Hz, H-1'$_\alpha$), 5.55 (s, 1H, C*H*Ph$_\alpha$), 5.50 (s, 0.5H, C*H*Ph$_\beta$), 5.02 (d, 1H, *J* = 11.8 Hz, C*H*H Bn$_\alpha$), 4.96 – 4.88 (m, 2H, 2xCH*H* Bn$_\beta$, C*H*H Bn$_\alpha$), 4.87 – 4.81 (m, 1.5H, CH*H* Bn$_\beta$, CH*H* Bn$_\alpha$), 4.81 – 4.62 (m, 6.0H, CH*H* Bn$_\beta$, 2xC*H*H Bn$_\alpha$, 2xCH$_2$ Bn$_\beta$, CH$_2$ Bn$_\alpha$, H-1'$_\beta$), 4.55 (d, 1H, *J* = 12.0 Hz, CH*H* Bn$_\alpha$), 4.57 – 4.47 (m, 2.5H, CH*H* Bn$_\alpha$, H-1$_\alpha$, H-1$_\beta$), 4.26 (dd, 1H, *J* = 10.3, 4.8 Hz, H-6'$_\alpha$), 4.16 (dd, 1H, *J* = 10.5, 5.0 Hz, H-6'$_\beta$), 4.08 – 3.99 (m, 2H, H-3$_\alpha$, H-3'$_\alpha$), 3.98 – 3.78 (m, 2H, H-5$_\alpha$, H-5'$_\alpha$), 3.78 – 3.66 (m, 2H, H-4'$_\beta$, H-6'$_\alpha$, H-5$_\beta$), 3.63 (m, 2H, m, H-4$_\alpha$, H-4'$_\alpha$), 3.58 – 3.50 (m, 2.5H, H-2'$_\alpha$, H-2$_\alpha$, H-2$_\beta$), 3.50 – 3.40 (m, 1.5H, H-6'$_\beta$, H-4$_\beta$, H-2'$_\beta$), 3.39 (s, 1.5H, CH$_3$ OMe$_\beta$), 3.37 (s, 3H, CH$_3$ OMe$_\alpha$), 3.29 (td, 0.5H, *J* = 9.7, 4.9 Hz, H-5'$_\beta$), 1.34 (d, 3H, *J* = 6.2 Hz, H-6$_\alpha$), 1.27 (d, 1.5H, *J* = 6.4 Hz, H-6$_\beta$); ^{13}C-APT NMR (CDCl$_3$, 101 MHz, HSQC, HMBC): δ 139.1, 138.7, 138.6, 138.4, 138.3, 138.0, 137.4 (C$_\alpha$), 129.0, 129.0, 128.5, 128.4, 128.3, 128.1, 127.7, 127.2, 126.6, 126.1, 126.1(CH$_{arom}$), 103.7(C-1'$_\beta$), 101.2(CHPh$_\alpha$), 101.2 (CHPh$_\beta$), 98.1 (C-1$_\beta$) , 97.9 (C-1'$_\alpha$), 97.6 (C-1$_\alpha$), 83.8 (C-4$_\beta$), 82.8 (C-2'$_\beta$), 82.3 (C-4$_\alpha$), 81.8 (C-3$_\alpha$), 81.4 (C-4'$_\beta$), 80.7 (C-2'$_\alpha$), 80.0 (C-3$_\beta$), 79.5 (C-3'$_\beta$), 79.0 (C-3'$_\alpha$), 78.8 (C-4'$_\alpha$), 78.3 (C-2$_\alpha$), 75.8, 75.5, 75.4, 75.2, 74.2, 74.0, 73.6, 73.3 (CH$_2$ Bn), 68.9 (C-6'$_\alpha$), 68.8 (C-6'$_\beta$), 66.6 (C-5$_\beta$), 66.0 (C-5'$_\beta$), 65.7 (C-5$_\alpha$), 63.3 (C-5'$_\alpha$), 55.4 (OMe$_\beta$), 55.2 (OMe$_\alpha$), 19.2 (C-6$_\alpha$), 18.0 (C-6$_\beta$); HRMS: [M+NH$_4$]$^+$ calcd for $C_{48}H_{56}NO_{10}$ 806.38987, found 806.39030.

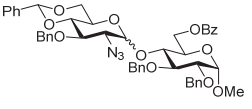


Methyl 4-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranosyl)-2,3-di-*O*-benzyl-6-deoxy-α-D-glucopyranoside (2B). Donor **B** and acceptor **2** were condensed using the general procedure for Tf$_2$O/Ph$_2$SO mediated glycosylations (E) yielding product **2B** (50 mg, 69 µmol, 69%, α:β = 1:5) as a white solid. R$_f$: 0.50 (4/1 pentane/EtOAc); IR (thin film): 698, 737, 999, 1049, 1092, 1177, 1277, 1366, 1454, 2110, 2912, 3032; Data for the β-anomer: ^{1}H NMR (CDCl$_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 7.51 – 7.20 (m, 20H, CH$_{arom}$), 5.48 (s, 1H, C*H*Ph), 4.94 –

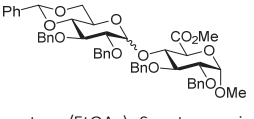
4.69 (m, 5H, 2xCH$_2$ Bn, C*H*H Bn), 4.66 – 4.58 (m, 1H, CH*H* Bn), 4.54 – 4.46 (m, 2H, H-1, H-1'), 4.07 – 3.98 (m, 1H, H-6'), 3.89 – 3.82 (m, 1H, H-3), 3.79 (dd, 1H, *J* = 9.7, 6.2 Hz, H-5), 3.63 (t, 1H, *J* = 9.1 Hz, H-4'), 3.57 (t, 1H, *J* = 9.1 Hz, H-3'), 3.51 – 3.48 (m, 1H, H-2), 3.48 – 3.39 (m, 3H, H-6', H-2', H-4), 3.38 (s, 3H, CH$_3$ OMe), 3.25 – 3.16 (m, 1H, H-5'), 1.35 (d, 3H, *J* = 6.2 Hz, H-6); ^{13}C-APT NMR (CDCl$_3$, 101 MHz, HSQC, HMBC): δ 139.4, 138.3, 137.8, 137.2 (C$_q$), 129.2, 128.5, 128.4, 128.3, 128.3, 128.2, 128.0, 128.0, 127.4, 127.2, 126.1 (CH$_{arom}$), 102.4 (C-1'), 101.3 (C*H*Ph), 97.9 (C-1), 84.0 (C-4), 81.7 (C-4'), 80.1 (C-3), 79.7 (C-2), 79.5 (C-3'), 75.3, 75.0, 73.5 (CH$_2$ Bn), 68.5 (C-6'), 67.2 (C-2'), 66.2 (C-5), 66.2 (C-5'), 55.3 (OMe), 18.1 (C-6); Diagnostic peaks for the α-anomer: ^{1}H NMR (CDCl$_3$, 400 MHz): δ 5.66 (d, 1H, *J* = 4.2 Hz, H-1'), 5.57 (s, 1H, C*H*Ph), 5.10 (d, 1H, *J* = 10.6 Hz), 4.98 (d, 1H, *J* = 10.9 Hz), 4.22 (dd, 1H, *J* = 10.4, 4.9 Hz, H-6'), 3.92 (td, 1H, *J* = 10.1, 4.9 Hz, H-5'), 3.31 (dd, 1H, *J* = 10.1, 4.2 Hz, H-2'), 1.30 (d, 3H, *J* = 6.2 Hz, H-6); ^{13}C-APT NMR (CDCl$_3$, 101 MHz): δ 101.3, 98.8, 97.7, 82.6, 80.9, 79.9, 76.3, 75.2, 75.1, 73.3, 68.6, 65.5, 63.3, 62.8, 18.8; HRMS: [M+NH$_4$]$^+$ calcd for $C_{41}H_{49}N_4O_9$ 741.34941, found 741.34989.



Methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranosyl)-2,3-di-*O*-benzyl-6-*O*-benzoyl-α-D-glucopyranoside (3A). Donor **A** and acceptor **3** were condensed using the general procedure for Tf$_2$O/Ph$_2$SO mediated glycosylations (E) yielding product **3A** (84 mg, 92 µmol, 92%, α:β = 5:1) as a colorless oil. R$_f$: 0.49 (4/1 pentane/EtOAc); IR (thin film): 737, 999, 1026, 1049, 1092, 1273, 1454, 1721, 2928; Data for the α-anomer: ^{1}H NMR (CDCl$_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 8.10 – 8.00 (m, 2H, CH$_{arom}$), 7.59 – 7.11 (m, 28H, CH$_{arom}$), 5.73 (d, 1H, *J* = 4.0 Hz, H-1'$_\alpha$), 5.47 (s, 1H, C*H*Ph), 4.99 (d, 1H, *J* = 11.5 Hz, C*H*H Bn), 4.89 (d, 1H, *J* = 11.1 Hz, C*H*H Bn), 4.80 (d, 1H, *J* = 8.3 Hz, C*H*H Bn), 4.76 – 4.69 (m, 3H, 2xCH*H* Bn, H-6), 4.66 (d, 1H, *J* = 8.7 Hz, C*H*H Bn), 4.60 (d, 1H, *J* = 3.5 Hz, H-1), 4.59 – 4.50 (m, 3H, 2xCH*H* Bn, H-6), 4.16 – 4.08 (m, 1H, H-3), 4.07 (m, 4H, H-5, H-3', H-4, H-6'), 3.81 (td, 1H, *J* = 9.9, 4.7 Hz, H-5'), 3.63 – 3.52 (m, 4H, H-2, H-4', H-6', H-2'), 3.39 (s, 3H, CH$_3$ OMe); ^{13}C-APT NMR (CDCl$_3$, 101 MHz, HSQC, HMBC): δ 166.2 (C=O), 138.9, 138.6, 137.8, 137.4 (C$_q$), 133.2 (CH$_{arom}$), 129.9 (C$_q$), 129.8, 128.9, 128.5, 127.7, 126.9, 126.2, 126.1 (CH$_{arom}$), 101.3 (CHPh), 98.2 (C-1'), 97.6 (C-1), 82.4 (C-2), 81.7 (C-3), 80.4 (C-4') , 78.7 (C-3'), 78.7 (C-2'), 75.3, 74.6, 74.2 (CH$_2$ Bn), 73.7 (C-4), 73.4 (CH$_2$ Bn), 68.8 (C-6'), 68.1 (C-5), 63.7 (C-5'), 62.8 (C-6), 55.4 (OMe); Diagnostic peaks β-anomer: ^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.99 – 7.94 (m, 2H), 5.51 (s, 1H), 4.46 (dd, 1H, *J* = 12.1, 4.7 Hz), 4.19 (dd, 1H, *J* = 10.5, 5.0 Hz), 3.32 – 3.18 (m, 1H, H-5'$_\beta$); ^{13}C-APT NMR (CDCl$_3$, 101 MHz): δ 166.0, 139.1, 138.3, 138.2, 137.3, 129.6, 128.3, 127.3, 103.3, 101.2, 98.0, 82.7, 81.4, 80.1, 77.8, 75.8, 68.7, 66.1, 63.7, 41.1; HRMS: [M+NH$_4$]$^+$ calcd for $C_{55}H_{60}NO_{12}$ 926.41100, found 926.41196.

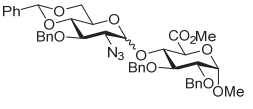


Methyl 4-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranosyl)-2,3-di-*O*-benzyl-6-*O*-benzoyl-α-D-glucopyranoside (3B). Donor **B** and acceptor **3** were condensed using the general procedure for Tf$_2$O/Ph$_2$SO mediated glycosylations (E) yielding product **3B** (61 mg, 67 µmol, 67%, α:β = 1:1.1) as a colorless oil. R$_f$: 0.50 (4/1 pentane/EtOAc); IR (thin film): 698, 741, 914, 999, 1030, 1092, 1273, 1369, 1454, 1721, 2110, 2870, 3032; Data reported for a 0.9:1 mixture of anomers. ^{1}H NMR (CDCl$_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 8.04 (ddd, 3.8H, *J* = 8.4, 6.7, 1.4 Hz, CH$_{arom}$), 7.61 – 7.15 (m, 43.7H, CH$_{arom}$), 5.71 (d, 0.9H, *J* = 4.2 Hz, H-1'$_\alpha$), 5.50 (s, 0.9H, C*H*Ph$_\alpha$), 5.49 (s, 1H, C*H*Ph$_\beta$), 5.13 (d, 1H, *J* = 10.4 Hz, C*H*H Bn), 5.00 – 4.83 (m, 5H, CH*H* Bn, 2xCH$_2$ Bn, C*H*H Bn), 4.83 – 4.68 (m, 4.9H, H-6$_\alpha$, H-6$_\beta$, CH*H* Bn, 2xCH*H* Bn), 4.68 – 4.54 (m, 4.8H, 2xCH*H* Bn, H-6$_\alpha$, H-1$_\alpha$, H-1$_\beta$), 4.51 – 4.40 (m, 2H, H-6$_\beta$, H-1'$_\beta$), 4.13 (dd, 1H, *J* = 9.5, 8.4 Hz, H-3$_\beta$), 4.08 – 3.88 (m, 7.5H, H-3$_\alpha$, H-3'$_\alpha$, H-4$_\beta$, H-4$_\alpha$, H-5$_\alpha$, H-5$_\beta$, H-6'$_\alpha$, H-6'$_\beta$), 3.83 (td, 0.9H, *J* = 9.9, 4.8 Hz, H-5'$_\alpha$), 3.71 – 3.51 (m, 5H, H-2$_\alpha$, H-2$_\beta$, H-3'$_\beta$, H-4'$_\beta$ H-4'$_\beta$, H-6'$_\alpha$), 3.49 (t, 1H, *J* = 10.3 Hz, H-6'$_\beta$), 3.46 – 3.41 (m, 1H, H-2'$_\beta$), 3.41 (s, 3H, CH$_3$ OMe$_\beta$), 3.40 (s, 2.7H, CH$_3$ OMe$_\alpha$), 3.35 (dd, 0.9H, *J* = 10.1, 4.2 Hz, H-2'$_\alpha$), 3.22 – 3.10 (m, 1H, H-5'$_\beta$); ^{13}C-APT NMR (CDCl$_3$, 101 MHz, HSQC, HMBC): δ 166.2, 166.1 (C=O), 139.1, 138.6, 138.2, 137.9, 137.8, 137.7, 137.2, 137.1 (C$_q$), 133.4, 133.3 (CH$_{arom}$), 129.9 (C$_q$), 129.7, 129.2, 129.1, 128.7, 128.6, 128.6, 128.6, 128.5, 128.5, 128.4, 128.3, 128.3, 128.3, 128.2, 128.2, 128.1, 128.0, 128.0, 127.9, 127.8, 127.6, 127.5, 126.1, 126.0 (CH$_{arom}$), 102.0 (C-1'$_\beta$), 101.4 (CHPh$_\alpha$), 101.3 (CHPh$_\beta$), 99.0 (H-1$_\alpha$), 98.0, 97.7 (C-1$_\alpha$, C-1$_\beta$), 82.7 (C-4'$_\alpha$), 81.6, 81.6 (C-3$_\beta$, C-4'$_\beta$), 80.8 (C-2$_\alpha$), 80.1 (C-3$_\alpha$), 79.7 (C-3'$_\beta$), 79.6, (C-2$_\beta$), 78.0 (C-4$_\beta$), 76.1 (C-3'$_\alpha$), 75.7, 75.3, 75.2, 75.1 (CH$_2$ Bn), 74.9 (C-4$_\alpha$), 73.6, 73.4 (CH$_2$ Bn), 68.6, 68.5 (C-6'$_{\alpha,\beta}$) , 68.5, 68.0 (C-5$_\alpha$, C-5$_\beta$), 66.8 (C-2'$_\beta$), 66.3 (C-5'$_\beta$), 63.7 (C-5'$_\alpha$), 63.5 (C-6$_\beta$), 63.1 (C-6$_\alpha$), 62.8 (C-2'$_\alpha$), 55.6 (OMe$_\beta$), 55.5 (OMe$_\alpha$); HRMS: [M+Na]$^+$ calcd for $C_{48}H_{49}N_3O_{11}Na$ 866.3290, found 866.3259.

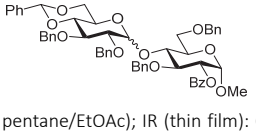


Methyl (methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranosyl)-2,3-di-*O*-benzyl-α-D-glucopyranosyl uronate) (4A). Donor **A** and acceptor **4** were condensed using the general procedure for Tf$_2$O/Ph$_2$SO mediated glycosylations (E) yielding product **4A** (75.2 mg, 90 µmol, 90%, α:β = 5:1) as a white solid. R$_f$: 0.77 (7/3 pentane/EtOAc); Spectroscopic data were in accord with those previously reported.[32] IR (thin film): 694, 732, 912, 988, 1026, 1043, 1074, 1086, 1358, 1454, 1749, 28866, 2932; Data for the α-anomer: ^{1}H NMR (CDCl$_3$, 400 MHz, HH-

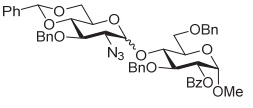
COSY, HSQC, HMBC): δ 7.48 – 7.43 (m, 2H, CH_{arom}), 7.40 – 7.16 (m, 23H, CH_{arom}), 5.51 (s, 1H, C*H*Ph), 5.44 (d, 1H, *J* = 3.8 Hz, H-1'), 4.95 – 4.86 (m, 3H, CH_2 Bn, C*H*H Bn), 4.78 (d, 1H, *J* = 11.2 Hz, CH*H* Bn), 4.71 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.67 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.59 – 4.53 (m, 3H, 2xCH*H* Bn, H-1), 4.28 (dd, 1H, *J* = 6.5, 3.8 Hz, H-6'), 4.25 (d, 1H, *J* = 9.5 Hz, H-5), 4.11 (t, 1H, *J* = 9.1 Hz, H-4), 4.05 (t, 1H, *J* = 8.9 Hz, H-3), 3.98 (t, 1H, *J* = 9.1 Hz, H-3'), 3.76 (s, 3H, CH_3 CO_2Me), 3.64 (t, 1H, *J* = 10.0 Hz, H-6'), 3.61 – 3.54 (m, 3H, H-2, H-4', H-5'), 3.48 (dd, 1H, *J* = 5.6, 3.9 Hz, H-2'), 3.40 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 170.1 (C=O CO_2Me), 139.0, 138.6, 138.0, 137.8, 137.6 (C_q), 129.0, 128.6, 128.4, 128.4, 128.3, 128.3, 128.3, 128.2, 128.1, 128.1, 127.8, 127.7, 127.7, 127.3, 127.0, 126.1 (CH_{arom}), 101.3 (CHPh), 98.6 (C-1), 98.4 (C- 1'), 82.0 (C-4'), 80.8 (C-3), 79.2 (C-2), 78.7 (C-2'), 78.4 (C-3'), 76.1 (C-4), 75.3, 75.0, 73.7, 73.7 (CH_2 Bn), 70.3 (C-5), 68.6 (C-6'), 63.1 (C-5'), 55.8 (OMe), 52.9 (CO_2Me); ^{13}C-HMBC NMR ($CDCl_3$, 101 MHz): δ 98.4 ($J_{C1',H1'}$ = 174 Hz, C-1'$_\alpha$); Diagnostic peaks β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.47 (s, 1H, C*H*Ph), 4.62 (d, 1H, *J* = 12.1 Hz), 3.87 (dd, 1H, J = 9.6, 8.4 Hz), 3.50 (s, 3H, CH_3 CO_2Me), 3.44 (s, 0.54H, CH_3 OMe), 3.38 – 3.28 (m, 2H, H-2', H-5'); ^{13}CAPT NMR ($CDCl_3$, 101 MHz): δ 170.1, 139.2, 138.6, 138.2, 137.4, 129.0, 128.5, 128.3, 128.1, 127.7, 127.5, 126.1, 102.9 (C- 1'), 101.2 (CHPh), 99.0 (C-1), 82.3, 81.8, 81.3, 79.6, 78.5, 78.2, 75.6, 75.5, 75.2, 73.9, 70.0, 68.8, 65.9, 55.9, 52.7; ^{13}C-HMBC NMR ($CDCl_3$, 101 MHz): δ 102.9 ($J_{C1',H1'}$ = 164 Hz, C-1'$_\beta$); HRMS: $[M+Na]^+$ calcd for $C_{49}H_{52}O_{12}Na$ 855.33510, found 855.33496.



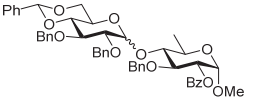
Methyl (methyl 4-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranosyl)-2,3-di-*O*-benzyl-α-D-glucopyranosyl uronate (4B). Donor **B** and acceptor **4** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **4B** (mg, 93 μmol, 93%, α:β = 1.1 :1) as a white solid. R_f 0.54 (4:1 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[11] IR (thin film): 696, 735, 914, 989, 1028, 1045, 1090, 1267, 1369, 1454, 1749, 2108, 2870, 2916. Data reported for a 1:1 mixture of anomers: ^{1}H NMR ($CDCl_3$, 400 MHz, H–H COSY, HSQC, HMBC): δ 7.48–7.41 (m, 4H, CH_{arom}), 7.41–7.24 (m, 36H, CH_{arom}), 5.53 (s, 1H, C*H*Ph$_\alpha$), 5.51 (d, 1H, J = 3.9 Hz, H-1'$_\alpha$), 5.47 (s, 1H, C*H*Ph$_\beta$), 5.04 (d, 1H, J = 10.5 Hz, C*H*H Bn), 4.94 (d, 1H, J = 11.0 Hz, C*H*H Bn), 4.91–4.82 (m, 4H, 2xCH*H* Bn, 2xC*H*H Bn), 4.81–4.72 (m, 4H, 2xCH*H* Bn, 2xC*H*H Bn), 4.64–4.58 (m, 2H, 2xCH*H* Bn), 4.57 (d, 2H, *J* = 3.5 Hz, H-1$_{\alpha,\beta}$), 4.43 (d, 1H, J = 8.1 Hz, H-1'$_\beta$), 4.26 (dd, 1H, J = 10.3, 4.8 Hz, H-6'$_\alpha$), 4.24–4.19 (m, 2H, H-5α, H-5$_\beta$), 4.09–3.99 (m, 4H, H-3$_\beta$, H-4$_\alpha$, H-4$_\beta$, H-6'$_\beta$), 3.97 (t, 1H, J = 9.5 Hz, H-3'$_\alpha$), 3.89 (t, 1H, J = 9.2 Hz, H-3$_\alpha$), 3.82 (s, 3H, CH_3 CO_2Me), 3.81 (s, 3H, CH_3 CO_2Me), 3.72–3.56 (m, 4H, H-2$_\beta$, H-4'$_\alpha$, H-4'$_\beta$, H-6'$_\alpha$), 3.56–3.46 (m, 3H, H-2$_\alpha$, H-3'$_\beta$, H-5'$_\alpha$), 3.46–3.38 (m, 7H, 2×CH_3 OMe$_{\alpha,\beta}$, H-6'$_\beta$), 3.36–3.29 (m, 2H, H-2'$_\alpha$, H-2'$_\beta$), 3.26 (td, 1H, J = 9.7, 5.0 Hz, H-5'$_\beta$). ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 170.0, 170.0 (C=O), 139.1, 138.5, 138.0, 137.9, 137.9, 137.8, 137.4, 137.2 (C_q), 129.2, 129.1, 128.7, 128.6, 128.5, 128.5, 128.4, 128.3, 128.3, 128.3, 128.3, 128.2, 128.1, 128.0, 128.0, 127.8, 127.7, 127.5, 127.4, 126.1, 126.1 (CH_{arom}), 102.3 (C-1'β), 101.4 (CHPh$_\beta$), 101.3 (CHPh$_\alpha$), 98.9, 98.6 (C-1$_\alpha$, C-1$_\beta$), 98.5 (C-1'$_\alpha$), 82.4 (C-4'$_\alpha$), 81.6 (C-4'$_\beta$), 81.1 (C-3$_\beta$), 79.6 (C-2$_\beta$, C-4$_\beta$), 79.5 (C-3$_\alpha$), 79.4 (C-3'$_\beta$), 78.7 (C-2$_\alpha$), 76.3 (C-3'$_\alpha$), 75.6 (CH_2 Bn), 75.5 (C-4$_\alpha$), 75.1, 75.0, 73.9, 73.7 (CH_2 Bn), 70.0, 69.9 (C-5$_\alpha$, C-5$_\beta$), 68.5, 68.5 (C-6$_\alpha$, C-6$_\beta$), 66.7 (C-2'$_\beta$), 66.2 (C-5'$_\beta$), 63.0 (C-5'$_\alpha$), 62.8 (C-2'$_\alpha$), 55.9, 55.9 (OMe), 53.0, 52.8 (CO_2Me); HRMS: $[M+NH_4]^+$ calcd for $C_{42}H_{49}N_4O_{11}$ 785.33923, found 785.34007.



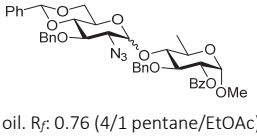
Methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranosyl)-2-*O*-benzoyl-3,6-di-*O*-benzyl-α-D-glucopyranoside (5A). Donor **A** and acceptor **5** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **5A** (74 mg, 81 μmol, 81%, α:β = 1:1.1) as a white solid. R_f: 0.50 (4/1 pentane/EtOAc); IR (thin film): 696, 737, 916, 995, 1047, 1088, 1271, 1366, 1452, 1721, 2926; Data reported for a 1:1.1 mixture of anomers: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 8.02 (td, 4H, *J* = 8.2, 1.4 Hz, CH_{arom}), 7.60 – 6.99 (m, 56H, CH_{arom}), 5.64 (d, 1H, *J* = 3.8 Hz, H-1'$_\alpha$), 5.54 (s, 1H, C*H*Ph$_\alpha$), 5.49 (s, 1.1H, C*H*Ph$_\beta$), 5.18 (dd, 1H, *J* = 9.7, 3.7 Hz, H-2$_\alpha$), 5.11 – 5.02 (m, 3.2H, H-2$_\beta$, H-1$_\beta$, H-1$_\alpha$), 4.96 – 4.55 (m, 15.7H, 7xCH_2 Bn, C*H*H Bn$_\beta$), 4.45 (d, 1.1H, *J* = 7.8 Hz, H-1'$_\beta$), 4.38 (d, 1.1H, *J* = 12.0 Hz, CH*H* Bn$_\beta$), 4.32 (t, 1H, *J* = 9.2 Hz, H-3$_\alpha$), 4.25 (t, 1H, *J* = 9.0 Hz, H-4$_\alpha$), 4.21 – 4.08 (m, 3.2H, H-6α, H-6'$_\beta$, H-3$_\beta$), 4.08 – 3.99 (m, 2.1H, H-3'$_\alpha$, H-3$_\beta$), 3.99 – 3.82 (m, 4.1H, H-5'$_\alpha$, H-6$_\alpha$, H-6$_\beta$, H-5$_\alpha$), 3.78 – 3.66 (m, 2.2H, H-6$_\alpha$, H-5$_\beta$), 3.63 – 3.49 (m, 6.3H, H-6$_\beta$, H-4'$_\beta$, H-4$_\beta$, H-4'$_\alpha$, H-6$_\alpha$, H-2'$_\alpha$), 3.45 (t, 1.1H, *J* = 10.3 Hz, H-6'$_\beta$), 3.41 – 3.38 (m, 7.4H, H-2'$_\beta$, CH_3 OMe$_\beta$, CH_3 OMe$_\alpha$), 3.20 – 3.09 (m, 1.1H, H-5'$_\beta$); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 166.0, 165.9 (C=O), 138.8, 138.8, 138.6, 138.5, 138.3, 138.3, 138.1, 138.0, 137.7 (C_q), 133.3, 133.2, 129.9, 129.9 (CH_{arom}), 129.7 (C_q), 129.1, 129.0, 128.6, 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.1, 128.0, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7, 127.6, 127.6, 127.5, 127.4, 127.0, 126.2 (CH_{arom}), 103.0 (C-1'$_\beta$), 101.2 (CHPh$_{\alpha,\beta}$), 97.7 (C-1'$_\alpha$), 97.3 (C-1$_\alpha$), 97.0 (C-1$_\beta$), 82.7 (C-2'$_\beta$), 82.4 (C-4'$_\alpha$), 81.9 (C-4'$_\beta$), 81.1 (C-3'$_\beta$), 80.6 (C-3$_\alpha$), 79.0 (C-2'$_\alpha$), 78.8 (C-3'$_\alpha$), 77.9 (C-3$_\beta$), 76.9 (C-4$_\beta$), 75.6, 75.4, 75.3, 75.1 (CH_2 Bn), 74.2 (C-2$_\alpha$), 74.1, 73.8, 73.6, 73.5 (CH_2 Bn), 73.4 (C-2$_\beta$), 72.7 (C-4$_\alpha$), 70.3 (C-5$_\beta$), 69.8 (C-5$_\alpha$), 69.0, 68.8, 68.8 (C-6'$_{\alpha,\beta}$, C-6$_\beta$), 67.6 (C-6$_\alpha$), 65.8 (C-5'$_\beta$), 63.5 (C-5'$_\alpha$), 55.5 (OMe$_\alpha$), 55.3 (OMe$_\beta$); HRMS: $[M+NH_4]^+$ calcd for $C_{55}H_{60}NO_{12}$ 926.41100, found 926.41192.



Methyl 4-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranosyl)-2-*O*-benzoyl-3,6-di-*O*-benzyl-α-D-glucopyranoside (5B). Donor **B** and acceptor **5** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **5B** (74 mg, 88 µmol, 88%, α:β = 1:6) as a light yellow oil. R_f: 0.50 (4/1 pentane/EtOAc); IR (thin film): 698, 737, 999, 1092, 1173, 1273, 1366, 1454, 1721, 2110, 2870; Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 8.05 – 7.98 (m, 2H, CH_{arom}), 7.60 – 7.10 (m, 23H, CH_{arom}), 5.47 (s, 1H, C*H*Ph), 5.12 – 5.03 (m, 2H, H-1, H-2), 4.90 (d, 1H, *J* = 11.2 Hz, C*H*H Bn), 4.85 (d, 1H, *J* = 11.0 Hz, C*H*H Bn), 4.78 (d, 1H, *J* = 4.3 Hz, C*H*H Bn), 4.75 (d, 1H, *J* = 3.5 Hz, CH*H* Bn), 4.70 (d, 1H, *J* = 11.0 Hz, CH*H* Bn), 4.47 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.29 – 4.24 (m, 1H, H-1'), 4.17 – 4.00 (m, 4H, H-3, H-6', H-3', H-6), 3.86 (dt, 1H, *J* = 9.4, 2.3 Hz, H-5), 3.77 (dd, 1H, *J* = 11.0, 1.8 Hz, H-6), 3.60 – 3.54 (m, 1H, H-4'), 3.44 – 3.34 (m, 2H, H-3', H-6', H-2', CH_3 OMe), 3.03 (td, 1H, *J* = 9.8, 5.0 Hz, H-5'); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 165.9 (C=O), 138.7, 137.9, 137.3 (C_q), 133.3, 129.9 (CH_{arom}), 129.8 (C_q), 129.2, 128.7, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 127.7, 127.5, 126.1 (CH_{arom}), 101.3, 101.3 (C-1', CHPh), 97.3 (C-1), 81.8 (C-4'), 79.2 (C-3'), 77.9 (C-3), 76.9 (C-4), 75.3, 74.9, 73.6 (CH_2 Bn), 73.5 (C-2), 70.0 (C-5), 68.6 (C-6'), 67.9 (C-6), 66.7 (C-2'), 65.9 (C-5'), 55.5 (OMe); Diagnostic peaks for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.11 – 8.06 (m, 2H), 5.68 (d, 1H, *J* = 4.0 Hz, H-1'), 5.55 (s, 1H, C*H*Ph), 5.17 (dd, 1H, *J* = 9.8, 3.6 Hz, H-2), 4.98 (d, 1H, *J* = 10.9 Hz), 4.33 (dd, 1H, *J* = 9.8, 8.7 Hz), 3.67 (t, 1H, *J* = 9.3 Hz); ^{13}C-APT NMR ($CDCl_3$, 101 MHz): δ 165.9, 138.2, 137.9, 137.4, 133.4, 129.6, 129.1, 128.6, 127.6, 98.2, 97.1, 82.7, 80.9, 76.3, 75.2, 75.0, 74.7, 69.7, 69.1, 68.8, 63.5, 62.9; HRMS: $[M+NH_4]^+$ calcd for $C_{48}H_{51}N_4O_{12}$ 861.37053, found 861.37082.

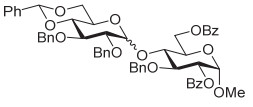


Methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranosyl)-2-*O*-benzoyl-3-*O*-benzyl-6-deoxy-α-D-glucopyranoside (6A). Donor **A** and acceptor **6** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **6A** (69 mg, 86 µmol, 86%, α:β = 1.1:1) as a white solid. R_f: 0.55 (4/1 pentane/EtOAc); IR (thin film): 696, 737, 995, 1051, 1086, 1273, 1366, 1452, 1720, 2932; Data reported for a 1.1:1 mixture of anomers: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.05 – 8.01 (m, 2H, CH_{arom}), 8.01 – 7.95 (m, 2.2H, CH_{arom}), 7.60 – 7.16 (m, 42.8H, CH_{arom}), 7.14 – 7.08 (m, 3.3H, CH_{arom}), 7.04 – 6.97 (m, 2.2H, CH_{arom}), 5.66 (d, 1.1H, *J* = 4.0 Hz, H-1'$_\alpha$), 5.57 (s, 1.1H, C*H*Ph$_\alpha$), 5.50 (s, 1H, C*H*Ph$_\beta$), 5.12 (dd, 1.1H, *J* = 9.9, 3.7 Hz, H-2$_\alpha$), 5.06 (dd, 1H, *J* = 10.0, 3.8 Hz, H-2$_\beta$) 4.97 (d, 1.1H, *J* = 3.8 Hz, H-1$_\beta$), 4.95 (d, 1H, *J* = 4.0 Hz, H-1$_\beta$), 4.95 – 4.70 (m, 11.5H, 2xCH_2 Bn$_\alpha$, 3xCH_2 Bn$_\beta$, C*H*H Bn$_\alpha$), 4.67 (d, 1H, *J* = 7.7 Hz, H-1'$_\beta$), 4.57 (d, 1.1H, *J* = 11.8 Hz, CH*H* Bn$_\alpha$), 4.33 – 4.22 (m, 2.2H, H-3$_\alpha$, H-6'$_\alpha$), 4.18 (dd, 1H, *J* = 10.4, 4.8 Hz, H-6'$_\beta$), 4.12 – 4.00 (m, 2.1H, H-3'$_\alpha$, H-3$_\beta$), 4.03 – 3.89 (m, 2.2H, H-5$_\alpha$, H-5'$_\alpha$), 3.85 – 3.74 (m, 2H, H-3$_\beta$, H-5$_\beta$), 3.74 (t, 1.1H, *J* = 10.3 Hz, H-6'$_\alpha$), 3.68 (dd, 1.1H, *J* = 9.5, 8.6 Hz, H-4$_\alpha$), 3.68 – 3.61 (m, 2.1H, H-4'$_\alpha$, H-4'$_\beta$), 3.58 (dd, 1H, *J* = 9.7, 8.8 Hz, H-4$_\beta$), 3.56 (dd, 1.1H, *J* = 9.5, 4.1 Hz, H-2$_\alpha$), 3.48 (dd, 1H, *J* = 8.8, 7.7 Hz, H-2'$_\beta$), 3.45 (t, 1H, *J* = 10.2 Hz, H-6'$_\beta$), 3.38 (s, 3H, CH_3 OMe$_\beta$), 3.36 (s, 3.3H, CH_3 OMe$_\alpha$), 3.32 (dt, 0.9H, *J* = 9.7, 4.8 Hz, H-5'$_\beta$), 1.42 (d, 3H, *J* = 6.2 Hz, H-6$_\alpha$), 1.36 (d, 2.7H, *J* = 6.3 Hz, H-6$_\beta$); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 166.0 (C=O), 138.8, 138.7, 138.6, 138.4, 138.3, 138.1, 137.4 (C_q), 133.3, 133.3 (CH_{arom}), 129.9 (C_q), 129.9, 129.1, 129.0, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.3, 128.2, 128.2, 128.1, 127.9, 127.8, 127.8, 127.7, 127.7, 127.5, 127.3, 126.7, 126.1, 126.1 (CH_{arom}), 103.8 (C-1'$_\beta$), 101.2 (CHPh$_\alpha$), 101.2 (CHPh$_\beta$), 98.3 (C-1'$_\alpha$), 97.0 (C-1$_\beta$), 96.9 (C-1$_\alpha$), 83.6 (C-4$_\beta$), 82.9 (C-2'$_\beta$), 82.3 (C-4'$_\alpha$), 81.8 (C-4'$_\beta$) , 81.4 (C-3'$_\beta$), 80.3 (C-3$_\alpha$), 79.2 (C-3'$_\alpha$), 78.9 (C-4$_\alpha$), 78.9 (C-2'$_\alpha$), 77.8 (C-3$_\beta$), 75.8, 75.4, 75.3 (CH_2 Bn), 74.7 (C-2$_\alpha$), 74.0 (CH_2 Bn), 73.8 (C-2$_\beta$), 68.9 (C-6'$_\alpha$), 68.8 (C-6'$_\beta$), 66.8 (C-5$_\beta$), 66.0 (C-5'$_\beta$), 65.9 (C-5$_\alpha$), 63.4 (C-5'$_\alpha$), 55.4 (OMe$_\beta$), 55.2 (OMe$_\alpha$) , 19.1 (C-6$_\alpha$), 17.9 (C-6$_\beta$); HRMS: $[M+NH_4]^+$ calcd for $C_{48}H_{54}NO_{11}$ 820.36914, found 820.36967.

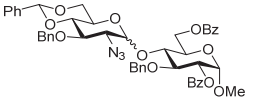


Methyl 4-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranosyl)-2-*O*-benzoyl-3-*O*-benzyl-6-deoxy-α-D-glucopyranoside (6B). Donor **B** and acceptor **6** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **6B** (65 mg, 88 µmol, 88%, α:β = 1:5) as a colorless oil. R_f: 0.76 (4/1 pentane/EtOAc); IR (thin film): 698, 737, 995, 1092, 1273, 1366, 1454, 1721, 2110, 2878; Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 8.05 – 7.98 (m, 2H, CH_{arom}), 7.60 – 7.11 (m, 18H, CH_{arom}), 5.49 (s, 1H, C*H*Ph), 5.06 (dd, 1H, *J* = 10.0, 3.7 Hz, H-2), 4.97 (d, 1H, *J* = 3.8 Hz, H-1), 4.94 – 4.82 (m, 2H, 2xC*H*H Bn), 4.79 (d, 1H, *J* = 11.2 Hz, CH*H* Bn), 4.74 (d, 1H, *J* = 11.1 Hz, CH*H* Bn), 4.53 (d, 1H, *J* = 8.1 Hz, H-1'), 4.12 – 4.01 (m, 2H, H-6', H-3), 3.89 (qd, 1H, *J* = 6.3, 3.4 Hz, H-5), 3.65 (t, 1H, *J* = 9.0 Hz, H-4'), 3.62 – 3.52 (m, 2H, H-3', H-4), 3.49 – 3.40 (m, 2H, H-2', H-6'), 3.37 (s, 3H, CH_3 OMe), 3.25 (td, 1H, *J* = 9.6, 4.9 Hz, H-5'), 1.43 (d, 3H, *J* = 6.2 Hz, H-6); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 166.0 (C=O), 138.7, 137.8, 137.2 (C_q), 133.3, 129.9 (CH_{arom}), 129.8 (C_q), 129.2, 128.6, 128.6, 128.5, 128.4, 128.4, 128.3, 128.3, 128.0, 127.7, 127.5, 127.4, 126.1 (CH_{arom}), 102.4 (C-1'), 101.3 (CHPh), 96.9 (C-1), 83.8 (C-4), 81.7 (C-4'), 79.4 (C-3'), 78.1 (C-3), 75.3, 75.1 (CH_2 Bn), 74.0 (C-2), 68.5 (C-6'), 67.2 (C-2'), 66.4 (C-5), 66.2 (C-5'), 55.4 (OMe), 18.0 (CO_2Me); Diagnostic peaks for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.11 –

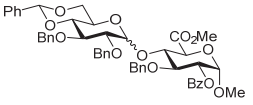
8.06 (m, 2H), 5.62 (d, 1H, *J* = 4.2 Hz, H-1'), 5.58 (s, 1H, C*H*Ph), 5.12 (dd, 1H, *J* = 9.8, 3.7 Hz, H-2), 4.31 – 4.23 (m, 2H), 3.78 – 3.66 (m, 2H) 1.39 (d, 3H, *J* = 6.2 Hz); ^{13}C-APT NMR ($CDCl_3$, 101 MHz): δ 166.0, 138.1, 137.9, 137.2, 133.5, 129.6, 127.7, 126.0, 98.8, 82.6, 80.4, 80.1, 76.4, 75.2, 75.0, 68.6, 65.6, 63.4, 62.8, 18.8; HRMS: $[M+Na]^+$ calcd for $C_{41}H_{43}N_3O_{10}Na$ 760.2841, found 760.2853.



Methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranosyl)-2,6-di-*O*-benzoyl-3-*O*-benzyl-α-D-glucopyranoside (7A). Donor **A** and acceptor **7** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **7A** (81 mg, 88 µmol, 88%, α:β = 3.5:1) as a white solid. R_f: 0.67 (4/1 pentane/EtOAc); IR (thin film): 698, 712, 737, 995, 1026, 1090, 1271, 1371, 1452, 1720, 2920; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC, HMBC): δ 8.12 – 8.06 (m, 2H, CH_{arom}), 8.01 – 7.97 (m, 2H, CH_{arom}), 7.61 – 6.99 (m, 26H, CH_{arom}), 5.57 (d, 1H, *J* = 3.9 Hz, H-1'$_\alpha$), 5.49 (s, 1H, C*H*Ph), 5.17 (dd, 1H, *J* = 9.9, 3.7 Hz, H-2), 5.02 (d, 1H, *J* = 3.5 Hz, H-1), 4.96 – 4.88 (m, 1H, C*H*H Bn), 4.87 – 4.82 (m, 1H, C*H*H Bn), 4.81 – 4.71 (m, 4H, C*H*H Bn, 2xCH*H* Bn, H-6), 4.65 – 4.55 (m, 2H, H-6, CH*H* Bn), 4.33 (ddd, 1H, *J* = 9.9, 6.5, 1.7 Hz, H-3), 4.17 – 4.02 (m, 4H, H-4, H-6', H-5, H-3'), 3.88 (td, 1H, *J* = 9.8, 4.7 Hz, H-5'), 3.63 – 3.57 (m, 2H, H-6', H-4'), 3.55 (dd, 1H, *J* = 9.5, 3.9 Hz, H-2'), 3.40 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC, HMBC): δ 166.2, 165.9 (C=O), 138.7, 138.3, 138.2, 137.5 (C_q), 133.4, 133.3 (CH_{arom}), 129.9 (C_q), 129.9, 129.7 (CH_{arom}), 129.6 (C_q), 129.0, 128.6, 128.5, 128.4, 128.3, 128.3, 128.1, 127.9, 127.7, 127.7, 127.4, 127.0, 126.2 (CH_{arom}), 101.4 (CHPh), 98.9 (C-1'), 97.0 (C-1), 82.4 (C-4'), 80.2 (C-3), 78.8 (C-2'), 78.7 (C-3'), 75.3 (CH_2 Bn) , 75.1 (C-4), 74.5 (CH_2 Bn) , 74.1 (C-2), 74.1 (CH_2 Bn), 68.9 (C-6'), 68.4 (C-5), 63.8 (C-5'), 63.7 (C-6), 55.5 (OMe); Diagnostic peaks for the β-anomer: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.06 – 8.01 (m, 2H), 5.50 (s, 1H, C*H*Ph), 5.08 (dd, 1H, *J* = 9.3, 3.8 Hz, H-2), 4.53 (dd, 1H, *J* = 12.1, 4.5 Hz, H-6), 3.76 (t, 1H, *J* = 9.0 Hz, H-3'), 3.27 (td, 1H, *J* = 9.1, 8.4, 4.3 Hz, H-5'); ^{13}C-APT NMR ($CDCl_3$, 126 MHz): δ 166.0, 165.9 (C=O), 138.5, 138.5, 137.3, 133.4, 130.0, 130.0, 129.8, 129.1, 128.6, 128.4, 128.1, 127.8, 127.8, 127.7, 126.1 (CH_{arom}), 103.4 (C-1'), 101.2 (CHPh), 97.1 (C-1), 82.8 (C-2'), 81.8 (C-4'), 81.4 (C-3'), 77.9, 77.8 (C-3, C-4), 75.9, 75.6, 75.3 (CH_2 Bn), 73.4 (C-2), 68.9 (C-5), 68.8 (C-6'), 66.2 (C-5'), 62.7 (C-6), 55.5 (OMe); HRMS: $[M+NH_4]^+$ calcd for $C_{55}H_{58}NO_{13}$ 940.39027, found 940.39106.

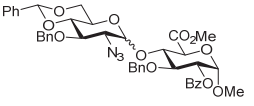


Methyl 4-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranosyl)-2,6-di-*O*-benzoyl-3-*O*-benzyl-α-D-glucopyranoside (7B). Donor **B** and acceptor **7** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **7B** (75 mg, 87 µmol, 87%, α:β = 1.3:1) as a colorless oil. R_f: 0.66 (4/1 pentane/EtOAc); IR (thin film): 698, 737, 918, 995, 1026, 1092, 1173, 1269, 1369, 1450, 1721, 2110, 2866; Data reported for a 1.3:1 mixture of anomers: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 8.14 – 7.98 (m, 9.2H, CH_{arom}), 7.64 – 7.13 (m, 48.3H, CH_{arom}), 5.67 (d, 1.3H, *J* = 4.1 Hz, H-1'$_\alpha$), 5.51 (s, 1.3H, C*H*Ph$_\alpha$), 5.49 (s, 1H, C*H*Ph$_\beta$), 5.18 (dd, 1.3H, *J* = 9.8, 3.6 Hz, H-2$_\alpha$), 5.12 (dd, 1H, *J* = 9.6, 3.7 Hz, H-2$_\beta$), 5.05 (d, 1H, *J* = 3.7 Hz, H-1$_\beta$), 5.03 (d, 1.3H, *J* = 3.6 Hz, H-1$_\alpha$), 4.98 (d, 1.3H, *J* = 10.9 Hz, C*H*H Bn$_\alpha$), 4.96 – 4.85 (m, 4.6H, CH_2 Bn$_\alpha$, 2xC*H*H Bn$_\beta$), 4.80 – 4.73 (m, 5.6H, H-6$_\beta$, 2xCH*H* Bn$_\beta$, CH*H* Bn$_\alpha$ H-6$_\alpha$, H-6$_\beta$), 4.67 (dd, 1H, *J* = 12.2, 2.9 Hz, H-6$_\beta$), 4.53 (dd, 1.3H, *J* = 12.0, 2.6 Hz, H-6$_\alpha$), 4.49 (d, 1H, *J* = 8.0 Hz, H-1'$_\beta$), 4.42 – 4.33 (m, 1.3H, H-3$_\alpha$), 4.21 – 4.13 (m, 1H, H-3$_\beta$), 4.12 – 4.01 (m, 8.2H, H-3'$_\alpha$, H-4$_\alpha$, H-4$_\beta$, H-5$_\beta$, H-5$_\alpha$, H-6'$_\alpha$, H-6'$_\beta$), 3.87 (td, 1.3H, *J* = 9.9, 4.9 Hz, H-5'$_\alpha$), 3.72 – 3.53 (m, 4.6H, H-3'$_\beta$, H-4'$_\alpha$, H-4'$_\beta$, H-6'$_\alpha$), 3.51 – 3.40 (m, 8.9H, H-2'$_\beta$, H-6'$_\beta$, CH_3 OMe$_\alpha$, CH_3 OMe$_\beta$), 3.36 (dd, 1.3H, *J* = 10.0, 4.1 Hz, H-2'$_\alpha$), 3.18 (td, 1H, *J* = 9.4, 4.9 Hz, H-5'$_\beta$); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 166.2, 166.2, 165.9, 165.9 (C=O), 138.4, 137.9, 137.8, 137.7, 137.2, 137.1 (C_q), 133.6, 133.5, 133.4, 133.3 (CH_{arom}), 129.9, 129.9 (C_q), 129.8 (CH_{arom}), 129.8, 129.7 (C_q), 129.7, 129.5, 129.2, 129.1, 128.7, 128.6, 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.0, 127.8, 127.8, 127.7, 127.6, 126.2, 126.0 (CH_{arom}), 102.0 (C-1'$_\beta$), 101.4 (CHPh$_\alpha$), 101.3 (CHPh$_\beta$), 99.0 (C-1'$_\alpha$), 97.1 (C-1$_\alpha$). 97.1 (C-1$_\beta$), 82.6 (C-4'$_\alpha$), 81.7 (C-4'$_\beta$), 80.4 (C-3$_\alpha$), 79.7 (C-3'$_\beta$), 78.1 (C-3$_\beta$), 77.9 (C-4$_\beta$), 76.2 (C-3'$_\alpha$), 75.6, 75.2 (CH_2 Bn), 75.0(C-4$_\alpha$), 74.6 (C-2$_\alpha$), 73.5 (C-2$_\beta$), 68.6 (C-5$_\beta$), 68.5, 68.5 (C-6'$_\alpha$, C-6'$_\beta$), 68.1 (C-5$_\alpha$), 66.8 (C-2'$_\beta$), 66.3 (C-5'$_\beta$), 63.8 (C-5'$_\alpha$), 63.4 (C-6$_\alpha$), 62.9 (C-6$_\beta$), 62.8 (C-2'$_\alpha$), 55.6 (OMe$_\alpha$), 55.6 (OMe$_\beta$); HRMS: $[M+NH_4]^+$ calcd for $C_{48}H_{49}N_4O_{13}$ 875.34980, found 875.35039.

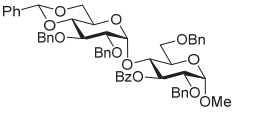


Methyl (methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranosyl)-2-*O*-benzoyl-3-*O*-benzyl-α-D-glucopyranosyl uronate) (8A). Donor **A** and acceptor **8** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **8A** (81 mg, 96 µmol, 96%, α:β = 4.8 : 1) as a colorless oil. R_f: 0.57 (4/1 pentane/EtOAc); IR (thin film): 698, 914, 995, 1045, 1088, 1200, 1267, 1369, 1452, 1722, 1751, 2938; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC, HMBC): δ 8.00 – 7.94 (m, 2H, CH_{arom}), 7.59 – 7.01 (m, 23H), 5.54 (s, 1H, C*H*Ph), 5.28 (d, 1H, *J* = 3.8 Hz, H-1'), 5.16 – 5.12 (m, 1H, H-2), 5.06 (d, 1H, *J* = 3.6 Hz, H-1), 4.95 – 4.68 (m, 5H, 2xCH_2 Bn, C*H*H Bn), 4.60 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.31 (dd, 1H, *J* = 8.9, 3.6 Hz, H-6'), 4.28 – 4.19 (m, 3H, H-3, H-4, H-5), 4.02 (t, 1H, *J* = 9.3 Hz, H-3'), 3.78 (s, 3H, CH_3 CO_2Me), 3.74 – 3.63 (m, 2H, H-5', H-6'), 3.60 (t, 1H, *J* = 9.2 Hz,

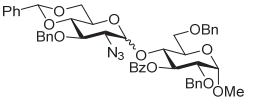
H-4'), 3.52 (dd, 1H, *J* = 9.5, 3.8 Hz, H-2'), 3.41 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC, HMBC): δ 169.5 (C=O CO_2Me), 165.9 (C=O OBz), 138.6, 138.3, 138.0, 137.6 (C_q), 133.4 (CH_{arom}), 130.0, 129.9 (CH_{arom}), 129.6 (C_q), 129.0, 128.5, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.8, 127.7, 127.4, 127.4, 126.1 (CH_{arom}), 101.3 (CHPh), 98.9 (C-1'), 97.6 (C-1), 82.1 (C-4'), 79.0 (C-2), 78.4 (C-4), 78.2 (C-3'), 77.8 (C-3), 75.2, 74.9, 73.7 (CH_2 Bn), 73.1 (C-2), 70.7 (C-5), 68.6 (C-6'), 63.4 (C-5'), 55.9 (OMe), 52.8 (CO_2Me); Diagnostic peaks for the β-anomer: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.05 – 8.00 (m, 1H), 5.46 (s, 1H, CHPh), 5.10 (dd, 1H, *J* = 9.4, 3.6 Hz, H-2), 4.09 (ddd, 1H, *J* = 9.4, 6.7, 1.5 Hz, H-3), 3.34 (td, 1H, *J* = 9.6, 4.7 Hz, H-5'); ^{13}C-APT NMR ($CDCl_3$, 126 MHz): δ 169.7 (C=O), 138.6, 138.5, 137.4 (C_q), 129.8, 128.3, 128.3, 128.1, 127.8, 127.7, 127.6, 126.1 (CH_{arom}), 103.1 (C-1'), 101.2 (CHPh), 97.6 (C-1), 82.4 (C-2'), 81.8, 81.3, 78.0, 77.0, 75.6 (C-3), 75.2, 72.6 (C-2), 70.4, 68.7, 65.9 (C-5'), 56.1 (OMe), 52.8 (CO_2Me); HRMS: $[M+NH_4]^+$ calcd for $C_{49}H_{54}NO_{13}$ 864.35897, found 864.36009.



Methyl (methyl 4-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranosyl)-2-*O*-benzoyl-3-*O*-benzyl-α-D-glucopyranosyl uronate) (8B). Donor **B** and acceptor **8** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **8B** (64 mg, 82 µmol, 82%, α:β = 1.18 : 1) as a colorless oil. R_f: 0.73 (4/1 pentane/EtOAc); IR (thin film): 698, 737, 918, 991, 1045, 1092, 1200, 1265, 1366, 1454, 1724, 1751, 2110, 2940; Data reported for a 1.18 : 1 mixture of anomers: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.11 – 8.04 (m, 2H, CH_{arom}), 8.04 – 7.97 (m, 2.2H, CH_{arom}), 7.63 – 7.09 (m, 39.6H, CH_{arom}), 5.55 (s, 1H), 5.48 (d, 2H, *J* = 3.3 Hz), 5.16 (dd, 1H, *J* = 9.6, 3.6 Hz), 5.55 (s, 1.2H, C*H*Ph$_\alpha$), 5.50 – 5.44 (m, 2.2H, H-1'$_\alpha$, C*H*Ph$_\beta$), 5.16 (dd, 1H, *J* = 9.6, 3.6 Hz, H-2$_\alpha$), 5.12 – 5.07 (m, 3.2H, H-1$_\alpha$, H-1$_\beta$, H-2$_\beta$), 4.96 (d, 1.2H, *J* = 11.0 Hz, C*H*H Bn$_\alpha$), 4.93 – 4.83 (m, 4.4H, 2xC*H*H Bn$_\beta$, CH_2 Bn$_\alpha$), 4.82 – 4.74 (m, 2.2H, CH*H* Bn$_\alpha$, CH*H* Bn$_\beta$), 4.73 (d, 1H, *J* = 11.1 Hz, CH*H* Bn$_\beta$), 4.51 (d, 1H, *J* = 8.1 Hz, H-1'$_\beta$), 4.37 – 4.26 (m, 4.6H, H-5$_\alpha$, H-5$_\beta$, H-3$_\alpha$, H-6'$_\alpha$), 4.26 – 4.16 (m, 2.2H, H-4$_\alpha$, H-4$_\beta$), 4.16 – 4.05 (m, 2H, H-3$_\beta$, H-6'$_\beta$), 4.00 (dd, 1.2H, *J* = 10.0, 9.0 Hz, H-3'$_\alpha$), 3.86 (s, 3H, CH_3 CO_2Me_β), 3.85 (s, 3.6H, CH_3 CO_2Me_α), 3.71 – 3.64 (m, 2.4H, H-6'$_\alpha$, H-4'$_\alpha$), 3.63 – 3.50 (m, 3.2H, H-3'$_\beta$, H-5'$_\alpha$, H-4'$_\beta$), 3.47 – 3.33 (m, 8.8H, CH_3 OMe_α, CH_3 OMe_β, H-2'$_\alpha$ H-2'$_\beta$, H-6'$_\beta$), 3.29 (td, 1H, *J* = 9.5, 4.8 Hz, H-5'$_\beta$); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 169.7, 169.6 (C=O CO_2Me), 165.9, 165.8 (C=O OBz), 138.4, 137.9, 137.9, 137.8, 137.4, 137.2 (C_q), 133.6, 133.4, 129.9, 129.9 (CH_{arom}), 129.6, 129.4 (C_q), 129.2, 129.1, 128.7, 128.5, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 128.0, 128.0, 127.8, 127.8, 127.6, 127.6, 126.1, 126.1 (CH_{arom}), 102.3 (C-1'$_\beta$), 101.5 (CHPh$_\alpha$), 101.4 (CHPh$_\beta$), 98.6 (C-1'$_\alpha$), 97.7 (C-1$_\alpha$), 97.7 (C-1$_\beta$), 82.5 (C-4'$_\alpha$), 81.6 (C-3'$_\beta$), 79.6 (C-3$_\alpha$), 79.4 (C-4'$_\beta$), 79.3 (C-4$_\beta$), 77.3 (C-3$_\beta$), 76.4 (C-3'$_\alpha$), 75.7 (C-4$_\alpha$), 75.5, 75.4, 75.1, 75.1 (CH_2 Bn), 73.9 (C-2$_\alpha$), 72.9 (C-2$_\beta$), 70.1 (C-5$_\alpha$), 70.0 (C-5$_\beta$), 68.5 (C-6'$_\alpha$), 66.7(C-2'$_\beta$), 66.2 (C-5'$_\beta$), 63.2 (C-5'$_\alpha$), 62.9 (C-2'$_\alpha$), 56.0 ($OMe_{\alpha,\beta}$), 53.1 (CO_2Me_α), 52.9 (CO_2Me_β); HRMS: $[M+NH_4]^+$ calcd $C_{42}H_{47}N_4O_{12}$ for 799.31850, found 799.31937.

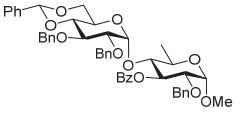


Methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranosyl)-2,6-di-*O*-benzyl-3-*O*-benzoyl-α-D-glucopyranoside (9A). Donor **A** and acceptor **9** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **9A** (86 mg, 95 µmol, 95%, α:β = >20:1) as a colorless oil. R_f: 0.26 (4/1 pentane/EtOAc); $[\alpha]_D^{20}$ = -0.9° (*c* = 1.0, $CHCl_3$); IR (thin film): 696, 746, 912, 995, 1047, 1088, 1269, 1369, 1452, 1728, 2924; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 8.09 – 8.02 (m, 2H, CH_{arom}), 7.61 – 7.11 (m, 28H, CH_{arom}), 5.94 (t, 1H, *J* = 9.6 Hz, H-3), 5.46 (s, 1H, C*H*Ph), 5.03 (d, 1H, *J* = 3.5 Hz, H-1'), 4.79 – 4.72 (m, 2H, H-1, C*H*H Bn), 4.63 – 4.50 (m, 5H, 2xCH_2 Bn, CH*H* Bn), 4.40 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.21 (t, 1H, *J* = 9.4 Hz, H-4), 4.13 – 4.04 (m, 2H, CH*H* Bn, H-6'), 3.97 – 3.88 (m, 3H, H-3', H-5, H-6), 3.85 (dd, 1H, *J* = 9.9, 4.8 Hz, H-5'), 3.71 – 3.67 (m, 1H, H-6), 3.65 (t, 1H, *J* = 3.0 Hz, H-2'), 3.55 (t, 1H, *J* = 10.2 Hz, H-6'), 3.44 (t, 1H, *J* = 9.7 Hz, H-4'), 3.41 (s, 3H, CH_3 OMe), 3.26 (dd, 1H, *J* = 9.4, 3.5 Hz, H-2'); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 165.4 (C=O), 138.8, 138.0, 137.9, 137.8, 137.6 (C_q), 132.9 (CH_{arom}), 130.7 (C_q), 129.9, 128.9, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.2, 128.1, 127.9, 127.9, 127.8, 127.7, 127.6, 126.2 (CH_{arom}), 101.3 (CHPh), 98.0 (C-1'), 97.7 (C-1), 81.9 (C-4), 78.8 (C-2'), 78.3 (C-3'), 77.2 (C-2), 75.4 (CH_2 Bn), 73.9 (C-3), 73.7 (C-4), 73.6, 72.9, 72.8 (CH_2 Bn), 69.7 (C-5), 69.0 (C-6'), 68.3 (C-6), 63.6 (C-5'), 55.4 (OMe); HRMS: $[M+NH_4]^+$ calcd for $C_{55}H_{60}NO_{12}$ 926.41100, found 926.41201.

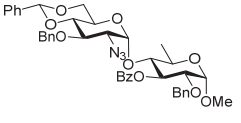


Methyl 4-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranosyl)-2,6-di-*O*-benzyl-3-*O*-benzoyl-α-D-glucopyranoside (9B). Donor **B** and acceptor **9** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **9B** (65 mg, 77 µmol, 77%, α:β = 6.7:1) as a light yellow oil. R_f: 0.28 (4/1 pentane/EtOAc); $[\alpha]_D^{20}$ = -25.5° (*c* = 1.0, $CHCl_3$); IR (thin film): 698, 745, 995, 1092, 1165, 1269, 1369, 1454, 1732, 2110, 2866; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 8.11 – 8.05 (m, 2H, CH_{arom}), 7.61 – 7.09 (m, 23H, CH_{arom}), 5.85 (t, 1H, *J* = 9.6 Hz, H-3), 5.50 (s, 1H, C*H*Ph), 5.04 (d, 1H, *J* = 3.7 Hz, H-1'), 4.82 (d, 1H,

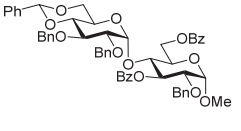
J = 10.6 Hz, C*H*H Bn), 4.75 (d, 1H, *J* = 3.5 Hz, H-1), 4.64 – 4.54 (m, 5H, CH*H* Bn, 2xCH$_2$ Bn), 4.10 (dd, 1H, *J* = 10.3, 4.8 Hz, H-6), 4.05 (t, 1H, *J* = 9.5 Hz, H-4), 3.96 – 3.81 (m, 4H, H-3', H-5', H-5, H-6), 3.76 – 3.67 (m, 1H, H-6'), 3.64 – 3.57 (m, 2H, H-2, H-6'), 3.56 (t, 1H, *J* = 9.3 Hz, H-4'), 3.42 (s, 3H, CH$_3$ OMe), 3.23 (dd, 1H, *J* = 9.9, 3.7 Hz, H-2'); ^{13}C-APT NMR (CDCl$_3$, 101 MHz, HSQC, HMBC): δ 165.4 (C=O), 137.9, 137.8, 137.7, 137.2 (C$_q$), 132.8 (CH$_{arom}$), 130.7 (C$_q$), 129.7, 129.1, 128.7, 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 128.0, 127.9, 127.9, 127.8, 126.1 (CH$_{arom}$), 101.5 (CHPh), 99.5 (C-1'), 97.7 (C-1), 82.5 (C-4'), 77.1 (C-4), 76.7 (C-3'), 76.5 (C-2), 75.3, 73.7 (CH$_2$ Bn), 73.5 (C-3), 72.8 (CH$_2$ Bn), 69.6 (C-5), 68.8 (C-6'), 68.7 (C-6), 63.8 (C-5'), 63.5 (C-2'), 55.6 (OMe); Diagnostic peaks for the β-anomer: ^{1}H NMR (CDCl$_3$, 400 MHz): δ 5.66 (dd, 1H, *J* = 10.0, 8.7 Hz, H-3), 5.19 (s, 1H, C*H*Ph), 4.70 (d, 1H, *J* = 11.9 Hz, C*H*H Bn), 4.69 (d, 1H, *J* = 11.4 Hz, CH*H* Bn), 4.44 (d, 1H, *J* = 11.9 Hz, CH*H* Bn), 3.99 (dd, 1H, *J* = 10.8, 2.5 Hz, H-6) 2.87 (td, 1H, *J* = 9.3, 4.9 Hz, H-5'), 2.52 (t, 1H, *J* = 10.4 Hz, H-6'); ^{13}C-APT NMR (CDCl$_3$, 101 MHz): δ 101.5 (C-1'), 101.0 (CHPh), 98.0 (C-1), 81.2, 79.1, 76.1, 74.6, 73.7, 72.8, 72.6, 69.4, 67.8, 67.6, 65.9, 65.7; HRMS: [M+NH$_4$]$^+$ calcd for $C_{48}H_{53}N_4O_{11}$ 861.37053, found 861.37106.



Methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranosyl)-2-*O*-benzyl-3-*O*-benzoyl-6-deoxy-α-D-glucopyranoside (10A). Donor **A** and acceptor **10** were condensed using the general procedure for Tf$_2$O/Ph$_2$SO mediated glycosylations (E) yielding product **10A** (67 mg, 83 µmol, 83%, α:β = >20:1) as a white solid. R$_f$: 0.38 (4/1 pentane/EtOAc); $[\alpha]_D^{20}$ = -3.6° (*c* = 1.0, CHCl$_3$); IR (thin film): 698, 745, 995, 1053, 1092, 1269, 1454, 1728, 2866; ^{1}H NMR (CDCl$_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 8.07 – 8.01 (m, 2H, CH$_{arom}$), 7.62 – 7.06 (m, 23H, CH$_{arom}$), 5.98 – 5.87 (m, 1H, H-3), 5.48 (s, 1H, C*H*Ph), 5.10 (d, 1H, *J* = 3.8 Hz, H-1'), 4.80 (d, 1H, *J* = 11.1 Hz, C*H*H Bn), 4.70 – 4.62 (m, 2H, H-1, CH*H* Bn), 4.57 (d, 1H, *J* = 12.5 Hz, C*H*H Bn), 4.52 (d, 1H, *J* = 12.5 Hz, CH*H* Bn), 4.42 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.24 – 4.13 (m, 2H, H-6', CH*H* Bn), 4.02 – 3.85 (m, 3H, H-3', H-5, H-5'), 3.70 – 3.62 (m, 2H, H-4', H-6'), 3.62 – 3.55 (m, 1H, H-2), 3.49 (t, 1H, *J* = 9.5 Hz, H-4), 3.41 (s, 3H, CH$_3$ OMe), 3.33 (dd, 1H, *J* = 9.5, 3.8 Hz, H-2'), 1.36 (d, 3H, *J* = 6.2 Hz, H-6); ^{13}C-APT NMR (CDCl$_3$, 101 MHz, HSQC, HMBC): δ 165.2 (C=O), 138.7, 137.8, 137.4 (C$_q$), 133.0 (CH$_{arom}$), 130.6 (C$_q$), 129.9, 129.0, 128.5, 128.4, 128.3, 128.3, 128.2, 128.1, 127.9, 127.7, 127.6, 126.1 (CH$_{arom}$), 101.3 (CHPh), 98.1 (C-1'), 97.3 (C-1), 81.9 (C-4), 79.4 (C-4'), 78.5 (C-2'), 78.4 (C-3'), 77.6 (C-2), 75.5 (CH$_2$ Bn), 73.9 (C-3), 73.1, 72.6 (CH$_2$ Bn), 68.9 (C-6'), 66.1 (C-5), 63.5 (C-5'), 55.3 (OMe), 18.7 (C-6); HRMS: [M+NH$_4$]$^+$ calcd for $C_{48}H_{54}NO_{11}$ 820.36914, found 820.36983.

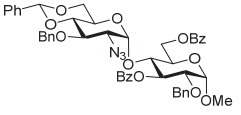


Methyl 4-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranosyl)-2-*O*-benzyl-3-*O*-benzoyl-6-deoxy-α-D-glucopyranoside (10B). Donor **B** and acceptor **10** were condensed using the general procedure for Tf$_2$O/Ph$_2$SO mediated glycosylations (E) yielding product **10B** (60 mg, 81 µmol, 81%, α:β = 14:1) as a colorless oil. R$_f$: 0.25 (4/1 pentane/EtOAc); $[\alpha]_D^{20}$ = -30.0° (*c* = 1.0, CHCl$_3$); IR (thin film): 698, 748, 995, 1053, 1096, 1269, 1373, 1454, 1732, 2110, 2931; Data for the α-anomer: ^{1}H NMR (CDCl$_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 8.07 – 8.01 (m, 2H, CH$_{arom}$), 7.61 – 7.09 (m, 18H, CH$_{arom}$), 5.84 (t, 1H, *J* = 9.6 Hz, H-3), 5.53 (s, 1H, C*H*Ph), 5.07 (d, 1H, *J* = 4.0 Hz, H-1'), 4.87 (d, 1H, *J* = 10.8 Hz, C*H*H Bn), 4.71 – 4.64 (m, 2H, CH*H* Bn, H-1), 4.61 – 4.47 (m, 2H, CH$_2$ Bn), 4.21 (dd, 1H, *J* = 10.4, 5.0 Hz, H-6'), 4.00 – 3.83 (m, 3H, H-3', H-5', H-5), 3.69 (t, 1H, *J* = 10.4 Hz, H-6'), 3.61 (t, 1H, *J* = 9.3 Hz, H-4'), 3.57 – 3.46 (m, 2H, H-2, H-4), 3.42 (s, 3H, CH$_3$ OMe), 3.19 (dd, 1H, *J* = 10.0, 4.0 Hz, H-2'), 1.35 (d, 3H, *J* = 6.2 Hz, H-6); ^{13}C-APT NMR (CDCl$_3$, 101 MHz, HSQC, HMBC): δ 165.3 (C=O), 137.8, 137.7, 137.1 (C$_q$), 132.8 (CH$_{arom}$), 130.6 (C$_q$), 129.6, 129.1, 128.5, 128.4, 128.4, 128.4, 128.3, 128.0, 127.9, 127.9, 126.0 (CH$_{arom}$), 101.3 (CHPh), 100.0 (C-1'), 97.5 (C-1), 82.4 (C-4'), 82.4 (C-4), 77.4 (C-2), 76.6 (C-3'), 75.2 (CH$_2$ Bn), 73.5 (C-3), 72.6 (CH$_2$ Bn), 68.5 (C-6'), 65.7 (C-5), 63.5 (C-5'), 63.0 (C-2'), 55.4 (OMe), 18.3 (C-6); Diagnostic peaks for the β-anomer: ^{1}H NMR (CDCl$_3$, 400 MHz): δ 5.66 (t, 1H, *J* = 9.5 Hz, H-3), 5.23 (s, 1H, C*H*Ph), 3.04 (td, 1H, *J* = 9.7, 5.1 Hz, H-5'), 2.63 (t, 1H, *J* = 10.4 Hz, H-6'), 1.38 (d, 3H, *J* = 6.3 Hz, H-6); ^{13}C-APT NMR (CDCl$_3$, 101 MHz): δ 102.6 (C-1'), 101.0 (CHPh), 97.5 (C-1), 83.3, 81.3, 81.1, 79.2, 74.8, 72.7, 67.8, 66.4, 66.1, 65.9, 17.7; HRMS: [M+Na]$^+$ calcd for $C_{41}H_{43}N_3O_{10}Na$ 760.2841, found 760.2852.

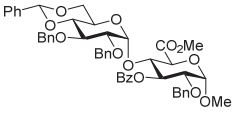


Methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranosyl)-2-*O*-benzyl-3,6-di-*O*-benzoyl-α-D-glucopyranoside (11A). Donor **A** and acceptor **11** were condensed using the general procedure for Tf$_2$O/Ph$_2$SO mediated glycosylations (E) yielding product **11A** (88 mg, 95 µmol, 95%, α:β = >20:1) as a white solid. R$_f$: 0.25 (4/1 pentane/EtOAc); $[\alpha]_D^{20}$ = +21.1° (*c* = 1.0, CHCl$_3$); IR (thin film): 698, 712, 748, 995, 1026, 1090, 1267, 1371, 1452, 1724; ^{1}H NMR (CDCl$_3$, 400 MHz, HH-COSY, HSQC): δ 8.12 – 8.06 (m, 2H, CH$_{arom}$), 8.06 – 8.01 (m, 2H, CH$_{arom}$), 7.62 – 7.51 (m, 2H, CH$_{arom}$), 7.46 – 7.32 (m, 9H, CH$_{arom}$), 7.29 – 7.11 (m, 15H, CH$_{arom}$), 5.99 (dd, 1H, *J* = 9.9, 9.0 Hz, H-3), 5.42 (s, 1H, C*H*Ph), 4.97 (d, 1H, *J* = 3.6 Hz, H-1'), 4.84 – 4.68 (m, 3H, H-1, H-6, C*H*H Bn), 4.67 – 4.51 (m, 4H, CH*H* Bn, CH$_2$ Bn, H-6), 4.36 (d, 1H, *J* = 12.2 Hz, C*H*H Bn), 4.15 (ddd, 1H, *J* = 10.0, 4.4, 2.1 Hz, H-5), 4.11 – 4.01 (m, 3H, H-6', H-4, CH*H* Bn), 3.98 (t, 1H, *J* = 9.4 Hz, H-3'), 3.88 (td, 1H, *J* = 9.9, 4.8 Hz, H-5'), 3.67 (dd, 1H, *J* = 9.9, 3.5 Hz,

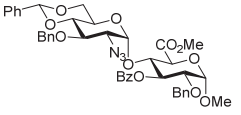
H-2), 3.54 (t, 1H, *J* = 10.3 Hz, H-6'), 3.46 (d, 1H, *J* = 9.5 Hz, H-4'), 3.44 (s, 3H, CH_3 OMe), 3.29 (dd, 1H, *J* = 9.5, 3.6 Hz, H-2'); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 166.1, 165.3 (C=O), 138.7, 138.1, 137.7, 137.4 (C_q), 133.2, 133.0 (CH_{arom}), 130.7, 130.0 (C_q), 129.9, 129.8, 128.9, 128.5, 128.5, 128.4, 128.3, 128.2, 128.2, 128.2, 128.0, 127.9, 127.7, 127.6, 126.2 (CH_{arom}), 101.4 (CHPh), 99.2 (C-1'), 97.5 (C-1), 81.9 (C-4'), 78.5 (C-2'), 78.3 (C-3'), 77.3 (C-2), 75.9 (C-4), 75.4 (CH_2 Bn), 73.3 (C-3), 73.2 (CH_2 Bn), 72.8 (CH_2 Bn), 68.8 (C-6'), 68.6 (C-5), 63.9 (C-5'), 63.5 (C-6), 55.5 (OMe); HRMS: $[M+NH_4]^+$ calcd for $C_{55}H_{58}NO_{13}$ 940.39027, found 940.39105.



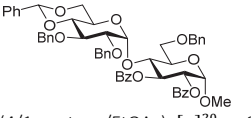
Methyl 4-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranosyl)-2-*O*-benzyl-3,6-di-*O*-benzoyl-α-D-glucopyranoside (11B). Donor **B** and acceptor **11** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **11B** (73 mg, 85 µmol, 85%, α:β = >20:1) as a colorless oil. R_f: 0.31 (4/1 pentane/EtOAc); $[\alpha]_D^{20}$ = +0.6° (*c* = 1.0, $CHCl_3$); IR (thin film): 748, 995, 1030, 1096, 1169, 1269, 1315, 1373, 1450, 1724, 2110, 2924; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 8.08 (td, 4H, *J* = 8.2, 1.4 Hz, CH_{arom}), 7.61 – 7.10 (m, 21H, CH_{arom}), 5.91 (t, 1H, *J* = 9.6 Hz, H-3), 5.49 (s, 1H, C*H*Ph), 5.07 (d, 1H, *J* = 3.9 Hz, H-1'), 4.85 (d, 1H, *J* = 10.7 Hz, C*H*H Bn), 4.76 (d, 1H, *J* = 3.4 Hz, H-1), 4.72 (dd, 1H, *J* = 12.2, 2.1 Hz, H-6), 4.67 (d, 1H, *J* = 10.7 Hz, CH*H* Bn), 4.63 – 4.53 (m, 2H, CH_2 Bn), 4.50 (dd, 1H, *J* = 12.1, 4.7 Hz, H-6), 4.23 (dd, 1H, *J* = 10.4, 4.9 Hz, H-6'), 4.12 (ddd, 1H, *J* = 9.9, 4.6, 2.0 Hz, H-5), 4.00 – 3.86 (m, 3H, H-3', H-4, H-5'), 3.67 – 3.53 (m, 3H, H-4', H-6', H-2), 3.45 (s, 3H, CH_3 OMe), 3.25 (dd, 1H, *J* = 10.0, 3.9 Hz, H-2'); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 166.2, 165.4 (C=O), 137.8, 137.1 (C_q), 133.3, 132.9 (CH_{arom}), 130.5, 129.9 (C_q), 129.8, 129.1, 128.6, 128.5, 128.4, 128.3, 128.3, 128.0, 127.9, 127.9, 126.1 (CH_{arom}), 101.4 (CHPh), 100.5 (C-1'), 97.6 (C-1), 82.4 (C-4'), 77.8 (C-4), 77.2 (C-2), 76.6 (C-3'), 75.2 (CH_2 Bn), 73.2 (C-3), 72.7 (CH_2 Bn), 68.5 (C-6'), 68.3 (C-5), 64.0 (C-5'), 63.6 (C-6), 63.2 (C-2'), 55.6 (OMe); HRMS: $[M+NH_4]^+$ calcd for $C_{48}H_{51}N_4O_{12}$ 875.34980, found 875.35050.



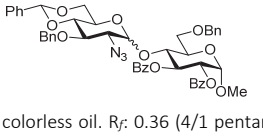
Methyl (methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranosyl)-2-*O*-benzyl-3-*O*-benzoyl-α-D-glucopyranosyl uronate) (12A). Donor **A** and acceptor **12** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **12A** (73 mg, 86 µmol, 86%, α:β = >20:1) as a white solid. R_f: 0.40 (4/1 pentane/EtOAc); $[\alpha]_D^{20}$ = -18.4° (*c* = 1.0, $CHCl_3$); IR (thin film): 698, 748, 914, 995, 1047, 1088, 1201, 1267, 1452, 1732, 2931; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.11 – 8.01 (m, 2H, CH_{arom}), 7.59 – 7.51 (m, 1H, CH_{arom}), 7.47 – 7.33 (m, 7H, CH_{arom}), 7.33 – 7.13 (m, 13H, CH_{arom}), 7.09 – 7.02 (m, 2H, CH_{arom}), 5.96 (t, 1H, *J* = 9.6 Hz, H-3), 5.45 (s, 1H, C*H*Ph), 4.93 (d, 1H, *J* = 3.7 Hz, H-1'), 4.80 (d, 1H, *J* = 11.1 Hz, C*H*H Bn), 4.75 (d, 1H, *J* = 3.4 Hz, H-1), 4.69 (d, 1H, *J* = 11.1 Hz, CH*H* Bn), 4.61 – 4.52 (m, 2H, CH_2 Bn), 4.40 – 4.28 (m, 2H, C*H*H Bn, H-5), 4.27 – 4.16 (m, 2H, H-4, H-6'), 3.99 (d, 1H, *J* = 12.2 Hz, CH*H* Bn), 3.92 (t, 1H, *J* = 9.4 Hz, H-3'), 3.74 (s, 3H, CH_3 CO_2Me), 3.69 (dd, 1H, *J* = 10.0, 3.4 Hz, H-2), 3.63 – 3.52 (m, 2H, H-5', H-6'), 3.46 (s, 3H, CH_3 OMe), 3.42 (d, 1H, *J* = 9.2 Hz, H-4'), 3.25 (dd, 1H, *J* = 9.4, 3.7 Hz, H-2'); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 169.9 (C=O CO_2Me), 165.1 (C=O OBz), 138.7, 137.8, 137.5 (C_q), 133.1 (CH_{arom}), 130.5 (C_q), 129.9, 129.0, 128.5, 128.5, 128.3, 128.3, 128.3, 128.2, 128.2, 128.2, 128.1, 127.7, 127.6, 126.1 (CH_{arom}), 101.3 (CHPh), 98.8 (C-1'), 98.4 (C-1), 81.6 (C-4'), 78.2 (C-2'), 78.0 (C-3'), 76.5 (C-2), 76.1 (C-4), 75.4, 73.0, 72.8 (CH_2 Bn), 72.7 (C-3), 70.5 (C-5), 68.5 (C-6'), 63.5 (C-5'), 55.9 (OMe), 52.9 (CO_2Me); HRMS: $[M+NH_4]^+$ calcd for $C_{49}H_{54}NO_{13}$ 864.35897, found 864.36004.



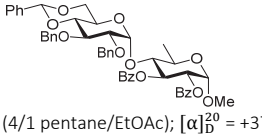
Methyl (methyl 4-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranosyl)-2-*O*-benzyl-3-*O*-benzoyl-α-D-glucopyranosyl uronate) (12B). Donor **B** and acceptor **12** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **12B** (73 mg, 93 µmol, 93%, α:β = >20:1) as a colorless oil. R_f: 0.33 (4/1 pentane/EtOAc); $[\alpha]_D^{20}$ = -35.8° (*c* = 1.0, $CHCl_3$); IR (thin film): 698, 748, 914, 995, 1045, 1092, 1200, 1265, 1373, 1454, 1732, 2110, 2936; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 8.09 – 7.99 (m, 2H, CH_{arom}), 7.62 – 7.53 (m, 1H, CH_{arom}), 7.52 – 7.42 (m, 4H, CH_{arom}), 7.42 – 7.33 (m, 3H, CH_{arom}), 7.29 – 7.16 (m, 10H, CH_{arom}), 5.87 (t, 1H, *J* = 9.7 Hz, H-3), 5.50 (s, 1H, C*H*Ph), 4.96 (d, 1H, *J* = 3.8 Hz, H-1'), 4.84 (d, 1H, *J* = 10.8 Hz, C*H*H Bn), 4.74 (d, 1H, *J* = 3.4 Hz, H-1), 4.67 (d, 1H, *J* = 10.8 Hz, CH*H* Bn), 4.60 – 4.51 (m, 2H, CH_2 Bn), 4.30 (d, 1H, *J* = 9.8 Hz, H-5), 4.28 – 4.21 (m, 1H, H-6'), 4.12 (t, 1H, *J* = 9.5 Hz, H-4), 3.92 (dd, 1H, *J* = 10.0, 9.0 Hz, H-3'), 3.79 (s, 3H, CH_3 CO_2Me), 3.73 – 3.59 (m, 3H, H-5', H-6', H-2), 3.55 (t, 1H, *J* = 9.0 Hz, H-4'), 3.46 (s, 3H, CH_3 OMe), 3.20 (dd, 1H, *J* = 9.9, 3.8 Hz, H-2'); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 169.4 (C=O CO_2Me), 165.2 (C=O OBz), 137.8, 137.5, 137.3 (C_q), 133.0 (CH_{arom}), 130.4 (C_q), 129.7, 129.1, 128.5, 128.5, 128.4, 128.4, 128.2, 128.1, 128.1, 127.9, 126.1 (CH_{arom}), 101.5 (CHPh), 99.7 (C-1'), 98.5 (C-1), 82.3 (C-4'), 77.7 (C-4), 76.6 (C-3'), 76.4 (C-2), 75.2 (CH2 Bn), 73.0 (CH2 Bn), 72.3 (C-3), 70.4 (C-5), 68.4 (C-6'), 63.5 (C-5'), 63.1 (C-2'), 56.0 (OMe), 52.9 (CO_2Me); HRMS: $[M+NH_4]^+$ calcd for $C_{42}H_{47}N_4O_{12}$ 799.31850, found 799.31924.



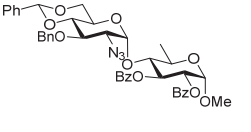
Methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranosyl)-2,3-di-*O*-benzoyl-6-*O*-benzyl-α-D-glucopyranoside (13A). Donor **A** and acceptor **13** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **13A** (83 mg, 90 µmol, 90%, α:β = >20:1) as a colorless oil. R_f: 0.53 (4/1 pentane/EtOAc); $[\alpha]_D^{20}$ = +33.1° (*c* = 1.0, $CHCl_3$); IR (thin film): 698, 710, 748, 997, 1088, 1275, 1367, 1452, 1724, 2934; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 8.03 – 7.91 (m, 4H, CH_{arom}), 7.54 – 7.10 (m, 26H, CH_{arom}), 6.17 (dd, 1H, *J* = 10.2, 9.2 Hz, H-3), 5.48 (s, 1H, C*H*Ph), 5.23 (dd, 1H, *J* = 10.2, 3.6 Hz, H-2), 5.18 (d, 1H, *J* = 3.6 Hz, H-1), 5.05 (d, 1H, *J* = 3.5 Hz, H-1'), 4.78 (d, 1H, *J* = 11.1 Hz, C*H*H Bn), 4.67 – 4.56 (m, 3H, CH_2 Bn, CH*H* Bn), 4.43 – 4.33 (m, 2H, H-4, C*H*H Bn), 4.12 (dd, 1H, *J* = 10.1, 4.8 Hz, H-6'), 4.07 (d, 1H, *J* = 12.3 Hz, CH*H* Bn), 4.05 – 3.97 (m, 2H, H-5, H-6), 3.96 – 3.85 (m, 2H, H-3, H-5'), 3.74 (dd, 1H, *J* = 10.8, 1.6 Hz, H-6), 3.57 (t, 1H, *J* = 10.2 Hz, H-6'), 3.48 (t, 1H, *J* = 9.5 Hz, H-4'), 3.41 (s, 3H, CH_3 OMe), 3.29 (dd, 1H, *J* = 9.4, 3.5 Hz, H-2'); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 166.1, 165.7 (C=O), 138.8, 138.0, 138.0, 137.6 (C_q), 133.3, 133.0 (CH_{arom}), 130.2 (C_q), 130.0, 129.8 (CH_{arom}), 129.2 (C_q), 129.0, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 127.8, 127.8, 127.7, 127.6, 126.2 (CH_{arom}), 101.3 (CHPh), 98.4 (C-1), 96.9 (C-1'), 81.9 (C-4'), 78.7 (C-2'), 78.3 (C-3'), 75.4 (CH_2 Bn), 73.9 (C-4), 73.6, 73.0 (CH_2 Bn), 72.4 (C-2), 72.3 (C-3), 70.0 (C-5), 69.0 (C-6'), 68.3 (C-6), 63.7 (C-5'), 55.4 (OMe); HRMS: $[M+NH_4]^+$ calcd for $C_{55}H_{58}NO_{13}$ 940.39027, found 940.39109.



Methyl 4-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranosyl)-2,3-di-*O*-benzoyl-6-*O*-benzyl-α-D-glucopyranoside (13B). Donor **B** and acceptor **13** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **13B** (80 mg, 93 µmol, 93%, α:β = 10:1) as a colorless oil. R_f: 0.36 (4/1 pentane/EtOAc); $[\alpha]_D^{20}$ = +27.3° (*c* = 1.0, $CHCl_3$); IR (thin film): 710, 748, 999, 1030, 1092, 1277, 1728, 2110, 2932; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 8.05 – 7.92 (m, 4H, CH_{arom}), 7.56 – 7.19 (m, 21H, CH_{arom}), 6.09 (dd, 1H, *J* = 10.2, 9.2 Hz, H-3), 5.53 (s, 1H, C*H*Ph), 5.18 – 5.06 (m, 3H, H-1, H-1', H-2), 4.86 (d, 1H, *J* = 10.8 Hz, C*H*H Bn), 4.68 – 4.63 (m, 3H, CH*H* Bn, CH_2 Bn), 4.25 (t, 1H, *J* = 9.5 Hz, H-4), 4.14 (dd, 1H, *J* = 10.3, 4.9 Hz, H-6'), 4.00 (ddd, 1H, *J* = 10.2, 3.9, 2.0 Hz, H-5), 3.96 – 3.86 (m, 3H, H-3', H-5', H-6), 3.79 (dd, 1H, *J* = 11.0, 1.8 Hz, H-6), 3.70 – 3.55 (m, 2H, H-6', H-4'), 3.42 (s, 3H, CH_3 OMe), 3.23 (dd, 1H, *J* = 10.0, 3.8 Hz, H-2'); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 166.1, 165.6 (C=O), 138.1, 137.8, 137.2 (C_q), 133.4, 133.0, 130.1, 129.6 (CH_{arom}), 129.2 (C_q), 129.2, 128.5, 128.5, 128.5, 128.4, 128.3, 127.9, 127.8, 127.7 (CH_{arom}), 101.5 (CHPh), 99.7 (C-1'), 96.9 (C-1), 82.5 (C-4'), 76.6 (C-3'), 76.1 (C-4), 75.2, 73.8 (CH_2 Bn), 72.4 (C-2), 72.3 (C-3), 69.8 (C-5), 68.8 (C-6'), 68.8 (C-6), 63.8 (C-5'), 63.3 (C-2'), 55.6 (OMe); Diagnostic peaks β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.90 (dd, 1H, *J* = 10.2, 9.1 Hz, H-3), 5.22 (dd, 1H, *J* = 10.1, 3.7 Hz, H-2), 4.77 (d, 1H, *J* = 11.9 Hz, C*H*H Bn), 4.51 (d, 1H, *J* = 11.9 Hz, CH*H* Bn), 2.97 – 2.88 (m, 1H, H-5'), 2.58 (t, 1H, *J* = 10.4 Hz, H-6'); ^{13}C-APT NMR ($CDCl_3$, 101 MHz): δ 166.0, 165.5, 137.9, 137.2, 133.1, 130.5, 130.0, 129.8, 129.3, 128.7, 128.2, 126.0, 101.6 (CHPh), 101.1 (C-1'), 97.1, 81.3, 79.1, 75.9, 74.7, 71.9, 70.8, 69.7, 67.9, 67.6, 66.0, 65.7, 55.5; HRMS: $[M+NH_4]^+$ calcd for $C_{48}H_{51}N_4O_{12}$ 875.34980, found 875.35038.

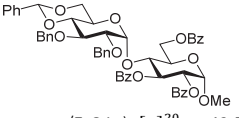


Methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranosyl)-2,3-di-*O*-benzoyl-6-deoxy-α-D-glucopyranoside (14A). Donor **A** and acceptor **14** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **14A** (68 mg, 83 µmol, 83%, α:β = >20:1) as a colorless oil. R_f: 0.50 (4/1 pentane/EtOAc); $[\alpha]_D^{20}$ = +37.1° (*c* = 1.0, $CHCl_3$); IR (thin film): 696, 708, 748, 995, 1026, 1051, 1088, 1177, 1275, 1452, 1722, 2934; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 8.01 – 7.92 (m, 4H, CH_{arom}), 7.54 – 7.04 (m, 21H, CH_{arom}), 6.15 (dd, 1H, *J* = 10.2, 9.1 Hz, H-3), 5.51 (s, 1H, C*H*Ph), 5.15 (dd, 1H, *J* = 10.2, 3.6 Hz, H-2), 5.10 (d, 1H, *J* = 3.8 Hz, H-1'), 5.07 (d, 1H, *J* = 3.6 Hz, H-1), 4.83 (d, 1H, *J* = 11.1 Hz, C*H*H Bn), 4.67 (d, 1H, *J* = 11.1 Hz, CH*H* Bn), 4.36 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.25 (dd, 1H, *J* = 10.3, 4.9 Hz, H-6'), 4.16 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.06 (dq, 1H, *J* = 9.5, 6.2 Hz, H-5), 4.02 – 3.90 (m, 2H, H-3', H-5'), 3.80 (t, 1H, *J* = 9.3 Hz, H-4), 3.68 (t, 1H, *J* = 10.3 Hz, H-6'), 3.53 (t, 1H, *J* = 9.5 Hz, H-4'), 3.40 (s, 3H, CH_3 OMe), 3.35 (dd, 1H, *J* = 9.5, 3.8 Hz, H-2'), 1.45 (d, 3H, *J* = 6.2 Hz, H-6); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 166.2, 165.5 (C=O), 138.7, 137.9, 137.4 (C_q), 133.4, 133.1 (CH_{arom}), 130.1 (C_q), 130.0, 129.8 (CH_{arom}), 129.2 (C_q), 129.0, 128.5, 128.5, 128.4, 128.3, 128.2, 128.1, 127.7, 127.7, 126.1 (CH_{arom}), 101.3 (CHPh), 98.7 (C-1'), 96.7 (C-1), 82.0 (C-4'), 79.8 (C-4), 78.5 (C-2'), 78.5 (C-3'), 75.5, 73.2 (CH_2 Bn), 72.9 (C-2), 72.4 (C-3), 68.9 (C-6'), 66.2 (C-5), 63.6 (C-5'), 55.3 (OMe), 18.6 (C-6); HRMS: $[M+NH_4]^+$ calcd for $C_{48}H_{52}NO_{12}$ 834.34840, found 834.34900.

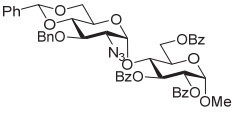


Methyl 4-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranosyl)-2,3-di-*O*-benzoyl-6-deoxy-α-D-glucopyranoside (14B). Donor **B** and acceptor **14** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **14B** (72 mg, 96 µmol, 96%, α:β = 20:1) as a colorless oil. R_f: 0.40 (4/1

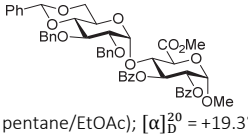
pentane/EtOAc); $[\alpha]_D^{20}$ = +22.9° (*c* = 1.0, $CHCl_3$); IR (thin film): 710, 753, 999, 1030, 1057, 1092, 1177, 1277, 1369, 1450, 1724, 2110, 2936; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 7.99 (dt, 4H, *J* = 8.3, 1.2 Hz, CH_{arom}), 7.54 – 7.18 (m, 16H, CH_{arom}), 6.11 – 6.01 (m, 1H, H-3), 5.56 (s, 1H, C*H*Ph), 5.15 (d, 1H, *J* = 4.0 Hz, H-1'), 5.09 – 5.02 (m, 2H, H-1, H-2), 4.90 (d, 1H, *J* = 10.8 Hz, C*H*H Bn), 4.72 (d, 1H, *J* = 10.8 Hz, CH*H* Bn), 4.26 (dd, 1H, *J* = 10.3, 4.9 Hz, H-6'), 4.06 – 3.89 (m, 3H, H-5, H-5', H-3'), 3.77 – 3.68 (m, 2H, H-4, H-6'), 3.65 (t, 1H, *J* = 9.3 Hz, H-4'), 3.41 (s, 3H, CH_3 OMe), 3.20 (dd, 1H, *J* = 10.1, 4.0 Hz, H-2'), 1.44 (d, 3H, *J* = 6.2 Hz, H-6); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 166.2, 165.5 (C=O), 137.8, 137.1 (C_q), 133.4, 133.0, 130.1 (CH_{arom}), 130.1 (C_q), 129.5 (CH_{arom}), 129.2 (C_q), 129.2, 128.5, 128.5, 128.4, 128.3, 128.0, 126.0 (CH_{arom}), 101.4 (CHPh), 100.1 (C-1'), 96.8 (C-1), 82.4 (C-4'), 82.1 (C-4), 76.5 (C-3'), 75.2 (CH_2 Bn), 72.8 (C-2), 72.3 (C-3), 68.5 (C-6'), 65.7 (C-5), 63.6 (C-5'), 62.9 (C-2'), 55.5 (OMe), 18.3 (C-6); HRMS: $[M+NH_4]^+$ calcd for $C_{41}H_{45}N_4O_{11}$ 769.30793, found 769.30861.



Methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranosyl)-2,3,6-tri-*O*-benzoyl-α-D-glucopyranoside (15A). Donor **A** and acceptor **15** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **15A** (85 mg, 91 µmol, 91%, α:β = >20:1) as a colorless oil. R_f: 0.47 (4/1 pentane/EtOAc); $[\alpha]_D^{20}$ = +43.5° (*c* = 1.0, $CHCl_3$); IR (thin film): 710, 748, 997, 1028, 1090, 1271, 1452, 1724, 2936; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.11 – 8.06 (m, 2H, CH_{arom}), 8.03 – 7.95 (m, 4H, CH_{arom}), 7.63 – 7.57 (m, 1H, CH_{arom}), 7.52 – 7.41 (m, 6H, CH_{arom}), 7.39 – 7.23 (m, 13H, CH_{arom}), 7.19 – 7.14 (m, 3H, CH_{arom}), 7.12 – 7.07 (m, 2H, CH_{arom}), 6.21 (ddd, 1H, *J* = 10.2, 7.0, 1.8 Hz, H-3), 5.44 (s, 1H, C*H*Ph), 5.27 (dd, 1H, *J* = 10.3, 3.6 Hz, H-2), 5.15 (d, 1H, *J* = 3.6 Hz, H-1), 4.94 (d, 1H, *J* = 3.6 Hz, H-1'), 4.85 – 4.75 (m, 2H, C*H*H Bn, H-6), 4.69 – 4.58 (m, 2H, CH*H* Bn, H-6), 4.30 (d, 1H, *J* = 12.4 Hz, C*H*H Bn), 4.26 – 4.18 (m, 2H, H-5, H-4), 4.13 (dd, 1H, *J* = 10.2, 4.8 Hz, H-6'), 4.04 – 3.96 (m, 2H, CH*H* Bn, H-3'), 3.92 (td, 1H, *J* = 10.0, 4.8 Hz, H-5'), 3.57 (t, 1H, *J* = 10.3 Hz, H-6'), 3.49 (d, 1H, *J* = 9.5 Hz, H-4'), 3.44 (s, 3H, CH_3 OMe), 3.29 (dd, 1H, *J* = 9.5, 3.6 Hz, H-2'); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 166.2, 165.6 (C=O), 138.7, 138.0, 137.4 (C_q), 133.5, 133.3, 133.1 (CH_{arom}), 130.1 (C_q), 130.1 (CH_{arom}), 129.9 (C_q), 129.8, 129.8 (CH_{arom}), 129.1 (C_q), 129.0, 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 128.2, 128.1, 127.8, 127.7, 126.2 (CH_{arom}), 101.4 (CHPh), 99.7 (C-1'), 96.9 (C-1), 81.9 (C-4'), 78.4 (C-2'), 78.4 (C-3'), 76.2 (C-4), 75.4 (CH_2 Bn), 73.3 (CH_2 Bn), 72.2 (C-2), 71.7 (C-3), 68.8 (C-6'), 68.7 (C-5), 64.0 (C-5'), 63.4 (C-6), 55.6 (OMe); HRMS: $[M+NH_4]^+$ calcd for $C_{55}H_{56}NO_{14}$ 954.36953, found 954.37046.

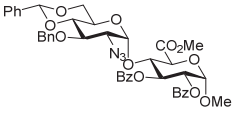


Methyl 4-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranosyl)-2,3,6-tri-*O*-benzoyl-α-D-glucopyranoside (15B). Donor **B** and acceptor **15** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **15B** (60 mg, 69 µmol, 69%, α:β = >20:1) as a white solid. R_f: 0.42 (4/1 pentane/EtOAc); $[\alpha]_D^{20}$ = +38.5° (*c* = 1.0, $CHCl_3$); IR (thin film): 710, 752, 999, 1030, 1096, 1269, 1450, 1724, 2110, 2936; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 8.15 – 7.94 (m, 6H, CH_{arom}), 7.64 – 7.20 (m, 19H, CH_{arom}), 6.14 (dd, 1H, *J* = 9.8, 8.7 Hz, H-3), 5.51 (s, 1H, C*H*Ph), 5.20 – 5.08 (m, 3H, H-1, H-1', H-2), 4.89 (d, 1H, *J* = 10.8 Hz, C*H*H Bn), 4.75 (dd, 1H, *J* = 12.2, 2.0 Hz, H-6), 4.70 (d, 1H, *J* = 10.8 Hz, CH*H* Bn), 4.59 (dd, 1H, *J* = 12.2, 4.1 Hz, H-6), 4.28 (dd, 1H, *J* = 10.4, 4.8 Hz, H-6'), 4.22 (ddd, 1H, *J* = 10.1, 4.1, 1.9 Hz, H-5), 4.20 – 4.12 (m, 1H, H-4), 4.03 – 3.89 (m, 2H, H-3', H-5'), 3.68 – 3.57 (m, 2H, H-6', H-4'), 3.45 (s, 3H, CH_3 OMe), 3.25 (dd, 1H, *J* = 10.0, 4.0 Hz, H-2'); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 166.2, 166.1, 165.6 (C=O), 137.7, 137.1 (C_q), 133.5, 133.5, 133.4, 133.1, 130.1 (CH_{arom}), 130.0 (C_q), 129.9 (CH_{arom}), 129.8 (C_q), 129.5, 129.1 (CH_{arom}), 129.1 (C_q), 128.7, 128.6, 128.5, 128.5, 128.4, 128.3, 128.0, 126.1 (CH_{arom}), 101.4 (CHPh), 100.6 (C-1'), 96.9 (C-1), 82.4 (C-4'), 77.4 (C-4), 76.6 (C-3'), 75.2 (CH_2 Bn), 72.3 (C-2), 72.1 (C-3), 68.5 (C-6'), 68.2 (C-5), 64.0 (C-5'), 63.4 (C-6), 63.0 (C-2'), 55.7 (OMe); HRMS: $[M+Na]^+$ calcd for $C_{48}H_{45}N_3O_{13}Na$ 894.2845, found 894.2878.

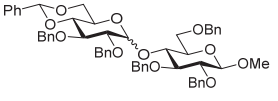


Methyl (methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranosyl)-2,3-di-*O*-benzoyl-α-D-glucopyranosyl uronate) (16A). Donor **A** and acceptor **16** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **16A** (72 mg, 84 µmol, 84%, α:β = >20:1) as a colorless oil. R_f: 0.58 (4/1 pentane/EtOAc); $[\alpha]_D^{20}$ = +19.3° (*c* = 1.0, $CHCl_3$); IR (thin film): 710, 748, 916, 997, 1049, 1090, 1271, 1452, 1732, 2938; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.05 – 7.91 (m, 4H, CH_{arom}), 7.53 – 7.43 (m, 4H, CH_{arom}), 7.41 – 7.24 (m, 12H, CH_{arom}), 7.21 – 7.15 (m, 3H, CH_{arom}), 7.07 – 7.02 (m, 2H, CH_{arom}), 6.17 (dd, 1H, *J* = 10.2, 8.8 Hz, H-3), 5.48 (s, 1H, C*H*Ph), 5.24 (dd, 1H, *J* = 10.1, 3.5 Hz, H-2), 5.20 (d, 1H, *J* = 3.5 Hz, H-1), 4.94 (d, 1H, *J* = 3.7 Hz, H-1'), 4.81 (d, 1H, *J* = 11.2 Hz, C*H*H Bn), 4.70 (d, 1H, *J* = 11.2 Hz, CH*H* Bn), 4.45 (d, 1H, *J* = 9.7 Hz, H-5), 4.39 (dd, 1H, *J* = 9.7, 8.9 Hz, H-4), 4.34 – 4.22 (m, 2H, C*H*H Bn, H-6'), 3.99 (d, 1H, *J* = 12.4 Hz, CH*H* Bn), 3.95 (t, 1H, *J* = 9.4 Hz, H-3'), 3.79 (s, 3H, CH_3 CO_2Me), 3.72 – 3.64 (m, 1H, H-5), 3.64 – 3.56 (m, 1H, H-6'), 3.52 – 3.40 (m, 4H, H-4', CH_3 OMe), 3.28 (dd, 1H, *J* = 9.4, 3.7 Hz, H-

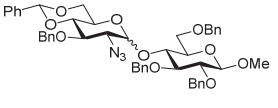
2'); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 169.4 (C=O CO_2Me), 166.0, 165.4 (C=O OBz), 138.7, 137.9, 137.5 (C_q), 133.5, 133.2, 130.1 (CH_{arom}), 130.0 (C_q), 129.8 (CH_{arom}), 129.0 (C_q), 129.0, 128.5, 128.4, 128.3, 128.2, 128.0, 127.7, 127.7, 126.1 (CH_{arom}), 101.3 (CHPh), 99.2 (C-1'), 97.5 (C-1), 81.6 (C-4'), 78.2 (C-2'), 78.0 (C-3'), 76.3 (C-4), 75.4, 72.8 (CH_2 Bn), 71.7 (C-2), 71.3 (C-3), 70.6 (C-5), 68.6 (C-6'), 63.6 (C-5'), 56.0 (OMe), 53.0 (CO_2Me); HRMS: $[M+NH_4]^+$ calcd for $C_{49}H_{52}NO_{14}$ 878.33823, found 878.33866.



Methyl (methyl 4-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranosyl)-2,3-di-*O*-benzoyl-α-D-glucopyranosyl uronate) (16B). Donor **B** and acceptor **16** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **16B** (79 mg, 99 µmol, 99%, α:β = >20:1) as a white solid. R_f: 0.51 (4/1 pentane/EtOAc); $[\alpha]_D^{20}$ = +13.1° (*c* = 1.0, $CHCl_3$); IR (thin film): 710, 752, 995, 1092, 1269, 1369, 1450, 1728, 2110, 2936; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 8.03 – 7.94 (m, 4H, CH_{arom}), 7.54 – 7.19 (m, 16H, CH_{arom}), 6.09 (dd, 1H, *J* = 10.2, 9.0 Hz, H-3), 5.53 (s, 1H, C*H*Ph), 5.21 (d, 1H, *J* = 3.5 Hz, H-1), 5.15 (dd, 1H, *J* = 10.2, 3.5 Hz, H-2), 5.06 (d, 1H, *J* = 3.9 Hz, H-1'), 4.87 (d, 1H, *J* = 10.8 Hz, C*H*H Bn), 4.70 (d, 1H, *J* = 10.8 Hz, CH*H* Bn), 4.45 – 4.26 (m, 3H, H-5, H-4, H-6'), 3.95 (dd, 1H, *J* = 10.0, 8.9 Hz, H-3'), 3.85 (s, 3H, CH_3 CO_2Me), 3.75 – 3.63 (m, 2H, H-5', H-6'), 3.59 (t, 1H, *J* = 9.1 Hz, H-4'), 3.47 (s, 3H, CH_3 OMe), 3.22 (dd, 1H, *J* = 10.0, 3.8 Hz, H-2'); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 169.0 (C=O CO_2Me), 166.0, 165.5 (C=O OBz), 137.8, 137.3 (C_q), 133.5, 133.2, 130.1 (CH_{arom}), 129.8 (C_q), 129.6, 129.2 (CH_{arom}), 129.0 (C_q), 128.6, 128.5, 128.4, 128.3, 127.9, 126.1 (CH_{arom}), 101.5 (C*H*Ph), 99.8 (C-1'), 97.6 (C-1), 82.4 (C-4'), 77.4 (C-4), 76.5 (C-3'), 75.2 (CH_2 Bn), 71.8 (C-2), 71.1 (C-3), 70.3 (C-5), 68.5 (C-6'), 63.6 (C-5'), 63.0 (C-2'), 56.1 (OMe), 53.0 (CO_2Me); HRMS: $[M+NH_4]^+$ calcd for $C_{42}H_{45}N_4O_{13}$ 813.29776, found 813.29765.

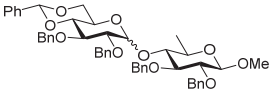


Methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranosyl)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (17A). Donor **A** and acceptor **17** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **17A** (71 mg, 79 µmol, 79%, α:β = 1:1) as a colorless oil. R_f: 0.67 (4/1 pentane/EtOAc); IR (thin film): 698, 737, 910, 999, 1072, 1211, 1277, 1366, 1454, 2866; Data reported for a 1:1 mixture of anomers: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 7.55 – 7.05 (m, 60H, CH_{arom}), 5.71 (d, 1H, *J* = 3.9 Hz, H-1'$_\alpha$), 5.53 (s, 1H, C*H*Ph$_\alpha$), 5.49 (s, 1H, C*H*Ph$_\beta$), 5.00 – 4.84 (m, 6H, 6xC*H*H Bn), 4.84 – 4.66 (m, 9H, CH_2 Bn, 5xCH*H* Bn, 2xC*H*H Bn), 4.66 – 4.50 (m, 5H, 3xCH*H* Bn, C*H*H Bn, H-1'$_\beta$), 4.38 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.34 (d, 1H, *J* = 7.8 Hz, H-1$_\alpha$), 4.29 (d, 1H, *J* = 7.7 Hz, H-1$_\beta$), 4.23 – 4.14 (m, 2H, H-6'$_\beta$, H-6$_\alpha$), 4.12 (dd, 1H, *J* = 9.7, 8.7 Hz, H-3'$_\beta$), 4.02 – 3.94 (m, 2H, H-3$_\alpha$, H-3$_\beta$), 3.91 – 3.73 (m, 5H, H-5$_\alpha$, H-6$_\beta$, H-6$_\alpha$, H-6$_\alpha$, H-3'$_\alpha$), 3.68 (dd, 1H, *J* = 10.9, 1.8 Hz, H-6$_\beta$), 3.66 – 3.52 (m, 12H, H-2$_\alpha$, H-4'$_\beta$, H-4'$_\alpha$, H-4$_\alpha$, H-5$_\beta$, H-6'$_\alpha$, CH_3 OMe$_\alpha$, CH_3 OMe$_\beta$), 3.51 – 3.28 (m, 6H, H-2'$_\alpha$, H-2$_\beta$, H-2'$_\beta$, H-3$_\beta$, H-4$_\beta$, H-6'$_\beta$), 3.14 (td, 1H, *J* = 9.4, 4.9 Hz, H-5'$_\beta$); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 139.1, 138.8, 138.8, 138.6, 138.4, 138.3, 138.2, 137.9, 137.7, 137.5 (C_q), 129.1, 128.9, 128.5, 128.4, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 128.1, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7, 127.7, 127.5, 127.3, 126.7, 126.1 (CH_{arom}), 104.8 (C-1$_\beta$), 104.6 (C-1$_\alpha$), 102.9 (C-1'$_\beta$), 101.2 (CHPh$_{\alpha,\beta}$), 97.3 (C-1'$_\alpha$), 84.9 (C-3'$_\alpha$), 82.9 (C-2$_\alpha$), 82.6 (C-2'$_\beta$), 82.5, 82.4, 81.9, 81.8, 81.2 (C-4$_\alpha$ C-4'$_\beta$ C-5$_\alpha$ C-2$_\beta$ C-4'$_\alpha$), 78.8, 78.8 (C-2'$_\alpha$ C-3$_\beta$), 76.9 (C-3$_\alpha$), 75.5, 75.5, 75.4, 75.1, 75.1 (CH_2 Bn), 75.0 (C-4$_\beta$), 74.7, 74.3 (CH_2 Bn), 73.9 (C-5$_\beta$), 73.8, 73.5, 73.3 (CH_2 Bn), 72.0 (C-3'$_\beta$), 69.0 (C-6$_\alpha$), 68.9 (C-6'$_{\alpha,\beta}$) 68.0 (C-6$_\beta$), 65.9 (C-5'$_\beta$), 63.4 (C-5'$_\alpha$), 57.2 (OMe$_\alpha$), 57.1 (OMe$_\beta$); HRMS: $[M+NH_4]^+$ calcd for $C_{48}H_{56}NO_{10}$ 912.43174, found 912.43238.

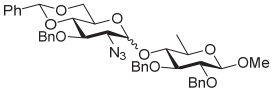


Methyl 4-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranosyl)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (17B). Donor **B** and acceptor **17** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **17B** (66 mg, 80 µmol, 80%, α:β = 1:7) as a colorless oil. R_f: 0.78 (4/1 pentane/EtOAc); IR (thin film): 698, 737, 914, 999, 1092, 1277, 1366, 1454, 2110, 2870; Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 7.54 – 7.14 (m, 25H, CH_{arom}), 5.47 (s, 1H, C*H*Ph), 4.90 – 4.82 (m, 3H, CH_2 Bn, C*H*H Bn), 4.82 – 4.67 (m, 4H, CH*H* Bn, CH_2 Bn, C*H*H Bn), 4.48 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.35 (d, 1H, *J* = 7.8 Hz, H-1'), 4.30 (d, 1H, *J* = 7.7 Hz, H-1), 4.11 (dd, 1H, *J* = 10.5, 5.0 Hz, H-6'), 4.02 (t, 1H, *J* = 9.4 Hz, H-4), 3.99 – 3.92 (m, 1H, H-6), 3.82 (dd, 1H, *J* = 11.0, 1.8 Hz, H-6), 3.60 – 3.52 (m, 5H, CH_3 OMe, H-3, H-4'), 3.49 – 3.29 (m, 5H, H-2, H-2', H-3', H-5, H-6'), 3.01 (td, 1H, *J* = 9.8, 5.0 Hz, H-5'); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 139.1, 138.7, 138.1, 137.9, 137.3 (C_q), 129.2, 128.6, 128.5, 128.4, 128.3, 128.3, 128.1, 128.0, 128.0, 127.7, 127.7, 127.5, 126.1 (CH_{arom}), 104.8 (C-1), 101.3 (C*H*Ph), 101.3 (C-1'), 82.8 (C-4'), 81.8 (C-2), 81.8 (C-3), 79.2 (C-3'), 76.9 (C-4), 75.5, 75.0, 74.9 (CH_2 Bn), 74.7 (C-5), 73.5 (CH_2 Bn), 68.6 (C-6'), 68.2 (C-6), 66.7 (C-2'), 65.9 (C-5'), 57.3 (OMe); Diagnostic peaks for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.69 (d, 1H, *J* = 4.1 Hz, H-1'), 5.54 (s, 1H, C*H*Ph), 5.07 (d, 1H, *J* = 10.7 Hz), 3.26 (dd, 1H, *J* = 10.1, 4.0 Hz, H-2'); ^{13}C-APT NMR ($CDCl_3$, 101 MHz): δ 138.5, 138.4, 138.3, 137.4,

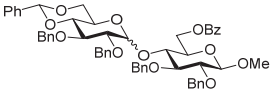
129.1, 128.5, 128.4, 128.2, 127.8, 127.6, 126.1, 104.7, 98.0, 85.0, 82.7, 76.2, 75.1, 74.3, 73.7, 73.1, 69.2, 68.8, 63.4, 62.8, 57.1; HRMS: $[M+NH_4]^+$ calcd for $C_{48}H_{55}N_4O_{10}$ 847.39127, found 847.39197.



Methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranosyl)-2,3-di-*O*-benzyl-6-deoxy-β-D-glucopyranoside (18A). Donor **A** and acceptor **18** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **18A** (69 mg, 87 µmol, 87%, α:β = 1.1:1) as a colorless oil. R_f: 0.68 (4/1 pentane/EtOAc); IR (thin film): 698, 737, 999, 1030, 1072, 1454, 2870, 3032; Data reported for a 1.1:1 mixture of anomers: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 7.53 – 7.06 (m, 47.5H, CH_{arom}), 5.71 (d, 1H, *J* = 4.1 Hz, H-1'$_\alpha$), 5.55 (s, 1H, C*H*Ph$_\alpha$), 5.52 (s, 0.9H, C*H*Ph$_\beta$), 4.99 – 4.87 (m, 5H, 3xC*H*H Bn, CH_2 Bn), 4.87 – 4.74 (m, 6H, 2xCH*H* Bn, 2xCH_2 Bn), 4.74 – 4.62 (m, 3.9H, CH*H* Bn, 2xC*H*H Bn, H-1'$_\beta$), 4.57 (d, 1H, *J* = 10.9 Hz, CH*H* Bn), 4.52 (d, 1H, *J* = 11.7 Hz, CH*H* Bn), 4.34 – 4.28 (m, 1.9H, H-1$_\alpha$, H-1$_\beta$), 4.26 (dd, 1H, *J* = 10.3, 4.9 Hz, H-6'$_\alpha$), 4.18 (dd, 0.9H, *J* = 10.4, 4.9 Hz, H-6'$_\beta$), 4.02 (t, 1H, *J* = 9.3 Hz, H-3'$_\alpha$), 3.94 (td, 1H, *J* = 10.0, 4.8 Hz, H-5'$_\alpha$), 3.81 – 3.68 (m, 3H. H-3$_\alpha$, H-4$_\alpha$, H-6'$_\alpha$), 3.67 – 3.58 (m, 4.7H, H-3'$_\beta$, H-3$_\beta$, H-4'$_\beta$, H-5$_\alpha$, H-4'$_\alpha$), 3.57 (s, 3H, CH_3 OMe$_\alpha$), 3.56 (s, 2.7H, CH_3 OMe$_\beta$), 3.54 – 3.43 (m, 5.7H, H-2'$_\alpha$, H-2$_\alpha$, H-6'$_\beta$, H-4$_\beta$, H-5$_\alpha$, H-2'$_\beta$), 3.43 – 3.35 (m, 1.8H, H-2$_\beta$, H-5$_\beta$), 3.31 (td, 0.9H, *J* = 9.7, 4.9 Hz, H-5'$_\beta$), 1.42 (d, 3H, *J* = 5.8 Hz, H-6$_\alpha$), 1.38 (d, 2.7H, *J* = 6.1 Hz, H-6$_\beta$); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 139.2, 139.0, 138.7, 138.7, 138.5, 138.4, 138.2, 137.9, 137.4 (C_q), 129.1, 129.0, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.1, 128.1, 127.9, 127.8, 127.7, 127.7, 127.7, 127.7, 127.5, 127.2, 126.5, 126.1, 126.0 (CH_{arom}), 104.5 (C-1$_\beta$), 104.5 (C-1$_\alpha$), 103.7 (C-1'$_\beta$), 101.2 (CHPh$_{\alpha,\beta}$), 97.8 (C-1'$_\alpha$), 84.6 (C-3$_\alpha$), 83.2 (C-4$_\beta$), 82.9, 82.7, 82.7, 82.3, 82.1 (C-3$_\beta$ C-3'$_\beta$ C-2$_\beta$ C-2'$_\beta$ C-2$_\alpha$), 81.8 (C-4'$_\beta$), 81.4 (C-4$_\alpha$), 78.9 (C-3'$_\alpha$), 78.7 (C-2'$_\alpha$), 78.2 (C-4'$_\alpha$), 75.7, 75.5, 75.4, 75.3, 75.0, 74.7, 74.0, 73.8 (CH_2 Bn), 71.4 (C-5$_\beta$), 70.4 (C-5$_\alpha$), 68.9 (C-6'$_\alpha$), 68.8 (C-6'$_\beta$), 66.0 (C-5'$_\alpha$), 63.3 (C-5'$_\alpha$), 57.2 (OMe$_\alpha$), 57.2 (OMe$_\beta$), 19.3 (C-6$_\alpha$), 18.1 (C-6$_\beta$); HRMS: $[M+Na]^+$ calcd for $C_{48}H_{52}O_{10}Na$ 811.3453, found 811.3475.

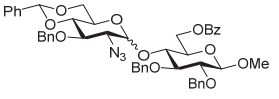


Methyl 4-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranosyl)-2,3-di-*O*-benzyl-6-deoxy-β-D-glucopyranoside (18B). Donor **B** and acceptor **18** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **18B** (62 mg, 86 µmol, 86%, α:β = 1:5) as a white solid. R_f: 0.84 (4/1 pentane/EtOAc); IR (thin film): 698, 737, 999, 1072, 1169, 1277, 1366, 1454, 2110, 2873; Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.54 – 7.11 (m, 20H, CH_{arom}), 5.49 (s, 1H, C*H*Ph), 4.91 (d, 1H, *J* = 11.3 Hz, C*H*H Bn), 4.87 (d, 1H, *J* = 11.1 Hz, C*H*H Bn), 4.85 – 4.81 (m, 2H, CH_2 Bn), 4.77 (d, 1H, *J* = 11.2 Hz, CH*H* Bn), 4.68 (d, 1H, *J* = 11.0 Hz, CH*H* Bn), 4.52 (d, 1H, *J* = 8.1 Hz, H-1'), 4.30 (d, 1H, *J* = 7.8 Hz, H-1), 4.06 (dd, 1H, *J* = 10.5, 5.0 Hz, H-6'), 3.63 (t, 1H, *J* = 9.1 Hz, H-4'), 3.60 – 3.50 (m, 5H, CH3 OMe, H-3, H-3'), 3.50 – 3.36 (m, 6H, H-2, H-2', H-4, H-5, H-6'), 3.22 (td, 1H, *J* = 9.6, 5.0 Hz, H-5'), 1.44 (d, 2H, *J* = 5.5 Hz, H-6); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 139.1, 138.6, 137.8, 137.2 (C_q), 129.2, 128.5, 128.4, 128.4, 128.3, 128.3, 128.1, 128.0, 127.7, 127.6, 127.5, 127.3, 126.1 (CH_{arom}), 104.5 (C-1), 102.3 (C-1'), 101.3 (CHPh), 83.5 (C-4), 82.9 (C-3), 82.3 (C-2), 81.7 (C-4'), 79.4 (C-3'), 75.4, 75.0, 74.9 (CH_2 Bn), 71.0 (C-5), 68.5 (C-6'), 67.2 (C-2'), 66.2 (C-5'), 57.2 (OMe), 18.1 (C-6); Diagnostic peaks for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.64 (d, 1H, *J* = 4.2 Hz, (H-1'), 5.57 (s, 1H, C*H*Ph), 5.08 (d, 1H, *J* = 10.6 Hz, C*H*H Bn), 4.98 (d, 1H, *J* = 10.9 Hz, C*H*H Bn), 4.23 (dd, 1H, *J* = 10.4, 4.9 Hz, H-6'), 3.93 (td, 1H, *J* = 9.9, 4.9 Hz, H-5'), 3.29 (dd, 1H, *J* = 10.1, 4.2 Hz, H-2'), 1.39 (d, 3H, *J* = 5.2 Hz, H-6); ^{13}C-APT NMR ($CDCl_3$, 101 MHz): δ 138.6, 138.4, 137.9, 128.6, 128.2, 127.8, 126.0, 101.3, 98.6, 84.6, 83.1, 82.6, 79.5, 76.3, 75.2, 75.0, 74.7, 70.2, 68.6, 63.3, 62.8, 57.2, 19.0; HRMS: $[M+NH_4]^+$ calcd for $C_{41}H_{49}N_4O_9$ 741.34941, found 741.35004.

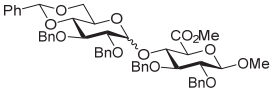


Methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranosyl)-2,3-di-*O*-benzyl-6-*O*-benzoyl-β-D-glucopyranoside (19A). Donor **A** and acceptor **19** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **19A** (66 mg, 73 µmol, 73%, α:β = 3:1) as a white solid. R_f: 0.65 (4/1 pentane/EtOAc); IR (thin film): 698, 999, 1030, 1088, 1273, 1454, 1721, 2862, 3032; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 8.13 – 8.03 (m, 2H, CH_{arom}), 7.60 – 7.01 (m, 28H, CH_{arom}), 5.65 (d, 1H, *J* = 4.0 Hz, H-1'), 5.46 (s, 1H, C*H*Ph), 4.95 – 4.65 (m, 7H, 2xC*H*H Bn, 2xCH_2 Bn, H-6), 4.65 – 4.50 (m, 3H, 2x CH*H* Bn, H-6), 4.38 (d, 1H, *J* = 7.7 Hz, H-1), 4.12 – 4.00 (m, 3H, H-4', H-6', H-5'), 3.87 – 3.74 (m, 3H, H-3, H-5, H-3'), 3.62 – 3.45 (m, 7H, H-2', H-2, H-4, H-6', CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 166.2 (C=O), 138.8, 138.6, 138.3, 138.0, 137.4 (C_q), 133.2 (CH_{arom}), 130.0 (C_q), 129.9, 129.7, 129.0, 128.5, 128.5, 128.4, 128.4, 128.4, 128.3, 128.2, 128.1, 127.8, 127.7, 126.8, 126.2 (CH_{arom}), 104.5 (C-1), 101.4 (CHPh), 98.3 (C-1'), 84.5 (C-3), 82.4 (C-4), 82.4 (C-2), 78.8 (C-5'), 78.6 (C-2'), 75.3, 74.7, 74.3 (CH_2 Bn), 74.2 (C-4'), 74.1 (CH_2 Bn), 72.6 (C-3'), 68.9 (C-6'), 63.8 (C-6), 63.7 (C-5), 57.2 (OMe); Diagnostic peaks for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.50 (s, 1H, C*H*Ph), 4.47 (dd, 1H, *J* = 12.0, 4.9 Hz), 4.33 (d, 1H, *J* = 7.7 Hz, H-1), 4.19 (dt, 1H, *J* = 9.3, 4.6 Hz), 3.72 (d, 1H, *J* = 8.9 Hz), 3.67 – 3.62 (m, 1H), 3.44 –

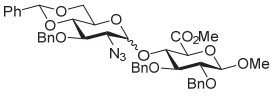
3.39 (m, 1H, H-2'), 3.23 (td, 1H, *J* = 9.7, 5.0 Hz, H-5'); ^{13}C-APT NMR ($CDCl_3$, 101 MHz): δ 166.0, 138.8, 138.6, 138.5, 138.2, 137.3, 133.3, 129.7, 129.0, 128.5, 128.0, 127.4, 126.1, 104.6 (C-1), 103.1 (C-1'), 101.2 (CHPh), 82.7, 82.6, 81.8, 81.4, 77.4, 75.8, 75.7, 75.3, 75.0, 73.3, 66.1, 62.9; HRMS: $[M+Na]^+$ calcd for $C_{55}H_{56}O_{12}Na$ 931.3664, found 931.3695.



Methyl 4-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranosyl)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (19B). Donor **B** and acceptor **19** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **19B** (59 mg, 70 μmol, 70%, α:β = 1:1.2) as a colorless oil. R_f: 0.59 (4/1 pentane/EtOAc); IR (thin film): 698, 737, 999, 1030, 1069, 1092, 1273, 1369, 1454, 1721, 2110, 2870, 3032; Data reported for a 1:1.2 mixture of anomers: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.10 – 8.00 (m, 4.4H, CH_{arom}), 7.61 – 7.18 (m, 50.6H, CH_{arom}), 5.68 (d, 1H, *J* = 4.2 Hz, H-1'$_\alpha$), 5.49 (s, 1H, C*H*Ph$_\alpha$), 5.48 (s, 1.2H, C*H*Ph$_\beta$), 5.10 (d, 1H, *J* = 10.5 Hz, C*H*H Bn$_\alpha$), 4.95 (d, 1H, *J* = 11.0 Hz, C*H*H Bn$_\alpha$), 4.94 (d, 1H, *J* = 11.0 Hz, C*H*H Bn$_\alpha$), 4.92 – 4.82 (m, 7H, 2xC*H*H Bn$_\beta$, CH_2 Bn$_\beta$, CH*H* Bn$_\alpha$, H-6$_\beta$), 4.80 – 4.72 (m, 3.2H, CH*H* Bn$_\alpha$, CH*H* Bn$_\beta$, H-6$_\alpha$), 4.70 (d, 1.2H, *J* = 11.0 Hz,, CH*H* Bn$_\beta$), 4.68 (d, 1H, *J* = 11.0 Hz, CH*H* Bn$_\alpha$), 4.57 (dd, 1H, *J* = 12.2, 4.4 Hz, H-6$_\beta$), 4.51 – 4.43 (m, 2.2H, H-1'$_\beta$, H-6$_\alpha$), 4.43 – 4.33 (m, 2.2H, H-1$_\alpha$, H-1$_\beta$), 4.09 – 3.92 (m, 5.4H, H-3'$_\alpha$, H-4$_\alpha$, H-4$_\beta$, H-6'$_\alpha$, H-6'$_\beta$), 3.88 – 3.77 (m, 2.2H, H-3$_\beta$, H-5'$_\alpha$), 3.76 – 3.60 (m, 5.4H, H-3$_\alpha$, H-4'$_\alpha$, H-4'$_\beta$, H-5$_\alpha$, H-5$_\beta$), 3.60 – 3.39 (m, 13.4H, CH_3 OMe$_\alpha$, CH_3 OMe$_\beta$, H-2$_\alpha$, H-2$_\beta$, H-2'$_\beta$, H-3'$_\beta$, H-6'$_\alpha$, H-6'$_\beta$), 3.31 (dd, 1H, *J* = 10.1, 4.1 Hz, H-2'$_\alpha$), 3.13 (td, 1.2H, *J* = 9.6, 5.0 Hz, H-5'$_\beta$); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 166.1 (C=O), 138.8, 138.5, 138.4, 138.3, 137.8, 137.7, 137.2, 137.1 (C_q), 133.4, 133.3, 129.9 (CH_{arom}), 129.9 (C_q), 129.7, 129.2, 129.1, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.7, 127.5, 126.2, 126.0 (CH_{arom}), 104.7 (C-1$_\beta$), 104.6 (C-1$_\alpha$), 101.9 (C-1'$_\beta$), 101.4 (CHPh$_\alpha$), 101.3 (CHPh$_\beta$), 98.8 (C-1'$_\alpha$), 84.5 (C-3$_\beta$), 82.8 (C-2$_\beta$), 82.7 (C-4'$_\alpha$), 82.6 (C-3$_\alpha$), 81.9 (C-2$_\beta$), 81.6 (C-4'$_\beta$), 79.6 (C-3'$_\beta$), 77.7 (C-4$_\beta$), 76.0 (C-3'$_\alpha$), 75.7, 75.1, 75.1, 75.0 (CH_2 Bn), 74.8 (C-4$_\alpha$), 74.7, 74.7 (CH_2 Bn), 73.0 (C-5$_\beta$), 72.3 (C-5$_\alpha$), 68.5 (C-6$_{\alpha,\beta}$), 66.8 (C-2'$_\beta$), 66.3 (C-5'$_\beta$), 63.7 (C-5'$_\alpha$), 63.6 (C-6$_\alpha$), 63.1 (C-6$_\beta$), 62.8(C-2'$_\alpha$),, 57.3 (OMe$_\beta$), 57.2 (OMe$_\alpha$); HRMS: $[M+Na]^+$ calcd for $C_{48}H_{49}N_3O_{11}Na$ 866.3289, found 866.3259.

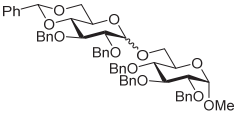


Methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranosyl)-2,3-di-*O*-benzyl-β-D-glucopyranosyl uronate) (20A). Donor **A** and acceptor **20** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **20A** (69 mg, 83 μmol, 83%, α:β = 5:1) as a white solid. R_f: 0.75 (4/1 pentane/EtOAc); IR (thin film): 698, 737, 995, 1030, 1207, 1454, 1751, 2866, 3032; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 7.50 – 7.08 (m, 25H, CH_{arom}), 5.51 (s, 1H, C*H*Ph), 5.38 (d, 1H, *J* = 3.8 Hz, H-1'), 4.94 – 4.75 (m, 4H, 2xC*H*H Bn, CH_2 Bn), 4.67 – 4.50 (m, 4H, 2xCH*H* Bn, CH_2 Bn), 4.36 (d, 1H, *J* = 7.6 Hz, H-1), 4.32 – 4.25 (m, 1H, H-6'), 4.19 (t, 1H, *J* = 9.0 Hz, H-4), 4.00 (d, 1H, *J* = 9.5 Hz, H-5), 3.78 (s, 3H, CH_3 CO_2Me), 3.75 (t, 1H, *J* = 8.9 Hz, H-3), 3.65 – 3.55 (m, 3H, H-6', H-5', H-4'), 3.54 (s, 3H, CH_3 OMe), 3.52 – 3.43 (m, 3H, H-3', H-2, H-2'); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 169.0 (C=O), 138.7, 138.6, 138.2, 137.9, 137.5 (C_q), 129.0, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.2, 128.1, 127.9, 127.8, 127.7, 127.7, 127.3, 127.0, 126.1 (CH_{arom}), 104.9 (C-1), 101.3 (C*H*Ph), 98.4 (C-1'), 83.4 (C-3), 82.0 (C-4'), 81.5 (C-2), 78.6 (C-2'), 78.4 (C-3'), 76.3 (C-4), 75.3 (CH_2 Bn), 74.8 (C-5), 74.8, 74.7, 73.6 (CH_2 Bn), 68.6 (C-6'), 63.2 (C-5'), 57.5 (OMe), 52.9 (CO_2Me); Diagnostic peaks for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.48 (s, 1H, C*H*Ph), 4.39 (d, 1H, *J* = 7.6 Hz), 3.91 (d, 1H, *J* = 9.4 Hz), 3.41 – 3.29 (m, 1H); ^{13}C-APT NMR ($CDCl_3$, 101 MHz): δ 169.1, 138.9, 138.5, 138.5, 138.5, 137.4, 129.0, 127.6, 126.1, 105.0, 102.8, 101.2, 82.3, 81.8, 81.3, 78.0, 75.6, 75.4, 75.0, 74.8, 74.5, 68.8, 66.0, 52.7; HRMS: $[M+Na]^+$ calcd for $C_{49}H_{52}O_{12}Na$ 855.3351, found 855.3370.

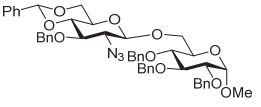


Methyl (methyl 4-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranosyl)-2,3-di-*O*-benzyl-β-D-glucopyranosyl uronate) (20B). Donor **B** and acceptor **20** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **20B** (65 mg, 85 μmol, 85%, α:β = 1.2:1) as a white solid. R_f: 0.55 (4/1 pentane/EtOAc); IR (thin film): 698, 741, 999, 1030, 1211, 1277, 1369, 1454, 1751, 2110, 2870, 2932; Data reported for a 1.2:1 mixture of anomers: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 7.51 – 7.19 (m, 36H, CH_{arom}), 5.53 (s, 1H, C*H*Ph$_\alpha$), 5.50 (d, 1H, *J* = 3.9 Hz, H-1'$_\alpha$), 5.48 (s, 0.8H, C*H*Ph$_\beta$), 5.01 (d, 1H, *J* = 10.6 Hz, C*H*H Bn), 4.92 – 4.72 (m, 9H, C*H*H Bn, 4xCH_2 Bn), 4.69 (d, 1H, *J* = 4.8 Hz, C*H*H Bn), 4.66 (d, 1H, *J* = 4.8 Hz, CH*H* Bn), 4.46 (d, 0.8H, *J* = 8.1 Hz, H-1'$_\beta$), 4.42 – 4.34 (m, 1.8H, H-1$_\beta$, H-1$_\alpha$), 4.27 (dd, 1H, *J* = 10.3, 4.8 Hz, H-6'$_\alpha$), 4.19 – 4.04 (m, 2.8H, H-3$_\alpha$, H-5$_\alpha$, H-6'$_\beta$), 4.01 – 3.91 (m, 2.8H, H-5$_\beta$, H-4$_\alpha$, H-3'$_\alpha$), 3.85 (s, 2.4H, CH_3 CO_2Me$_\beta$), 3.83 (s, 3H, CH_3 OMe$_\alpha$), 3.76 (t, 1H, *J* = 8.9 Hz, H-3$_\beta$), 3.70 – 3.63 (m, 2H, H-6'$_\alpha$, H-4'$_\alpha$), 3.59 (dd, 0.8H, *J* = 9.1, 1.6 Hz, H-4'$_\beta$), 3.56 (s, 5.4H, CH_3 OMe$_{\alpha,\beta}$), 3.54 – 3.51 (m, 1.8H, H-2$_\alpha$, H-4$_\beta$) 3.51 – 3.47 (m, 0.8H, H-2$_\beta$), 3.47 – 3.40 (m, 2.6H, H-3$_\beta$, H-5'$_\alpha$, H-6'$_\beta$), 3.36 – 3.27 (m, 2.6H, H-2'$_\beta$, H-2'$_\alpha$, H-5'$_\beta$); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 169.0, 169.0 (C=O),

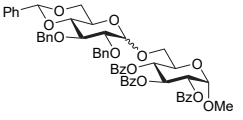
138.8, 138.3, 138.3, 138.2, 137.9, 137.9, 137.4, 137.2 (C_q), 129.2, 129.1, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.1, 128.0, 128.0, 127.9, 127.8, 127.7, 127.7, 127.6, 127.5 (CH_{arom}), 105.1 (C-1$_\beta$), 105.0 (C-1$_\alpha$), 102.3 (C-1'$_\beta$), 101.5 (CHPh$_\alpha$), 101.4 (CHPh$_\beta$), 98.4 (C-1'$_\alpha$), 83.9 (C-3$_\beta$), 82.4 (C-4'$_\alpha$), 82.0 (C-4$_\beta$), 81.9 (C-2$_\alpha$), 81.6 (C-4'$_\beta$), 81.4 (C-2$_\beta$), 79.3 (C-5$_\alpha$), 79.2 (C-3'$_\beta$), 76.2 (C-3'$_\alpha$), 75.5, 75.4 (CH_2 Bn), 75.2 (C-3$_\alpha$), 75.1, 75.0, 75.0, 74.8 (CH_2 Bn), 74.4 (C-4$_\alpha$), 74.3 (C-5$_\beta$), 68.5 (C-6'$_{\alpha,\beta}$), 66.7 (C-2'$_\beta$), 66.2 (C-5'$_\beta$), 63.1 (C-5'$_\alpha$), 62.8 (C-2'$_\alpha$), 57.6 (OMe$_{\alpha,\beta}$), 53.0 (CO_2Me_β), 52.9 (CO_2Me_α); HRMS: $[M+Na]^+$ calcd for $C_{42}H_{45}N_3O_{11}Na$ 790.2946, found 790.2962.



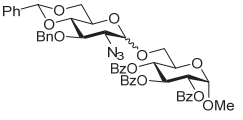
Methyl 6-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (21A). See Chapter 3, compound **25** for synthesis and analytical data.



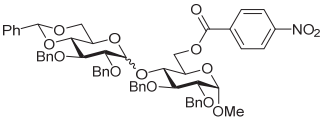
Methyl 6-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (21B). See Chapter 4, compound **3C** for synthesis and analytical data.



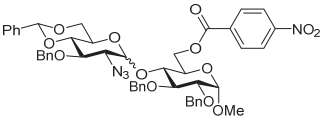
Methyl 6-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranosyl)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (22A). Donor **A** and acceptor **22**[53] were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **22A** (80 mg, 86 µmol, 86%, α:β = 3 : 1) as a colorless oil. R_f: 0.40 (4/1 pentane/EtOAc). Spectroscopic data were in accord with those previously reported for the α-anomer.[59] IR (thin film): 648, 696, 708, 727, 906, 1026, 1053, 1068, 1088, 1261, 1277, 1452, 1726; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 – 7.91 (m, 4H, CH_{arom}), 7.90 – 7.82 (m, 2H, CH_{arom}), 7.56 – 7.43 (m, 4H, CH_{arom}), 7.43 – 7.16 (m, 20H, CH_{arom}), 6.24 – 6.12 (m, 1H, H-3), 5.57 – 5.46 (m, 2H, C*H*Ph, H-4), 5.33 – 5.19 (m, 2H, H-1, H-2), 4.94 – 4.64 (m, 5H, 2xCH_2 Bn, H-1'), 4.41 – 4.30 (m, 1H, H-5), 4.18 (dd, 1H, *J* = 10.0, 4.8 Hz, H-6'), 4.11 – 3.96 (m, 2H, H-3', H-5'), 3.91 – 3.82 (m, 1H, H-6), 3.78 – 3.52 (m, 5H, H-2', H-4', H-6, H-6'), 3.52 – 3.36 (m, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 165.9, 165.9, 165.5 (C=O), 138.8, 138.4, 137.7 (C_q), 133.5, 133.4, 133.2, 130.0, 130.0, 129.8 (CH_{arom}), 129.3, 129.2, 129.0 (C_q), 128.5, 128.5, 128.5, 128.5, 128.4, 128.3, 128.3, 128.3, 128.1, 128.1, 128.0, 127.9, 127.6, 126.2 (CH_{arom}), 101.3 (CHPh), 98.3 (C-1'), 97.0 (C-1), 82.2 (C-4'), 79.4 (C-2'), 78.3 (C-3'), 75.2, 73.6 (CH_2 Bn), 72.2 (C-2), 70.6 (C-3), 69.7 (C-4), 69.0 (C-6'), 68.7 (C-5), 67.3 (C-6), 62.6 (C-5'), 55.8 (OMe); Diagnostic peaks β-anomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.01 (d, 1H, *J* = 10.7 Hz, H-), 4.59 (d, *J* = 7.6 Hz, 1H); ^{13}C-APT NMR ($CDCl_3$, 101 MHz): δ 165.9, 165.9, 165.5, 138.6 (C=O), 138.4, 137.4, 133.6 (C_q), 133.5-127.6 (CH_{arom}), 104.4 (C-1'), 101.2 (CHPh), 97.0 (C-1) 82.3, 81.4, 80.9, 75.4, 72.1, 70.5, 70.0, 69.2, 69.0, 66.1, 55.7; HRMS: $[M+Na]^+$ calcd for $C_{55}H_{52}O_{14}Na$ 959.3255, found 959.3292.



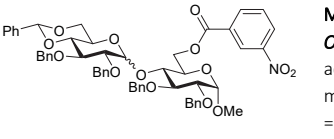
Methyl 6-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranosyl)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (22B). Donor **B** and acceptor **22**[53] were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **22B** (83 mg, 95 µmol, 95%, α:β = 1 : 1.5) as a colorless oil. R_f: 0.32 and 0.50 (4/1 pentane/EtOAc); product was contaminated with 10% of the 6-6 homocoupled acceptor. IR (thin film): 698, 706, 735, 999, 1026, 1069, 1090, 1175, 1250, 1261, 1450, 1724, 2110; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 8.01 – 7.93 (m, 10H, CH_{arom}), 7.89 – 7.84 (m, 5H, CH_{arom}), 7.54 – 7.25 (m, 47.5H, CH_{arom}), 6.22 – 6.14 (m, 2.5H, H-3$_\alpha$, H-3$_\beta$), 5.64 – 5.53 (m, 5H, C*H*Ph$_{\alpha,\beta}$, H-4$_\alpha$, H-4$_\beta$), 5.31 – 5.23 (m, 5H, H-1$_\alpha$, H-1$_\beta$, H-2$_\alpha$, H-2$_\beta$), 4.97 (d, 1H, *J* = 11.1 Hz, C*H*H Bn$_\alpha$), 4.95 – 4.89 (m, 2H, C*H*H Bn$_\beta$, H-1'$_\alpha$), 4.87 – 4.76 (m, 2H, CH*H* Bn$_\alpha$, CH*H* Bn$_\beta$), 4.44 (d, 1.5H, *J* = 8.0 Hz, H-1'$_\beta$), 4.34 – 4.26 (m, 4H, H-5$_\alpha$, H-5$_\beta$, H-6'$_\beta$), 4.20 – 4.11 (m, 2H, H-3', H-6'), 4.07 (dd, 1.5H, *J* = 11.2, 2.2 Hz, H-6), 3.99 – 3.89 (m, 2H, H-5', H-6), 3.80 (dd, 1.5H, *J* = 11.3, 6.3 Hz, H-6), 3.77 – 3.64 (m, 6H, H-4'$_\alpha$, H-4'$_\beta$, H-6$_\alpha$, H-6'$_\alpha$, H-6'$_\beta$), 3.57 (t, 1.5H, *J* = 9.3 Hz, H-3'$_\beta$), 3.50 (s, 4.5H, CH_3 OMe$_\beta$), 3.48 – 3.43 (m, 4.5H, CH_3 OMe$_\alpha$, H-2'$_\beta$), 3.41 – 3.33 (m, 2.5H, H-2'$_\alpha$, H-5'$_\beta$); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 165.9, 165.9, 165.9, 165.5, 165.5 (C=O), 137.9, 137.4, 137.2 (C_q), 133.6, 133.5, 133.5, 133.2, 130.0, 130.0, 129.9, 129.8 (CH_{arom}), 129.3, 129.2, 129.1, 129.1, 129.0, 128.9 (C_q/CH_{arom}), 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 128.2, 128.0, 126.2, 126.1 (CH_{arom}), 102.9 (C-1'$_\beta$), 101.4, 101.4 (CHPh$_{\alpha,\beta}$), 98.8 (C-1'$_\alpha$), 97.1, 97.0 (C-1$_\alpha$, C-1$_\beta$), 82.8 (C-4'$_\alpha$), 81.5 (C-4'$_\beta$), 79.0 (C-3'$_\beta$), 75.8 (C-3'$_\alpha$), 75.1 (CH_2 Bn), 72.1 (C-2, C-2$_\beta$), 70.5, 70.4 (C-3$_\alpha$, C-3$_\beta$), 69.7 (C-4$_\beta$), 69.5 (C-4$_\alpha$), 68.9 (C-5$_\alpha$), 68.8 (C-6$_\beta$), 68.6 (C-6'$_\alpha$, C-6'$_\beta$), 68.5 (C-5$_\alpha$), 67.0 (C-6$_\alpha$), 66.4 (C-2'$_\beta$), 66.3 (C-5'$_\beta$), 63.0 (C-2'$_\alpha$), 62.9 (C-5'$_\alpha$), 55.8 (OMe); HRMS: $[M+Na]^+$ calcd for $C_{48}H_{45}N_3O_{13}Na$ 894.2850, found 894.2874.



Methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranosyl)-2,3-di-*O*-benzyl-6-*O*-(4-nitrobenzoyl)-α-D-glucopyranoside (23A). Donor **A** and acceptor **23** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **23A** (88 mg, 92 µmol, 92%, α:β = 3 : 1) as a colorless oil. R_f: 0.36 (4/1 pentane/EtOAc); IR (thin film): 696, 719, 735, 997, 1028, 1047, 1076, 1088, 1273, 1348, 1454, 1525, 1726, 2866, 2910, 2926; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.22 – 8.15 (m, 4H, pNO_2Bz), 7.44 – 7.17 (m, 25H, CH_{arom}), 5.71 (d, 1H, *J* = 4.0 Hz, H-1'), 5.47 (s, 1H, C*H*Ph), 5.00 (d, 1H, *J* = 11.5 Hz, C*H*H Bn), 4.94 – 4.88 (m, 1H, C*H*H Bn), 4.82 – 4.61 (m, 5H, 2xCH*H* Bn, 2x C*H*H Bn, H-6), 4.61 – 4.52 (m, 4H, 2x CH*H* Bn, H-1, H-6), 4.15 – 4.07 (m, 2H, H-3', H-5), 4.03 (t, 1H, *J* = 9.4 Hz, H-3), 4.01 – 3.95 (m, 2H, H-4, H-6'), 3.81 – 3.73 (m, 1H, H-5'), 3.63 – 3.52 (m, 4H, H-2, H-2', H-4', H-6'), 3.39 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 164.4 (C=O), 150.6, 138.8, 138.5, 137.9, 137.8, 137.3, 135.2 (C_q), 130.9, 128.6, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.1, 128.0, 127.8, 127.8, 127.7, 127.7, 126.8, 126.1, 123.6 (CH_{arom}), 101.2 (CHPh), 98.1 (C-1'), 97.7 (C-1), 82.3 (C-4'), 81.6 (C-3'), 80.4 (C-2), 78.8, 78.7 (C-2', C-3), 75.3, 74.6, 74.3 (CH_2 Bn), 73.5 (C-4), 73.4 (CH_2 Bn), 68.8 (C-6'), 67.9 (C-5), 64.8 (C-6), 63.7 (C-5'), 55.5 (OMe); Diagnostic peaks for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.28 – 8.23 (m, 2H, pNO_2Bz), 8.10 – 8.06 (m, 2H, pNO_2Bz), 5.52 (s, 1H, C*H*Ph), 3.91 (dd, 1H, *J* = 9.5, 8.3 Hz), 3.66 (t, 1H, *J* = 9.3 Hz), 3.39 (s, 3H, CH_3 OMe), 3.27 (td, 1H, *J* = 9.8, 5.0 Hz, H-5'); ^{13}C-APT NMR ($CDCl_3$, 101 MHz): δ 164.1, 139.0, 138.4, 138.2, 138.1, 137.2, 135.2, 130.7, 129.0, 128.5, 128.3, 128.2, 128.2, 128.1, 127.8, 127.7, 127.4, 126.0, 103.6 (C-1'), 101.2 (CHPh), 98.0 (C-1), 82.7 (C-2'), 81.7 (C-4'), 81.4 (C-3'), 79.9 (C-3), 79.2 (C-2), 78.5 (C-4), 75.8, 75.1, 73.7 (CH_2 Bn), 68.8 (C-6'), 68.6 (C-5), 66.2 (C-5'), 63.9 (C-6), 55.5 (OMe); HRMS: $[M+H]^+$ calcd for $C_{55}H_{56}NO_{14}$ 954.3701, found 954.3745.

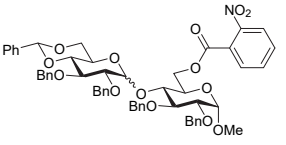


Methyl 4-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranosyl)-2,3-di-*O*-benzyl-6-*O*-(4-nitrobenzoyl)-α-D-glucopyranoside (23B). Donor **A** and acceptor **23** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **23B** (49 mg, 55 µmol, 55%, α:β = 1 : 1) as a colorless oil. R_f: 0.33 and 0.33 (4/1 pentane/EtOAc); IR (thin film): 698, 719, 739, 999, 1015, 1028, 1049, 1094, 1275, 1454, 1528, 1728, 2110, 2868, 2922; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 8.34 – 8.25 (m, 2H, pNO_2Bz), 8.24 – 8.15 (m, 8H, pNO_2Bz), 7.46 – 7.25 (m, 40H, CH_{arom}), 5.68 (d, 1H, *J* = 4.2 Hz, H-1'$_\alpha$), 5.51 (s, 1H, C*H*Ph$_\alpha$), 5.49 (s, 1H, C*H*Ph$_\beta$), 5.13 (d, 1H, *J* = 10.4 Hz, C*H*H Bn), 4.99 – 4.86 (m, 5H, 2xC*H*H Bn, CH*H* Bn, CH_2 Bn), 4.81 (dd, 1H, *J* = 12.0, 2.1 Hz, H-6$_\beta$), 4.81 – 4.73 (m, 4H, 2xCH*H* Bn, 2xC*H*H Bn), 4.71 (dd, 1H, *J* = 12.1, 2.4 Hz, H-6$_\alpha$), 4.65 (dd, 1H, *J* = 12.0, 4.8 Hz, H-6$_\beta$), 4.65 – 4.59 (m, 4H, 2xCH*H* Bn, H-1$_\alpha$, H-1$_\beta$), 4.53 (dd, 1H, *J* = 12.0, 4.2 Hz, H-6$_\alpha$), 4.45 (d, 1H, *J* = 8.1 Hz, H-1'$_\beta$), 4.13 (dd, 1H, *J* = 9.4, 8.8 Hz, H-3$_\alpha$), 4.06 – 3.94 (m, 6H, H-3$_\beta$, H-3'$_\alpha$, H-5$_\alpha$, H-5$_\beta$, H-6'$_\alpha$, H-6'$_\beta$), 3.90 – 3.78 (m, 3H, H-4$_\alpha$, H-4$_\beta$, H-5'$_\alpha$), 3.71 – 3.53 (m, 6H, H-2$_\alpha$, H-2$_\beta$, H-3'$_\beta$, H-4'$_\alpha$, H-4'$_\beta$, H-6'$_\alpha$), 3.48 (t, 1H, *J* = 10.3 Hz, H-6'$_\beta$), 3.43 (dd, 1H, *J* = 9.1, 8.3 Hz, H-2'$_\beta$), 3.40 (s, 3H, CH_3 OMe), 3.40 (s, 3H, CH_3 OMe), 3.36 (dd, 1H, *J* = 10.1, 4.2 Hz, H-2'$_\alpha$), 3.15 (ddd, 1H, *J* = 10.0, 9.0, 5.0 Hz, H-5'$_\beta$); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 164.4, 164.3 (C=O), 150.7, 150.7 (C_q NO_2), 139.0, 138.5, 138.0, 137.8, 137.7, 137.6, 137.0, 137.0, 135.3, 135.1 (C_q), 130.9, 130.8, 129.2, 129.2, 128.7, 128.6, 128.6, 128.6, 128.5, 128.4, 128.4, 128.4, 128.3, 128.2, 128.1, 128.1, 128.0, 127.8, 127.6, 127.1, 126.1, 126.0, 123.8, 123.7 (CH_{arom}), 102.3 (C-1'), 101.3, 101.3 (CHPh), 99.0 (C-1'), 98.0, 97.8 (C-1, C-1), 82.5 (C-4'), 81.6 (C-3), 81.4 (C-4'), 80.7 (C-2), 80.1 (C-3), 79.7, 79.6 (C-2, C-3'), 78.5 (C-4), 76.1 (C-3'), 75.5, 75.3, 75.1 (CH_2 Bn), 75.1 (C-4), 75.0, 73.6, 73.4 (CH_2 Bn), 68.5 (C-6'), 68.4 (C-6'), 68.3 (C-5), 67.8 (C-5), 66.8 (C-2'), 66.4 (C-5'), 64.7 (C-6), 64.1 (C-6), 63.7 (C-5'), 62.8 (C-2'), 55.6, 55.6 (OMe); HRMS: $[M+H]^+$ calcd for $C_{48}H_{49}N_4O_{13}$ 889.3296, found 889.3331.

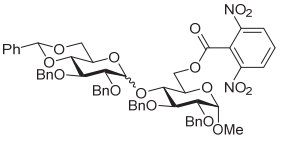


Methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranosyl)-2,3-di-*O*-benzyl-6-*O*-(3-nitrobenzoyl)-α-D-glucopyranoside (24A). Donor **A** and acceptor **24** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **24A** (47 mg, 49 µmol, 49%, α:β = 3.3 : 1) as a colorless oil. R_f: 0.30 (4/1 pentane/EtOAc); IR (thin film): 696, 719, 737, 1028, 1047, 1076, 1088, 1261, 1350, 1454, 1533, 1730, 2868, 2908, 2926; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC, HMBC): δ 8.85 – 8.83 (m, 1H, CH_{arom} NO_2Bz), 8.37 (ddd, 1H, *J* = 8.2, 2.3, 1.1 Hz, CH_{arom} NO_2Bz), 8.33 (dt, 1H, *J* = 7.8, 1.3 Hz, CH_{arom} NO_2Bz), 7.57 (t, 1H, *J* = 8.0 Hz, CH_{arom} NO_2Bz), 7.45 – 7.17 (m, 25H, CH_{arom}), 5.70 (d, 1H, *J* = 4.0 Hz, H-1'), 5.47 (s, 1H, C*H*Ph), 5.00 (d, 1H, *J* = 11.5 Hz, C*H*H Bn), 4.90 (d, 1H, *J* = 11.2 Hz, C*H*H Bn), 4.79 – 4.72 (m, 4H, C*H*H Bn, 2xCH*H* Bn, H-6), 4.69 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.60 – 4.52 (m, 4H, 2xCH*H* Bn, H-1, H-6), 4.16 – 4.09 (m, 2H, H-3, H-5), 4.07 – 4.01 (m, 2H, H-3', H-6'), 3.97 (dd, 1H, *J* = 9.9, 8.7 Hz, H-4), 3.80 – 3.74 (m, 1H, H-5'), 3.63 – 3.57 (m, 3H, H-2, H-4', H-6'), 3.55 (dd, 1H, *J* = 9.4, 4.0 Hz, H-2'), 3.40 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC, HMBC): δ 164.2 (C=O), 148.4 (C_q NO_2), 138.9, 138.6, 138.0, 137.9 (C_q Bn), 137.3 (CH_{arom}),

135.4 (C_q Bz), 131.7, 129.7, 129.0, 128.6, 128.6, 128.4, 128.4, 128.3, 128.3, 128.3, 128.2, 128.1, 128.1, 127.9, 127.8, 127.7, 127.7, 127.6, 127.4, 126.9, 126.1, 124.8 (CH_{arom}), 101.3 (CHPh), 98.2 (C-1), 97.8 (C-1'), 82.3 (C-4'), 81.6 (C-3), 80.5 (C-2), 78.8, 78.7 (C-2', C-3'), 75.4, 74.6, 74.2 (CH_2 Bn), 73.7 (C-4), 73.5 (CH_2 Bn), 68.8 (C-6'), 68.0 (C-5), 64.8 (C-6), 63.8 (C-5'), 55.5 (OMe); Diagnostic peaks for the β-anomer: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.76 – 8.72 (m, 1H, CH_{arom} NO_2Bz), 8.41 (ddd, 2H, *J* = 8.2, 2.3, 1.1 Hz, CH_{arom} NO_2Bz), 8.24 (dt, 1H, *J* = 7.7, 1.3 Hz, CH_{arom} NO_2Bz), 7.62 (t, 1H, *J* = 8.0 Hz, CH_{arom} NO_2Bz), 5.51 (s, 1H, C*H*Ph), 4.48 (dd, 1H, *J* = 11.8, 5.6 Hz, H-6), 4.19 (dd, 1H, *J* = 10.5, 5.0 Hz, H-6'), 3.93 – 3.87 (m, 1H, H-3), 3.65 (t, 1H, *J* = 9.3 Hz, H-4'), 3.41 (s, 3H, CH_3 OMe), 3.30 (td, 1H, *J* = 9.7, 5.0 Hz, H-5'); ^{13}C-APT NMR ($CDCl_3$, 126 MHz): δ 163.9 (C=O), 139.1 (C_q NO_2), 138.5, 138.2, 138.2, 135.2 (C_q) - 124.7 (CH_{arom}), 103.7 (C-1'), 101.2 (CHPh), 98.1 (C-1), 82.8 (C-2'), 81.8 (C-4'), 81.5 (C-3'), 80.0 (C-3), 79.3 (C-2), 78.6 (C-4), 75.8, 75.8, 75.2, 73.7 (CH_2 Bn), 68.8 (C-6'), 68.7 (C-5), 66.3 (C-5'), 63.9 (C-6), 55.5 (OMe); HRMS: $[M+Na]^+$ calcd for $C_{55}H_{55}NO_{14}Na$ 976.3520, found 976.3550.



Methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranosyl)-2,3-di-*O*-benzyl-6-*O*-(2-nitrobenzoyl)-α-D-glucopyranoside (25A). Donor **A** and acceptor **25** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **25A** (79 mg, 83 µmol, 83%, α:β = 3.5 : 1) as a colorless oil. R_f: 0.20 (4/1 pentane/EtOAc); IR (thin film): 696, 733, 995, 1028, 1045, 1074, 1088, 1254, 1290, 1352, 1454, 1533, 1736, 2868, 2907; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.86 – 7.82 (m, 1H, CH_{arom}), 7.78 – 7.75 (m, 1H, CH_{arom}), 7.62 – 7.54 (m, 2H, CH_{arom}), 7.51 – 7.46 (m, 2H, CH_{arom}), 7.41 – 7.16 (m, 23H, CH_{arom}), 5.60 (d, 1H, *J* = 3.9 Hz, H-1'), 5.50 (s, 1H, C*H*Ph), 4.99 – 4.87 (m, 2H, 2xC*H*H Bn), 4.82 – 4.64 (m, 5H, 2xCH*H* Bn, 2xC*H*H Bn, H-6), 4.63 (d, 1H, *J* = 3.3 Hz, H-1), 4.61 – 4.50 (m, 3H, 2xCH*H* Bn, H-6), 4.11 – 4.05 (m, 2H, H-3', H-6'), 4.05 – 3.98 (m, 2H, H-3, H-5), 3.87 (dd, 1H, *J* = 9.8, 8.6 Hz, H-4), 3.84 – 3.77 (m, 1H, H-5'), 3.64 – 3.57 (m, 3H, H-2, H-4', H-6'), 3.52 (dd, 1H, *J* = 9.5, 3.9 Hz, H-2'), 3.39 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 164.9 (C=O), 148.6 (C_q NO_2), 139.1, 138.7, 138.1, 137.9, 137.5 (C_q), 132.7, 132.0, 130.4, 129.0, 128.5, 128.5, 128.4, 128.3, 128.3, 128.2, 128.1, 128.1, 128.0, 127.9, 127.8, 127.7, 127.2 (CH_{arom}), 127.0 (C_q Bz), 126.9, 126.2, 126.1, 123.8 (CH_{arom}), 101.4 (CHPh), 98.3 (C-1'), 97.7 (C-1), 82.3 (C-4'), 81.2 (C-3'), 80.2 (C-2), 78.8, 78.7 (C-2', C-3), 75.3 (CH_2 Bn), 74.5 (C-4), 74.4, 73.9, 73.4 (CH_2 Bn), 68.9 (C-6'), 68.1 (C-5), 65.3 (C-6), 63.6 (C-5'), 55.5 (OMe); Diagnostic peaks for the β-anomer: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 5.51 (s, 1H, C*H*Ph), 4.22 (dd, 1H, *J* = 9.8, 4.4 Hz, H-6'), 3.73 (dd, 1H, *J* = 10.0, 8.7 Hz, H-4), 3.37 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 126 MHz): δ 164.8, 148.6, 139.3, 138.4, 138.4, 132.7 - 123.8 (CH_{arom}), 103.2 (C-1'), 101.2 (CHPh), 98.2 (C-1), 82.9 (C-2'), 81.8 (C-4'), 81.6 (C-3'), 79.9 (C-3), 79.1 (C-2), 77.8 (C-4), 75.8, 75.5, 75.2, 73.7 (CH_2 Bn), 68.9 (C-6'), 68.5 (C-5), 65.9 (C-5'), 64.1 (C-6), 55.6 (OMe); HRMS: $[M+Na]^+$ calcd for $C_{55}H_{55}NO_{14}Na$ 976.3520, found 976.3566.



Methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranosyl)-2,3-di-*O*-benzyl-6-*O*-(2,6-dinitrobenzoyl)-α-D-glucopyranoside (26A). Donor **A** and acceptor **26** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations (E) yielding product **26A** (83 mg, 83 µmol, 83%, α:β = 5.6 : 1) as a colorless oil. R_f: 0.12 (4/1 pentane/EtOAc); IR (thin film): 696, 735, 918, 1028, 1045, 1074, 1088, 1267, 1344, 1454, 1541, 1749, 2870; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.36 (d, 2H, *J* = 8.3 Hz, NO_2Bz_{meta}), 7.69 (t, 1H, *J* = 8.3 Hz, NO_2Bz_{para}), 7.40 – 7.17 (m, 25H, CH_{arom}), 5.52 (d, 1H, *J* = 3.9 Hz, H-1), 5.46 (s, 1H, C*H*Ph), 5.01 (dd, 1H, *J* = 11.8, 2.2 Hz, H-6), 4.95 – 4.74 (m, 4H, 2xCH_2 Bn), 4.73 – 4.62 (m, 4H, 2xC*H*H Bn, H-1, H-6), 4.59 – 4.51 (m, 2H, 2xCH*H* Bn), 4.09 (dd, 1H, *J* = 9.6, 8.5 Hz, H-3), 4.10 – 3.87 (m, 4H, H-3', H-5, H-5', H-6'), 3.82 (dd, 1H, *J* = 9.8, 8.5 Hz, H-4), 3.63 – 3.51 (m, 4H, H-2, H-2', H-4', H-6'), 3.40 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 162.3 (C=O), 146.7 (C_q NO_2), 139.1, 138.6, 138.1, 137.9, 137.5 (C_q), 129.7, 128.5, 128.4, 128.3, 128.3, 128.3, 128.2, 128.1, 128.0, 127.8, 127.7, 127.6, 127.0, 126.2 (CH_{arom}), 125.5 (C_q Bz), 101.3 (CHPh), 98.5 (C-1'), 97.7 (C-1), 82.2 (C-4'), 81.0 (C-3), 80.0 (C-2), 78.8 (C-2'), 78.6 (C-3'), 75.6 (C-4), 75.3, 74.6, 73.8, 73.4 (CH_2 Bn), 68.9 (C-6'), 68.5 (C-5), 66.2 (C-6), 63.5 (C-5'), 55.6 (OMe); Diagnostic peaks for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 8.42 (d, 2H, *J* = 8.3 Hz, NO_2Bz_{meta}), 7.75 (t, 1H, *J* = 8.3 Hz, NO_2Bz_{para}), 4.45 (dd, 1H, *J* = 12.1, 2.4 Hz, H-6), 4.19 (dd, 1H, *J* = 10.1, 4.7 Hz, H-6'), 3.79 – 3.72 (m, 1H), 3.47 (dd, 1H, *J* = 8.8, 7.7 Hz, H-2'), 3.42 (dd, 2H, *J* = 9.5, 3.6 Hz, H-2), 3.38 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 162.2, 146.7, 139.1, 138.6, 138.5, 138.3, 137.5, 131.2, 129.8, 129.0, 128.9, 128.5, 128.4, 128.3, 128.1, 127.9, 127.9, 127.7, 127.5, 127.2, 126.1, 125.5, 103.0 (C-1'), 101.1 (CHPh), 98.2 (C-1), 82.9, 81.8, 81.6, 79.9, 78.8, 77.4, 75.7, 73.5, 68.3, 65.8, 65.5, 55.7; HRMS: $[M+NH_4]^+$ calcd for $C_{55}H_{58}N_3O_{16}$ 1016.3817, found 1016.3864.

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Chapter 7

Synthesis of C-2- and C-5-modified furanosides

Introduction

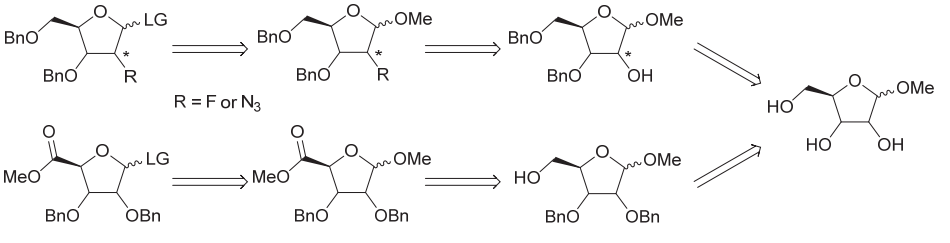
Furanosides are key structural components in a variety of bacterial and plant oligosaccharides.[1–3] In this framework, the glycosylation of furanosides has been studied to obtain specific target oligosaccharides with the required anomeric configuration. Furanosylation is more extensively investigated for the synthesis of modified nucleosides and oligonucleotides.[4–6] Besides structural variants, in which the ring oxygen is replaced by sulfur, selenium, nitrogen, or carbon, furanosides with differently configured amino or fluoro substituents have been studied.[7–9] Uronic acid furanosides occur in natural compounds and have attracted attention as biomimics. Modified (oligo)nucleotides are studied as potential therapeutics and as radio-tracer compounds (primarily ^{18}F, but also ^{11}C, ^{13}N) in Positron Emission Tomography (PET).[10–13] Despite their biological relevance, the synthesis of the differently substituted furanosides and their glycosylating properties are scarcely investigated.[5] The development of effective routes of synthesis for these compounds and insight in their reactivity will contribute to the application of these

saccharides.[14] For instance, oligosaccharides containing furanosyl moieties can be relevant for the development of carbohydrate based vaccines.[4,7,15] Furthermore, insight in the reactivity of differently substituted furanosides will be a valuable asset to understand the mechanisms of the glycosylation reaction of both furanosides and pyranosides. This chapter describes the synthesis of all four diastereoisomers of the D-pentofuranosides as their 2-fluoro, 2-azido, and 5-uronic acid derivatives. The influence of these functional groups in glycosylation reactions is the subject of Chapter 8, where they are studied using experimental and computational means.

Results and discussion

The strategy to obtain the three modifications on all four diastereoisomers is shown in Scheme 1. The C-2-modified furanoside donors were obtained by inversion of the 2-hydroxy group in otherwise protected methyl furanosides. The C-5-methyl esters were generated from their suitably protected 5-hydroxy methyl furanosides. Subsequent anomeric hydrolysis and installation of the anomeric leaving group (LG), will then give all twelve D-pentofuranoside donors, four configurations for each functional group.

Scheme 1. Retrosynthesis of C-2- and C-5-modified furanosides.

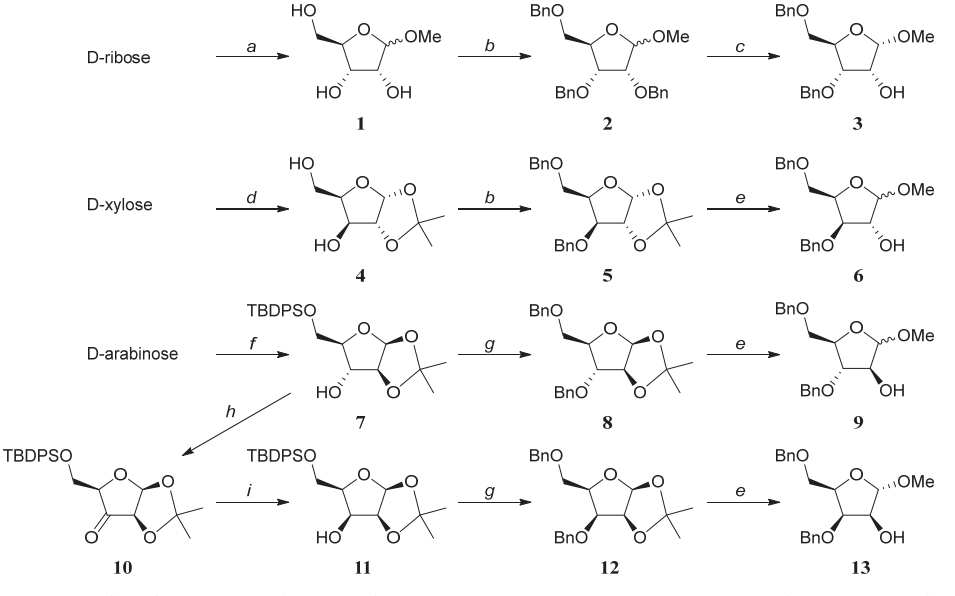


*Center of inversion. LG = leaving group.

The syntheses of the protected 2-hydroxy pentofuranoses is outlined in Scheme 2. Adapting literature procedures, the 2-hydroxy pentofuranoses could be obtained on large scale (10-150 mmol). *Ribo*-configured structure **3** was prepared by treatment of fully protected **2** with $SnCl_4$, inducing both anomerization and regioselective benzyl cleavage.[16] Similarly protected *xylo*se derivative **6** was obtained from 1,2-isopropylidene-xylofuranose **4** in high yield (97%) by benzylation and CSA mediated acetal exchange.

The syntheses of *arabino*- and *lyxo*-derivatives **9** and **13** required more steps, as di-isopropylidenation of arabinose yields the pyranoside and regioselective removal of the C-2–*O*-benzyl, as reported for ribose derivative **3**, is unknown for these epimers.[17] First, the primary alcohol of arabinose was protected with a bulky TBDPS group to force the carbohydrate in the furanose form. Subsequent isopropylidene protection gave **7**. Conveniently, the epimeric lyxose compound could be easily obtained from **7** by an oxidation-reduction sequence.[18] Dess-Martin oxidation proved superior over the Sarett (CrO_3, pyridine in DCM)[19] and Moffat (DMSO, Ac_2O)[20] oxidations both in yield and ease of purification.[21] Reduction of ulose **10** with $NaBH_4$ gave optically pure *lyxo*-configured **11**. Both **7** and **11** were silyl-deprotected and benzylated in a one-pot procedure using KOH and BnCl in THF.[22] An alternative two-step reaction sequence of removing the TBDPS (with TBAF, AcOH in THF) and subsequent benzylation (NaH, BnBr in DMF) was less efficient. Finally, acetal exchange yielded both the *arabino*-configured **9** and *lyxo*-configured **13**.

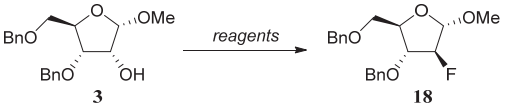
Scheme 2. Synthesis of 2-hydroxy pentofuranosides **3**, **6**, **9**, and **13**.



Reagents and conditions: (a) AcCl, MeOH; (b) BnBr, NaH, DMF, **2**: 89% (two steps); (c) $SnCl_4$, DCM, 92%; (d) *i*. H_2SO_4, acetone; *ii*. HCl, H_2O, aceton, 90% (two steps); (e) CSA, MeOH, **6**: 97% (two steps), **9**: 91%, **13**: 84%; (f) *i*. TBDPSCl, imidazole, DMF; *ii*. dimethoxypropane, CSA, DCM, 53% (two steps); (g) BnCl, KOH, THF, **8**: 71%, **12**: 99%; (h) Dess-Martin periodinane, DCM, 77%; (i) $NaBH_4$, DCM, MeOH, 73%.

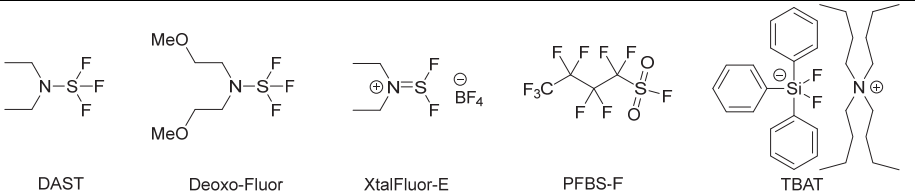
Having synthesized all 2-hydroxy pentofuranosides (**3**, **6**, **9**, **13**), the inversion procedures were investigated. Fluoride substitutions were considered first, since a range of fluorination reagents are commercially available. Table 1 summarizes the results of the direct substitution reactions on ribose derivative **3**. Unfortunately, none of the reagents was successful in substituting the 2-hydroxy group to provide 2-fluoroarabinoside **18** in decent yield.

Table 1. Inversion of riboside **3** with different fluorination reagents.



3 **18**

Entry	Scale (mmol)	Reagents[a] (eq.)	Temperature (°C)	Time (h)	Yield (%)
1	0.5	DAST (1.8)	-60 to 20	72	12
2	2.0	DAST (4)	-60 to 45	24	13
3	0.5	Deoxo-Fluor® (1.2)	0 to 20	72	15
4	0.5	PFBS-F (2.2), TBAT (0.8), DiPEA (2.5)	0 to 20	30	< 25
5	0.5	XtalFluor-E® (1.5), 3HF·Et_3N (1.5)	0 to 20	30	-



[a]Concentration for all reactions was 0.2 M in DCM.

Therefore, the 2-hydroxy groups in the projected furanoses were converted into the corresponding triflates followed by substitution with fluoride or azide anions, respectively.[23] Figure 1 provides an overview of the triflates, readily prepared from the alcohols, the targeted substitution products as well as the side products obtained in the reactions (deviations colored red).

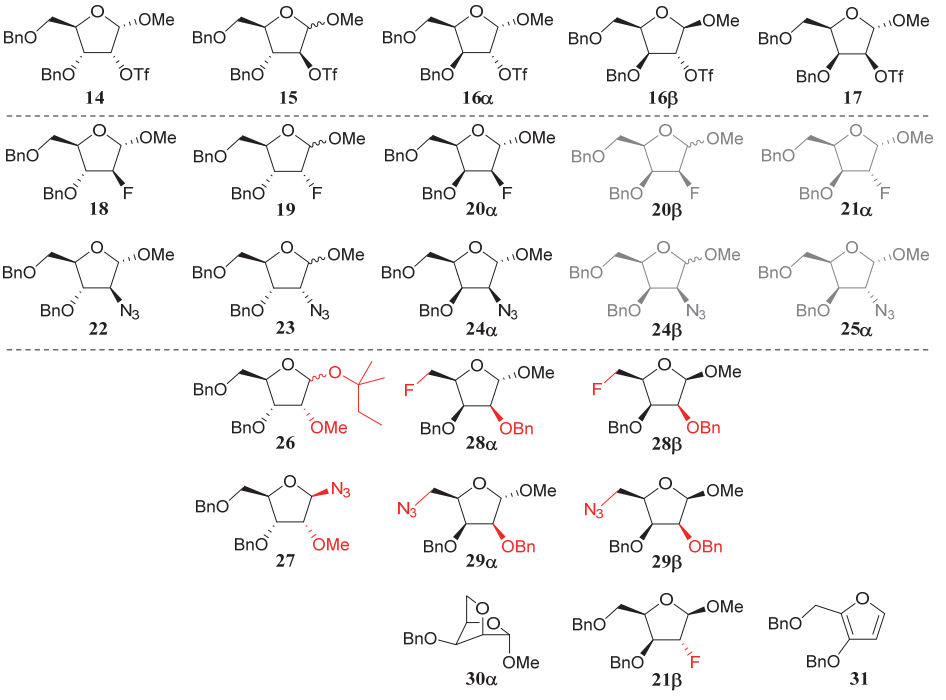


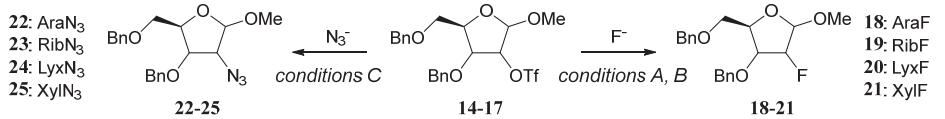
Figure 1. Furanosyl C-2–*O*-triflates (**14-17**) and their substitution products by fluoride inversion (**18-21**), and azide inversion (**22-25**). Major side products isolated from the reaction mixture (**26-31**), red color indicates the deviations from the expected products. Formation of the structures in grey was not observed.

Table 2 reports the outcome of all substitution reactions. Entries 1-3 show that *ribo*-configured triflate **14** is readily substituted with the fluoride (TBAF, or CsF) and azide anions (NaN_3), respectively. The yield of the fluoride substitution on triflate **14** with TBAF in THF (71%) was increased to 86% when CsF was used in a polar protic solvent (*tert*-amyl alcohol, entry 2).[24] Azide **22** was obtained in 93% yield. Substitution of the arabinotriflate **15** (a mixture of anomers), with fluorine and azide nucleophiles gave **19** and **23**, respectively in reasonable to good yields. As reported by the group of Woerpel,[22] only the β-anomer of **15** reacted with TBAF (entry 4), and the triflate of the α-anomer could be recovered.

Under conditions B (entry 5) both anomers of **15** reacted and despite the generation of side product **26**, the yield was increased to 63%. Azide **23** was obtained in high yield, although a similar migration to side product **27** occurred during the azide substitution (entry 6).[25] The possible reaction pathways for the formation of these side products are displayed in Figure 2. The anomeric methoxy substituent can substitute the neighboring triflate and form a highly reactive methyl oxiranium ion, which is attacked

with inversion at the anomeric center, explaining the stereochemistry of the anomeric azide side product found (**27**). Alternatively, an S_N1 reaction on the oxocarbenium ion, formed upon opening of the oxiranium ion, happens in entry 4 with the solvent, explaining the mixture of anomers found in product **26**.

Table 2. Results of substitution reactions on triflates **14-17**.



Entry	Triflate[b]	Conditions[a]	Substitution product	Yield (%)	Side product 1	Side product 2
1	**14**	A (TBAF)	**18**	71	-	-
2	**14**	B (CsF)	**18**	86	-	-
3	**14**	C (N_3)	**22**	93	-	-
4	**15**	A	**19**, β only	42	**15α**, 17%	-
5	**15**	B	**19**	63	**26**[g], 17%	-
6	**15**	C	**23**	86[c]	**27**[c]	-
7	**16α**	A[d]	**20α**	44	**6**, 17%	**16α**, 3%
8	**16α**	B[e]	**20α**	-	**28α**, 57%	**30α**, 21%
9	**16α**	C[f]	**24α**	67	**29α**, 12%	**30α**, 7%
10	**16β**	A[d]	**20β**	-	**28β**, 18%	**31**[h]
11	**16β**	B	**20β**	-	**28β**, 47%	**21β**, 10%
12	**16β**	C[f]	**24β**	-	**29β**, 30%	-
13	**17**	A,B,C	**21 / 25**	-	**31**[h]	-

[a]*Reagents and conditions*: (A) 0.2 M solution in THF, 2.5 eq. TBAF, 0°C to 20°C, overnight; (B) 0.35 M solution in *tert*-amyl alcohol, 4 eq. CsF, 90°C, overnight; (C) 0.2 M solution in DMF, 5 eq. NaN_3, 80°C, 2 h. [b]See experimental section for the general procedure of the triflate formation. [c]Combined yield of **23** and **27**, as a 4:1 mixture. [d]70°C, 5 h for entry 7, overnight for entry 10. [e]110°C overnight. [f]overnight. [g]α : β = 88 : 12. . [h]Yield not determined.

Both anomers of xyloside **6** were obtained, therefore both triflates **16α** and **16β** could be independently studied. Substitution of **16α**, using CsF in *tert*-amyl alcohol at 90°C, only gave the side products 5-fluorolyxoside **28α** and the bicycle **30α** (entry 8). The formation of these products can be explained by participation of the C-5–*O*-benzyl group followed by substitution from the least hindered sites (path A and B, Figure 2B), to yield 5-fluorolyxoside **28α** and the bicycle **30α**, respectively. No products arising from double inversion (path C) or elimination were detected. Fortunately, heating **16α** in a

THF solution with TBAF for 5 hours did give the desired fluoride inversion and product **20α** was isolated in 44% yield (entry 7). Interestingly, the only observed side products were unreacted and hydrolysed triflate and no products derived from C-5–*O*-benzyl participation were found. Subjection of **16α** to conditions C led to effective azide substitution to give the desired product **24α** (entry 9) together with small amounts of bicycle **30α** and 5-azidolyxoside **29α** originating from pathways A and B, respectively (Figure 2B).

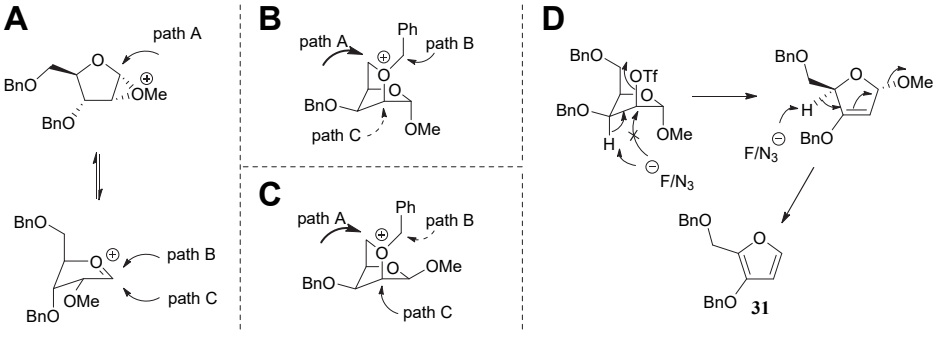


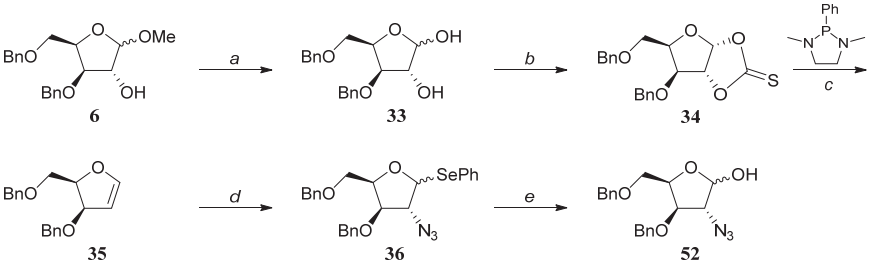
Figure 2. Mechanistic pathways underlying the formation of side products **26**-**31**.

Similar reactions with β-xylotriflate **16β** did not lead to the required substitutions (entries 10-12, Table 2). Both conditions A and B gave 5-fluoroxyloside **28β**, and condition A led to elimination product **31**, while condition B gave **21β**. The more nucleophilic and basic fluoride ion in condition A resulted in substitution on triflate **16α**, but elimination to furan **31** for **16β**. The formation of 2-fluoroxyloside **21β** with net retention of configuration can be explained by a double inversion mechanism as shown in Figure 2C (path C). Since **21β** is one of the target compounds and its formation from lyxotriflate **17** was ineffective, generation of **21β** through this route proved advantageous. Azide substitution at the C-5-position (path A) resulted in the formation of the 5-azidolyxoside side product **29α**.

All substitutions with lyxotriflate **17** to attain the target C-2-substituted xylofuranosides were ineffective and resulted in the elimination product **31**. The fast elimination of triflate **17** into furan **31** can be explained by the steric hindrance that is experienced during nucleophilic attack and the favorable H-OTf alignment for elimination (Figure 2D).[26]

An alternative approach towards the missing C-2-substituted xylofuranosides **21** and **25** was devised (Scheme 3). This synthetic route started with the preparation of glycal **35**. Among the various procedures to generate glycals,[27–31] two methods, using relatively neutral conditions, were examined. Direct conversion of diol **33** by the Garegg olefination conditions (I_2, Ph_3P, imidazole) led to the glycal but it could only be isolated in low yield.[32–34] A two-step procedure via thionocarbonate **34** proved more effective and this method was reproducible and scalable.[35,36] This Corey-Winter olefination method cleanly converted **34** into glycal **35** when 1,3-dimethyl-2-phenyl-1,3,2-diazaphospholidine was used as desulfurization agent.[37]

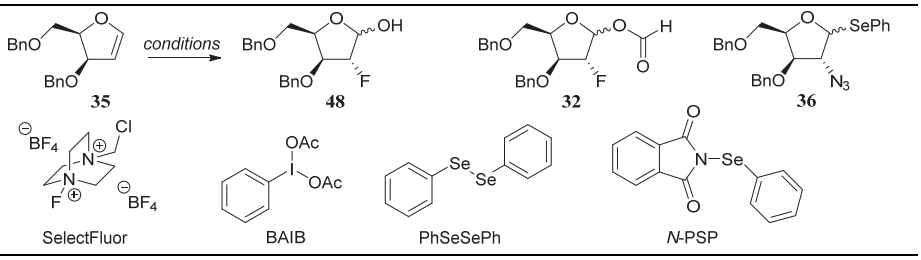
Scheme 3. Synthetic route towards 2-azidoxylose **52** via azidophenylselenation of glycal **35**.



Reagents and conditions: (a) TFA, THF, H_2O, 84%; (b) DMAP, DiPEA, thiophosgene, DCM, 78%; (c) 1,3-dimethyl-2-phenyl-1,3,2-diazaphospholidine, toluene, 76%; (d) *N*-(phenylseleno)phthalimide, $TMSN_3$, TBAF, DCM, 65%; (e) NIS, H_2O, acetone, THF, 87%.

The glycal **35** can be transformed to 2-fluoroxyloside **48** by electrophilic fluorination or to 2-azidoselenoxyloside **36** by azidophenylselenation respectively, see Table 3. Although the diastereoselectivity of the addition with SelectFluor in 4:1 DMF/H_2O was good (9:1, *xylo*:*lyxo*),[38] the yield was low (**48**, 36%) and a 2-fluoro-1-*O*-formyl (**32**) side product was isolated in 18%, resulting from reaction with DMF. Standard azidophenylselenation conditions (entry 2) delivered **36** as a 9:1 *xylo*:*lyxo* product mixture, which proved difficult to purify. The incompatibility of this reagent system with *O*-benzyl groups has been noted before[39,40] and a switch to an alternative reagent proved beneficial. The *N*-(phenylseleno)phthalimide (*N*-PSP) mediated azidophenylselenation proceeded much cleaner and with equally good regio- and diastereoselectivity to give product **36** (entry 3).[41–46]

Table 3. Conversion of glycal **35** to 2-fluoro- and 2-azidoxylosides **48** and **36**.

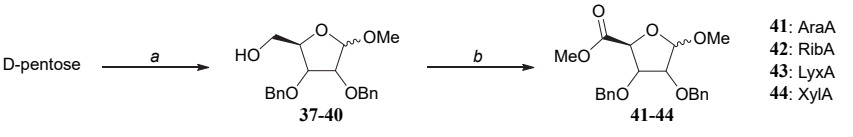


Entry	Conditions[a]	Product, yield[c]	*xylo*:*lyxo*[c]
1	SelectFluor, DMF, H_2O	**48**, 36% **32**, 18%	9 : 1
2	$TMSN_3$, BAIB, PhSeSePh, DCM	**36**, 50%	9 : 1
3	$TMSN_3$, TBAF, *N*-PSP, DCM	**36**, 65%	9 : 1

[a]Reaction time was 20 h, stirred from 0°C to 20°C. [b]Yield of the isolated *xylo*-configuration. [c]Ratio obtained by crude ^{1}H-NMR.

With the critical functionalizations at C-2 completed, the attention was turned to modification of the C-5-position. The general synthetic route towards the uronic acid esters is presented in Scheme 4. The intermediates **37-40** are synthesized from the D-aldopentose by a straightforward four-step procedure giving roughly the same yield for all the diastereoisomers (41%-50%). The subsequent oxidation reaction was carried out in a biphasic system of DCM and H_2O with catalytic TEMPO as the oxidating agent and BAIB as co-oxidant. Yields of the oxidation were high but loss of product was observed in the subsequent methylation step to give **41-44**. Shorter reaction times and aqueous work up, without concentration of the reaction mixture, were crucial to a higher isolated yield. Quenching with acetic acid instead of water or methanol also helped to increase the yield.

Scheme 4. Synthesis of 5-uronic acid functionalized methyl glycosides **41**-**44**.

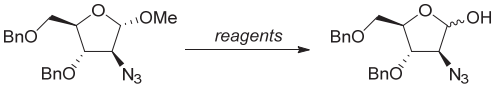


Reagents and conditions: (a) *i*. AcCl, MeOH; *ii*. TrtCl, Et_3N, DMF; *iii*. BnBr, NaH, DMF; *iv*. pTsOH·H_2O, MeOH, **37**: 41%, **38**: 43%, **39**: 46%, **40**: 50%, (all over four steps); (b) *i*. TEMPO, BAIB, DCM, H_2O; *ii*. MeI, K_2CO_3, DMF, **41**: 70%, **42**: 87%, **43**: 89%, **44**: 88%, (all over two steps).

With all methyl furanosides **18**-**24** and **41**-**44** available, the conversion of these furanosides into suitable glycosyl donors was undertaken. The first step comprises the hydrolysis of the methyl acetals to give lactols **45**-**56**. Because of the electron-withdrawing nature of the azido, fluoro, and uronic acid ester substituents in the furanosides, the anomeric acetals proved relatively stable and optimization of the acidic hydrolysis was required to prevent concomitant C-5–*O*-benzyl cleavage. The results of the optimization studies are summarized in Table 4.

In an attempt to obtain the acetyl donor **57**, methyl furanoside **22** was treated with H_2SO_4 in acetic anhydride, but this led to formation of diacetyl compound **61** instead (entry 1, see experimental section). Heating an 80% aq. AcOH solution of **22** overnight (entry 2) gave no conversion, and upon HCl addition decomposition occurred (entry 3).[47] Aqueous 70-90% TFA at room temperature (entries 5-7) gave **49** in low yield with significant concurrent decomposition.[48] Fortunately, using 50% aqueous TFA at 75°C significantly improved the outcome (entry 10), and also the use of 80% aqueous formic acid at this temperature provided the target compound. The best results were obtained with formic acid at a temperature of 60°C (entries 10 and 11).[24]

Table 4. Evaluation of acidic hydrolysis conditions.



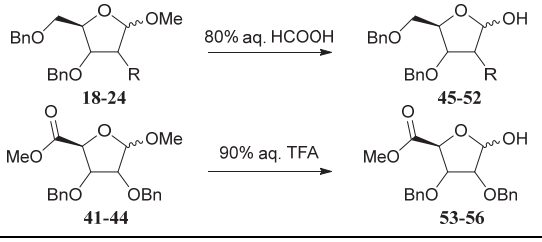
22 **49**

Entry	Conc.[a]	Conditions	Temperature (°C)	Time (h)	Yield (%)
1	0.3 M	1.5% H_2SO_4 in Ac_2O	0	0.3	[b]
2	0.1 M	80% aq. AcOH	115	24	-
3	0.2 M	20% 5M HCl in AcOH	85	16	-
4	0.3 M	Ph_3C-BF_4 in DCM	20	70	-
5	0.2 M	90% aq. TFA	20	40	17
6	0.2 M	80% aq. TFA	20	300	23
7	0.2 M	70% aq. TFA	20	300	50
8	0.1 M	50% aq. TFA	75	24	50
9	0.05 M	80 aq. formic acid	75	24	51
10	0.1 M	50% aq. TFA	60	80	73
11	0.05 M	80 aq. formic acid	60	80	76

[a]Concentration. Scale is 0.4 mmol except entry 1 (1.0 mmol) and entries 10 and 11 (1.5 mmol). [b]Yield of 1,5-di-*O*-acetyl-2-azido-3-*O*-benzyl-2-deoxy-α/β-D-arabinofuranoside **61** was 85%.

The hydrolysis of all other furanosides are listed in Table 5. The formic acid conditions proved effective for the 2-fluoro (entries 1-4), and 2-azido (entries 5-7) series, to give the corresponding lactols in good yield. The reactivity of the different substrates varied greatly, and changing the temperature and reaction time was needed to push the reactions to completion. The uronic acids (entries 8-11) were hydrolysed with 90% aqueous TFA to give the lactol products in good yield.

Table 5. Hydrolysis reaction results for methyl glycosides **18**-**24**, and **41**-**44**.



R = F
45: AraF
46: RibF
47: LyxF
48: XylF

R = N_3
49: $AraN_3$
50: $RibN_3$
51: $LyxN_3$
52: $XylN_3$

53: AraA
54: RibA
55: LyxA
56: XylA

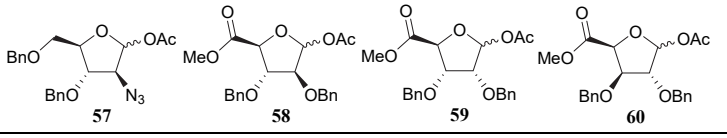
Entry	Substrate	Configuration	Product	Conditions	Temperature (°C)	Time (h)	Yield (%)
1	**18**	AraF	**45**	A	65	64	63
2	**19**	RibF	**46**	A	60	18	78
3	**20**	LyxF	**47**	A	65	6	75
4	**21**	XylF	**48**	A	60	6	75
5	**22**	$AraN_3$	**49**	A	60	80	76
6	**23**	$RibN_3$	**50**	A	65	6	70[a]
7	**24**	$LyxN_3$	**51**	A	60	18	62
8	**41**	AraA	**53**	B	0 to 20	8	60
9	**42**	RibA	**54**	B	0 to 20	7.5	73
10	**43**	LyxA	**55**	B	0 to 20	6	85
11	**44**	XylA	**56**	B	0 to 20	4	90

Reagents and conditions: (A) $HCOOH/H_2O$ (4/1 v/v, 0.05 M); (B) TFA/H_2O (9/1 v/v, 0.2 M). [a]Yield over two steps (including inversion), the combined yield of the 4:1 mixture of **23** and **27** was 89%.

The acetyl donors were prepared by treatment of the lactol precursors with acetic anhydride in pyridine (Table 6). But as a pilot study revealed that TMSOTf catalyzed glycosylations with allyl-trimethylsilane and deuterated triethylsilane were not productive using the acetyl donors even at room temperature, it was decided to generate the trifluoro-*N*-phenylimidate donors (Table 7, **62-73**), as these are more reactive and can be activated under catalytical conditions.[49]

The majority of the imidates were synthesized using an acetone/H_2O mixture and Cs_2CO_3 as a base. However, since some of the reactions were slow and purification

Table 6. Conversion of lactols to acetyl donors **57**-**60**.

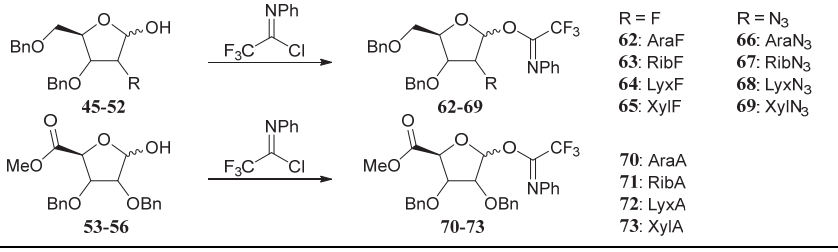


Entry	Substrate	Configuration	Product	α : β	Yield (%)
1	**49**	$AraN_3$	**57**	2.3 : 1	90
2	**53**	AraA	**58**	5.7 : 1	90
3	**54**	RibA	**59**	0 : 1	91
4	**56**	XylA	**60**	1.2 : 1	98

Reagents and conditions: Ac_2O (1.25 eq.) in pyridine (0.25 M), 0°C to r.t.

issues occurred, separating the target compounds from the hydrolyzed or unreacted 2,2,2-trifluoro-*N*-phenylacetimidoyl chloride, an anhydrous DCM/DBU procedure was explored. These reactions were complete within minutes, successfully generating the target compounds, even though work up and purification led to some degradation.

Table 7. Conversion of lactols **45**-**56** to imidate donors **62**-**73**.



Entry	Substrate	Configuration	Product	Conditions	α : β	Yield (%)
1	**45**	AraF	**62**	A	5 : 1	85 (69 + 16)
2	**46**	RibF	**63**	A	0 : 1	98
3	**47**	LyxF	**64**	A	1 : 0	82
4	**48**	XylF	**65**	A	1 : 2	91
5	**49**	$AraN_3$	**66**	B	1.6 : 1	71 (44 + 27)
6	**50**	$RibN_3$	**67**	A	1 : 8	77 (8 + 69)
7	**51**	$LyxN_3$	**68**	B	1 : 1.2	67 (30 + 37)
8	**52**	$XylN_3$	**69**	A	1 : 1	100
9	**53**	AraA	**70**	A	1 : 1	97
10	**54**	RibA	**71**	A	0 : 1	85
11	**55**	LyxA	**72**	A	5 : 1	85 (70 + 15)
12	**56**	XylA	**73**	A	0 : 1	81

Reagents and conditions: (A) 2,2,2-trifluoro-*N*-phenylacetimidoyl chloride (0.95 eq.), Cs_2CO_3 (1.1 eq.) in acetone/H_2O (9/1 v/v, 0.2 M), 0°C to r.t. (B) 2,2,2-trifluoro-*N*-phenylacetimidoyl chloride (0.95 eq.), DBU (1 eq.) in DCM (0.25 M), 0°C.

Conclusions

This chapter presents the synthesis of C-2- (2-fluoro, 2-azido) and C-5- (5-methyl uronates) modified furanosides of all four diastereoisomers. While the synthesis of the C-5-modified furanosides was relatively straightforward, the inversion reactions of the C-2-alcohols to provide the azides and fluorides, proved challenging. Eventually all synthetic pitfalls were overcome, leading to the successful synthesis of all twelve pentofuranoside imidate donors. The stereoelectronic effects originating from the newly introduced functional groups on C-2 and C-5 in glycosylation reactions will be discussed in Chapter 8.

Experimental section

General procedure for the formation of 2-*O*-trifluoromethanesulfonyl-furanosides (14-17). A 0.2 M solution of the alcohol (1 eq.) in DCM was cooled to 0°C followed by the addition of pyridine (2 eq.) and Tf_2O (1.2 eq.). After stirring for 40 min the reaction mixture was poured into cold 1 M aq. HCl and extracted twice with DCM. The combined organic layers were washed with cold H_2O, cold sat. aq. $NaHCO_3$, and brine. The organic layer was dried (Na_2SO_4), filtered, and concentrated under reduced pressure. After coevaporated with toluene the crude triflated furanoside was dissolved in the solvent required for the next synthetic step.

General procedure for the inversion of 2-*O*-trifluoromethanesulfonyl-furanosides (18-24). Conditions **A**: The triflate (1 eq.) was dissolved in *tert*-amyl alcohol (0.35 M) and CsF (4 eq.) was added. The reaction mixture was heated overnight at 90°C, followed by aqueous work up. Conditions **B**: The triflate (1 eq.) was dissolved in THF (0.2 M) and TBAF (1 M in THF, 2.5 eq.) was added at 0°C. The reaction mixture was allowed to reach room temperature and stirred overnight, followed by aqueous work up. Conditions **C**: The triflate (1 eq.) was dissolved in DMF (0.2 M) and NaN_3 (5 eq.) was added. The reaction mixture was heated for 2 h at 80°C, followed by aqueous work up. Work up conditons: the reaction mixture was diluted with H_2O (volume×10) and extracted with Et_2O three times. The combined organic layers were washed with H_2O, sat .aq. $NaHCO_3$, and brine. The organic layer was dried (MgSO4), filtered and concentrated *in vacuo*. Flash column chromatography (1/0 to 9/1 pentane/EtOAc) provided the target inverted furanosides as colourless oils.

General procedure for the synthesis of primary furanoside alcohols (37-40). To a suspension of D-pentose in MeOH (0.2 M) was added AcCl (0.3-0.9 eq) and the reaction was stirred until complete conversion to the methyl furanoside was observed (TLC). $NaHCO_3$ (s) was added to the reaction mixture until neutral. The slurry was filtered and concentrated under reduced pressure, followed by coevaporated with toluene. The residue was dissolved in DMF (0.2 M) and Et_3N (2.0 eq.), TrtCl (1.5 eq.), and DMAP (0.05 eq.) were successively added. After stirring for 1-2 days the mixture was diluted with H_2O and extracted twice with DCM. The combined DCM fractions were washed with H_2O and brine, then dried with $MgSO_4$, filtered and concentrated in vacuo followed by coevaporation with toluene. The crude tritylated product was redissolved in DMF (0.2 M) and cooled to 0°C. NaH (60% dispersion in mineral oil, 2.5 eq.) and TBAI (0.05 eq.) were added, followed by drop wise addition of BnBr (2.5 eq.). After stirring overnight at room temperature, the reaction was quenched by the addition of H_2O and extracted three times with Et_2O. The combined organic layers were washed with H_2O and brine, dried ($MgSO_4$), filtered over a short plug of silica gel, and concentrated under reduced pressure. The crude material was dissolved in MeOH/DCM (1/1, v/v, 0.2 M) and pTsOH·H_2O (0.1 eq.) was added and the reaction stirred at room temperature overnight and then quenched with Et_3N (0.15 eq.) The solvent was removed under reduced pressure and the residue was purified by flash column chromatography (19/1 to 6/4 pentane/EtOAc) to yield the primary furanoside alcohols as yellow oils.

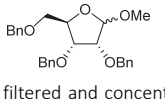
General procedure for the synthesis furanosyl methyl uronates by TEMPO/BAIB oxidation and methylation (41-44). The primary alcohol was dissolved in DCM/H_2O (2/1, v/v, 0.17 M) and the mixture was cooled to 0°C. TEMPO (0.2 eq.) and BAIB (2.5 eq.) were added and the reaction mixture was stirred vigorously overnight. A 10 % aq. NaS_2O_3 solution was added and the mixture stirred for 15 min at room temperature. The mixture was diluted with 0.01 M aq. HCl and DCM and phase separated and the aqueous layer extracted three times with DCM. The combined DCM layers were washed with H_2O and brine, dried ($MgSO_4$), filtered and concentrated under reduced pressure. The crude carboxylic acid was dissolved in DMF (0.2 M) and K_2CO_3 (3 eq.) and MeI (3 eq.) were added at 0°C. The reaction was stirred for 3 h and then quenched with AcOH (5 eq). The solution was diluted with H_2O and extracted three times with Et_2O. The combined organic layers were washed with sat. aq. $NaHCO_3$ and brine, dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (19/1 to 7/3) to give the uronic acid methyl ester.

General procedure for the hydrolysis of methyl furanosides (49-64). Conditions **A**: The methyl glycoside was mixed with 80% aq. formic acid to a concentration of 0.05 M and stirred at 60-65°C for 6-64 h as mentioned for each experiment. After the reaction mixture was cooled to room temperature and transferred to a seperatory funnel, it was diluted 5× with H_2O and extracted three times with DCM. The combined DCM layers were washed with sat. aq. $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The resulting residue was purified by flash column chromatography (pentane/EtOAc mixtures) to provide the target lactol as a mixture of anomers. Conditions **B**: The methyl glycoside was dissolved in 90% aq. TFA at 0°C and stirred for 4-8 h. The reaction was diluted with DCM and washed with H_2O three times. The aqueous layers were extracted twice with DCM and the combined organic layers

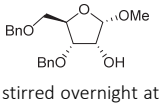
were washed with sat. aq. $NaHCO_3$ and brine. The organic layer was dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residu was purified by flash column chromatography (19/1 to 6/4 pentane/EtOAc) to provide the target lactol as a mixture of anomers.

General procedure for the synthesis of acetyl donors from lactols (65-69). The furanose lactol was dissolved in pyridine (0.25 M) and cooled to 0°C. Ac_2O (1.3 eq.) was added and the reaction mixture was stirred overnight at room temperature. The solution was diluted with 0.1 M aq. HCl and extracted three times with Et_2O. The combined organic layers were washed with 0.1 M HCl, H_2O, sat. aq. $NaHCO_3$, and brine. The organic layer was dried ($MgSO_4$), filtered, and concentrated in vacuo. Purification of the residue by flash column chromatography (1/0 to 8/2 pentane/EtOAc) gave the acetylated compound as a light yellow oil.

General procedure for the installation of the trifluoro-*N*-phenylacetimidoyl group (71-86). Conditions **A**: The furanose lactol was dissolved in acetone/H_2O (0.2 M, 9/1 v,v) and cooled to 0°C. Cs_2CO_3 (1.1 eq.) and 2,2,2-trifluoro-*N*-phenylacetimidoyl chloride (0.95 eq.) were added and the reaction mixture stirred until TLC-analysis showed complete conversion (1-4 days). The reaction mixture was reduced in volume under reduced pressure and H_2O was added. The aqueous phase was extracted twice with DCM and the combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure. Flash column chromatography (0-15% Et_2O/pentane) of the residue provided the target imidate donors. Conditions **B**: The furanose lactol was dissolved in DCM (0.25 M) and cooled to 0°C. 2,2,2-Trifluoro-*N*-phenylacetimidoyl chloride (0.95 eq.) was added followed bu DBU (1 eq.). The reaction mixture was stirred for 1 h and then concentrated under reduced pressure. Flash column chromatography (1/0 to 85/15 pentane/Et_2O) of the residue provided the target imidate donors.

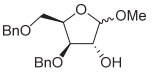


Methyl 2,3,5-tri-*O*-benzyl-α/β-D-ribofuranoside (2). D-Ribose (25 g, 167 mmol, 1 eq.) was dissolved in 600 mL MeOH and AcCl (4 mL, 56 mmol, 0.3 eq.) was added. The reaction mixture was stirred for 5 h and then quenched by the addition of solid $NaHCO_3$ (30 g). The mixture was filtered and concentrated under reduced pressure. The crude product **1** was coevaporated with toluene and then dissolved in 800 mL DMF and cooled to 0°C. NaH (60% dispersion in mineral oil, 26.7 g, 668 mmol, 4 eq.) was added in four portion while BnBr (80 mL, 668 mmol, 4 eq.) was slowly added over the course of 1 h. After stirring overnight the reaction was quenched by the addition of 75 mL MeOH and the reaction mixture was concentrated under reduced pressure. The crude mixture was taken up in H_2O and extracted twice with Et_2O. The combined Et_2O layers were washed with brine, dried with $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash column chromatography (19/1 to 2/1 pentane/EtOAc) gave compound **2** as a colourless oil (65 g, 150 mmol, 89%). Spectroscopic data were in accord with those previously reported.[50] Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.36 – 7.25 (m, 13H, CH_{arom}), 7.23 – 7.19 (m, 2H, CH_{arom}), 4.88 (d, 1H, *J* = 4.2 Hz, H-1), 4.68 (d, 1H, *J* = 12.8 Hz, C*H*H Bn), 4.64 (d, 1H, *J* = 12.3 Hz, C*H*H Bn), 4.61 – 4.56 (m, 2H, 2xCH*H* Bn), 4.49 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.42 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.25 (td, 1H, *J* = 4.1, 2.9 Hz, H-4), 3.82 (dd, 1H, *J* = 6.8, 3.0 Hz, H-3), 3.77 (dd, 1H, *J* = 6.8, 4.2 Hz, H-2), 3.46 (s, 3H, CH_3 OMe), 3.41 (dd, 1H, *J* = 10.4, 4.1 Hz, H-5), 3.35 (dd, 1H, *J* = 10.4, 4.2 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.6, 138.0, 137.9 (C_q), 128.5, 128.5, 128.4, 128.4, 128.2, 127.9, 127.8, 127.8 (CH_{arom}), 102.6 (C-1), 82.3 (C-4), 77.9 (C-2), 75.1 (C-3), 73.6, 72.6, 72.5 (CH_2 Bn), 70.3 (C-5), 55.7 (OMe); Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.40 – 7.25 (m, 15H, CH_{arom}), 4.92 (d, 1H, *J* = 1.0 Hz, H-1), 4.67 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.61 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.59 (d, 1H, *J* = 12.2 Hz, C*H*H Bn), 4.55 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.54 (d, 1H, *J* = 12.2 Hz, CH*H* Bn), 4.45 (d, 1H, *J* = 11.9 Hz, CH*H* Bn), 4.34 (ddd, 1H, *J* = 7.1, 5.8, 3.7 Hz, H-4), 4.01 (dd, 1H, *J* = 7.1, 4.7 Hz, H-3), 3.84 (dd, 1H, *J* = 4.6, 1.0 Hz, H-2), 3.61 (dd, 1H, *J* = 10.6, 3.7 Hz, H-5), 3.51 (dd, 1H, *J* = 10.6, 5.8 Hz, H-5), 3.31 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.3, 137.8, 137.8 (C_q), 128.4, 128.4, 128.3, 128.0, 127.9, 127.8, 127.8, 127.6, 127.5 (CH_{arom}), 106.3 (C-1), 80.5 (C-4), 79.6 (C-2), 78.3 (C-3), 73.2, 72.4, 72.3 (CH_2 Bn), 71.3 (C-5), 55.1 (OMe).

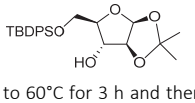


Methyl 3,5-di-*O*-benzyl-α-D-ribofuranoside (3). Compound **2** (4.35 g, 10 mmol, 1 eq.) was coevaporated with toluene twice and then was dissolved in 50 mL DCM at 0°C, followed by the addition of a 1 M $SnCl_4$ solution in DCM (10 mL, 10 mmol, 1 eq.). The reaction mixture was stirred overnight at 4°C and then quenched by the addition of sat. aq. $NaHCO_3$. The organic layer was washed with H_2O and brine, then dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (9/1 to 7/3 pentane/EtOAc) to yield the title compound as a colourless oil (3.19 g, 9.26 mmol, 93%). Spectroscopic data were in accord with those previously reported.[17] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.36 – 7.22 (m, 10H, CHarom), 4.88 (d, 1H, *J* = 4.6 Hz, H-1), 4.72 (d, 1H, *J* = 12.4 Hz, C*H*H Bn), 4.57 (d, 1H, *J* = 12.3 Hz, CH*H* Bn), 4.50 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.44 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.16 (td, 1H, *J* = 4.1, 3.1 Hz, H-4), 4.14 –

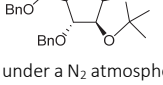
4.06 (m, 1H, H-2), 3.78 (dd, 1H, *J* = 7.1, 3.2 Hz, H-3), 3.47 (s, 3H, CH_3 OMe), 3.43 (dd, 1H, *J* = 10.4, 4.1 Hz, H-5), 3.35 (dd, 1H, *J* = 10.4, 4.3 Hz, H-5), 2.96 (bd, 1H, *J* = 10.1 Hz, 2-OH); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 137.9, 137.9 (C_q), 128.5, 128.5, 128.0, 127.9, 127.8, 127.7 (CH_{arom}), 103.0 (C-1), 82.0 (C-4), 76.4 (C-3), 73.5, 73.0 (CH_2 Bn), 71.9 (C-2), 70.1 (C-5), 55.7 (OMe); HRMS: $[M+Na]^+$ calcd for $C_{20}H_{24}O_5Na$ 367.15160, found 367.15139.



Methyl 3,5-di-*O*-benzyl-α/β-D-xylofuranoside (6). 1,2-*O*-Isopropylidene-α-D-xylofuranoside **4**[51] (28.6 g, 150 mmol, 1 eq.) was dissolved in 750 mL DMF and cooled to 0°C. NaH (60% dispersion in mineral oil, 15 g, 375 mmol, 2.5 eq.) was added followed by the slow addition of BnBr (45 mL, 375 mmol, 2.5 eq.). After 4 h the reaction was quenched by the addition of 50 mL MeOH and the reaction mixture was concentrated under reduced pressure. The crude mixture was taken up in H_2O and extracted twice with Et_2O. The combined Et_2O layers were washed with brine and dried with $MgSO_4$. After filtration and concentration, the crude product **5** was dissolved in 750 mL MeOH and CSA (3.5 g, 15 mmol, 0.1 eq.) was added and the reaction mixture was refluxed for 4 h. The reaction was quenched by addition of solid $NaHCO_3$, which after stirring for 15 min, was removed by filtration followed by concentration on the reaction mixture *in vacuo*. The residue was redissolved in EtOAc and was washed with H_2O and brine, dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (9/1 to 1/1 pentane/EtOAc) yielded compound **6** as a light yellow oils in three fractions (1: α only, 21.8 g, 63.4 mmol, 2: α/β mixture, 7.6 g, 22.2 mmol, 3: β only, 20.8 g, 60.5 mmol) combined yield: 146.1 mmol, 97%. Spectroscopic data were in accord with those previously reported.[52] Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.37 – 7.24 (m, 10H, CH_{arom}), 4.99 (d, 1H, *J* = 4.7 Hz, H-1), 4.73 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.63 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.55 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.53 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.39 (td, 1H, *J* = 6.4, 4.2 Hz, H-4), 4.26 (dt, 1H, *J* = 7.5, 4.4 Hz, H-2), 4.00 (dd, 1H, *J* = 6.0, 4.1 Hz, H-3), 3.72 (dd, 1H, *J* = 10.5, 4.2 Hz, H-5), 3.65 (dd, 1H, *J* = 10.5, 6.7 Hz, H-5), 3.49 (s, 3H, CH_3 OMe), 2.71 (d, 1H, *J* = 7.6 Hz, 2-OH); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.4, 138.1 (C_q), 128.5, 128.5, 127.9, 127.8, 127.7, 127.7 (CH_{arom}), 101.9 (C-1), 83.7 (C-3), 77.5 (C-4), 77.1 (C-2), 73.6, 72.0 (CH_2 Bn), 69.2 (C-5), 55.9 (OMe); Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.37 – 7.25 (m, 10H, CH_{arom}), 4.80 (d, 1H, *J* = 1.7 Hz, H-1), 4.66 – 4.58 (m, 2H, 2xC*H*H Bn), 4.55 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.54 (d, 1H, *J* = 12.2 Hz, CH*H* Bn), 4.47 (ddd, 1H, *J* = 7.2, 6.1, 4.6 Hz, H-4), 4.21 (ddd, 1H, *J* = 4.7, 2.9, 1.7 Hz, H-2), 3.95 (dd, 1H, *J* = 6.1, 2.9 Hz, H-3), 3.77 (dd, 1H, *J* = 10.3, 4.7 Hz, H-5), 3.70 (dd, 1H, *J* = 10.3, 7.3 Hz, H-5), 3.40 (s, 3H, CH_3 OMe), 1.95 (d, 1H, *J* = 4.8 Hz, 2-OH); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.4, 137.9 (C_q), 128.6, 128.5, 128.0, 127.9, 127.9, 127.7 (CH_{arom}), 109.6 (C-1), 83.5 (C-3), 80.1 (C-4), 79.8 (C-2), 73.6, 72.5 (CH_2 Bn), 70.0 (C-5), 55.9 (OMe).

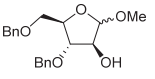


1,2-*O*-Isopropylidene-5-*O*-(*tert*-butyldiphenylsilyl)-β-D-arabinofuranoside (7). D-Arabinose (30 g, 200 mmol, 1 eq.) was dissolved in 1 L DMF and imidazole (27.2 g, 400 mmol, 2 eq.) and TBDPSCl (52 mL, 200 mmol, 1 eq.) were added sequentially. The reaction mixture was heated to 60°C for 3 h and then two thirds of the DMF was removed under reduced pressure. The remaining solution was mixed with H_2O (1.5 L) and conc. HCl (15 mL) and the aqueous phase extracted four times with EtOAc. The organic layers were combined and washed with sat. aq. $NaHCO_3$ and brine. The organic phase was dried with $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was coevaporated with toluene and then dissolved in DCM (1.1 L) and cooled to 0°C. CSA (2.5 g, 10.8 mmol, 0.05 eq.) was added followed by dropwise addition of 2,2-dimethoxypropane (44 mL, 360 mmol, 1.8 eq.). After 4 h, the reaction was quenched with Et_3N (2.8 mL) and concentrated under reduced pressure. Flash column chromatography (19/1 to 8/2 pentane/EtOAc) yielded compound 7 as a colourless oil (43.7 g, 102 mmol, 51%). Spectroscopic data were in accord with those previously reported.[53] ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.73 – 7.61 (m, 4H, CH_{arom}), 7.46 – 7.33 (m, 6H, CH_{arom}), 5.88 (d, 1H, *J* = 4.0 Hz, H-1), 4.54 (d, 1H, *J* = 4.0 Hz, H-2), 4.43 (t, 1H, *J* = 3.1 Hz, H-3), 4.05 (ddd, 1H, *J* = 7.9, 5.7, 2.6 Hz, H-4), 3.86 – 3.78 (m, 2H, H-5), 2.00 (d, 1H, *J* = 4.3 Hz, 3-OH), 1.32 (s, 3H, CH_3 Me), 1.28 (s, 3H, CH_3 Me), 1.06 (s, 9H, CH_3 ^{t}Bu); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 135.7, 135.7 (CH_{arom}), 133.3, 133.2 (C_q Ph), 129.9, 129.9, 127.9, 127.9 (CH_{arom}), 112.6 (C_q), 105.7 (C-1), 87.5 (C-4), 87.1 (C-2), 76.5 (C-3), 63.8 (C-5), 27.0, 27.0 (^{t}Bu), 26.2 (Me), 19.3 (C_q ^{t}Bu).

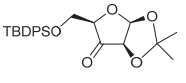


Methyl 3,5-di-*O*-benzyl-1,2-*O*-isopropylidene-β-D-arabinofuranoside (8). Compound **7** (14.1 g, 32.8 mmol, 1 eq.) and BnCl (22.6 mL, 197 mmol, 6 eq.) were dissolved in 140 mL THF. Freshly crushed KOH pellets (35 g, 623 mmol, 19 eq.) were added and the reaction mixture was stirred under a N_2 atmosphere at reflux overnight. Once the mixture was cooled to room temperature, it was filtered through glass wool and concentrated *in vacuo*. Flash column chromatography (1/0 to 9/1 pentane/EtOAc) afforded the title compound as a yellow oil (9.0 g, 24.3 mmol, 74%). Spectroscopic data were in accord with those previously reported.[22] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.34 – 7.26 (m, 10H, CH_{arom}), 5.90 (d, 1H, *J* = 4.0 Hz, H-1), 4.64 (d, 1H, *J* = 4.1 Hz, H-2), 4.62 – 4.57 (m, 2H, CH_2 Bn), 4.57 – 4.51 (m, 2H, CH_2 Bn), 4.27 (td, 1H, *J* = 6.3, 3.0 Hz, H-4), 4.02 (d, 1H,

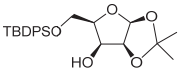
J = 2.7 Hz, H-3), 3.63 (d, 2H, *J* = 6.2 Hz, H-5), 1.44 (s, 3H, CH_3 Me), 1.32 (s, 3H, CH_3 Me); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.1, 137.4 (C_q Bn), 128.6, 128.5, 128.0, 127.9, 127.8, 127.8 (CH_{arom}), 112.8 (C_q), 105.8 (C-1), 85.3 (C-2), 83.7 (C-4), 83.2 (C-3), 73.5, 71.8 (CH_2 Bn), 70.1 (C-5), 27.2, 26.4 (Me).



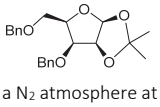
Methyl 3,5-di-*O*-benzyl-α/β-D-arabinofuranoside (9). Fully protected compound **8** (11 g, 30 mmol, 1 eq.) and CSA (0.7 g, 3.0 mmol, 0.1 eq.) were dissolved in 150 mL MeOH and brought to reflux. After stirring for 5 h, the reaction mixture was cooled down and solid $NaHCO_3$ was added. The reaction mixture was concentrated and then H_2O was added. Extraction with EtOAc twice and those combined organic layers were washed with brine, then dried with $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash column chromatography (19/1 to 8/2 pentane/EtOAc) afforded the title compound (9.4 g, 27 mmol, 91%) as a colourless oil. Spectroscopic data were in accord with those previously reported.[22] Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.37 – 7.21 (m, 10H, CH_{arom}), 4.89 (s, 1H, H-1), 4.68 (d, 1H, *J* = 12.3 Hz, C*H*H Bn), 4.61 (d, 1H, *J* = 11.9 Hz, C*H*H Bn), 4.51 (d, 1H, *J* = 12.4 Hz, CH*H* Bn), 4.46 (d, 1H, *J* = 11.9 Hz, CH*H* Bn),4.26 (s, 1H, H-4), 4.12 (d, 1H, *J* = 10.9 Hz, H-2), 3.84 (s, 1H, H-3), 3.64 (dd, 1H, *J* = 10.4, 2.4 Hz, H-5), 3.43 (dd, 1H, *J* = 10.4, 2.5 Hz, H-5), 3.40 (s, 3H, CH_3 OMe), 3.34 (d, 1H, *J* = 10.8 Hz, OH); Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.39 – 7.22 (m, 10H, CH_{arom}), 4.84 (d, 1H, *J* = 4.7 Hz, H-1), 4.74 (d, 1H, *J* = 11.9 Hz, C*H*H Bn), 4.59 (d, 1H, *J* = 11.9 Hz, CH*H* Bn), 4.57 (s, 2H, CH_2 Bn), 4.31 – 4.21 (m, 1H, H-2), 4.19 – 4.09 (m, 1H, H-4), 3.84 (t, 1H, *J* = 5.8 Hz, H-3), 3.53 (d, 2H, *J* = 5.6 Hz, H-5), 3.41 (s, 3H, CH_3 OMe), 2.57 (d, 1H, *J* = 9.4 Hz, OH); Data for the both anomers: ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.1, 138.0, 137.8, 137.1 (C_q), 128.6, 128.5, 128.4, 128.1, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7 (CH_{arom}), 110.5 (C-1α), 102.8 (C-1β), 85.0 (C-3α), 84.7 (C-3β), 83.5 (C-4α), 80.8 (C-4β), 78.1 (C-2α), 78.0 (C-2β), 73.8, 73.4, 72.2 (CH_2 Bn), 72.1 (C-5β), 71.9 (CH_2 Bn), 69.8 (C-5α), 55.4, 55.3 (OMe).



1,2-O-Isopropylidene 5-O-(*tert*-butyldiphenylsilyl)-β-D-arabinofuran-3-uloside (10). Compound **7** (9.95 g, 23.2 mmol, 1 eq.) was dissolved in 230 mL DCM and Dess-Martin periodinane (13.4 g, 31 mmol, 1.36 eq.) was added. After stirring 4 h, $Na_2S_2O_3$ (20 g) was added and the reaction mixture was poured into sat. aq. $NaHCO_3$. The mixture was extracted with DCM three times and the combined organic layers were washed with H_2O and brine. The organic layer was dried with $MgSO_4$, filtered and concentrated under reduced pressure. Flash column chromatography (1/0 to 8/2 pentane/EtOAc) afforded the title compound as a colourless oil (7.65 g, 17.9 mmol, 77%). Spectroscopic data were in accord with those previously reported.[18] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.75 – 7.63 (m, 4H, CH_{arom}), 7.45 – 7.33 (m, 6H, CH_{arom}), 6.03 (d, 1H, *J* = 4.3 Hz, H-1), 4.39 (d, 1H, *J* = 4.3 Hz, H-2), 4.29 (dd, 1H, *J* = 6.3, 4.2 Hz, H-4), 3.99 – 3.87 (m, 2H, H-5), 1.37 (s, 3H, CH_3 Me), 1.35 (s, 3H, CH_3 Me), 1.05 (s, 9H, CH_3 ^{t}Bu); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 207.3 (C=O), 135.9, 135.7 (CH_{arom}), 133.2, 132.9 (C_q Ph), 129.9, 127.9 (CH_{arom}), 114.9 (C_q), 102.7 (C-1), 82.5 (C-4), 76.9 (C-2), 64.6 (C-5), 27.6 (Me), 26.9 (^{t}Bu), 19.4 (C_q ^{t}Bu);

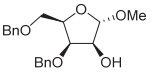


1,2-*O*-Isopropylidene-5-*O*-(*tert*-butyldiphenylsilyl)-β-D-lyxofuranoside (11). Ketone **9** (6.9 g, 16.2 mmol, 1 eq.) was dissolved in DCM/MeOH (100 mL, 1/1) and cooled to 0C. $NaBH_4$ (1.8 g, 48 mmol, 3 eq.) was added in three equal portions and the reaction mixture was stirred for 30 min after each addition. After 1.5 h sat. aq. NH_4Cl was added and the mixture was extracted three times with DCM. The combined organic layers were washed with sat. aq. NH_4Cl, H_2O, and brine. The organic layer was then dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Flash column chromatography (2% to 14% EtOAc/pentane) afforded the title compound as a yellow oil (5.2 g, 13.1 mmol, 75%). Spectroscopic data were in accord with those previously reported.[54] ^{1}H NMR ($CDCl_3$, HH-COSY, HSQC): δ 7.78 – 7.62 (m, 4H, CH_{arom}), 7.48 – 7.31 (m, 6H, CH_{arom}), 5.71 (d, 1H, *J* = 4.1 Hz, H-1), 4.60 (dd, 1H, *J* = 5.8, 4.1 Hz, H-2), 4.33 (q, 1H, *J* = 5.9 Hz, H-3), 4.20 – 4.11 (m, 2H, H-4, H-5), 3.93 – 3.84 (m, 1H, H-5), 3.10 (d, 1H, *J* = 6.4 Hz, 3-OH), 1.42 (s, 3H, CH_3 Me), 1.34 (s, 3H, CH_3 Me), 1.06 (s, 9H, CH_3 ^{t}Bu); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 135.7, 135.7 (CH_{arom}), 133.2, 133 (C_q Ph).1, 129.8, 127.8, 127.8 (CH_{arom}), 114.1 (C_q), 105.0 (C-1), 81.4 (C-4), 79.9 (C-2), 71.0 (C-3), 63.3 (C-5), 26.9 (CH_3 ^{t}Bu), 26.8, 26.6 (Me), 19.2 (C_q ^{t}Bu).

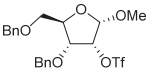


Methyl 3,5-di-*O*-benzyl-1,2-*O*-isopropylidene-β-D-lyxofuranoside (12). Compound **11** (9.0 g, 21 mmol, 1 eq.) and BnCl (14 mL, 123 mmol, 5.9 eq.) were dissolved in 90 mL THF. Freshly crushed KOH pellets (19.7 g, 351 mmol, 16.7 eq.) were added and the reaction mixture was stirred under a N_2 atmosphere at reflux overnight. Once the mixture was cooled to room temperature, it was filtered through glass wool and concentrated *in vacuo*. Flash column chromatography (1/0 to 8/2 pentane/EtOAc) afforded the title compound as a colourless oil (7.9 g, 21 mmol, 100%). Spectroscopic data were in accord with those previously reported for the L-enantiomer.[55] R*f*: 0.16 (9/1 pentane/EtOAc). $[\alpha]_D^{20}$ = +15° (*c* = 0.44, $CHCl_3$). IR (thin film): 698, 737,

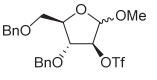
1026, 1097, 1152, 1209, 1255, 1454, 2868, 2946, 2986; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.41 – 7.18 (m, 10H, CH_{arom}), 5.70 (d, 1H, *J* = 4.0 Hz, H-1), 4.67 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.63 – 4.57 (m, 3H, CH_2 Bn, CH*H* Bn), 4.55 (dd, 1H, *J* = 5.1, 4.0 Hz, H-2), 4.32 (dt, 1H, *J* = 7.2, 5.8 Hz, H-4), 4.05 (dd, 1H, *J* = 7.3, 5.1 Hz, H-3), 3.88 (d, 2H, *J* = 5.9 Hz, 2xH-5), 1.48 (s, 3H, CH_3 Me), 1.30 (s, 3H, CH_3 Me); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.4, 137.5 (C_q Bn), 128.5, 128.3, 128.0, 127.9, 127.8, 127.5 (CH_{arom}), 113.5 (C_q), 104.7 (C-1), 80.0 (C-4), 78.4 (C-2), 77.2 (C-3), 73.3, 72.6 (CH_2 Bn), 69.9 (C-5), 26.6, 26.1 (Me); HRMS: $[M+NH_4]^+$ calcd for $C_{22}H_{30}NO_5$ 388.21185, found 388.21226.



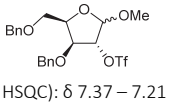
Methyl 3,5-di-*O*-benzyl-α-D-lyxofuranoside (13). Fully protected compound **12** (7.8 g, 21 mmol, 1 eq.) and CSA (0.46 g, 2.0 mmol, 0.1 eq.) were dissolved in 100 mL MeOH and brought to reflux. After stirring for 5 h, the reaction mixture was cooled down and solid $NaHCO_3$ was added. The reaction mixture was concentrated and then H_2O was added. Extraction with EtOAc twice and those combined organic layers were washed with brine, then dried with $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash column chromatography (19/1 to 8/2 pentane/EtOAc) afforded the title compound (6.1 g, 17.7 mmol, 84%) as a colourless oil and a single anomer. Spectroscopic data were in accord with those previously reported.[56] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.39 – 7.24 (m, 10H, CH_{arom}), 4.86 (s, 1H, H-1), 4.72 (d, 1H, *J* = 11.4 Hz, C*H*H Bn), 4.64 (d, 1H, *J* = 11.8 Hz, C*H*H Bn), 4.55 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.48 (d, 1H, *J* = 11.4 Hz, CH*H* Bn), 4.40 (dd, 1H, *J* = 8.0, 4.9 Hz, H-3), 4.35 – 4.28 (m, 2H, H-4, 2-OH), 4.05 (dd, 1H, *J* = 10.2, 4.9 Hz, H-2), 3.67 (dd, 1H, *J* = 10.5, 3.3 Hz, H-5), 3.61 (dd, 1H, *J* = 10.5, 2.3 Hz, H-5), 3.34 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 137.9, 137.3 (C_q), 128.6, 128.5, 128.0, 128.0, 127.9 (CH_{arom}), 108.6 (C-1), 77.8 (C-3), 77.5 (C-4), 74.0, 72.6 (CH_2 Bn), 72.2 (C-2), 68.0 (C-5), 55.2 (OMe).



Methyl 3,5-di-*O*-benzyl-2-*O*-trifluoromethanesulfonate-α-D-ribofuranoside (14). The title compound was generated by the general procedure for triflate formation and used crude. Spectroscopic data were in accord with those previously reported.[57] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.37 – 7.21 (m, 10H, CH_{arom}), 5.09 (d, 1H, *J* = 4.3 Hz, H-1), 5.01 (dd, 1H, *J* = 6.5, 4.3 Hz, H-2), 4.75 (d, 1H, *J* = 12.2 Hz, C*H*H Bn), 4.53 – 4.44 (m, 2H, CH*H* Bn, C*H*H Bn), 4.40 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.19 (dt, 1H, *J* = 5.8, 3.1 Hz, H-4), 4.07 (dd, 1H, *J* = 6.5, 5.0 Hz, H-3), 3.53 (dd, 1H, *J* = 10.9, 2.9 Hzm H-5), 3.51 (s, 3H, CH_3 OMe), 3.33 (dd, 1H, *J* = 10.8, 3.3 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 137.7, 137.1 (C_q), 128.7, 128.6, 128.4, 128.3, 128.0, 127.9 (CH_{arom}), 118.7 (d, *J* = 319.6 Hz), 101.1 (C-1), 81.4 (C-2), 81.1 (C-4), 74.6 (C-3), 73.7, 73.5 (CH_2 Bn), 68.5 (C-5), 56.4 (OMe); HRMS: $[M+NH_4]^+$ calcd for $C_{21}H_{27}F_3NO_7S$ 494.14548, found 494.14526.

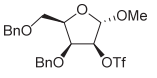


Methyl 3,5-di-*O*-benzyl-2-*O*-trifluoromethanesulfonate-α/β-D-arabinofuranoside (15). The title compound was generated by the general procedure for triflate formation and used crude. Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.38 – 7.23 (m, 10H, CH_{arom}), 5.20 (s, 1H, H-2), 5.10 (s, 1H, H-1), 4.70 (d, 1H, *J* = 11.9 Hz, C*H*H Bn), 4.55 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.52 – 4.45 (m, 2H, 2x CH*H* Bn), 4.22 – 4.18 (m, 1H, H-4), 4.13 (ddd, 1H, *J* = 5.9, 1.7, 0.9 Hz, H-3), 3.61 (dd, 1H, *J* = 10.9, 3.6 Hz, H-5), 3.54 (dd, 1H, *J* = 10.9, 4.6 Hz, H-5), 3.42 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 137.8, 136.7 (C_q), 128.7, 128.5, 128.3, 128.1, 127.9, 127.9 (CH_{arom}), 118.5 (q, *J* = 319.8 Hz), 105.9 (C-1), 92.7 (C-2), 82.6 (C-3), 81.8 (C-4), 73.7, 72.8 (CH_2 Bn), 68.6 (C-5), 55.2 (OMe); Diagnostic peaks β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.11 – 5.07 (m, 1H, H-1), 5.00 (d, 1H, *J* = 4.4 Hz, H-2), 4.62 (d, 1H, *J* = 11.8 Hz, C*H*H Bn), 4.57 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.55 – 4.48 (m, 2H, CH_2 Bn), 4.29 (dd, 1H, *J* = 6.5, 5.4 Hz, H-3), 4.17 – 4.12 (m, 1H, H-4), 3.57 – 3.53 (m, 1H, H-5), 3.47 (dd, 1H, *J* = 9.9, 6.2 Hz, H-5), 3.39 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 100.4 (C-1), 88.3 (C-2), 80.9 (C-3), 79.8 (C-4), 73.5, 72.6 (CH_2 Bn), 71.4 (C-5), 55.5 (OMe).

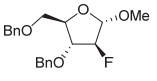


Methyl 3,5-di-*O*-benzyl-2-*O*-trifluoromethanesulfonate-α/β-D-xylofuranoside (16). The title compound was generated by the general procedure for triflate formation (anomers were treated separately) and used crude. Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.37 – 7.21 (m, 10H, CH_{arom}), 5.18 (t, 1H, *J* = 5.1 Hz, H-2), 5.06 (d, 1H, *J* = 4.4 Hz, H-1), 4.66 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.57 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.55 – 4.50 (m, 2H, 2xCH*H* Bn), 4.44 (dd, 1H, *J* = 6.9, 5.8 Hz, H-3), 4.33 (dt, 1H, *J* = 7.0, 4.6 Hz, H-4), 3.67 (dd, 1H, *J* = 10.5, 4.2 Hz, H-5), 3.59 (dd, 1H, *J* = 10.5, 5.1 Hz, H-5), 3.44 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 137.9, 136.9 (C_q), 128.7, 128.5, 128.3, 127.9, 127.8, 127.8 (CH_{arom}), 118.6 (q, *J* = 319.6 Hz), 99.6 (C-1), 87.9 (C-2), 79.3 (C-3), 75.7 (C-4), 73.7, 73.3 (CH_2 Bn), 68.4 (C-5), 56.0 (OMe); Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.42 – 7.23 (m, 10H, CH_{arom}), 5.17 (s, 1H, H-2), 5.05 (s, 1H, H-1), 4.71 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.59 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.54 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.53 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.48 (dt, 1H, *J* = 6.7, 5.5 Hz, H-4), 4.21 (dd, 1H, *J* = 5.9, 1.8 Hz, H-3), 3.74 (dd, 1H, *J* = 10.3, 5.1 Hz, H-5), 3.69 (dd, 1H, *J* = 10.3, 7.0 Hz, H-5), 3.42 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.0, 136.6,

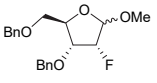
128.7, 128.5, 128.4, 128.1, 128.0, 127.9, 106.4, 91.2, 80.6, 80.4, 73.7, 72.8, 69.2, 56.1; HRMS: $[M+NH_4]^+$ calcd for $C_{21}H_{27}F_3NO_7S$ 494.14548, found 494.14515.



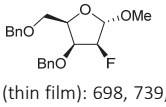
Methyl 3,5-di-*O*-benzyl-2-*O*-trifluoromethanesulfonate-α-D-lyxofuranoside (17). The title compound was generated by the general procedure for triflate formation and used crude. ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.43 – 7.13 (m, 10H, CH_{arom}), 5.08 (s, 1H, H-1), 5.05 (d, 1H, *J* = 4.3 Hz, H-2), 4.73 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.63 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.51 (d, 1H, *J* = 11.7 Hz, CH*H* Bn), 4.50 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.46 – 4.37 (m, 2H, H-3, H-4), 3.74 (dd, 1H, *J* = 10.5, 4.1 Hz, H-5), 3.64 (dd, 1H, *J* = 10.5, 7.3 Hz, H-5), 3.38 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.0, 136.9 (C_q), 128.7, 128.5, 128.3, 128.0, 128.0, 127.8 (CH_{arom}), 118.6 (q, *J* = 319.6 Hz, CF_3), 104.0 (C-1), 86.2 (C-2), 77.5 (C-4), 76.4 (C-3), 73.9, 73.7 (CH_2 Bn), 69.6 (C-5), 55.7 (OMe).



Methyl 3,5-di-*O*-benzyl-2-deoxy-2-fluoro-α-D-arabinofuranoside (18). Employing conditions **A** of the general experimental for inversion of furanosyl triflates gave **18** in 86% yield (0.95 mmol) from triflate **14**. Spectroscopic data were in accord with those previously reported.[24] IR (thin film): 696, 737, 947, 988, 1039, 1055, 1098, 1193, 1364, 1454, 2862, 2922; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.37 – 7.25 (m, 10H, CH_{arom}), 5.06 (d, 1H, *J* = 12.0 Hz, H-1), 4.94 (dd, 1H, *J* = 51.3, 1.8 Hz, H-2), 4.67 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.58 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.56 – 4.51 (m, 2H, 2xCH*H* Bn), 4.21 (ddd, 1H, *J* = 6.4, 5.2, 3.8 Hz, H-4), 3.99 (dddd, 1H, *J* = 24.7, 6.4, 1.9, 1.0 Hz, H-3), 3.63 (dd, 1H, *J* = 10.8, 3.8 Hz, H-5), 3.58 (dd, 1H, *J* = 10.8, 5.1 Hz, H-5), 3.40 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 138.0, 137.2 (C_q), 128.5, 128.4, 128.0, 127.7, 127.7 (CH_{arom}), 106.5 (d, *J* = 36.0 Hz, C-1), 99.6 (d, *J* = 181.3 Hz, C-2), 83.0 (d, *J* = 25.6 Hz, C-3), 81.3 (d, *J* = 4.0 Hz, C-4), 73.4, 72.5 (CH_2 Bn), 69.3 (C-5), 54.9 (OMe); ^{19}F NMR ($CDCl_3$, 471 MHz): δ -188.39 (ddd, *J* = 51.3, 24.6, 12.0 Hz); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): $^2J_{C1\text{-}H2}$ = -0.7 Hz, $^2J_{C2\text{-}H1}$ = -2.0 Hz; HRMS: $[M+NH_4]^+$ calcd for $C_{20}H_{27}NFO_4$ 364.19186, found 364.19196.

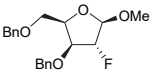


Methyl 3,5-di-*O*-benzyl-2-deoxy-2-fluoro-α/β-D-ribofuranoside (19). Employing conditions **A** of the general experimental for inversion of furanosyl triflates gave **19** in 63% yield (3.2 mmol), as two anomers (*Rf*: 0.47, and Rf: 0.15, 9/1 pentane/EtOAc) and two anomers of **26**. Spectroscopic data were in accord with those previously reported for the β-anomer.[22] Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.41 – 7.27 (m, 10H, CH_{arom}), 5.09 (dd, 1H, *J* = 4.1, 3.5 Hz, H-1), 4.88 (ddd, 1H, *J* = 51.1, 6.1, 4.2 Hz), 4.82 (d, 1H, *J* = 12.4 Hz, C*H*H Bn), 4.59 (d, 1H, *J* = 12.4 Hz, CH*H* Bn), 4.58 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.49 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.30 (dt, 1H, *J* = 5.3, 3.4 Hz, H-4), 4.00 (ddd, 1H, *J* = 7.6, 6.0, 5.2 Hz, H-3), 3.63 (dd, 1H, *J* = 10.9, 2.9 Hz, H-5), 3.56 (s, 3H, CH3 OMe), 3.49 (dd, 1H, *J* = 10.8, 3.7 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 137.9, 137.8 (C_q), 128.5, 128.5, 128.0, 128.0, 127.8, 127.7 (CH_{arom}), 101.8 (d, *J* = 15.9 Hz, C-1), 88.2 (d, *J* = 202.7 Hz, C-2), 80.9 (d, *J* = 2.1 Hz, C-4), 74.6 (d, *J* = 14.8 Hz, C-3), 73.6 (CH_2 5-OBn), 72.9 (d, *J* = 2.2 Hz, CH_2 3-OBn), 69.1 (C-5), 56.1 (OMe); ^{19}F NMR ($CDCl_3$, 470 MHz): δ -216.73 (ddd, *J* = 51.2, 7.6, 3.3 Hz); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): $^2J_{C1\text{-}H2}$: +2.4 Hz, $^2J_{C2\text{-}H1}$: -+3.2 Hz; Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.35 – 7.26 (m, 10H, CH_{arom}), 5.00 (d, 1H, *J* = 10.6 Hz, H-1), 4.76 (dd, 1H, *J* = 53.2, 3.7 Hz, H-2), 4.66 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.59 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.54 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.54 (d, 1H, *J* = 11.7 Hz, CH*H* Bn), 4.30 (ddd, 1H, *J* = 8.0, 5.7, 3.4 Hz, H-4), 4.07 (ddd, 1H, *J* = 24.6, 7.7, 3.7 Hz, H-3), 3.64 (dd, 1H, *J* = 10.6, 3.4 Hz, H-5), 3.53 (dd, 1H, *J* = 10.6, 5.7 Hz, H-5), 3.32 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.3, 137.4 (C_q), 128.6, 128.4, 128.1, 128.0, 127.7 (CH_{arom}), 105.7 (d, *J* = 29.3 Hz, C-1), 91.2 (d, *J* = 185.1 Hz, C-2), 80.1 (C-4), 77.8 (d, *J* = 15.6 Hz, C-3), 73.3, 72.8 (CH_2 Bn), 71.0 (C-5), 55.1 (OMe); ^{19}F NMR ($CDCl_3$, 471 MHz): δ -209.71 (ddd, *J* = 53.2, 24.6, 10.6 Hz); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): $^2J_{C1\text{-}H2}$: +1.6 Hz, $^2J_{C2\text{-}H1}$: -1.6 Hz; HRMS: $[M+NH_4]^+$ calcd for $C_{20}H_{24}FNO_4$ 364.19186, found 364.19205.

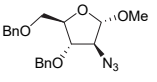


Methyl 3,5-di-*O*-benzyl-2-deoxy-2-fluoro-α-D-lyxofuranoside (20). Employing conditions **B** of the general experimental for inversion of furanosyl triflates, with an additional 70°C reflux for 7 h, gave **20** in 44% yield (2.19 mmol) from triflate **16α**. Conditions **A** yielded 57% **28** and 21% **30**. IR (thin film): 698, 739, 1056, 1452, 2932; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.40 – 7.24 (m, 10H, CH_{arom}), 5.08 (dd, 1H, *J* = 10.0, 1.0 Hz, H-1), 4.80 (ddd, 1H, *J* = 52.8, 4.1, 1.0 Hz, H-2), 4.68 (d, 1H, *J* = 11.9 Hz, C*H*H Bn), 4.65 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.53 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.52 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.42 (ddd, 1H, *J* = 8.0, 7.1, 3.8 Hz, H-4), 4.30 (ddd, 1H, *J* = 20.9, 7.1, 4.1 Hz, H-3), 3.77 (dd, 1H, *J* = 10.5, 3.8 Hz, H-5), 3.67 (ddd, 1H, *J* = 10.5, 8.0, 1.4 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 138.4, 137.5 (C_q), 128.6, 128.5, 128.1, 128.0, 127.8, 127.7 (CH_{arom}), 105.0 (d, *J* = 29.8 Hz, C-1), 92.4 (d, *J* = 187.9 Hz, C-2), 77.7 (C-4), 77.1 (d, *J* = 14.9 Hz, C-3), 73.6, 73.3 (CH_2 Bn), 70.3 (C-5), 55.5 (OMe); ^{19}F NMR ($CDCl_3$, 471 MHz, HH-COSY, HSQC): δ -207.58 (dddd, *J* = 52.8, 20.9, 10.0, 1.0 Hz); ^{13}C

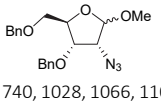
HSQC-HECADE NMR ($CDCl_3$, 126 MHz): $^2J_{C2,H1}$ = -2.5 Hz; HRMS: $[M+Na]^+$ calcd for $C_{20}H_{23}FO_4Na$ 369.14726, found 369.14734.



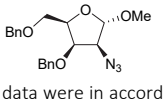
Methyl 3,5-di-*O*-benzyl-2-deoxy-2-fluoro-β-D-xylofuranoside (21). Employing conditions **A** of the general experimental for inversion of furanosyl triflates gave **21** in 10% yield (0.52 mmol) as the minor product from triflate **16β**. IR (thin film): 698, 712, 978, 1068, 1107, 2929; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.37 – 7.26 (m, 10H, CH_{arom}), 5.02 (d, 1H, *J* = 14.8 Hz, H-1), 4.93 (d, 1H, *J* = 50.6 Hz, H-2), 4.68 (d, 1H, *J* = 12.2 Hz, C*H*H Bn), 4.60 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.55 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.54 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.52 – 4.48 (m, 1H, H-4), 4.15 (ddd, 1H, *J* = 18.2, 6.1, 1.7 Hz, H-3), 3.76 (dd, 1H, *J* = 10.3, 4.9 Hz, H-5), 3.70 (dd, 1H, *J* = 10.3, 7.3 Hz, H-5), 3.41 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 138.3, 137.4 (C_q), 128.6, 128.5, 128.1, 127.9, 127.9, 127.8 (CH_{arom}), 107.1 (d, *J* = 35.2 Hz, C-1), 98.4 (d, *J* = 181.0 Hz, C-2), 80.9 (d, *J* = 25.9 Hz, C-3), 80.7 (d, *J* = 1.9 Hz, C-4), 73.6, 72.7 (CH_2 Bn), 69.7 (C-5), 55.8 (OMe); ^{19}F NMR ($CDCl_3$, 471 MHz): δ -192.85 (ddd, *J* = 50.6, 18.1, 14.9 Hz); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): $^2J_{C1,H2}$ = -2.6 Hz, $^2J_{C2,H1}$ = -0.2 Hz; HRMS: $[M+NH_4]^+$ calcd for $C_{20}H_{27}FNO_4$ 364.19186, found 364.19192.



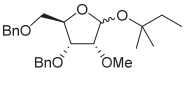
Methyl 2-azido-3,5-di-*O*-benzyl-2-deoxy-α-D-arabinofuranoside (22). Employing conditions **C** of the general experimental for inversion of furanosyl triflates gave **22** in 93% yield (5.37 mmol) from triflate **14**. $[\alpha]_D^{20}$ = +76.4° (*c* = 1.0, $CHCl_3$). IR (thin film): 698, 714, 1026, 1070, 1097, 1107, 1271, 1452, 2104, 2932; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.35 – 7.23 (m, 10H, CH_{arom}), 4.88 (d, 1H, *J* = 1.5 Hz, H-1), 4.61 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.56 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.49 (d, 1H, *J* = 12.2 Hz, CH*H* Bn), 4.49 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.23 – 4.15 (m, 1H, H-4), 3.92 – 3.85 (m, 2H, H-2, H-3), 3.60 (dd, 1H, *J* = 10.8, 3.6 Hz, H-5), 3.54 (dd, 1H, *J* = 10.8, 4.8 Hz, H-5), 3.39 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 137.9, 137.2 (C_q), 128.5, 128.4, 128.0, 128.0, 127.8, 127.7 (CH_{arom}), 107.0 (C-1), 83.1 (C-3), 81.2 (C-4), 73.5, 72.6 (CH_2 Bn), 70.8 (C-2), 69.0 (C-5), 55.3 (OMe); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): $^2J_{C1,H2}$ = -2.1 Hz, $^2J_{C2,H1}$ = -0.3 Hz; HRMS: $[M+NH_4]^+$ calcd for $C_{20}H_{27}N_4O_4$ 387.20268, found 387.20271.



Methyl 2-azido-3,5-di-*O*-benzyl-2-deoxy-α/β-D-ribofuranoside (23). Employing conditions **C** of the general experimental for inversion of furanosyl triflates gave **23** as an α:β = 1:2 mixture from triflate **15**, and as a 4:1 mixture of **23** and **27**, combined yield 86% (4.3 mmol). IR (thin film): 698, 740, 1028, 1066, 1107, 1271, 1452, 2108, 2918; Data for the α-anomer (intermixed with **27**, *vide infra*): ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.35 – 7.20 (m, 10H, CH_{arom}), 5.03 (d, 1H, *J* = 4.6 Hz, H-1), 4.76 (d, 1H, *J* = 12.5 Hz, C*H*H Bn), 4.58 (d, 1H, *J* = 12.5 Hz, CH*H* Bn), 4.47 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.40 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.30 – 4.22 (m, 1H, H-4), 3.99 (dd, 1H, *J* = 7.2, 3.7 Hz, H-3), 3.49 (s, 3H, OMe), 3.45 (dd, 1H, *J* = 10.5, 3.7 Hz, H-5), 3.36 – 3.28 (m, 2H, H-2, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 137.8, 137.6 (C_q), 128.4, 128.4, 128.0, 128.0, 127.7 (CH_{arom}), 104.5 (C-1), 82.5 (C-4), 77.8 (C-3), 73.5, 72.9 (CH_2 Bn), 69.5 (C-5), 61.0 (C-2), 55.7 (OMe); Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.38 – 7.23 (m, 10H, CH_{arom}), 4.83 (s, 1H, H-1), 4.63 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.56 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.51 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.51 (d, 1H, *J* = 11.7 Hz, CH*H* Bn), 4.28 – 4.21 (m, 2H, H-3, H-4), 3.80 (d, 1H, *J* = 3.8 Hz, H-2), 3.59 – 3.54 (m, 1H, H-5), 3.52 – 3.47 (m, 1H, H-5), 3.29 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.1, 137.3 (C_q), 128.5, 128.4, 128.1, 127.9, 127.6 (CH_{arom}), 106.6 (C-1), 80.7 (C-4), 79.8 (C-3), 73.2, 73.0 (CH_2 Bn), 71.2 (C-5), 64.6 (C-2), 55.0 (OMe); HRMS: $[M-N_2+H]^+$ calcd for $C_{20}H_{24}NO_4$ 387.20268, found 387.20275.

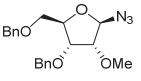


Methyl 2-azido-3,5-di-*O*-benzyl-2-deoxy-α-D-lyxofuranoside (24). Employing conditions **C** of the general experimental for inversion of furanosyl triflates, with additional 16 h stirring, gave **24** in 67% yield (3.36 mmol) from triflate **16α**, and side products **29α** (12%) and **30** (7%). Spectroscopic data were in accord with those previously reported.[58] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.34 – 7.27 (m, 10H, CH_{arom}), 4.95 (d, 1H, *J* = 2.1 Hz, H-1), 4.69 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.60 (d, 1H, *J* = 11.9 Hz, C*H*H Bn), 4.52 (d, 1H, *J* = 11.7 Hz, CH*H* Bn), 4.49 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.38 – 4.31 (m, 2H, H-3, H-4), 3.79 – 3.66 (m, 3H, H-2, H-5, H-5), 3.36 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.1, 137.4 (C_q), 128.5, 128.4, 128.0, 127.9, 127.8, 127.7 (CH_{arom}), 105.9 (C-1), 79.0 (C-3), 78.2 (C-4), 73.9, 73.6 (CH_2 Bn), 69.2 (C-5), 65.9 (C-2), 55.6 (OMe); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): $^2J_{C1,H2}$ = -3.2 Hz, $^2J_{C2,H1}$ = -0.1 Hz, $^3J_{C1,H3}$ = +2.3 Hz, $^3J_{C3,H1}$ = +2.4 Hz; HRMS: $[M+Na]^+$ calcd for $C_{20}H_{23}N_3O_4$ 392.15808, found 392.15787.

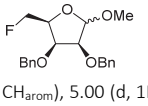


(2-Methyl-2-butyl) 3,5-di-*O*-benzyl-2-methyl-α/β-D-ribofuranoside (26). Formed as an 88:12 α:β anomeric mixture. Data for the isolated α-anomer: $[\alpha]_D^{20}$ = +86.3° (*c* = 0.35, $CHCl_3$).IR (thin film): 698, 739, 1026, 1042, 1109, 1211, 1454, 2928, 2970; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HH-NOESY, HSQC, HMBC): δ 7.37 – 7.20 (m, 10H, CH_{arom}), 5.34 (d, 1H, *J* = 4.1 Hz, H-1), 4.70 (d, 1H, *J* = 12.6

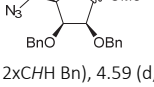
Hz, C*H*H Bn), 4.55 – 4.49 (m, 2H, C*H*H Bn, CH*H* Bn), 4.42 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.22 (q, 1H, *J* = 3.9 Hz, H-4), 3.91 (dd, 1H, *J* = 6.5, 4.5 Hz, H-3), 3.57 (dd, 1H, *J* = 6.5, 4.2 Hz, H-2), 3.50 – 3.44 (m, 4H, CH_3 OMe, H-5), 3.36 (dd, 1H, *J* = 10.6, 3.9 Hz, H-5), 1.60 (q, 2H, *J* = 7.5 Hz, CH_2CH_3 *t*-amyl), 1.26 (s, 3H, CH_3 *t*-amyl), 1.24 (s, 3H, CH_3 *t*-amyl), 0.93 (t, 3H, *J* = 7.5 Hz, CH_2CH_3 *t*-amyl); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 138.5, 138.2 (C_q), 128.3, 128.2, 128.0, 127.6, 127.5, 127.5 (CH_{arom}), 95.9 (C-1), 80.6, 80.5 (C-2, C-4), 77.0 (C_q t-amylOH)75.7 (C-3), 73.3, 72.2 (CH_2 Bn), 70.0 (C-5), 58.8 (OMe), 34.5 (CH_2 *t*-amyl), 26.1, 25.9 (C_qCH_3 *t*-amyl), 8.6 (CH_2CH_3 *t*-amyl); HRMS: $[M+Na]^+$ calcd for $C_{25}H_{34}O_5Na$ 437.22985, found 437.22953.



1-Azido 3,5-di-*O*-benzyl-1-deoxy-2-methyl-β-D-ribofuranoside (27). Intermixed with **24**. (*vide supra).* ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.34 – 7.20 (m, 10H, CH_{arom}), 5.32 (d, 1H, *J* = 1.9 Hz, H-1), 4.60 – 4.56 (m, 2H, 2xC*H*H Bn), 4.53 (d, 1H, *J* = 11.9 Hz, CH*H* Bn), 4.51 (d, 1H, *J* = 12.2 Hz, CH*H* Bn), 4.29 – 4.22 (m, 1H, H-4), 4.08 (dd, 1H, *J* = 6.9, 4.6 Hz, H-3), 3.64 (dd, 1H, *J* = 10.8, 3.3 Hz, H-5), 3.52 (dd, 1H, *J* = 10.9, 4.6 Hz, H-5), 3.50 – 3.47 (m, 1H, H-2), 3.40 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.1, 137.5 (C_q), 128.4, 128.4, 128.0, 127.9, 127.8, 127.6 (CH_{arom}), 92.2 (C-1), 82.5 (C-2), 81.3 (C-4), 77.1 (C-3), 73.4, 72.7 (CH_2 Bn), 69.8 (C-5), 58.3 (OMe); After hydrolysis of the mixture of **24** an **27**, **3,5-di-*O*-benzyl-2-*O*-methyl-α/β-D-ribofuranose** could be isolated as a α:β = 1:0.7 anomeric mixture. Spectroscopic data were in accord with those previously reported.[59] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.39 – 7.22 (m, 17H), 5.32 (dd, 1H, *J* = 11.2, 4.1 Hz, H-1α), 5.28 (d, 0.7H, *J* = 6.4 Hz, H-1β), 4.68 (d, 1H, *J* = 11.9 Hz, C*H*H Bnα), 4.63 (d, 0.7H, *J* = 12.0 Hz, C*H*H Bnβ), 4.61 (d, 1H, *J* = 11.9 Hz, CH*H* Bnα), 4.59 – 4.42 (m, 4.1H, CH_2 Bnα,β, CH*H* Bnβ), 4.35 (td, 1H, *J* = 4.2, 2.4 Hz, H-4α), 4.27 – 4.17 (m, 1.4H, H-3β, H-4β), 4.12 (d, 1H, *J* = 11.2 Hz, 1-OHα), 4.01 (dd, 1H, *J* = 5.0, 2.4 Hz, H-3α), 3.78 (dd, 1H, *J* = 4.9, 4.3 Hz, H-2α), 3.67 – 3.59 (m, 2.1H, H-2β, H-5β, 1-OHβ), 3.52 – 3.43 (m, 7.8H, CH_3 OMeα,β, H-5β, 2xH-5α); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 137.9, 137.8, 137.5, 137.4 (C_q), 128.6, 128.6, 128.5, 128.5, 128.1, 128.0, 128.0, 127.9, 127.8, 127.7 (CH_{arom}), 99.7 (C-1β), 96.1 (C-1α), 83.4 (C-2β), 81.0 (C-4α), 80.7 (C-3β), 80.2 (C-2β), 77.4 (C-3α), 77.2 (C-4β), 73.6, 73.5, 72.8, 72.7 (CH_2 Bn), 70.0 (C-5α), 69.6 (C-5β), 58.6, 58.4 (OMe); HRMS: $[M+Na]^+$ calcd for $C_{20}H_{24}O_5Na$ 367.15160, found 367.15164.

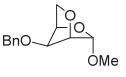


Methyl 2,5-di-*O*-benzyl-5-deoxy-5-fluoro-α/β-D-lyxofuranoside (28). Data for the α-anomer: m.p. 62-64 °C. $[\alpha]_D^{20}$ = +16.6° (*c* = 0.62, $CHCl_3$); IR (thin film): 698, 737, 1009, 1026, 1069, 1107, 1150, 1454, 2922, 3032; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HH-NOESY, HSQC): δ 7.36 – 7.28 (m, 10H, CH_{arom}), 5.00 (d, 1H, *J* = 1.6 Hz, H-1), 4.74 – 4.62 (m, 4H, 2xC*H*H Bn, H-5, H-5), 4.60 (d, 1H, *J* = 11.9 Hz, CH*H* Bn), 4.50 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.44 (dtd, 1H, *J* = 15.6, 6.8, 4.4 Hz, H-4), 4.30 (dd, 1H, *J* = 6.6, 4.6 Hz, H-3), 3.88 (dt, 1H, *J* = 4.6, 1.6 Hz, H-2), 3.36 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 137.8, 137.7 (C_q), 128.5, 128.5, 128.0, 127.9, 127.8, 127.8 (CH_{arom}), 106.2 (C-1), 84.0 (d, *J* = 164.8 Hz, C-5), 81.1 (C-2), 77.8 (d, *J* = 7.1 Hz, C-3), 77.3 (d, *J* = 20.2 Hz, C-4), 73.2, 72.7 (CH_2 Bn), 55.5 (OMe); ^{19}F NMR ($CDCl_3$, 471 MHz): δ -228.75 (td, *J* = 47.6, 15.7 Hz); ^{13}C HSQC-HECADE NMR: $^2J_{C1,H2}$ = -0.8 Hz, $^2J_{C2,H1}$ = -0.8 Hz; HRMS: $[M+NH_4]^+$ calcd for $C_{20}H_{27}NFO_4$ 364.19186, found 364.19199. Data for the β-anomer: $[\alpha]_D^{20}$ = -100.5° (*c* = 0.95, $CHCl_3$); IR (thin film): 698, 737, 1003, 1066, 1109, 1163, 1348, 1454, 2910, 2924; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HH-NOESY, HSQC): δ 7.37 – 7.27 (m, 10H, CH_{arom}), 4.84 (dd, 1H, *J* = 4.5, 1.2 Hz, H-1), 4.82 (d, 1H, *J* = 12.5 Hz, C*H*H Bn), 4.70 – 4.64 (m, 2H, C*H*H Bn, H-5), 4.63 – 4.59 (m, 2H, 2xCH*H* Bn), 4.59 – 4.52 (m, 1H, H-5), 4.28 (dddd, 1H, *J* = 14.4, 7.0, 6.0, 5.1 Hz, H-4), 4.11 (t, 1H, *J* = 6.0 Hz, H-3), 3.80 (dd, 1H, *J* = 5.9, 4.5 Hz, H-2), 3.46 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 138.2, 137.7 (C_q), 128.6, 128.5, 128.3, 128.1, 128.0, 127.9 (CH_{arom}), 101.7 (C-1), 83.8 (d, *J* = 165.6 Hz, C-5), 79.1 (d, *J* = 0.9 Hz, C-2), 78.5 (d, *J* = 21.4 Hz, C-4), 74.7 (d, *J* = 6.0 Hz, C-3), 73.9, 72.7 (CH_2 Bn), 55.8 (OMe); ^{19}F NMR ($CDCl_3$, 471 MHz): δ -227.76 (td, *J* = 47.5, 14.4 Hz); HRMS: $[M+NH_4]^+$ calcd for $C_{20}H_{27}NFO_4$ 364.19186, found 364.19178.

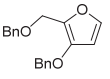


Methyl 5-azido-2,5-di-*O*-benzyl-5-deoxy-α/β-D-lyxofuranoside (29). Data for the α-anomer: IR (thin film):695, 734, 923, 1047, 1101, 1145, 1270, 1454, 2095; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 7.38 – 7.24 (m, 10H, CH_{arom}), 4.98 (d, 1H, *J* = 1.6 Hz, H-1), 4.71 – 4.63 (m, 2H, 2xC*H*H Bn), 4.59 (d, 1H, *J* = 11.9 Hz, CH*H* Bn), 4.47 (d, 1H, *J* = 11.7 Hz, CH*H* Bn), 4.29 – 4.19 (m, 2H, H-3, H-4), 3.88 (dd, 1H, *J* = 4.3, 1.7 Hz, H-2), 3.62 (dd, 1H, *J* = 12.8, 7.6 Hz, H-5), 3.45 (dd, 1H, *J* = 12.9, 3.8 Hz, H-5), 3.34 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 137.8 (C_q), 128.5, 128.0, 127.9, 127.9, 127.8 (CH_{arom}), 106.1 (C-1), 81.5 (C-2), 77.9, 77.8 (C-3, C-4), 73.2, 72.8 (CH_2 Bn), 55.5 (OMe), 52.1 (C-5); ^{13}C HSQC-HECADE NMR: $^2J_{C1,H2}$ = -0.9 Hz, $^2J_{C2,H1}$ = -1.0 Hz, $^2J_{C3,H2}$ = +0.7 Hz; HRMS: $[M+NH_4]^+$ calcd for $C_{20}H_{27}N_4O_4$ 387.20268, found 387.20275. Data for the β-anomer: $[\alpha]_D^{20}$ = -58.5° (*c* = 0.48, $CHCl_3$); IR (thin film): 698, 737, 999, 1053, 1105, 1157, 1454, 2096, 2874, 2914, 3030; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.41 – 7.27 (m, 10H, CH_{arom}), 4.89 – 4.83 (m, 2H, C*H*H Bn, H-1), 4.72 (d, 1H, *J* = 12.2 Hz, C*H*H Bn), 4.62 (d, 1H, *J* = 12.2 Hz, CH*H* Bn), 4.58 (d, 1H, *J* = 12.3 Hz, CH*H* Bn), 4.13 (ddd, 1H, *J* = 8.7, 5.9, 4.3 Hz, H-4), 4.05 (t, 1H, *J* = 5.9 Hz, H-3), 3.83 (dd, 1H, *J* = 5.8, 4.5 Hz, H-2), 3.66 (dd, 1H, *J* = 13.0, 8.7 Hz, H-5), 3.47 (s,

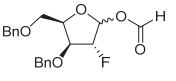
3H, CH_3 OMe), 3.29 (dd, 1H, *J* = 13.0, 4.3 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.1, 137.7 (C_q), 128.6, 128.5, 128.3, 128.1, 128.0, 127.9 (CH_{arom}), 102.0 (C-1), 79.3 (C-4), 79.0 (C-2), 75.0 (C-3), 73.8, 72.8 (CH_2 Bn), 55.9 (OMe), 52.8 (C-5); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): $^2J_{C1,H2}$ = +1.0 Hz, $^2J_{C2,H1}$ = +2.5 Hz; HRMS: $[M+NH_4]^+$ calcd for $C_{20}H_{27}N_4O_4$ 387.20268, found 387.20272.



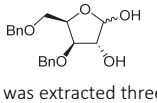
Methyl 2,5-anhydro-3-*O*-benzyl-α-D-lyxofuranoside (30). $[\alpha]_D^{20}$ = +88.3° (*c* = 0.41, $CHCl_3$); IR (thin film): 698, 741, 880, 989, 1028, 1051, 1107, 11998, 1454, 2882, 2940; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.38 – 7.28 (m, 5H, CH_{arom}), 4.74 (s, 1H, H-1), 4.66 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.55 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.25 (d, 1H, *J* = 2.7 Hz, H-4), 4.23 (d, 1H, *J* = 2.6 Hz, H-3), 4.10 (s, 1H, H-2), 3.99 (d, 1H, *J* = 7.8 Hz, H-5), 3.70 (d, 1H, *J* = 7.8 Hz, H-5), 3.36 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 137.7 (C_q), 128.6, 128.1, 127.9 (CH_{arom}), 106.2 (C-1), 78.6 (C-3), 76.7 (C-2), 75.0 (C-4), 72.5, 70.9 (CH_2 Bn), 55.5 (OMe); HRMS: $[M+NH_4]^+$ calcd for $C_{13}H_{20}NO_4$ 254.13868, found 254.13878.



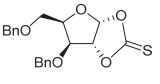
3-benzyloxy-2-(benzyloxy)methyl-furan (31). Spectroscopic data were in accord with those previously reported.[57] ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.36 – 7.21 (m, 10H), 7.20 (d, 1H, *J* = 2.1 Hz), 6.25 (d, 1H, *J* = 2.1 Hz), 4.95 (s, 2H), 4.47 (s, 2H), 4.46 (s, 2H).



Formyl 3,5-di-*O*-benzyl-2-deoxy-2-fluoro-α/β-D-xylofuranoside (32). Data for the α-anomer: IR (thin film):698, 737, 1026, 1088, 1271, 1454, 1732, 2868, 2926; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 8.09 (d, 1H, *J* = 0.5 Hz, *H*C=O), 7.37 – 7.26 (m, 10H, CH_{arom}), 6.45 (dd, 1H, *J* = 4.2, 1.9 Hz, H-1), 5.23 (dt, 1H, *J* = 52.7, 4.7 Hz, H-2), 4.73 (d, 1H, *J* = 11.9 Hz, C*H*H Bn), 4.59 – 4.54 (m, 3H, CH_2 Bn, CH*H* Bn), 4.53 – 4.50 (m, 1H, H-4), 4.39 (ddd, 1H, *J* = 15.9, 6.7, 5.0 Hz, H-3), 3.70 (ddd, 1H, *J* = 10.6, 4.1, 0.8 Hz, H-5), 3.64 (dd, 1H, *J* = 10.6, 5.1 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 159.5 (HC=O), 138.0, 137.2 (C_q), 128.7, 128.2, 127.8 (CH_{arom}), 93.7 (d, *J* = 199.3 Hz, C-1), 93.4 (d, *J* = 17.4 Hz, C-2), 79.4 (d, *J* = 22.4 Hz, C-3), 78.7 (d, *J* = 7.1 Hz, C-4), 73.7, 72.7 (CH_{arom}), 68.1 (C-5); ^{19}F NMR ($CDCl_3$, 471 MHz): -202.33 (dd, 0.3F *J* = 52.6, 15.9 Hz, F-2α); ^{13}C HSQC-HECADE NMR: $^2J_{C1,H2}$ = +2.8 Hz, $^2J_{C2,H1}$ = +3.3 Hz; Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 8.03 (dd, 1H, *J* = 2.2, 0.9 Hz, *H*C=O), 7.40 – 7.25 (m, 10H, CH_{arom}), 6.33 (d, 1H, *J* = 13.3 Hz, H-1), 5.07 (dd, 1H, *J* = 49.5, 1.4 Hz, H-2), 4.67 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.60 – 4.53 (m, 4H, CH*H* Bn, CH_2 Bn, H-4), 4.22 (ddd, 1H, *J* = 14.9, 5.6, 1.3 Hz, H-3), 3.80 (dd, 1H, *J* = 10.3, 5.4 Hz, H-5), 3.72 (dd, 1H, *J* = 10.3, 6.5 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 159.5 (HC=O), 138.0, 137.0 (C_q), 128.7, 128.5, 128.3, 127.9, 127.8 (CH_{arom}), 98.8 (d, *J* = 37.3 Hz, C-1), 96.8 (d, *J* = 184.2 Hz, C-2), 82.7 (C-4), 79.7 (d, *J* = 25.7 Hz, C-3), 73.6, 73.0 (CH_2 Bn), 68.4 (C-5); ^{19}F NMR ($CDCl_3$, 471 MHz): δ -193.49 – -193.70 (m, 1F, F-2β); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): $^2J_{C1,H2}$ = +0.3 Hz, $^2J_{C2,H1}$ = -1.7 Hz; HRMS: $[M+Na]^+$ calcd for $C_{20}H_{21}FO_5Na$ 383.1271, found 383.1276.

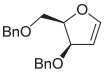


3,5-di-*O*-benzyl-α/β-D-xylofuranose (33). Xyloside **6** (7.6 g, 22 mmol) was dissolved in 20 mL THF and 40 mL H_2O and cooled to 0°C, followed by the slow addition of 100 mL TFA. After stirring overnight, the reaction mixture was partitioned between DCM and H_2O, and the aqueous layer was extracted three times with DCM. The combined DCM layers were washed with sat. aq. $NaHCO_3$ and brine, dried with $MgSO_4$, filtered and concentrated *in vacuo*. Flash column chromatography (9/1 to 1/1 pentane/EtOAc) afforded the title compound (6.1 g, 18.5 mmol, 84%) as a waxy material of a α:β = 70:30 anomeric composition. Spectroscopic data were in accord with those previously reported.[60] ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.34 – 7.23 (m, 10H, CH_{arom}), 5.44 (t, 0.7H, *J* = 4.8 Hz, H-1α), 5.11 (d, 0.3H, *J* = 10.9 Hz, H-1β), 4.87 (d, 0.7H, *J* = 5.5 Hz, 1-OHα), 4.66 – 4.53 (m, 2H, 2x*CH*H Bnα, 2x*CH*H Bnβ), 4.52 – 4.43 (m, 2.7H, 2xCH*H* Bnα, 2xCH*H* Bnβ, H-4α), 4.40 (q, 0.3H, *J* = 5.2 Hz, H-4β), 4.19 (t, 0.3H, *J* = 2.9 Hz, H-2β), 4.13 – 4.08 (m, 1H, H-2α, 1-OHβ), 3.98 – 3.93 (m, 1H, H-3α, H-3β), 3.77 – 3.70 (m, 0.6H, H-5β, H-5β), 3.66 – 3.64 (m, 1.4H, H-5α, H-5α), 3.30 (d, 0.7H, *J* = 5.8 Hz, 2-OHα), 3.14 (d, 0.3H, *J* = 4.3 Hz, 2-OHβ); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 137.9, 137.7, 137.4 (C_q), 128.6, 128.5, 128.5, 128.5, 128.1, 128.0, 128.0, 127.9, 127.8, 127.8, 127.8, 127.6 (CH_{arom}), 103.5 (C-1β), 96.1 (C-1α), 83.6 (C-3α), 82.9 (C-3β), 80.0 (C-4β), 79.2 (C-2β), 77.5 (C-4α), 75.6 (C-2α), 73.7 (CH_2 Bnα), 73.6 (CH_2 Bnβ), 72.7 (CH_2 Bnα), 72.0 (CH_2 Bnβ), 69.2 (C-5), 69.1 (C-5α); HRMS: $[M+Na]^+$ calcd for $C_{19}H_{22}O_5Na$ 353.13594, found 353.13594.

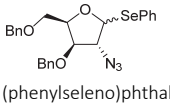


1,2-*O*-thiocarbonate-3,5-di-*O*-benzyl-α/β-D-xylofuranose (34). Diol **33** (1.65 g, 5 mmol, 1 eq.) was dissolved in 25 mL DCM and cooled to 0°C. DiPEA (7 ml, 40 mmol, 8 eq.) and DMAP (122 mg, 1 mmol, 0.2 eq.) were added, followed by the addition of thiophosgene (0.5 mL, 6.25 mmol, 1.25 eq., dissolved in 25 mL DCM). After 15 min the reaction was complete as concluded from TLC analysis. The reaction mixture was diluted with DCM and washed with 1 M aq. HCl, sat. aq. NH_4Cl, sat. aq. $NaHCO_3$, and brine. The organic layer was dried with Na_2SO_4, filtered and concentrated *in vacuo*. Flash column chromatography (19/1 to 8/2

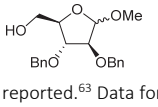
pentane/EtOAc) afforded the title compound (1.45 g, 3.9 mmol, 78%) as a light orange oil. Spectroscopic data were in accord with those previously reported.[61,62] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.38 – 7.25 (m, 10H, CH_{arom}), 6.40 (d, 1H, *J* = 4.7 Hz, H-1), 5.08 (d, 1H, *J* = 4.7 Hz, H-2), 4.65 (d, 1H, *J* = 11.9 Hz, C*H*H Bn), 4.60 (d, 1H, *J* = 11.9 Hz, C*H*H Bn), 4.56 (d, 1H, *J* = 11.9 Hz, CH*H* Bn), 4.52 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.35 (td, 1H, *J* = 5.8, 3.5 Hz, H-4), 4.20 (d, 1H, *J* = 3.5 Hz, H-3), 3.78 (d, 2H, *J* = 5.8 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 189.8 (C=S), 137.6, 136.3 (C_q), 128.9, 128.7, 128.6, 128.1, 128.1, 127.9 (CH_{arom}), 107.8 (C-1), 86.0 (C-2), 80.7 (C-4), 79.4 (C-3), 73.8, 73.0 (CH_2 Bn), 66.5 (C-5).



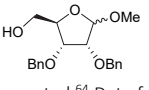
3-benzyloxy-2-(benzyloxy)methyl-2,3-dihydrofuran (35). Thionocarbonate **34** (330 mg, 0.89 mmol, 1 eq.) was dissolved in toluene (1.8 mL) and heated to 70°C. When the target temperature was reached 1,3-dimethyl-2-phenyl-1,3,2-diazaphospholidine (0.18 mL, 0.98 mmol, 1.1 eq.) was added, and the reaction was continued to stir for 20 min. The reaction mixture was concentrated in vacuo and flash column chromatography (1/0 to 85/15 pentane/Et_2O) afforded the title compound (191 mg, 0.68 mmol, 76%) as a colourless oil. Spectroscopic data were in accord with those previously reported.[36] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.38 – 7.23 (m, 10H, CHarom), 6.61 (d, 1H, *J* = 2.8 Hz, H-1), 5.24 (t, 1H, *J* = 2.6 Hz, H-2), 4.64 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.61 (ddd, 2H, *J* = 7.1, 2.5, 0.7 Hz, H-3), 4.55 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.50 – 4.44 (m, 2H, C*H*H Bn, H-4), 4.42 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 3.96 (dd, 1H, *J* = 10.6, 4.6 Hz, H-5), 3.85 (dd, 1H, *J* = 10.6, 7.7 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 150.6 (C-1), 138.5, 138.1 (C_q), 128.4, 128.4, 127.8, 127.7, 127.6, 127.5 (CH_{arom}), 101.4 (C-2), 83.3 (C-4), 79.5 (C-3), 73.6, 70.7 (CH_2 Bn), 67.8 (C-5).



Phenyl 2-azido-3,5-di-*O*-benzyl-2-deoxy-1-seleno-α/β-D-xylofuranoside (36). Glycal **35** (314 mg, 1.11 mmol, 1 eq.) was dissolved in DCM (5.5 mL) followed by the subsequent addition of $TMSN_3$ (295 µL, 2.22 mmol, 2 eq.), TBAF (1M solution in THF, 220 µL, 0.22 mmol, 0.2 eq.), and *N*-(phenylseleno)phthalimide (671 mg, 2.22 mmol, 2 eq.). The reaction was stirred overnight, diluted with DCM and washed with sat. aq. $NaHCO_3$ and brine. The organic layer was dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residu was purified by flash column chromatography (1/0 to 85/15 pentane/Et_2O) to give the still impure title compound (360 mg, 0.72 mmol, <65%) and was used direct in the subsequent hydrolysis (*vide infra*, **52**). The major product was confirmed as the trans-*xylo* isomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, NOESY, HSQC): δ 7.66 – 7.59 (m, 2H, CH_{arom}), 7.36 – 7.27 (m, 13H, CH_{arom}), 5.46 (d, 1H, *J* = 3.7 Hz, H-1), 4.66 (d, 1H, *J* = 11.8 Hz, C*H*H Bn), 4.62 – 4.53 (m, 3H, CH*H* Bn, CH_2 Bn), 4.34 (q, 1H, *J* = 5.4 Hz, H-4), 4.27 (t, 1H, *J* = 3.4 Hz, H-2), 4.01 (dd, 1H, *J* = 5.4, 3.2 Hz, H-3), 3.78 (dd, 1H, *J* = 10.2, 5.2 Hz, H-5), 3.73 (dd, 1H, *J* = 10.2, 6.0 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.1, 137.1 (C_q), 134.3 (CH_{arom}), 130.0 (C_q), 129.2, 128.7, 128.6, 128.4, 128.1, 127.9, 127.9, 127.8, 127.8, 127.7 (CH_{arom}), 85.7 (C-1), 81.6 (C-3), 81.1 (C-4), 73.6, 72.7 (CH_2 Bn), 70.1 (C-2), 68.6 (C-5); ^{13}C HSQC-HECADE NMR: $^2J_{C1,H2}$ = -1.1 Hz, $^2J_{C2,H1}$ = -3.1 Hz, $^2J_{C2,H1}$ = -4.0 Hz. And minor products are identified as cis-xylo (^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): $^2J_{C1,H2}$ = +0.9 Hz, $^2J_{C2,H1}$ = +1.3 Hz), and trans-lyxo (^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz):$^2J_{C1,H2}$ = -0.7 Hz, $^2J_{C2,H1}$ = -3.0 Hz).

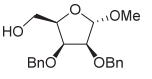


Methyl 2,3-di-*O*-benzyl-α/β-D-arabinofuranoside (37). The title compound was prepared by the general procedure for the synthesis of primary furanoside alcohols from D-arabinose (200 mmol) in 41% as a yellow oil (28.2 g, 82 mmol). Spectroscopic data were in accord with those previously reported.[63] Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.39 – 7.26 (m, 10H, CH_{arom}), 4.94 (s, 1H, H-1), 4.69 – 4.41 (m, 4H, CH_2Bn), 4.19 – 4.11 (m, 1H, H-3), 4.03 – 3.93 (m, 2H, H-2, H-4), 3.83 (ddd, 1H, *J* = 12.1, 4.2, 2.8 Hz, H-5), 3.64 (ddd, 1H, *J* = 12.0, 7.9, 4.1 Hz, H-5), 3.38 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 137.8, 137.4 (C_q), 128.6, 128.6, 128.1, 128.1, 128.0, 128.0 (CH_{arom}), 107.6 (C-1), 87.8 (C-2), 82.6 (C-4), 82.5 (C-3), 72.5, 72.0 (CH_2Bn), 62.4 (C-5), 55.1 (OMe); Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.42 – 7.27 (m, 10H, CH_{arom}), 4.73 – 4.56 (m, 5H, H-1, 2xCH_2Bn), 4.27 (dd, 1H, *J* = 6.9, 6.1 Hz, H-3), 4.07 (m, 2H, *J* = 9.4, 6.4, 3.8 Hz, H-2, H-3), 3.69 (d, 1H, *J* = 11.8 Hz, H-5), 3.57 (dt, 1H, *J* = 11.6, 5.6 Hz, H-5), 3.40 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.0, 137.6 (C_q), 128.6, 128.6, 128.3, 128.2, 128.0, 127.9 (CH_{arom}), 101.9 (C-1), 84.4 (C-2), 82.4 (C-4), 81.1 (C-3), 72.8, 72.7 (CH_2 Bn), 64.1 (C-5), 55.9 (OMe); HRMS: $[M+NH_4]^+$ calcd for $C_{20}H_{28}NO_5$ 362.19620, found 362.19611.

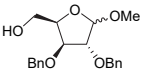


Methyl 2,3-di-*O*-benzyl-α/β-D-ribofuranoside (38). The title compound was prepared by the general procedure for the synthesis of primary furanoside alcohols from D-ribose (100 mmol) in 43% as a yellow oil (14.8 g, 43 mmol). Spectroscopic data were in accord with those previously reported.[64] Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.40 – 7.27 (m, 10H, CH_{arom}), 4.87 (d, 1H, *J* = 4.3 Hz, H-1), 4.74 (d, *J* = 12.7 Hz, C*H*H Bn), 4.65 (d, *J* = 12.3 Hz, C*H*H Bn), 4.61 (d, *J* = 12.3 Hz, CH*H* Bn), 4.58

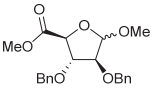
(d, *J* = 12.7 Hz, CH*H* Bn), 4.17 (q, 1H, *J* = 3.5 Hz, H-3), 3.84 (dd, 1H, *J* = 6.9, 3.6 Hz, H-4), 3.73 (dd, 1H, *J* = 6.9, 4.3 Hz, H-2), 3.66 (dd, 1H, *J* = 12.0, 3.2 Hz, H-5), 3.46 (s, 3H, CH_3OMe), 3.44 – 3.37 (m, 1H, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.3, 137.9 (C_q), 128.5, 128.5, 128.3, 128.1, 128. 0, 127.9 (CH_{arom}), 102.8 (C-1), 83.2 (C-3), 78.3 (C-2), 74.8 (C-4), 72.8, 72.7 (CH_2Bn), 62.9 (C-5), 55.7 (OMe); Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.44 – 7.25 (m, 10H, CH_{arom}), 4.89 (s, 1H, H-1), 4.65 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.61 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.56 (d, 1H, *J* = 11.7 Hz, CH*H* Bn), 4.48 (d, 1H, *J* = 11.7 Hz, CH*H* Bn), 4.27 (dt, 1H, *J* = 6.8, 3.4 Hz, H-4), 4.11 (dd, 1H, *J* = 7.0, 4.7 Hz, H-3), 3.86 (d, 1H, *J* = 4.7 Hz, H-2), 3.79 (dt, 1H, *J* = 12.0, 3.4 Hz, H-5), 3.56 (ddd, 1H, *J* = 12.1, 8.5, 3.8 Hz, H-5), 3.35 (s, 3H, CH_3 OMe), 2.06 (dd, 1H, *J* = 8.5, 4.1 Hz, OH); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 137.8, 137.7 (C_q), 128.5, 128.1, 128.0, 127.9 (CH_{arom}), 106.9 (C-1), 82.4 (C-4), 80.2 (C-2), 77.3 (C-3), 72.7, 72.5 (CH_2 Bn), 62.8 (C-5), 55.7 (OMe); HRMS: $[M+Na]^+$ calcd for $C_{20}H_{24}O_5Na$ 367.15160, found 367.15159.



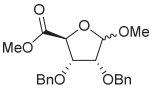
Methyl 2,3-di-*O*-benzyl-α-D-lyxofuranoside (39). The title compound was prepared by the general procedure for the synthesis of primary furanoside alcohols from D-lyxose (160 mmol) in 42% as a yellow oil (23.1 g, 67.2 mmol). Spectroscopic data were in accord with those previously reported.[65] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.39 – 7.26 (m, 10H, CH_{arom}), 5.00 (s, 1H, H-1), 4.72 (d, 1H, *J* = 11.8 Hz, C*H*H Bn), 4.64 (d, 1H, *J* = 11.8 Hz, C*H*H Bn), 4.59 (d, 1H, *J* = 11.9 Hz, CH*H* Bn), 4.46 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.36 (dd, 1H, *J* = 7.3, 4.9 Hz, H-3), 4.26 (dt, 1H, *J* = 7.5, 4.2 Hz, H-4), 3.88 (dd, 1H, *J* = 4.8, 0.8 Hz, H-2), 3.85 – 3.80 (m, 2H, H-5), 3.34 (s, 3H, CH_3 OMe), 2.68 (t, 1H, *J* = 6.1 Hz, OH); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 137.7, 137.4 (C_q), 128.6, 128.6, 128.1, 128.0, 128.0, 127.7 (CH_{arom}), 105.5 (C-1), 80.0 (C-2), 78.4 (C-4), 78.3 (C-3), 73.0, 72.8 (CH_2 Bn), 62.0 (C-5), 55.3 (OMe); HRMS: $[M+H]^+$ calcd for $C_{20}H_{25}O_5$ 345.16965, found 345.16967.



Methyl 2,3-di-*O*-benzyl-α/β-D-xylofuranoside (40). The title compound was prepared by the general procedure for the synthesis of primary furanoside alcohols from D-xylose (200 mmol) in 50% as a yellow oil (34.4 g, 100 mmol). Spectroscopic data were in accord with those previously reported.[66] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.40 – 7.25 (m, 18H, CH_{arom}), 4.90 (d, 1H, *J* = 1.9 Hz, H-1β), 4.80 (d, 0.8H, *J* = 4.2 Hz, H-1α), 4.73 (d, 0.8H, *J* = 11.8 Hz, C*H*H Bnα), 4.67 – 4.47 (m, 6.4H, CH*H* Bnα, CH_2 Bnα, 2xCH_2 Bnβ), 4.43 (dd, 0.8H, *J* = 7.8, 6.5 Hz, H-3α), 4.31 (dt, 1H, *J* = 6.8, 4.8 Hz, H-4β), 4.22 (dd, 0.8H, *J* = 7.7, 3.9 Hz, H-4α), 4.18 (dd, 1H, *J* = 6.8, 3.8 Hz, H-3β), 4.10 (dd, 1H, *J* = 3.9, 1.9 Hz, H-2β), 4.05 (dd, 0.8H, *J* = 6.5, 4.2 Hz, H-2α), 3.83 – 3.70 (m, 3.6H, 2xH-5α, 2xH-5β), 3.40 (s, 3H, CH_3 OMeβ), 3.38 (s, 2.4H, CH_3 OMeα), 2.58 (t, 1H, *J* = 6.6 Hz, 5-OHβ), 2.43 (dd, 0.8H, *J* = 8.7, 5.0 Hz, 5-OHα); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 137.6, 137.5 (C_q), 128.6, 128.6, 128.6, 128.3, 128.1, 128.1, 128.0, 127.9, 127.9, 127.8 (CH_{arom}), 108.0 (C-1β), 100.2 (C-1α), 87.2 (C-2β), 84.6 (C-2α), 82.9 (C-3β), 82.3 (C-3α), 80.6 (C-4β), 76.3 (C-4α), 72.8, 72.7, 72.5, 72.3 (CH_2 Bn), 62.3, 62.3 (C-5α,β), 55.7 (OMeβ), 55.2 (OMeα); HRMS: $[M+Na]^+$ calcd for $C_{20}H_{24}O_5Na$ 367.15160, found 367.15152.

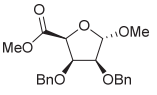


Methyl (methyl 2,3-di-*O*-benzyl-α/β-D-arabinofuranosyl uronate) (41). The title compound was generated from **37** (28.2 g, 78.8 mmol) by the general procedure for TEMPO/BAIB oxidation. Yield: 70% (20.6 g, 55.3 mmol) as a yellow oil. R*f*: 0.75 (7/3 pentane/EtOAc). IR (thin film): 698, 737, 1028, 1059, 1099, 1207, 1360, 1454, 1734, 1755, 2874, 2916, 2949, 3030. Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.44 – 7.21 (m, 10H, CH_{arom}), 5.09 (s, 1H, H-1), 4.63 (d, 1H, *J* = 4.8 Hz, H-4), 4.67 – 4.54 (m, 2H, CH_2 Bn), 4.47 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.41 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.15 (dd, 1H, *J* = 4.8, 1.8 Hz, H-3), 3.96 (dd, 1H, *J* = 1.8, 0.8 Hz, H-2), 3.73 (s, 3H, CH_3 CO_2Me), 3.41 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 170.6 (C=O), 137.2, 137.2 (C_q), 128.4, 128.2, 128.0, 127.9, 127.9, 127.9 (CH_{arom}), 108.0 (C-1), 86.5 (C-2), 84.9 (C-3), 80.9 (C-4), 72.1, 71.7 (CH_2 Bn), 55.5 (CH_3 OMe), 52.4 (CH_3 CO_2Me); Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.37 – 7.22 (m, 10H, CH_{arom}), 4.76 (d, 1H, *J* = 4.2 Hz, H-1), 4.73 (d, 1H, *J* = 11.8 Hz, C*H*H Bn), 4.67 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.64 – 4.58 (m, 2H, CH_2 Bn), 4.53 (dd, 1H, *J* = 6.6, 4.9 Hz, H-3), 4.42 (d, 1H, *J* = 4.9 Hz, H-4), 4.01 (dd, 1H, *J* = 6.6, 4.2 Hz, H-2), 3.73 (s, 3H, CH_3 CO_2Me), 3.42 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 171.5 (C=O), 137.7, 137.4 (C_q), 128.4, 128.4, 128.3, 128.1, 127.9, 127.7 (CH_{arom}), 102.3 (C-1), 83.8, 83.8 (C-2, C-3), 79.4 (C-4), 72.5, 72.5 (CH_2 Bn), 55.5 (CH_3 OMe), 52.2 (CH_3 CO_2Me); HRMS: $[M+NH_4]^+$ calcd for $C_{21}H_{28}NO_6$ 390.19111, found 390.19094.

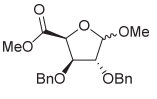


Methyl (methyl 2,3-di-*O*-benzyl-α/β-D-ribofuranosyl uronate) (42). The title compound was generated from **38** (13.3 g, 38.7 mmol) by the general procedure for TEMPO/BAIB oxidation. Yield: 87% (12.5 g, 33.7 mmol) as a yellow oil. R*f*: 0.73 (7/3 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[67] Data for the β-anomer: IR (thin film): 698, 739, 957, 1026, 1063, 1111, 1136, 1205, 1358, 1454, 1738, 1753, 2930, 3030; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HH-NOESY, HSQC): δ 7.38 – 7.26 (m, 10H, CH_{arom}), 4.97 (s, 1H, H-1), 4.68 – 4.62 (m, 3H, CH_2 Bn, H-4), 4.61 (d, 1H, *J* = 12.0

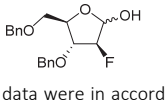
Hz, C*H*H Bn), 4.57 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.35 (dd, 1H, *J* = 6.4, 4.7 Hz, H-3), 3.85 (d, 1H, *J* = 4.6 Hz, H-2), 3.74 (s, 3H, CH_3CO_2Me), 3.38 (s, 3H, CH_3OMe); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 172.0 (C=O), 137.6, 137.5 (C_q), 128.5, 128.4, 128.0, 127.9, 127.9 (CH_{arom}), 107.1 (C-1), 80.6 (C-3), 79.8 (C-2), 79.6 (C-4), 72.8, 72.7 (CH_2 Bn), 55.3 (CH_3OMe), 52.3 (CH_3CO_2Me); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): $^2J_{C1,H2}$: +0.3 Hz, $^2J_{C2,H1}$: -0.6 Hz; HRMS: $[M+NH_4]^+$ calcd for $C_{21}H_{28}NO_6$ 390.19111, found 390.19105.



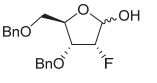
Methyl (methyl 2,3-di-*O*-benzyl-α-D-lyxofuranosyl uronate) (43). The title compound was generated from **39** (9.91 g, 28.8 mmol) by the general procedure for TEMPO/BAIB oxidation. Yield: 89% (9.5 g, 25.5 mmol) as a white solid. R*f*: 0.70 (7/3 pentane/EtOAc). m.p. 76-80 °C. $[\alpha]_D^{20}$ = +29.7° (*c* = 0.92, $CHCl_3$); IR (thin film): 698, 739, 1028, 1065, 1145, 1211, 1454, 1734, 1767, 2949; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.38 – 7.23 (m, 10H, CH_{arom}), 5.23 (d, 1H, *J* = 3.6 Hz, H-1), 4.76 (d, 1H, *J* = 11.8 Hz, C*H*H Bn), 4.72 (d, 1H, *J* = 4.7 Hz, H-4), 4.69 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.63 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.59 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.35 (t, 1H, *J* = 4.7 Hz, H-3), 3.93 (dd, 1H, *J* = 4.6, 3.6 Hz, H-2), 3.72 (s, 3H, CH_3CO_2Me), 3.43 (s, 3H, CH_3OMe); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 169.1 (C=O), 138.0, 137.8 (C_q), 128.5, 128.4, 127.9, 127.9, 127.8, 127.8 (CH_{arom}), 108.0 (C-1), 83.3 (C-2), 79.0 (C-3), 78.5 (C-4), 73.9, 72.8 (CH_2 Bn), 56.5 (CH_3OMe), 52.3 (CH_3CO_2Me); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): $^2J_{C1,H2}$ = -2.8 Hz, $^2J_{C2,H1}$ = -1.6 Hz; HRMS: $[M+H]^+$ calcd for $C_{21}H_{25}O_6$ 373.16456, found 373.16471.



Methyl (methyl 2,3-di-*O*-benzyl-α/β-D-xylofuranosyl uronate) (44). The title compound was generated from **40** (34.4 g, 100 mmol) by the general procedure for TEMPO/BAIB oxidation. Yield: 88% (30.8 g, 88.2 mmol) as a yellow oil. R*f*: 0.65 (7/3 pentane/EtOAc). IR (thin film): 698, 739, 1063, 1119, 1207, 1454, 1738, 1765, 2916, 2949, 3030. Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.39 – 7.21 (m, 10H, CH_{arom}), 4.94 (d, 1H, *J* = 4.3 Hz, H-1), 4.79 (d, 1H, *J* = 7.4 Hz, H-4), 4.64 – 4.57 (m, 4H, 2xCH_2 Bn), 4.47 (dd, 1H, *J* = 7.4, 6.2 Hz, H-3), 4.11 (dd, 1H, *J* = 6.2, 4.3 Hz, H-2), 3.73 (s, 3H, CH_3CO_2Me), 3.40 (s, 3H, CH_3OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 169.7 (C=O), 137.6, 137.4 (C_q), 128.5, 128.4, 128.2, 128.1, 127.7, 127.5 (CH_{arom}), 101.6 (C-1), 82.5 (C-2), 81.8 (C-3), 76.5 (C-4), 73.0, 72.9 (CH_2 Bn), 55.7 (OMe), 52.2 (CO_2Me); Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.40 – 7.23 (m, 10H, CH_{arom}), 5.04 (s, 1H, H-1), 4.90 (d, 1H, *J* = 6.2 Hz, H-4), 4.61 – 4.56 (m, 1H, C*H*H Bn) 4.53 (d, 1H, *J* = 12.5 Hz, C*H*H Bn), 4.43 (d, 1H, *J* = 11.9 Hz, C*H*H Bn), 4.39 (d, 1H, *J* = 11.9 Hz, CH*H* Bn), 4.23 (dd, 1H, *J* = 6.2, 1.4 Hz, H-2), 3.98 – 3.97 (m, 1H, H-2), 3.77 (s, 3H, CH_3CO_2Me), 3.53 (s, 3H, CH_3OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 169.7 (C=O), 137.2, 137.2 (C_q), 128.5, 128.5, 128.1, 128.0, 127.7, 127.5 (CH_{arom}), 108.8 (C-1), 85.1 (C-2), 81.2 (C-3), 81.1 (C-4), 72.7, 71.9 (CH_2 Bn), 56.0 (OMe), 52.1 (CO_2Me); HRMS: $[M+H]^+$ calcd for $C_{21}H_{25}O_6$ 373.16456, found 373.16448.

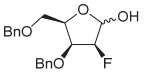


3,5-di-*O*-benzyl-2-deoxy-2-fluoro-α/β-D-arabinofuranose (45). The title compound was generated from **18** (470 mg, 1.36 mmol) by the general procedure for methyl furanoside hydrolysis, conditions A (65°C, 64 h). Yield: 63% α:β = 70:30 (0.85 mmol) as a colourless oil**.** Spectroscopic data were in accord with those previously reported.[24] Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.37 – 7.23 (m, 10H, CH_{arom}), 5.45 (dd, 1H, *J* = 10.7, 2.9 Hz, H-1), 4.93 (d, 1H, *J* = 50.2 Hz, H-2), 4.62 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.57 – 4.47 (m, 3H, CH_2 Bn, CH*H* Bn), 4.43 (q, 1H, *J* = 5.2 Hz, H-4), 3.98 (dd, 1H, *J* = 21.0, 4.8 Hz, H-3), 3.76 (d, 1H, *J* = 4.1 Hz, OH), 3.58 – 3.54 (m, 1H, H-5), 3.51 (dd, 1H, *J* = 10.3, 5.1 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 137.9, 137.0 (C_q), 128.6, 128.4, 128.1, 128.0, 127.8, 127.8 (CH_{arom}), 100.4 (d, *J* = 34.5 Hz, C-2), 98.4 (d, *J* = 182.7 Hz, C-1), 82.6 (d, *J* = 25.6 Hz, C-3), 81.9 (d, *J* = 2.0 Hz, C-4), 73.5, 72.4 (CH_2 Bn), 69.7 (C-5); ^{19}F NMR ($CDCl_3$, 471 MHz): δ -189.12 (ddd, *J* = 50.7, 21.0, 10.8 Hz); ^{13}C HSQC-HECADE NMR: $^2J_{C1\text{-}H2}$ = +1.8 Hz, $^2J_{C2\text{-}H1}$ = +3.9 Hz; Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.36 – 7.23 (m, 10H, CH_{arom}), 5.32 – 5.24 (m, 1H, H-1), 5.00 – 4.85 (m, 1H, H-2), 4.66 (d, 1H, *J* = 11.8 Hz, C*H*H Bn), 4.57 – 4.47 (m, 3H, CH*H* Bn, CH_2 Bn), 4.28 (dt, 1H, *J* = 17.8, 4.9 Hz, H-3), 4.22 (d, 1H, *J* = 9.5 Hz, OH), 4.09 (q, 1H, *J* = 3.8 Hz, H-4), 3.58 – 3.54 (m, 1H, H-5), 3.47 (dd, 1H, *J* = 10.3, 3.8 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 137.3, 137.1 (C_q), 128.6, 128.6, 128.1, 128.1, 128.0, 127.9 (CH_{arom}), 95.8 (d, *J* = 194.1 Hz, C-2), 95.4 (d, *J* = 18.8 Hz, C-1), 80.6 (d, *J* = 22.8 Hz, C-3), 80.1 (d, *J* = 8.2 Hz, C-4), 73.7, 72.2 (CH_2 Bn), 70.0 (C-5); ^{19}F NMR ($CDCl_3$, 471 MHz): δ -202.72 (dd, *J* = 52.7, 17.8 Hz); HRMS: $[M+Na]^+$ calcd for $C_{19}H_{21}FO_4Na$ 355.13161, found 355.13160.

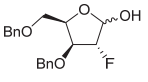


3,5-di-*O*-benzyl-2-deoxy-2-fluoro-α/β-D-ribofuranose (46). The title compound was generated from **19** (205 mg, 0.59 mmol) by the general procedure for methyl furanoside hydrolysis, conditions A (60°C, 18 h). Yield: 78% α:β = 25:75 (0.46 mmol). Spectroscopic data were in accord with those previously reported.[22] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.40 – 7.21 (m, 10H, CH_{arom}), 5.35 (dd, 0.75H, *J* = 8.5, 6.7 Hz, H-1β), 5.33 (dt, 0.25H, *J* = 11.7, 3.6 Hz, H-1α), 4.91 (dt, 0.25H, *J* = 51.8, 4.3 Hz, H-2α), 4.76 (dd,

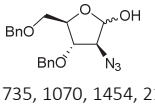
0.75H, *J* = 53.3, 3.4 Hz, H-2β), 4.72 (d, 0.25H, *J* = 11.8 Hz, C*H*H Bnα), 4.66 (d, 0.75H, *J* = 11.7 Hz, C*H*H Bnβ), 4.60 – 4.42 (m, 3H, CH*H* Bnα, CH*H* Bnβ, CH_2 Bnα, CH_2 Bnβ), 4.34 (qd, 0.25H, *J* = 3.4, 1.0 Hz, H-4α), 4.31 – 4.21 (m, 1.5H, H-3β, H-4β), 4.09 – 4.01 (m, 0.5H, H-3α, 1-OHα), 3.89 (dd, 0.75H, *J* = 6.7, 0.9 Hz, 1-OHβ), 3.66 (dd, 0.75H, *J* = 10.4, 2.4 Hz, H-5β), 3.54 (dd, 0.25H, *J* = 10.7, 3.3 Hz, H-5α), 3.51 – 3.45 (m, 1H, H-5α, H-5β); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 137.8, 137.3, 137.1 (C_q), 128.6, 128.6, 128.5, 128.2, 128.1, 128.1, 128.0, 127.9, 127.7 (CH_{arom}), 99.8 (d, *J* = 29.2 Hz, C-1β), 95.9 (d, *J* = 18.5 Hz, C-1α), 91.9 (d, *J* = 187.5 Hz, C-2β), 88.8 (d, *J* = 197.2 Hz, C-2α), 80.7 (d, *J* = 3.5 Hz, C-4α), 76.8 (C-4β), 76.8 (d, *J* = 14.7 Hz, C-3α), 76.5 (d, *J* = 15.5 Hz, C-3β), 73.6 (CH_2 Bnα), 73.6 (CH_2 Bnβ), 73.2 (d, *J* = 2.2 Hz, CH_2 Bnα), 72.8 (CH_2 Bnβ), 69.4 (C-5α), 69.1 (C-5β); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): α-anomer: $^2J_{C1\text{-}H2}$: +1.8 Hz, $^2J_{C2\text{-}H1}$: -+2.0 Hz, β-anomer: $^2J_{C2\text{-}H1}$: -0.3 Hz; HRMS: $[M+Na]^+$ calcd for $C_{19}H_{21}FO_4Na$ 355.13161, found 355.13147.



3,5-di-*O*-benzyl-2-deoxy-2-fluoro-α/β-D-lyxofuranose (47). The title compound was generated from **20** (340 mg, 0.98 mmol) by the general procedure for methyl furanoside hydrolysis, conditions A (65°C, 6 h). Yield: 75% α:β = 1:1 (0.73 mmol). IR (thin film): 696, 735, 1027, 1045, 1454, 2864, 2926, 3410; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.42 – 7.29 (m, 20H, CH_{arom}), 5.58 (dd, 1H, *J* = 9.8, 2.6 Hz, H-1α), 5.28 (dd, 1H, *J* = 12.5, 4.5 Hz, H-1β), 4.94 (dt, 1H, *J* = 50.3, 4.4 Hz, H-2α), 4.87 (d, 1H, *J* = 11.3 Hz, C*H*H Bn), 4.87 (ddd, 1H, *J* = 52.6, 4.1, 1.0 Hz, H-2β), 4.73 (d, 1H, *J* = 11.9 Hz, C*H*H Bn), 4.68 – 4.61 (m, 3H, CH*H* Bn 2xC*H*H Bn), 4.60 – 4.53 (m, 4H, 3xCH*H* Bn, H-4α), 4.40 (ddd, 1H, *J* = 20.3, 7.1, 4.1 Hz, H-3α), 4.25 (td, 1H, *J* = 4.2, 1.8 Hz, H-3β), 4.23 – 4.18 (m, 1H, H-4β), 4.17 (dd, 1H, *J* = 12.6, 1.0 Hz, 1-OHβ), 3.85 (dd, 1H, *J* = 9.7, 6.6 Hz, H-5β), 3.79 (dd, 1H, *J* = 10.5, 3.6 Hz, H-5α), 3.76 – 3.67 (m, 2H, H-5α, H-5β), 3.43 (t, 1H, *J* = 2.9 Hz, 1-OHα); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.1, 137.8, 137.4, 137.0 (C_q), 128.7, 128.6, 128.6, 128.5, 128.4, 128.1, 128.1, 128.0, 127.9, 127.8, 127.7 (CH_{arom}), 99.0 (d, *J* = 30.5 Hz, C-1α), 95.1 (d, *J* = 19.2 Hz, C-1β), 92.9 (d, *J* = 187.9 Hz, C-2α), 89.5 (d, *J* = 202.2 Hz, C-2β), 77.7 (C-4α), 77.4 (d, *J* = 5.9 Hz, C-4β), 76.9 (d, *J* = 15.0 Hz, C-3α), 76.3 (d, *J* = 14.6 Hz, C-3β), 74.5 (d, *J* = 3.1 Hz, CH_2 Bn), 73.8, 73.6 (CH_2 Bn), 73.2 (d, *J* = 1.3 Hz, CH_2 Bn), 70.3 (d, *J* = 1.2 Hz, C-5α), 68.9 (C-5β); ^{19}F NMR ($CDCl_3$, 471 MHz): δ -207.67 (ddd, *J* = 52.6, 20.1, 9.3 Hz, C2-Fα), -214.36 (d, *J* = 50.4 Hz, C2-Fβ); HRMS: $[M+Na]^+$ calcd for $C_{19}H_{21}FO_4Na$ 355.13161, found 355.13164.

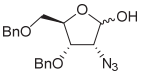


3,5-di-*O*-benzyl-2-deoxy-2-fluoro-α/β-D-xylofuranose (48). The title compound was generated from **21** (181 mg, 0.52 mmol) by the general procedure for methyl furanoside hydrolysis, conditions A (60°C, 6 h). Yield: 75% α:β = 30:70 (0.40 mmol) as a colourless oil**.** Spectroscopic data were in accord with those previously reported for the L-enantiomer.[68] IR (thin film): 696, 735, 1026, 1047, 1454, 2868, 2924, 3400; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.37 – 7.24 (m, 10H), 5.48 (td, 0.3H, *J* = 8.3, 3.7 Hz, H-1α), 5.29 (dd, 0.7H, *J* = 13.9, 11.6 Hz, H-1β), 4.95 (ddd, 0.7H, *J* = 52.2, 3.2, 0.8 Hz, H-2β), 4.90 (dt, 0.3H, *J* = 52.1, 3.4 Hz, H-2α), 4.68 (d, 0.7H, *J* = 11.7 Hz, C*H*H Bnβ), 4.65 (d, 0.3H, *J* = 11.9 Hz, C*H*H Bnα), 4.60 – 4.50 (m, 3H, CH*H* Bnα, CH*H* Bnβ, CH_2 Bnα, CH_2 Bnβ), 4.50 – 4.46 (m, 0.3H, H-4α), 4.39 (dt, 0.7H, *J* = 6.1, 4.2 Hz, H-4β), 4.27 (ddd, 0.3H, *J* = 13.2, 5.3, 3.1 Hz, H-3α), 4.23 (dddd, 0.7H, *J* = 17.8, 6.1, 3.0, 0.7 Hz, H-3β), 4.14 (d, 0.7H, *J* = 11.6 Hz, 1-OHβ), 3.73 (ddd, 0.7H, *J* = 10.1, 4.6, 1.2 Hz, H-5β), 3.71 – 3.67 (m, 1H, H-5α, H-5β), 3.64 (dd, 0.3H, *J* = 10.2, 5.9 Hz, H-5α), 3.57 (dd, 0.3H, *J* = 8.5, 3.2 Hz, 1-OHα); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 138.1, 137.4, 137.3, 137.0 (C_q), 128.7, 128.6, 128.6, 128.4, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7 (CH_{arom}), 101.0 (d, *J* = 34.4 Hz, C-1β), 99.1 (d, *J* = 185.0 Hz, C-2β), 95.6 (d, *J* = 17.1 Hz, C-1α), 93.8 (d, *J* = 191.1 Hz, C-2α), 80.9 (d, *J* = 24.6 Hz, C-3β), 80.3 (d, *J* = 24.1 Hz, C-3α), 80.0 (d, *J* = 3.4 Hz, C-4β), 77.2 (d, *J* = 4.1 Hz, C-4α), 73.9 (CH_2 Bnβ), 73.6 (CH_2 Bnα), 73.0 (CH_2 Bnβ), 72.7 (CH_2 Bnα), 68.4 (C-5α), 68.4 (C-5β); ^{19}F NMR ($CDCl_3$, 471 MHz): δ -189.88 (ddd, 0.7F, *J* = 52.2, 17.7, 14.1 Hz, F-2β), -204.74 (dt, 0.3F, *J* = 52.2, 9.7 Hz, F-2α); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): α-anomer: $^2J_{C1,H2}$ = +3.1 Hz, $^2J_{C2,H1}$ = +5.6 Hz, β-anomer: $^2J_{C2,H1}$ = -2.3 Hz; HRMS: $[M+Na]^+$ calcd for $C_{19}H_{21}FO_4Na$ 355.1322, found 355.1326.

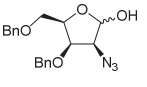


2-azido-3,5-di-*O*-benzyl-2-deoxy-α/β-D-arabinofuranose (49). The title compound was generated from **22** (554 mg, 1.50 mmol) by the general procedure for methyl furanoside hydrolysis, conditions A (60°C, 64 h). Yield: 76% α:β = 1:1 (1.1 mmol) as a colourless oil**.** IR (thin film): 696, 735, 1070, 1454, 2108, 3320; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.45 – 7.10 (m, 20H), 5.33 (d, 1H, *J* = 7.0 Hz, H-1α), 5.30 (dd, 1H, *J* = 9.1, 4.6 Hz, H-1β), 4.68 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.62 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.58 – 4.54 (m, 4H, 2x CH_2 Bn), 4.52 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.50 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.45 – 4.38 (m, 1H, H-4α), 4.24 (dd, 1H, *J* = 7.0, 5.2 Hz, H-3β), 4.16 (dt, 1H, *J* = 5.2, 3.0 Hz, H-4β), 3.98 – 3.94 (m, 2H, H-2α, OHβ), 3.91 (ddd, 1H, *J* = 4.3, 2.6, 0.6 Hz, H-3α), 3.80 (dd, 1H, *J* = 6.9, 4.5 Hz, H-2β), 3.59 (dd, 1H, *J* = 10.3, 3.2 Hz, H-5β), 3.60 – 3.50 (m, 2H, 2xH-5α), 3.41 (dd, 1H, *J* = 10.3, 3.0 Hz, H-5β), 3.30 (d, 1H, *J* = 6.9 Hz, OHα); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 137.9, 137.4, 136.9, 136.8 (C_q), 128.8, 128.7, 128.7, 128.6, 128.4, 128.3, 128.3, 128.1, 128.1, 128.1, 127.9 (CH_{arom}), 101.0 (C-1α), 97.4 (C-1β), 82.9 (C-3α), 82.2 (C-4α), 81.8 (C-4β), 80.3 (C-3β), 73.9, 73.6, 72.7, 72.6 (CH_2 Bn), 70.2 (C-2α),

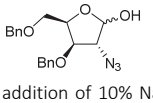
69.9 (C-5β), 69.6 (C-5α), 68.7 (C-2β); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): α-anomer: $^2J_{C1\text{-}H2}$ = -2.2 Hz, $^2J_{C2\text{-}H1}$ = -0.1 Hz. β-anomer: $^2J_{C1\text{-}H2}$ = -2.1 Hz, $^2J_{C2\text{-}H1}$ = +2.2 Hz; HRMS: $[M+Na]^+$ calcd for $C_{19}H_{26}N_3O_4Na$ 378.14243, found 378.14248.



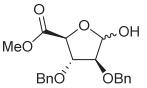
2-azido-3,5-di-*O*-benzyl-2-deoxy-α/β-D-ribofuranose (50). The title compound was generated from a 4:1 mixture of **23** and **27** by the general procedure for methyl furanoside hydrolysis, conditions A (65°C, 6 h). Combined yield: 89%, Yield of **42** was 70% over two steps (from **15**), α:β = 33:67 (0.29 mmol) as a colourless oil**.** IR (thin film): 696, 741, 1094, 1454, 2105, 2866, 3330; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.37 – 7.22 (m, 15H, CH_{arom}), 5.35 (bs, 0.5H, H-1α), 5.23 (s, 1H, H-1β), 4.68 – 4.58 (m, 2H, CH2 Bnα, C*H*H Bnβ), 4.53 (d, 1H, *J* = 11.8 Hz, C*H*H Bnβ), 4.49 – 4.35 (m, 4.5H, 2xCH*H* Bnβ, CH_2 Bnα, H-3β, H-4α), 4.21 (dt, 1H, *J* = 6.4, 3.1 Hz, H-4β), 4.13 (bs, 1H, 1-OHβ), 4.09 (dd, 0.5H, *J* = 5.4, 2.7 Hz, H-3α), 3.96 (bs, 0.5H, 1-$OH_α$), 3.78 (d, 1H, *J* = 5.1 Hz, H-2β), 3.66 (dd, 0.5H, *J* = 5.4, 4.4 Hz, H-2α), 3.62 (dd, 1H, *J* = 10.4, 2.9 Hz, H-5β), 3.49 – 3.40 (m, 1.5H, H-5β, 2xH-5α); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 137.6, 137.2, 137.0, 136.8 (C_q), 128.6, 128.6, 128.6, 128.5, 128.3, 128.2, 128.1, 128.0, 128.0, 127.9, 127.7 (CH_{arom}), 100.8 (C-1β), 97.6 (C-1α), 81.6 (C-4α), 80.9 (C-4β), 78.8 (C-3α), 78.4 (C-3β), 73.6, 73.6, 73.1, 73.0 (CH_2 Bn), 69.6 (C-5α), 69.3 (C-5β), 65.9 (C-2β), 62.1 (C-2α); HRMS: $[M+NH_4]^+$ calcd for $C_{19}H_{25}N_4O_4$ 373.18703, found 373.18699.



2-azido-3,5-di-*O*-benzyl-2-deoxy-α/β-D-lyxofuranose (51). The title compound was generated from **24** (620 mg, 1.68 mmol) by the general procedure for methyl furanoside hydrolysis, conditions A (60°C, 18 h). Yield: 62% α:β = 60:40 (1.04 mmol) as a colourless oil. IR (thin film): 696, 734, 1026, 1070, 1269, 1454, 2110, 2868, 2924, 3400; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.37 – 7.28 (m, 10H, CH_{arom}), 5.45 (t, 0.6H, *J* = 2.7 Hz, H-1α), 5.28 (dd, 0.4H, *J* = 12.2, 4.6 Hz, H-1β), 4.80 (d, 0.4H, *J* = 11.0 Hz, C*H*H Bnβ), 4.72 (d, 0.6H, *J* = 11.7 Hz, C*H*H Bnα), 4.65 (d, 0.4H, *J* = 11.0 Hz, CH*H* Bnβ), 4.62 – 4.47 (m, 3.2H, CH_2 Bnα, CH_2 Bnβ, CH*H* Bnα, H-4α), 4.41 (t, 0.6H, *J* = 5.5 Hz, H-3α), 4.22 (t, 0.4H, *J* = 4.0 Hz, H-3β), 4.17 (ddd, 0.4H, *J* = 7.2, 5.5, 3.8 Hz, H-4β), 3.84 – 3.76 (m, 1.4H, H-2α, H-5β, OHβ), 3.74 – 3.67 (m, 1.6H, H-5β, H-5α, H-5α), 3.63 (t, 0.4H, *J* = 4.4 Hz, H-2β), 3.06 (d, 0.6H, *J* = 3.1 Hz, $OH_α$); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 128.7, 128.6, 128.6, 128.5, 128.5, 128.4, 128.2, 128.1, 128.0, 128.0, 127.8 (CH_{arom}), 99.8 (C-1α), 97.3 (C-1β), 79.6 (C-4α), 79.0 (C-3), 78.5, 78.4 (C-3β, C-4β), 75.0, 74.0, 73.9, 73.7 (CH_2 Bn), 69.4 (C-5α), 68.8 (C-5β), 66.6 (C-2α), 63.0 (C-2β); HRMS: $[M+Na]^+$ calcd for $C_{19}H_{21}N_3O_4Na$ 378.14243, found 378.14233.

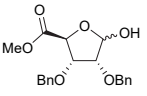


2-azido-3,5-di-*O*-benzyl-2-deoxy-α/β-D-xylofuranose (52). Selenoglycoside **36** (360 mg, 0.72 mmol, 1 eq.) was dissolved in THF/H_2O/acetone (3/2/3 v/v/v, 8 mL) and cooled to 0°C, followed by addition of NIS (180 mg, 0.8 mmol, 1.1 eq.). After 1 h the reaction mixture was quenched by addition of 10% $Na_2S_2O_3$, diluted with H_2O and extracted with DCM three times. The combined organic layer was washed with brine, dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by flash column chromatography (19/1 to 8/2 pentane/EtOAc) gave the title compound as a colourless oil (222 mg, 0.62 mmol, 87%). IR (thin film): 696, 737, 1053, 1255, 1454, 2102, 2866, 2924, 3390; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, NOESY, HSQC): δ 7.37 – 7.25 (m, 20H, CH_{arom}), 5.48 (dd, 1H, *J* = 5.4, 4.6 Hz, H-1α), 5.15 (dd, 1H, *J* = 11.4, 1.7 Hz, H-1β), 4.66 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.65 (d, 1H, *J* = 11.8 Hz, C*H*H Bn), 4.61 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.59 – 4.54 (m, 4H, C*H*H Bn, 3xCH*H* Bn), 4.52 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.47 (td, 1H, *J* = 6.1, 4.5 Hz, H-4α), 4.29 (dt, 1H, *J* = 5.6, 4.5 Hz, H-4β), 4.23 (dd, 1H, *J* = 5.9, 5.2 Hz, H-3α), 4.15 (d, 1H, *J* = 11.4 Hz, 1-OHβ), 4.03 (dd, 1H, *J* = 5.6, 3.7 Hz, H-3β), 3.99 (dd, 1H, *J* = 4.1, 1.7 Hz, H-2β), 3.89 – 3.85 (m, 1H, H-2α), 3.73 (dd, 1H, *J* = 10.1, 4.7 Hz, H-5β), 3.70 (dd, 1H, *J* = 10.1, 4.3 Hz, H-5β), 3.68 (dd, 1H, *J* = 10.3, 4.6 Hz, H-5α), 3.61 (dd, 1H, *J* = 10.3, 6.2 Hz, H-5α), 3.61 (d, 1H, *J* = 5.6 Hz, 1-$OH_α$); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 137.9, 137.3, 136.9 (C_q), 128.7, 128.6, 128.5, 128.4, 128.1, 128.1, 128.0, 128.0, 127.9, 127.9, 127.8 (CH_{arom}), 101.2 (C-1β), 96.2 (C-1α), 81.6 (C-3β), 80.8 (C-3α), 79.5 (C-4β), 77.1 (C-4α), 73.9, 73.6, 73.2, 73.0 (CH_2 Bn), 70.5 (C-2β), 68.8 (C-5α), 68.5 (C-5β), 66.9 (C-2α); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): α-anomer: $^2J_{C1,H2}$ = -0.5 Hz, $^2J_{C2,H1}$ = +3.9 Hz, β-anomer: $^2J_{C1,H2}$ = -2.4 Hz, $^2J_{C2,H1}$ = -0.2 Hz; As additional confirmation of the xylo-configuration: α -anomer: $^2J_{C2,H3}$ = -2.8 Hz, $^2J_{C3,H2}$ = -5.0 Hz, β -anomer: $^2J_{C2,H3}$ = -3.3 Hz, $^2J_{C3,H2}$ = -4.6 Hz). HRMS: $[M+Na]^+$ calcd for $C_{19}H_{21}N_3O_4Na$ 378.14243, found 378.14235.

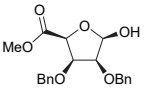


Methyl (2,3-di-*O*-benzyl-α/β-D-arabinofuranosyl uronate) (53). The title compound was generated from **41** (11.9 g, 32 mmol) by the general procedure for methyl furanoside hydrolysis, conditions B (8 h). Yield: 60% α:β = 2:1 (6.87 g, 19.2 mmol) as a yellow oil. *Rf*: 0.38 (7/3 pentane/EtOAc). IR (thin film): 698, 739, 1028, 1076, 1090, 1207, 1454, 1740. Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.40 – 7.22 (m, 10H, CH_{arom}), 5.51 (d, 1H, *J* = 10.2 Hz, H-1), 4.86 (d, 1H, *J* = 1.7 Hz, H-4),

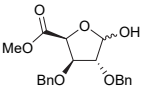
4.70 (d, 1H, *J* = 11.8 Hz, C*H*H Bn), 4.59 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.53 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.46 (d, 1H, *J* = 11.7 Hz, CH*H* Bn), 4.38 – 4.34 (m, 1H, H-3), 3.94 (d, 1H, *J* = 0.9 Hz, H-2), 3.69 (s, 3H, CH_3CO_2Me), 3.41 (d, 1H, *J* = 10.3 Hz, OH); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 170.5 (C=O), 137.1, 136.7 (C_q), 128.6, 128.5, 128.4, 128.0, 128.0, 127.7 (CH_{arom}), 102.1 (C-1), 84.6 (C-2), 84.1 (C-3), 81.1 (C-4), 72.3, 71.6 (CH_2 Bn), 52.4 (CH_3CO_2Me); Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.40 – 7.22 (m, 10H, CH_{arom}), 5.55 (dd, 1H, *J* = 10.0, 3.9 Hz, H-1), 4.66 (d, 1H, *J* = 11.9 Hz, C*H*H Bn), 4.57 – 4.54 (m, 1H, CH*H* Bn), 4.53 (d, 1H, *J* = 2.2 Hz, H-4), 4.38 – 4.34 (m, 1H, H-3), 3.91 (dd, 1H, *J* = 3.9, 2.7 Hz, H-2), 3.85 (d, 1H, *J* = 10.0 Hz, OH), 3.72 (s, 3H, CH_3CO_2Me); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 171.8 (C=O), 137.2, 136.9 (C_q), 128.5, 128.2, 128.2, 128.0, 127.9, 127.8 (CH_{arom}), 98.2 (C-1), 84.2 (C-3), 81.5 (C-2), 79.7 (C-4), 72.7, 72.1 (CH_2 Bn), 52.5 (CH_3CO_2Me); HRMS: $[M+NH_4]^+$ calcd for $C_{20}H_{26}NO_6$ 376.17546, found 376.17566.



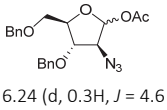
Methyl (2,3-di-*O*-benzyl-α/β-D-ribofuranosyl uronate) (54). The title compound was generated from **42** (8.33 g, 22.38 mmol) by the general procedure for methyl furanoside hydrolysis, conditions B (7.5 h). Yield: 73% α:β = 1.1:1 (5.87 g, 16.4) as a colourless oil. R*f*: 0.54 (7/3 pentane/EtOAc). IR (thin film): 698, 739, 1026, 1070, 1209, 1358, 1454, 1740, 2870, 2951, 3030, 3441; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.40 – 7.25 (m, 10H, CH_{arom}), 5.45 (dd, 1H, *J* = 11.1, 4.3 Hz, H-1), 4.82 – 4.44 (m, 5H, 2xCH_2Bn, H-4), 4.19 (d, 1H, *J* = 11.5 Hz, OH), 4.16 – 4.06 (m, 1H, H-3), 3.89 (d, 1H, *J* = 4.5 Hz, H-2), 3.71 (d, 3H, *J* = 4.2 Hz, CH_3CO_2Me); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 170.6 (C=O), 137.11, 136.74 (C_q), 128.5 – 127.9 (CH_{arom}), 96.8 (C-1), 80.2 (C-2), 79.1 (C-4), 77.5 (C-3), 72.5, 72.4 (CH_2Bn), 52.6 (CH_3CO_2Me); Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.40 – 7.25 (m, 10H, CH_{arom}), 5.55 (s, 1H, H-1), 5.07 – 4.88 (m, 1H, OH), 4.78, (d, *J* = 1.4 Hz, H-4), 4.82 – 4.44 (m, 4H, 2xCH_2Bn), 4.38 (dd, 1H, *J* = 6.5, 4.5 Hz, H-3), 3.93 (t, 1H, *J* = 4.6 Hz, H-2), 3.71 (d, 3H, *J* = 4.2 Hz, CH_3CO_2Me); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 173.3 (C=O), 137.6, 137.4 (C_q), 128.5 – 127.9 (CH_{arom}), 101.1 (C-1), 80.4 (C-3), 80.2 (C-2), 79.7 (C-4), 73.0, 72.7 (CH_2Bn), 52.6 (CH_3CO_2Me); HRMS: $[M+Na]^+$ calcd for $C_{20}H_{22}O_6Na$ 381.13086, found 381.13084.



Methyl (2,3-di-*O*-benzyl-β-D-lyxofuranosyl uronate) (55). The title compound was generated from **43** (1.0 g, 2.7 mmol) by the general procedure for methyl furanoside hydrolysis, conditions B (6 h). Yield: 85% β only (818 mg, 2.28 mmol) as a white solid. R*f*: 0.35 (1/1 pentane/EtOAc). IR (thin film): 698, 739, 1026, 1065, 1141, 1211, 1360, 1437, 1454, 1738, 1763, 2874, 2951, 3466. ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.43 – 7.22 (m, 10H, CH_{arom}), 5.40 (dd, 1H, *J* = 12.6, 4.3 Hz, H-1), 4.85 (d, 1H, *J* = 11.2 Hz, C*H*H Bn), 4.80 (d, 1H, *J* = 11.6 Hz, C*H*H Bn), 4.63 – 4.59 (m, 3H, 2xCH*H* Bn, H-4), 4.37 (t, 1H, *J* = 4.4 Hz, H-3), 4.33 (d, 1H, *J* = 12.6 Hz, OH), 3.91 (t, 1H, *J* = 4.2 Hz, H-2), 3.73 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 169.5 (C=O), 137.3, 137.2 (C_q), 128.7, 128.5, 128.2, 128.2, 128.1, 127.9 (CH_{arom}), 97.0 (C-1), 78.8 (C-4), 78.5, 78.4 (C-2, C-3), 74.8, 72.2 (CH_2 Bn), 52.4 (CH_3CO_2Me); HRMS: $[M+Na]^+$ calcd for $C_{20}H_{22}O_6Na$ 376.17546, found 376.17580.

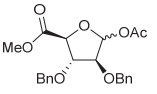


Methyl (2,3-di-*O*-benzyl-α/β-D-xylofuranosyl uronate) (56). The title compound was generated from **44** (17.7 g, 47.6 mmol) by the general procedure for methyl furanoside hydrolysis, conditions B (4 h). Yield: 90% α:β = 1:1.3 (15.3 mg, 42.7 mmol) as a light yellow oil. R*f*: 0.2 (8/2 pentane/EtOAc). IR (thin film): 698, 739, 1028, 1061, 1072, 1209, 1366, 1437, 1454, 1738, 1759, 2951, 3030, 3430; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.45 – 7.21 (m, 17.5H, CH_{arom}), 5.65 (dd, 0.75H, *J* = 10.1, 4.0 Hz, H-1α), 5.39 (d, 1H, *J* = 11.3 Hz, H-1β), 4.90 (d, 1H, *J* = 5.9 Hz, H-4β), 4.83 (d, 0.75H, *J* = 5.2 Hz, H-4α), 4.61 – 4.49 (m, 7H, CH_2 Bn), 4.28 (ddd, 1H, *J* = 5.9, 2.4, 0.8 Hz, H-3β), 4.25 (ddd, 1H, *J* = 5.2, 2.5, 0.4 Hz, H-3α), 4.00 (d, 1H, *J* = 11.6 Hz, 1-OHβ), 4.00 (dt, 1H, *J* = 2.4, 0.8 Hz, H-2β), 3.94 (dd, 0.75H, *J* = 3.9, 2.6 Hz, H-2α), 3.84 (d, 0.75H, *J* = 10.1 Hz, 1-OHα), 3.77 (s, 3H, CH_3CO_2Meβ), 3.74 (s, 2.25H, CH_3CO_2Meα); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 171.2, 169.7 (C=O), 137.1, 136.7 (C_q), 128.7, 128.6, 128.5, 128.5, 128.3, 128.1, 128.1, 127.9, 127.8 (CH_{arom}), 102.8 (C-1β), 97.4 (C-1α), 85.2 (C-2β), 82.1 (C-3β), 81.7 (C-3α), 80.8 (C-4β), 80.4 (C-2α), 77.9 (C-4α), 73.2, 73.0, 72.8, 72.1 (CH_2 Bn), 52.5 (CO_2Meβ), 52.1 (CO_2Meα); HRMS: $[M+NH_4]^+$ calcd for $C_{20}H_{26}NO_6$ 376.17546, found 376.17564.

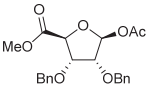


Acetyl 2-azido-3,5-di-*O*-benzyl-2-deoxy-α/β-D-arabinofuranoside (57). The title compound was generated from **49** (107 mg, 0.3 mmol) by the general procedure for acetyl donor synthesis. Yield: 90% α:β = 2.3:1 ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.41 – 7.22 (m, 10H, CH_{arom}), 6.24 (d, 0.3H, *J* = 4.6 Hz, H-1β), 6.11 (d, 0.7H, *J* = 1.0 Hz, H-1α), 4.71 – 4.47 (m, 4H, 4xCH_2 Bnα,β), 4.33 (dt, 0.7H, *J* = 5.8, 4.5 Hz, H-4α), 4.25 – 4.15 (m, 0.6H, H-3β, H-4β), 4.05 (dd, 0.7H, *J* = 3.1, 1.3 Hz, H-2α), 3.95 (ddd, 1H, *J* = 10.3, 6.8, 3.9 Hz, H-2β, H-3α), 3.63 – 3.55 (m, 1.4H, H-5α), 3.53 (dd, 0.6H, *J* = 4.7, 1.9 Hz, H-5β); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 169.8, 169.4 (C=O), 137.8, 137.7, 137.3, 137.1 (C_q), 128.5, 128.5, 128.4, 128.1, 128.1, 127.9, 127.8, 127.8, 127.7,

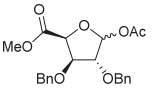
127.6 (CH_{arom}), 100.4 (C-1β), 95.2 (C-1α), 83.4 (C-4β), 83.0 (C-3β), 82.1 (C-4α), 80.4 (C-3α), 73.5, 73.3, 72.8, 72.6 (CH_2 Bn), 70.5 (C-2β), 70.3 (C-5α), 68.7 (C-5β), 66.4 (C-2α), 21.1, 21.0 (CH_3 OAc); HRMS: $[M+Na]^+$ calcd for $C_{19}H_{21}N_3O_4Na$ 378.1424, found 378.1425.



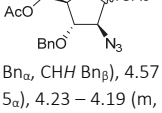
Methyl (acetyl 2,3-di-*O*-benzyl-α/β-D-arabinofuranosyl uronate) (58). The title compound was generated from **53** (5.20 g, 14.5 mmol) by the general procedure for acetyl donor synthesis. Yield: 91% α:β = 6.7:1 (5.29 g, 13.2 mmol) as a light yellow oil. R*f*: 0.80 (7/3 pentane/EtOAc). IR (thin film): 698, 1011, 1223, 1371, 1454, 1734, 1749, 2872, 2951, 3030. Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.39 – 7.26 (m, 8.5H, CH_{arom}), 6.36 (s, 0.85H, H-1), 4.76 (d, 0.85H, *J* = 3.9 Hz, H-4), 4.62 (d, 0.85H, *J* = 12.0 Hz, C*H*H Bn), 4.62 (d, 0.85H, *J* = 12.0 Hz, C*H*H Bn), 4.54 (d, 0.85H, *J* = 12.0 Hz, CH*H* Bn), 4.49 (d, 0.85H, *J* = 12.1 Hz, CH*H* Bn), 4.25 (ddd, 0.85H, *J* = 3.9, 1.4, 0.7 Hz, H-3), 4.04 (dd, 0.85H, *J* = 1.4, 0.5 Hz, H-2), 3.74 (s, 2.55H, CH_3 CO_2Me), 2.08 (s, 2.55H, CH_3 OAc); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 169.8, 169.7 (C=O), 137.2, 137.0 (C_q), 128.5, 128.1, 127.9, 127.9 (CH_{arom}), 100.7 (C-1), 85.3 (C-2), 85.0 (C-3), 82.8 (C-4), 72.2, 72.0 (CH_2 Bn), 52.6 (CH_3 CO_2Me), 21.2 (OAc); Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.37 – 7.26 (m, 1.5H, CH_{arom}), 6.24 (d, 0.15H, *J* = 4.3 Hz, H-1), 4.75 (d, 0.15H, *J* = 11.7 Hz, C*H*H Bn), 4.68 (d, 0.15, *J* = 11.8 Hz, CH*H* Bn), 4.57 – 4.46 (m, 0.6H, CH2 Bn, H-3, H-4), 4.18 (dd, 0.15H, *J* = 6.4, 4.2 Hz, H-2), 3.76 (s, 0.45H, CH_3 CO_2Me), 2.07 (s, 0.45H, CH_3 OAc); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 170.9, 170.0 (C=O), 137.5, 137.1 (C_q), 128.6, 128.5, 128.5, 128.2, 128.0, 128.0 (CH_{arom}), 94.5 (C-1), 83.4 (C-3), 83.2 (C-2), 80.4 (C-4), 73.1, 72.8 (CH_2 Bn), 52.6 (CO_2Me), 21.2 (OAc); HRMS: $[M+NH_4]^+$ calcd for $C_{22}H_{28}NO_7$ 418.18603, found 418.18598.



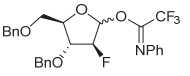
Methyl (acetyl 2,3-di-*O*-benzyl-β-D-ribofuranosyl uronate) (59). The title compound was generated from **54** (5.9 g, 16.4 mmol) by the general procedure for acetyl donor synthesis. Yield: 90% β only (5.9 g, 14.7 mmol) as a light yellow oil. R*f*: 0.67 (7/3 pentane/EtOAc). IR (thin film): 698, 738, 959, 1013, 1094, 1138, 1209, 1371, 1454, 1749, 2870, 2951; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.40 – 7.30 (m, 10H, CH_{arom}), 6.24 (s, 1H, H-1), 4.73 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.69 (d, 1H, *J* = 6.7 Hz, H-4), 4.64 (d, 1H, *J* = 12.2 Hz, CH*H* Bn), 4.60 (d, *J* = 12.0 Hz, C*H*H Bn), 4.57 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.32 (dd, 1H, *J* = 6.7, 4.7 Hz, H-3), 3.94 (d, 1H, *J* = 4.6 Hz, H-2), 3.76 (s, 3H, CH_3 CO_2Me), 2.05 (s, 3H, CH_3 OAc); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 171.3 (C=O CO_2Me), 169.7 (C=O OAc), 137.3, 137.2 (C_q), 128.6, 128.6, 128.2, 128.1, 127.9 (CH_{arom}), 99.4 (C-1), 80.4 (C-4), 79.7 (C-3), 79.0 (C-2), 72.8, 72.6 (CH_2 Bn), 52.7 (CH_3 CO_2Me), 21.3 (CH_3 OAc); HRMS: $[M+NH_4]^+$ calcd for $C_{22}H_{28}NO_7$ 418.18603, found 418.18605.



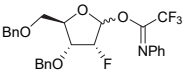
Methyl (acetyl 2,3-di-*O*-benzyl-α/β-D-xylofuranosyl uronate) (60). The title compound was generated from **56** (15.3 g, 42.7 mmol) by the general procedure for acetyl donor synthesis. Yield: 89% α:β = 1.3:1 (15.2 g, 38.1 mmol) as a light yellow oil. R*f*: 0.60 and 0.73 (8/2 pentane/EtOAc). IR (thin film): 698, 739, 1016, 1026, 1098, 1211, 1369, 1454, 1748, 2872, 2951, 3030. ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.39 – 7.21 (m, 17.5H), 6.42 (d, 1H, *J* = 4.4 Hz, H-1α), 6.24 (s, 0.75H, H-1β), 4.95 (d, 0.75H, *J* = 5.8 Hz, H-4β), 4.87 (d, 1H, *J* = 7.3 Hz, H-4α), 4.66 – 4.48 (m, 7H, 2xCH_2 Bnα, 2x CH_2 Bnβ), 4.47 – 4.43 (m, 1H, H-3α), 4.30 (dd, 1H, *J* = 6.6, 4.4 Hz, H-2α), 4.27 (ddd, 0.75H, *J* = 5.8, 1.5, 0.6 Hz, H-3β), 4.08 (dt, 0.75H, *J* = 1.4, 0.7 Hz, H-2β), 3.74 (s, 2.25H, CH_3 CO_2Meα), 3.73 (s, 3H, CH_3 CO_2Meβ), 2.09 (s, 2.25H, CH_3 OAcα), 2.07 (s, 3H, CH_3 OAcβ); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 170.3, 169.7, 169.2, 168.8 (C=O), 137.4, 137.2, 137.2, 137.0 (C_q), 128.6, 128.6, 128.5, 128.5, 128.2, 128.2, 128.0, 128.0, 127.9, 127.8, 127.6, 127.5 (CH_{arom}), 100.7 (C-1β), 94.4 (C-1α), 83.9 (C-2β), 82.2 (C-4β), 81.8 (C-2α), 81.6 (C-3β), 81.0 (C-3α), 77.7 (C-4α), 73.6, 73.1, 72.6, 72.2 (CH_2 Bn), 52.3 (C-5α), 52.2 (C-5β), 21.3 (OAcβ), 21.2 (OAcα); HRMS: $[M+NH_4]^+$ calcd for $C_{22}H_{28}NO_7$ 418.18603, found 418.18599.



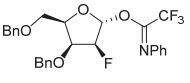
1,5-Di-*O*-acetyl 2-azido-3-*O*-benzyl-2-deoxy-α/β-D-arabinofuranoside. (61). ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 7.39 – 7.29 (m, 7.9H, CH_{arom}), 6.29 (d, 0.58H, *J* = 4.5 Hz, H-1β), 6.11 (d, 1H, *J* = 1.2 Hz, H-1α), 4.73 (d, 0.58H, *J* = 11.7 Hz, C*H*H Bnβ), 4.69 – 4.61 (m, 1.58H, C*H*H Bnα, CH*H* Bnβ), 4.57 (d, 1H, *J* = 11.8 Hz, CH*H* Bnα), 4.36 (td, 1H, *J* = 5.6, 3.4 Hz, H-4α), 4.26 (dd, 1H, *J* = 12.2, 3.5 Hz, H-5α), 4.23 – 4.19 (m, 0.58H, H-4β), 4.17 – 4.04 (m, 3.74H, H-2α, H-3β, H-5α, H-5β, H-5β), 3.99 (dd, 0.58H, *J* = 7.8, 4.6 Hz, H-2β), 3.86 (dd, 1H, *J* = 6.2, 3.1 Hz, H-3α), 2.09 (s, 1.74H, CH_3 OAcβ), 2.09 (s, 3H, CH_3 OAcα), 2.05 (s, 1.74H, CH_3 OAcβ), 2.02 (s, 3H, CH_3 OAcα); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 170.4, 170.3, 169.6, 169.1 (C=O, Ac), 136.8, 136.7 (C_q Bn), 128.6, 128.2, 128.2, 127.8, 127.8 (CH_{arom}), 100.4 (C-1α), 95.2 (C-1β), 82.7 (C-3α), 81.8 (C-4α), 80.6 (C-4β), 80.1 (C-3β), 72.9 (CH_2 Bnβ), 72.7 (CH_2 Bnα), 70.2 (C-2α), 66.3 (C-2β), 64.6 (C-5β), 62.8 (C-5α), 21.0, 21.0, 20.6, 20.6 (CH_3 OAc); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): α-anomer: $^2J_{C1,H2}$ = -3.5 Hz, $^2J_{C2,H1}$ = -0.5 Hz, β-anomer: $^2J_{C1,H2}$ = -0.6 Hz, $^2J_{C2,H1}$ = +1.9 Hz; HRMS: $[M+Na]^+$ calcd for $C_{16}H_{19}N_3O_6Na$ 372.11661, found 372.11646.



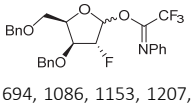
3,5-di-*O*-benzyl-2-deoxy-2-fluoro-1-*O*-(*N*-[phenyl]trifluoroacetimidoyl)-α/β-D-arabinofuranoside (62). The title compound was generated from **45** by the general procedure for imidate donor synthesis, conditions A. Yield: 85% α:β = 5:1 as separate anomers (0.14 mmol and 0.60 mmol respectively) as colourless oils. Data for the α-anomer: $[\alpha]_D^{20}$ = +67.7° (*c* = 1.39, $CHCl_3$); IR (thin film): 696, 933, 1101, 1153, 1159, 1207, 1327, 1454, 1714, 2866, 3032; ^{1}H NMR ($CDCl_3$, *T* = 323 K, 500 MHz, HH-COSY, HSQC): δ 7.35 – 7.24 (m, 12H, CH_{arom}), 7.11 – 7.06 (m, 1H, NPh), 6.83 (d, 2H, *J* = 7.5 Hz, NPh), 6.37 (d, 1H, *J* = 8.3 Hz, H-1), 5.17 (dd, 1H, *J* = 50.5, 1.6 Hz, H-2), 4.65 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.61 – 4.55 (m, 2H, CH*H* Bn, C*H*H Bn), 4.53 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.44 (q, 1H, *J* = 4.9 Hz, H-4), 4.16 (dddd, 1H, *J* = 23.1, 5.8, 1.8, 0.9 Hz, H-3), 3.64 (d, 2H, *J* = 4.7 Hz, H-5, H-5); ^{13}C-APT NMR ($CDCl_3$, *T* = 323 K, 126 MHz, HSQC): δ 143.8 (C_q NPh), 138.1, 137.4 (C_q Bn), 128.9, 128.7, 128.6, 128.2, 127.9, 127.9, 124.6, 119.8 (CH_{arom}), 116.2 (q, *J* = 286.8 Hz, CF_3), 102.7 (d, *J* = 38.8 Hz, C-1), 98.9 (d, *J* = 184.9 Hz, C-2), 84.3 (d, *J* = 3.4 Hz, C-4), 82.9 (d, *J* = 25.7 Hz, C-3), 73.8, 72.8 (CH_2 Bn), 69.2 (C-5); ^{19}F NMR ($CDCl_3$, *T* = 323 K, 471 MHz, HH-COSY, HSQC): δ -66.34 (bs, 3F, CF_3), -188.59 (ddd, 1F, *J* = 50.5, 23.1, 11.0 Hz, F-2); Data for the β-anomer: $[\alpha]_D^{20}$ = -43.0° (*c* = 0.6, $CHCl_3$); IR (thin film): 696, 1026, 1072, 1092, 1153, 1159, 1207, 1319, 1717, 2864; ^{1}H NMR ($CDCl_3$, *T* = 323 K, 500 MHz, HH-COSY, HSQC): δ 7.35 – 7.24 (m, 12H, CH_{arom}), 7.10 – 7.05 (m, 1H, NPh), 6.80 (dd, 2H, *J* = 8.4, 1.1 Hz, NPh), 6.46 (bs, 1H, H-1), 5.17 (ddd, 1H, *J* = 52.0, 5.8, 4.5 Hz, H-2), 4.69 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.60 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.57 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.54 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.32 (dt, 1H, *J* = 16.7, 5.9 Hz, H-3), 4.25 (q, 1H, *J* = 5.7 Hz, H-4), 3.63 (dd, 1H, *J* = 10.4, 5.6 Hz, H-5), 3.60 (dd, 1H, *J* = 10.5, 5.5 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, *T* = 323 K, 126 MHz, HSQC): δ 143.8 (C_q NPh), 138.1, 137.5 (C_q Bn), 128.9, 128.6, 128.6, 128.1, 127.9, 127.9, 127.9, 124.4, 119.7 (CH_{arom}), 116.1 (q, *J* = 285.9 Hz, CF_3), 96.9 (d, *J* = 18.1 Hz, C-1), 95.1 (d, *J* = 201.9 Hz, C-2), 81.9 (d, *J* = 9.0 Hz, C-4), 81.2 (d, *J* = 21.4 Hz, C-3), 73.7, 72.7 (CH_2 Bn), 70.9 (C-5); ^{19}F NMR ($CDCl_3$, *T* = 323 K, 471 MHz, HH-COSY, HSQC): δ -66.45 (bs, 3F, CF_3), -203.20 (dd, 1F, *J* = 52.1, 16.7 Hz, F-2); HRMS: $[M+H]^+$ calcd for $C_{27}H_{26}F_4NO_4$ 504.17925, found 504.17933.



3,5-di-*O*-benzyl-2-deoxy-2-fluoro-1-*O*-(*N*-[phenyl]trifluoroacetimidoyl)-α/β-D-ribofuranoside (63). The title compound was generated from **46** by the general procedure for imidate donor synthesis, conditions A. Yield: 98% β only (0.45 mmol) as a white solid, includes ~10% acetamide. IR (thin film): 694, 1092, 1151, 1207, 1712, 2869; ^{1}H NMR ($CDCl_3$, *T* = 328 K, 400 MHz, HH-COSY, HSQC): δ 7.36 – 7.21 (m, 12H, CH_{arom}), 7.11 – 7.04 (m, 1H, NPh), 6.79 (d, 2H, *J* = 8.2 Hz, NPh), 6.36 (d, 1H, *J* = 9.1 Hz, H-1), 4.95 (dd, 1H, *J* = 52.3, 3.5 Hz, H-2), 4.66 (d, 1H, *J* = 11.6 Hz, C*H*H Bn), 4.60 – 4.49 (m, 3H, CH_2 Bn, CH*H* Bn), 4.38 (dt, 1H, *J* = 7.6, 3.9 Hz, H-4), 4.24 (ddd, 1H, *J* = 23.6, 7.6, 3.6 Hz, H-3), 3.69 (dd, 1H, *J* = 11.1, 3.1 Hz, H-5), 3.58 (dd, 1H, *J* = 11.1, 4.4 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, *T* = 328 K, 101 MHz, HSQC): δ 143.6 (C_q NPh), 138.2, 137.3 (C_q Bn), 129.4, 128.8, 128.6, 128.5, 128.2, 128.0, 127.8, 127.7, 124.6, 119.6 (CH_{arom}), 116.0 (q, *J* = 286.1 Hz, CF_3), 101.2 (d, *J* = 32.4 Hz, C-1), 91.0 (d, *J* = 188.6 Hz, C-2), 82.0 (C-4), 77.0 (d, *J* = 15.7 Hz, C-3), 73.5, 73.2 (CH_2 Bn), 69.7 (C-5); ^{19}F NMR ($CDCl_3$, *T* =298 K, 471 MHz): δ -65.81 (bs, 3F, CF_3), -209.42 (ddd, 1F, *J* = 52.3, 23.9, 9.4 Hz); HRMS: $[M+H]^+$ calcd for $C_{27}H_{26}F_4NO_4$ 504.17925, found 504.17889.

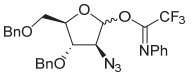


3,5-di-*O*-benzyl-2-deoxy-2-fluoro-1-*O*-(*N*-[phenyl]trifluoroacetimidoyl)-α/β-D-lyxofuranoside (64). The title compound was generated from **47** by the general procedure for imidate donor synthesis, conditions A. Yield: 82% α only (0.54 mmol) as a colourless oil. $[\alpha]_D^{20}$ = +50.2° (*c* = 1.30, $CHCl_3$); IR (thin film): 694, 737, 931, 1086, 1097, 1150, 1207, 1321, 1715, 2872, 3032; ^{1}H NMR ($CDCl_3$, *T* = 323 K, 500 MHz, HH-COSY, HSQC): δ 7.36 – 7.22 (m, 12H, CH_{arom}), 7.11 – 7.04 (m, 1H, NPh), 6.82 (d, 2H, *J* = 7.5 Hz, NPh), 6.41 (bs, 1H, H-1), 5.02 (dd, 1H, *J* = 51.7, 3.8 Hz, H-2), 4.69 (d, 1H, *J* = 11.6 Hz, C*H*H Bn), 4.60 – 4.53 (m, 3H, C*H*H Bn, CH*H* Bn, H-4), 4.50 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.34 (ddd, 1H, *J* = 17.6, 6.4, 4.3 Hz, H-3), 3.83 (dd, 1H, *J* = 10.7, 4.5 Hz, H-5), 3.68 (dd, 1H, *J* = 9.8, 7.3 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 143.6 (C_q NPh), 142.9 (q, *J* = 36.4 Hz, F_3CC=N), 138.3, 137.4 (C_q Bn), 128.9, 128.6, 128.5, 128.2, 127.9, 127.7, 124.6, 119.7 (CH_{arom}), 116.2 (q, *J* = 285.9 Hz, CF_3), 101.3 (d, *J* = 33.4 Hz, C-1), 92.6 (d, *J* = 192.3 Hz, C-2), 80.2 (C-4), 76.6 (d, *J* = 15.0 Hz, C-3), 73.7, 73.7 (CH_2 Bn), 69.5 (C-5); ^{19}F NMR ($CDCl_3$, *T* = 323 K, 471 MHz): δ -66.49 (bs, 3F, CF_3), -207.43 (ddd, 1F *J* = 51.8, 17.6, 9.5 Hz, C2-F); HRMS: $[2M+NH_4]^+$ calcd for $C_{54}H_{54}F_8N_3O_8$ 1024.37777, found 1024.37849.

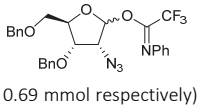


3,5-di-*O*-benzyl-2-deoxy-2-fluoro-1-*O*-(*N*-[phenyl]trifluoroacetimidoyl)-α/β-D-xylofuranoside (65). The title compound was generated from **48** by the general procedure for imidate donor synthesis, conditions A. Yield: 91% α:β = 37:63 (0.36 mmol) as a colourless oil. IR (thin film): 694, 1086, 1153, 1207, 1323, 1715; ^{1}H NMR ($CDCl_3$, *T* = 323 K, 500 MHz, HH-COSY, HSQC): δ 7.35 – 7.22 (m, 12H, CH_{arom}), 7.11 – 7.04 (m, 1H, NPh), 6.84 – 6.78 (m, 2H, NPh), 6.46 (bs, 0.37H, H-1α), 6.34 (d, 0.63H, *J* = 12.5 Hz, H-1β), 5.23 (dt, 0.37H, *J* = 51.9, 4.0 Hz, H-2α), 5.18 (dd, 0.63H, *J* = 49.8, 1.6 Hz, H-2β), 4.71 (d, 0.37H, *J* = 11.8 Hz, C*H*H Bnα), 4.68 – 4.50 (m, 3.63H, CH*H* Bnα, CH_2 Bnα, 2xCH_2 Bnβ, H-4α, H-4β), 4.41 (ddd, 0.37H, *J* = 15.7, 6.5, 4.8 Hz, H-3α), 4.26

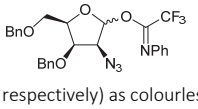
(ddd, 0.63H, *J* = 16.2, 5.8, 1.6 Hz, H-3β), 3.85 (dd, 0.63H, *J* = 10.5, 5.4 Hz, H-5β), 3.75 (dd, 0.63H, *J* = 10.4, 6.6 Hz, H-5β), 3.72 (dd, 0.37H, *J* = 10.7, 4.5 Hz, H-5α), 3.65 (dd, 0.37H, *J* = 10.6, 5.0 Hz, H-5α); ^{13}C-APT NMR ($CDCl_3$, *T* = 323K, 126 MHz, HSQC): δ 143.9, 143.8 (C_q NPh), 138.4, 138.2, 137.4, 137.4 (C_q Bn), 128.9, 128.9, 128.7, 128.5, 128.5, 128.2, 128.1, 127.8, 127.8, 127.8, 127.6, 124.5, 124.4, 119.7 (CH_{arom}), 116.1 (q, *J* = 286.3 Hz, CF_3), 102.1 (d, *J* = 37.5 Hz, H-1β), 97.0 (d, *J* = 16.8 Hz, H-1α), 97.0 (d, *J* = 184.5 Hz, H-2β), 94.1 (d, *J* = 200.0 Hz, H-2α), 83.1 (C-4β), 80.5 (d, *J* = 25.6 Hz, C-3β), 79.9 (d, *J* = 22.9 Hz, C-3α), 79.0 (d, *J* = 6.8 Hz, C-4α), 73.8 (CH_2 Bnα), 73.7, 73.2 (CH_2 Bnβ), 72.9 (CH_2 Bnα), 68.9 (C-5β), 68.2 (C-5α); ^{19}F NMR ($CDCl_3$, *T* = 323 K, 471 MHz): δ -66.32 (s, 3F, CF_3), -193.57 (dt, 0.63F, *J* = 49.8, 14.1 Hz, F-2β), -202.33 (dd, 0.37F, *J* = 52.1, 15.6 Hz, F-2α); HRMS: $[2M+NH_4]^+$ calcd for $C_{54}H_{54}F_8N_3O_8$ 1024.37777, found 1024.37842.



2-azido-3,5-di-*O*-benzyl-2-deoxy-1-*O*-(*N*-[phenyl]trifluoroacetimidoyl)-α/β-D-arabinofuranoside (66). The title compound was generated from **49** by the general procedure for imidate donor synthesis, conditions B. Yield: 71% α:β = 1.6:1 as separate anomers (0.31 mmol and 0.19 mmol respectively) as colourless oils. Data for the α-anomer: $[\alpha]_D^{20}$ = +5.4° (*c* = 0.50, $CHCl_3$); IR (thin film): 696, 929, 1103, 1161, 1207, 1329, 1456, 1700, 1717, 2106, 2866, 3032; ^{1}H NMR ($CDCl_3$, *T* = 323 K, 500 MHz, HH-COSY, HSQC): δ 7.38 – 7.22 (m, 12H, CH_{arom}), 7.08 (t, 1H, *J* = 7.5 Hz, NPh), 6.82 (d, 2H, *J* = 7.7 Hz, NPh), 6.18 (bs, 1H, H-1), 4.63 – 4.56 (m, 2H, CH_2 Bn), 4.56 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.51 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.42 (q, 1H, *J* = 4.6 Hz, H-4), 4.17 (d, 1H, *J* = 2.2 Hz, H-2), 4.00 (dd, 1H, *J* = 6.0, 3.1 Hz, H-3), 3.64 (dd, 1H, *J* = 11.0, 4.2 Hz, H-5), 3.61 (dd, 1H, *J* = 11.0, 4.8 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, *T* = 323 K, 126 MHz, HSQC): δ 143.7 (C_q NPh), 138.0, 137.4 (C_q Bn), 128.9, 128.7, 128.5, 128.2, 127.9, 127.9, 127.9, 124.6, 119.8 (CH_{arom}), 116.1 (q, *J* = 286.7 Hz, CF_3), 104.0 (C-1), 84.2 (C-4), 83.4 (C-3), 73.7, 73.0 (CH_2 Bn), 70.8 (C-5), 68.9 (C-2); HRMS: $[2M+NH_4]^+$ calcd for $C_{54}H_{54}F_6N_9O_8$ 1070.39941, found 1070.40019. Data for the β-anomer: $[\alpha]_D^{20}$ = -56.1° (*c* = 1.30, $CHCl_3$); IR (thin film): 696, 1024, 1094, 1144, 1161, 1207, 1317, 1713, 2110, 2864; ^{1}H NMR ($CDCl_3$, *T* = 323 K, 500 MHz, HH-COSY, HSQC): δ 7.36 – 7.22 (m, 12H, CH_{arom}), 7.12 – 7.03 (m, 1H, NPh), 6.81 (d, 2H, *J* = 7.5 Hz, NPh), 6.43 (bs, 1H, H-1), 4.67 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.63 (d, 1H, *J* = 11.7 Hz, CH*H* Bn), 4.59 – 4.52 (m, 2H, CH_2 Bn), 4.26 (q, 1H, *J* = 5.6 Hz, H-4), 4.21 (dd, 1H, *J* = 7.5, 6.0 Hz, H-3), 4.04 (dd, 1H, *J* = 7.5, 4.5 Hz, H-2), 3.63 – 3.53 (m, 2H, H-5); ^{13}C-APT NMR ($CDCl_3$, *T* = 323 K, 126 MHz, HSQC): δ 143.8 (C_q NPh), 138.0, 137.5 (C_q Bn), 128.9, 128.7, 128.6, 128.2, 128.0, 127.9, 127.9, 124.5, 119.6 (CH_{arom}), 116.1 (d, *J* = 286.6 Hz, CF_3), 98.6 (C-1), 82.9 (C-4), 81.5 (C-3), 73.7, 73.1 (CH_2 Bn), 70.9 (C-5), 67.4 (C-2); HRMS: $[M+NH_4]^+$ calcd for $C_{27}H_{29}F_3N_5O_4$ 544.21662, found 544.21623.

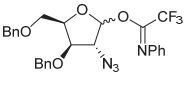


2-azido-3,5-di-*O*-benzyl-2-deoxy-1-*O*-(*N*-[phenyl]trifluoroacetimidoyl)-α/β-D-ribofuranoside (67). The title compound was generated from **50** by the general procedure for imidate donor synthesis, conditions A. Yield: 77% α:β = 1:8 as separate anomers (0.085 mmol and 0.69 mmol respectively) as a white soild. Data for the α-anomer: $[\alpha]_D^{20}$ = +52.4° (*c* = 0.46, $CHCl_3$); IR (thin film): 696, 1101, 1144, 1161, 1207, 1319, 1713, 2114, 2864; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.36 – 7.25 (m, 10H, CH_{arom}), 7.25 – 7.21 (m, 2H, CH_{arom}), 7.11 – 7.05 (m, 1H, NPh), 6.87 (d, 2H, *J* = 7.7 Hz, NPh), 6.45 (bs, 1H, H-1), 4.74 (d, 1H, *J* = 12.2 Hz, C*H*H Bn), 4.61 (d, 1H, *J* = 12.2 Hz, CH*H* Bn), 4.49 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.45 – 4.40 (m, 2H, CH*H* Bn, H-4), 4.18 (dd, 1H, *J* = 6.6, 3.1 Hz, H-3), 3.63 – 3.58 (m, 1H, H-2), 3.51 (dd, 1H, *J* = 10.8, 3.7 Hz, H-5), 3.45 (dd, 1H, *J* = 10.7, 3.3 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 144.0 (C_q NPh), 137.8, 137.7 (C_q Bn), 128.9, 128.6, 128.6, 128.0, 127.8, 124.5, 119.9 (CH_{arom}), 99.9 (C-1), 84.8 (C-4), 78.3 (C-3), 73.9, 73.1 (CH_2 Bn), 69.6 (C-5), 61.4 (C-2); HRMS: $[M+Na]^+$ calcd for $C_{27}H_{25}F_3N_4O_4Na$ 549.17201, found 549.17174. Data for the β-anomer: $[\alpha]_D^{20}$ = -1.6° (*c* = 0.70, $CHCl_3$); IR (thin film): 696, 1090, 1144, 1159, 1207, 1331, 1715, 2108, 2862; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.35 – 7.24 (m, 12H, CH_{arom}), 7.08 (t, 1H, *J* = 7.4 Hz, NPh), 6.80 (d, 2H, *J* = 7.7 Hz, NPh), 6.18 (bs, 1H, H-1), 4.64 (d, 1H, *J* = 11.6 Hz, C*H*H Bn), 4.58 (d, 1H, *J* = 11.6 Hz, CH*H* Bn), 4.56 (d, 1H, *J* = 12.2 Hz, C*H*H Bn), 4.53 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.39 (dd, 1H, *J* = 7.0, 5.0 Hz, H-3), 4.33 (dt, 1H, *J* = 7.0, 4.3 Hz, H-4), 4.03 (d, 1H, *J* = 5.0 Hz, H-2), 3.64 (dd, 1H, *J* = 10.9, 4.0 Hz, H-5), 3.57 (dd, 1H, *J* = 10.9, 4.7 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 143.7 (C_q NPh), 138.1, 137.2 (C_q Bn), 128.9, 128.7, 128.5, 128.3, 128.1, 127.8, 127.8, 124.6, 119.7 (CH_{arom}), 116.06 (q, *J* = 286.0 Hz, CF_3), 102.5 (C-1), 82.6 (C-4), 79.0 (C-3), 73.6, 73.6 (CH_2 Bn), 70.0 (C-5), 64.8 (C-2); HRMS: $[2M+NH_4]^+$ calcd for $C_{54}H_{54}F_6N_9O_8$ 1070.39941, found 1070.40023.

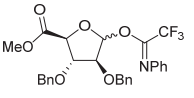


2-azido-3,5-di-*O*-benzyl-2-deoxy-1-*O*-(*N*-[phenyl]trifluoroacetimidoyl)-α/β-D-lyxofuranoside (68). The title compound was generated from **51** by the general procedure for imidate donor synthesis, conditions B. Yield: 67% α:β = 1:1.2 (0.30 mmol and 0.37 mmol respectively) as colourless oils. Data for the α-anomer: $[\alpha]_D^{20}$ = -57.5° (*c* = 0.69, $CHCl_3$); IR (thin film): 696, 1045, 1098, 1144, 1207, 1323, 1714, 2112, 2866, 2926; ^{1}H NMR ($CDCl_3$, *T* = 323 K, 500 MHz, HH-COSY, HSQC): δ 7.37 – 7.22 (m, 12H, CH_{arom}), 7.11 – 7.03 (m, 1H, NPh), 6.82 (d, 2H, *J* = 7.5 Hz, NPh), 6.27 (bs, 1H, H-1), 4.71 (d, 1H, *J* = 11.5 Hz, C*H*H Bn), 4.59 (d, 1H, *J* = 11.6 Hz, CH*H* Bn), 4.56 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.53 – 4.47 (m, 2H, CH*H* Bn, H-4), 4.41 (t, 1H,

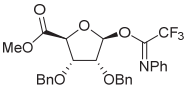
J = 5.5 Hz, H-3), 4.02 (dd, 1H, *J* = 5.1, 1.9 Hz, H-1), 3.81 (dd, 1H, *J* = 10.4, 5.4 Hz, H-5), 3.71 (dd, 1H, *J* = 10.4, 6.5 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, *T* = 323 K, 126 MHz, HSQC): δ 143.7 (C_q NPh), 138.2, 137.2 (C_q Bn), 128.9, 128.7, 128.5, 128.2, 127.9, 127.9, 127.8, 124.6, 119.7 (CH_{arom}), 116.2 (q, *J* = 286.9 Hz, CF_3), 102.3 (C-1), 80.7 (C-4), 78.6 (C-3), 74.4, 73.7 (CH_2 Bn), 68.7 (C-5), 66.2 (C-2); HRMS: $[M+NH_4]^+$ calcd for $C_{27}H_{29}F_3N_5O_4$ 544.21662, found 544.21667. Data for the β-anomer: $[\alpha]_D^{20}$ = +24.9° (*c* = 0.68, $CHCl_3$); IR (thin film): 696, 1094, 1144, 1153, 1207, 1319, 1717, 2110, 2926; ^{1}H NMR ($CDCl_3$, *T* = 323 K, 500 MHz, HH-COSY, HSQC): δ 7.37 – 7.21 (m, 12H, CH_{arom}), 7.10 – 7.02 (m, 1H, NPh), 6.84 (d, 2H, *J* = 7.5 Hz, NPh), 6.41 (bs, 1H, H-1), 4.83 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.66 (d, 1H, *J* = 11.7 Hz, CH*H* Bn), 4.51 (d, 1H, *J* = 11.8 Hz, C*H*H Bn), 4.46 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.36 (q, 1H, *J* = 6.3 Hz, H-4), 4.26 (t, 1H, *J* = 5.4 Hz, H-3), 3.82 (dd, 1H, *J* = 9.9, 6.7 Hz, H-5), 3.70 (dd, 1H, *J* = 9.9, 6.2 Hz, H-5), 3.51 (t, 1H, *J* = 4.9 Hz, H-2); ^{13}C-APT NMR ($CDCl_3$, *T* = 323 K, 126 MHz, HSQC): δ 143.9 (C_q NPh), 138.1, 137.6 (C_q Bn), 128.8, 128.5, 128.5, 127.9, 127.8, 127.5, 124.4, 119.7 (CH_{arom}), 116.2 (q, *J* = 286.3 Hz, CF_3), 98.5 (C-1), 82.2 (C-4), 77.7 (C-3), 74.7, 73.8 (CH_2 Bn), 69.0 (C-5), 62.2 (C-2); HRMS: $[2M+NH_4]^+$ calcd for $C_{54}H_{54}F_6N_9O_8$ 1070.39941, found 1070.39931.



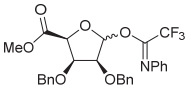
2-azido-3,5-di-*O*-benzyl-2-deoxy-1-*O*-(*N*-[phenyl]trifluoroacetimidoyl)-α/β-D-xylofuranoside (69). The title compound was generated from **52** by the general procedure for imidate donor synthesis, conditions A. Yield: 100% α:β = 1:1 (0.33 mmol) as a colourless oil. IR (thin film): 696, 1044, 1099, 1143, 1207, 1321, 1712, 2114; ^{1}H NMR ($CDCl_3$, *T* = 323 K, 500 MHz, HH-COSY, HSQC): δ 7.36 – 7.23 (m, 24H, CH_{arom}), 7.10 – 7.06 (m, 2H, NPh), 6.84 (d, 2H, *J* = 7.7 Hz, NPh), 6.80 (d, 2H, *J* = 7.6 Hz, NPh), 6.43 (bs, 1H, H-1α), 6.15 (bs, 1H, H-1β), 4.69 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.64 – 4.57 (m, 4H, CH_2 Bn, CH*H* Bn, C*H*H Bn), 4.56 – 4.50 (m, 4H, CH_2 Bn, CH*H* Bn, H-4β), 4.50 – 4.45 (m, 1H, H-4α), 4.32 (t, 1H, *J* = 6.7 Hz, H-3α), 4.22 (bs, 1H, H-2β), 4.17 – 4.11 (m, 1H, H-2α), 4.08 (dd, 1H, *J* = 5.8, 2.8 Hz, H-3β), 3.85 (dd, 1H, *J* = 10.5, 5.3 Hz, H-5β), 3.76 (dd, 1H, *J* = 10.5, 6.5 Hz, H-5β), 3.71 (dd, 1H, *J* = 10.7, 4.4 Hz, H-5α), 3.61 (dd, 1H, *J* = 10.7, 4.9 Hz, H-5α); ^{13}C-APT NMR ($CDCl_3$, *T* = 323 K, 126 MHz, HSQC): δ 143.8, 143.8 (C_q NPh), 138.3, 138.2, 137.4, 137.4 (C_q Bn), 128.9, 128.9, 128.7, 128.5, 128.5, 128.3, 128.3, 127.9, 127.9, 127.8, 127.8, 127.8, 127.8, 124.5, 119.8, 119.7 (CH_{arom}), 103.2 (C-1β), 98.4 (C-1α), 82.7 (C-4β), 81.6 (C-3β), 79.1 (C-3α), 73.8 (C-4α), 73.8, 73.6, 73.3 (CH_2 Bn), 69.1 (C-2β), 69.0 (C-5β), 68.5 (C-5α), 66.7 (C-2α); HRMS: only mass of hydrolysis found $[M+Na]^+$ calcd for $C_{19}H_{21}N_3O_4Na$ 378.1430, found 378.1433.



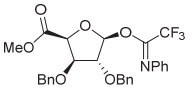
Methyl (2,3-di-*O*-benzyl-1-*O*-(*N*-[phenyl]trifluoroacetimidoyl)-α/β-D-arabinofuranosyl uronate) (70). The title compound was generated from **53** (466 mg, 1.3 mmol) by the general procedure for imidate donor synthesis, conditions A. Yield: 97%, α:β = 1:1.2 (670 mg, 1.27 mmol) as a white solid. R*f*: 0.51 (8/2 pentane/Et_2O). IR (thin film): 696, 1074, 1105, 1318, 1712, 1769; ^{1}H NMR ($CDCl_3$, *T* = 323 K, 500 MHz, HH-COSY, HSQC): δ 7.35 – 7.20 (m, 24H, CH_{arom}), 7.10 – 7.02 (m, 2H, NPh), 6.79 (d, 2H, *J* = 7.7 Hz, NPh), 6.77 – 6.74 (m, 2H, NPh), 6.41 (bs, 1H, H-1β), 6.29 (bs, 1H, H-1α), 4.82 (d, 1H, *J* = 3.8 Hz, H-4β), 4.76 (d, 1H, *J* = 11.8 Hz, C*H*H Bn), 4.72 – 4.61 (m, 4H, CH_2 Bn, CH*H* Bn, C*H*H Bn), 4.60 – 4.53 (m, 4H, CH_2 Bn, H-3α, H-4α), 4.50 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.29 (d, 1H, *J* = 3.1 Hz, H-3β), 4.24 – 4.18 (m, 2H, H-2α, H-2β), 3.74 (s, 3H, CH_3 CO_2Me), 3.73 (s, 3H, CH_3 CO_2Me); ^{13}C-APT NMR ($CDCl_3$, *T* = 323 K, 126 MHz, HSQC): δ 170.7, 169.6 (C=O), 144.0, 143.8, 137.8, 137.5, 137.4, 137.1 (C_q), 128.8, 128.7, 128.6, 128.6, 128.5, 128.5, 128.2, 128.1, 128.0, 128.0, 128.0, 127.9, 127.9, 127.8, 124.5, 124.2, 119.8, 119.6 (CH_{arom}), 116.1 (q, *J* = 286.7 Hz, CF_3), 116.1 (q, *J* = 286.5 Hz, CF_3), 104.0 (C-1α), 97.3 (C-1β), 85.2, 85.2 (C-2β, C-3α), 84.0 (C-2α), 83.7 (C-3β), 83.3 (C-4α), 80.9 (C-4β), 73.4, 73.0, 72.4, 72.2 (CH_2 Bn), 52.5 (OMe); ^{19}F NMR ($CDCl_3$, 471 MHz): δ -66.18; HRMS: $[M+Na]^+$ calcd for $C_{28}H_{26}F_3NO_6Na$ 552.16044, found 552.16010.



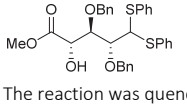
Methyl (2,3-di-*O*-benzyl-1-*O*-(*N*-[phenyl]trifluoroacetimidoyl)-β-D-ribofuranosyl uronate) (71). The title compound was generated from **54** (1.0 g, 2.8 mmol) by the general procedure for imidate donor synthesis, conditions A. Yield: 85% β only (1.26 g, 2.38 mmol) as a white solid. R*f*: 0.54 (7/3 pentane/Et_2O). $[\alpha]_D^{20}$ = +18.6° (*c* = 0.90, $CHCl_3$); IR (thin film): 696, 1090, 1146, 1206, 1456, 1717, 1740; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.35 – 7.25 (m, 12H, CH_{arom}), 7.08 (t, 1H, *J* = 7.5 Hz, NPh), 6.81 (d, 2H, *J* = 7.5 Hz, NPh), 6.29 (bs, 1H, H-1), 4.72 (d, 1H, *J* = 6.4 Hz, H-4), 4.68 – 4.63 (m, 3H, CH_2 Bn, C*H*H Bn), 4.62 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.43 (dd, 1H, *J* = 6.3, 4.7 Hz, H-3), 4.09 (d, 1H, *J* = 4.5 Hz, H-2), 3.76 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 170.9 (C=O), 143.9 (C_q NPh), 137.5, 137.4 (C_q Bn), 128.9, 128.7, 128.6, 128.2, 128.2, 128.1, 128.1, 124.5, 119.7 (CH_{arom}), 116.11 (q, *J* = 285.8 Hz, CF_3), 102.6 (C-1), 81.2 (C-4), 80.3 (C-3), 79.7 (C-2), 73.3, 73.0 (CH_2 Bn), 52.5 (CH_3 CO_2Me); ^{19}F NMR ($CDCl_3$, 471 MHz): δ -66.62; HRMS: $[M+H]^+$ calcd for $C_{28}H_{27}F_3NO_6$ 530.17850, found 530.17802.



Methyl (2,3-di-*O*-benzyl-1-*O*-(*N*-[phenyl]trifluoroacetimidoyl)-α/β-D-lyxofuranosyl uronate) (72). The title compound was generated from **55** (1.05 g, 2.90 mmol) by the general procedure for imidate donor synthesis, conditions A. Yield: 85% as two separate anomers (487 mg, 0.92 mmol α and 105 mg, 0.20 mmol β respectively) as colourless oils. R*f*: 0.24 and 0.69 (8/2 pentane/Et_2O). Data for the α-anomer: $[\alpha]_D^{20}$ = -5.5° (*c* = 1.23, $CHCl_3$); IR (thin film): 696, 1026, 1101, 1159, 1207, 1327, 1707, 1734, 1770; ^{1}H NMR ($CDCl_3$, *T* = 323 K, 500 MHz, HH-COSY, HSQC): δ 7.33 – 7.22 (m, 12H, CH_{arom}), 7.10 – 7.02 (m, 1H, NPh), 6.80 (d, 2H, *J* = 7.5 Hz, NPh), 6.49 (bs, 1H, H-1), 4.81 (d, 1H, *J* = 5.3 Hz, H-4), 4.71 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.66 (s, 2H, CH_2 Bn), 4.61 (d, 1H, *J* = 11.7 Hz, CH*H* Bn), 4.43 (t, 1H, *J* = 5.1 Hz, H-3), 4.20 (dd, 1H, *J* = 4.6, 2.7 Hz, H-2), 3.68 (s, 3H, CH_3 CO_2Me); ^{13}C-APT NMR ($CDCl_3$, *T* = 323 K, 126 MHz, HSQC): δ 167.9 (C=O), 143.7 (C_q NPh), 143.1 (q, *J* = 36.2 Hz, CF_3-*C*=N), 137.7, 137.3 (C_q Bn), 128.8, 128.5, 128.4, 128.1, 127.9, 127.8, 124.5, 119.7, (CH_{arom}), 116.1 (q, *J* = 285.8 Hz, CF_3), 103.5 (C-1), 82.0 (C-2), 79.7 (C-4), 78.4 (C-3), 73.9, 73.0 (CH_2 Bn), 52.1 (CH_3 CO_2Me); HRMS: $[M+NH_4]^+$ calcd for $C_{28}H_{30}F_3N_2O_6$ 547.20505, found 547.20459. Data for the β-anomer: $[\alpha]_D^{20}$ = -66.4° (*c* = 0.70, $CHCl_3$); IR (thin film): 696, 1074, 1086, 1144, 1327, 1715, 1769; ^{1}H NMR ($CDCl_3$, *T* = 323 K, 500 MHz, HH-COSY, HSQC): δ 7.35 – 7.25 (m, 10H, CH_{arom}), 7.25 – 7.19 (m, 3H, NPh), 7.09 – 6.99 (m, 1H, NPh), 6.79 (d, 2H, *J* = 7.7 Hz, NPh), 6.40 (bs, 1H, H-1), 4.89 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.74 (d, 1H, *J* = 5.5 Hz, H-4), 4.69 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.66 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.62 (d, 1H, *J* = 11.7 Hz, CH*H* Bn), 4.39 (t, 1H, *J* = 5.3 Hz, H-3), 3.98 (t, 1H, *J* = 4.6 Hz, H-2), 3.64 (s, 3H, CH_3 CO_2Me); ^{13}C-APT NMR ($CDCl_3$, *T* = 323 K, 126 MHz, HSQC): δ 168.3 (C=O), 144.4 (C_q NPh), 138.4, 137.4 (C_q Bn), 128.7, 128.7, 128.2, 128.2, 127.7, 127.4, 127.3, 124.0, 119.8 (CH_{arom}), 116.3 (q, *J* = 286.8 Hz, CF_3), 96.4 (C-1), 81.1 (C-4), 79.9 (C-2), 76.4 (C-3), 74.2, 73.3 (CH_2 Bn), 52.0 (CH_3 CO_2Me); HRMS: $[M+H]^+$ calcd for $C_{28}H_{27}F_3NO_6$ 530.17850, found 530.17835.



Methyl (2,3-di-*O*-benzyl-1-*O*-(*N*-[phenyl]trifluoroacetimidoyl)-β-D-xylofuranosyl uronate) (73). The title compound was generated from **56** (1.20 g, 3.0 mmol) by the general procedure for imidate donor synthesis, conditions A. Yield: 81% β only (561 mg, 1.06 mmol) as a colourless oil. R*f*: 0.28 (8/2 pentane/Et_2O). $[\alpha]_D^{20}$ = +10.2° (*c* = 0.55, $CHCl_3$); IR (thin film): 696, 1105, 1159, 1207, 1325, 1717, 1732, 1771; ^{1}H NMR ($CDCl_3$, *T* = 323 K, 500 MHz, HH-COSY, HSQC): δ 7.34 – 7.22 (m, 12H, CH_{arom}), 7.15 – 7.02 (m, 1H, NPh), 6.82 (d, 1H, *J* = 7.5 Hz, NPh), 6.32 (bs, 1H, H-1), 5.00 (d, 1H, *J* = 6.0 Hz, H-4), 4.57 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.55 – 4.50 (m, 3H, CH_2 Bn, CH*H* Bn), 4.32 (dd, 1H, *J* = 6.0, 1.2 Hz, H-3), 4.23 (s, 1H, H-2), 3.72 (s, 3H, CH_3 CO_2Me); ^{13}C-APT NMR ($CDCl_3$, *T* = 323 K, 126 MHz, HSQC): δ 168.6 (C=O), 144.1 (C_q NPh), 137.5, 137.1 (C_q Bn), 128.8, 128.7, 128.5, 128.3, 128.0, 127.9, 127.6, 124.2, 119.8 (CH_{arom}), 116.1 (q, *J* = 286.8 Hz, CF_3), 103.3 (C-1), 84.0 (C-2), 82.9 (C-4), 82.0 (C-3), 73.1, 72.5 (CH_2 Bn), 52.0 (CH_3 CO_2 Me); HRMS: $[M+Na]^+$ calcd for $C_{28}H_{26}F_3NO_6Na$ 552.16044, found 552.15999.



Methyl (2,3-di-*O*-benzyl-D-ribosyl uronate) diphenyl mercaptal (74). Compound **59** (200 mg, 0.5 mmol) was dissolved in 2 mL DCM and cooled to 0°C. Thiophenol (90 µL, 0.88 mmol, 1.75 eq.) and $BF_3{\cdot}OEt_2$ (105 µL, 0.85 mmol, 1.7 eq.) were added and the reaction stirred for 4 h. The reaction was quenched by the addition of sat. aq. $NaHCO_3$ and the mixture was extracted with DCM three times. The combined organic layers were washed with H_2O and brine, then dried ($MgSO_4$), filtered and concentrated in vacuo. Purfication by flash column chromatography (1/0 to 8/2 pentane/EtOAc) gave the dithioacetal as a colourless oil (156, 0.28 mmol, 56%). IR (thin film): 696, 737, 1026, 1101, 1217, 1230, 1267, 1439, 1454, 1481, 1581, 1734, 2873, 2922, 2949, 3030, 3059, 3466; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.50 – 7.11 (m, 20H, CH_{arom}), 5.19 (d, 1H, *J* = 10.5 Hz, C*H*H Bn), 5.05 (s, 1H, H-1), 4.76 (d, 1H, *J* = 11.3 Hz, C*H*H Bn), 4.56 (d, 1H, *J* = 10.5 Hz, CH*H* Bn), 4.53 (bs, 1H, H-4), 4.48 (d, 1H, *J* = 11.3 Hz, CH*H* Bn), 4.39 – 4.30 (m, 2H, H-2, H-3), 3.42 (s, 3H, CH_3 CO_2Me), 3.02 (bs, 1H, OH); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 172.8 (C=O), 137.9, 137.5, 136.0, 135.1 (C_q), 131.3, 130.7, 129.2, 129.1, 128.5, 128.4, 128.3, 127.9, 127.8, 127.3, 127.0 (CH_{arom}), 81.4, 78.8 (C-2, C-3), 74.8, 73.4 (CH_2 Bn), 69.8 (C-4), 60.4 (C-1), 52.6 (CH_3 CO_2Me); HRMS: $[M+Na]^+$ calcd for $C_{32}H_{32}O_5S_2Na$ 583.158.34, found 583.15803.

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Chapter 8

Stereoselectivity of C-2- and C-5-modified furanosides: a computational and experimental study

Introduction

Of the many structurally different carbohydrates, furanosides, the five-membered ring carbohydrates, are common components of plant- and bacterial oligosaccharides, and form the basis of DNA/RNA as nucleotides.[1–7] Glycosylation reactions with furanosides proceed with much the same chemistry as six-membered ring pyranosides. The glycosylation mechanism therefore proceeds through a pathway having S_N1-like and S_N2-like character. Furanosides are typically more reactive than pyranosides because they have one electron-withdrawing oxygen substituent less, and they are conformationally more flexible and can easier accommodate the double bond character upon oxocarbenium ion formation in the ring. In this chapter the stereoselectivity of S_N1-type glycosylations are investigated for furanosides, bearing different ring substituents. The stereoelectronic effects brought about by fluorine, azide, or the benzyloxy groups on C-2 and a methyl uronate or benzyloxymethyl group at C-5 are probed, as these can have tremendous influence on both the reactivity and the stereoselectivity of the glycosylation

reaction. The stereochemical outcome of experimental glycosylations of the differently functionalized furanosides is interpreted using computational analysis of the stability of the reactive intermediates in the dissociative mechanism, the furanosyl oxocarbenium ion.

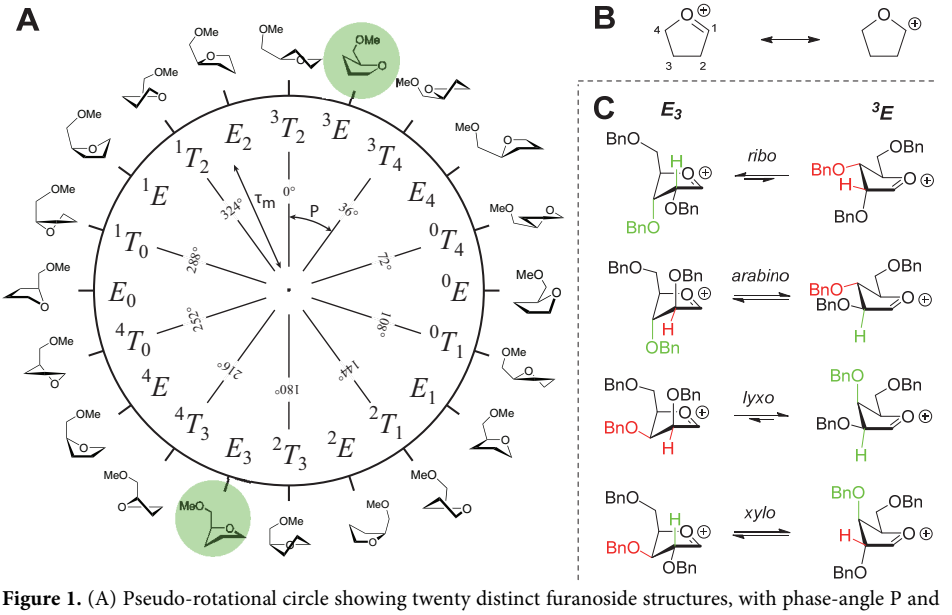


Figure 1. (A) Pseudo-rotational circle showing twenty distinct furanoside structures, with phase-angle P and puckering amplitude τ_m.[8] Green circles indicate the two major conformations of oxocarbenium ions. (B) Two resonance structures of a cyclic furanosyl oxocarbenium ion. (C) The two principal conformations of the two-conformer model (E_3-^3E) shown for every carbohydrate configuration, example taken as their tri-*O*-benzyl protected form. Colors indicate relative preferential orientations for H-2 and O-3 (see Chapter 1), green is relatively stabilizing whereas red is relatively destabilizing.

Furanosides readily attain different conformations, and all the different possible geometric shapes a five-membered ring can adopt can be described by a pseudo-rotational circle (Figure 1A).[9,10] The phase angle (P) defines the conformation of the ring, and the puckering amplitude (τ_m) describes the amount of distortion from the median plane the outlying atoms have.[8,11] In the middle of this circle, all five ring atoms are in the same plane, and all the substituents suffer from eclipsing interactions. Each furanoside, neutral or charged, has its own preferential conformation or suite of conformations, depending on the nature of the ring substituents and their orientation.

The conformations adopted by the reactive intermediates in S_N1-type substitutions, the oxocarbenium ions, are limited to a smaller region of the pseudo-rotational circle.[12] The oxocarbenium ion has two extreme resonance structures (Figure 1B), the most stable of the two features a C=O double bond which places four of the five

ring atoms in the same plane. The remaining ring-atom, C-3, will be out of the oxocarbenium ion plane, to minimize eclipsing interactions of its substituents. Therefore, the two most likely structures of an oxocarbenium ion will be the E_3 and ^3E conformations, or conformations closely related to those. The orientational preferences of each substituent in these two conformations has been investigated by the group of Woerpel (see also Chapter 1), the results of which are graphically displayed in Figure 1C.[13–17] The substituent on C-2 is preferentially placed in a sterically less demanding *pseudo*-equatorial orientation, simultaneously allowing the *pseudo*-axially orientated C–H bond to be aligned for hyperconjugative stabilization ($\sigma \rightarrow p/\pi^*$) of the anomeric carbocation. The substituent on C-3, on the other hand, is preferentially placed in a *pseudo*-axial orientation, as this brings the electron density of the electronegative oxygen atom closer to the oxocarbenium ion than it would in a *pseudo*-equatorial setting. This makes the effect of the C-3–O-3 bond less electron-withdrawing and allows for through-space electrostatic stabilization by the lone electron pairs on oxygen.

The stereoselectivity in glycosylations with furanosides that follow an S_N1 mechanism can be traced to the stereoselectivity inferred by the oxocarbenium ion. Woerpel and co-workers have established a model to account for the selectivity based on the E_3 and ^3E oxocarbenium ion conformations (Figure 2).[17–20] In this model, coined the two-conformer model, attack on the inside of the oxocarbenium ion is preferred over attack on the outside of the oxocarbenium ion. The basis of this rationale is the developing eclipsing interactions that occur in the transition state of the glycosylation reaction. When nucleophilic attack occurs on the outside of the oxocarbenium ion, the incoming nucleophile experiences eclipsing interactions with the *pseudo*-axially orientated substituent at C-2. The *pseudo*-equatorially orientated substituents at C-1 and C-2 also experience increased eclipsing interactions in the transition state upon rehybridization when a nucleophile attacks from the outside.

The stability of the oxocarbenium ion, dictated by its substituents, and the preference for inside attack leading to a more favorable transition state, leads to a model that can predict stereoselectivity based on oxocarbenium ion stability. The reasoning of this model is valid by the Hammond postulate: the geometry of the product-forming transition state is assumed to resemble the structure of the oxocarbenium ion intermediate, and the stereoselective preference of the ground-state oxocarbenium ion can therefore be taken as indicative of the reaction outcome (Figure 2). The ground state

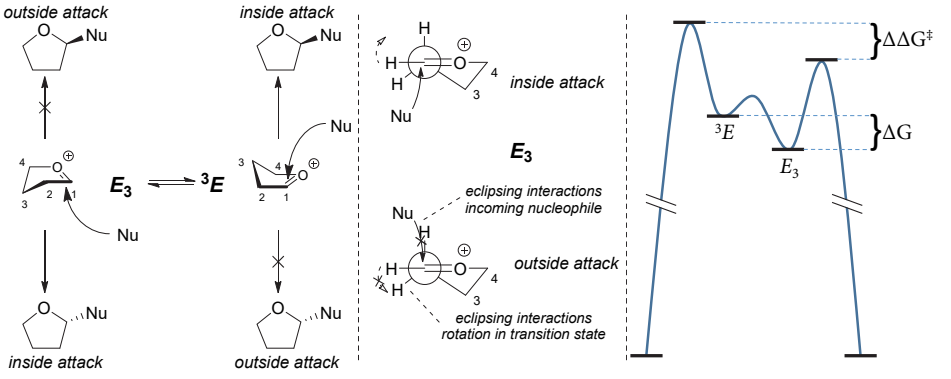


Figure 2. (left, middle) The two-conformer model, visualizing preferential nucleophilic attack from the inside face. Important rotations are denoted by dashed arrows. (right) Ground-state approximation to oxocarbenium ion stereoselectivity. $\Delta G \approx \Delta\Delta G^{\ddagger}$, energy levels are arbitrarily chosen for illustrative purposes. Reaction coordinate only visualized for the two inside attack pathways.

energy difference of two oxocarbenium ions (ΔG) is assumed to be similar to their transition state energy difference ($\Delta\Delta G^{\ddagger}$), thereby resulting in similar reaction rates of both inside attack pathways, and a product ratio mirroring the oxocarbenium ion ratio.

It can be difficult to predict which of the E_3-^3E envelopes is the more stable conformation on the basis of individual substituent effects, especially when there are conflicting orientational interests between the substituents. Furthermore, a change in protecting- or functional groups on the furanoside ring may have an unforeseen stereoelectronic influence, leading to less obvious geometries.[21,22] To assess the conformational behavior of furanosyl oxocarbenium ions, a method was devised based on Density Functional Theory (DFT), with which the relative stabilities of each conformation in the complete pseudo-rotational circle can be calculated, generating Conformational Energy Landscape (CEL) maps.[23] This method has been previously used by van Rijssel *et al.* to calculate the relative energies of furanosyl oxocarbenium ions of all four pentose furanosyl configurations (*arabino*-, *ribo*-, *lyxo*-, and *xylo*-configured, **49**, **53**, **57**, and **61**, Figure 3), bearing three *O*-methyl groups.[24,25] The results obtained by this method were in excellent agreement with experimental glycosylations (using the per-benzylated substrates, see also Table 1), and prompted further application of the DFT method to study relevant structural modifications. This chapter describes in detail the effects of the 2-fluoro, 2-azido, and 5-methyl uronate groups on the stability of the oxocarbenium ion conformations. The stereochemical outcome of experimental glycosylations is related to the structures of the intermediate oxocarbenium ions as revealed by the CEL maps.

Results and discussion

Glycosylations

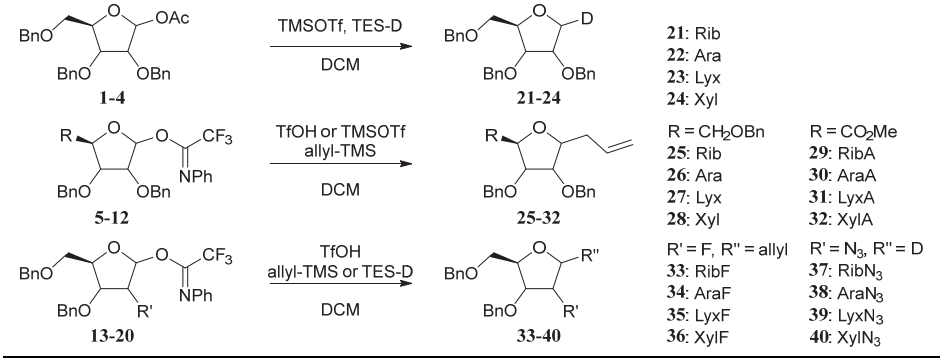
Sixteen furanosides, comprising all four configurations of the D-pentofuranoses, with a 2-fluoro, 2-azido, or a 5-uronic acid ester substituent are studied, while the previously investigated fully benzylated donors are used for comparison.[24] The synthesis of all used furanosyl donors is described in Chapter 7.

The glycosyl donors of the C-2- and C-5-modified furanosides feature a trifluoro-*N*-phenylimidate anomeric leaving group (**9**-**20**, Table 1), since the corresponding acetyl donors proved inactive due to the presence of more electron-withdrawing substituents. Besides, allylations were preferred here over reactions with triethylsilane-*d* (TES-D) because the structure of the products could be determined with more ease, generally less side products were formed, the products could be easier separated from the contaminants, and the yields of the reactions were generally higher.[26] For the reactions of the C-2-azido donors TES-D was used because allyltrimethylsilane (allyl-TMS) did not lead to product formation even at higher temperatures (+5°C) and further increase of temperature led to degradation of the donor.

First the effect of these changes was probed by the condensation of tri-*O*-benzyl trifluoro-*N*-phenylimidate donors **5**-**8**, with allyl-TMS), showing nearly identical selectivities as those obtained previously by van Rijssel *et al*. with the four perbenzylated furanosyl acetates **1**-**4** with TES-D as the acceptor (see entries 1-4 *vs* entries 5-8, Table 1).[24] The high 1,2-*cis*-selectivity of all tri-*O*-benzyl furanosides (**1**-**8**, entries 1-8, Table 1) is apparent (α for *ribo*- and *xylo*-configured, β for *arabino*- and *lyxo*-configured substrates). The *ribo*- and *lyxo*-configured donors give solely the 1,2-*cis*-glycosylated products (**21**, **23**, **25**, **27**). The *xylo*-configured donors show poorer selectivity and a 85:15 α:β product ratio is obtained when both xylosyl donors are condensed with allyl-TMS (**28**) or TES-D (**24**). Arabinoside **1** is highly β-selective with TES-D (**21**) and forms a small amount of the other anomer when glycosylated as imidate **5** with allyl-TMS (**25**).

This 1,2-*cis*-selectivity largely remains in the series of C-2- and C-5-modified furanosides: all configurations except xylose are highly 1,2-*cis*-selective for all modifications tested. Rather strikingly, it thus appears that the nature of the substituents on furanosyl donors, have relatively little effect on the stereochemical outcome of the glycosylation reactions, when following a S_N1-like pathway. The 2-fluoroxyloside **36** is formed in a 70:30 α:β ratio, and the 2-azidoxyloside donor **20** gives a 85:15 mixture of

Table 1. Glycosylations of imidate donors **5-20**.[a]



Entry	Donor	Donor configuration[b]	Acceptor	Temp. (°C)	Time (h)	Product	α : β	Yield (%)
1	**1**	β-Rib	2 eq. TES-D	-78	70	**21**	>98 : 2	50
2	**2**	α/β-Ara (2/1)	2 eq. TES-D	-78	165	**22**	<2 : 98	62
3	**3**	α-Lyx	2 eq. TES-D	-78	165	**23**	<2 : 98	100
4	**4**	α/β-Xyl (1/3)	2 eq. TES-D	-78	165	**24**	85 : 15	40
5	**5**	β-Rib	2 eq. allyl-TMS	-78	24	**25**	>98 : 2	[e]
6	**6**	α-Ara	2 eq. allyl-TMS	-78	24	**26**	10 : 90	[e]
7	**7**	α-Lyx	2 eq. allyl-TMS	-78	24	**27**	<2 : 98	[e]
8	**8**	α/β-Xyl (1/6)	2 eq. allyl-TMS	-78	24	**28**	85 : 15	[e]
9	**9**	β-RibA	4 eq. allyl-TMS	-20	100	**29**	>98 : 2	79
10	**10**	α/β-AraA (1/1)	4 eq. allyl-TMS	-20	100	**30**	5 : 95	76
11	**11**	α-LyxA[c]	4 eq. allyl-TMS	-20	100	**31**	<2 : 98	76
12	**12**	β-XylA	4 eq. allyl-TMS	-20	100	**32**	45 : 55	57[d]
13	**13**	β-RibF	4 eq. allyl-TMS	-20	100	**33**	>98 : 2	76
14	**14**	α-AraF[c]	4 eq. allyl-TMS	-20	100	**34**	<2 : 98	79
15	**15**	α-LyxF	4 eq. allyl-TMS	-20	100	**35**	<2 : 98	90
16	**16**	α/β-XylF (3/5)	4 eq. allyl-TMS	-20	100	**36**	70 : 30	62
17	**17**	β-RibN$_3$[c]	4 eq. TES-D	+5	100	**37**	>98 : 2	68
18	**18**	α-AraN$_3$[c]	4 eq. TES-D	+5	100	**38**	<2 : 98	57
19	**19**	β-LyxN$_3$[c]	4 eq. TES-D	+5	100	**39**	<2 : 98	59
20	**20**	α/β-XylN$_3$ (1/1)	4 eq. TES-D	+5	100	**40**	85 : 15	68[d]

Anomeric configuration established by HSQC-HECADE and NOESY NMR.[27–29] [a]Detailed experimental conditions are provided in the experimental section. [b]Imidates were assigned by ^{1}H NMR at +50°C in $CDCl_3$, but rotational dynamics still interfered with definite anomeric determination and the imidates are tentatively assigned based on ^{13}C chemical shift; imidate anomeric mixtures served as a reference. [c]These imidates were formed as an anomeric mixture and isolated as separate anomers, indicated is the anomer used in the reaction. [d]Calculated yields from isolated mixed fractions. [e]Yield not determined, ratios obtained from crude ^{1}H NMR.

anomers (product **40**), identical to the reaction of the corresponding tri-*O*-benzyl donor. The uronic acid xyloside donor **12** is the least selective (entry 12, Table 1), giving roughly equal amounts of both the α- and the β-product (**32**). The reactions of the xylosides also provided significant quantities of different side products. Beside **45**, the product originating from an intramolecular electrophilic aromatic substitution, the yet unreported trifluoro-*N*-phenylacetamide linked glycosides (**41**-**44**) were formed (Figure 4). The furanosides with other configurations only showed minor amounts of these side products.

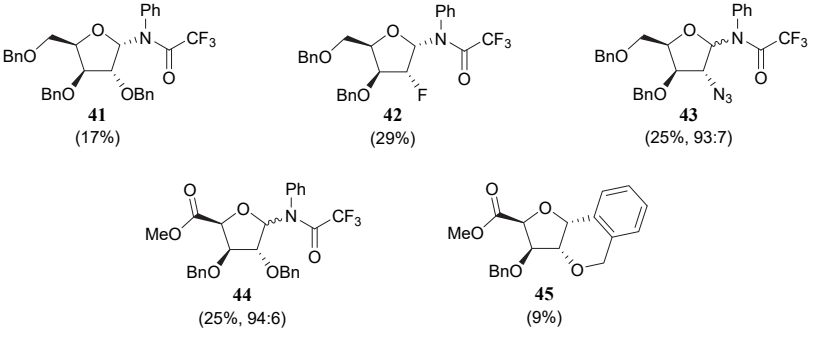


Figure 4. Side products **41**-**45** identified as side products, percentages obtained from the crude ^{1}H NMR.

Computations

With the experimental glycosylation stereoselectivity data available, the computational studies of the intermediate oxocarbenium ions were undertaken next. The oxocarbenium ions which are used in DFT calculations are displayed in Figure 3 and they are all protected with *O*-methyl ethers to limit rotational degrees of freedom and reduce computational cost.

The DFT calculations were executed by screening all the conformations on the pseudo-rotational circle, akin to the method described by van Rijssel *et al*. An initial geometry-optimized structure was taken as the base conformation and by changing the dihedral angles of the ring atoms, a set of 81 conformations was generated, with a maximum ring puckering of 40° (See Experimental section). While these dihedral angles were constrained, the other internal coordinates were allowed to change in the subsequent energy optimization calculations, performed by the Gaussian 03 software package,[30] at a computational level of B3LYP/6-311G**. Three separate sets of 81 conformations each were generated for the *gg*, *gt*, and *tg* C-4–C-5 rotamers respectively,

totaling 243 data points. For the uronic acids, two sets of 81 conformations, for the eclipsed and bisected structures, were assessed providing 162 data points. The energy obtained from the DFT calculations was corrected for solvation in DCM by a polarized continuum model (PCM). Additionaly, a Gibbs free energy correction was applied at the temperature of the glycosylation reactions.[31] The energy of all conformers was then visualized as a polar contour plot on the pseudo-rotational circle, with isoenergetic values as the contour lines, resulting in the Conformational Energy Landscape (CEL) maps (*vide infra*). Separate CEL maps are generated for the C-4–C-5 bond rotamers (*gg*, *gt*, *tg*, or eclipsed and bisected).

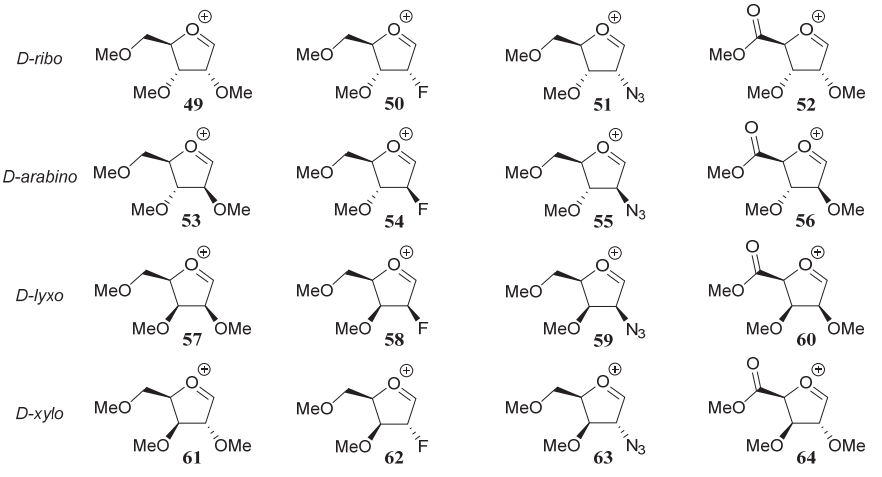
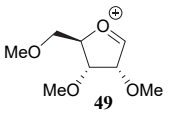
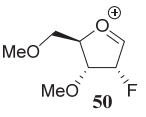
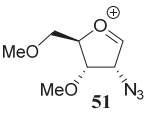
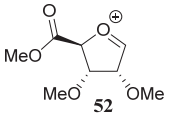
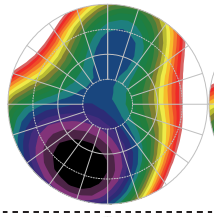
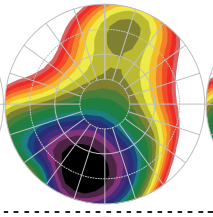
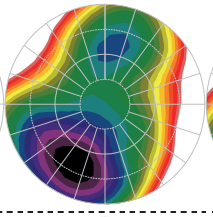
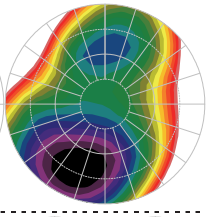
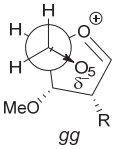
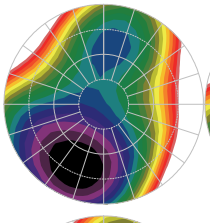
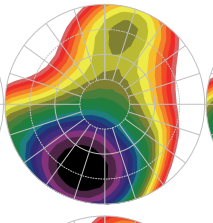
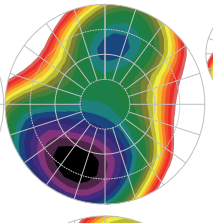
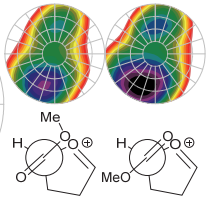
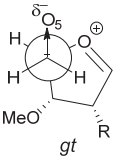
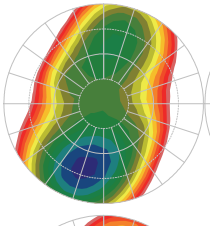
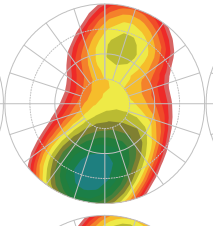
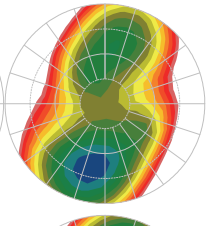
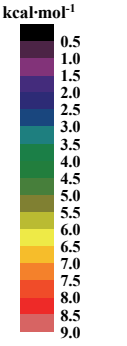
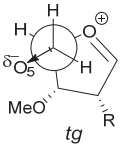
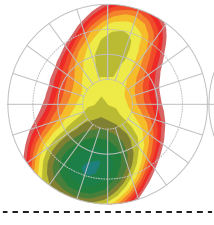
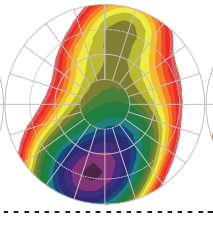
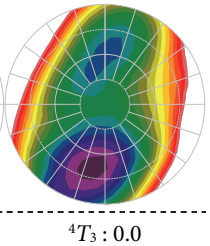
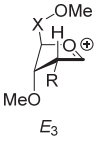
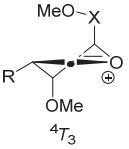
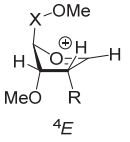
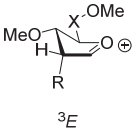


Figure 3. Oxocarbenium ions evaluated computationally in this chapter.

The modifications at C-2 and C-5 have been be examined for each configuration and Tables 2-5 report the CEL maps for each configuration, the contributions of each C-4–C-5 rotamer, the relative energy of the most favorable conformations, as well as the experimental stereoselectivities.

The results of the computational study of the *ribo*-configured furanosyl oxocarbenium ions **49-52** are provided in Table 2. The overall shape of the energy landscape is comparable for all four ions in the combined rotamer CEL maps, with the energy minima centered on the E_3 conformation, which places all the individual substituents in their most favorable orientation. The three individual rotamers provide similar maps for the different C-2 modifications, with *gg* being clearly the most favorable rotamer, as this species benefits from a stabilizing interaction of the O-5 lone pairs and the electron depleted anomeric center. The uronic acid has two low-energy C-4–C-5

Table 2. CEL maps of *ribo*-configured oxocarbenium ions **49**-**52**.

Ribose	 **49**	 **50**	 **51**	 **52**
Combined rotamers				
gg	 			
gt	 			
tg	 			
Energies (kcal·mol^{-1})	E_3 : 0.0 $^4T_3$: 1.1 ^4E : 1.1 ^3E : 1.9	E_3 : 0.0 $^4T_3$: 0.5 ^4E : 1.5 ^3E : 5.2	$^4T_3$: 0.0 E_3 : 0.1 ^4E : 1.4 ^3E : 2.8	E_3 : 0.0 $^4T_3$: 0.3 ^3E : 2.5
	 E_3	 $^4T_3$	 ^4E	 ^3E
Experimental (α : β)	>98 : 2	>98 : 2	>98 : 2	>98 : 2

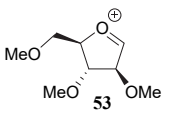
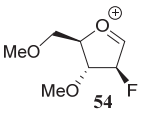
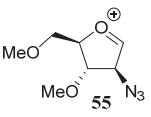
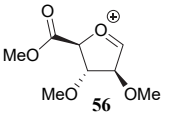
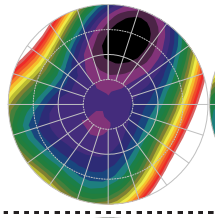
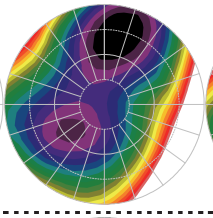
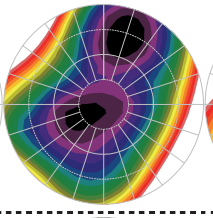
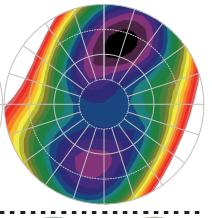
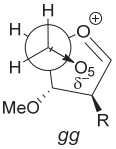
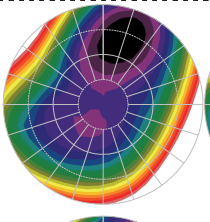
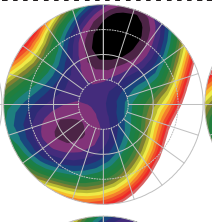
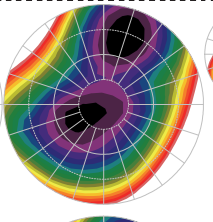
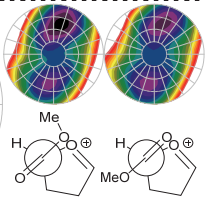
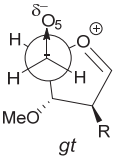
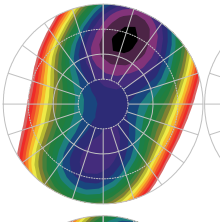
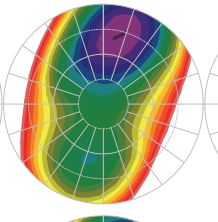
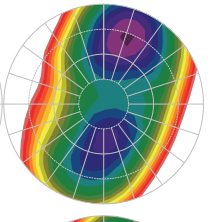
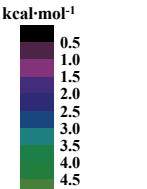
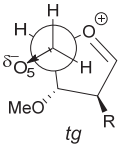
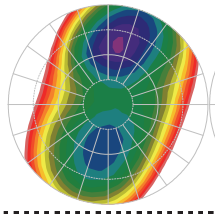
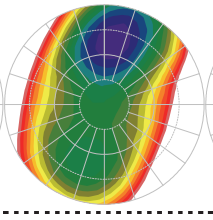
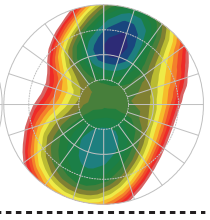
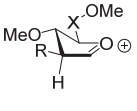
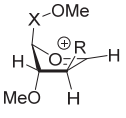
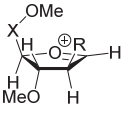
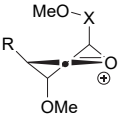
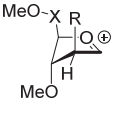
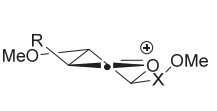
R =OMe, F, or N_3; X = CH_2 or C=O.

rotamers, being the eclipsed and bisected ones. Apparently both can benefit from a charge-stabilizing interaction by the lone pairs of the oxygen atoms of the uronic acid ester. The CEL maps of both are similar, with the stabilization originating from the C=O being somewhat more favorable than the stabilization of the OMe group. The most appreciable structural difference that can be derived from the CEL maps of the four ribosyl oxocarbenium ions, is the stronger tendency of the fluorine atom to occupy a *pseudo*-equatorial orientation. The ^{3}E conformer of **50** is 5.2 kcal·mol^{-1} higher in energy than the lowest energy E_3 conformer, whereas this difference is only 1.9 kcal·mol^{-1} for **49** and around 2.5 kcal·mol^{-1} for **51** and **52**. The introduction of an electron-withdrawing substituent on C-2 or C-5 also led to the decrease of the relative energy of the twist $^{4}T_3$ structures, closely related to the E_3 conformation. Using the lowest energy E_3 conformers, or closely related $^{4}T_3$ structures, as product forming intermediates the formation of the 1,2-*cis*-products can be accounted for using the inside attack model. Thus the stereoelectronic effects of the C-2–OBn, C-2–F and C-2–N_3 on the stability and reactivity of the intermediate oxocarbenium ions appear to be very similar.

The CEL maps for *arabino*-configured furanosyl oxocarbenium ions **53-56** (depicted in Tabel 3) also have a very similar overall shape, with the energy minima at the ^{3}E conformations. The substituents for *arabino*-configured furanosyl oxocarbenium ions cannot simultaneously take up a most stabilizing orientation and the contribution of the C-2–H hyperconjugation seems to be most dominating, resulting in the ^{3}E as the lowest energy structure. The three C-4–C-5 rotamers show the expected order of stability: *gg* > *gt* > *tg*. There are small structural differences apparent caused by the stereoelectronic effects of the fluoro, and azido groups respectively. The ^{3}E conformation is clearly the most stable structure, but a second minimum appears on the other side of the CEL map at a minimally puckered E_3 conformation. The largest difference is seen for the C-2–N_3 *gg*-rotamer, where a second minimum-energy conformer can be found for structures adopting a $^{4}T_3/^{4}E$ conformation with minimal puckering, and one without any puckering (Figure 5). The uronic acid oxocarbenium ion **56** preferentially takes up a ^{3}E structure, with the related $^{3}T_4$ conformation being relatively close in energy (0.9 kcal·mol^{-1}).

The stereoselectivity of the condensation reactions of the arabinofuranosyl donors, which are all highly 1,2-*cis*-selective, may be explained using the $^{3}E/^{3}T_4$ structures as product forming intermediates. This would indicate that attack on the more flat C-2–N_3 oxocarbenium ions is relatively unfavorable.

Table 3. CEL maps of *arabino*-configured oxocarbenium ions **53-56**.

Arabinose	 **53**	 **54**	 **55**	 **56**
Combined rotamers				
gg	 			
gt	 			
tg	 			
Energies (kcal·mol^{-1})	^3E : 0.0 *flat*-E_3 : 1.2 E_3 : 2.2	^3E : 0.0 *flat*-^4E : 0.6 *flat*-$^4T_3$: 1.1 *flat*-E_3 : 1.2	^3E : 0.0 *flat*-^4E : 0.3 *flat*: 0.4 *flat*-E_3 : 0.9	^3E : 0.0 $^3T_4$: 0.9 E_3 : 1.2
	 ^3E	 ^4E	 *flat*	 $^4T_3$	 E_3	 $^3T_4$
Experimental (α : β)	<2 : 98	<2 : 98	<2 : 98	5 : 95

R =OMe, F, or N_3; X = CH_2 or C=O.

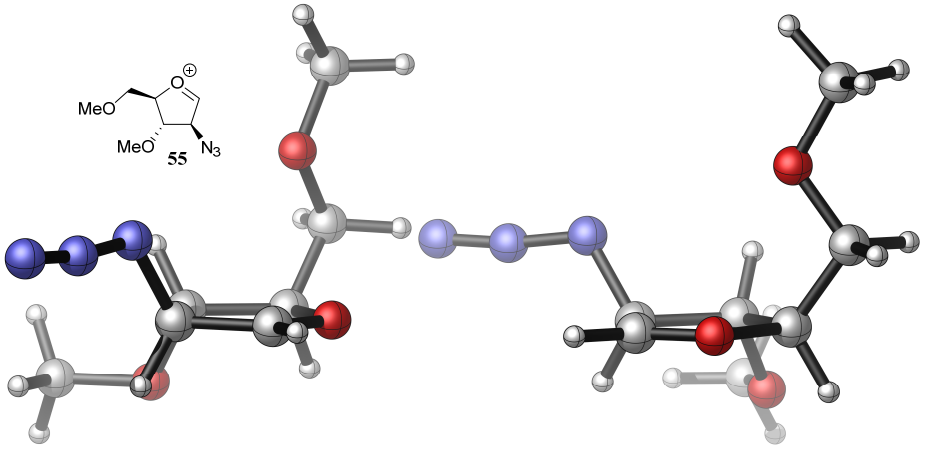
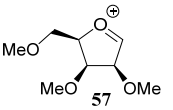
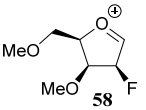
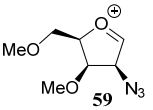
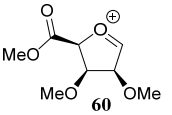
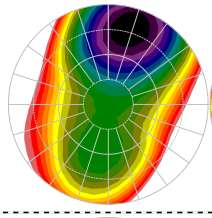
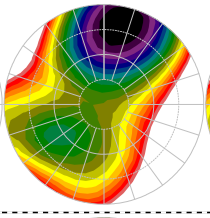
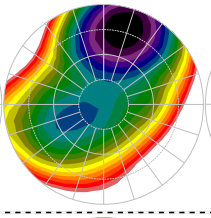
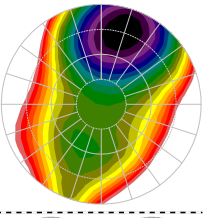
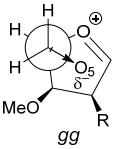
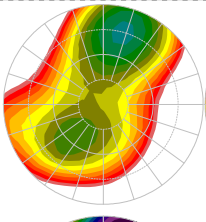
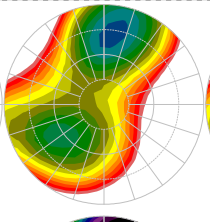
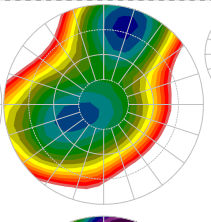
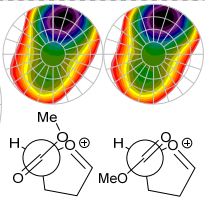
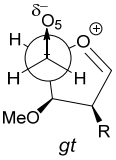
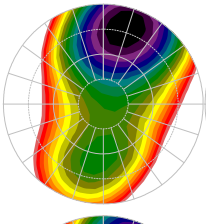
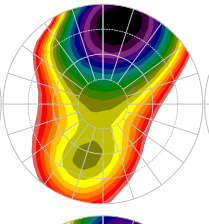
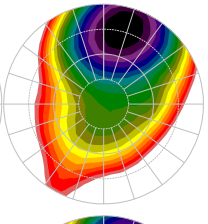
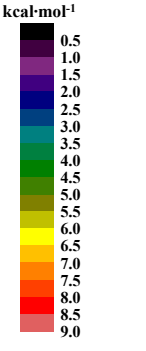
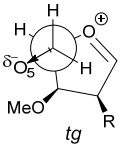
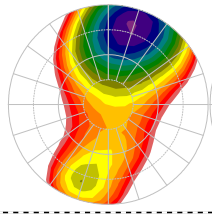
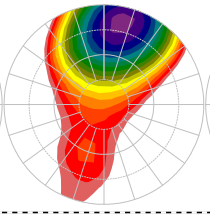
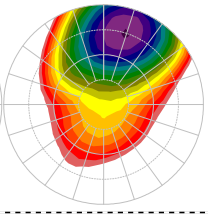
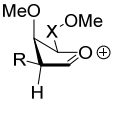
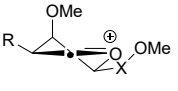
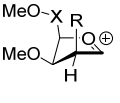


Figure 5. Ball-stick model of the *flat* conformation of 2-azidoarabinosyl oxocarbenium ion **55**, viewed through the C-2–C-3 bond and C-1–C-2 bond respectively.

All *lyxo*-configured oxocarbenium ions **57**-**60** (Table 4) show a single energy minimum on the ^{3}E side of the CEL map. The difference in energy between this structure and the other conformers appears to be even larger than the energy differences observed for the ribosyl oxocarbenium ions. This can be understood by realizing that the 'inverted' envelope, the E_3, not only loses the stabilizing interactions of the C-2 and C-3 substituents, but also experiences severe 1,3-diaxial interactions between the C-2 and C-4 groups, especially for the electronically most favorable *gg*-rotamer. In the most stable ^{3}E conformer, the steric interaction between the C-5–OMe and the C-3–OMe (a 1,3-diaxial like interaction) increases the relative energy of the *gg*-rotamer, and the *gt*-rotamer is the most favorable rotamer providing the energy minimum in the overall CEL map. Also in the *lyxo*-case, the effect of the different substituents is minimal, although structures occupying a $^{3}T_{4}$ conformation are relatively favorable for all three modifications (being 1.2-2.1 kcal·mol^{-1} higher in energy than the neighboring E_3 envelopes). Again the lowest energy oxocarbenium ions account for the observed experimental all-*cis* stereoselectivity, following the inside attack model.

Table 4. CEL maps of *lyxo*-configured oxocarbenium ions **57-60**.

Lyxose	 **57**	 **58**	 **59**	 **60**
Combined rotamers				
gg	 			
gt	 			
tg	 			
Energies (kcal·mol^{-1})	^3E : 0.0 E_3 : 4.2	^3E : 0.0 *flat*-$^3T_4$: 2.1 E_3 : 4.7	^3E : 0.0 $^3T_4$: 1.4 *flat*-E_3 : 3.2	^3E : 0.0 $^3T_4$: 1.2 E_3 : 4.4
	 ^3E	 $^3T_4$	 E_3	
Experimental (α : β)	<2 : 98	<2 : 98	<2 : 98	<2 : 98

R =OMe, F, or N_3; X = CH_2 or C=O.

Finally, the *xylo*-configured oxocarbenium ions **61**-**64** (Table 5) were assessed. Again, the CEL maps of the differently functionalized xylosides appear to be rather similar. Two minima are apparent on either side of the CEL maps. These minima originate from C-4–C-5 rotamers, with the *gg*- and *gt*-rotamers leading to low energy E_3-like and ^3E-like structures respectively. The energy minima located on the south side of the CEL maps are relatively 'broad' and not only encompass the E_3 conformations but also, as noted earlier by van Rijssel *et al.*, the $^4T_3$ structures, and perhaps more striking, the ^4E envelope conformation. This latter conformer is in fact the lowest energy species for 2-fluoroxyloside **62** and xylosyl uronate **64**. This conformation is unable to use the stabilizing effect of the O-3 lone electron pairs, or the hyperconjugation of the C–H bond on C-2 to its full extent (Figure 6). Instead, the driving stabilization now appears to be the interaction of the C-5–*O*-benzyl with the anomeric center. In the ^4E conformation, the steric interactions between C-5 and the substituents at C-3 and the C-2–H are reduced when compared to the sterically unfavorable situation in the E_3 conformer.

When the relative energy of the different configurations is compared, it becomes clear that the xylose oxocarbenium ions are higher in energy than their configurational counterparts. This may, in part, account for the higher amount of side products formed in the reactions of the xylosyl donors.[32] The established broad energy minima may be at the basis for the poor stereoselectivity observed in the condensations of the xylosyl donors as attack of the ^4E conformers (See Figure 6) may occur from both sides of the ring.

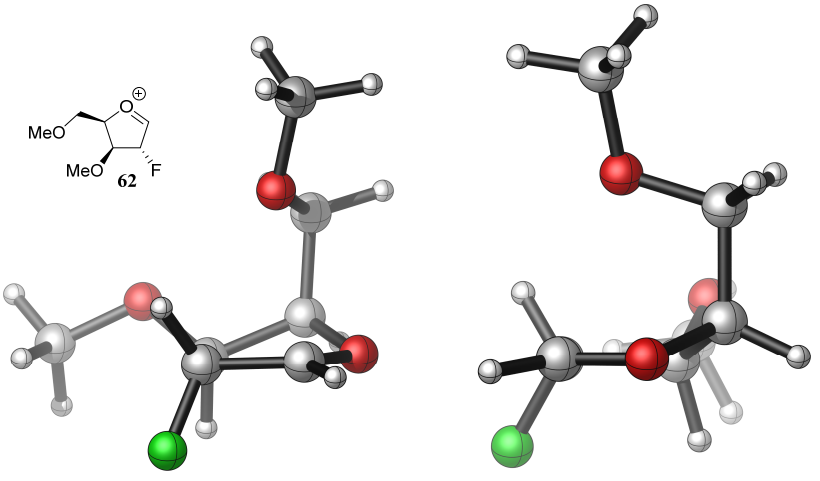
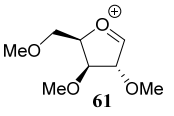
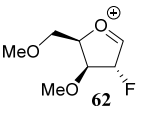
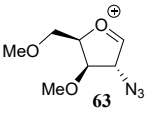
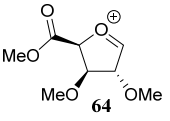
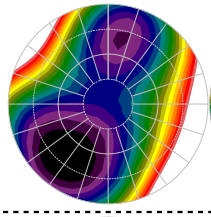
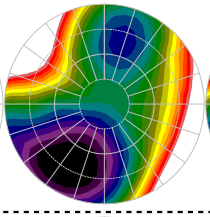
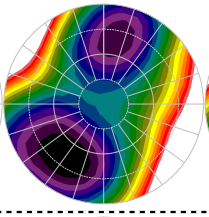
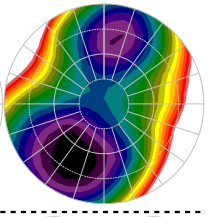
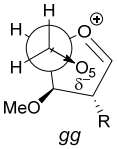
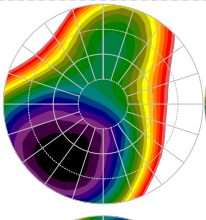
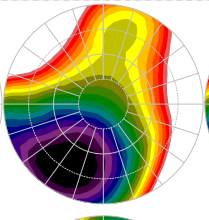
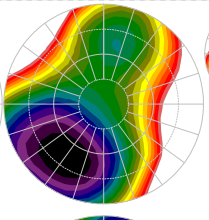
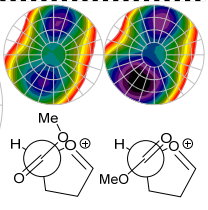
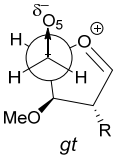
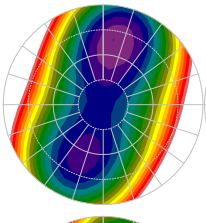
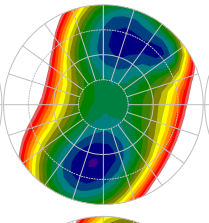
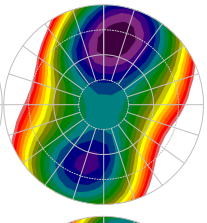
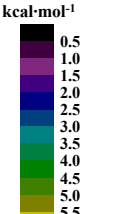
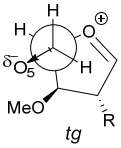
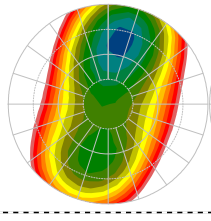
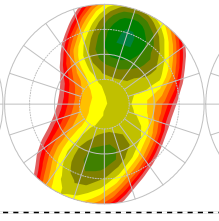
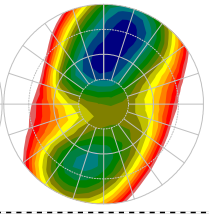
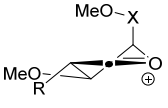
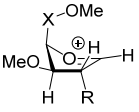
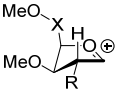
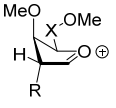


Figure 6. Ball-stick model of the ^4E conformation of 2-fluoroxylosyl oxocarbenium ion **62**, viewed through the C-2–C-3 bond and C-1–C-2 bond respectively.

Table 5. CEL maps of *xylo*-configured oxocarbenium ions **61-64**.

Xylose	 **61**	 **62**	 **63**	 **64**
Combined rotamers				
gg	 			
gt	 			
tg	 			
Energies (kcal·mol^{-1})	$^4T_3$: 0.0 ^4E : 0.4 E_3 : 0.4 ^3E : 1.0	$^4T_3$: 0.0 ^4E : 0.0 E_3 : 0.1 ^3E : 2.3	$^4T_3$: 0.0 E_3 : 0.2 ^4E : 0.5 ^3E : 0.8	^4E : 0.0 E_3 : 0.2 *flattened*-$^4T_3$: 0.4 ^3E : 1.1
	 $^4T_3$	 ^4E	 E_3	 ^3E
Experimental (α : β)	85 : 15	70 : 30	85 : 15	45 : 55

R =OMe, F, or N_3; X = CH_2 or C=O.

Conclusions

A set of twelve functionalized furanosides has been glycosylated under conditions favoring an S_N1-type substitution reaction with allyltrimethylsilane or triethylsilane-*d* to investigate the stereoselectivity of these reactions. The experimental results have been complemented by computational studies, generating Conformational Energy Landscape (CEL) maps for the intermediate oxocarbenium ions. Striking similarities have been observed for the CEL maps of the oxocarbenium ions featuring different C-2 and C-5 substituents and –as a result– very similar stereoselectivities are obtained in the glycosylations of the different donors. Nonetheless, the CEL map method also revealed conformers different from the ^3E-E_3 pair as relatively stable conformers and structural deviations to ^4E, $^4T_3$, $^3T_4$ and flat conformations have been revealed in some cases for the 2-fluoro, 2-azido, and 5-methyl uronate substituted species. The changes in the population of the different conformational states of the reactive intermediate only had a minor effect on the outcome of the glycosylations, which where across the board highly 1,2-*cis*-selective, except for the *xylo*-configured furanosides which consistently provided anomeric mixtures. The appearance of more low-energy conformations for the *xylo*-configured oxocarbenium ions could account for the erosion of stereoselectivity. CEL maps with a localized single energy minimum corresponded to reactions that are completely stereoselective. Overall, the study described here has shown that the nature of the substituent, C-2–OBn *vs* –F or $-N_3$ and C-4–CH_2OBn *vs* $-CO_2$Me, does not significantly affect the structure of the intermediate ions and the course of the S_N1-type reactions studied here. This stands in sharp contrast to the effect that these substituents have in glycosylations of pyranosyl donors (See for example chapter 4 and 6). The effect of the different substituents in this case can probably best be reconciled with a change in the S_N2-S_N1 reaction mechanism continuum.

Experimental section

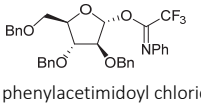
General procedure for furanoside imidate glycosylations. The imidate donor (0.1 mmol, 1 eq.) was coevaporated twice with dry toluene and then dissolved in dry DCM (1 mL). Activated 3 Å molecular sieves and the acceptor (2 or 4 eq.) were added and the solution was stirred for 30 min at room temperature under an inert atmosphere (N_2 or Ar). The reaction mixture was cooled to the indicated temperature and a freshly prepared stock solution (0.2 M in DCM) of TMSOTf or TfOH was introduced via syringe (50 µL, 0.01 mmol, 0.1 eq.). The reaction mixture was stirred for 1-4 days at the indicated temperature, and was then quenched by the addition of sat. aq. $NaHCO_3$. The mixture was diluted with H_2O and twice extracted with DCM. The combined organic layers were dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (1/0 to 80/20 pentane/Et_2O) to provide the glycosylated furanoside.

General procedure for quantum mechanical calculations. Analogous to the work of van Rijssel,[24] all calculations were performed with DFT calculations with the B3LYP hybrid functional. The starting conformer for the Conformational Energy Landscapes (CEL) was obtained by a conformer distribution search in the Spartan 10 program in the gas phase, with a 6-31G(d) basis set. All resulting geometries were further optimized at the 6-311G(d,p) level in the Gaussian 03 program, with a polarized continuum model (PCM) to correct for solvation in dichloromethane, and further corrected for their zero-point energy (ZPE). The geometry with the lowest, ZPE corrected solvated energy, was selected and used as the starting geometry for the CEL. Two dihedral angles of the five-membered ring were constrained: C4-O4-C1-C2 and C1-C2-C3-C4 by scanning with 10° per step, over 9 steps (-40° to 40°), totaling 81 conformations spanning the entire pseudo rotational sphere with a maximum puckering amplitude (τ_m) of 40°. All other internal coordinates were unconstrained. Three separate staggered rotamers (*gg*, *gt*, *tg*) of the O4-C4-C5-O5 dihedral angle (-65°, 65°, 175°) were considered and their CEL maps were calculated separately by pre-rotating the C4-C5 bond (not constrained), bringing the total conformations for each configuration to 243 geometries. The final denoted free Gibbs energy was calculated using Equation (1) in which ΔE_{gas} is the gas-phase energy (electronic energy), ΔG^T_{gas} (T = 298.15 K and pressure = 1 atm.) is the sum of corrections from the electronic energy to free Gibbs energy in the harmonic oscillator approximation also including zero-point-vibrational energy, and ΔG^T_{solv} is their corresponding free solvation Gibbs energy.

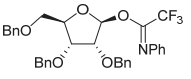
$$\Delta G^T_{in\ solution} = \Delta E_{gas} + \Delta G^T_{gas} + \Delta G_{solv} \quad (1)$$

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

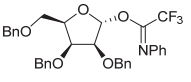
All found minima were checked for negative frequencies. The CEL was visualized as a polar contour plot by the Origin pro 9 software, with the energy plotted as 0.5 kcal·mol^{-1} colored intervals, the phase angle P as the azimuth angle and the puckering amplitude (τ_m) as the radius, with a smoothing factor of 0.001. The computed stereoselectivity was based on the ^3E - E_3 two conformer (inside-attack) model, as the ratio of conformers obtained from the Boltzmann distribution over these two conformers, at the temperature of the experiment.



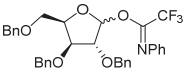
2,3,5-tri-*O*-benzyl-1-*O*-(*N*-[phenyl]trifluoroacetimidoyl)-α-D-arabinofuranoside (6). The arabinofuranose lactol[24] (421 mg, 1 mmol) was dissolved in acetone (6 mL) and H_2O (0.1 mL) and cooled to 0°C. Cs_2CO_3 (358 mg, 1,1 mmol, 1.1 eq.) and 2,2,2-trifluoro-*N*-phenylacetimidoyl chloride (317 µL, 2 mmol, 2 eq.) were added and the reaction mixture stirred overnight. Very little conversion was observed (TLC-analysis), therefore DBU (0.12 mL) was added and the conversion was complete immediately. The reaction mixture was reduced in volume under reduced pressure and H_2O was added. The aqueous phase was extracted twice with DCM and the combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure. Flash column chromatography (0-15% Et_2O/pentane, with 0.5% Et_3N) of the residue provided the target imidate donor. Yield = 425 mg, 0.72 mmol, 72% as a waxy solid. R_f: 0.81 (85/15 pentane/Et_2O). ^{1}H NMR ($CDCl_3$, *T* = 323 K, 400 MHz, HH-COSY, HSQC): δ 7.32 – 7.22 (m, 17H, CH_{arom}), 7.09 – 7.01 (m, 1H, NPh), 6.80 (d, 2H, *J* = 8.0 Hz, NPh), 6.27 (bs, 1H, H-1), 4.60 – 4.47 (m, 6H, 3xCH_2 Bn), 4.45 (q, 1H, *J* = 5.1 Hz, H-4), 4.23 (d, 1H, *J* = 1.8 Hz, H-2), 4.03 (dd, 1H, *J* = 5.5, 2.0 Hz, H-3), 3.63 (d, 2H, *J* = 5.1 Hz, H-5, H-5); ^{13}C-APT NMR ($CDCl_3$, *T* = 323 K, 101 MHz, HSQC): δ 144.0 (C_q NPh), 138.1, 137.9, 137.4 (C_q Bn), 128.8, 128.5, 128.5, 128.4, 127.9, 127.9, 127.8, 127.7, 124.3, 119.8 (CH_{arom}), 104.0 (C-1), 87.0 (C-2), 84.1 (C-4), 83.8 (C-3), 73.5, 72.3 (CH_2 Bn), 69.7 (C-5); HRMS: $[M+Na]^+$ calcd for $C_{34}H_{32}F_3NO_5Na$ 614.21217, found 614.21248.



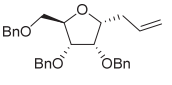
2,3,5-tri-*O*-benzyl-1-*O*-(*N*-[phenyl]trifluoroacetimidoyl)-β-D-ribofuranoside (5). The ribofuranose lactol[24] (421 mg, 1 mmol) was dissolved in acetone (6 mL) and H_2O (0.1 mL) and cooled to 0°C. Cs_2CO_3 (489 mg, 1,5 mmol, 1.5 eq.) and 2,2,2-trifluoro-*N*-phenylacetimidoyl chloride (238 µL, 1.5 mmol, 1.5 eq.) were added and the reaction mixture stirred for 2 days. The reaction mixture was reduced in volume under reduced pressure and H_2O was added. The aqueous phase was extracted twice with DCM and the combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure. Flash column chromatography (0-15% Et_2O/pentane, with 0.5% Et_3N) of the residue provided the target imidate donor. Yield = 327 mg, 0.55 mmol, 55% as a colourless oil. R_f: 0.15 (95/5 pentane/Et_2O). Spectroscopic data were in accord with those previously reported.[33] ^{1}H NMR ($CDCl_3$, *T* = 295 K, 400 MHz, HH-COSY, HSQC): δ 7.34 – 7.26 (m, 17H, CH_{arom}), 7.14 – 7.06 (m, 1H, NPh), 6.80 (d, 2H, *J* = 7.5 Hz, NPh), 6.33 (bs, 1H, H-1), 4.75 – 4.50 (m, 5H, 2xCH_2 Bn, C*H*H Bn), 4.49 – 4.43 (m, 2H, CH*H* Bn, H-4), 4.16 (dd, 1H, *J* = 7.3, 4.7 Hz, H-3), 4.07 (d, 1H, *J* = 4.0 Hz, H-2), 3.71 (dd, 1H, *J* = 11.0, 3.1 Hz, H-5), 3.59 (dd, 1H, *J* = 11.0, 4.9 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, *T* = 295 K, 101 MHz, HSQC): δ 143.8 (C_q NPh), 138.2, 137.5, 137.4 (C_q Bn), 128.8, 128.5, 128.5, 128.4, 128.2, 128.1, 128.0, 127.9, 127.6, 124.3, 119.7 (CH_{arom}), 102.5 (C-1), 82.2 (C-4), 78.5 (C-2), 77.3 (C-3), 73.3, 72.7, 72.3 (CH_2 Bn), 70.0 (C-5).



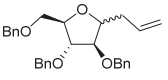
2,3,5-tri-*O*-benzyl-1-*O*-(*N*-[phenyl]trifluoroacetimidoyl)-α-D-lyxofuranoside (7). The lyxofuranose lactol[24] (660 mg, 1,58 mmol) was dissolved in acetone (8 mL) and H_2O (0.5 mL) and cooled to 0°C. Cs_2CO_3 (619 mg, 1,9 mmol, 1.2 eq.) and 2,2,2-trifluoro-*N*-phenylacetimidoyl chloride (500 µL, 3.17 mmol, 2 eq.) were added and the reaction mixture stirred overnight. Very little conversion was observed (TLC-analysis), therefore DBU (0.2 mL) was added and the conversion was complete immediately. The reaction mixture was reduced in volume under reduced pressure and coevaporated with dioxane and toluene. The residue was dissolved in DCM and filtered over Celite, the filtrate was concentrated under reduced pressure. Flash column chromatography (0-15% Et_2O/pentane, with 0.5% Et_3N) of the residue provided the target imidate donor. Yield = 930 mg, 1.57 mmol, 100% as a white solid. R_f: 0.8 (85/15 pentane/Et_2O). ^{1}H NMR ($CDCl_3$, *T* = 323 K, 400 MHz, HH-COSY, HSQC): δ 7.34 – 7.20 (m, 17H, CH_{arom}), 7.09 – 7.01 (m, 1H, NPh), 6.78 (d, 2H, *J* = 8.0 Hz, NPh), 6.31 (bs, 1H, H-1), 4.68 – 4.44 (m, 7H, 3xCH_2 Bn, H-4), 4.25 (t, 1H, *J* = 5.1 Hz, H-3), 4.13 (d, 1H, *J* = 4.2 Hz, H-2), 3.83 (dd, 1H, *J* = 10.5, 4.7 Hz, H-5), 3.76 (dd, 1H, *J* = 10.4, 7.3 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, *T* = 323 K, 101 MHz, HSQC): δ 143.9 (C_q NPh), 138.2, 137.9, 137.5 (C_q Bn), 129.3, 128.8, 128.5, 128.4, 128.4, 128.0, 127.9, 127.8, 127.7, 124.4, 119.7 (CH_{arom}), 103.0 (C-1), 81.7 (C-2), 80.5 (C-4), 77.4 (C-3), 73.5, 73.5, 72.9 (CH_2 Bn), 69.5 (C-5).



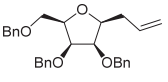
2,3,5-tri-*O*-benzyl-1-*O*-(*N*-[phenyl]trifluoroacetimidoyl)-α/β-D-xylofuranoside (8). The xylofuranose lactol[24] (421 mg, 1 mmol) was dissolved in acetone (10 mL) and cooled to 0°C. 2,2,2-Trifluoro-*N*-phenylacetimidoyl chloride (190 µL, 1.2 mmol, 1.2 eq.) and DBU (165 µL, 1.1 mmol, 1.1 eq.) were added and the reaction mixture stirred for 1 h. The reaction mixture was reduced in volume under reduced pressure and H_2O was added. The aqueous phase was extracted twice with DCM and the combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure. Flash column chromatography (0-15% Et_2O/pentane, with 0.5% Et_3N) of the residue provided the target imidate donor. Yield = 427 mg, 0.72 mmol, 72% as a waxy solid. R_f: 0.38 and 0.47 (9/1 pentane/Et_2O). Data for the β-anomer: ^{1}H NMR ($CDCl_3$, *T* = 295 K, 400 MHz, HH-COSY, HSQC): δ 7.34 – 7.18 (m, 17H, CH_{arom}), 7.05 (t, 1H, *J* = 7.4 Hz, NPh), 6.77 (d, 2H, *J* = 7.6 Hz, NPh), 6.30 (bs, 1H, H-1), 4.65 (q, 1H, *J* = 5.6 Hz, H-4), 4.60 – 4.42 (m, 6H, 3xCH_2 Bn), 4.24 (s, 1H, H-2), 4.10 (d, 1H, *J* = 5.4 Hz, H-3), 3.86 (dd, 1H, *J* = 10.4, 5.1 Hz, H-5), 3.80 (dd, 1H, *J* = 10.2, 7.2 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, *T* = 295 K, 101 MHz, HSQC): δ 143.9 (C_q NPh), 138.2, 137.7, 137.2 (C_q Bn), 129.1, 128.7, 128.5, 128.4, 128.3, 128.0, 127.8, 127.7, 127.6, 127.5, 124.2, 119.6 (CH_{arom}), 103.5 (C-1), 84.5 (C-2), 83.0 (C-4), 81.1 (C-3), 73.4, 72.4, 72.1 (CH_2 Bn), 69.1 (C-5).



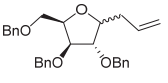
Allyl 2,3,5-tri-*O*-benzyl-1-deoxy-α-D-ribofuranoside (25). Donor **5** and allyltrimethylsilane (2 eq.) were condensed using the general procedure for furanosyl imidate glycosylations at -78°C for 24 h with TMSOTf as the promotor. R_f: 0.27 (19/1 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[34] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.40 – 7.23 (m, 15H, CH_{arom}), 5.79 (ddt, 1H, *J* = 17.1, 10.2, 6.9 Hz, CH allyl), 5.10 (dq, 1H, *J* = 17.2, 1.5 Hz, C*H*H allyl), 5.04 (ddt, 1H, *J* = 10.2, 2.1, 1.1 Hz, CH*H* allyl), 4.81 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.64 – 4.45 (m, 5H, CH*H* Bn, 2xCH_2 Bn), 4.21 (dt, 1H, *J* = 7.1, 3.5 Hz, H-4), 4.10 (dd, 1H, *J* = 7.1, 4.3 Hz, H-3), 4.05 (td, 1H, *J* = 7.0, 3.9 Hz, H-1), 3.98 (t, 1H, *J* = 4.1 Hz, H-2), 3.63 (dd, 1H, *J* = 10.7, 3.3 Hz, H-5), 3.52 (dd, 1H, *J* = 10.7, 3.8 Hz, H-5), 2.51 (t, 2H, *J* = 7.0 Hz, CH_2 allylic); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.6, 138.4, 138.1 (C_q Bn), 135.1 (CH allyl), 128.5, 128.4, 128.4, 127.9, 127.8, 127.8, 127.7, 127.7 (CH_{arom}), 117.0 (CH_2 allyl), 80.2 (C-1), 80.1 (C-3), 79.6 (C-4), 77.7 (C-2), 73.5, 73.4, 72.8 (CH_2 Bn), 70.2 (C-5), 34.4 (CH_2 allylic); HRMS: $[M+NH_4]^+$ calcd for $C_{29}H_{36}NO_4$ 462.26389, found 462.26382.



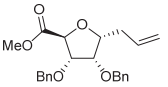
Allyl 2,3,5-tri-*O*-benzyl-1-deoxy-α/β-D-arabinofuranoside (26). Donor **6** and allyltrimethylsilane (2 eq.) were condensed using the general procedure for furanosyl imidate glycosylations at -78°C for 24 h with TMSOTf as the promotor. (α:β = 10:90). Spectroscopic data were in accord with those previously reported.[35] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.36 – 7.23 (m, 15H, CH_{arom}), 5.80 (ddt, 1H, *J* = 17.1, 10.2, 7.0 Hz, CH allyl), 5.15 – 5.00 (m, 2H, CH_2 allyl), 4.61 – 4.47 (m, 5H, 2x CH_2 Bn, C*H*H Bn), 4.36 (d, 1H, *J* = 11.9 Hz, CH*H* Bn), 4.08 (td, 1H, *J* = 6.7, 2.8 Hz, H-4), 4.03 (td, 1H, *J* = 7.0, 3.5 Hz, H-1), 3.92 (d, 1H, *J* = 2.7 Hz, H-3), 3.81 (d, 1H, *J* = 3.5 Hz, H-2), 3.63 (dd, 1H, *J* = 9.8, 5.8 Hz, H-5), 3.51 (dd, 1H, *J* = 9.8, 6.9 Hz, H-5), 2.52 – 2.47 (m, 2H, CH_2 allylic); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.3, 138.0, 137.9 (C_q Bn), 135.0 (CH allyl), 128.6, 128.5, 128.4, 127.9, 127.8, 127.8, 127.8, 127.7 (CH_{arom}), 117.1 (CH_2 allyl), 83.8 (C-3), 82.9 (C-2), 82.8 (C-4), 81.1 (C-1), 73.4, 71.5, 71.4 (CH_2 Bn), 70.7 (C-5), 33.3 (CH_2 allylic).



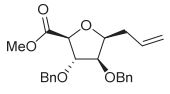
Allyl 2,3,5-tri-*O*-benzyl-1-deoxy-β-D-lyxofuranoside (27). Donor **7** and allyltrimethylsilane (2 eq.) were condensed using the general procedure for furanosyl imidate glycosylations at -78°C for 24 h with TMSOTf as the promotor. R_f: 0.47 (9/1 pentane/EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.36 – 7.24 (m, 15H, CH_{arom}), 5.82 (ddt, 1H, *J* = 17.1, 10.2, 7.0 Hz, CH allyl), 5.07 (dq, 1H, *J* = 17.1, 1.5 Hz, C*H*H allyl), 5.02 (ddt, 1H, *J* = 10.2, 2.2, 1.2 Hz, CH*H* allyl), 4.76 (d, 1H, *J* = 11.8 Hz, C*H*H Bn), 4.68 (d, 1H, *J* = 11.9 Hz, C*H*H Bn), 4.61 (d, 1H, *J* = 11.9 Hz, CH*H* Bn), 4.59 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.54 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.52 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.24 – 4.19 (m, 1H, H-4), 4.17 (dd, 1H, *J* = 6.1, 3.9 Hz, H-3), 4.01 – 3.94 (m, 2H, H-1, H-2), 3.83 (dd, 1H, *J* = 10.1, 4.8 Hz, H-5), 3.72 (dd, 1H, *J* = 10.1, 6.6 Hz, H-5), 2.53 – 2.46 (m, 2H, CH_2 allylic); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.6, 138.5, 138.4 (C_q Bn), 135.6 (CH allyl), 128.5, 128.4, 128.4, 127.9, 127.7, 127.7, 127.6, 127.5 (CH_{arom}), 116.7 (CH_2 allyl), 79.6 (C-3), 79.1 (C-1), 78.9 (C-2), 78.0 (C-4), 73.4, 73.3, 73.3 (CH_2 Bn), 70.5 (C-5), 35.4 (CH allylic); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 101 MHz): $^2J_{C1,H2}$ = +1.0 Hz, $^2J_{C2,H1}$ = +1.5 Hz, $^3J_{H2,C\text{-}allyl}$ = +1.6 Hz; HRMS: $[M+H]^+$ calcd for $C_{29}H_{33}O_4$ 445.23709, found 445.23704.



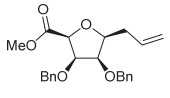
Allyl 2,3,5-tri-*O*-benzyl-1-deoxy-α/β-D-xylofuranoside (28). Donor **8** and allyltrimethylsilane (2 eq.) were condensed using the general procedure for furanosyl imidate glycosylations at -78°C for 24 h with TMSOTf as the promotor. R_f: 0.38 (92/8 pentane/Et_2O). Spectroscopic data were in accord with those previously reported for the β-anomer.[36] Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.40 – 7.22 (m, 15H, CH_{arom}), 5.78 (ddt, 1H, *J* = 17.1, 10.2, 6.9 Hz, CH allyl), 5.10 (dq, 1H, *J* = 17.2, 1.6 Hz, C*H*H allyl), 5.02 (ddd, 1H, *J* = 10.2, 2.2, 1.1 Hz, CH*H* allyl), 4.64 – 4.35 (m, 6H, 3xCH_2 Bn), 4.37 (td, 1H, *J* = 6.3, 4.1 Hz, H-4), 4.16 (td, 1H, *J* = 7.1, 3.7 Hz, H-1), 4.03 (dd, 1H, *J* = 4.1, 1.1 Hz, H-3), 3.83 (dd, 1H, *J* = 3.7, 1.1 Hz, H-2), 3.72 (dd, 1H, *J* = 9.6, 6.4 Hz, H-5), 3.67 (dd, 1H, *J* = 9.6, 6.3 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.4, 138.1, 138.0 (C_q Bn), 135.2 (CH allyl), 128.6, 128.5, 128.4, 127.9, 127.9, 127.8, 127.7 (CH_{arom}), 116.9 (CH_2 allyl), 81.8 (C-2), 81.4 (C-3), 80.1 (C-1), 78.8 (C-4), 73.5, 72.4, 72.1 (CH_2 Bn), 68.5 (C-5), 33.7 (CH_2 allylic); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 101 MHz): $^2J_{C1,H2}$ = +4.2 Hz, $^2J_{C2,H1}$ = +2.2 Hz, $^3J_{Callyl,H2}$ = +0.5 Hz; Diagnostic peaks for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 4.24 – 4.18 (m, 1H, H-4), 3.96 (dd, 1H, *J* = 3.9, 1.0 Hz, H-3), 3.92 (ddd, 1H, *J* = 7.1, 6.4, 3.5 Hz, H-1), 3.81 – 3.70 (m, 3H, H-2, H-5, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 134.6 (CH allyl), 117.3 (CH_2 allyl), 85.9 (C-2), 83.4 (C-1), 83.0 (C-3), 80.1 (C-4), 73.6, 71.7, 71.7 (CH_2 Bn), 68.5 (C-5), 38.5 (CH_2 allylic); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 101 MHz): $^2J_{C2,H1}$ = -4.0 Hz, $^3J_{Callyl,H2}$ = +4.5 Hz; HRMS: $[M+H]^+$ calcd for $C_{29}H_{33}O_4$ 445.23709, found 445.23734.



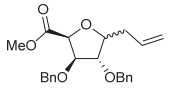
Methyl (1-allyl-2,3-di-*O*-benzyl-1-deoxy-α-D-ribofuranosyl uronate) (29). Donor **9** and allyltrimethylsilane (4 eq.) were condensed using the general procedure for furanosyl imidate glycosylations at -20°C for 100 h with TfOH as the promotor. Yield = 30.5 mg, 79 µmol, 79% as a white solid. R_f: 0.57 (4/1 pentane/EtOAc). $[\alpha]_D^{20}$ = +28.3° (*c* = 0.60, $CHCl_3$); IR (thin film): 698, 737, 916, 1026, 1099, 1144, 1206, 1275, 1356, 1454, 1748, 2868, 2922, 3030; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.38 – 7.27 (m, 10H, CH_{arom}), 5.77 (ddt, 1H, *J* = 17.1, 10.2, 6.9 Hz, CH allyl), 5.11 (dq, 1H, *J* = 17.2, 1.6 Hz, C*H*H allyl), 5.04 (ddt, 1H, *J* = 10.2, 2.0, 1.1 Hz, CH*H* allyl), 4.82 (d, 1H, *J* = 11.6 Hz, C*H*H Bn), 4.67 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.63 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.59 (d, 1H, *J* = 6.0 Hz, H-4), 4.56 (d, 1H, *J* = 11.6 Hz, CH*H* Bn), 4.22 (dd, 1H, *J* = 6.0, 4.5 Hz, H-3), 4.17 (td, 1H, *J* = 7.0, 4.1 Hz, H-1), 3.99 (t, 1H, *J* = 4.3 Hz, H-2), 3.73 (s, 3H, CH_3CO_2Me), 2.56 – 2.48 (m, 2H, CH_2 allylic); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 172.7 (C=O), 138.2, 137.6 (C_q), 134.6 (CH allyl), 128.6, 128.5, 128.1, 128.0, 127.9 (CH_{arom}), 117.3 (CH_2 allyl), 82.7 (C-3), 81.1 (C-1), 79.3 (C-4), 77.8 (C-2), 73.6, 72.8 (CH_2 Bn), 52.4 (CH_3CO_2Me), 34.0 (CH_2 allylic); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): $^2J_{C2,H1}$: +1.5 Hz, $^3J_{Callyl,H2}$: +0.7 Hz; HRMS: $[M+NH_4]^+$ calcd for $C_{23}H_{30}NO_5$ 400.21185, found 400.21173.



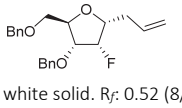
Methyl (1-allyl-2,3-di-*O*-benzyl-1-deoxy-β-D-arabinofuranosyl uronate) (30). Donor **10** and allyltrimethylsilane (4 eq.) were condensed using the general procedure for furanosyl imidate glycosylations at -20°C for 100 h with TfOH as the promotor. Yield = 29 mg, 76 µmol, 76% as a white solid (α:β = 5:95). R_f: 0.64 (4/1 pentane/EtOAc). $[\alpha]_D^{20}$ = +32.4° (*c* = 0.38, $CHCl_3$); IR (thin film): 698, 737, 916, 1028, 1101, 1207, 1279, 1454, 1726, 1761, 2920; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.44 – 7.18 (m, 10H, CH_{arom}), 5.79 (ddt, 1H, *J* = 17.1, 10.2, 7.0 Hz, CH allyl), 5.14 (dq, 1H, *J* = 17.1, 1.5 Hz, C*H*H allyl), 5.08 – 5.02 (m, 1H, CH*H* allyl), 4.66 (d, 1H, *J* = 11.9 Hz, C*H*H Bn), 4.56 (d, 1H, *J* = 11.9 Hz, CH*H* Bn), 4.51 (d, 1H, *J* = 1.7 Hz, H-4), 4.49 (d, 1H, *J* = 11.8 Hz, C*H*H Bn), 4.39 – 4.34 (m, 2H, CH*H* Bn, H-3), 4.21 (td, 1H, *J* = 7.2, 3.5 Hz, H-1), 3.81 (dd, 1H, *J* = 3.5, 0.8 Hz, H-2), 3.68 (s, 3H, CH_3 CO_2Me), 2.64 – 2.50 (m, 2H, CH_2 allylic); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 171.4 (C=O) 137.7, 137.5 (C_q), 134.7 (CH allyl), 128.6, 128.5, 128.1, 127.9, 127.9, 127.8 (CH_{arom}), 117.3 (CH_2 allyl), 85.2 (C-3), 82.4 (C-1), 81.6 (C-4), 81.3 (C-2), 71.9, 71.8 (CH_2 Bn), 52.3 (CO_2Me), 33.3 (CH_2 allylic); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): $^2J_{C1,H2}$ = +2.5 Hz, $^2J_{C2,H1}$ = +2.5 Hz, $^3J_{Callyl,H2}$ = +0.3 Hz; HRMS: $[M+Na]^+$ calcd for $C_{23}H_{26}O_5Na$ 405.16725, found 405.16656.



Methyl (1-allyl-2,3-di-*O*-benzyl-1-deoxy-β-D-lyxofuranosyl uronate) (31). Donor **11** and allyltrimethylsilane (4 eq.) were condensed using the general procedure for furanosyl imidate glycosylations at -20°C for 100 h with TfOH as the promotor. Yield = 29 mg, 76 µmol, 76% as a white solid. R_f: 0.32 (4/1 pentane/EtOAc). $[\alpha]_D^{20}$ = +3.6° (*c* = 0.58, $CHCl_3$); IR (thin film): 698, 737, 1028, 1072, 1084, 1099, 1152, 1207, 1356, 1437, 1454, 1732, 1763, 2870, 2920, 2949. ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.39 – 7.21 (m, 10H, CH_{arom}), 5.92 (ddt, 1H, *J* = 17.2, 10.2, 7.0 Hz, CH allyl), 5.15 (dq, 1H, *J* = 17.2, 1.4 Hz, C*H*H allyl), 5.09 – 5.04 (m, 1H, CH*H* allyl), 4.76 – 4.67 (m, 3H, CH_2 Bn, C*H*H Bn), 4.62 (d, 1H, *J* = 6.0 Hz, H-4), 4.56 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.34 (dd, 1H, *J* = 6.0, 4.4 Hz, H-3), 4.13 (dt, 1H, *J* = 8.8, 5.4 Hz, H-1), 4.04 (dd, 1H, *J* = 6.0, 4.4 Hz, H-2), 3.66 (s, 3H, CH_3 CO_2Me), 2.75 – 2.64 (m, 1H, C*H*H allylic), 2.58 – 2.48 (m, 1H, CH*H* allylic); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 170.3 (C=O), 138.2, 138.2 (C_q), 135.8 (CH allyl), 128.5, 128.4, 127.8, 127.7, 127.6 (CH_{arom}), 116.8 (CH_2 allyl), 80.5 (C-1), 80.1 (C-3), 79.2 (C-2), 78.3 (C-4), 73.9, 73.2 (CH_2 Bn), 51.9 (CO_2Me), 35.0 (CH_2 allylic); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): $^2J_{C2,H1}$ = -0.25 Hz, $^3J_{Callyl,H2}$ = +2.9 Hz; HRMS: $[M+NH_4]^+$ calcd for $C_{23}H_{30}NO_5$ 400.21185, found 400.21167.

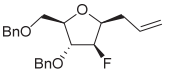


Methyl (1-allyl-2,3-di-*O*-benzyl-1-deoxy-α/β-D-xylofuranosyl uronate) (32). Donor **12** and allyltrimethylsilane (4 eq.) were condensed using the general procedure for furanosyl imidate glycosylations at -20°C for 100 h with TfOH as the promotor. Four fractions were isolated: amide **44** (1 mg, R_f: 0.66), mixed fraction (22 mg, product **32**, α:β = 35:65 as 68 wt%, and amide **44** as 32 wt%), title product **45** (7 mg, α:β = 69:33), cyclized product **61** (2 mg, R_f: 0.38) Calculated total title product yield = 22 mg, 57 µmol, 57%, (α:β = 45:55). R_f: 0.61 and 0.57 (4/1 pentane/EtOAc). Reported as a 1:1 mixture. IR (thin film): 698, 737, 1028, 1078, 1094, 1206, 1290, 1454, 1732, 1765, 2862, 2949. ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.38 – 7.24 (m, 20H, CH_{arom}), 5.88 – 5.72 (m, 2H, CH allyl), 5.16 – 5.03 (m, 4H, CH_2 allyl), 4.82 (d, 1H, *J* = 5.1 Hz, H-4α), 4.69 (d, 1H, *J* = 4.8 Hz, H-4β), 4.54 – 4.38 (m, 8H, 4xCH_2 Bn), 4.36 (ddd, 1H, *J* = 7.9, 6.5, 3.3 Hz, H-1α), 4.27 (dd, 1H, *J* = 5.1, 1.0 Hz, H-3α), 4.24 (dd, 1H, *J* = 4.8, 1.7 Hz, H-3β), 4.01 (td, 1H, *J* = 6.9, 3.3 Hz, H-1β), 3.82 (d, 1H, *J* = 3.5 Hz, H-2α), 3.82 (d, 1H, *J* = 3.4 Hz, H-2β), 3.76 (s, 3H, CH_3 CO_2Meβ), 3.73 (s, 3H, CH_3 CO_2Meα), 2.64 – 2.41 (m, 4H, CH2 allylic); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 170.6 (C=Oα), 169.6 (C=Oβ), 137.7 ($C_{qα}$), 137.7 ($C_{qβ}$), 137.6 ($C_{qβ}$), 137.5 ($C_{qα}$), 134.5 (CH allylα), 134.4 (CH allylβ), 128.6, 128.6, 128.6, 128.6, 128.1, 128.1, 128.1, 127.9, 127.9, 127.9 (CH_{arom}), 117.6 (CH_2 allylicβ), 117.3 (CH_2 allylicα), 84.7 (C-2β), 84.0 (C-1β), 83.9 (C-3β), 82.9 (C-3α), 81.6 (C-1α), 81.4 (C-2α), 80.4 (C-4β), 80.0 (C-4α), 73.0, 72.5, 72.3, 72.0 (CH_2 Bn), 52.1 (CO_2Meβ), 52.0 (CO_2Meα), 38.1 (CH_2 allylicβ), 33.1 (CH_2 allylicα); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): α-anomer: $^2J_{C1,H2}$ = +1.5 Hz, $^2J_{C2,H1}$ = +2.4 Hz, $^3J_{Callyl,H2}$ = +0.2 Hz, β-anomer: $^2J_{C1,H2}$ = -1.5 Hz, $^2J_{C2,H1}$ = -4.5 Hz, $^3J_{Callyl,H2}$ = +2.9 Hz; HRMS: $[M+NH_4]^+$ calcd for $C_{23}H_{30}NO_5$ 400.21185, found 400.21153.

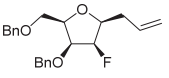


Allyl 3,5-di-*O*-benzyl-1,2-dideoxy-2-fluoro-α-D-ribofuranoside (33). Donor **13** and allyltrimethylsilane (4 eq.) were condensed using the general procedure for furanosyl imidate glycosylations at -20°C for 100 h with TfOH as the promotor. Yield = 27 mg, 76 µmol, 76% as a white solid. R_f: 0.52 (8/2 pentane/Et_2O). Spectroscopic data were in accord with those previously reported.[13] ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.40 – 7.19 (m, 10H, CH_{arom}), 5.80 (ddtd, 1H, *J* = 17.3, 10.2, 7.0, 0.8 Hz, CH allyl), 5.20 – 5.14 (m, 1H, C*H*H allyl), 5.09 (ddt, 1H, *J* = 10.2, 2.1, 1.1 Hz, CH*H* allyl), 4.89 (dt, 1H, *J* = 55.2, 2.9 Hz, H-2), 4.69 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.59 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.52 (d, 1H, *J* = 11.7 Hz, CH*H* Bn), 4.49 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.21 – 4.16 (m, 1H, H-4), 4.11 (ddd, 1H, *J* = 8.6, 3.5, 0.5 Hz, H-3), 4.05 (dtd, 1H, *J* = 29.3, 7.4, 2.4 Hz, H-1), 3.71 (dd, 1H, *J* = 10.8, 2.4 Hz, H-5), 3.56 (dd, 1H, *J* = 10.9, 3.4 Hz, H-5), 2.49 (ddt, 2H, *J* = 7.0, 5.6, 1.4 Hz, CH_2 allylic); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 138.3, 137.6 (C_q), 133.6 (CH allyl), 128.6, 128.5, 128.1, 128.0, 127.8, 127.7

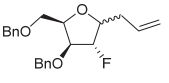
(CH_{arom}), 118.0 (CH allyl), 90.1 (d, *J* = 191.0 Hz, C-2), 80.0 (d, *J* = 18.3 Hz, C-1), 79.2 (C-4), 78.6 (d, *J* = 16.5 Hz, C-3), 73.6, 72.5 (CH_2 Bn), 69.6 (C-5), 33.7 (d, *J* = 9.3 Hz, CH allylic); ^{19}F NMR ($CDCl_3$, 471 MHz): δ -215.30 (ddd, *J* = 53.7, 29.4, 23.5 Hz, F-2); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): $^2J_{C2,H1}$ = +4.9 Hz, $^3J_{Callyl,H2}$ = +0.2 Hz; HRMS: $[M+NH_4]^+$ calcd for $C_{22}H_{29}FNO_3$ 374.21260, found 374.21252.



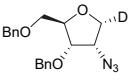
Allyl 3,5-di-*O*-benzyl-1,2-dideoxy-2-fluoro-β-D-arabinofuranoside (34). Donor **14** and allyltrimethylsilane (4 eq.) were condensed using the general procedure for furanosyl imidate glycosylations at -20°C for 100 h with TfOH as the promotor. Yield = 28 mg, 79 µmol, 79% as a colourless oil. R_f: 0.80 (9/1 pentane/EtOAc). $[\alpha]_D^{20}$ = -29.7° (*c* = 0.93, $CHCl_3$); IR (thin film):700, 712, 1026, 1070, 1096, 1269, 1452, 2924; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HH-NOESY, HSQC): δ 7.36 – 7.25 (m, 10H, CH_{arom}), 5.84 (ddtd, 1H, *J* = 17.2, 10.2, 7.1, 0.7 Hz, CH allyl), 5.17 (dq, 1H, *J* = 17.1, 1.5 Hz, C*H*H allyl), 5.10 (ddt, 1H, *J* = 10.2, 2.0, 1.1 Hz, CH*H* allyl), 4.88 (dd, 1H, *J* = 52.0, 2.8 Hz, H-2), 4.66 – 4.53 (m, 4H, 2xCH_2 Bn), 4.04 – 3.98 (m, 2.5H, H-1, H-3, H-4), 3.95 (td, 0.5H, *J* = 7.2, 2.8 Hz, H-3), 3.65 – 3.59 (m, 1H, H-5), 3.56 – 3.51 (m, 1H, H-5), 2.55 – 2.42 (m, 2H, CH_2 allylic);^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 138.2, 137.4 (C_q), 133.8 (CH allyl), 128.6, 128.5, 128.1, 127.9, 127.9, 127.8 (CH_{arom}), 117.8 (CH_2 allyl), 95.89 (d, *J* = 186.6 Hz, C-2), 84.71 (d, *J* = 27.3 Hz, C-3), 82.5 (C-4), 80.70 (d, *J* = 20.9 Hz, C-1), 73.6, 72.2 (CH_2 Bn), 70.2 (C-5), 32.63 (d, *J* = 8.1 Hz, CH_2 allylic); ^{19}F NMR ($CDCl_3$, 471 MHz): δ -198.80 (ddd, *J* = 50.6, 29.6, 20.2 Hz); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): $^2J_{C1,H2}$ = +4.2 Hz, $^2J_{C2,H1}$ = +5.6 Hz, $^3J_{Callyl,H2}$ = 0.1 Hz; HRMS: $[M+NH_4]^+$ calcd for $C_{22}H_{29}FNO_3$ 374.21260, found 374.21280.



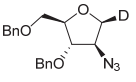
Allyl 3,5-di-*O*-benzyl-1,2-dideoxy-2-fluoro-β-D-lyxofuranoside (35). Donor **15** and allyltrimethylsilane (4 eq.) were condensed using the general procedure for furanosyl imidate glycosylations at -20°C for 100 h with TfOH as the promotor. Yield = 32 mg, 90 µmol, 90% as a white solid. R_f: 0.28 (9/1 pentane/EtOAc). $[\alpha]_D^{20}$ = -10.5° (*c* = 1.07, $CHCl_3$); IR (thin film): 696, 711, 737, 1026, 1070, 1271, 1452, 2870, 2922; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.42 – 7.21 (m, 10H, CH_{arom}), 5.82 (ddt, 1H, *J* = 17.2, 10.2, 7.0 Hz, CH allyl), 5.17 (dd, 1H, *J* = 17.1, 1.5 Hz, C*H*H allyl), 5.12 – 5.06 (m, 1H, CH*H* allyl), 4.89 (ddd, 1H, *J* = 54.6, 4.0, 2.9 Hz, H-2), 4.69 (d, 1H, *J* = 11.9 Hz, C*H*H Bn), 4.62 (d, 1H, *J* = 12.2 Hz, C*H*H Bn), 4.58 – 4.51 (m, 2H, 2xCH*H* Bn), 4.28 (td, 1H, *J* = 7.7, 3.6 Hz, H-4), 4.19 (ddd, 1H, *J* = 22.8, 7.8, 4.0 Hz, H-3), 3.84 (dtd, 1H, *J* = 27.3, 7.2, 2.8 Hz, H-1), 3.80 (dd, 1H, *J* = 10.6, 3.7 Hz, H-5), 3.65 (ddd, 1H, *J* = 10.6, 7.7, 1.7 Hz, H-5), 2.51 (t, 2H, *J* = 7.1 Hz, CH_2 allylic); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 138.6, 137.5 (C_q), 133.7 (CH allyl), 128.6, 128.4, 128.1, 127.9, 127.8, 127.6 (CH_{arom}), 117.9 (CH_2 allyl), 90.2 (d, *J* = 193.1 Hz, C-2), 79.3 (d, *J* = 18.8 Hz, C-1), 78.6 (d, *J* = 15.7 Hz, C-3), 78.2 (C-4), 73.5, 72.8 (CH_2 Bn), 70.6 (d, *J* = 2.7 Hz, C-5), 33.9 (d, *J* = 8.1 Hz, CH_2 allylic); ^{19}F NMR ($CDCl_3$, 471 MHz): δ -213.57 (ddd, *J* = 54.5, 27.2, 22.9 Hz); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): $^2J_{C1,H2}$ = +1.2 Hz, $^2J_{C2,H1}$ = +5.2 Hz, $^3J_{Callyl,H2}$ = +0.4 Hz; HRMS: $[M+NH_4]^+$ calcd for $C_{22}H_{29}FNO_3$ 374.21260, found 374.21295.



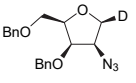
Allyl 3,5-di-*O*-benzyl-1,2-dideoxy-2-fluoro-α/β-D-xylofuranoside (36). Donor **16** and allyltrimethylsilane (4 eq.) were condensed using the general procedure for furanosyl imidate glycosylations at -20°C for 100 h with TfOH as the promotor. Yield = 22 mg, 62 µmol, 62% as a colourless oil (α:β = 70:30), and 12 mg (24%) of the anomeric amide (**42**). R_f: 0.53 and 0.40 (9/1 pentane/Et_2O). IR (thin film): 696, 735, 1028, 1076, 1088, 1454, 2868, 2922; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.37 – 7.25 (m, 10H, CH_{arom}), 5.88 – 5.77 (m, 1H, CH allyl), 5.19 – 5.07 (m, 2H, CH_2 allyl), 4.91 (ddd, 0.7H, *J* = 51.4, 2.8, 1.3 Hz, H-2α), 4.79 (ddd, 0.3H, *J* = 52.6, 2.9, 1.4 Hz, H-2β), 4.65 (d, 0.3H, *J* = 11.9 Hz, C*H*H Bnβ), 4.65 – 4.58 (m, 1.7H, 2xC*H*H Bnα, C*H*H Bnβ), 4.56 (d, 0.7H, *J* = 11.9 Hz, CH*H* Bnα), 4.53 – 4.49 (m, 1.3H, 2xCH*H* Bnβ, CH*H* Bnα), 4.42 – 4.36 (m, 0.7H, H-4α), 4.26 – 4.12 (m, 1.7H, H-1α, H-3α, H-4β), 4.08 (ddd, 0.3H, *J* = 8.9, 4.3, 1.3 Hz, H-3β), 4.02 (dddd, 0.3H, *J* = 13.9, 7.3, 6.5, 2.8 Hz, H-1β), 3.76 (dd, 0.3H, *J* = 10.0, 5.3 Hz, H-5β), 3.73 – 3.69 (m, 1H, H-5α, H-5β), 3.67 (dd, 0.7H, *J* = 9.8, 6.4 Hz, H-5α), 2.54 – 2.36 (m, 2H, CH_2 allylic); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 138.3, 138.2, 137.6 (C_q), 134.0 (CH allylα), 133.8 (CHallylβ), 128.6, 128.6, 128.5, 128.1, 128.0, 127.9, 127.9, 127.8, 127.7, 127.7, 127.7 (CH_{arom}), 117.8 (CH_2 allylβ), 117.7 (CH_2 allylα), 97.7 (d, *J* = 182.9 Hz, C-2β), 94.4 (d, *J* = 187.9 Hz, C-2α), 82.4 (d, *J* = 35.5 Hz, C-3β), 82.4 (d, *J* = 13.9 Hz, C-1β), 81.8 (d, *J* = 25.8 Hz, C-3α), 79.8 (d, *J* = 1.6 Hz, C-4β), 79.6 (d, *J* = 19.0 Hz, C-1α), 78.9 (C-4α), 73.6 (CH_2 Bnβ), 73.6, 72.9 (CH_2 Bnα), 72.1 (CH_2 Bnβ), 68.3 (C-5β), 68.2 (C-5α), 37.4 (d, *J* = 7.6 Hz, CH_2 allylicβ), 33.1 (d, *J* = 10.3 Hz, CH_2 allylicα); ^{19}F NMR ($CDCl_3$, 471 MHz): δ -183.53 (dddd, 0.3F, *J* = 52.6, 28.0, 13.2, 1.8 Hz), -201.43 (dddd, 0.7F, *J* = 51.4, 31.9, 9.9, 2.5 Hz); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): α-anomer: $^2J_{C1,H2}$ = +5.0 Hz, $^2J_{C2,H1}$ = +4.5 Hz, $^3J_{Callyl,H2}$ = +0.3 Hz, β-anomer: $^2J_{C1,H2}$ = +1.3 Hz, $^2J_{C2,H1}$ = -5.4 Hz, $^3J_{Callyl,H2}$ = +2.8 Hz; HRMS: $[M+Na]^+$ calcd for $C_{22}H_{25}FO_3Na$ 379.1685, found 379.1685.



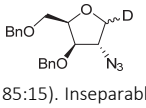
1-[^{2}H]-1,4-anhydro-2-azido-3,5-di-*O*-benzyl-2-deoxy-α-D-ribitol (37). Donor **17** and triethylsilane-*d* (4 eq.) were condensed using the general procedure for furanosyl imidate glycosylations at 0-5°C for 100 h with TfOH as the promotor. Yield = 23 mg, 68 µmol, 68% as a colourless oil. Inseparable mixture of **37** and amide **46** (in a 95:5 ratio). R_f: 0.26 (9/1 pentane/EtOAc). $[\alpha]_D^{20}$ = +88° (*c* = 0.77, $CHCl_3$) IR (thin film): 698, 738, 1028, 1089, 1269, 1454, 2104, 2864; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HH-NOESY, HSQC): δ 7.38 – 7.26 (m, 10H, CH_{arom}), 4.69 (d, 1H, *J* = 11.8 Hz, C*H*H Bn), 4.57 – 4.52 (m, 2H, C*H*H Bn, CH*H* Bn), 4.48 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.14 (dd, 1H, *J* = 6.1, 5.5 Hz, H-3), 4.09 – 4.02 (m, 2H, H-1, H-4), 3.89 (t, 1H, *J* = 5.4 Hz, H-2), 3.61 (dd, 1H, *J* = 10.7, 3.3 Hz, H-5), 3.50 (dd, 1H, *J* = 10.7, 4.0 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 138.1, 137.4 (C_q), 128.6, 128.5, 128.2, 128.1, 127.8, 127.8 (CH_{arom}), 80.9 (C-4), 79.9 (C-3), 73.6, 73.0 (CH_2 Bn), 70.2 (t, *J* =22.8 Hz, C-1), 69.8 (C-5), 60.8 (C-2); ^{2}H NMR ($CHCl_3$, 77 MHz): δ 3.90; ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): $^2J_{C1\text{-}H2}$: +1.5 Hz, $^2J_{C2\text{-}H1}$: +1.3 Hz; HRMS: $[M+Na]^+$ calcd for $C_{19}H_{20}DN_3O_3Na$ 363.1543, found 363.1546.



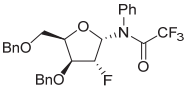
1-[^{2}H]-1,4-anhydro-2-azido-3,5-di-*O*-benzyl-2-deoxy-β-D-arabitol (38). Donor **18** and triethylsilane-*d* (4 eq.) were condensed using the general procedure for furanosyl imidate glycosylations at 0-5°C for 100 h with TfOH as the promotor. Yield = 19.5 mg, 57 µmol, 57% as a colourless oil. R_f: 0.38 (9/1 pentane/EtOAc). Spectroscopic data were in accord with those previously reported for the non-deuterated compound.[37] $[\alpha]_D^{20}$ = -14.6° (*c* = 0.98, $CHCl_3$); IR ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.37 – 7.26 (m, 10H, CH_{arom}), 4.59 (d, 1H, *J* = 11.8 Hz, C*H*H Bn), 4.56 (s, 2H, CH_2 Bn), 4.54 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.02 (td, 1H, *J* = 5.3, 4.3 Hz, H-4), 4.00 (bs, 1H, H-1), 3.98 (dd, 1H, *J* = 5.0, 1.9 Hz, H-2), 3.92 (dd, 1H, *J* = 4.3, 1.9 Hz, H-3), 3.59 (dd, 1H, *J* = 10.3, 5.5 Hz, H-5), 3.57 (dd, 1H, *J* = 10.3, 5.2 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 138.1, 137.4 (C_q), 128.7, 128.5, 128.2, 128.0, 127.9, 127.8 (CH_{arom}), 85.0 (C-3), 83.4 (C-4), 73.6, 72.4 (CH_2 Bn), 70.7 (t, *J* = 23.0 Hz, C-1), 70.5, 70.0 (C-5), 65.9 (C-2); ^{2}H NMR ($CHCl_3$, 77 MHz): δ 4.02; ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): $^2J_{C1\text{-}H2}$: +1.1 Hz, $^2J_{C2\text{-}H1}$: +2.3 Hz; HRMS: $[M+NH_4]^+$ calcd for $C_{19}H_{24}DN_4O_3$ 358.19839, found 358.19858.



1-[^{2}H]-1,4-anhydro-2-azido-3,5-di-*O*-benzyl-2-deoxy-β-D-lyxitol (39). Donor **19** and triethylsilane-*d* (4 eq.) were condensed using the general procedure for furanosyl imidate glycosylations at 0-5°C for 100 h with TfOH as the promotor. Yield = 20 mg, 59 µmol, 59% as a colourless oil. R_f: 0.13 (9/1 pentane/EtOAc). $[\alpha]_D^{20}$ = -37° (*c* = 1.0, $CHCl_3$); IR (thin film): 698, 738, 1984, 1269, 1452, 2104, 2868, 2922, 3032; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.36 – 7.26 (m, 10H, CH_{arom}), 4.77 (d, 1H, *J* = 11.6 Hz, C*H*H Bn), 4.61 – 4.56 (m, 2H, C*H*H Bn, CH*H* Bn), 4.50 (d, 1H, *J* = 11.9 Hz, CH*H* Bn), 4.20 (t, 1H, *J* = 5.2 Hz, H-3), 4.15 (dt, 1H, *J* = 6.9, 5.2 Hz, H-4), 3.92 (d, 1H, *J* = 6.4 Hz, H-1), 3.86 (dd, 1H, *J* = 6.3, 5.1 Hz, H-2), 3.73 (dd, 1H, *J* = 10.1, 5.0 Hz, H-5), 3.68 (dd, 1H, *J* = 10.1, 7.0 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 138.2, 137.5 (C_q), 128.6, 128.5, 128.1, 128.0, 127.9, 127.8 (CH_{arom}), 79.6, 79.6 (C-3, C-4), 74.0, 73.7 (CH_2 Bn), 69.0 (C-5), 68.7 (t, *J* = 22.8 Hz, C-1), 61.3 (C-2); ^{2}H NMR ($CHCl_3$, 77 MHz): δ 3.95; ^{13}C HSQC-HECADE NMR: $^2J_{C2,H1}$ = +0.2 Hz; HRMS: $[M+Na]^+$ calcd for $C_{19}H_{20}DN_3O_3Na$ 363.1543, found 363.1551.

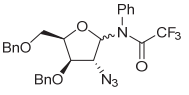


1-[^{2}H]-1,4-anhydro-2-azido-3,5-di-*O*-benzyl-2-deoxy-α/β-D-xylitol (40). Donor **20** and triethylsilane-*d* (4 eq.) were condensed using the general procedure for furanosyl imidate glycosylations at 0-5°C for 100 h with TfOH as the promotor. Yield = 23 mg, 68 µmol, 68% as a colourless oil (α:β = 85:15). Inseparable mixture of **40** and amide **43** (in a 73:27 ratio) R_f: 0.30 (85/15 pentane/Et_2O). IR (thin film): 696, 735, 1061, 1088, 1207, 1454, 1494, 1690, 2106, 2916; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.38 – 7.24 (m, 10H, CH_{arom}), 4.65 – 4.58 (m, 2H, 2x*CH*H Bn), 4.54 (d, 1H, *J* = 11.9 Hz, CH*H* Bn), 4.52 (d, 1H, *J* = 11.9 Hz, CH*H* Bn), 4.21 – 4.15 (m, 1.85H, H-1α, H-4), 4.04 (dd, 1H, *J* = 5.5, 1.9 Hz, H-2), 3.99 (dd, 1H, *J* = 4.4, 1.9 Hz, H-3), 3.74 – 3.70 (m, 1.15H, H-1β, H-5), 3.68 (dd, 1H, *J* = 10.0, 6.4 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 138.2, 137.4 (C_q), 128.7, 128.5, 128.2, 127.9, 127.8, 127.8 (CH_{arom}), 82.9 (C-3), 79.7 (C-4), 73.7, 72.6 (CH_2 Bn), 70.0 (t, *J* = 22.7 Hz C-1β), 70.0 (t, *J* = 22.7, C-1α) 68.4 (C-5), 65.0 (C-2); ^{2}H NMR ($CHCl_3$, 77 MHz): δ 4.19 (s, 0.15H), 3.75 (s, 0.85H);^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): α-anomer: $^2J_{C2,H1}$ = +0.7 Hz; β-anomer: $^2J_{C2,H1}$ = -4.3 Hz; HRMS: $[M+Na]^+$ calcd for $C_{19}H_{20}DN_3O_3Na$ 363.1543, found 363.1549.

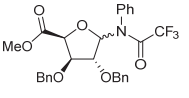


3,5-di-*O*-benzyl-1,2-dideoxy-2-fluoro-1-*N*-[phenyl]trifluoroacetyl-α/β-D-xylofuranoside (42). IR (thin film): 698, 737, 1070, 1153, 1188, 1207, 1454, 1495, 1595, 1690, 2862, 2922; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.43 – 7.19 (m, 15H, CH_{arom}), 6.31 (dd, 1H, *J* = 11.0, 5.1 Hz, H-1), 5.45 (ddd, 1H, *J* = 52.9, 5.0, 3.8 Hz, H-2), 4.65 (d, 1H, *J* = 11.9 Hz, C*H*H Bn), 4.47 (d, 1H, *J* = 11.9 Hz, CH*H* Bn), 4.40 (s, 2H, CH_2 Bn), 3.91 (dt, 1H, *J* = 14.3, 4.1 Hz, H-3), 3.77 (qd, 1H, *J* = 4.7, 1.7 Hz, H-4), 3.56 (ddd, 1H, *J* = 10.5, 4.4, 0.7 Hz, H-5), 3.49 (dd, 1H, *J* = 10.6, 4.8 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.0, 137.1 (C_q), 134.2, 132.0, 130.5, 129.6, 128.6, 128.5, 128.2, 127.9, 127.8, 127.7 (CH_{arom}), 93.5 (d, *J* =

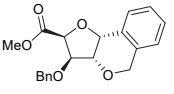
194.8 Hz, C-2), 87.2 (d, *J* = 17.4 Hz, C-1), 80.1 (d, *J* = 23.2 Hz, C-3), 79.1 (d, *J* = 3.5 Hz, C-4), 73.4, 72.6 (CH_2 Bn), 68.0 (C-5); ^{19}F NMR ($CDCl_3$, 471 MHz): δ -68.17 (s, 3F, CF_3), -196.37 (dt, 1F, *J* = 53.1, 12.7 Hz, F-2).



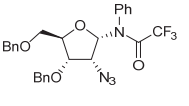
2-azido-3,5-di-*O*-benzyl-1,2-dideoxy-1-*N*-[phenyl]trifluoroacetyl-α/β-D-xylofuranoside (43). Intermixed with **40**. The anomeric amide was formed in an α:β = 93:7 ratio. Data for the α-anomer: ^1H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.17 (dd, 2H, *J* = 6.6, 2.6 Hz, NPh), 6.33 (d, 1H, *J* = 6.6 Hz, H-1), 4.59 (t, 1H, *J* = 6.6 Hz, H-2), 4.50 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.46 – 4.40 (m, 3H, CH_2 Bn, CH*H* Bn), 3.66 (t, 1H, *J* = 4.3 Hz, H-4), 3.59 (t, 1H, *J* = 6.8 Hz, H-3), 3.49 (dd, 1H, *J* = 10.7, 4.0 Hz, H-5), 3.41 (dd, 1H, *J* = 10.7, 4.5 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 157.0 (q, *J* = 36.4 Hz, F_3C-*C*=O), 138.0, 137.0 (C_q), 132.0, 130.7, 129.6, 129.5, 128.7, 128.3, 128.1, 127.8, 127.8, 127.7, 126.5, 120.6 (CH_{arom}), 116.0 (q, *J* = 288.7 Hz, CF_3), 86.9 (C-1), 80.9 (C-3), 78.6 (C-4), 73.5, 73.3 (CH_2 Bn), 68.6 (C-5), 67.1 (C-2); ^{19}F NMR ($CDCl_3$, 471 MHz): δ -68.04 (s, $CF_{3,\alpha}$), -68.18 (s, $CF_{3,\beta}$); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): α-anomer: $^2J_{C1,H2}$ = -0.2 Hz, $^2J_{C2,H1}$ = +1.1 Hz; Diagnostic peaks for the β-anomer: ^1H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): 5.98 (d, 0.07H, *J* = 6.2 Hz, H-1), 4.28 (td, 0.07H, *J* = 6.3, 4.6 Hz, H-4); ^{13}C HSQC-HECADE NMR: $^2J_{C1,H2}$ = -4.0 Hz, $^2J_{C2,H1}$ = -2.1 Hz.



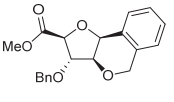
Methyl (2,3-di-*O*-benzyl-1-deoxy-1-*N*-[phenyl]trifluoroacetyl-α/β-D-xylofuranosyl uronate) (44). ^1H NMR ($CDCl_3$, 500 MHz, HH-COSY, HH-NOESY, HSQC, HMBC): δ 7.41 – 7.28 (m, 18H, CH_{arom}), 7.15 (dd, 2H, *J* = 7.3, 2.0 Hz, CH_{arom}), 6.59 (d, 1H, *J* = 6.1 Hz, H-1), 4.70 (d, 1H, *J* = 11.2 Hz, C*H*H Bn), 4.58 (d, 1H, *J* = 11.2 Hz, CH*H* Bn), 4.51 (t, 1H, *J* = 6.1 Hz, H-2), 4.44 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.38 (d, 1H, *J* = 11.9 Hz, CH*H* Bn), 4.15 (d, 1H, *J* = 6.5 Hz, H-4), 3.77 – 3.72 (m, 1H, H-3), 3.67 (s, 3H, CH_3 CO_2Me); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC, HMBC): δ 169.5 (C=O), 137.3, 137.1 (C_q), 129.6, 128.7, 128.6, 128.5, 128.3, 128.2, 128.1, 127.9 (CH_{arom}), 87.6 (C-1), 81.9 (C-2), 81.1 (C-3), 78.2 (C-4), 74.3, 72.9 (CH_2 Bn), 52.3 (CO_2Me); ^{19}F NMR ($CDCl_3$, 471 MHz): δ -68.09; ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): $^2J_{C1,H2}$ = +1.5 Hz.



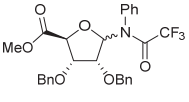
Methyl (2*S*,3*R*,3a*S*,9b*R*)-3-(benzyloxy)-3,3a,5,9b-tetrahydro-2*H*-furo[3,2-*c*]isochromene-2-carboxylate (45). ^1H NMR ($CDCl_3$, 500 MHz, HH-COSY, HH-NOESY, HSQC): δ 7.61 – 7.57 (m, 1H, CH_{arom}), 7.37 – 7.28 (m, 7H, CH_{arom}), 7.08 – 7.04 (m, 1H, CH_{arom}), 5.16 (d, 1H, *J* = 2.8 Hz, H-1), 4.92 (d, 1H, *J* = 4.9 Hz, H-4), 4.78 (d, 1H, *J* = 14.6 Hz, C*H*H Bn $_{(C\text{-}2)}$), 4.72 (d, 1H, *J* = 11.9 Hz, C*H*H Bn $_{(C\text{-}3)}$), 4.65 (d, 1H, *J* = 14.8 Hz, CH*H* Bn $_{(C\text{-}2)}$), 4.64 (d, 1H, *J* = 12.0 Hz, CH*H* Bn $_{(C\text{-}3)}$), 4.44 (d, 1H, *J* = 5.1 Hz, H-3), 4.26 (d, 1H, *J* = 3.0 Hz, H-2), 3.76 (s, 3H, CH_3 CO_2Me); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 170.2 (C=O), 134.4, 130.9, 130.3 (C_q), 128.7, 128.6, 128.1, 127.7, 127.7, 124.2 (CH_{arom}), 85.2 (C-3), 80.4 (C-4), 79.5 (C-2), 74.9 (C-1), 73.2 (CH_2 $Bn_{(C\text{-}3)}$), 67.2 (CH_2 $Bn_{(C\text{-}2)}$), 52.1 (CO_2Me).



3,5-di-*O*-benzyl-1,2-dideoxy-2-fluoro-1-*N*-[phenyl]trifluoroacetyl-α-D-ribofuranoside (46). Intermixed with **37**. Diagnostic peaks: ^1H NMR ($CDCl_3$, 500 MHz): δ 6.04 (d, 1H, *J* = 5.1 Hz, H-1), 4.61 (t, 1H, *J* = 5.5 Hz, H-2), 4.44 (d, 1H, *J* = 11.6 Hz, C*H*H Bn), 4.41 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.30 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 3.44 (dd, 1H, *J* = 11.3, 2.5 Hz, H-5), 3.32 (dd, 1H, *J* = 11.3, 3.5 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 88.1 (C-1), 80.3 (C-4), 77.0 (C-3), 73.4, 73.3 (CH_2 Bn), 68.0 (C-5), 62.9 (C-2).



Methyl (2*S*,3*S*,3a*R*,9b*S*)-3-(benzyloxy)-3,3a,5,9b-tetrahydro-2*H*-furo[3,2-*c*]isochromene-2-carboxylate (47). Intermixed with **30**. ^1H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.52 (dd, 1H, *J* = 5.5, 3.6 Hz, CH_{arom}), 7.44 – 7.25 (m, 7H, CH_{arom}), 7.07 (dd, 1H, *J* = 5.4, 3.8 Hz, CH_{arom}), 4.93 (d, 1H, *J* = 2.9 Hz, H-1), 4.79 (d, 1H, *J* = 12.1 Hz, C*H*H 3-OBn), 4.79 (d, 1H, *J* = 14.7 Hz, C*H*H 2-OBn), 4.72 (d, 1H, *J* = 12.1 Hz, CH*H* 3-OBn), 4.66 (d, 1H, *J* = 14.7 Hz, CH*H* 2-OBn), 4.64 (d, 1H, *J* = 2.8 Hz, H-4), 4.46 (dd, 1H, *J* = 2.7, 0.7 Hz, H-3), 4.21 (d, 1H, *J* = 3.0 Hz, H-2), 3.71 (s, 3H, CH_3 CO_2Me); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 170.6 (C=O), 137.4, 134.7, 130.7 (C_q), 129.8, 128.7, 128.1, 128.0, 128.0, 127.5, 124.2 (CH_{arom}), 87.8 (C-3), 82.2 (C-4), 79.8 (C-2), 75.3 (C-1), 72.4, 67.0 (CH_2 Bn), 52.4 (CO_2Me); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): $^2J_{C1,H2}$ = +6.0 Hz, $^2J_{C2,H1}$ = +2.4 Hz.



Methyl (2,3-di-*O*-benzyl-1-deoxy-1-*N*-[phenyl]trifluoroacetyl-α-D-ribofuranosyl uronate) (48). ^1H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.43 – 7.16 (m, 14H, CH_{arom}), 7.09 – 7.00 (m, 1H, NPh), 6.44 (d, 1H, *J* = 5.8 Hz, H-1), 4.75 (d, 1H, *J* = 11.1 Hz, C*H*H Bn), 4.65 (d, 1H, *J* = 11.0 Hz, CH*H* Bn), 4.48 – 4.39 (m, 2H, C*H*H Bn, H-2), 4.35 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.02 – 3.99 (m, 2H, H-3, H-4), 3.67 (s, 3H, CH_3 CO_2Me); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 170.5 (C=O), 137.4, 137.0, 133.5 (C_q), 132.1, 131.8, 129.1, 128.6, 128.5, 128.3, 128.2, 128.2, 128.1 (CH_{arom}), 88.5 (C-1), 79.9, 79.0 (C-3, C-4), 77.2 (C-2), 74.5, 72.8 (CH_2 Bn), 52.7 (CO_2Me); ^{19}F NMR ($CDCl_3$, 471 MHz): δ -68.03.

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Chapter 9

Summary and future prospects

Summary

The demand for biologically relevant oligosaccharides and glycoconstructs is ever increasing. Chemical synthesis can provide pure and well-defined carbohydrates, which are generally difficult to obtain from nature. One of the challenges in synthetic carbohydrate chemistry is the efficient construction of 1,2-*cis*-glycosidic linkages. The synthesis of this type of glycosidic bond often requires time-consuming, trial-and-error based optimization experiments. It would be highly beneficial if more insight into the mechanism of the glycosylation reaction in general, and the formation of 1,2-*cis*-bonds in particular, could be obtained. In this thesis, systematic studies on the reactivity of both reaction partners, the glycosyl donor and the glycosyl acceptor, and the influence thereof on the selectivity of a glycosylation reaction, are conducted. With these studies more insight into the glycosylation mechanism is obtained and it provides a direction how to improve the stereoselectivity in the formation of 1,2-*cis*-glycosidic linkages.

The general glycosylation reaction mechanism and the reactivity of carbohydrate building blocks in glycosylation reactions is described in **Chapter 1** and **Chapter 2**. The first chapter describes the reactivity from the perspective of the glycosyl donor, the electrophilic species. In the second chapter the focus is laid on the nucleophilic reaction partner, the acceptor. The reactivity of both species depends on the protecting groups they carry. Although much insight has been gained how the protecting groups on the donor glycoside impact the reactivity of this coupling partner, the reactivity of acceptor glycosides as a function of the protecting and functional group pattern is rather ill-documented. It also remains unclear how the changing reactivity impacts the change in mechanisms from an S_N2- to S_N1-like substitution reaction, which can have far reaching consequences for the stereoselectivity of a glycosylations reaction. Chapter 2 provides an overview of recent and older examples that show how small changes in the structure and reactivity of the acceptor can lead to large changes in yield, selectivity, and reaction rates.

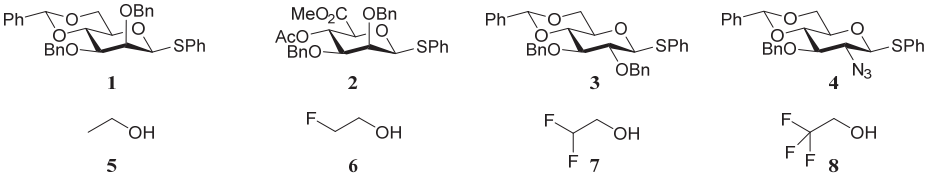


Figure 1. Donors **1**-**4** and model acceptors **5**-**8** used in Chapters **3** and **4**.

Chapter 3 describes how the reactivity of the acceptor affects the glycosylation reaction mechanism. A set of model acceptors (**5**-**8**, Figure 1) of gradually changing reactivity is used to unveil the influence of the reactivity of the acceptor on the stereochemical outcome of the glycosylation reaction. The model acceptors are based on ethanol with a varying amount of fluorine substituents (up to three fluorine atoms). The presence of more electron-withdrawing fluorine atoms makes the acceptor less reactive. The glycosylation method chosen was based on the preactivation of thioglycoside donors, to ensure the formation of an anomeric triflate intermediate and prevent alternative reaction pathways associated with *in situ* glycosylation protocols. Ethanol **5**, the most reactive model acceptor, gave high β-selectivity in glycosylations with three donors tested: benzylidene glucose **3**, benzylidene mannose **1** and mannuronic acid methyl ester **2**. The significantly less reactive trifluoroethanol **8** gave high α-selectivity for the benzylidene glucose donor, in contrast to the other two donors, that provided mostly the β-products. The mono- and difluoroethanols **6** and **7** gave mixtures of

anomeric products with the glucose donor, with more α-product for the less reactive difluoroethanol. These results indicated that the glycosylations of benzylidene glucose donor **3** are very susceptible to changes in acceptor reactivity, while the outcome of the glycosylations of the benzylidene mannose and mannuronic acid proved to be less sensitive to changes in acceptor nucleophilicity. Subsequently, carbohydrate acceptors were tested and it was found that the reactivity of these larger acceptors also proved decisive for the glycosylation outcome. Primary and secondary equatorial hydroxyls gave relatively high β-selectivity, while secondary axial hydroxyls gave α-selectivity for the benzylidene glucose donor. Benzylidene mannose and mannuronic acid donors were consistently β-selective for the carbohydrate acceptors. With these results the correlation between reactivity of the acceptor and a change in the glycosylation mechanism was established. Stronger nucleophiles participate in a more S_N2-like mechanism, providing the β-product, while weaker nucleophiles react with more S_N1-substitution character. For benzylidene glucose the S_N1 intermediate is an oxocarbenium ion in the $^4H_3/^4E$ conformation, preferably attacked from the α-face, whereas the benzylidene mannose and mannuronic acid preferentially take up a $B_{2,5}$ and $^3H_4$ conformation respectively, which are attacked on the β-face.

The donor scope was extended in **Chapter 4** to study the effect of the azide as an amine masking group on benzylidene glucosamine donors, and to compare the results of glycosylations with these donors with the benzylidene glucose donor from Chapter 3. The azide is an electron-withdrawing group and destabilizes the formation of positive charge on the anomeric center more than an *O*-benzyl group does. As a consequence, the glycosylations with benzylidene glucosazide donors (such as **4**, Figure 1) proceed with more S_N2-character when compared to reactions with benzylidene glucose, and the 2-azido group is therefore β-directing. Further structural modifications on the donor were also investigated. Changing the C-3 position of the donor from an *O*-benzyl to an *O*-benzoyl group made the donor slightly more β-selective, as a result of the electron-withdrawing effect of the benzoyl group. Changing the benzylidene ring for a silylidene ring made the donor less β-selective, and in combination with a poorly nucleophilic acceptor, high α-selectivity can be achieved.

Instead of the benzylidene or silylidene ring, which span over positions C-4 and C-6, a tethering group spanning C-3 and C-4, the butanediacetal (BDA) group, is studied as a protecting group of glucosazide donors in **Chapter 5**. Glycosylations with the set of fluorinated model acceptors showed that the glucosazide donor bearing the BDA group

glycosylates significantly more β-selective than its benzylidene counterpart. Likely, the conformational restriction inferred by the cyclic BDA group, prevents the formation of charge on the anomeric center, making S_N1-pathways less favorable. Consequently, reactions with this donor proceed with a high degree of S_N2 substitution.

The reactivity of glycosyl acceptors was studied in more detail in **Chapter 6**. With a large selection of C-4–OH glucose acceptors bearing *O*-benzyl and *O*-benzoyl groups in all possible patterns, the influence of acceptor reactivity on the glycosylation stereoselectivity was studied. The benzylidene protected glucose and glucosazide donors from Chapters 3 and 4 served as donors to map the acceptor structure-reactivity-stereoselectivity relationships. The outcome of glycosylations of these two donors is very sensitive to changes in acceptor reactivity and complement each other, with the benzylidene glucosazide donor providing more β-product (resulting from more S_N2 character in the condensation reactions) than the benzylidene glucose donor. From this study it became evident that the reactivity of carbohydrate acceptors can also be changed by the manipulation of protecting groups. The strategic placement of a single benzoyl group is sufficient to turn the glycosylation with the benzylidene glycose donor completely α-selective. With a second benzoyl group, also the glucosazide donor becomes completely α-selective, providing a method to construct 1,2-*cis*-glucosamine linkages. Also, the effect of electron-withdrawing substituents on the aromatic ring of the benzoates were studied. These substituents had a minor influence, and only the presence of two nitro groups, at both ortho-positions, gave the required drop in reactivity and increase in α-selectivity.

Chapter 7 and **Chapter 8** focus on five-membered ring sugars, the furanoses, and their selectivity in glycosylations. In the first chapter different functionalities are installed on the furanoses. The C-2 position is modified with an azido or a fluoro group and the C-5 position is oxidized to the methyl ester. The chosen strategy to install the azide and fluoride via inversion of a triflate leaving group, was not without problems. The inversion of 2-*O*-triflylriboside smoothly gave the 2-fluoro- and 2-azidoarabinosides. The success of the nucleophilic substitution on arabinose to give the ribosides, depended on the anomeric configuration, with partial migration of the anomeric *O*-methyl group to the C-2 position in the α-anomer. The inversion of 2-*O*-triflylxylosides to give the corresponding lyxose products only proceeded with the α-anomer. Side products during this reaction originated from intramolecular participation of the C-5-*O*-benzyl group. Inverting 2-*O*-triflyllyxoside was unsuccessful and only the aromatic furan was formed.

The 2-fluoro- and 2-azidoxylosides therefore had to be made via an alternative route, for which the electrophilic addition to a glycal was chosen. Further modifications to generate a set of twelve imidate donors went uneventful. These donors were glycosylated with model acceptors in Chapter 8.

The selectivity of furanosides in glycosylation reactions, under S_N1-conditions, was investigated in **Chapter 8**. The oxocarbenium ions that serve as reactive intermediates in these glycosylations are responsible for the observed stereoselectivity. First, the stereoselectivities were experimentally determined with nucleophilic model acceptors allyltrimethylsilane and triethylsilane-*d*. Almost all glycosylations proceeded with exclusive 1,2-*cis*-selectivity, except for *xylo*-configured donors which gave anomeric mixtures. Next, the relative energies of all possible conformations of the oxocarbenium ions were assessed using Density Functional Theory (DFT). The collective set of data points for each configuration and C-2/C-5 modification was then plotted as a Conformational Energy Landscape (CEL) map. From the computational data it became evident that when a single conformation was strongly preferred, the experimental glycosylations proceeded with excellent stereoselectivity. In the *arabino*-configuration multiple low in energy conformations were found, of which several were nearly flat. The influence of these conformers on the stereochemical outcome of the glycosylations proved to be limited and also for the studied C-2/C-5 arabinofuranosides high 1,2-*cis*-selectivity was found. The CEL maps of the *xylo*-configured oxocarbenium ions also displayed multiple low in energy conformations. Besides the ^3E and E_3 conformations, which are the most common furanosyl oxocarbenium ion conformations, the ^4E envelope was found as one of the major contributors to the conformer population. The multitude of available conformations led to anomeric mixtures in the glycosylation reactions. The computational method is able to effectively show the differences in conformer population distribution when groups exhibiting different stereoelectronic effects are introduced, like the azido, fluoro, and uronic acid ester groups. With the relative stabilities of each conformation of an oxocarbenium ion available, it can be determined whether a glycosylation reaction under S_N1-conditions proceeds with exclusive stereoselectivity. Erosion of stereoselectivity may occur when the oxocarbenium ion can take up multiple conformations.

Future prospects

The main goal of this thesis was to shed more light on the glycosylation reaction mechanism. The influence the acceptor has on the glycosylation mechanism is profound, but is difficult to quantify. Several techniques referred to in the previous chapters can be extended to the model systems used in Chapters 3-5 as well as applied to the carbohydrate acceptors of Chapter 6. A few approaches to obtain both qualitative and quantitative information on the glycosylation mechanism and/or acceptor reactivity will be discussed below. The two extreme situations of the glycosylation mechanism, the S_N1 or S_N2 substitution reactions, can be discerned by experimental kinetics and transition state models as studied by computational methods.

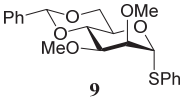
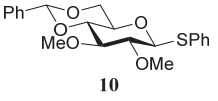
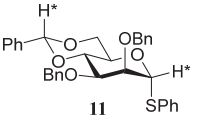
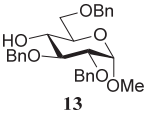
Kinetic Isotope Effects

The rate-determining step for a typical S_N1 mechanism is dissociation of the leaving group and generation of an (oxo)carbenium ion. This is followed by addition of the nucleophile in the product-forming step. In a S_N2 reaction, the rate-determining step is also the product-forming step. Dissecting the mechanism of glycosylation into its S_N1 and S_N2 extremes can be effectively done by studying Kinetic Isotope Effects (KIEs).[1,2] Primary KIEs are measured by integrating NMR signals of the electrophilic anomeric carbon atom, either with isotopically enriched substances or using the naturally abundant $^{13}C/^{12}C$ isotopes. The vibrational energy levels of the bonds to the heavier ^{13}C isotope (8% mass increase compared to ^{12}C) are lower than those to the ^{12}C atom, resulting in a slightly higher bond dissociation energy for the former. This has an immediate effect on the S_N2 reaction transition state, creating an energy difference between the pathways having a ^{13}C or ^{12}C anomeric center carbon (rate constants $k_{12}>k_{13}$). The rate of S_N1 reactions is much less effected by the difference between ^{13}C and ^{12}C atoms and the ratio of reaction rates (k_{12}/k_{13}) is close to unity. Secondary deuterium KIEs (SDKIEs) are measured of an atom at which the reaction does not take place, but which is in (close) proximity to the reacting center. The deuterium atom in isotopically labelled carbohydrates can be directly attached to the anomeric center (α-SDKIE), or positioned further away (β-SDKIE, γ-SDKIE). The ratio of reaction rates is again indicative of the reaction mechanism, but it is reversed as compared to primary-KIEs. The S_N1 SDKIE is often observed to be high (>1.20), while that of the S_N2 pathway is around unity.

KIEs have been studied in the context of glycosylations by the groups of Crich, Tantillo, and Bennet, among others, a selection of the results are summarized in

Table 1.[3–12] Primary KIEs obtained with the strongly nucleophilic acceptor isopropanol **12** are indicative of an S_N2 mechanism for the formation of both anomeric products from benzylidene glucose donor **10**, and the β-product from benzylidene mannose donor **9** (entries 1 and 2). The α-product of benzylidene mannose gave a value indicating an S_N1 mechanism of formation, consistent with the postulates given in Chapter 3 that an oxocarbenium ion in the $^4H_3$ conformation is at play here. Secondary KIEs measured for a weaker carbohydrate acceptor (**13**, entry 3) gave values corresponding to an S_N2 reaction with significant oxocarbenium ion character (an "exploded S_N2-reaction) for the formation of both anomers of benzylidene mannose **11**.

Table 1. Kinetic isotope effects measured for glycosylation reactions.

Entry	Donor[a]	Acceptor	KIE	Value[b]	Verdict[c]
1[5]	 **9**	 **12**	^{13}C primary KIE	α: 1.005±0.002 β: 1.023±0.003	S_N1 S_N2
2[5]	 **10**	 **12**	^{13}C primary KIE	α: 1.023±0.006 β: 1.019±0.001	S_N2 S_N2
3[4]	 **11**	 **13**	^2H secondary α-KIE	β: 1.12±0.01	S_N2/S_N1

[a]H* indicates partial deuterium labelling. [b]Values for the anomers are indicated. [c]S_N2 is described in each case to be a loosened-S_N2 transition state.

It would be worthwhile to determine KIEs of a range of donor-acceptor pairs, in which the reactivity of both partners is gradually changed. For example, the two donors used in Chapter 6 (**3** and **4**, Figure 2) can be used in conjunction with the set of fluorinated model acceptors (**5**-**8**, Figure 2) in a broad KIE study. The set of model acceptors is expected to show a steady decline of primary KIEs or steady increase of secondary KIEs due to the increased oxocarbenium ion contribution in the transition states for these reactions.

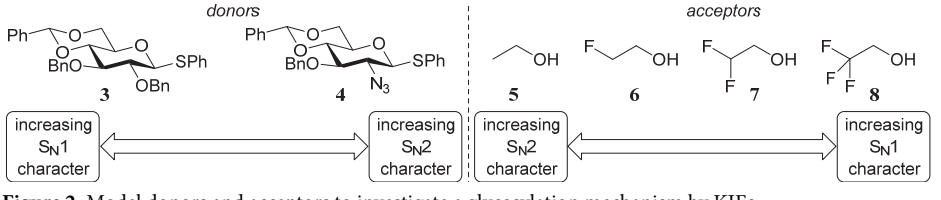


Figure 2. Model donors and acceptors to investigate a glycosylation mechanism by KIEs.

Cation-clock kinetics

Another approach to derive kinetic data for glycosylation reactions is based on the competition reactions using the cation-clock methodology. The reaction rate in an S_N2 reaction is dependent on the concentration of the electrophile and the nucleophile, while the rate of the S_N1 reaction is independent of the nucleophile. Changing the concentration of a nucleophile and establishing the reaction rate, is therefore a practical means to determine whether a reaction proceed through an S_N1 or S_N2 path. Since glycosylation reactions are very fast, when using a preactivation setup (see also the next section), and rates of conversion are difficult to measure on a practical time-scale, Crich and co-workers have developed a cation-clock competition set-up in which an internal and external nucleophile compete for the electrophilic species.[13–15] The internal nucleophile is a weak nucleophile and will only react with the more electrophilic oxocarbenium ion via an S_N1 mechanism, giving a cyclized product at a fixed rate (clock). In the presence of a competing nucleophile, the oxocarbenium ion or the covalent triflate may be captured. A strong external nucleophile will outcompete the internal nucleophile (following the S_N2-path), while weaker nucleophiles will have more competition from internal cyclization. Crich and co-workers used the strong nucleophile isopropanol **12** and allyltrimethylsilane **14** (Figure 3) as acceptors in combination with benzylidene mannose donor **15** and benzylidene glucose donor **16** and found that

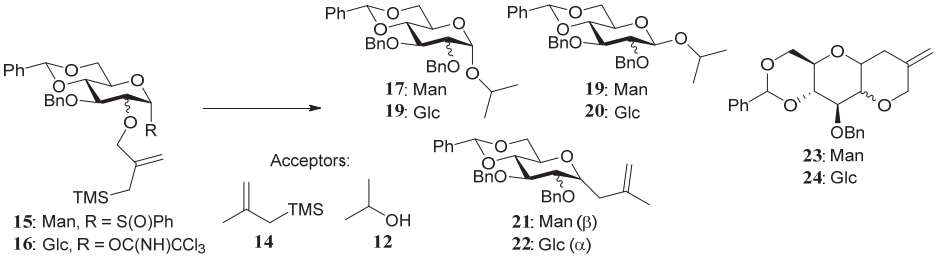


Figure 3. Cation-clock substitution products from external and internal nucleophiles.

the β-*manno*-anomer **19** is formed with a much higher concentration dependence than internal cyclization product **23**, consistent with an S_N2 scenario. It was also shown that formation of the α-anomer **17** was not concentration dependent. In contrast, the *gluco*-β-anomer **20** is formed with the same concentration dependence as α-anomer **18**, and both react with significant S_N2 character. The reactions of *C*-nucleophile **14**, followed S_N1 kinetics (pseudo-first order in these experiments).

As the research in this thesis has shown that secondary carbohydrate alcohols are significantly weaker nucleophlies than *iso*-propanol it would be of interest to perform this type of cation clock experiments with the set of partially fluorinated ethanols. Systematic variation in the reactivity of the donors (by slightly changing the protecting group pattern as described in Chapters 3 and 4) will be of interest, to pinpoint when the mechanism most radically changes.

Preactivation-based competition experiments

Decreasing the reactivity of an acceptor has consequences for the stereoselectivity of the glycosylation reaction by a change in the mechanism, as the results from Chapters 3-6 confirm. How the reactivity of the acceptor changes by its structural modifications can be effectively studied by competition of two acceptors for a limiting amount of donor, as was demonstrated in Chapter 2 by the work of the group of Crich and the group of Rúveda. The set of fluorinated model acceptors and the array of carbohydrate acceptors from Chapter 6 would serve as excellent substrates for acceptor competition experiments (Figure 4). Donors varying in reactivity, for example one favoring S_N2 and the other favoring S_N1 reactions would further help to establish the reactivities of acceptors under different circumstances. To keep the mechanistic picture of the competition experiments close to the actual glycosylations reported throughout this thesis, a preactivation setup would be the preferred method for competitive glycosylations. Preliminary results indicate that the preactivation setup may be too reactive for efficient competition between two nucleophiles either from the set of model acceptors or carbohydrate acceptors. Further studies in the field of preactivation glycosylations are necessary to develop this method of competitive glycosylations.

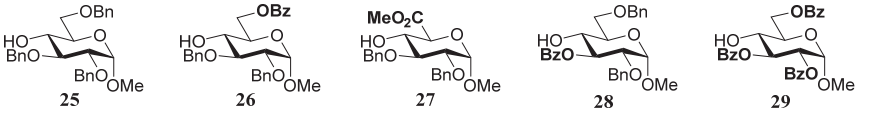
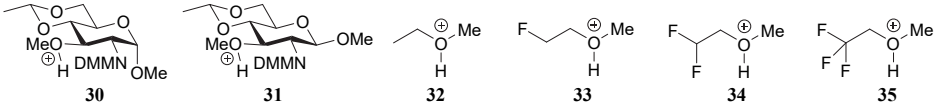


Figure 4. Selection of carbohydrate acceptors bearing functional groups influencing the reactivity of the acceptor.

Computational evaluation of the reactivity of the acceptor

In Chapter 2 the work of Stortz was described quantifying the reactivity of glycosyl acceptors.[16] They calculated the energy of formation of cationic species originating from the reaction of glycosyl alcohols with a methyl cation (Figure 5). The difference in energy of formation (ΔΔE) explained the relative reactivities of two acceptors **30** and **31** (**30**/**31**, 5:1). It would be of interest to probe this method to a wider range of glycosyl acceptors and to find out how the ΔΔE found for various acceptors correlates with experimentally obtained stereoselectivities or relative reactivity values. The set of model acceptors introduced in Chapter 3 may serve to benchmark the system and a range of acceptors like those from Chapter 6 can then be studied following the computational approach of Stortz and co-workers.



30 **31** **32** **33** **34** **35**

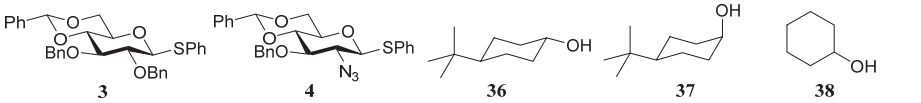
ΔE = -107.6 kcal·mol^{-1} ΔE = -99.7 kcal·mol^{-1}

Figure 5. Methylated acceptors **30** and **31**, and methylated model acceptors **32**-**35**.

Assessing steric and conformational effects in acceptor reactivity

The set of model acceptors introduced in Chapter 3 (**5-8**, *vide supra*) was used to determine how electronic effects in the acceptor affected the stereoselectivity in glycosylation reactions. It is clear that in a glycosylation reaction, that unites two bulky coupling partners, sterics also play a major role. Therefore, it would be of interest to develop a system to systematically gauge the effect of different steric environments on

Table 4. Glycosylations with model acceptors **36**-**38**.



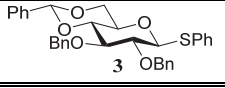
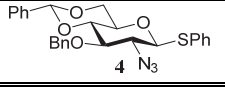
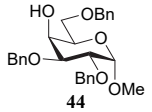
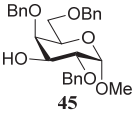
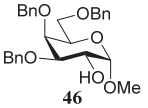
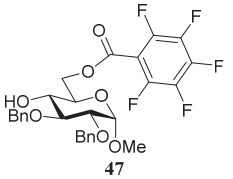
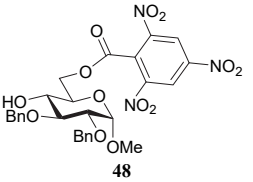
3 **4** **36** **37** **38**

Entry	Donor	Acceptor	Yield	Ratio	Product
1	**3**	**36**	65	1 : 2.5	**39**
2	**3**	**37**	52	1.5 : 1	**40**
3	**3**	**38**	71	1 : 5.1	**41**
4	**4**	**36**	96	1 : 17	**42**
5	**4**	**38**	77	<1 : 20	**43**[18]

the stereochemical outcome of a glycosylation reaction. A systematic series of acceptors could be formed by ethanol, *iso*-propanol, and *tert*-butanol. More substituted systems in which the orientation of the alcohol and neighboring groups can be modulated should be considered next. Initial experiments in this direction are displayed in Table 4. Conformationally locked cyclohexanols **36** and **37** were glycosylated with donors **3** and **4** to assess the difference in reactivity between an axial and equatorial alcohol. Interestingly, both stereoisomers were less β-selective than cyclohexanol **38** (entries 3 and 5), indicating that flexibility of the acceptor can have an important effect on the glycosylation reaction, as was previously also noted by Zhang *et al.*[17]

In Chapter 6 the stereoselectivity of condensation reactions of several C-4–OH *gluco*-configured carbohydrate acceptors with donor **3** and **4** was determined. It is of interest to expand the set of acceptors to carbohydrates having a different configuration and vary the protecting group pattern. This will further prove the generality of the approach and may lead to an acceptor reactivity chart that will serve as a reference for

Table 5. Additional glycosylations with donors **3** and **4** and carbohydrate acceptors **44**-**48**.

Acceptor	 **3**	 **4**
 **44**	**49** 12 : 1 (72 %)	**50** 3 : 1 (86 %)
 **45**	**51** 6 : 1 (85 %)	**52** 1 : 1.3 (88 %)
 **46**	**53** 10 : 1 (87 %)	**54** 1 : 1.3 (73 %)
 **47**	**55** 1.4 : 1 (71 %)	**56** 1 : 1.6 (80 %)
 **48**	**57** 2.1 : 1 (75 %)	

many future glycosylation reactions. For example, galactoside acceptors **44**-**46** have been used and glycosylations of these acceptors with donors **3** and **4** show that all three of them are moderately α-selective (Table 5). Further decreasing their reactivity by placing benzoyl groups on the acceptors should further increase their α-selectivity. Other relevant systems to investigate, include *manno*-configured acceptors, acceptors of the L-configuration such as fucose and rhamnose, but also disaccharides or thioglycosides.

Changing the substituents of the benzoyl groups may increase their electron-withdrawing capacity offering another way to fine-tune acceptor reactivity (Table 5). A series of mono-nitrated *ortho*-, *meta*-, and *para*- nitrobenzoyl groups was successfully glycosylated and a small increase in α-selectivity was observed from *para*- to *ortho*-nitrobenzoyl (from α/β = 3 : 1 to α/β = 3.5 : 1). Placing two nitro groups enhanced the α-selectivity further (5.6:1) as shown in Chapter 6. Surprisingly, installing a third nitro group (**48**) had an adverse effect, decreasing the selectivity to α/β = 2.1 : 1. The pentafluorobenzoate in acceptor **47** was even less selective providing product **55** in an α/β = 1.4 : 1 anomeric mixture.[19]

Experimental and computational evaluation of 5-deoxy furanosyl oxocarbenium ions

In Chapter 7 and 8 furanoses bearing different substituents on the C-2- and C-5-position were synthesized and studied under S_N1-glycosylation conditions to probe the effect of these substituents on the stereoselectivity of the reactions. The intermediate oxocarbenium ions were studied by the CEL map method. Initial studies into the effect of a 5-deoxy functionality have also been undertaken to investigate the effect of this modification on the stereoselectivity of the glycosylation reactions. To this end furanosyl donors **59**-**62** were synthesized and glycosylated with allyl trimethyl silane (Figure 6).

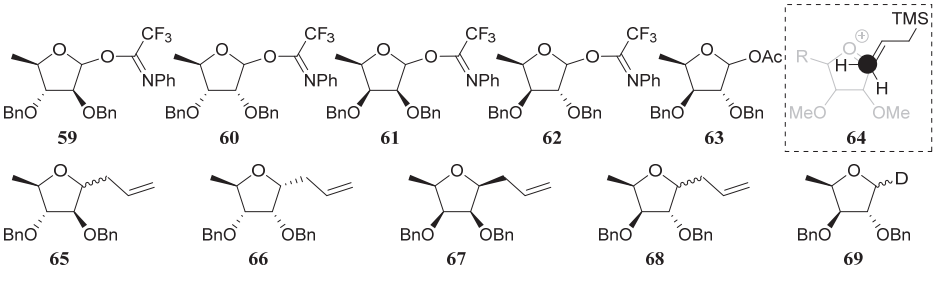
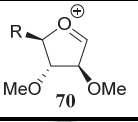
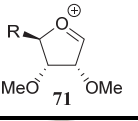
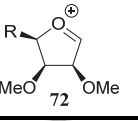
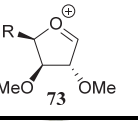
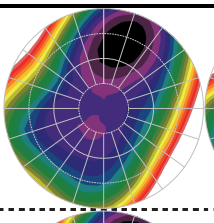
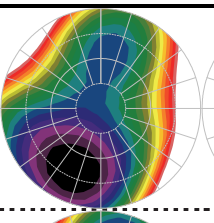
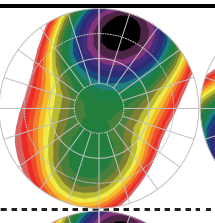
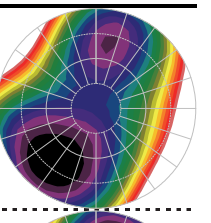
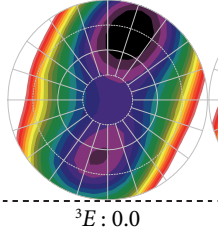
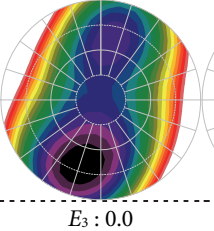
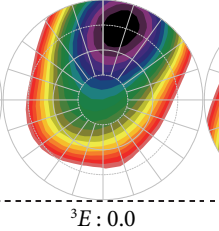
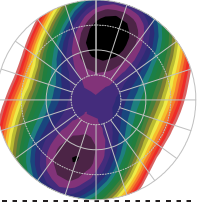
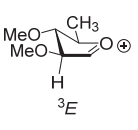
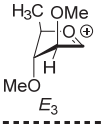
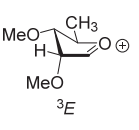
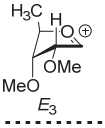
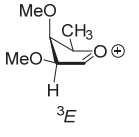
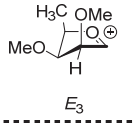
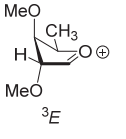
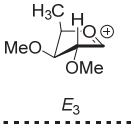


Figure 6. Imidate donors **59**-**62**, acetyl donor **63** and glycosylation products **65**-**69** of 5-deoxy furanosides. Inset: top view of the protruding C–H bonds on the acceptor.

The results of these glycosylations and the CEL maps of the 5-deoxyfuranosyl oxocarbenium ions are shown in Table 6. For the 5-deoxyribose and 5-deoxylyxose oxocarbenium ions **71** and **72** the C-2 and C-3 substituents can take up a most stabilizing orientation in the E_3 and ^3E conformation, respectively. The *ribo*- and *lyxo*-configured 5-deoxyfuranoside imidate donors **60** and **61** provide exclusively the 1,2-*cis*-product in glycosylations with allyl-TMS (**66**, **67**, Figure 6), in line with all other modifications on these two configurations. The *arabino*- and *xylo*-configured 5-deoxyfuranosides give

Table 6: CEL maps of *ribo*-configured oxocarbenium ions **70**-**73**.

	Arabinose	**Ribose**	**Lyxose**	**Xylose**
	 **70**	 **71**	 **72**	 **73**
R = CH_2OBn				
R = CH_3				
Energies (kcal·mol^{-1})	^3E : 0.0 $^3T_4$: 0.5 E_3 : 1.0	E_3 : 0.0 $^4T_3$: 0.85 ^3E : 1.5	^3E : 0.0 $^3T_4$: 1.7 E_3 : 4.5	^3E : 0.0 E_3 : 0.4
	 ^3E  E_3	 ^3E  E_3	 ^3E  E_3	 ^3E  E_3
Experimental (α : β)	**65**; 40 : 60[a]	**66**; >98 : 2[a]	**67**; <2 : 98[a]	**68**; 60 : 40[a] **69**; 40 : 60[b]
Yield (%)	86	89	56	60 and 77

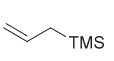
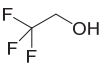
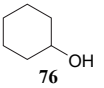
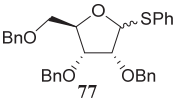
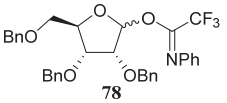
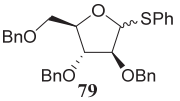
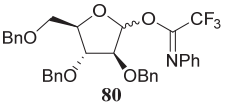
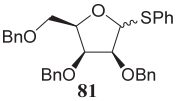
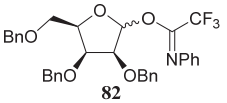
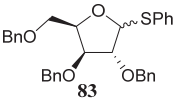
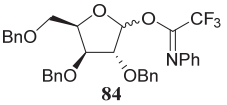
[a]Allyl-TMS was the acceptor. [b]TES-D was the acceptor, acetyl donor **63**, see experimental section. *Reagents and conditions:* donor (0.1 mmol), acceptor (0.4 mmol), TfOH (0.01 mmol), DCM (1 mL), 3Å M.S., -75°C

anomeric mixtures. This is not surprising considering the conflicting interest of the C-2 and C-3 substituents in both the *arabino*- and *xylo*-configurations. However, the CEL maps predict a different stereochemical outcome. There is no clear explanation for this discrepancy. It may be that the use of an acetyl donor and TES-D as a nucleophile provides a different outcome. Indeed, the use of these conditions slightly changed the anomeric ratio in the case of the 5-deoxyxylose donor (**63**).

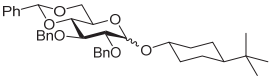
Furanoside *O*-glycosylations

Chapter 7 and 8 have reported on glycosylation reactions of differently substituted furanosyl donors with allyl-TMS and TES-D as nucleophiles. In line with previous studies by van Rijssel *et al.* the stereoselectivity in these condensations could be adequately accounted for using the CEL maps of the intermediate oxocarbenium ions.[20] Thus, these glycosylations very likely proceed with an S_N1-like mechanism. To investigate how *O*-nucleophiles react with the set of furanosyl donors the imidate donors of all perbenzylated pentofuranoses and their thiophenyl equivalents (**77**-**84**) have been glycosylated with acceptors **5**, **8**, and **76**. Table 7 lists the outcome of these experiments and compares them to the reaction with allyl-TMS **75**. It is clear that there is a relatively poor correlation between the outcome of the reactions of the *O*- versus the *C*-nucleophiles. Even the results of the condensations of the weak *O*-nucleophile, trifluoroethanol, deviate form those using TES-D and allyl-TMS. It is difficult to distill a trend from the results in Table 7, and no clear single mechanistic explanation is available to account for the observed selectivities. It is likely that the more nucleophilic acceptors **5** and **76** react in glycosylations with more S_N2-character. Therefore the nature, stability and reactivity of the intermediate anomeric triflates should be investigated by Low-Temperature NMR.[21] It may also be that the inside attack model, devised by Woerpel and co-workers, does not hold for glycosylations of *O*-nucleophiles and furanosyl oxocarbenium ions. Computational models of the triflates, and the transition states of the S_N1 and S_N2 reactions should help to build a better understanding of *O*-glycosylation of furanosides.

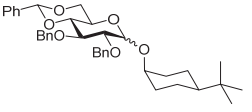
Table 7. Glycosylations of furanosides with model acceptors.

	 **75**	 **8**	 **76**	 **5**
Donor	α : β (yield)	α : β (yield)	α : β (yield)	α : β (yield)
 **77**	**85** >98 : 2 -	**86** 68 : 32 (85%)	**87** 64 : 36 (52%)	**88** 81 : 19 (72%)
 **78**	**85** >98 : 2 (31%)	**86** 65 : 35 (86%)	**87** 67 : 33 -	**88** 58 : 42 (76%)
 **79**	**89** 5 : 95 -	**90** 13 : 87 (80%)	**91** 44 : 56 (78%)	**92** 30 : 70 (51%)
 **80**	**89** 10 : 90 (25%)	**90** 14 : 86 (85%)	**91** 9 : 91 (88%)	-
 **81**	**93** <2 : 98 (54%)	**94** 48 : 52 (98%)	**95** 73 : 26 (72%)	**96** 78 : 22 (76%)
 **82**	**93** <2 : 98 (22%)	-	**95** 25 : 75 -	**96** 20 : 80 -
 **83**	**97** 80 : 20 (68%)	**98** 84 : 16 (85%)	**99** 62 : 38 (79%)	-
 **84**	**97** 85 : 15 (35%)	**98** 71 : 29 (74%)	**99** 70 : 30 (56%)	-

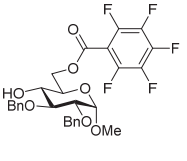
Experimental section



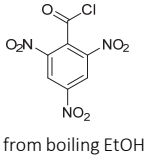
Trans-4-*tert*-butylcyclohexyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranoside (39). Donor **3** and acceptor **36** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 yielding product **39** (38 mg, 65 µmol, 65%, α:β = 1 : 2.5) as a white solid. R_f: 0.28 (toluene). IR (thin film): 696, 732, 997, 1028, 1074, 1365, 2862, 2940; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.53 – 7.46 (m, 2.6H, CH_{arom}), 7.41 – 7.24 (m, 16.9H, CH_{arom}), 5.55 (s, 1.3H, C*H*Ph$_{α,β}$), 4.96 – 4.66 (m, 5.5H, 2xCH_2 Bn$_{α,β}$, H-1α), 4.62 (d, 1H, *J* = 7.7 Hz, H-1β), 4.33 (dd, 1H, *J* = 10.5, 5.0 Hz, H-6β), 4.26 (dd, 0.3H, *J* = 10.2, 4.9 Hz, H-6β), 4.06 (t, 0.3H, *J* = 9.3 Hz, H-3α), 3.95 (td, 0.3H, *J* = 10.0, 4.8 Hz, H-5α), 3.79 (t, 1H, *J* = 10.3 Hz, H-6β), 3.76 – 3.52 (m, 3.9H, H-2α, H-3β, H-4α, H-4β, H-6α, CH Cyβ), 3.49 – 3.35 (m, 2.3H, H-2β, H-5β, CH Cyα), 2.20 – 0.95 (m, 11.7H, CH_2 Cy), 0.85 (s, 11.7H, ^{t}Bu); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 139.0, 138.6, 138.5, 138.4, 137.5, 137.4 (C_q), 131.6, 130.3, 129.3, 128.9, 128.9, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.1, 128.0, 128.0, 127.8, 127.7, 127.6, 127.5, 126.0, 126.0, 124.4 (CH_{arom}), 102.5 (C-1β), 101.2 (CHPh), 101.1 (C-1α), 96.1, 82.4, 82.2, 81.5, 81.1, 79.4, 79.3, 78.7, 76.8, 75.4, 75.1, 73.4, 69.1, 68.9, 66.0, 62.4, 47.2, 47.2, 34.2, 33.8, 32.7, 32.3, 31.9, 27.7, 25.9, 25.7, 25.6, 25.6; HRMS: $[M+H]^+$ calcd for $C_{37}H_{47}O_6$ 587.33672, found 587.33666.



Cis-4-tert-butylcyclohexyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranoside (40). Donor **3** and acceptor **37** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 yielding product **40** (31 mg, 52 µmol, 52%, α:β = 1.5 : 1) as a white solid. R_f: 0.25 and 0.22 (toluene). IR (thin film): 660, 733, 999, 1028, 1072, 1084, 1365, 2864, 2938; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.62 – 7.18 (m, 25.5H, CH_{arom}), 5.56 (s, 1H, C*H*Ph$_α$), 5.55 (s, 0.7H, C*H*Ph$_β$), 5.02 – 4.66 (m, 7.8H, 2xCH_2 Bn, H-1α), 4.58 (d, 0.7H, *J* = 7.7 Hz, H-1β), 4.32 (dd, 0.7H, *J* = 10.4, 5.0 Hz, H-6β), 4.25 (dd, 1H, *J* = 10.2, 4.8 Hz, H-6α), 4.09 (t, 1H, *J* = 9.2 Hz, H-3α), 4.02 (t, 0.7H, *J* = 2.6 Hz, CH Cyβ), 3.94 (td, 1H, *J* = 10.0, 5.0 Hz, H-5α), 3.85 – 3.66 (m, 4.4H, H-3β, H-4β, H-6α, H-6β, CH Cyα), 3.62 (t, 1H, *J* = 9.4 Hz, H-4α), 3.57 (dd, 1H, *J* = 9.3, 3.7 Hz, H-2α), 3.48 (t, 0.7H, *J* = 8.0 Hz, H-2β), 3.39 (td, 0.7H, *J* = 9.5, 4.9 Hz, H-5β), 2.09 – 1.88 (m, 3.4H, CH_2 Cy), 1.61 – 1.24 (m, 10.2H, CH_2 Cy), 1.05 – 0.94 (m, 1.7H, CH Cy), 0.83 (s, 9H, ^{t}Bu), 0.81 (s, 6.3H, ^{t}Bu); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 139.0, 138.7, 138.6, 137.6, 137.5, 129.0, 129.0, 128.4, 128.4, 128.3, 128.1, 128.1, 127.9, 127.7, 127.7, 127.7, 127.6, 126.1, 102.1 (C-1β), 101.3, 101.2 (CHPh), 96.1 (C-1α), 82.6 (C-4α), 82.1 (C-2α), 81.7, 81.2 (C-3β, C-4β), 79.8 (C-2α), 78.5 (C-3α), 75.3, 75.2, 75.2, 73.2 (CH_2 Bn), 73.1 (CH Cy), 71.8 (CH Cyα), 69.4 (C-6α), 69.0 (C-6β), 66.2 (C-5α), 62.8 (C-5β), 48.0, 48.0, 32.7, 32.7, 32.6, 32.4, 29.8, 27.7, 27.6, 21.9, 21.8, 21.7, 21.5; HRMS: $[M+H]^+$ calcd for $C_{37}H_{47}O_6$ 587.33672, found 587.33660.

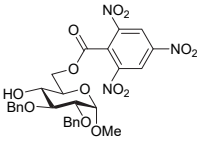


Methyl 2,3-di-*O*-benzyl-6-O-(2,3,4,5,6-pentafluorobenzoyl)-α-D-glucopyranoside (47). Methyl 2,3-di-*O*-benzyl-α-D-glucopyranoside[22] (374 mg, 1.0 mmol, 1 eq.) was converted to the title compound **47** following general procedure **C** of Chapter 6 (pentafluorobenzoyl chloride; 145 µL, 1.05 mmol, 1.05 eq.). Yield: 550 mg, 0.97 mmol, 97%. $[\alpha]_D^{20}$ = +22.7° (*c* = 0.6, $CHCl_3$); IR (thin film): 698, 739, 1007, 1057, 1229, 1325, 1497, 1524, 1653, 1740, 2916, 3500; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.40 – 7.30 (m, 10H, CH_{arom}), 5.03 (d, 1H, *J* = 11.5 Hz, C*H*H Bn), 4.78 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.71 (d, 1H, *J* = 11.5 Hz, CH*H* Bn), 4.66 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.62 (d, 1H, *J* = 3.5 Hz, H-1), 4.62 (dd, 1H, *J* = 11.9, 2.2 Hz, H-6), 4.54 (dd, 1H, *J* = 11.9, 5.4 Hz, H-6), 3.86 (ddd, 1H, *J* = 10.0, 5.4, 2.2 Hz, H-5), 3.80 (t, 1H, *J* = 9.2 Hz, H-3), 3.52 (dd, 1H, *J* = 9.6, 3.5 Hz, H-2), 3.51 – 3.45 (m, 1H, H-4), 3.39 (s, 3H, CH_3 OMe), 2.33 (d, 1H, *J* = 2.7 Hz, 4-OH); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 159.0 (C=O), 146.7, 144.5, 142.4, ($CF_{ortho/para}$), 138.8, 138.7 (CF_{meta}), 138.0 (C_q), 136.9, 136.8 (CF_{meta}), 128.8, 128.7, 128.2, 128.2 (CH_{arom}), 108.0 ($C_{q\text{-}ipso}$), 98.3 (C-1), 81.2 (C-3), 79.8 (C-2), 75.6, 73.3 (CH_2 Bn), 70.0 (C-4), 68.9 (C-5), 65.6 (C-6), 55.5 (OMe); ^{19}F NMR ($CDCl_3$, 471 MHz): δ -137.87 (dp, 2F, *J* = 16.5, 5.4 Hz, *ortho*-F_5Bz), -148.29 (tt, 1F, *J* = 20.9, 4.8 Hz, *para*-F_5Bz), -160.46 (tt, 2F, *J* = 21.0, 5.9 Hz, *meta*-F_5Bz); HRMS: $[M+Na]^+$ calcd for $C_{28}H_{25}F_5O_7Na$ 591.1418, found 591.1431.

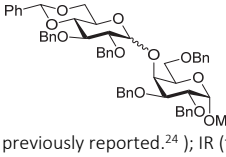


2,4,6-Trinitrobenzoyl chloride (S1). Toluene (2.1 mL, 20 mmol) was dissolved in 17 mL H_2SO_4 and cooled to 0°C. To this mixture a solution of HNO_3 (99%, 4.2 mL) in 15 mL H_2SO_4 was slowly added (15 min, temperature remains below 40°C). When addition was complete, the reaction mixture was slowly heated to 95°C and kept at that temperature for 3 h. The solution was cooled and poured over ice. The precipitate was collected, washed with cold H_2O, air-dried, and crystallized from boiling EtOH (50 mL) to form large needles of 2,4,6-trinitrotoluene (TNT) (3.8 g, 16.8 mmol, 84%). ^{1}H NMR (DMSO, 400 MHz): δ 9.03 (s, 2H), 2.57 (s, 3H). The TNT (2.27 g, 10 mmol) was dissolved in H_2SO_4 (18 mL) and $K_2Cr_2O_7$ (3.18 g,

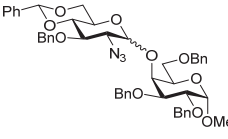
10.8 mmol) was added in small portions, mainting a temperature below 35°C (ice-bath). After stirring overnight at room temperature, the reaction mixture was poured on ice and the precipitate collected, washed with cold H_2O, dried and crystallized from boiling H_2O to yield 2,4,5-trinitrobenzoic acid (TNBA) as yellow crystals (1,1 g, 4.3 mmol, 43%). ^{1}H NMR (MeOD, 400 MHz): δ 9.23 (s, 2H); ^{13}C-APT NMR (MeOD, 101 MHz): δ 164.1, 149.3, 148.6, 131.6, 125.6. The TNBA (390 mg, 1.5 mmol) was suspended in DCE (300 µL) and DMF (15 µL), thionyl chloride was slowly added (375 µL) and the mixture heated to 80°C for 2 h. The reaction mixture was cooled to 0°C and the precipitate was collected by filtration and washed with cold DCE to yield the 2,4,6-trinitrobenzoyl chloride as a yellow solid (250 mg, 0.9 mmol, 60%). Spectroscopic data were in accord with those previously reported.[23] ^{1}H NMR (DMSO, 400 MHz): δ 9.14 (s, 2H); ^{13}C-APT NMR (DMSO, 101 MHz): δ 162.4, 147.6, 146.7, 129.7, 125.0.



Methyl 2,3-di-*O*-benzyl-6-O-(2,4,6-trinitrobenzoyl)-α-D-glucopyranoside (48). Methyl 2,3-di-*O*-benzyl-α-D-glucopyranoside[22] (374 mg, 1.0 mmol, 1 eq.) was converted to the title compound **48** following general procedure **C** of Chapter 6 (2,4,6-trinitrobenzoyl chloride **S1**; 250 mg , 0.9 mmol, 0.9 eq. and 90 µL pyridine, 1.2 eq.). Yield: 137 mg, 0.22 mmol, 22%. $[\alpha]_D^{20}$ = +29.7° (*c* = 0.67, $CHCl_3$); IR (thin film): 700, 735, 1059, 1261, 1279, 1342, 1454, 1545, 1553, 1609, 1751, 2922, 3600; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 9.23 (s, 2H, CH_{arom} NO_2Bz), 7.37 – 7.26 (m, 10H, CH_{arom} Bn), 4.99 (d, 1H, *J* = 11.4 Hz, C*H*H Bn), 4.78 – 4.72 (m, 2H, C*H*H Bn, H-6), 4.72 – 4.66 (m, 2H, CH*H* Bn, H-6), 4.66 – 4.62 (m, 2H, CH*H* Bn, H-1), 3.89 (ddd, 1H, *J* = 10.1, 4.9, 2.2 Hz, H-5), 3.80 (t, 1H, *J* = 9.2 Hz, H-3), 3.50 – 3.44 (m, 2H, H-2, H-4), 3.36 (s, 3H, CH_3 OMe), 2.42 (d, 1H, *J* = 2.9 Hz, 4-OH); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 160.7 (C=O), 147.9, 147.3 (C_q NO_2), 138.7, 138.0 (C_q Bn), 129.9 (C_q Bz), 128.7, 128.6, 128.2, 128.1, 128.1, 124.6 (CH_{arom}), 98.4 (C-1), 81.2 (C-3), 79.6 (C-2), 75.6, 73.2 (CH_2 Bn), 69.8 (C-4), 68.9 (C-5), 67.0 (C-6), 55.6 (OMe); HRMS: $[M+Na]^+$ calcd for $C_{28}H_{27}N_3O_{13}Na$ 636.1442, found 636.1451.

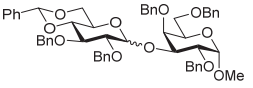


Methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranosyl)-2,3,6-tri-*O*-benzyl-α-D-galactopyranoside (49). Donor **3** and acceptor **44** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 yielding product **49** (60 mg, 72 µmol, 72%, α:β = 12 : 1) as a colorless oil. R_f: 0.50 (4/1 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[24]); IR (thin film): 694, 733, 995, 1026, 1049, 1076, 1086, 1364, 1452, 1498, 2864, 2926; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC, HMBC): δ 7.53 – 7.49 (m, 2H, CH_{arom}), 7.45 – 7.15 (m, 28H, CH_{arom}), 5.52 (s, 1H, C*H*Ph), 4.97 – 4.93 (m, 2H, C*H*H Bn, H-1'), 4.89 (d, 1H, *J* = 12.3 Hz, C*H*H Bn), 4.87 (d, 1H, *J* = 11.9 Hz, C*H*H Bn), 4.81 – 4.74 (m, 4H, CH_2 Bn, 2xCH*H* Bn), 4.70 (d, 1H, *J* = 11.9 Hz, CH*H* Bn), 4.65 (d, 1H, *J* = 3.5 Hz, H-1), 4.29 (td, 1H, *J* = 10.0, 4.9 Hz, H-5'), 4.26 (d, 1H, *J* = 11.9 Hz, C*H*H Bn), 4.22 (d, 1H, *J* = 11.9 Hz, CH*H* Bn), 4.06 (d, 1H, *J* = 2.3 Hz, H-4), 4.02 (t, 1H, *J* = 9.3 Hz, H-3'), 3.97 – 3.78 (m, 5H, H-2, H-3, H-5, H-6, H-6'), 3.60 (dd, 1H, *J* = 9.7, 9.3 Hz, H-4'), 3.56 (dd, 1H, *J* = 9.5, 3.6 Hz, H-2'), 3.52 – 3.46 (m, 2H, H-6, H-6'), 3.36 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC, HMBC): δ 138.9, 138.6, 138.4, 138.3, 138.3, 137.8 (C_q), 128.8, 128.6, 128.5, 128.5, 128.5, 128.4, 128.3, 128.3, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 127.5, 126.1 (CH_{arom}), 101.2 (CHPh), 100.6 (C-1'), 99.1 (C-1), 82.9 (C-4'), 79.7 (C-2'), 79.2 (C-3'), 77.8 (C-3), 77.3 (C-4), 75.2, 74.4 (CH_2 Bn), 74.4 (C-2), 73.6, 73.0, 73.0 (CH_2 Bn), 69.4 (C-5), 69.1 (C-6'), 68.1 (C-6), 63.1 (C-5'), 55.5 (OMe); HRMS: $[M+Na]^+$ calcd for $C_{55}H_{58}O_{11}Na$ 917.3877, found 917.3903.

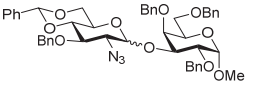


Methyl 4-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranosyl)-2,3,6-tri-*O*-benzyl-α-D-galactopyranoside (50). Donor **4** and acceptor **44** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 yielding product **50** (70 mg, 86 µmol, 86%, α:β = 3 : 1) as a colorless oil. R_f: 0.60 (4/1 pentane/EtOAc); IR (thin film): 696, 737,997, 1034, 1055, 1092, 1369, 1454, 1497, 2106, 2866, 2928, 3030; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.54 – 7.15 (m, 25H, CH_{arom}), 5.52 (s, 1H, C*H*Ph), 4.95 (d, 1H, *J* = 10.7 Hz, C*H*H Bn), 4.84 – 4.78 (m, 5H, 2xCH$_2$ Bn, H-1'), 4.74 (d, 1H, *J* = 10.7 Hz, CH*H* Bn), 4.68 (d, 1H, *J* = 3.3 Hz, H-1), 4.57 (d, 1H, *J* = 11.8 Hz, C*H*H Bn), 4.49 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.32 (td, 1H, *J* = 10.0, 4.9 Hz, H-5'), 4.13 (d, 1H, *J* = 2.3 Hz, H-4), 3.97 – 3.84 (m, 5H, H-2, H-3, H-3', H-5, H-6), 3.77 (dd, 1H, *J* = 10.1, 4.9 Hz, H-6'), 3.64 (t, *J* = 9.5 Hz, 1H, H-4'), 3.55 – 3.46 (m, 2H, H-6, H-6'), 3.36 (s, 3H, CH_3 OMe), 3.33 (dd, 1H, *J* = 10.0, 3.8 Hz, H-2'); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.5, 138.2, 138.1, 137.7, 137.6 (C_q), 128.6, 128.6, 128.6, 128.5, 128.3, 128.2, 127.6, 126.1 (CH_{arom}), 101.2 (CHPh), 99.0 (C-1'), 98.9 (C-1), 83.0 (C-4'), 77.3 (C-2), 77.0 (C-3'), 75.7 (C-4), 75.2 (CH_2 Bn), 74.7 (C-3), 73.6, 73.4, 73.2 (CH_2 Bn), 68.8, 68.8 (C-5, C-6'), 67.1 (C-6), 63.8 (C-2'), 62.9 (C-5'), 55.5 (OMe); Diagnostic peaks β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 4.95 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.90 (d, 1H, *J* = 11.4 Hz, C*H*H Bn), 4.62 (d, 1H, *J* = 3.7 Hz, H-1), 4.55 (d, 1H, *J* = 11.9 Hz, C*H*H Bn), 4.47 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.11 (dd, 1H, *J* = 10.1, 3.7 Hz, H-2), 3.37 (s, 3H, CH_3 OMe), 3.20 (td, 1H,

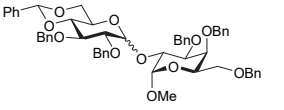
J = 9.8, 5.0 Hz, H-5'); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 139.0, 138.6, 138.3, 138.0, 137.2 (C_q), 102.1 (C-1'), 101.4 (CHPh), 98.9 (C-1), 81.6, 79.0, 78.4, 76.4, 75.0, 73.9, 73.8, 73.4, 69.6, 69.0, 68.6, 66.5 (C-2'), 66.0 (C-5'), 55.5 (OMe); HRMS: $[M+Na]^+$ calcd for $C_{48}H_{51}N_3O_{10}Na$ 852.3472, found 852.3488.



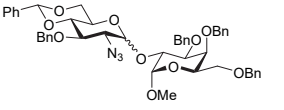
Methyl 3-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranosyl)-2,4,6-tri-*O*-benzyl-α-D-galactopyranoside (51). Donor **3** and acceptor **45** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 yielding product **51** (76 mg, 85 µmol, 85%, α:β = 6 : 1) as a colorless oil. R_f: 0.25 and 0.51 (4/1 pentane/EtOAc); IR (thin film): 696, 735, 1028, 1049, 1074, 1088, 1350, 1368, 154, 2864, 2914; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.48 – 7.45 (m, 2H, CH_{arom}), 7.40 – 7.14 (m, 28H, CH_{arom}), 5.54 (s, 1H, C*H*Ph), 5.06 (d, 1H, *J* = 3.6 Hz, H-1'), 5.00 (d, 1H, *J* = 11.3 Hz, C*H*H Bn), 4.91 (d, 1H, *J* = 11.5 Hz, C*H*H Bn), 4.84 (d, 1H, *J* = 11.4 Hz, C*H*H Bn), 4.80 – 4.75 (m, 2H, CH*H* Bn, C*H*H Bn), 4.68 (d, 1H, *J* = 11.5 Hz, CH*H* Bn), 4.62 (d, 1H, *J* = 3.5 Hz, H-1), 4.56 (d, 1H, *J* = 11.9 Hz, CH*H* Bn), 4.47 (d, 1H, *J* = 11.8 Hz, C*H*H Bn), 4.37 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.36 (d, 1H, *J* = 11.4 Hz, CH*H* Bn), 4.23 (td, 1H, *J* = 10.0, 4.9 Hz, H-5'), 4.16 (dd, 1H, *J* = 10.1, 4.9 Hz, H-6'), 4.10 (t, 1H, *J* = 9.3 Hz, H-3'), 4.04 (dd, 1H, *J* = 10.2, 2.8 Hz, H-3), 3.96 (dd, 1H, *J* = 10.2, 3.6 Hz, H-2), 3.91 (dd, 1H, *J* = 2.8, 1.1 Hz, H-4), 3.83 (t, 1H, *J* = 6.9 Hz, H-6), 3.64 (t, 1H, *J* = 9.5 Hz, H-4'), 3.63 (t, 1H, *J* = 10.2 Hz, H-6'), 3.62 (dd, 1H, *J* = 9.4, 3.5 Hz, H-2'), 3.48 – 3.46 (m, 2H, H-5, H-6), 3.31 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 139.1, 138.7, 138.3, 138.1, 138.1, 137.8 (C_q), 128.5, 128.5, 128.5, 128.4, 128.2, 128.2, 128.2, 128.2, 128.1, 127.9, 127.9, 127.8, 127.7, 127.4, 126.3 (CH_{arom}), 101.3 (CHPh), 98.5 (C-1'), 98.5 (C-1), 82.7 (C-4'), 79.8 (C-2'), 78.7 (C-3'), 78.2 (C-3), 75.8 (C-2), 75.5 (C-4), 75.1, 75.0, 74.6, 73.6, 73.4 (CH_2 Bn), 69.3 (C-5), 69.2 (C-6), 69.0 (C-6'), 63.1 (C-5'), 55.3 (OMe); Diagnostic peaks β-anomer: ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.52 – 7.48 (m, 2H, CH_{arom}), 7.42 – 7.16 (m, 28H, CH_{arom}), 5.57 (s, 1H, C*H*Ph), 5.04 (d, 1H, *J* = 7.7 Hz, H-1'), 5.00 (d, 1H, *J* = 11.5 Hz, C*H*H Bn), 4.98 (d, 1H, *J* = 11.4 Hz, C*H*H Bn), 4.94 (d, 1H, *J* = 11.3 Hz, C*H*H Bn), 4.84 (d, 1H, *J* = 11.5 Hz, CH*H* Bn), 4.82 (d, 1H, *J* = 11.3 Hz, CH*H* Bn), 4.65 (d, 1H, *J* = 11.5 Hz, CH*H* Bn), 4.63 (d, 1H, *J* = 11.8 Hz, C*H*H Bn), 4.55 (d, 1H, *J* = 3.7 Hz, H-1), 4.48 (d, 1H, *J* = 11.6 Hz, C*H*H Bn), 4.40 (d, 1H, *J* = 11.6 Hz, CH*H* Bn), 4.32 (dd, 1H, *J* = 10.5, 5.1 Hz, H-6'), 4.32 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.24 (dd, 1H, *J* = 10.1, 3.1 Hz, H-3), 3.99 (dd, 1H, *J* = 10.1, 3.7 Hz, H-2), 3.97 – 3.93 (m, 2H, H-4, H-6), 3.79 – 3.74 (m, 2H, H-3', H-6'), 3.69 (t, 1H, *J* = 9.3 Hz, H-4), 3.54 – 3.52 (m, 2H, H-5, H-6), 3.46 (dd, 1H, *J* = 8.7, 7.8 Hz, H-2'), 3.40 (td, 1H, *J* = 9.9, 5.1 Hz, H-5'), 3.31 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 103.9 (C-1'), 101.2 (CHPh), 98.5 (C-1), 82.9 (C-2'), 81.9 (C-4'), 81.1(C-3'), 77.9, 75.3, 75.3, 75.2, 73.7, 73.6, 69.1, 69.1, 68.9, 65.8 (C-5'), 55.4 (OMe); HRMS: $[M+Na]^+$ calcd for $C_{55}H_{58}O_{11}Na$ 917.3877, found 917.3885.



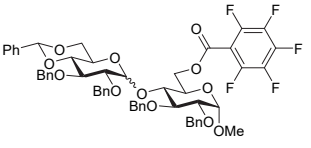
Methyl 3-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranosyl)-2,4,6-tri-*O*-benzyl-α-D-galactopyranoside (52). Donor **4** and acceptor **45** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 yielding product **52** (73 mg, 88 µmol, 88%, α:β = 1 : 1.3) as a colorless oil. R_f: 0.43 and 0.66 (4/1 pentane/EtOAc); IR (thin film): 696, 735, 995, 1028, 1047, 1092, 1350, 1369, 1454, 2108, 2866, 2910; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.48 – 7.21 (m, 57.5H, CH_{arom}), 5.57 (s, 1.3H, C*H*Phβ), 5.55 (s, 1H, C*H*Phα), 5.13 (d, 1H, *J* = 3.6 Hz, H-1'α), 5.01 (d, 1H, *J* = 11.2 Hz, C*H*H Bnα), 4.94 – 4.84 (m, 6.2H, 4xC*H*H Bn, H-1'β), 4.80 (d, 1.3H, *J* = 11.2 Hz, CH*H* Bnβ), 4.76 (d, 1H, *J* = 11.9 Hz, C*H*H Bnα), 4.75 (d, 1H, *J* = 11.0 Hz, CH*H* Bnα), 4.65 (d, 1H, *J* = 3.6 Hz, H-1α), 4.60 – 4.53 (m, 5.9H, 4xCH*H* Bn, H-1β), 4.48 (d, 1H, *J* = 11.7 Hz, C*H*H Bnα), 4.48 (d, 1.3H, *J* = 11.8 Hz, C*H*H Bnβ), 4.40 (d, 1H, *J* = 11.7 Hz, CH*H* Bnα), 4.40 (d, 1.3H, *J* = 11.7 Hz, CH*H* Bnβ), 4.31 (dd, 1.3H, *J* = 10.4, 5.1 Hz, H-6'β), 4.27 – 4.22 (m, 2H, H-5'α, H-6'α), 4.19 (dd, 1.3H, *J* = 10.1, 3.2 Hz, H-3β), 4.12 (dd, 1H, *J* = 10.3, 2.9 Hz, H-3α), 4.10 – 4.04 (m, 2.3H, H-2β, H-3'α), 4.02 – 3.97 (m, 2H, H-2α, H-4α), 3.95 – 3.87 (m, 3.6H, H-4β, H-5α, H-5β), 3.78 – 3.64 (m, 4.6H, H-4'α, H-4'β, H-6'α, H-6'β), 3.56 – 3.49 (m, 6.9H, H-2'α, H-3'β, H-6α, H-6α, H-6β, H-6β), 3.42 (dd, 1.3H, *J* = 9.5, 8.0 Hz, H-2'β), 3.36 (td, 1.3H, *J* = 9.9, 5.1 Hz, H-5'β), 3.33 (s, 3H, CH_3 OMeα), 3.31 (s, 3.9H, CH_3 OMeβ); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 138.7, 138.7, 138.3, 138.2, 138.1, 138.0, 137.9, 137.8, 137.6, 137.2 (C_q), 129.1, 129.0, 128.6, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.2, 128.1, 128.1, 128.0, 128.0, 127.9, 127.9, 127.9, 127.9, 127.8, 127.7, 126.3, 126.1 (CH_{arom}), 102.9 (C-1'β), 101.5 (CHPhα), 101.4 (CHPhβ), 98.5 (C-1α), 98.3 (C-1β), 96.1 (C-1'α), 83.0 (C-4'α), 81.8 (C-4'β), 79.1 (C-3'β), 77.4, 77.3 (C-2β, C-4β), 76.8 (C-3β), 76.2 (C-3'α), 75.8 (C-3α), 75.3 (C-2α), 75.2, 75.1, 75.0, 75.0 (CH_2 Bn), 74.1 (C-4α), 73.7, 73.6, 73.6, 73.6 (CH_2 Bn), 69.1, 69.0 (C-5α, C-5β), 69.0, 68.9, 68.8, 68.7 (C-6α, C-6β, C-6'α, C-6'β), 66.9 (C-2'β), 66.0 (C-5'β), 63.6 (C-2'α), 62.9 (C-5'α), 55.4, 55.4 (OMe); HRMS: $[M+Na]^+$ calcd for $C_{48}H_{51}N_3O_{10}Na$ 852.3472, found 852.3482.



Methyl 2-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-galactopyranoside (53). Donor **3** and acceptor **46** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 yielding product **53** (78 mg, 87 µmol, 87%, α:β = 10 : 1) as a colorless oil. R_f: 0.60 (4/1 pentane/EtOAc); IR (thin film): 696, 734, 1028, 1053, 1076, 1085, 1366, 1454, 2864, 2914; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.44 – 7.12 (m, 30H, CH_{arom}), 5.51 (s, 1H, C*H*Ph), 4.92 – 4.86 (m, 4H, 2xC*H*H Bn, H-1, H-1'), 4.86 – 4.80 (m, 3H, 2xC*H*H Bn, CH*H* Bn), 4.71 (d, 1H, *J* = 12.3 Hz, CH*H* Bn), 4.67 (d, 1H, *J* = 11.5 Hz, CH*H* Bn), 4.52 (d, 1H, *J* = 11.3 Hz, CH*H* Bn), 4.51 (d, 1H, *J* = 11.8 Hz, C*H*H Bn), 4.43 (d, 1H, *J* = 11.7 Hz, CH*H* Bn), 4.33 (dd, 1H, *J* = 10.3, 3.5 Hz, H-2), 4.25 (td, 1H, *J* = 10.0, 5.0 Hz, H-5'), 4.15 (dd, 1H, *J* = 10.1, 5.0 Hz, H-6'), 4.13 (t, 1H, *J* = 9.2 Hz, H-3'), 4.02 (dd, 1H, *J* = 10.3, 2.8 Hz, H-3), 3.95 (dd, 1H, *J* = 2.9, 1.2 Hz, H-4), 3.94 – 3.91 (m, 1H, H-6), 3.62 (t, 1H, *J* = 10.2 Hz, H-6'), 3.61 – 3.53 (m, 4H, H-2', H-4', H-5, H-6), 3.42 (s, 3H); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 138.9, 138.7, 138.6, 138.2, 138.0, 137.8 (C_q), 128.8, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.1, 128.1, 128.1, 127.9, 127.9, 127.9, 127.9, 127.7, 127.6, 127.6, 126.3 (CH_{arom}), 101.3 (CHPh), 97.0 (C-1), 95.5 (C-1'), 82.3 (C-4'), 78.9 (C-2'), 78.6 (C-3'), 77.6 (C-3), 75.2 (CH_2 Bn), 75.1 (C-4), 75.0, 73.7, 73.4, 73.4 (CH_2 Bn), 72.0 (C-2), 69.5 (C-5), 69.2 (C-6), 69.0 (C-6'), 62.4 (C-5'), 55.2 (OMe); Diagnostic peaks β-anomer: ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 5.54 (s, 1H, C*H*Ph), 5.00 (d, 1H, *J* = 11.2 Hz, C*H*H Bn), 3.76 (t, 1H, *J* = 10.3 Hz), 3.77 – 3.66 (m, 2H), 3.41 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 105.0 (C-1'), 101.2 (CHPh), 100.0 (C-1), 82.1, 81.4, 81.0, 78.4, 75.1, 75.0, 73.6, 73.0, 69.3, 69.1, 68.8, 66.0, 62.4, 55.2; HRMS: $[M+Na]^+$ calcd for $C_{55}H_{58}O_{11}Na$ 917.3877, found 917.3874.

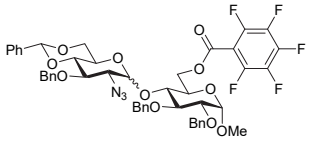


Methyl 2-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-galactopyranoside (54). Donor **4** and acceptor **46** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 yielding product **54** (60 mg, 73 µmol, 73%, α:β = 1 : 1.3) as a colorless oil. R_f: 0.74 (4/1 pentane/EtOAc); IR (thin film): 696, 735, 997, 1028, 1051, 1090, 1356, 1368, 1454, 2108, 2866, 2912; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.49 – 7.22 (m, 57.5H, CH_{arom}), 5.55 (s, 1.3H, C*H*Phβ), 5.54 (s, 1H, C*H*Phα), 4.98 (d, 1H, *J* = 3.7 Hz, H-1'α), 4.94 – 4.86 (m, 6.9H, 5xC*H*H Bn, H-1α), 4.85 (d, 1.3H, *J* = 3.7 Hz, H-1β), 4.79 (d, 1.3H, *J* = 11.3 Hz, CH*H* Bn), 4.75 (d, 1H, *J* = 11.0 Hz, CH*H* Bn), 4.74 (d, 1H, *J* = 11.6 Hz, C*H*H Bn), 4.69 (d, 1.3H, *J* = 11.5 Hz, CH*H* Bn), 4.65 (d, 1H, *J* = 11.5 Hz, CH*H* Bn), 4.58 (d, 1H, *J* = 8.0 Hz, H-1'β), 4.54 – 4.50 (m, 3.3H, C*H*H Bn, 2xCH*H* Bn), 4.47 (d, 1.3H, *J* = 11.8 Hz, C*H*H Bn), 4.43 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.39 (d, 1.3H, *J* = 11.8 Hz, CH*H* Bn), 4.31 – 4.23 (m, 3.3H, H-2α, H-5', H-6'β), 4.17 (dd, 1H, *J* = 10.2, 5.0 Hz, H-6'α), 4.16 (dd, 1.3H, *J* = 9.7, 3.7 Hz, H-2β), 4.08 (dd, 1H, *J* = 9.8, 9.2 Hz, H-3'α), 3.97 – 3.89 (m, 6.9H, H-3α, H-3β, H-4α, H-4β, H-5α, H-5β), 3.74 (t, 1.3H, *J* = 10.3 Hz, H-6'β), 3.73 – 3.65 (m, 3.3H, H-4'α, H-4'β, H-6'α), 3.62 – 3.55 (m, 3.9H, H-2'β, H-3'β, H-6β), 3.52 (dd, 2H, *J* = 6.4, 3.2 Hz, H-6α), 3.43 (s, 3H, CH_3 OMeα), 3.43 (dd, 1H, *J* = 9.9, 3.7 Hz, H-2'α), 3.39 (s, 3.9H, CH_3 OMeβ), 3.36 (td, 1.3H, *J* = 10.0, 5.0 Hz, H-5'β); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 138.7, 138.6, 138.6, 138.1, 138.1, 138.0, 137.9, 137.9, 137.6, 137.2 (C_q), 129.1, 129.0, 128.6, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.0, 127.9, 127.9, 127.8, 127.8, 127.8, 127.8, 127.7, 126.3, 126.1 (CH_{arom}), 103.6 (C-1'β), 101.5, 101.4 (CHPh), 100.0 (C-1β), 97.1 (C-1α), 95.6 (C-1'α), 82.9 (C-4'α), 81.6 (C-4'β), 79.6 (C-3'β), 78.1, 77.9, 77.5 (C-2β, C-3α, C-3β), 76.2 (C-3'α), 75.2, 74.9 (C-4α, C-4β), 75.1, 75.1, 75.0, 75.0 (CH_2 Bn), 73.7, 73.6, 73.3, 73.3 (CH_2 Bn), 72.5 (C-2α), 69.4, 69.2 (C-5α, C-5β), 69.1, 69.0 (C-6α, C-6β), 68.9 (C-6'α), 68.6 (C-6'β), 66.1 (C-5'β), 65.9 (C-2'β), 63.0 (C-2'α), 62.7 (C-5'α); HRMS: $[M+Na]^+$ calcd for $C_{48}H_{51}N_3O_{10}Na$ 852.3472, found 852.3488.

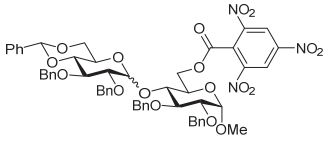


Methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranosyl)-2,3-di-*O*-benzyl-6-*O*-(2,3,4,5,6-pentafluorobenzoyl)-α-D-glucopyranoside (55). Donor **3** and acceptor **47** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 yielding product **55** (71 mg, 71 µmol, 71%, α:β = 1.4 : 1) as a colorless oil. R_f: 0.82 (4/1 pentane/EtOAc); IR (thin film): 696, 735, 1007, 1028, 1047, 1076, 1088, 1227, 1325, 1454, 1496, 1524, 1740, 2870, 2926; Data reported as a 1 : 0.7 mixture of anomers: ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC, HMBC): δ 7.51 – 7.18 (m, 42.5H), 5.56 (d, 1H, *J* = 3.9 Hz, H-1'α), 5.52 (s, 0.7H, C*H*Phβ), 5.49 (s, 1H, C*H*Phα), 4.97 (d, 1H, *J* = 11.5 Hz, C*H*H Bnα), 4.95 – 4.90 (m, 3.1H, C*H*H Bnα, 3xC*H*H Bnβ), 4.83 (d, 0.7H, *J* = 10.7 Hz, CH*H* Bnβ), 4.81 – 4.74 (m, 5.1H, 2xCH*H* Bnα, 2xCH*H* Bnβ, C*H*H Bnβ, H-6α), 4.73 – 4.67 (m, 2H, 2xC*H*H Bnα), 4.63 (dd, 0.7H, *J* = 12.0, 2.0 Hz, H-6β), 4.62 (d, 0.7H, *J* = 12.1 Hz, CH*H* Bnβ), 4.59 – 4.51 (m, 5.4H, 2xCH*H* Bnα, H-1α, H-1β, H-1'β, H-6α), 4.49 (dd, 0.7H, *J* = 12.0, 4.2 Hz, H-6β), 4.20 (dd, 0.7H, *J* = 10.5, 5.0 Hz, H-6'β), 4.12 (dd, 1H, *J* = 10.3, 4.7 Hz, H-6'α), 4.08 (dd, 1H, *J* = 9.4, 8.7 Hz, H-3α), 4.05 – 4.00 (m, 2H, H-3'α, H-5α), 3.91 – 3.84 (m, 1.7H, H-3β, H-4α), 3.82 – 3.73 (m, 2.4H, H-

3'$_\beta$, H-4$_\beta$, H-5'$_\alpha$), 3.70 (ddd, 0.7H, *J* = 9.8, 4.1, 1.9 Hz, H-5$_\beta$), 3.67 – 3.58 (m, 2.7H, H-4'$_\alpha$, H-4'$_\beta$, H-6'$_\alpha$), 3.56 – 3.50 (m, 2.7H, H-2$_\alpha$, H-2'$_\alpha$, H-6'$_\beta$), 3.48 – 3.44 (m, 1.4H, H-2$_\beta$, H-2'$_\beta$), 3.39 (s, 3H, CH_3 OMe$_\alpha$), 3.38 (s, 2.1H, CH_3 OMe$_\beta$), 3.29 (td, 0.7H, *J* = 9.9, 5.0 Hz, H-5'$_\beta$); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC, HMBC): δ 158.7, 158.5 (C=O), 146.8, 144.8 (CF-*ortho*), 144.5, 142.4 (CF-*para*), 139.1, 139.0 (C_q), 138.8 (CF-meta), 138.6, 138.5, 138.3, 138.1, 137.9, 137.4, 137.3 (C_q), 136.8 (CF-*meta*), 129.1, 129.0, 128.6, 128.6, 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.1, 128.1, 128.0, 128.0, 127.8, 127.8, 127.7, 127.7, 127.6, 127.3, 126.9, 126.1, 126.0 (CH_{arom}), 107.8 ($C_{q\text{-}ipso}$), 103.4 (C-1'$_\beta$), 101.3 (CHPh$_\alpha$), 101.2 (CHPh$_\beta$), 98.4 (C-1'$_\alpha$), 98.3 (C-1$_\beta$), 97.9 (C-1$_\alpha$), 82.8 (C-2'$_\beta$), 82.3 (C-4'$_\alpha$), 81.8 (C-4'$_\beta$), 81.6 (C-3'$_\beta$), 81.2 (C-3$_\alpha$), 80.3 (C-2$_\alpha$), 79.9 (C-3$_\beta$), 79.2 (C-2$_\beta$), 78.8 (C-2'$_\alpha$), 78.6 (C-3'$_\alpha$), 78.1 (C-4$_\beta$), 75.9, 75.7, 75.3, 75.2, 74.7 (CH_2 Bn), 74.6 (C-4$_\alpha$), 74.1, 73.8, 73.5 (CH_2 Bn), 69.0 (C-6'$_\alpha$), 68.8 (C-6'$_\beta$), 68.4 (C-5$_\beta$), 67.9 (C-5$_\alpha$), 66.2 (C-5'$_\beta$), 65.4 (C-6$_\alpha$), 64.5 (C-6$_\beta$), 63.7 (C-5'$_\alpha$), 55.6 (OMe$_\beta$), 55.5 (OMe$_\alpha$); ^{19}F NMR ($CDCl_3$, 471 MHz): δ -137.33 (dp, 2F, *J* = 16.6, 5.4 Hz, *ortho*F$_5$Bz$_\alpha$), -137.83 (dp, 1.4F, *J* = 16.5, 5.4 Hz, *ortho*F$_5$Bz$_\beta$), -147.86 – -148.26 (m, 1.7F, *para*F$_5$Bz$_{\alpha,\beta}$), -160.23 (tt, 1.4F, *J* = 21.1, 5.8 Hz, *meta*F$_5$Bz$_\beta$), -160.41 (tt, 2F, *J* = 21.1, 5.8 Hz, *meta*F$_5$Bz$_\alpha$); HRMS: $[M+Na]^+$ calcd for $C_{55}H_{51}F_5O_{12}Na$ 1021.3198, found 1021.3237.



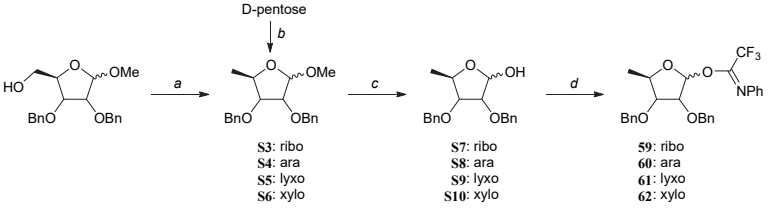
Methyl 4-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranosyl)-2,3-di-*O*-benzyl-6-*O*-(2,3,4,5,6-pentafluorobenzoyl)-α-D-glucopyranoside (56). Donor **4** and acceptor **47** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 yielding product **56** (75 mg, 80 µmol, 80%, α:β = 1 : 1.7) as a colorless oil. R_f: 0.69 and 0.82 (4/1 pentane/EtOAc); IR (thin film): 696, 735, 997, 1003, 1028, 1047, 1092, 1227, 1325, 1454, 1498, 1524, 1653, 1740, 2110, 2872, 2914; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.46 – 7.42 (m, 5.4H, CH_{arom}), 7.40 – 7.25 (m, 48.6H, CH_{arom}), 5.58 (d, 1H, *J* = 4.1 Hz, H-1'$_\alpha$), 5.53 (s, 1H, C*H*Ph$_\alpha$), 5.49 (s, 1.7H, C*H*Ph$_\beta$), 5.12 (d, 1H, *J* = 10.6 Hz, C*H*H Bn$_\alpha$), 4.97 (d, 1H, *J* = 10.9 Hz, C*H*H Bn$_\alpha$), 4.94 – 4.88 (m, 6.1H, 3xCHH Bn$_\beta$, CHH Bn$_\alpha$), 4.84 (dd, 1.7H, *J* = 12.1, 2.1 Hz, H-6$_\beta$), 4.79 – 4.73 (m, 5.4H, 2xCHH Bn$_\alpha$, 2xCHH Bn$_\beta$), 4.68 (dd, 1H, *J* = 11.9, 2.4 Hz$_\alpha$), 4.65 (dd, 1.7H, *J* = 12.2, 4.0 Hz, H-6$_\beta$), 4.63 – 4.57 (m, 5.4H, CH*H* Bn$_\alpha$, CH*H* Bn$_\beta$, H-1$_\alpha$, H-1$_\beta$), 4.50 (dd, 1H, *J* = 11.9, 4.4 Hz, H-6$_\alpha$), 4.41 (d, 1.7H, *J* = 8.1 Hz, H-1'), 4.16 (dd, 1H, *J* = 10.3, 4.9 Hz, H-6'$_\alpha$), 4.10 (dd, 1H, *J* = 9.4, 8.8 Hz, H-3$_\alpha$), 4.05 – 4.00 (m, 2.7H, H-3'$_\alpha$, H-6'$_\beta$), 3.99 – 3.90 (m, 4.4H, H-3$_\beta$, H-5$_\alpha$, H-5$_\beta$), 3.84 – 3.76 (m, 3.7H, H-4$_\alpha$, H-4$_\beta$, H-5'$_\alpha$), 3.70 – 3.60 (m, 5.4H, H-3'$_\beta$, H-4$_\alpha$, H-4'$_\beta$, H-6'$_\alpha$), 3.54 (dd, 1H, *J* = 9.6, 3.5 Hz, H-2$_\alpha$), 3.49 (dd, 1.7H, *J* = 9.6, 3.6 Hz, H-2$_\beta$), 3.47 (t, 1.7H, *J* = 10.3 Hz, H-6'$_\beta$), 3.43 (dd, 1.7H, *J* = 9.2, 8.2 Hz, H-2'$_\beta$), 3.40 (s, 5.1H, CH_3 OMe$_\beta$), 3.39 (s, 3H, CH_3 OMe$_\alpha$), 3.35 (dd, 1H, *J* = 10.1, 4.1 Hz, H-2'$_\alpha$), 3.20 (ddd, 1.7H, *J* = 9.9, 9.0, 5.0 Hz, H-5'$_\beta$); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 158.8, 158.7 (m, C=O), 146.7, 144.7, 144.4, 142.5 (m, CF_{arom}), 139.2 (C_q), 138.8 (m, CF_{arom}), 138.7, 138.1, 137.8, 137.8, 137.7, 137.1 (C_q), 136.8 (m, CF_{arom}), 129.2, 129.1, 128.7, 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.3, 128.2, 128.2, 128.0, 128.0, 127.6, 127.6, 127.6, 127.3, 126.1, 126.0 (CH_{arom}), 107.8 (m, $C_{q(ipso\text{-}F5Bz)}$), 102.2 (C-1'$_\beta$), 101.3, 101.3 (CHPh), 99.1 (C-1'$_\alpha$), 98.2 (C-1$_\beta$), 97.8 (C-1$_\alpha$), 82.6 (C-4$_\alpha$), 81.7 (C-4'$_\beta$), 81.2 (C-3$_\alpha$), 80.6 (C-2$_\alpha$), 79.9 (C-3$_\beta$), 79.8 (C-3'$_\beta$), 79.4 (C-2$_\beta$), 78.3 (C-4$_\beta$), 76.2 (C-3'$_\alpha$), 75.6 (C-4$_\alpha$), 75.5, 75.2, 75.1, 75.0, 73.7, 73.4 (CH_2 Bn), 68.6 (C-6'$_\alpha$), 68.5 (C-6'$_\beta$), 68.1, 67.7 (C-5$_\alpha$, C-5$_\beta$), 66.8 (C-2'$_\beta$), 66.3 (C-5'$_\beta$), 65.4 (C-6$_\alpha$), 64.8 (C-6$_\beta$), 63.7 (C-5'$_\alpha$), 62.9 (C-2'$_\alpha$), 55.7 (OMe$_\alpha$), 55.6 (OMe$_\beta$); ^{19}F NMR ($CDCl_3$, 471 MHz): δ -137.42 (dp, *J* = 16.7, 5.5 Hz), -137.96 (dp, *J* = 16.5, 5.5 Hz), -147.83 – -148.02 (m), -160.08 (tt, *J* = 21.1, 5.8 Hz), -160.31 (tt, *J* = 21.1, 5.9 Hz); HRMS: $[M+Na]^+$ calcd for $C_{48}H_{44}F_5N_3O_{11}Na$ 956.2794, found 956.2816.



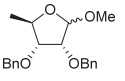
Methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranosyl)-2,3-di-*O*-benzyl-6-*O*-(2,4,6-trinitrobenzoyl)-α-D-glucopyranoside (57). Donor **3** and acceptor **48** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 yielding product **57** (78 mg, 75 µmol, 75%, α:β = 2.1 : 1) as a colorless oil. R_f: 0.43 (4/1 pentane/EtOAc); IR (thin film): 698, 735, 1028, 1047, 1074, 1088, 1269, 1342, 1454, 1545, 1557, 1755, 2872, 2928; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC, HMBC): δ 8.97 (s, 2H, CH_{arom} NO_2Bz), 7.38 – 7.14 (m, 25H, CH_{arom}), 5.53 (d, 1H, *J* = 3.9 Hz, H-1'), 5.38 (s, 1H, C*H*Ph), 5.06 (dd, 1H, *J* = 11.7, 2.2 Hz, H-6), 4.97 – 4.86 (m, 3H, 2xC*H*H Bn, H-6), 4.80 – 4.64 (m, 6H, 2xC*H*H Bn, 2xCH*H* Bn, H-1, H-6), 4.57 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.54 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.11 – 4.04 (m, 2H, H-3, H-5), 4.01 (t, 1H, *J* = 9.3 Hz, H-3'), 3.87 – 3.83 (m, 2H, H-5', H-6'), 3.80 (dd, 1H, *J* = 9.8, 8.6 Hz, H-4), 3.57 – 3.49 (m, 4H, H-2, H-2', H-4', H-6'), 3.41 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC, HMBC): δ 160.6 (C=O), 147.8, 147.1 (C_q NO_2), 138.9, 138.6, 138.1, 137.9, 137.3, 129.6 (C_q), 129.0, 128.6, 128.5, 128.4, 128.3, 128.3, 128.3, 128.1, 128.1, 128.1, 128.1, 127.8, 127.8, 127.7, 127.3, 127.0, 126.1, 125.9, 124.5 (CH_{arom}), 101.0 (CHPh), 98.0 (C-1'), 97.8 (C-1), 82.1 (C-4'), 81.1 (C-3), 80.3 (C-2), 78.9 (C-2'), 78.5 (C-3'), 75.3, 74.6 (CH_2 Bn), 74.3 (C-4), 73.9, 73.4 (CH_2 Bn), 68.9 (C-6'), 68.3 (C-5), 66.9 (C-6), 63.3 (C-5'), 55.7 (OMe); Diagnostic peaks for the β-anomer: ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 9.13 (s, 2H, CH_{arom} NO_2Bz), 5.49 (s, 1H, C*H*Ph), 4.49 (dd, 1H, *J* = 12.0, 2.8 Hz, H-6), 4.17 (dd, 1H, *J* = 10.4, 4.9 Hz, H-6'), 3.63

(t, 1H, *J* = 9.3 Hz, H-4'), 3.45 (dd, 1H, *J* = 8.8, 7.7 Hz, H-2'), 3.42 (dd, 1H, *J* = 10.0, 4.0 Hz, H-2), 3.39 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 160.5 (C=O), 147.8, 147.2 (C_q NO_2), 139.1, 138.5, 138.3, 137.4, 129.7 (C_q), 129.0 - 124.6 (CH_{arom}), 103.0 (C-1'), 101.2 (CHPh), 98.2 (C-1), 83.1 (C-2'), 81.9 (C-4'), 81.5 (C-3'), 79.8 (C-3), 78.9 (C-2), 77.9 (C-4), 75.8 , 75.7, 73.5 (CH_2 Bn), 68.8 (C-6'), 68.2 (C-5), 66.6 (C-5'), 66.0 (C-6), 55.7 (OMe); HRMS: $[M+Na]^+$ calcd for $C_{55}H_{53}N_3O_{18}Na$ 1066.3222, found 1066.3257.

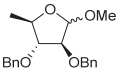
Preparation of 5-deoxy furanosyl imidates.



Reagents and conditions: (a) *i*. TsCl, pyridine, DCM; *ii*. $LiAlH_4$, Et_2O, **S5**: 75%, **S6**: 80%; (b) *i*. AcCl, MeOH; *ii*. Ph_3P, I_2, imidazole, THF, *iii*. $Pd(OH)_2$/C, H_2, DiPEA; *iv*. BnBr, NaH, DMF, **S3**: 40%, **S4**: 52%; (c) $HCOOH/H_2O$ (4/1 v/v, 0.05 M), 50°C, **S7**: 86%, **S8**: 72%, **S9**: 92%, **S10**: 92%; (d) 2,2,2-trifluoro-*N*-phenylacetimidoyl chloride (0.95 eq.), DBU (1 eq.) in DCM (0.25 M), 0°C, **77**: 48%, **79**: 56%, **81**: 44%, **83**: 66%.

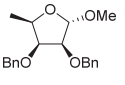


Methyl 2,3-di-*O*-benzyl-5-deoxy-α/β-D-ribofuranoside (S3). To a 0°C solution of D-ribose (3 g, 20 mmol) in MeOH (70 mL) was added AcCl (0.6 mL, 9 mmol, 0.45 eq.) and the reaction was stirred overnight at room temperature. The reaction was quenched by the addition of solid K_2CO_3 (5 g), stirred for 10 min, then filtered and concentrated under reduced pressure. The crude methyl glycoside was dissolved in THF (80 mL) and Ph_3P (7.9 g, 30 mmol, 1.5 eq.) and imidazole (2.7 g, 40 mmol, 2 eq.) were added and the reaction mixture brought to reflux. To the boiling reaction mixture was slowly added a solution of I_2 (7.6 g, 30 mmol, 1.5 eq.) in THF (30 mL). After 3 h the reaction was cooled to room temperature, MeOH (10 mL) was added and the reaction mixture was concentrated under reduced pressure. The residue was filtered over silica gel (5% MeOH in DCM) and the filtrate was concentrated under reduced pressure. The crude iodide was dissolved in MeOH (60 mL) and DiPEA (5 mL, 29 mmol). $Pd(OH)_2$ (20% on C, 0.85 g) was added and the reaction flask was purged with N_2. The flask was subsequently purged with H_2 for 5 min and then kept under a H_2 atmosphere (balloon) for 3 h. The reaction mixture was purged with N_2, filtered over Celite and evaporated. The residue was dissolved in 5% MeOH in DCM and filtered over silica gel, the filtrate concentrated under reduced pressure and coevaporated once with toluene. The crude material was dissolved in DMF (50 mL), cooled to 0°C, and treated with BnBr (4.2 mL, 35 mmol) and NaH (60% dispersion in mineral oil, 1.2 g, 30 mmol) and stirred overnight. The reaction mixture was quenched by the addition of H_2O, and then extracted three times with Et_2O. The combined organic layers were washed with 0.1 M aq. HCl, H_2O, and brine. The organic layer was dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography 0% to 10% EtOAc in pentane) to give the title compound as a colourless oil (1.93 g, 5.9 mmol, 30%, β anomer. The α anomer (10%) was impure and discarded). Data for the β-anomer: R*f*: 0.50 (9/1 pentane/EtOAc). $[\alpha]_D^{20}$ = +35.9° (*c* = 0.66, $CHCl_3$); IR (thin film): 698, 737, 935, 1028, 1038, 1111, 1454, 2911, 2926, 2972; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HH-NOESY, HSQC): δ 7.40 – 7.25 (m, 10H, CH_{arom}), 4.87 (s, 1H, H-1), 4.68 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.60 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.58 (d, 1H, *J* = 11.9 Hz, C*H*H Bn), 4.45 (d, 1H, *J* = 11.9 Hz, CH*H* Bn), 4.24 (dq, 1H, *J* = 7.3, 6.3 Hz, H-4), 3.84 (dd, 1H, *J* = 4.6, 1.0 Hz, H-2), 3.74 (dd, 1H, *J* = 7.3, 4.6 Hz, H-3), 3.33 (s, 3H, CH_3 OMe), 1.30 (d, 3H, *J* = 6.3 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.0, 137.9 (C_q), 128.5, 128.5, 128.1, 127.9, 127.9 (CH_{arom}), 106.3 (C-1), 83.2 (C-3), 80.0 (C-2), 77.3 (C-4), 72.5, 72.4 (CH_2 Bn), 55.0 (CH_3 OMe), 20.6 (C-5); HRMS: $[M+Na]^+$ calcd for $C_{20}H_{24}O_4Na$ 351.1572, found 351.1582.

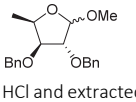


Methyl 2,3-di-*O*-benzyl-5-deoxy-α/β-D-arabinofuranoside (S4). To a 0°C solution of D-arabinose (3 g, 20 mmol) in MeOH (70 mL) was added AcCl (0.8 mL, 12 mmol, 0.6 eq.) and the reaction was stirred overnight at room temperature. The reaction was quenched by the addition of solid K_2CO_3 (5 g), stirred for 10 min, then filtered and concentrated under reduced pressure. The crude methyl glycoside was dissolved in THF (80 mL) and Ph_3P (7.9 g, 30 mmol, 1.5 eq.) and imidazole (2.7 g, 40 mmol, 2 eq.) were added and the reaction mixture brought to reflux. To the boiling reaction mixture was slowly added a solution of I_2 (7.6 g, 30 mmol, 1.5 eq.) in THF (30 mL). After 2 h the reaction was cooled to room temperature, MeOH (10 mL) was added and the reaction mixture was concentrated under reduced pressure. The residue was filtered over silica gel (5% MeOH in DCM) and the filtrate was concentrated under reduced pressure to give nearly pure methyl 5-iodo arabinoside (4.12 g, 15 mmol, 75%). The crude iodide (1.37 g, 5 mmol) was dissolved in MeOH (25 mL) and DiPEA (2.6 mL, 15 mmol, 3 eq.). $Pd(OH)_2$

(20% on C, 0.4 g) was added and the reaction flask was purged with N_2. The flask was subsequently purged with H_2 for 5 min and then kept under a H_2 atmosphere (balloon) for 3 h. The reaction mixture was purged with N_2, filtered over Celite and evaporated. The residue was dissolved in 5% MeOH in DCM and filtered over silica gel, the filtrate concentrated under reduced pressure and coevaporated once with toluene to give 4.15 mmol (83%) of reduced compound. The crude material (4 mmol) was dissolved in DMF (20 mL), cooled to 0°C, and treated with BnBr (1.43 mL, 12 mmol, 3 eq.) and NaH (60% dispersion in mineral oil, 480 mg, 12 mmol, 3 eq.) and stirred overnight. The reaction mixture was quenched by the addition of H_2O, and then extracted three times with Et_2O. The combined organic layers were washed with sat. aq. NH_4Cl, H_2O, and brine. The organic layer was dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (2% to 12% EtOAc in pentane) to give the title compound as a colourless oil (1.1 g, 3.5 mmol, 84%) in 52% over four steps, α:β = 2:1 anomeric mixture. IR (thin film): 698, 748, 1049, 1109, 1452, 2926; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.47 – 7.18 (m, 10H, CH_{arom}), 4.87 (s, 1H, H-1), 4.59 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.57 (d, 1H, *J* = 11.8 Hz, C*H*H Bn), 4.54 – 4.46 (m, 2H, 2xCH*H* Bn), 4.09 (p, 1H, *J* = 6.3 Hz, H-4), 3.97 (dd, 1H, *J* = 3.5, 1.0 Hz, H-2), 3.59 (dd, 1H, *J* = 7.1, 3.5 Hz, H-3), 3.37 (s, 3H, CH_3 OMe), 1.32 (d, 3H, *J* = 6.3 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.0, 137.7 (C_q), 128.6, 128.5, 128.1, 128.0, 127.9, 127.9 (CH_{arom}), 107.1 (C-1), 89.1 (C-2), 88.8 (C-3), 76.8 (C-4), 72.4, 72.2 (CH_2 Bn), 54.9 (OMe), 18.8 (C-5); Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.43 – 7.24 (m, 10H, CH_{arom}), 4.74 – 4.67 (m, 2H, C*H*H Bn, H-1), 4.66 – 4.57 (m, 3H, CH_2 Bn, CH*H* Bn), 4.06 – 3.95 (m, 3H, H-2, H-3, H-4), 3.37 (s, 3H, CH_3 OMe), 1.33 (d, 3H, *J* = 6.2 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.3, 137.8 (C_q), 128.5, 128.3, 128.0, 127.9, 127.8 (CH_{arom}), 101.5 (C-1), 87.1 (C-3/4), 84.5 (C-2), 77.6 (C-3/4), 72.6, 72.6 (CH_2 Bn), 54.9 (OMe), 22.3 (C-5); HRMS: $[M+NH_4]^+$ calcd for $C_{20}H_{28}NO_4$ 346.20128, found 346.20131.

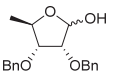


Methyl 2,3-di-*O*-benzyl-5-deoxy-α-D-lyxofuranoside (S5). To a solution of methyl 2,3-di-*O*-benzyl-α-D-lyxofuranoside[25] (1.03 g, 3.0 mmol, 1 eq.) and pyridine (1.4 mL, 18 mmol, 6 eq.) in DCM (15 mL) was added TsCl (2.3 g, 12 mmol, 4 eq.) and the reaction mixture was stirred for two days. The reaction mixture was poured into 1 M aq. HCl and extracted twice with Et_2O. The combined organic layers were washed with H_2O, sat. aq. $NaHCO_3$, and brine, then dried with $MgSO_4$, filtered and concentrated under reduced pressure. After coevaporation with dry toluene, the crude tosylate was dissolved in Et_2O (30 mL) and $LiAlH_4$ (4 M in Et_2O, 2.5 mL, 10 mmol, 5 eq.) was slowly added. The solution was refluxed for 3 h and then cooled to 0°C and quenched with EtOAc and H_2O. The reaction mixture was poured in 0.1 M HCl and extracted twice with Et_2O. The combined organic layers were washed with H_2O, sat. aq. $NaHCO_3$, and brine, then dried ($MgSO_4$), filtered and concentrated under reduced pressure. Purification by flash column chromatography (1/0 to 85/15 pentane/EtOAc) gave the title compound as a colourless oil, which crystalized on standing. Yield: 740 mg, 2.25 mmol, 75%. m.p. 34-36 °C. $[\alpha]_D^{20}$ = +16.0° (*c* = 1.0, $CHCl_3$); IR (neat): 692, 729, 955, 1015, 1028, 1051, 1098, 1132, 1159, 1366, 1450, 2899, 1933, 2976; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HH-NOESY, HSQC): δ 7.38 – 7.23 (m, 10H, CH_{arom}), 5.00 (d, 1H, *J* = 2.8 Hz, H-1), 4.73 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.66 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.62 – 4.53 (m, 2H, 2xCH*H* Bn), 4.23 (qd, 1H, *J* = 6.4, 4.6 Hz, H-4), 3.96 (t, 1H, *J* = 4.6 Hz, H-3), 3.92 (dd, 1H, *J* = 4.7, 2.8 Hz, H-2), 3.36 (s, 3H, CH_3 OMe), 1.32 (d, 3H, *J* = 6.5 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 138.4, 138.1 (C_q), 128.4, 128.3, 127.8, 127.7, 127.6 (CH_{arom}), 106.7 (C-1), 84.0 (C-2), 78.9 (C-3), 75.7 (C-4), 73.2, 72.6 (CH_2 Bn), 55.5 (OMe), 15.7 (C-5); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): $^2J_{C1,H2}$ = -2.5 Hz, $^2J_{C2,H1}$ = -1.2 Hz; HRMS: $[M+Na]^+$ calcd for $C_{20}H_{24}O_4Na$ 351.1572, found 351.1580.

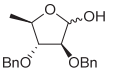


Methyl 2,3-di-*O*-benzyl-5-deoxy-α/β-D-xylofuranoside (S6). To a solution of methyl 2,3-di-*O*-benzyl-α-D-xylofuranoside[26] (2.2 g, 6.39 mmol, 1 eq.) in pyridine (15 mL) was added TsCl (2.4 g, 12.8 mmol, 2 eq.) and the reaction mixture was stirred overnight. The reaction mixture was poured into 1 M aq. HCl and extracted twice with Et_2O. The combined organic layers were washed with 1 M HCl, H_2O, sat. aq. $NaHCO_3$, and brine, then dried with $MgSO_4$, filtered and concentrated under reduced pressure. After coevaporation with dry toluene, the crude tosylate was dissolved in Et_2O (60 mL) and $LiAlH_4$ (4 M in Et_2O, 5 mL, 20 mmol, 3.1 eq.) was slowly added. The solution was refluxed for 8 h and then cooled to 0°C and quenched with EtOAc and H_2O. The reaction mixture was poured in 0.1 M HCl and extracted twice with Et_2O. The combined organic layers were washed with H_2O, sat. aq. $NaHCO_3$, and brine, then dried ($MgSO_4$), filtered and concentrated under reduced pressure. Purification by flash column chromatography (1/0 to 85/15 pentane/EtOAc) gave the title compound as a colourless oil. Yield: 1.68 g, 5.1 mmol, 80% as an α:β = 1:1.2 anomeric mixture. R*f*: 0.55 and 0.38 (9/1 pentane/EtOAc). IR (neat): 696, 735, 1026, 1063, 1107, 1454, 2870, 2909, 2930; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.39 – 7.26 (m, 22H, CH_{arom}), 4.86 (d, 1.2H, *J* = 1.9 Hz, H-1β), 4.77 (d, 1H, *J* = 4.3 Hz, H-1α), 4.65 (d, 1H, *J* = 12.0 Hz, C*H*H Bnα), 4.62 – 4.48 (m, 7.8H, CH*H* Bnα, CH_2 Bnα, 2xCH_2 Bnβ), 4.40 – 4.31 (m, 2.2H, H-4α, H-4β), 4.15 (dd, 1H, *J* = 6.7, 5.4 Hz, H-3α), 4.02 (dd, 1.2H, *J* = 3.2, 1.9 Hz, H-2β), 3.98 (dd, 1H, *J* = 5.4, 4.3 Hz, H-2α), 3.91 (dd, 1.2H, *J* = 5.8, 3.2 Hz, H-3β), 3.40 (s, 3.6H, CH_3 OMeβ), 3.39

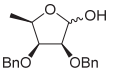
(s, 3H, CH_3 OMeα), 1.32 (d, 3.6H, *J* = 6.6 Hz, H-5β), 1.25 (d, 3H, *J* = 6.6 Hz, H-5α); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 138.3, 138.1, 137.8, 137.7 (C_q), 128.4, 128.4, 128.4, 128.1, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 127.5 (CH_{arom}), 108.1 (C-1β), 100.3 (C-1α), 87.4 (C-2β), 84.4 (C-2α), 82.5 (C-3β), 82.3 (C-3α), 76.9 (C-4β), 73.4 (C-4α), 72.6, 72.2, 72.0, 71.9 (CH_2 Bn), 55.5 (OMeβ), 55.0 (OMeα), 16.2 (C-5β), 15.6 (C-5α); HRMS: $[M+Na]^+$ calcd for $C_{20}H_{24}O_4Na$ 351.1572, found 351.1585.



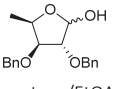
2,3-di-*O*-benzyl-5-deoxy-α/β-D-ribofuranose (S7). The title compound was generated from **S3** (1.1 g, 3.35 mmol) by the general procedure for methyl furanoside hydrolysis, conditions A (50°C, 2 h) as described in Chapter 7. Yield: 86% α:β = 1:2.5 (909 mg, 2.9 mmol) as a colourless oil. R*f*: 0.16 (8/2 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[27] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.42 – 7.26 (m, 15.5H, CH_{arom}), 5.34 (d, 0.55H, *J* = 2.9 Hz, H-1β), 5.30 (dd, 1H, *J* = 11.2, 4.2 Hz, H-1α), 4.74 – 4.67 (m, 3.1H, 2x C*H*H Bnα, 2x C*H*H Bnβ), 4.65 – 4.58 (m, 2.55H, C*H*H Bnβ, 2xCH*H* Bnα), 4.46 (d, 0.55H, *J* = 11.9 Hz, CH*H* Bnβ), 4.33 (qd, 1H, *J* = 6.5, 3.4 Hz, H-4α), 4.26 (d, 1H, *J* = 11.3 Hz, 1-OHα), 4.29 – 4.17 (m, 0.55H, H-4β), 3.93 (t, 1H, *J* = 4.5 Hz, H-2α), 3.85 (dd, 0.55H, *J* = 4.6, 0.9 Hz, H-2β), 3.79 (dd, 0.55H, *J* = 7.4, 4.6 Hz, H-3β), 3.62 (dd, 1H, *J* = 4.9, 3.4 Hz, H-3α), 3.16 (d, 0.55H, *J* = 3.4 Hz, 1-OHβ), 1.33 (d, 1.65H, *J* = 6.3 Hz, H-5β), 1.17 (d, 3H, *J* = 6.6 Hz, H-5α); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 137.9, 137.9, 137.6, 137.4 (C_q), 128.6, 128.6, 128.5, 128.5, 128.2, 128.1, 128.0, 127.9 (CH_{arom}), 100.1 (C-1β), 95.9 (C-1α), 82.8 (C-3β), 81.8 (C-3α), 80.4 (C-2β), 77.3, 77.3, 77.2 (C-2α, C-4α, C-4β), 72.9, 72.8, 72.6, 72.3 (CH_2 Bn), 20.6 (C-5β), 19.8 (C-5α); HRMS: $[M+Na]^+$ calcd for $C_{19}H_{22}O_4Na$ 337.1410, found 337.1425.



2,3-di-*O*-benzyl-5-deoxy-α/β-D-arabinofuranose (S8). The title compound was generated from **S4** (600 mg, 1.87 mmol) by the general procedure for methyl furanoside hydrolysis, conditions A (50°C, 2 h) as described in Chapter 7. Yield: 72% α:β = 1:2.5 (413 mg, 1.31 mmol) as a colourless oil. R*f*: 0.54 (7/3 pentane/EtOAc). IR (neat): 694, 733, 995, 1055, 1207, 1454, 1497, 2872, 2905, 2928, 2972, 3030, 3395; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.39 – 7.26 (m, 14H, CH_{arom}), 5.38 (d, 1H, *J* = 6.8 Hz, H-1α), 5.31 (dd, 0.4H, *J* = 8.6, 4.3 Hz, H-1β), 4.67 – 4.49 (m, 5.6H, 2xCH_2 Bnα, 2xCH_2 Bnβ), 4.35 (qd, 1H, *J* = 6.4, 4.8 Hz, H-4α), 3.98 (dd, 1H, *J* = 2.5, 0.9 Hz, H-2α), 4.00 – 3.89 (m, 0.8H, H-2β, H-4β), 3.78 (d, 0.4H, *J* = 8.6 Hz, 1-OHβ), 3.75 (dd, 0.4H, *J* = 5.1, 4.3 Hz, H-3β), 3.66 (ddd, 1H, *J* = 4.7, 2.5, 0.7 Hz, H-3α), 3.37 (d, 1H, *J* = 6.8 Hz, 1-OHα), 1.35 (d, 1.2H, *J* = 6.4 Hz, H-5β), 1.31 (d, 3H, *J* = 6.5 Hz, H-5α); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 137.8, 137.6, 137.5, 137.1 (C_q), 128.7, 128.6, 128.6, 128.3, 128.2, 128.1, 128.0, 128.0, 127.9, 127.9, 127.8 (CH_{arom}), 100.9 (C-1α), 96.0 (C-1β), 87.6 (C-2α), 87.4 (C-3α), 86.7 (C-3β), 83.2 (C-2β), 78.6 (C-4α), 76.5 (C-4β), 72.7, 72.3, 72.3, 72.0 (CH_2 Bn), 20.9 (C-5β), 19.4 (C-5α); HRMS: $[M+Na]^+$ calcd for $C_{19}H_{22}O_4Na$ 337.1410, found 337.1426.

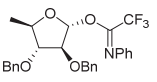


2,3-di-*O*-benzyl-5-deoxy-α/β-D-lyxofuranose (S9). The title compound was generated from **S5** (370 mg, 1.13 mmol) by the general procedure for methyl furanoside hydrolysis, conditions A (50°C, 1.5 h) as described in Chapter 7. Yield: 92% α:β = 1:4 (327 mg, 1.04 mmol) as a colourless oil. R*f*: 0.35 (7/3 pentane/EtOAc). IR (thin film): 698, 735, 1058, 1159, 1454, 2926, 3408; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.43 – 7.27 (m, 12.5H), 5.49 (t, 0.25H, *J* = 3.1 Hz, H-1α), 5.24 (dd, 1H, *J* = 12.2, 3.9 Hz, H-1β), 4.89 (d, 1H, *J* = 11.6 Hz, C*H*H Bnβ), 4.81 – 4.73 (m, 1.25H, CHH Bnα, CHH Bnβ), 4.70 (d, 0.25H, *J* = 12.1 Hz, C*H*H Bnα), 4.67 – 4.57 (m, 2.5H, 2xCH*H* Bnα, 2xCH*H* Bnβ), 4.37 (qd, 0.25H, *J* = 6.5, 4.7 Hz, H-4α), 4.25 (d, 1H, *J* = 12.2 Hz, 1-OHβ), 4.09 – 4.01 (m, 1.25H, H-3α, H-4β), 3.96 – 3.89 (m, 2.25H, H-2α, H-2β, H-3β), 3.04 (d, 0.25H, *J* = 3.5 Hz, 1-OHα), 1.35 (d, 3H, *J* = 6.5 Hz, H-5β), 1.31 (d, 1H, *J* = 6.5 Hz, H-5α); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.4, 138.1, 137.9, 137.7 (C_q), 128.6, 128.5, 128.5, 128.4, 128.0, 128.0, 127.9, 127.8, 127.8 (CH_{arom}), 100.2 (C-1α), 95.6 (C-1β), 84.7 (C-2α), 79.9 (C-3β), 78.8 (C-3α), 78.5 (C-2β), 76.0 (C-4α), 75.6 (C-4β), 74.2, 73.3, 72.6, 72.0 (CH_2 Bn), 16.6 (C-5β), 15.9 (C-5α); HRMS: $[M+Na]^+$ calcd for $C_{19}H_{22}O_4Na$ 337.1410, found 337.1428.

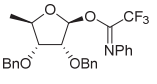


2,3-di-*O*-benzyl-5-deoxy-α/β-D-xylofuranose (S10). The title compound was generated from **S6** (887 mg, 2.7 mmol) by the general procedure for methyl furanoside hydrolysis, conditions A (50°C, 2 h) as described in Chapter 7. Yield: 92% α:β = 1.1:1 (778 mg, 2.47 mmol) as a colourless oil. R*f*: 0.37 (8/2 pentane/EtOAc). IR (neat): 694, 733, 1026, 1057, 1207, 1454, 1497, 2870, 2932, 3030, 3400; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.39 – 7.26 (m, 19H, CH_{arom}), 5.44 (dd, 0.9H, *J* = 9.0, 4.4 Hz, H-1α), 5.23 (d, 1H, *J* = 11.0 Hz, H-1β), 4.64 – 4.50 (m, 5.7H, CH_2 Bnα, CH_2 Bnβ, C*H*H Bnα, C*H*H Bnβ), 4.48 (d, 1H, *J* = 11.9 Hz, CH*H* Bnβ), 4.44 (d, 0.9H, *J* = 12.2 Hz, CH*H* Bnα), 4.39 – 4.30 (m, 1.9H, H-4α, H-4β), 3.98 (d, 1H, *J* = 1.2 Hz, H-2β), 3.95 (dd, 0.9H, *J* = 4.4, 2.1 Hz, H-2α), 3.91 (d, 0.9H, *J* = 9.0 Hz, 1-OHα), 3.81 (dd, 0.9H, *J* = 4.2, 2.1 Hz, H-3α), 3.77 (ddd, 1H, *J* = 3.9, 1.3, 0.7 Hz, H-3β), 3.35 (d, 1H, *J* = 11.0 Hz, 1-OHβ), 1.37 (d, 3H, *J* = 6.6 Hz, H-5β), 1.26 (d, 2.7H, *J* = 6.5 Hz, H-5α); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 138.0, 137.6, 137.3, 137.0 (C_q), 128.8, 128.7, 128.6, 128.6, 128.4, 128.2, 128.1, 128.1, 128.0, 127.9, 127.8, 127.7

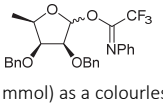
(CH_{arom}), 101.1 (C-1β), 95.7 (C-1α), 85.3 (C-2β), 82.5 (C-3α), 82.3 (C-2α), 81.5 (C-3β), 78.0 (C-4β), 74.7 (C-4α), 73.3, 72.5, 72.1, 72.0 (CH_2 Bn), 15.5 (C-5β), 14.6 (C-5α); HRMS: $[M+Na]^+$ calcd for $C_{19}H_{22}O_4Na$ 337.1410, found 337.1429.



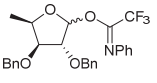
2,3-di-*O*-benzyl-5-deoxy-1-*O*-(*N*-[phenyl]trifluoroacetimidoyl)-α-D-arabinofuranoside (59). The title compound was generated from **61** (330 mg, 1.05 mmol) by the general procedure for imidate donor synthesis, conditions B as described in Chapter 7. Yield: 56% α only (286 mg, 0.59 mmol) as a colourless oil. R*f*: 0.55 (9/1 pentane/Et_2O). $[\alpha]_D^{20}$ = -1.1° (*c* = 0.75, $CHCl_3$); IR (thin film): 696, 905, 1103, 1120, 1161, 1207, 1330, 1454, 1707, 2932; ^{1}H NMR ($CDCl_3$, *T* = 323 K, 500 MHz, HH-COSY, HSQC): δ 7.36 – 7.24 (m, 12H, CH_{arom}), 7.11 – 7.02 (m, 1H, NPh), 6.81 (d, 2H, *J* = 7.7 Hz, NPh), 6.19 (bs, 1H, H-1), 4.65 – 4.50 (m, 4H, 2xCH_2 Bn), 4.32 (p, 1H, *J* = 6.2 Hz, H-4), 4.21 (d, 1H, *J* = 2.7 Hz, H-2), 3.69 (dd, 1H, *J* = 6.3, 2.8 Hz, H-3), 1.35 (d, 3H, *J* = 6.3 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, *T* = 323 K, 126 MHz, HSQC): δ 144.2 (C_q NPh), 138.0, 137.5 (C_q Bn), 128.8, 128.8, 128.6, 128.6, 128.2, 128.1, 128.0, 127.8, 124.4, 119.9 (CH_{arom}), 116.3 (q, *J* = 286.3 Hz, CF_3), 104.0 (C-1), 88.9 (C-3), 88.0 (C-2), 80.1 (C-4), 72.6, 72.6 (CH_2 Bn), 18.9 (C-5); HRMS: only mass of hydrolysis found $[M+Na]^+$ calcd for $C_{19}H_{22}O_4Na$ 337.1416, found 337.1416.



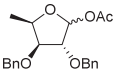
2,3-di-*O*-benzyl-5-deoxy-1-*O*-(*N*-[phenyl]trifluoroacetimidoyl)-β-D-ribofuranoside (60). The title compound was generated from **62** (355 mg, 1.13 mmol) by the general procedure for imidate donor synthesis, conditions B as described in Chapter 7. Yield: 48% β only (264 mg, 0.54 mmol) as a colourless oil. R*f*: 0.75 (8/2 pentane/Et_2O). $[\alpha]_D^{20}$ = +82.8° (*c* = 1.09, $CHCl_3$); IR (thin film): 696, 1092, 1151, 1207, 1454, 1712, 2872, 2930; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.35 – 7.24 (m, 12H, CH_{arom}), 7.08 (t, 1H, *J* = 7.5 Hz, NPh), 6.81 (d, 2H, *J* = 7.7 Hz, NPh), 6.19 (bs, 1H, H-1), 4.68 (d, 1H, *J* = 11.9 Hz, C*H*H Bn), 4.60 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.56 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.48 (d, 1H, *J* = 11.7 Hz, CH*H* Bn), 4.36 (p, 1H, *J* = 6.4 Hz, H-4), 4.05 (d, 1H, *J* = 4.3 Hz, H-2), 3.79 (dd, 1H, *J* = 7.6, 4.5 Hz, H-3), 1.35 (d, 3H, *J* = 6.3 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 144.1 (C_q NPh), 143.55 (q, *J* = 37.1 Hz, CF_3-*C*=NPh), 137.8, 137.7, 137.7, 128.9, 128.6, 128.2, 128.1, 128.1, 127.9, 124.4, 119.8 (CH_{arom}), 116.17 (q, *J* = 285.7 Hz, CF_3), 102.9 (C-1), 82.9 (C-3), 79.4 (C-2), 79.2 (C-4), 72.9, 72.5 (CH_2 Bn), 20.1 (C-5); HRMS: only mass of hydrolysis found $[M+Na]^+$ calcd for $C_{19}H_{22}O_4Na$ 337.1416, found 337.1420.



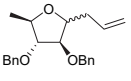
2,3-di-*O*-benzyl-5-deoxy-1-*O*-(*N*-[phenyl]trifluoroacetimidoyl)-α-D-lyxofuranoside (61). The title compound was generated from **63** (195 mg, 0.62 mmol) by the general procedure for imidate donor synthesis, conditions B as described in Chapter 7. Yield: 44% α:β = 1:4 (132 mg, 0.27 mmol) as a colourless oil. IR (thin film): 696, 1091, 1207, 1454, 1716, 2868; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, *T* = 328 K, 500 MHz, HH-COSY, HSQC): δ 7.34 – 7.24 (m, 12H, CH_{arom}), 7.09 – 7.05 (m, 1H, NPh), 6.82 (dd, 2H, *J* = 8.4, 1.0 Hz, NPh), 6.26 (bs, 1H, H-1), 4.69 (d, 1H, *J* = 11.8 Hz, C*H*H Bn), 4.68 – 4.60 (m, 2H, CH_2 Bn), 4.55 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.39 (p, 1H, *J* = 6.3 Hz, H-4), 4.15 (dd, 1H, *J* = 4.7, 1.9 Hz, H-2), 4.08 (t, 1H, *J* = 5.1 Hz, H-3), 1.34 (d, 3H, *J* = 6.5 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, *T* = 328 K, 126 MHz, HSQC): δ 144.2 (C_q NPh), 143.8 (q, *J* = 35.4 Hz, *C*=NPh), 138.3, 137.8 (C_q Bn), 128.8, 128.6, 128.5, 128.0, 127.9, 127.9, 127.8, 124.4, 119.9 (CH_{arom}), 116.38 (q, *J* = 286.0 Hz, CF_3) 103.5 (C-1), 82.8 (C-2), 78.3 (C-3), 78.1 (C-4), 73.4, 73.0 (CH_2 Bn), 15.8 (C-5); Diagnostic peaks β-anomer: ^{1}H NMR ($CDCl_3$, *T* = 328 K, 500 MHz, HH-COSY, HSQC): δ 7.40 – 7.18 (m, 12H, CH_{arom}), 7.04 – 6.99 (m, 1H, NPh), 6.75 (d, 2H, *J* = 7.9 Hz, NPh), 6.35 (bs, 1H, H-1), 4.90 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.74 – 4.60 (m, 3H, CH*H* Bn, CH_2 Bn), 4.23 (qd, 1H, *J* = 6.5, 4.7 Hz, H-4), 4.05 – 4.01 (m, 1H, H-2), 3.95 (t, 1H, *J* = 4.9 Hz, H-3), 1.37 (d, 3H, *J* = 6.6 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, *T* = 328 K, 126 MHz, HSQC): δ 144.6 (C_q NPh), 139.0, 137.9 (C_q Bn), 128.7, 128.6, 128.3, 128.0, 127.6, 127.5, 127.4, 124.0, 120.0 (CH_{arom}), 97.2 (C-1), 81.0 (C-2), 78.8 (C-4), 76.4 (C-3), 73.5, 73.3 (CH_2 Bn), 16.1 (C-5); HRMS: only mass of hydrolysis found $[M+Na]^+$ calcd for $C_{19}H_{22}O_4Na$ 337.1416, found 337.1422.



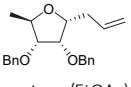
2,3-di-*O*-benzyl-5-deoxy-1-*O*-(*N*-[phenyl]trifluoroacetimidoyl)-α/β-D-xylofuranoside (62). The title compound was generated from **64** (285 mg, 0.91 mmol) by the general procedure for imidate donor synthesis, conditions B as described in Chapter 7. Yield: 66% α:β = 1:3 (290 mg, 0.59 mmol) as a colourless oil. R*f*: 0.41 (9/1 pentane/Et_2O). IR (thin film): 696, 1085, 1154, 1207, 1454, 1708, 2864; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.35 – 7.21 (m, 16H, CH_{arom}), 7.09 – 7.02 (m, 1.33H, NPh), 6.82 – 6.77 (m, 1H, NPh), 6.74 (d, 0.33H, *J* = 7.5 Hz, NPh), 6.32 (bs, 0.33H, H-1α), 6.18 (bs, 1H, H-1β), 4.67 – 4.47 (m, 6.67H, 2xCH_2 Bnα, 2xCH_2 Bnβ, H-4α, H-4β), 4.27 (d, 1H, *J* = 2.3 Hz, H-2β), 4.18 – 4.14 (m, 0.67H, H-2α, H-3α), 3.97 (dd, 1H, *J* = 5.7, 2.6 Hz, H-3β), 1.37 (d, 3H, *J* = 6.7 Hz, H-5β), 1.27 (d, 1H, *J* = 6.6 Hz, H-5α); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 144.3, 144.2 (C_q NPh), 138.2, 138.1, 137.8, 137.6 (C_q Bn), 129.5, 128.8, 128.6, 128.5, 128.1, 128.1, 128.0, 127.9, 127.8, 127.6, 127.6, 126.5, 124.2, 120.7, 119.8 (CH_{arom}), 116.23 (q, *J* = 286.4 Hz, CF_3), 103.8 (C-1β), 97.8 (C-1α), 86.1 (C-2β), 84.3 (C-2α), 82.6 (C-3β), 81.7 (C-3α), 80.1 (C-4β), 76.4 (C-4α), 73.4, 72.6, 72.5, 72.4 (CH_2 Bn), 15.8 (C-5β), 15.4 (C-5α); HRMS: only mass of hydrolysis found $[M+Na]^+$ calcd for $C_{19}H_{22}O_4Na$ 337.1416, found 337.1417.



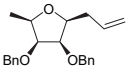
Acetyl 2,3-di-*O*-benzyl-5-deoxy-α/β-D-xylofuranoside (63). The title compound was generated from **S10** (220 mg, 0.7 mmol) by the general procedure for acetyl donor synthesis as described in Chapter 7. Yield: 95% α:β = 1:2.5 (236 mg, 0.66 mmol) as a colourless oil. IR (thin film): 604, 696, 735, 1007, 1090, 1231, 1373, 1454, 1741, 2934, 3030; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.39 – 7.23 (m, 14H, CH_{arom}), 6.28 (d, 0.4H, *J* = 4.1 Hz, H-1α), 6.12 (s, 1H, H-1β), 4.64 (d, 1H, *J* = 12.0 Hz, C*H*H Bnβ), 4.62 – 4.42 (m, 6H, CH*H* Bnβ, CH_2 Bnβ, 2xCH_2 Bnα, H-4α, H-4β), 4.15 – 4.08 (m, 1.8H, H-2α, H-2β, H-3α), 3.89 (dd, 1H, *J* = 5.2, 2.3 Hz, H-3β), 2.06 (s, 1.2H, CH_3 OAcα), 2.04 (s, 3H, CH_3 OAcβ), 1.34 (d, 3H, *J* = 6.6 Hz, H-5β), 1.27 (d, 1.2H, *J* = 6.5 Hz, H-5α); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 170.3, 170.2 (C=O), 138.0, 137.8, 137.4, 137.4 (C_q), 128.5, 128.4, 128.0, 128.0, 128.0, 127.8, 127.7, 127.5, 127.5 (CH_{arom}), 100.5 (C-1β), 94.2 (C-1α), 85.8 (C-2β), 83.6 (C-2α), 81.9 (C-3β), 81.5 (C-3α), 79.1 (C-4β), 75.7 (C-4α), 73.2, 72.2, 72.1, 71.8 (CH_2 Bn), 21.4 (CH_3 OAcβ), 21.2 (CH_3 OAcα), 15.5 (C-5β), 15.4 (C-5α); HRMS: $[M+Na]^+$ calcd for $C_{21}H_{24}O_5Na$ 379.1521, found 379.1525.



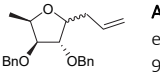
Allyl 2,3-di-*O*-benzyl-1,5-dideoxy-α/β-D-arabinofuranoside (65). Donor **59** and allyltrimethylsilane (4 eq.) were condensed using the general procedure for furanosyl imidate glycosylations at -78°C for 90 h with TfOH as the promotor. Yield = 28 mg, 83 µmol, 83% as a colourless oil (α:β = 40:60). R_f: 0.55 (85/15 pentane/EtOAc). IR (thin film): 698, 737, 1028, 1069, 1098, 1454, 2866, 2900, 2974; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HH-NOESY, HSQC): δ 7.39 – 7.27 (m, 10H, CH_{arom}), 5.89 – 5.77 (m, 1H, CH allyl), 5.17 – 5.03 (m, 2H, CH_2 allyl), 4.59 (d, 0.6H, *J* = 12.0 Hz, C*H*H Bnβ), 4.56 – 4.44 (m, 3.4H, CH*H* Bnβ, CH_2 Bnβ, 2xCH_2 Bnα), 4.14 (qd, 0.4H, *J* = 6.5, 4.4 Hz, H-4α), 4.08 (td, 0.4H, *J* = 6.7, 4.1 Hz, H-1α), 3.96 (td, 0.6H, *J* = 7.0, 3.7 Hz, H-1β), 3.92 (qd, 0.6H, *J* = 6.5, 3.8 Hz, H-4β), 3.84 (dd, 0.4H, *J* = 4.0, 2.8 Hz, H-2α), 3.82 (dd, 0.6H, *J* = 3.7, 0.9 Hz, H-2β), 3.75 (dd, 0.4H, *J* = 4.3, 2.8 Hz, H-3α), 3.65 (dd, 0.6H, *J* = 3.8, 1.0 Hz, H-3β), 2.51 (tq, 1.2H, *J* = 6.9, 1.3 Hz, CH_2 allylicβ), 2.44 – 2.34 (m, 0.4H, CH_2 allylicα), 1.34 (d, 1.8H, *J* = 6.5 Hz, H-5β), 1.31 (d, 1.2H, *J* = 6.5 Hz, H-5α); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.2, 138.1, 138.0, 138.0 (C_q), 135.1 (CH allylβ), 134.5 (CH allylα), 128.6, 128.6, 128.6, 128.5, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7 (CH_{arom}), 117.6 (CH_2 allylα), 117.0 (CH_2 allylβ), 89.7 (C-3α), 88.7 (C-3β), 87.6 (C-2α), 83.6 (C-2β), 81.4 (C-1α), 80.9 (C-1β), 79.9 (C-4β), 78.1 (C-4α), 72.1, 72.0, 71.8, 71.6 (CH_2 Bn), 38.0 (CH_2 allylicα), 33.5 (CH_2 allylicβ), 20.1 (C-5β), 19.5 (C-5α); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): α-anomer: $^2J_{C1,H2}$ = -0.7 Hz, $^2J_{C2,H1}$ = -4.2 Hz, $^3J_{Callyl,H2}$ = +3.7 Hz, β-anomer: $^2J_{C1,H2}$ = +2.2 Hz, $^2J_{C2,H1}$ = +3.4 Hz, $^3J_{Callyl,H2}$ = +0.3 Hz; HRMS: $[M+Na]^+$ calcd for $C_{22}H_{26}O_3Na$ 361.1780, found 361.1780.



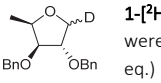
Allyl 2,3-di-*O*-benzyl-1,5-dideoxy-α-D-ribofuranoside (66). Donor **60** and allyltrimethylsilane (4 eq.) were condensed using the general procedure for furanosyl imidate glycosylations at -78°C for 90 h with TfOH as the promotor. Yield = 30 mg, 89 µmol, 89% as a colourless oil. R_f: 0.61 (85/15 pentane/EtOAc). $[\alpha]_D^{20}$ = +50.9° (*c* = 1.0, $CHCl_3$); IR (thin film): 696, 737, 914, 1026, 1094, 1273, 1454, 2926, 2970, 3032; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HH-NOESY, HSQC): δ 7.42 – 7.25 (m, 10H, CH_{arom}), 5.80 (ddt, 1H, *J* = 17.1, 10.2, 6.9 Hz, CH allyl), 5.10 (dq, 1H, *J* = 17.2, 1.6 Hz, C*H*H allyl), 5.04 (ddt, 1H, *J* = 10.2, 2.1, 1.1 Hz, CH*H* allyl), 4.81 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.67 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.59 (d, 1H, *J* = 11.7 Hz, CH*H* Bn), 4.54 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.17 (dq, 1H, *J* = 7.5, 6.2 Hz, H-4), 4.05 (td, 1H, *J* = 7.0, 4.0 Hz, H-1), 3.97 (t, 1H, *J* = 4.1 Hz, H-2), 3.61 (dd, 1H, *J* = 7.5, 4.2 Hz, H-3), 2.54 – 2.41 (m, 2H, CH_2 allylic), 1.24 (d, 3H, *J* = 6.2 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.6, 138.1 (C_q), 135.2 (CH allyl), 128.6, 128.4, 127.9, 127.8, 127.8, 127.7 (CH_{arom}), 117.0 (CH_2 allyl), 85.7 (C-3), 79.4 (C-1), 77.8 (C-2), 75.5 (C-4), 73.5, 72.8 (CH_2 Bn), 34.6 (CH_2 allylic), 19.6 (C-5); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): α-anomer: $^2J_{C1,H2}$ = +0.9 Hz, $^2J_{C2,H1}$ = +1.6 Hz, $^3J_{Callyl,H2}$ = +1.5 Hz; HRMS: $[M+Na]^+$ calcd for $C_{22}H_{26}O_3Na$ 361.1780, found 361.1779.



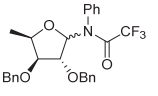
Allyl 2,3-di-*O*-benzyl-1,5-dideoxy-β-D-lyxofuranoside (67). Donor **61** and allyltrimethylsilane (4 eq.) were condensed using the general procedure for furanosyl imidate glycosylations at -78°C for 90 h with TfOH as the promotor. Yield = 19 mg, 56 µmol, 56% as a colourless oil. R_f: 0.25 (85/15 pentane/EtOAc). $[\alpha]_D^{20}$ = -7.1° (*c* = 0.63, $CHCl_3$); IR (thin film): 696, 735, 912, 1028, 1065, 1086, 1159, 1454, 2866, 2926, 3030, 3064; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.39 – 7.26 (m, 10H, CH_{arom}), 5.84 (ddt, 1H, *J* = 17.2, 10.2, 6.9 Hz, CH allyl), 5.10 (ddt, 1H, *J* = 17.2, 2.1, 1.5 Hz, C*H*H allyl), 5.03 (ddt, 1H, *J* = 10.2, 2.2, 1.2 Hz, CH*H* allyl), 4.79 (d, 1H, *J* = 11.8 Hz, C*H*H Bn), 4.70 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.61 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.57 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.16 – 4.08 (m, 1H, H-4), 4.04 – 3.98 (m, 2H, H-2, H-3), 3.94 – 3.88 (m, 1H, H-1), 2.53 – 2.46 (m, 2H, CH_2 allylic), 1.33 (d, 3H, *J* = 6.4 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.7, 138.6 (C_q), 135.7 (CH allyl), 128.5, 128.4, 127.7, 127.6, 127.6, 127.5 (CH_{arom}), 116.7 (CH_2 allyl), 80.4 (C-3), 79.4 (C-2), 78.8 (C-1), 75.1 (C-4), 73.4, 73.1 (CH_2 Bn), 35.4 (CH_2 allylic), 16.9 (C-5); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): $^2J_{C1,H2}$ = +1.5 Hz, $^2J_{C2,H1}$ = +1.5 Hz, $^3J_{Callyl,H2}$ = +0.5 Hz; HRMS: $[M+Na]^+$ calcd for $C_{22}H_{26}O_3Na$ 361.1780, found 361.1779.



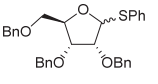
Allyl 2,3-di-*O*-benzyl-1,5-dideoxy-α/β-D-xylofuranoside (68). Donor **62** and allyltrimethylsilane (4 eq.) were condensed using the general procedure for furanosyl imidate glycosylations at -78°C for 90 h with TfOH as the promotor. Isolated yield = 28 mg, calculated product yield = 20 mg, 60 µmol, 60% (α:β = 60:40), intermixed with amide **74** (16%). R_f: 0.58 (80/20 pentane/EtOAc). IR (thin film): 696, 734, 914, 1028, 1067, 1086, 1205, 1454, 2866, 2930, 3032; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.39 – 7.19 (m, 17H, CH_{arom}), 5.87 – 5.76 (m, 1.7H, CH allyl), 5.14 – 5.02 (m, 3.4H, CH_2 allyl), 4.59 – 4.52 (m, 2.7H, 3xC*H*H Bn), 4.50 – 4.44 (m, 4.4H, 3xCH*H* Bn, CH_2 Bn), 4.29 (qd, 1H, *J* = 6.5, 4.0 Hz, H-4α), 4.17 (td, 1H, *J* = 7.1, 4.0 Hz, H-1α), 4.08 (qd, 0.7H, *J* = 6.4, 3.7 Hz, H-4β), 3.88 (dd, 1H, *J* = 4.0, 1.4 Hz, H-2α), 3.83 (td, 0.7H, *J* = 6.7, 3.9 Hz, H-1β), 3.80 (dd, 1H, *J* = 4.0, 1.4 Hz, H-3α), 3.77 – 3.73 (m, 1.4H, H-2β, H-3β), 2.49 – 2.34 (m, 3.4H, CH_2 allylic), 1.33 (d, 2.1H, *J* = 6.4 Hz, H-5β), 1.26 (d, 3H, *J* = 6.5 Hz, H-5α); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 138.3, 138.3, 138.1, 138.0 (C_q), 135.4 (CH allylα), 134.7 (CH allylβ), 129.2, 128.6, 128.6, 128.5, 128.4, 128.2, 127.9, 127.9, 127.9, 127.8, 127.8, 127.8, 127.7, 127.7, 127.6 (CH_{arom}), 117.3 (CH_2 allylβ), 116.8 (CH_2 allylα), 86.9 (C-2β), 84.2 (C-3β), 82.9 (C-1β), 82.8 (C-3α), 82.5 (C-2α), 79.4 (C-1α), 77.1 (C-4β), 75.8 (C-4α), 72.3, 72.2 (CH_2 Bnα), 71.8, 71.6 (CH_2 Bnβ), 38.6 (CH_2 allylicβ), 33.9 (CH_2 allylicα), 14.8 (C-5α), 14.3 (C-5β); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): α-anomer: $^2J_{C1,H2}$ = +2.0 Hz, $^2J_{C2,H1}$ = +2.0 Hz, $^3J_{Callyl,H2}$ = +0.4 Hz; β-anomer:$^2J_{C2,H1}$ = -4.4 Hz, $^3J_{Callyl,H2}$ = +3.7 Hz; HRMS: $[M+Na]^+$ calcd for $C_{22}H_{26}O_3Na$ 361.1780, found 361.1779.



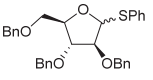
1-[^{2}H]-1,4-anhydro-2,3-di-*O*-benzyl-5-deoxy-α/β-D-xylitol (69). Donor **60** and triethylsilane-*d* (4 eq.) were condensed using the procedure published by van Rijssel *et al.*[20] -78°C for 90 h with TMSOTf (1.3 eq.) as the promotor. Yield = 23 mg, 77 µmol, 77% as a colourless oil (α:β = 40:60). R_f: 0.42 (9/1 pentane/EtOAc). IR (thin film): 709, 1026, 1096, 1109, 1267, 1452, 2933; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.38 – 7.27 (m, 10H, CH_{arom}), 4.61 (d, 1H, *J* = 12.2 Hz, C*H*H Bn), 4.50 (d, 1H, *J* = 12.2 Hz, CH*H* Bn), 4.49 (s, 2H, CH_2 Bn), 4.14 (t, 0.6H, *J* = 5.5 Hz, H-1β), 4.15 – 4.06 (m, 2H, H-2, H-4), 3.80 (dd, 1H, *J* = 3.8, 1.2 Hz, H-3), 3.71 (dt, 0.4H, *J* = 2.7, 1.3 Hz, H-1α), 1.30 (d, 3H, *J* = 6.4 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.2, 137.9 (C_q), 128.6, 128.6, 128.0, 127.9, 127.7 (CH_{arom}), 83.3 (C-3), 82.9 (C-2), 76.8 (C-4), 71.9, 71.7 (CH_2 Bn), 71.1 (t, *J* = 22.4 Hz, C-1), 71.1 (t, *J* = 22.4 Hz, C-1), 14.1 (C-5); ^{2}H NMR ($CHCl_3$, 77 MHz): δ 4.18 (s, 0.4D, D-1α), 3.74 (s, 0.6D, D-1β); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): α-anomer: $^2J_{C2,H1}$ = +1.2 Hz; β-anomer:$^2J_{C2,H1}$ = -4.5 Hz.



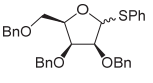
2,3-di-*O*-benzyl-1,5-dideoxy-1-*N*-[phenyl]trifluoroacetyl-α/β-D-xylofuranoside (74). Intermixed with **68**. The anomeric amide was formed in an α:β = 96:4 ratio. Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.40 – 7.20 (m, 15H, CH_{arom}), 6.31 (d, 1H, *J* = 5.6 Hz, H-1), 4.69 (d, 1H, *J* = 11.1 Hz, C*H*H Bn), 4.54 (d, 1H, *J* = 11.2 Hz, CH*H* Bn), 4.50 – 4.46 (m, 1H, C*H*H Bn), 4.42 (dd, 1H, *J* = 5.7, 3.3 Hz, H-4), 4.34 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 3.52 – 3.47 (m, 2H, H-2, H-3), 1.03 (d, 3H, *J* = 6.1 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 156.5 (C=O), 137.8, 137.4 (C_q Bn), 134.6 (C_q Ph), 132.1 - 127.6 (CH_{arom}), 116.1 (q, *J* = 289 Hz, CF_3, 87.8 (C-1), 83.1 (C-2), 81.6 (C-3), 76.6 (C-4), 74.1, 72.0 (CH_2 Bn), 15.1 (C-5); ^{19}F NMR ($CDCl_3$, 471 MHz): δ -68.08 ; ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): $^2J_{C1,H2}$ = +1.2 Hz, $^2J_{C2,H1}$ = +2.0 Hz;



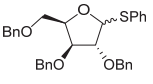
Phenyl 2,3,5-tri-*O*-benzyl-1-thio-α/β-D-ribofuranoside (77). A solution of 1,2,3,5-tetra-O-acetyl-α/β-D-ribofuranose[20] (1.59 g, 3.43 mmol, 1 eq.), thiophenol (0,40 mL, 3.77 mmol, 1.1 eq.) and $BF_3{\cdot}OEt_2$ (0.51 mL, 4.12 mmol, 1.2 eq.) at 0°C was stirred for 2 h. The reaction was quenched with sat. aq. $NaHCO_3$ and the mixture was extracted with EtOAc and washed with brine. The organic layer was dried ($MgSO_4$), filtered and concentrated *in vacuo*. Flash column chromatography of the residue (1/0 to 19/1 pentane/EtOAc) afforded the title compound as a colourless oil (Yield = 1.237 g, 2.41 mmol, 70%, α:β = 1:2.7). Spectroscopic data was previously reported[28] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.81 – 7.36 (m, 55.5H, CH_{arom}), 5.97 (d, 1H, *J* = 5.3 Hz, H-1α), 5.73 (d, 2.7H, *J* = 3.7 Hz, H-1β), 4.99 (d, 1H, *J* = 11.7 Hz, C*H*H Bnα), 4.92 (d, 1H, *J* = 12.1 Hz, C*H*H Bnα), 4.84 (d, 1H, *J* = 11.7 Hz, CH*H* Bnα), 4.80 (d, 2.7H, *J* = 11.9 Hz, C*H*H Bnβ), 4.75 – 4.63 (m, 16.5H, 2xC*H*H Bnβ, 3xCH*H* Bnβ, C*H*H Bnα, CH*H* Bnα, H-4α), 4.61 (d, 1H, *J* = 12.1 Hz, CH*H* Bnα), 4.58 – 4.54 (m, 2.7H, H-4β), 4.38 (t, 1H, *J* = 5.5 Hz, H-2α), 4.20 (t, 1H, *J* = 5.4 Hz, H-3α), 4.18 – 4.14 (m, 5.4H, H-2β, H-3β), 3.80 (dd, 1H, *J* = 10.9, 3.3 Hz, H-5α), 3.74 (d, 5.4H, *J* = 4.5 Hz, H-5β, H-5β), 3.71 (dd, 1H, *J* = 10.8, 3.5 Hz, H-5α); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 137.9, 137.9, 137.8, 137.5, 137.4, 137.2, 136.4, 133.3 (C_q), 131.9, 130.4, 128.6, 128.5, 128.1, 128.1, 128.0, 127.8, 127.7, 127.6, 127.5, 127.5, 127.4, 127.3, 127.3, 127.3, 127.3, 127.2, 126.2 (CH_{arom}), 90.4 (C-1α), 88.4 (C-1β), 81.7 (C-4β), 80.6 (C-4α), 80.2 (C-2β), 78.3 (C-2α), 77.2 (C-3β), 76.9 (C-3α), 73.0, 72.9, 72.9, 72.2, 71.8 (CH_2 Bn), 70.0 (C-5β), 69.0 (C-5α); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): α-anomer: $^2J_{C1,H2}$ = +2.0 Hz; β-anomer: $^2J_{C2,H1}$ = -2.9 Hz; HRMS: $[M+Na]^+$ calcd for $C_{32}H_{32}O_4SNa$ 535.19135, found 535.19064.



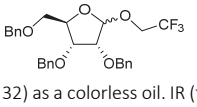
Phenyl 2,3,5-tri-*O*-benzyl-1-thio-α/β-D-arabinofuranoside (79). A solution of 1,2,3,5-tetra-O-acetyl-α/β-D-arabinofuranose[20] (889 mg, 1.92 mmol, 1 eq.), thiophenol (0.22 mL, 2.11 mmol, 1.1 eq.) and $BF_3{\cdot}OEt_2$ (0.30 mL, 2.31 mmol, 1.2 eq.) at 0°C was stirred for 2 h. The reaction was quenched with sat. aq. $NaHCO_3$ and the mixture was extracted with EtOAc and washed with brine. The organic layer was dried ($MgSO_4$), filtered and concentrated *in vacuo*. Flash column chromatography of the residue (1/0 to 19/1 pentane/EtOAc) afforded the title compound as a colourless oil (Yield = 291 mg, 0.57 mmol, 30%, α:β = 4:1). Spectroscopic data for the β-anomer was reported previously.[29] Data for the α-anomer: IR (thin film): 693, 734, 1026, 1068, 1270, 1361, 1453, 1722, 2864; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.54 – 7.46 (m, 2H, CH_{arom}), 7.38 – 7.18 (m, 18H, CH_{arom}), 5.62 (d, 1H, *J* = 2.8 Hz, H-1), 4.66 – 4.45 (m, 6H, 3xCH_2 Bn), 4.40 (dt, 1H, *J* = 6.7, 4.4 Hz, H-4), 4.13 (t, 1H, *J* = 3.1 Hz, H-2), 4.05 (dd, 1H, *J* = 6.7, 3.3 Hz, H-3), 3.68 (dd, 1H, *J* = 10.9, 3.9 Hz, H-5), 3.63 (dd, 1H, *J* = 10.9, 4.8 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.1, 137.7, 137.3, 134.9 (C_q), 131.2, 128.9, 128.5, 128.4, 128.4, 128.0, 128.0, 127.8, 127.8, 127.7, 127.6, 127.1 (CH_{arom}), 90.3 (C-1), 88.5 (C-2), 83.4 (C-3), 80.5 (C-4), 73.3, 72.3, 72.1 (CH_2 Bn), 69.0 (C-5); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): α-anomer: $^2J_{C1,H2}$ = +0.6 Hz, $^2J_{C2,H1}$ = -4.0 Hz; HRMS: $[M+Na]^+$ calcd for $C_{32}H_{32}O_4SNa$ 535.19135, found 535.19024.



Phenyl 2,3,5-tri-*O*-benzyl-1-thio-α/β-D-lyxofuranoside (81). A solution of 1,2,3,5-tetra-O-acetyl-α/β-D-lyxofuranose[20] (1.86 g, 4.02 mmol, 1 eq.), thiophenol (0.50 mL, 4.43 mmol, 1.1 eq.) and $BF_3{\cdot}OEt_2$ (0.60 mL, 4.83 mmol, 1.2 eq.) at 0°C was stirred for 2 h. The reaction was quenched with sat. aq. $NaHCO_3$ and the mixture was extracted with EtOAc and washed with brine. The organic layer was dried ($MgSO_4$), filtered and concentrated *in vacuo*. Flash column chromatography of the residue (1/0 to 19/1 pentane/EtOAc) afforded the title compound as a colourless oil (Yield = 1.11 g, 2.17 mmol, 54%, α:β = 97:3). Data for the α-anomer: IR (thin film): 693, 733, 1025, 1072, 1453, 2859; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.49 – 7.43 (m, 2H, CH_{arom}), 7.31 – 7.16 (m, 17H, CH_{arom}), 5.54 (d, 1H, *J* = 6.0 Hz, H-1), 4.70 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.60 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.55 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.53 (d, 1H, *J* = 11.7 Hz, CH*H* Bn), 4.51 (d, 1H, *J* = 11.9 Hz, C*H*H Bn), 4.44 (d, 1H, *J* = 11.9 Hz, CH*H* Bn), 4.27 (td, 1H, *J* = 6.2, 3.8 Hz, H-4), 3.99 (t, 1H, *J* = 4.1 Hz, H-3), 3.94 (dd, 1H, *J* = 5.9, 4.4 Hz, H-2), 3.80 (dd, 1H, *J* = 9.9, 6.3 Hz, H-5), 3.70 (dd, 1H, *J* = 9.9, 6.2 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.0, 138.0, 137.4, 134.0 (C_q), 131.7, 128.8, 128.4, 128.3, 128.2, 127.8, 127.8, 127.8, 127.7, 127.6, 127.6, 127.2 (CH_{arom}), 88.4 (C-1), 83.2 (C-2), 79.0 (C-4), 76.8 (C-3), 73.5, 73.3, 72.6 (CH_2 Bn), 68.2 (C-5); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): $^2J_{C1,H2}$ = -2.2 Hz, $^2J_{C2,H1}$ = -4.5 Hz; HRMS: $[M+Na]^+$ calcd for $C_{32}H_{32}O_4SNa$ 535.19135, found 535.19018.

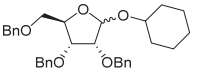


Phenyl 2,3,5-tri-*O*-benzyl-1-thio-α/β-D-xylofuranoside (81). A solution of 1,2,3,5-tetra-O-acetyl-α/β-D-xylofuranose[20] (3.55 g, 7.68 mmol, 1 eq.), thiophenol (0.90 mL, 8.45 mmol, 1.1 eq.) and $BF_3{\cdot}OEt_2$ (1.15 mL, 9.22 mmol, 1.2 eq.) at 0°C was stirred for 2 h. The reaction was quenched with sat. aq. $NaHCO_3$ and the mixture was extracted with EtOAc and washed with brine. The organic layer was dried ($MgSO_4$), filtered and concentrated *in vacuo*. Flash column chromatography of the residue (1/0 to 19/1 pentane/EtOAc) afforded the title compound as a colourless oil (Yield = 2.07 g, 4.04 mmol, 53%, α:β = 1:0.8). Spectroscopic data for the α-anomer was reported previously.[29] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.55 – 7.47 (m, 4H, CH_{arom}), 7.40 – 7.14 (m, 32H, CH_{arom}), 5.80 (d, 1H, *J* = 5.0 Hz, H-1α), 5.37 (d, 0.8H, *J* = 2.9 Hz, H-1β), 4.69 – 4.37 (m, 12.6H, 3xCH_2 Bnα,β, H-4α), 4.21 (dd, 1H, *J* = 5.0, 2.3 Hz, H-2α), 4.15 – 4.11 (m, 0.8H, H-2β), 4.09 (dd, 1H, *J* = 4.5, 2.3 Hz, H-3α), 4.03 (dd, 0.8H, *J* = 4.7, 1.8 Hz, H-3β), 3.87 – 3.76 (m, 2.6H, H-5α, H-5β,β), 3.71 (dd, 1H, *J* = 10.1, 5.8 Hz, H-5α); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.1, 137.7, 137.6, 137.3, 135.6, 135.3 (C_q), 130.9, 128.8, 128.7, 128.4, 128.3, 128.2, 127.9, 127.8, 127.7, 127.6, 127.6, 127.6, 127.5, 126.9, 126.5 (CH_{arom}), 90.0 (C-1α), 89.9 (C-1β), 86.6 (C-2β), 83.7 (C-2α), 81.6 (C-3α), 81.5 (C-3β), 81.2 (C-4β), 78.1 (C-4α), 73.3, 73.2, 72.8, 72.1, 71.8, 71.7 (CH_2 Bn), 68.6 (C-5β), 67.7 (C-5α); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): α-anomer: $^2J_{C1,H2}$ = +2.5 Hz, $^2J_{C2,H1}$ = +0.7 Hz; β-anomer: $^2J_{C1,H2}$ = 0 Hz, $^2J_{C2,H1}$ = -4.5 Hz; HRMS: $[M+Na]^+$ calcd for $C_{32}H_{32}O_4SNa$ 535.19135, found 535.19046.

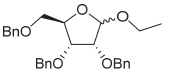


2,2,2-Trifluoroethyl 2,3,5-tri-*O*-benzyl-α/β-D-ribofuranoside (86). Donor **77** and acceptor **8** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 (2h at -60°C) yielding product **86** (42.7 mg, 85 µmol, 85%, α:β = 68 : 32) as a colorless oil. IR (thin film): 697, 735, 1028, 1046, 1114, 1153, 1279, 1454, 2861, 2930; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.39 – 7.26 (m, 13H, CH_{arom}), 7.20 (dd, 2H, *J* = 7.7, 1.8 Hz, CH_{arom}), 5.13 (t, 1H, *J* = 2.1 Hz, H-1), 4.72 (d, 1H, *J* = 12.5 Hz, C*H*H Bn), 4.68 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.62 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.53 (d, 1H, *J* = 12.5 Hz, CH*H* Bn), 4.48 (d, 1H, *J* = 12.2 Hz, C*H*H Bn), 4.41 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.28 – 4.22 (m, 1H, H-4), 4.04 (q, 2H, *J* = 8.9 Hz, CH_2 TFE), 3.89 – 3.84 (m, 2H, H-2, H-3), 3.45 (dd, 1H, *J* = 10.5, 3.6 Hz, H-5), 3.36

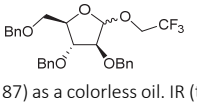
(dd, 1H, *J* = 10.6, 4.1 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.3, 137.9, 137.8 (C_q), 128.5, 128.4, 128.2, 128.0, 127.9, 127.8, 127.8, (CH_{arom}), 124.3 (d, *J* = 279.5 Hz), 101.5 (C-1), 82.6 (C-4), 77.9 (C-3), 75.3 (C-2), 73.6, 72.8, 72.6 (CH_2 Bn), 69.9 (C-5), 64.2 (q, *J* = 34.4 Hz, *CH*$_2$-CF_3); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): $^2J_{C1,H2}$ = +3.5 Hz, $^2J_{C2,H1}$ = +4.4 Hz; Data for the β-anomer:: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.36 – 7.24 (m, 15H, CH_{arom}), 5.06 (s, 1H, H-1), 4.69 – 4.42 (m, 6H, 3xCH_2 Bn), 4.36 (ddd, 1H, *J* = 7.4, 5.5, 3.3 Hz, H-4), 4.08 (dd, 1H, *J* = 7.4, 4.6 Hz, H-3), 3.95 (d, 1H, *J* = 4.6 Hz, H-2), 3.90 – 3.70 (m, 1H, CH_2 TFE), 3.63 (dd, 1H, *J* = 10.6, 3.3 Hz, H-5), 3.46 (dd, 1H, *J* = 10.6, 5.5 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.1, 137.6 (C_q), 128.6, 128.5, 128.1, 128.1, 128.0, 128.0, 128.0, 127.9, 127.8 (CH_{arom}), 124.0 (q, *J* = 278.3 Hz, CF_3), 105.1 (C-1), 81.2 (C-4), 79.5 (C-2), 78.0 (C-3), 73.3, 72.7, 72.7 (CH_2 Bn), 70.6 (C-5), 63.9 (q, *J* = 34.5 Hz, *CH*$_2$-CF_3); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): $^2J_{C2,H1}$ = -1.0 Hz; HRMS: $[M+Na]^+$ calcd for $C_{28}H_{29}F_3O_5Na$ 525.18593, found 525.18488.



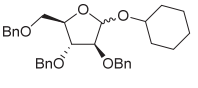
Cyclohexyl 2,3,5-tri-*O*-benzyl-α/β-D-ribofuranoside (87). Donor **77** and acceptor **76** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 (2h at -60°C) yielding product **87** (26.2 mg, 52 µmol, 52%, α:β = 64 : 36) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.42 – 7.19 (m, 22.5H, CH_{arom}), 5.19 – 5.15 (m, 1.5H, H-1α,β), 4.74 – 4.41 (m, 9H, 3xCH_2 Bnα,β), 4.32 (td, 0.5H, *J* = 6.3, 4.1 Hz, H-4β), 4.24 (q, 1H, *J* = 4.1 Hz, H-4α), 4.00 (dd, 0.5H, *J* = 6.8, 4.8 Hz, H-3β), 3.86 – 3.80 (m, 1.5H, H-2β, H-3α), 3.76 (dd, 1H, *J* = 6.9, 4.2 Hz, H-2α), 3.65 – 3.49 (m, 2.5H, H-5β,β, CH Cγα,β), 3.46 (dd, 1H, *J* = 10.6, 3.7 Hz, H-5α), 3.37 (dd, 1H, *J* = 10.6, 4.2 Hz, H-5α), 2.01 – 1.11 (m, 15H, CH_2 Cγα,β); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.7, 138.4, 138.3, 138.2, 138.1 (C_q), 128.5, 128.4, 128.4, 128.4, 128.3, 128.1, 128.1, 128.1, 127.9, 127.9, 127.8, 127.8, 127.7, 127.6 (CH_{arom}), 103.3 (C-1β), 99.7 (C-1α), 81.0 (C-4α), 80.3 (C-2β, C-4β), 78.9 (C-3β), 77.4 (C-2α), 76.3 (CH Cγα), 75.6 (C-3α), 75.3 (CH Cγβ), 73.5, 73.3, 72.4, 72.3 (CH_2 Bn), 71.9 (C-5β), 70.1 (C-5α), 33.9, 33.7, 32.1, 31.6, 25.8, 25.8, 24.7, 24.6, 24.3, 24.1 (CH_2 Cγ); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): α-anomer:: $^2J_{C1,H2}$ = +1.2 Hz; β-anomer:: $^2J_{C1,H2}$ = -0.5 Hz; HRMS: $[M+Na]^+$ calcd for $C_{32}H_{38}O_5Na$ 525.26115, found 525.26028.



Ethyl 2,3,5-tri-*O*-benzyl-α/β-D-ribofuranoside (88). Donor **77** and acceptor **5** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 (2h at -60°C) yielding product **88** (32.4 mg, 72 µmol, 72%, α:β = 81 : 19) as a colorless oil. IR (thin film): 694, 739, 1044, 1090, 1444, 2879, 2930, 3065; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.38 – 7.26 (m, 18H, CH_{arom}), 5.02 (d, 1.2H, *J* = 4.2 Hz, H-1α,β), 4.73 – 4.40 (m, 7.2H, 3xCH_2 Bnα,β), 4.37 – 4.30 (m, 0.2H, H-4β), 4.25 (q, 1H, *J* = 3.9 Hz, H-4α), 4.04 (dd, 0.2H, *J* = 7.0, 4.7 Hz, H-3β), 3.88 – 3.80 (m, 2.2H, H-2β, H-3α, C*H* Etα), 3.79 – 3.69 (m, 1.2H, H-2α, C*H* Etβ), 3.65 – 3.57 (m, 1.2H, H-5β, CH*H* Etα), 3.52 (dd, 0.2H, *J* = 10.6, 5.9 Hz, H-5β), 3.47 – 3.38 (m, 1.2H, H-5α, CH*H* Etβ), 3.35 (dd, 1H, *J* = 10.5, 4.2 Hz, H-5α), 1.28 (t, 3H, *J* = 7.1 Hz, CH_3 Etα), 1.11 (t, 0.6H, *J* = 7.1 Hz, CH_3 Etβ); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.4, 138.0, 138.0 (C_q), 131.2, 129.4, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.1, 128.0, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 124.9 (CH_{arom})105.1 (C-1β), 101.1 (C-1α), 81.6 (C-4α), 80.4 (C-4β), 79.9 (C-2β), 78.7 (C-3β), 77.6 (C-2α), 75.3 (C-3α), 73.5, 73.2, 72.5, 72.5, 72.4, 72.3 (CH_2 Bn), 71.6 (C-5β), 70.1 (C-5α), 63.8 (CH_2 Etα), 63.3 (CH_2 Etβ), 15.4 (CH_3 Etα), 15.1 (CH_3 Etβ); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): α-anomer: $^2J_{C1,H2}$ = +1.4 Hz, $^2J_{C2,H1}$ = +2.2 Hz HRMS: $[M+Na]^+$ calcd for $C_{28}H_{32}O_5Na$ 471.21420, found 471.21324.

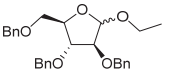


2,2,2-Trifluoroethyl 2,3,5-tri-*O*-benzyl-α/β-D-arabinofuranoside (90). Donor **79** and acceptor **8** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 (2h at -60°C) yielding product **90** (40 mg, 80 µmol, 80%, α:β = 13 : 87) as a colorless oil. IR (thin film): 697, 736, 1072, 1116, 1161, 1279, 1454, 2879, 2930; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.43 – 7.31 (m, 18H, CH_{arom}), 5.19 (s, 0.2H, H-1α), 5.01 (d, 1H, *J* = 3.8 Hz, H-1β), 4.77 – 4.49 (m, 7.2H, CH_2 Bnα,β), 4.29 – 4.25 (m, 0.2H, H-4α), 4.21 – 4.13 (m, 3.2H, H-2α, H-2β, H-3β, H-4β), 3.99 (dd, 0.2H, *J* = 6.9, 3.2 Hz, H-3α), 3.89 – 3.79 (m, 2.4H, CH_2 TFEα,β), 3.69 (dd, 0.2H, *J* = 10.8, 3.5 Hz, H-5α), 3.63 (dd, 0.2H, *J* = 10.8, 5.4 Hz, H-5α), 3.59 – 3.50 (m, 2H, H-5β, H-5β); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.1, 137.9, 137.7, 137.5 (C_q), 128.9, 128.6, 128.5, 128.5, 128.4, 128.2, 128.1, 128.0, 127.9, 127.9, 127.9, 127.8 (CH_{arom}), 124.1 (q, *J* = 278.8 Hz, CF_3), 106.4 (C-1α), 100.6 (C-1β), 87.9 (C-2α), 84.3 (C-2β), 83.4 (C-3α), 82.4 (C-3β), 81.3 (C-4α), 80.8 (C-4β), 73.5, 73.4, 72.7, 72.6, 72.3, 72.3 (CH_2 Bn), 71.8 (C-5β), 69.5 (C-5α), 64.0 (q, *J* = 34.6 Hz, *CH*$_2$-CF_3 α), 63.8 (q, *J* = 34.4 Hz, *CH*$_2$-CF_3 β); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): α-anomer: $^2J_{C1,H2}$ = -2.1 Hz, $^2J_{C2,H1}$ = -1.8 Hz; β-anomer: $^2J_{C1,H2}$ = +2.1 Hz, $^2J_{C2,H1}$ = +1.8 Hz; HRMS: $[M+Na]^+$ calcd for $C_{28}H_{29}F_3O_5Na$ 525.18593, found 525.18480.

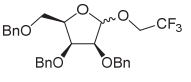


Cyclohexyl 2,3,5-tri-*O*-benzyl-α/β-D-arabinofuranoside (91). Donor **79** and acceptor **76** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as

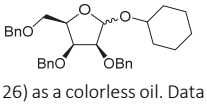
described in Chapter 3 (2h at -60°C) yielding product **91** (39mg, 78 µmol, 78%, α:β = 44 : 56) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.46 – 7.20 (m, 27H, CH_{arom}), 5.27 (d, 0.8H, *J* = 1.2 Hz, H-1α), 5.15 (d, 1H, *J* = 4.3 Hz, H-1β), 4.76 – 4.50 (m, 10.8H, 3xCH_2 Bnα,β), 4.26 (ddd, 0.8H, *J* = 7.3, 5.2, 3.4 Hz, H-4α), 4.17 – 4.08 (m, 3.8H, H-2β, H-3β, H-4β), 4.07 (dd, 0.8H, *J* = 3.6, 1.6 Hz, H-2α), 3.97 (dd, 0.8H, *J* = 7.2, 3.6 Hz, H-3α), 3.72 – 3.55 (m, 5.4H, H-5α,β, H-5α,β, CH Cyα,β), 2.00 – 1.12 (m, 18H, CH_2 Cyα,β); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.4, 138.3, 138.2, 138.1, 137.9, 137.8 (C_q), 128.5, 128.5, 128.4, 128.4, 128.2, 128.0, 128.0, 127.9, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7 (CH_{arom}), 104.1 (C-1α), 98.8 (C-1β), 88.9 (C-2α), 84.1, 83.8 (C-2β, C-3β), 83.6 (C-3α), 80.1, 80.1 (C-4α,β), 76.0, 75.0 (CH Cyα,β), 73.5 (CH_2 Bn), 73.4 (C-5β), 73.1, 72.4, 72.3, 72.2, 72.0 (CH_2 Bn), 69.8 (C-5α), 33.8, 33.8, 31.9, 31.8, 29.8, 25.8, 25.7, 24.6, 24.4, 24.4, 24.2 (CH_2 Cyα,β); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): α-anomer: $^{2}J_{C1,H2}$ = -2.2 Hz, $^{2}J_{C2,H1}$ = -1.5 Hz; β-anomer: $^{2}J_{C1,H2}$ = +1.2 Hz, $^{2}J_{C2,H1}$ = +4.0 Hz; HRMS: $[M+Na]^+$ calcd for $C_{32}H_{38}O_5Na$ 525.26115, found 525.25999.



Ethyl 2,3,5-tri-*O*-benzyl-α/β-D-arabinofuranoside (92). Donor **79** and acceptor **5** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 (2h at -60°C) yielding product **92** (22.7 mg, 51 µmol, 51%, α:β = 30 : 70) as a colorless oil. IR (thin film): 696, 735, 1099, 1453, 2862, 2902; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.37 – 7.22 (m, 15H, CH_{arom}), 5.06 (d, 0.7H, *J* = 1.3 Hz, H-1α), 4.85 (d, 0.3H, *J* = 4.2 Hz, H-1β), 4.69 – 4.45 (m, 6H, 3xCH_2 Bnα,β), 4.21 (ddd, 0.7H, *J* = 6.9, 5.3, 3.6 Hz, H-4α), 4.14 – 4.03 (m, 0.9H, H-2β, H-3β, H-4β), 4.02 (dd, 0.7H, *J* = 3.3, 1.4 Hz, H-2α), 3.91 (dd, 0.7H, *J* = 6.9, 3.2 Hz, H-3α), 3.79 (dq, 0.7H, *J* = 9.8, 7.1 Hz, C*H*H Etα), 3.74 – 3.35 (m, 3.3H, H-5β,β, H-5α,α, C*H*H Etα, CH_2 Etβ), 1.22 (t, 2.1H, *J* = 7.1 Hz, CH_3 Etα), 1.17 (t, 0.9H, *J* = 7.1 Hz, CH_3 Etβ); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.3, 138.2, 138.2, 138.0, 137.9, 137.8 (C_q), 128.5, 128.5, 128.5, 128.5, 128.3, 128.0, 127.9, 127.9, 127.8, 127.8, 127.8, 127.7, 127.7 (CH_{arom}), 106.0 (C-1α), 100.4 (C-1β), 88.6 (C-2α), 84.3 (C-2β), 83.6 (C-3α,β), 80.6 (C-4α), 80.3 (C-4β), 73.5, 73.4, 72.8, 72.6, 72.4, 72.2, 72.1, 69.9 (CH_2 Bn, C-5α,β), 63.3 (CH_2 Etβ), 63.2 (CH_2 Etα), 15.3 (CH_3 Etα), 15.2 (CH_3 Etβ); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): α-anomer: $^{2}J_{C1,H2}$ = -2.0 Hz, $^{2}J_{C2,H1}$ = -1.1 Hz; β-anomer: $^{2}J_{C1,H2}$ = +0.3 Hz, $^{2}J_{C2,H1}$ = +1.8 Hz; HRMS: $[M+Na]^+$ calcd for $C_{28}H_{32}O_5Na$ 471.21420, found 471.21298.

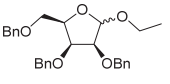


2,2,2-Trifluoroethyl 2,3,5-tri-*O*-benzyl-α/β-D-lyxofuranoside (94). Donor **81** and acceptor **8** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 (2h at -60°C) yielding product **94** (49 mg, 98 µmol, 98%, α:β = 48 : 52) as a colorless oil. Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.35 – 7.25 (m, 15H, CH_{arom}), 5.19 (d, 1H, *J* = 2.1 Hz, H-1), 4.68 (d, 1H, *J* = 11.8 Hz, C*H*H Bn), 4.66 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.61 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.60 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.52 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.50 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.37 (q, 1H, *J* = 5.7 Hz, H-4), 4.21 (t, 1H, *J* = 5.1 Hz, H-3), 4.06 – 3.94 (m, 2H, H-2, C*H*H-CF_3), 3.84 (dq, 1H, *J* = 12.4, 8.6 Hz, CH*H*-CF_3), 3.78 – 3.74 (m, 2H, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.2, 138.0, 137.7 (C_q), 128.6, 128.5, 128.0, 128.0, 127.9, 127.9, 127.8 (CH_{arom}), 124.0 (q, *J* = 278.3 Hz, CF_3), 105.7 (C-1), 82.3 (C-2), 79.1 (C-4), 77.9 (C-3), 73.6, 73.5, 72.8 (CH_2 Bn), 69.6 (C-5), 64.7 (q, *J* = 34.6 Hz, CH_2-CF_3); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): $^{2}J_{C1,H2}$ = -1.9 Hz, $^{2}J_{C2,H1}$ = -1.1 Hz; Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.39 – 7.22 (m, 15H, CH_{arom}), 5.12 (d, 1H, *J* = 4.6 Hz, H-1), 4.86 (d, 1H, *J* = 12.2 Hz, C*H*H Bn), 4.71 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.58 (d, 2H, *J* = 12.0 Hz, 2xCH*H* Bn), 4.54 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.51 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.19 (dt, 1H, *J* = 7.2, 5.1 Hz, H-4), 4.07 (t, 1H, *J* = 5.3 Hz, H-3), 4.00 (dd, 1H, *J* = 9.0, 1.2 Hz, C*H*H-CF_3), 3.96 (dd, 1H, *J* = 8.9, 0.9 Hz, CH*H*-CF_3), 3.89 (t, 1H, *J* = 5.2 Hz, H-2), 3.74 (dd, 1H, *J* = 10.2, 5.1 Hz, H-5), 3.68 (dd, 1H, *J* = 10.1, 7.2 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.5, 138.1, 137.7 (C_q), 128.6, 128.5, 128.3, 128.0, 128.0, 127.9, 127.8, 127.8, 127.6 (CH_{arom}), 124.3 (q, *J* = 279.1 Hz, CF_3), 100.1 (C-1), 79.7 (C-2), 79.5 (C-4), 75.1 (C-3), 73.6, 73.6, 72.6 (CH_2 Bn), 69.7 (C-5), 64.0 (q, *J* = 34.4 Hz, CH_2-CF_3); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): $^{2}J_{C1,H2}$ = +2.0 Hz, $^{2}J_{C2,H1}$ = +2.3 Hz; HRMS: $[M+Na]^+$ calcd for $C_{28}H_{29}F_3O_5Na$ 525.18593, found 525.18468.

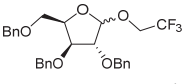


Cyclohexyl 2,3,5-tri-*O*-benzyl-α/β-D-lyxofuranoside (95). Donor **81** and acceptor **76** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 (2h at -60°C) yielding product **95** (36 mg, 72 µmol, 72%, α:β = 73 : 26) as a colorless oil. Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.36 – 7.23 (m, 15H, CH_{arom}), 5.27 (d, 1H, *J* = 2.7 Hz, H-1), 4.69 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.65 – 4.59 (m, 3H, 2x*CH*H Bn, CH*H* Bn), 4.54 (d, 1H, *J* = 11.9 Hz, CH*H* Bn), 4.50 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.36 (dt, 1H, *J* = 6.9, 5.2 Hz, H-4), 4.20 (t, 1H, *J* = 4.9 Hz, H-3), 3.90 (dd, 1H, *J* = 4.6, 2.7 Hz, H-2), 3.78 (dd, 1H, *J* = 10.1, 5.1 Hz, H-5), 3.72 (dd, 1H, *J* = 10.1, 7.0 Hz, H-5), 3.58 (tt, 1H, *J* = 9.2, 4.1 Hz, CH Cy), 1.92 – 1.84 (m, 2H, CH_2 Cy), 1.69 (d, 2H, *J* = 5.8 Hz, CH_2 Cy), 1.55 – 1.47 (m, 1H, CH_2 Cy), 1.34 – 1.15 (m, 5H, CH_2 Cy); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.4, 138.4, 138.2 (C_q), 128.5, 128.4, 128.4, 128.0, 127.8, 127.8, 127.8, 127.7, 127.7 (CH_{arom}), 103.3 (C-1), 83.0 (C-2), 78.2, 78.0 (C-3, C-4), 75.7 (CH Cy), 73.5, 73.4, 72.6 (CH_2

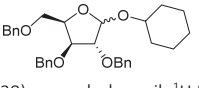
Bn), 69.8 (C-5), 33.8, 31.9, 25.8, 24.4, 24.2 (CH_2 Cy); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): $^2J_{C1,H2}$ = -2.2 Hz, $^2J_{C2,H1}$ = -1.5 Hz; Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.38 – 7.26 (m, 15H, CH_{arom}), 5.14 (d, 1H, *J* = 4.6 Hz, H-1), 4.85 (d, 1H, *J* = 12.4 Hz, C*H*H Bn), 4.74 (d, 1H, *J* = 12.2 Hz, C*H*H Bn), 4.58 (d, 1H, *J* = 12.4 Hz, CH*H* Bn), 4.57 (d, 1H, *J* = 12.2 Hz, CH*H* Bn), 4.56 (d, 1H, *J* = 11.9 Hz, C*H*H Bn), 4.51 (d, 1H, *J* = 11.9 Hz, CH*H* Bn), 4.19 (dt, 1H, *J* = 6.9, 5.3 Hz, H-4), 4.06 (t, 1H, *J* = 5.7 Hz, H-3), 3.82 – 3.71 (m, 3H, H-2, H-5, H-5), 3.62 (ddd, 1H, *J* = 13.6, 9.6, 3.8 Hz, CH Cy), 1.91 (d, 2H, *J* = 10.0 Hz, CH_2 Cy), 1.81 – 1.71 (m, 2H, CH_2 Cy), 1.57 – 1.48 (m, 1H, CH Cy), 1.40 – 1.18 (m, 5H, CH_2 Cy); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 139.0, 138.5, 138.3 (C_q), 128.5, 128.4, 128.2, 128.0, 127.9, 127.8, 127.7, 127.6, 127.4 (CH_{arom}), 98.6 (C-1), 79.0 (C-2), 78.9 (C-4), 76.1 (CH Cy), 75.8 (C-3), 73.6, 73.3, 72.3 (CH_2 Bn), 70.8 (C-5), 33.8, 32.0, 25.9, 24.6, 24.4 (CH_2 Cy); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): $^2J_{C1,H2}$ = +1.8 Hz, $^2J_{C2,H1}$ = +2.2 Hz; HRMS: $[M+Na]^+$ calcd for $C_{32}H_{38}O_5Na$ 525.26115, found 525.26001.



Ethyl 2,3,5-tri-*O*-benzyl-α/β-D-lyxofuranoside (96). Donor **81** and acceptor **5** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 (2h at -60°C) yielding product **96** (34 mg, 76 µmol, 76%, α:β = 78 : 22) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.36 – 7.25 (m, 19.5H), 5.13 (d, 1H, *J* = 2.6 Hz, H-1α), 4.97 (d, 0.3H, *J* = 4.6 Hz, H-1β), 4.83 (d, 0.3H, *J* = 12.5 Hz, C*H*H Bnβ), 4.70 – 4.48 (m, 7.5H, 3xCH_2 Bnα, 2xCH_2 Bnβ, CH*H* Bnβ), 4.36 (dt, 1H, *J* = 7.0, 5.2 Hz, H-4α), 4.20 (t, 1H, *J* = 5.0 Hz, H-3α), 4.18 (dt, 0.3H, *J* = 6.8, 5.5 Hz, H-4β), 4.05 (t, 0.3H, *J* = 5.6 Hz, H-3β), 3.91 (dd, 1H, *J* = 4.6, 2.6 Hz, H-2α), 3.82 – 3.68 (m, 4.2H, H-2β, H-5α,α, H-5β,β, C*H*H Etα,β), 3.60 (dq, 0.3H, *J* = 10.1, 7.0 Hz, CH*H* Etβ), 3.47 (dq, 1H, *J* = 9.7, 7.0 Hz, CH*H* Etα), 1.24 (t, 0.9H, *J* = 7.1 Hz, CH_3 Etβ), 1.18 (t, 3H, *J* = 7.1 Hz, CH_3 Etα); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.7, 138.4, 138.3, 138.1 (C_q), 128.5, 128.5, 128.4, 128.4, 128.3, 128.0, 128.0, 127.9, 127.9, 127.8, 127.8, 127.8, 127.7, 127.5 (CH_{arom}), 105.2 (C-1α), 99.9 (C-1β), 82.8 (C-2α), 79.1 (C-2β), 79.1 (C-4β), 78.2 (C4α), 78.1 (C-3α), 75.2 (C-3β), 73.5, 73.4, 72.6, 72.4 (CH_2 Bn), 70.5 (C-5β), 69.8 (C-5α), 63.9 (CH_2 Etα), 63.8 (CH_2 Etβ), 15.4 (CH_2 Etβ), 15.3 (CH_2 Etα); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): α-anomer: $^2J_{C1,H2}$ = -2.2 Hz, $^2J_{C2,H1}$ = -1.7 Hz; β-anomer: $^2J_{C1,H2}$ = +0.8 Hz, $^2J_{C2,H1}$ = +2.0 Hz; HRMS: $[M+Na]^+$ calcd for $C_{28}H_{32}O_5Na$ 471.21420, found 471.21299.



2,2,2-Trifluoroethyl 2,3,5-tri-*O*-benzyl-α/β-D-xylofuranoside (98). Donor **83** and acceptor **8** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 (2h at -60°C) yielding product **98** (42.7 mg, 85 µmol, 85%, α:β = 84 : 16) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.44 – 7.27 (m, 18H, CH_{arom}), 5.17 (s, 0.2H, H-1β), 5.11 (d, 1H, *J* = 4.2 Hz, H-1α), 4.72 – 4.44 (m, 8.4H, 3xCH_2 Bnα,β ,H-4α,β), 4.38 (dd, 1H, *J* = 7.2, 6.0 Hz, H-3α), 4.16 – 3.85 (m, 2.2H, H-2α,β, H-3β), 3.82 – 3.71 (m, 1.4H, H-5α,β,β), 3.65 (dd, 1H, *J* = 10.7, 6.8 Hz, H-5α); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.2, 138.1, 137.7, 137.5, 137.3 (C_q), 129.8, 128.6, 128.6, 128.5, 128.5, 128.4, 128.2, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7, (CH_{arom}), 124.1 (q, *J* = 278.8 Hz, CF_3), 106.9 (C-1β), 99.8 (C-1α), 86.5 (C-2β), 84.0 (C-2α), 81.8 (C-3β), 81.3 (C-3α), 81.0 (C-4β), 76.8 (C-4α), 73.6, 73.5, 72.8, 72.7, 72.3 (CH_2 Bn), 69.6 (C-5β), 69.3 (C-5α), 64.4 (q, *J* = 34.5 Hz, CH_2CF_3 β), 64.2 (q, *J* = 34.5 Hz CH_2CF_3 α); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): α-anomer: $^2J_{C1,H2}$ = +2.0 Hz, $^2J_{C2,H1}$ = +2.1 Hz; β-anomer: $^2J_{C1,H2}$ = -1.7 Hz, $^2J_{C2,H1}$ = -1.2 Hz; HRMS: $[M+Na]^+$ calcd for $C_{28}H_{29}F_3O_5Na$ 525.18593, found 525.18492.



Cyclohexyl 2,3,5-tri-*O*-benzyl-α/β-D-xylofuranoside (99). Donor **83** and acceptor **76** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 (2h at -60°C) yielding product **99** (39.7 mg, 79 µmol, 79%, α:β = 62 : 38) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.40 – 7.22 (m, 24H, CH_{arom}), 5.17 – 5.14 (m, 2H, H-1α,β), 4.69 – 4.35 (m, 11.2H, 3xCH_2 Bnα,β, H-4α,β), 4.33 (dd, 0.6H, *J* = 7.1, 5.9 Hz, H-3α), 4.08 (dd, 1H, *J* = 6.2, 3.5 Hz, H-3β), 4.03 – 3.95 (m, 1.6H, H-2α,β), 3.78 (dd, 1H, *J* = 10.3, 4.7 Hz, H-5β), 3.78 – 3.67 (m, 1.6H, H-5α,β), 3.68 – 3.54 (m, 2.2H, H-5α, CH Cyα,β), 1.95 – 1.86 (m, 3.2H, CH_2 Cyα,β), 1.80 – 1.66 (m, 3.2H, CH_2 Cyα,β), 1.52 (d, 1.6H, *J* = 5.9 Hz, CH_2 Cyα,β), 1.45 – 1.15 (m, 8H, CH_2 Cyα,β); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.5, 138.4, 138.1, 137.9, 137.9 (C_q), 128.5, 128.5, 128.4, 128.2, 128.0, 127.9, 127.9, 127.7, 127.7, 127.6, 127.6, 127.6 (CH_{arom}), 105.0 (C-1β), 97.8 (C-1α), 87.6 (C-2β), 84.2 (C-2α), 82.2 (C-3β), 82.0 (C-3α), 79.4 (C-4β), 75.9, 75.8, 75.7 (C-4α, CH_{Cy} α,β), 73.6, 73.5, 72.6, 72.3, 72.0 (CH_2 Bn), 70.1 (C-5β), 69.6 (C-5α), 33.9, 33.6, 32.1, 31.8, 25.8, 25.8, 24.6, 24.5, 24.3, 24.2 (CH_2 Cyα,β); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): α-anomer: $^2J_{C1,H2}$ = +1.4 Hz, $^2J_{C2,H1}$ = +2.0 Hz; β-anomer: $^2J_{C1,H2}$ = -2.5 Hz, $^2J_{C2,H1}$ = -1.5 Hz; HRMS: $[M+Na]^+$ calcd for $C_{32}H_{38}O_5Na$ 525.26115, found 525.26005.

Footnotes and references

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Samenvatting in het Nederlands

Reactiviteit en selectiviteit in glycosyleringsreacties

Koolhydraten, sachariden en suikers zijn benamingen voor in de natuur voorkomende moleculen die wat structuur betreft enorm divers zijn. Bijvoorbeeld niet alleen de polymeren zetmeel en glycogeen zijn koolhydraten, maar ook kleinere structuren zoals de oligosachariden die kenmerkend zijn voor de menselijke bloedgroepen. Sachariden spelen een belangrijke rol bij een groot aantal essentiële biologische processen in alle vormen van leven en zijn daardoor van belang voor bestaande en nog te ontwikkelen medicijnen. Koolhydraten die van belang zijn voor het ophelderen en beïnvloeden van biologische processen kunnen echter vaak in onvoldoende mate in zuivere toestand uit de natuur worden geïsoleerd. De chemische synthese van deze specifieke koolhydraatverbindingen is daarom van groot belang. Koolhydraten bestaan uit lineaire of vertakte ketens van verschillende monosacchariden zoals glucose en mannose. Een van de grootste uitdagingen bij het synthetiseren van koolhydraten is het aanbrengen van de juiste binding tussen de monosachariden onderling of tussen een monosaccharide en een groeiende koolhydraatketen. Deze glycosidische binding dient op één specifieke wijze te worden aangebracht. Deze selectiviteit betreft niet alleen de positie van de naburige suiker waaraan de suiker in kwestie vastgemaakt wordt (de zogenoemde *regiochemie*) maar ook de richting van de nieuw te vormen glycosidische binding (de zogenoemde *stereochemie*), die 1,2-*trans* of 1,2-*cis* kan zijn. De positie van de glycosidische binding en de introductie van 1,2-*trans*-bindingen kunnen veelal met beschermgroepen worden gestuurd. Voor het verkrijgen van 1,2-*cis*-glycosidische bindingen is geen degelijke algemene oplossing en de invoering verloopt vaak met vallen en opstaan. Een dergelijke procedure gaat gepaard met tijdrovende optimalisaties. Meer inzicht in hoe 1,2-*cis*-glycosidische bindingen tot stand komen is dus wenselijk. Dit proefschrift beschrijft systematische studies naar de invloed van de reactiviteit van de reactiepartners op de stereoselectiviteit van een chemische glycosylering. Deze reactiepartners zijn de elektrofiele donor en de nucleofiele acceptor, die met elkaar reageren onder invloed van een activator. Met behulp van deze studies is er meer inzicht verkregen in het mechanisme van de glycosyleringsreactie en hoe deze te beïnvloeden is om 1,2-*cis*-selectieve koppelingen te geven.

De bestaande kennis over de reactiviteit van donoren en acceptoren alsmede de invloed daarvan op de selectiviteit van glycosyleringen wordt in **Hoofdstukken 1** en **2**

beschreven. Het eerste hoofdstuk behandelt de bestaande inzichten in het mechanisme van de glycosyleringsreactie en de invloed van de reactiviteit van de donor, het elektrofiel, in deze reactie. In het tweede hoofdstuk ligt de nadruk op het nucleofiel, de acceptor. De reactiviteit van zowel de donor als de acceptor kan worden beïnvloed door de wijze waarop de niet reagerende functies in de bouwstenen zijn beschermd met beschermgroepen. In het algemeen verminderen sterk elektronenzuigende acylbeschermgroepen de reactiviteit meer dan relatief minder sterk elektronenzuigende alkylbeschermgroepen. Waar de reactiviteit van glycosyldonoren goed onderzocht is en het algemeen geaccepteerd is dat verschillen in donorreactiviteit een verschuiving van een S_N2-type naar een S_N1-type mechanisme tot gevolg kan hebben, is de reactiviteit van glycosylacceptoren nauwelijks systematisch onderzocht en is de invloed hiervan op het reactiemechanisme niet in kaart gebracht. Hoofdstuk 2 geeft een overzicht met voorbeelden uit het recente en minder recente verleden die aantonen dat kleine veranderingen in de reactiviteit van de acceptor kunnen leiden tot grote verschuivingen in opbrengst, selectiviteit en reactiesnelheden van glycosyleringsreacties.

Hoofdstuk 3 beschrijft het eerste systematische onderzoek naar hoe de reactiviteit van een acceptor het mechanisme van glycosyleringsreacties beïnvloedt. Daartoe is een set modelacceptoren van verschillende nucleofiliciteit gebruikt. De modelacceptoren zijn gebaseerd op ethanol en bevatten een verschillend aantal fluoratomen (0 tot 3). Hoe meer fluoratomen het molecuul bevat, hoe minder nucleofiel het is. Dit komt door de elektronenzuigende werking van de fluoratomen. Het reactieve ethanol bleek hoge β-selectiviteit te geven in glycosyleringen met benzylideen beschermde glucose- en mannosedonoren en met een mannuronzuurdonor. Het veel minder reactieve trifluorethanol gaf juist hoge α-selectiviteit met de benzylideenglucosedonor en liet slechts een kleine afname in β-selectiviteit zien voor de benzylideenmannose- en mannuronzuurdonoren. Mono- en difluorethanol gaven mengsels van beide anomere producten in glycosyleringen met de glucosedonor, waarbij meer α-product voor het minder reactieve difluorethanol werd gevormd. Deze resultaten tonen aan dat de koppelingen van de benzylideenglucosedonor gevoelig zijn voor veranderingen in acceptorreactiviteit, terwijl de koppelingen van benzylideenmannose- en mannuronzuurdonoren dat niet zijn. Vervolgens werden relevante suikeracceptoren getest. Suikeracceptoren met primaire of equatoriale secundaire hydroxylgroepen waren voornamelijk β-selectief; axiale secundaire hydroxylgroepen werden juist α-selectief voor de glucosedonor. Wederom bleven de mannose- en mannuronzuurdonoren β-

selectief. Hiermee kan het verband worden gelegd tussen de reactiviteit van de acceptor en de verschuiving van het reactiemechanisme: substituties met sterke nucleofielen hebben meer een S_N2-karakter en substituties met zwakke nucleofielen meer een S_N1-karakter. Voor glucose geven deze twee mechanismen twee verschillende producten. Een S_N2-reactie met het anomere triflaat als vetrekkende groep geeft het β-product, terwijl een S_N1-reactie via het oxocarbeniumion in de $^4H_3/^4E$-conformatie het α-product geeft. De reden dat benzylideenmannose- en mannuronzuurdonoren juist erg β-selectief bleven kan worden verklaard met de β-selectieve conformeren van de oxocarbeniumionen in de S_N1-reacties. Zowel de $B_{2,5}$-conformatie die de benzylideenmannosedonor kan aannemen als de $^3H_4$-conformatie die mannuronzuurdonoren prefereren, zijn β-selectief.

In **Hoofdstuk 4** wordt de invloed van een azide-functionaliteit als aminebeschermgroep in een glucosaminedonor behandeld door de glycosyleringen van benzylideenglucosazide te vergelijken met benzylideenglucose uit hoofdstuk 3. De 2-azido-substituent is een elektronenzuigende groep en destabiliseert de vorming van lading op het anomere centrum meer dan een 2-*O*-benzylgroep, waardoor het S_N1-S_N2-evenwicht van de glycosyleringen meer aan de S_N2-kant komt te liggen. Dit heeft als gevolg dat koppelingen van glucosazidedonoren met hogere β-selectiviteit verlopen. Omdat het α-product, met de 1,2-*cis*-configuratie, juist vaak gewenst is, werden ook de andere beschermgroepen op deze donor geëvalueerd. Het vervangen van de *O*-benzylgroep op de C-3-positie door een meer zuigende *O*-benzoylgroep had een gering effect en de donor werd, zoals verwacht, nog β-selectiever. De benzylideenring vervangen door een silylideenring maakte de donor juist reactiever en minder β-selectief. In combinatie met een zwak nucleofiel kan daarmee hoge α-selectiviteit worden verkregen.

Waar de silylideen- en benzylideenbeschermgroepen een ring spannen tussen de C-4- en C-6-posities in monosacchariden, wordt in **Hoofdstuk 5** de invloed van een cyclische bisacetaalgroep, die de alcoholen op C-3 en C-4 beschermd, besproken. Gebruik van de door butaandion-di-acetaal (BDA) beschermde glucosazidedonor geeft β-selectieve koppelingen. De BDA-ring vermindert de conformationele vrijheid van de donor en hindert als zodanig de vorming van het oxocarbeniumion, wat vervolgens leidt tot veel S_N2-karakter en hoge β-selectiviteit in de koppelingen.

De rol van de nucleofiliciteit van de acceptor wordt in detail behandeld in **Hoofdstuk 6**. Een uitgebreide reeks van suikeracceptoren met alle mogelijke beschermgroeppatronen van benzyl- en benzoylgroepen op een glucoseacceptor werd

geëvalueerd. De door benzylideen beschermde glucose- en glucosazidedonoren uit hoofdstukken 3 en 4 werden als modeldonoren gekozen om de reactiviteit-selectiviteitsrelatie van de acceptoren in kaart te brengen. De koppelingen van beide donoren zijn zeer gevoelig voor veranderingen van acceptorreactiviteit en zijn complementair aan elkaar, waarbij de glucosazidedonor steevast meer β-product geeft. Uit deze studie kwam naar voren dat verandering van reactiviteit van acceptoren, door variatie van beschermgroepen op de C-3- en C-4-posities, een grote invloed kan hebben op de stereoselectiviteit in glycosyleringen. Een enkele strategisch geplaatste benzoylgroep op de acceptor was voldoende om volledige α-selectiviteit te geven met de glucosedonor en hoge α-selectiviteit met de overeenkomstige glucosazidedonor. Door introductie van een tweede benzoylgroep in de acceptor kon ook de koppeling van deze laatste donor met volledige α-selectiviteit worden bewerkstelligd. Gesubstitueerde benzoylbeschermgroepen op de C-6-positie van de acceptor bleken echter minder effect te hebben en alleen twee nitrogroepen op beide ortho-posities gaf een afname in reactiviteit en een toename in α-selectiviteit.

Hoofdstuk 7 en 8 hebben vijfringsuikers, ook wel furanoses genoemd, als onderwerp. Het eerste hoofdstuk beschrijft de synthese van een set van furanoses met verschillende substituenten op de C-2- of C-5-positie. Op C-2 werd een fluor of een azide geïnstalleerd en C-5 werd geoxideerd tot een uronzuur (methylester). Oxidatie van de C-5-alcoholen in alle furanoses verliep zonder problemen maar het installeren van de substituenten op de C-2-positie bleek niet triviaal. De gekozen strategie omvatte in eerste instantie de inversie van de C-2-positie door gebruik te maken van een triflaat als *O*-vertrekkende groep en fluoride- of azide-anionen als nucleofielen. Voor de vier verschillende configuraties van de furanoses (arabinose, ribose, lyxose en xylose) verliep de inversie met verschillende uitkomsten. Het inverteren van ribose gaf geen problemen en de 2-fluoro- en 2-azidoarabinoses waren gemakkelijk te verkrijgen. Zowel het arabinosetriflaat inverteren om zo de riboseconfiguratie te verkrijgen, als de transformatie van een xylose- naar een lyxose-geconfigureerde bouwsteen, gaf bijproducten door participatie van de beschermgroepen. Voor arabinose was de β-anomeer probleemloos om te zetten naar 2-fluoro- en 2-azidoribose, maar de α-anomeer gaf een ongewenste en verrassende migratie van de anomere *O*-methylgroep naar de C-2-positie. In het geval van xylose gaf alleen de α-anomeer het gewenste lyxoseproduct en beide anomeren gaven significante hoeveelheden bijproducten als gevolg van participatie van de C-5–*O*-benzylgroep. Het inverteren van lyxose naar xylose bleek

onmogelijk en alleen furan werd gevormd. Om de gewenste 2-fluoro- en 2-azidoxyloses te kunnen maken werd gebruik gemaakt van een andere strategie: met behulp van een glycaal werden de azido- en fluorogroepen geïnstalleerd. Tenslotte werden er van de vier furanoseconfiguraties imidaatdonoren gesynthetiseerd, met in elk van de configuraties een variatie in de drie verschillende C-2- of C-5-modificaties. De glycosylerende eigenschappen van deze twaalf donoren met modelacceptoren wordt in Hoofdstuk 8 besproken.

Hoofdstuk 8 beschrijft een onderzoek naar de selectiviteit van furanosedonoren als de reacties worden uitgevoerd onder S_N1-condities, waarbij verondersteld wordt dat oxocarbeniumion-intermediairen verantwoordelijk zijn voor de selectiviteit. Allereerst werden de imidaatdonoren uit Hoofdstuk 7 geglycosyleerd met de modelacceptoren allyltrimethylsilaan of triethylsilaan-*d*. De koppelingen van de arabinose-, ribose- en lyxosedonoren verliepen met uitstekende 1,2-*cis*-selectiviteit, terwijl xylosedonoren anomere mengsels gaven. Vervolgens werd met behulp van kwantummechanische berekeningen de energie van alle mogelijke conformaties van de oxocarbeniumionen berekend en bepaald welke conformeren het meest stabiel waren. Daaruit kwam naar voren dat oxocarbeniumionen die een enkele conformatie sterk prefereerden ook zeer selectief waren in de experimentele glycosyleringen. In het geval van het arabinosyl-oxocarbeniumion werden meerdere conformaties laag in energie gevonden. Deze conformaties waren nagenoeg plat. Echter, dit had geen invloed op de experimentele glycosyleringen, welke volledig 1,2-*cis*-selectief bleken. Voor de verschillende xylosyl-oxocarbeniumionen werden ook meerdere conformaties gevonden die vergelijkbaar laag in energie waren. Naast de gebruikelijke conformaties uit het bestaande S_N1-model voor furanoseglycosyleringen, waarbij de E_3- en ^3E-conformaties de hoofdrol spelen, werd nu ook de ^4E-conformatie aangetroffen. Doordat er meerdere gunstige conformaties waren, gaven de glycosyleringsreacties anomere mengsels. Uit de studie kan geconcludeerd worden dat de gebruikte kwantummechanische methode in staat is verschuivingen in de populatieverdeling van de verschillende conformaties in kaart te brengen. Deze verschuivingen worden veroorzaakt door de stereo-elektronische effecten van functionele groepen zoals een azide, fluoride, of uronzuur. Met de berekende energieverdeling van de conformaties van een oxocarbeniumion kan vrij nauwkeurig worden voorspeld of een glycosyleringsreactie onder S_N1-condities selectief verloopt of dat erosie van selectiviteit verwacht kan worden.

List of publications

Stereoselective Glycosylations – Additions to Oxocarbenium Ions

Bas Hagen, Stefan van der Vorm, Thomas Hansen, Gijsbert A. van der Marel and Jeroen D.C. Codée

in: "Selective Glycosylations: Synthetic Methods and Catalysts", **2017**, editor: Clay S. Bennett, pp 1-28. ISBN: 978-3-527-33987-7

The influence of acceptor nucleophilicity on the glycosylation reaction mechanism

Stefan van der Vorm, Thomas Hansen, Herman S. Overkleeft, Gijsbert A. van der Marel and Jeroen D. C. Codée

Chemical Science, **2017**, *8* (3), pp. 1867-1875

Stereoselectivity of conformationally restricted glucosazide donors

Stefan van der Vorm, Herman S. Overkleeft, Gijsbert A. van der Marel and Jeroen D. C. Codée

The Journal of Organic Chemistry, **2017**, *82* (9), pp. 4793-4811

Mapping the relationship between glycosyl acceptor reactivity and glycosylation stereoselectivity

Stefan van der Vorm, Jacob M. A. van Hengst, Marloes Bakker, Herman S. Overkleeft, Gijsbert A. van der Marel and Jeroen D. C. Codée

Angewandte Chemie International Edition, **2018**, *57* (27), pp. 8240-8244
Angewandte Chemie, **2018**, *130* (27), pp. 8372-8376

The synthesis of O-1 to O-6 substituted positional isomers of D-glucose-thioether ligands and their ruthenium polypyridyl conjugates

Lucien N. Lameijer, Julien Le Roy, Stefan van der Vorm, Sylvestre Bonnet

Manuscript in press, The Journal of Organic Chemistry

Conformational Energy Landscapes as a tool to study the glycosylation stereoselectivity of 2-azidofuranoses, 2-fluorofuranoses, and methyl furanosyl uronates

Stefan van der Vorm, Thomas Hansen, Erwin R. van Rijssel, Rolf Dekkers, Jerre M. Madern, Herman S. Overkleeft, Dmitri V. Filippov, Gijsbert A. van der Marel and Jeroen D. C. Codée

Manuscript submitted

Synthesis, reactivity and stereoselectivity of 4-thio furanosides

Jerre M. Madern, Thomas Hansen, Erwin R. van Rijssel, Stefan van der Vorm, Herman S. Overkleeft, Gijsbert A. van der Marel, Dmitri V. Filippov and Jeroen D. C. Codée

Manuscript submitted

Defining the S_N1-side of glycosylation reactions: stereoselectivity of glycopyranosyl cations

Thomas Hansen, Ludivine Lebedel, Wouter A. Remmerswaal, Stefan van der Vorm, Dennis P.A. Wander, Herman S. Overkleeft, Dmitri V. Filippov, Yves Bleriot, Gijsbert A. van der Marel, Sebastien Thibaudeau, Jeroen D. C. Codée

Manuscript in preparation

Acceptor reactivity in glycosylations

Stefan van der Vorm, Herman S. Overkleeft, Gijsbert A. van der Marel and Jeroen D. C. Codée

Manuscript in preparation

The impact of 3,4-tethering on the stereoselectivity of a glucosazide donor

Stefan van der Vorm, Herman S. Overkleeft, Gijsbert A. van der Marel and Jeroen D. C. Codée

Manuscript in preparation

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Curriculum vitae - Nederlands

Stefan van der Vorm werd geboren op 28 juli 1988 te Rotterdam. Van 2000 tot 2007 volgde hij middelbaar onderwijs aan het Maerlant College Brielle, waar hij in 2005 het HAVO diploma (met het profiel Natuur & Gezondheid) en vervolgens in 2007 het VWO-atheneum diploma (profielen Natuur & Techniek en Natuur & Gezondheid) behaalde. In 2007 werd begonnen aan de bacheloropleiding Molecular Science & Technology aan de Universiteit Leiden en de Technische Universiteit Delft. Als afstudeerstage werd van januari tot en met augustus 2010 onderzoek verricht onder leiding van prof.dr.ir. J.G.E.M. Fraaije, waarbij eiwitten betrokken bij membraanfusie werden gemodelleerd met behulp van dissipatieve deeltjes dynamica. Na een jaar de opleiding Talen en Culturen van Japan aan de Universiteit Leiden te hebben gevolgd, werd in 2011 op dezelfde locatie begonnen aan de masteropleiding Chemistry, met een onderzoeksspecialisatie in Ontwerp & Synthese. In het kader van deze opleiding werd een onderzoeksstage gevolgd bij de vakgroep Bio-organische Synthese, onder leiding van prof.dr. H.S. Overkleeft en prof.dr. G.A. van der Marel. Dit project getiteld "Towards a library of sulfated mannuronic acid oligomers, to study structure-activity relationships" werd begeleid door dr. M.T.C. Walvoort en dr. A.G. Volbeda. In 2013 werd een tweede onderzoeksstage gevolgd aan de Universiteit van Kioto (京都大学), in de groep van prof.dr. J.-I. Yoshida (吉田 潤一), getiteld "Configurational stability of chiral oxyranyllithium intermediates from styrene oxide derivatives" waarbij gebruik werd gemaakt van microreactoren. Na het afronden van de masteropleiding werd het diploma met lof behaald. In december 2013 werd gestart met het in dit proefschrift beschreven promotieonderzoek bij de vakgroep Bio-organische Synthese, onder leiding van prof.dr. G.A. van der Marel, prof.dr. H.S. Overkleeft en dr. J.D.C. Codée.

Delen van het onderzoek hier beschreven zijn gepresenteerd op de jaarlijkse NWO-CHAINS conferentie te Veldhoven, middels posterpresentaties (2014, 2015, 2016, 2017) en mondelinge presentaties (2017). Een posterpresentatie is gegeven op het 19de European Carbohydrate Symposium 2017 in Barcelona, Spanje, waar het werd bekroond met de prijs voor beste poster.

Sinds april 2018 is hij aangesteld als vakdocent organische chemie aan de Universiteit Leiden.

Curriculum vitae - English

Stefan van der Vorm was born in Rotterdam, The Netherlands, on July 28th 1988. From 2000 until 2007 he attended the Maerlant College in Brielle, at which secondary education diplomas, with majors in science, were obtained in 2005 (HAVO) and 2007 (VWO-atheneum). In 2007 he commenced with the bachelor education Molecular Science & Technology at Leiden University and Delft University of Technology. As part of the bachelor program, a research internship in the field of molecular modelling was followed, concerning the dissipative particle dynamics study of protein-mediated membrane fusion, under guidance of prof.dr. J.G.E.M. Fraaije. The Bachelor of Science degree was subsequently obtained in 2010, after which he studied Languages and Cultures of Japan at Leiden University for one year. In 2011 the research master program in Chemistry was started with a specialization in Design and Synthesis. During this 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 Leiden University was pursued. The title of the project was "Towards a library of sulfated mannuronic acid oligomers, to study structure-activity relationships" and was under daily supervision of dr. M.T.C. Walvoort and dr. A.G. Volbeda. A second research internship was conducted in 2013 at Kyoto University (京都大学), in the group of prof.dr. J.-I. Yoshida (吉田 潤一), and was titled "Configurational stability of chiral oxyranyllithium intermediates from styrene oxide derivatives", making extensive use of microreactors. After conclusion of the master education, the Master of Science degree was received with honors. In December of 2013, the research described in this Ph.D. thesis was started under supervision of prof.dr. H.S. Overkleeft, prof.dr. G.A. van der Marel, and dr. J.D.C. Codée, in the Bio-organic Synthesis group of Leiden University.

Parts of the research described herein was presented at the annual Dutch chemistry conference "CHAINS", Veldhoven, by poster presentations (2014,2015, 2016, 2017) and an oral presentation (2017). A poster was presented at the 19th European Carbohydrate Symposium 2017, in Barcelona, Spain, and was rewarded the price for best poster.

Since April 2018 he is appointed as lecturer organic chemistry at Leiden University.

Appendix: General experimental procedures

All chemicals were of commercial grade and used as received unless stated otherwise. Dichloromethane (DCM) was stored over activated 4 Å molecular sieves for at least 24 h before use. Trifluoromethanesulfonic anhydride (Tf_2O) was distilled over P_2O_5 and stored at -20°C under a nitrogen atmosphere. Triethylamine (Et_3N) was distilled over CaH_2 and stored over KOH pellets. Overnight temperature control was achieved by a FT902 Immersion Cooler (Julabo). 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 Sephadex (LH-20, GE Healthcare Life Sciences) by isocratic elution with DCM/MeOH (1/1, v/v). Thin-layer chromatography (TLC) analysis was conducted on TLC silica gel 60 plates (Kieselgel 60 F_{254}, Merck) with UV detection by (254 nm) and by spraying with 20% sulfuric acid in ethanol 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% aq. sulfuric acid followed by charring at ±250 °C. TLC-MS analysis was performed on a Camag TLC-MS Interface combined 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). LC-MS analysis was conducted on a Finnigan LCQ Advantage Max mass spectrometer with a Finnigan Surveyor HPLC system eluted with a gradient solvent (8 min, 1 mL/min, 10%-90% CH_3CN in H_2O + 1% TFA, total sample run 12 min). High-resolution mass spectrometry (HRMS) was performed on a Thermo Finnigan LTQ Orbitrap mass spectrometer equipped with an electrospray ion source in positive-ion 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 of 150-4000) and dioctylphtalate (m/z=391.28428) as lock mass, or on a Waters Synapt G2-Si (TOF) equipped with an electrospray ion source in positive mode (source voltage 3.5 kV) and LeuEnk (m/z = 556.2771). as internal lock mass. ^{1}H, ^{2}H and ^{13}C NMR spectra were recorded on a Bruker AV-400 NMR, a Bruker DMX-400 NMR instrument (400, 61 and 101 MHz respectively), a Bruker AV-500 NMR instrument (500, 77, 126 MHz respectively), and ^{19}F spectra were recorded on a Bruker AV-500 NMR (470 MHz). 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 assignments were made using COSY and HSQC. If necessary additional NOESY, TOCSY, HMBC, (HMBC-)GATED, and HSQC-HECADE experiments were used to further elucidate the structure. The anomeric product ratios were based on careful analysis of the crude reaction mixture and the purified reaction product by integration of representative ^{1}H NMR signals. IR spectra were recorded on a Shimadzu FTIR-8300 IR spectrometer and are reported in cm^{-1}. Specific rotations were measured on a Propol automatic polarimeter or an Anton-Paar MCP-100 modular circular polarimeter at 589 nm unless otherwise stated.