

Structure-reactivity relationships in glycosylation chemistry Hengst, J.M.A. van

Citation

Hengst, J. M. A. van. (2023, December 7). *Structure-reactivity relationships in glycosylation chemistry*. Retrieved from https://hdl.handle.net/1887/3665922

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Structure-reactivity relationships in glycosylation chemistry

Proefschrift

ter verkrijging van

de graad van doctor aan de Universiteit Leiden,

op gezag van rector magnificus prof. dr. ir. H. Bijl

volgens besluit van het college voor promoties

te verdedigen op donderdag 7 december 2023

klokke 11:15 uur

door

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Cover design by Maaike de Wit Printed by Proefschriftspecialist

Printed on recycled paper

Dedicated to Desiree van Gastel

11-04-1958 / 03-05-2023

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Abbreviations

A.	Acinetobacter	
Ac	acetyl	
ACN	acetonitrile	
AIBN	2,2'-azobis(2-methyl-	
	propionitrile)	
APT	attached proton test	
aq.	aqueous	
Arom	aromatic	
В	boat	
B3LYP	Becke, 3-parameter, Lee-Yang-	
	Parr	
BAIB	(diacetoxyiodo)benzene	
Bn	benzyl	
bs	broad singlet	
Bu	butyl	
Bz	benzoyl	
С	chair	
cal	calorie	
calcd	calculated	
cat.	Catalytic	
CCSDT	coupled cluster single-double-	
	triple	
CEL	conformational energy landscape	
CIP	contact ion pair	
COSY	correlation spectroscopy	
Cq	quaternary carbon atom	
CSA	camphor-10-sulfonic acid	
δ	chemical shift	
d	doublet	
DBTO	dibutyltin oxide	
DCE	1,2-dichloroethane	
DCM	dichloromethane	
dd	double doublet	
ddd	doublet of double doublets	
dddd	double doublet of double	
	doublets	
DDQ	2,3-Dichloro-5,6-dicyano-1,4-	
	benzoquinone	

1.1.	1 11 4 6 1 11 4 1 4		
ddt	doublet of double triplets		
DFE	difluoroethanol		
DFT	density function theory		
DIAD	diisopropyl azocarboxylate		
DIPEA	diisopropylethylamine		
DLNPC) domain-based local pair natural		
	orbital		
DMAP	4-dimethylaminopyridine		
DMBA	1,3-Dimethylbarbituric acid		
DMF	N,N-dimethylformamide		
DMP	Dess-Martin periodinane		
DMSO	dimethylsulfoxide		
dq	double quartet		
dt	double triplet		
dtd	doublet of triple doublets		
DTBS	di-tert-butylsilylidene		
Е	energy		
Ε	envelope		
EDC(I)	1-Ethyl-3-(3-		
	dimethylaminopropyl)		
	carbodiimide		
eq.	molar equivalent		
Et	ethyl		
E-X	electrophilic activator system		
gg	gauche-gauche		
gt	gauche-trans		
GATED	proton decoupling applied only		
	during relaxation		
GlcNAc	c3NAcA		
	2,3-di-N-acetyl-D-		
	glucuronic acid		
h	hour(s)		
H	half-chair		
HFIP	hexafluoro-iso-propanol		
HMBC	heteronuclear multiple-bond		
	correlation spectroscopy		
HMDS	hexamethyldisilazane		
HRMS	high-resolution mass		
	spectroscopy		

HSQC	heteronuclear single quantum				
	coherence				
IR	infrared				
IRIS	infrared ion spectroscopy				
J	coupling constant				
LAH	lithium aluminium hydride				
Lev	Levulinoyl				
LG leaving group					
М	molar				
m	multiplet				
m.s.	molecular sieves				
m/z	mass over charge ratio				
min	minute(s)				
Me	methyl				
MFE	monofluoroethanol				
M.S. molecular sieves					
Ms	methanesulfonyl				
Nap	2-methylnaphthyl				
NIS	N-iodosuccinimide				
NMR	nuclear magnetic resonance				
NOESY	nuclear Overhauser effect				
	spectroscopy				
Nu	nucleophile				
р	para				
PG	protection group				
РСМ	polarizable continuum model				
Ph	phenyl				
PMB	4-methoxybenzyl				
ppm	parts per million				
PTFAI	2,2,2-Trifluoro-N-				
	phenylacetimidoyl				
PTSA	para-toluenesulfonic acid				
q	quartet				
qd quartet of doublets					
QuiNAc	4NAc				
	2,4-di-N-acetyl-D-				
	quinovose				
R^2 or r^2	coefficient of determination				
Rf	retention factor				
RRV	relative reactivity value				

	rt room temperature				
rxn		reaction			
	s	singlet			
	S	skew boat			
	sat.	saturated			
	$S_N 1$	uni-molecular nucleophilic			
		substitution			
	$S_N 2$	bi-molecular nucleophilic			
		substitution			
	SSIP	solvent-separated ion pair			
	SAR	structure-activity-relationships			
	t	triplet			
	t	tert			
	Т	twist			
	tg	trans-gauge			
	TBA	tetrabutylammonium			
	TBS	tert-butyldimethylsilyl			
	TBDMS	tert-butyldimethylsilyl			
	TBDPS	tert-butyldiphenylsilyl			
	TCA	trichloroacetyl			
	TES	triethylsilyl			
	ТЕМРО	2,2,6,6-tetramethylpiperidine 1-			
		oxyl			
	TFA	trifluoroacetic acid			
	TFAA	trifluoroacetic anhydride			
	TFE	trifluoroethanol			
	Tf	trifluoromethanesulfonyl			
	THF	tetrahydrofuran			
	TIPS	tri-isopropylsilyl			
	TLC	thin layer chromatography			
	TMS	trimethylsilyl			
	TOCSY	total correlation spectroscopy			
	Ts	4-methylbenzene-1-sulfonyl			
	TS	transition state			
	td	triple doublet			
	tt	triple triplet			
	TTBP	2,4,6-tri-tert-butylpyrimidine			
	UV	ultraviolet			
	VT	variable temperature			

Chapter 1: General introduction

Introduction

Carbohydrates are a class of biopolymers with large variety in terms of both structure and function in both prokaryotes and eukaryotes. The main difference that separates carbohydrates from the other biopolymers (nucleotides and proteins) is that when two carbohydrate building blocks are linked together, a new stereocenter is introduced. The stereocenter is important for the properties of the carbohydrate, for example starch is a polymer of α 1 \rightarrow 4 linked glucose and cellulose is a polymer of β 1 \rightarrow 4 linked glucose (*Figure 1*).



Figure 1: Structure differences between starch and cellulose

There are many (bio)medical applications of carbohydrates.¹⁻³ However, carbohydrates can be difficult to isolate from biological sources in sufficient quantify and purity. Therefore, chemical synthesis is an attractive alternative, because it allows for full control over the structure of the obtained product regarding properties including substitution pattern and chain length. The two main challenges in synthetic carbohydrate chemistry are regio- and/or chemoselective protection of hydroxyl- and other functional groups⁴⁻⁷ and the stereoselective formation of a glycosidic bond.⁸⁻¹² This thesis will focus mainly on the latter.

Carbohydrate synthesis

A typical synthesis of a glycosidic bond is depicted in *Scheme 1*. There are many variations in glycosylation protocols, but the vast majority of them follows this same scheme, where a donor with a latent leaving group reacts with an electrophilic activator. Examples of leaving groups include thio- or selenophenol, which are activated by a stoichiometric amount of an electrophilic promotor such as NIS/TMSOTf or a sulfoxonium ion, generated from, for example, Ph₂SO/Tf₂O¹³⁻¹⁶. A different class of leaving groups are the glycosyl imidates (most importantly the trichloroacetimidate (TCA) or *N*-phenyl trifluoroacetimidate (PTFAI) donors), which are activated by a catalytic amount of Lewis- or Brønsted acid such as BF₃.OEt₂, TMSOTf or TfOH.^{17, 18} Another type of donor, introduced by Yu and coworkers, are the alkynyl benzoates, which can react under mild conditions catalysed by Au(I).¹⁹ Upon activation of the

donor, a mixture of electrophilic species is generated, varying from oxocarbenium ions, which react via a S_N1 like mechanism, to covalent species which react via a S_N2 mechanism with a nucleophile (acceptor). These are attacked by the incoming nucleophile leading to either the α -product, the β -product or a mixture of the two.¹⁸



Scheme 1: General overview of a glycosylation reaction and the contents of this thesis

Stereoselective glycosylation methods

Many methods have been developed for the stereoselective formation of a glycosidic bond (*Figure 2*). 1,2-Trans glycosidic bonds are usually relatively easy to construct using neighbouring group participation (*Figure 2A*), where an acyl type protecting group, usually an ester, amide or carbamate, is placed on O-2 or N-2. Upon activation of the donor, the carbonyl group reacts to form a dioxolenium ion, which reacts with an acceptor to form a 1,2-trans glycosidic bond.^{20, 21} Participation of protecting groups on other positions has also been observed and used for the control of stereochemical outcome (*vide infra*). More recently, it has also been reported that alkoxymethyl protecting groups can provide 1,2-trans glycosidic bonds via a similar mechanism.²² For the formation of 1,2-cis glycosidic bond no such universally applicable technique exists, making the synthesis of these linkages more challenging.^{11, 23} Nevertheless, multiple methods for the construction of these glycosidic bonds have been developed and this chapter will discuss a few examples.

Historically, the β -mannosidic bond was one of the most difficult ones to synthesize.²⁴ One method to synthesize this kind of glycosidic bond was developed by the laboratory of Crich, in which a benzylidene is used as a protecting group for the C-4-OH and C-6-OH (*Figure 2B*).^{25, 26} Evidence based on variable temperature NMR,²⁷⁻²⁹ and a combination of kinetic isotope effect³⁰ and cation clock experiments³¹ show that the β -mannosidic bond is formed through a S_N2 reaction with the α -triflate, which is formed when the donor is activated with a triflate based promotor.³² However, there is also evidence that the stereoselectivity can be explained via an S_N1 reaction via an oxocarbenium ion adopting a B_{2,5}-conformation.³³

Another method for generating a 1,2-cis glycosidic bond based on the use of a cyclic protecting group on the C-4-OH and C-6-OH, is the use of a di-tert-butylsilylene (DTBS) group on galactose and galactosamine (*Figure 2C*). Introduced by Kiso and coworkers in 2003, glycosylation with this type of donor stereoselectively yields the α -galactoside, even when a participating group is present on C-2.³⁴ In the mechanism that explains this selectivity, an oxocarbenium ion is generated where the bulky DTBS group shields the top-side from attack by a nucleophile, so that only an attack from the bottom of the oxocarbenium ion is possible, which yields the α -product.³⁵

Participation of the protecting group on C-2 has also been used to introduce a 1,2-cis glycosidic bond via a chiral auxiliary (*Figure 2D*). In this system, a nucleophilic group (for example CO_2Et^{36} or SPh³⁷) on the protecting group on C-2 reacts with the oxocarbenium ion upon activation of the donor. The *S*-configuration of the protecting group is necessary for the stabilisation of the *trans*-decalin species to form the desired α -product. When the corresponding *R*-configured protecting group was used, the *cis*-decalin intermediate was generated, delivering the β -product.^{36, 37} Of note, the use of a non-chiral, nucleophilic protecting group on C-2 for the formation of α -glucosidic bonds was also described.³⁸⁻⁴⁰

The final two methods discussed in this chapter rely on "directing" the acceptor in the right direction, either through hydrogen bond formation (hydrogen bond mediated aglycon delivery, *Figure 2E*) or by covalently attaching the acceptor to a protecting group on C-2 (intramolecular aglycon delivery, *Figure 2F*). In hydrogen bond mediated aglycon delivery, a protecting group (in this case a picoloyl) with a hydrogen accepting functional group forms a hydrogen bond with the nucleophilic alcohol, which is then positioned on the "right" side of the reactive species to ensure a stereoselective glycosylation. This method has delivered β -mannosides using a C-3-picolyl ester⁴¹, α -glucosides and α -xylosides using a C-4-picolyl ester^{42,43}, and β -glycosides and β -fructosides using a C-6-picolyl ester^{44,45}. With intramolecular aglycon delivery, the protecting group on C-2 first forms a covalent bond with the acceptor. In the next step, an activator is added, and the 1,2-cis-glycosidic bond is formed. In the depicted example, the PMB protecting group is first oxidised to form an acetal with the acceptor,

which in the next step forms the desired β -mannosidic bond. Other acetals, as well as silyl based protecting groups have also been described.^{46,47}

The reason that stereoselective glycosylation remains challenging is two-fold. For one part, solutions are usually target-oriented and the other reason is that there are multiple different mechanistic pathways that can lead to two different products and that the mechanistic pathways are influenced by external factors such as solvent, temperature and concentration, as well as properties inherent to the donor and the acceptor.⁴⁸ A better understanding of the mechanistic pathways and the factors that influence these makes it easier to rationalize and eventually predict the outcome of glycosylation reaction and as such will streamline the total synthesis of biologically relevant carbohydrates.



Figure 2: Representative examples of methods for the stereoselective formation of glycosidic bonds. A: 1,2-Trans selective glycosylation through neighbouring group participation via a dioxolenium ion; B: β -Selective mannosylation via a conformationally restricted donor; C: α -Selective galactosylation using the bulky di-tert-butylsilylene (DTBS) group; D: α -Selective glucosylation using a chiral auxilary; E: 1,2-Cis selective glycosylation via hydrogen bond mediated aglycon delivery using the picoloyl (pico) protecting group; F) 1,2-Cis selective glycosylation via a covalent intermediate, using intramolecular aglycon delivery using the 4-methoxybenzyl (PMB) group as an example.

Oxocarbenium ions in glycosylation reactions

In a S_N1 type glycosylation reaction, the acceptor reacts with an oxocarbenium ion to form a glycosidic bond. The stereochemical outcome of these reactions is determined by the conformation and reactivity of the corresponding oxocarbenium ion. Oxocarbenium ions typically take up either a ${}^{3}H_{4}$ - or ${}^{4}H_{3}$ -like conformation (*Figure 3*) and the relative stability of the two conformers depends on the substituents on the ring.⁴⁹ The two different conformations can give rise to opposite stereochemical outcomes of the glycosylation reactions. For a ${}^{4}H_{3}$ oxocarbenium ion, a top-faced attack will result in an unfavourable twist-boat like transition state, while a bottom-face attack proceeds through a favourable chair-like transition state, causing the ${}^{4}H_{3}$ oxocarbenium ions to be bottom-face selective. For the same reasons, ${}^{3}H_{4}$ oxocarbenium ions are top face selective (see *Figure 3*).^{50, 51} Consequently, this means that for D-configured hexoses, the ${}^{4}H_{3}$ -configured oxocarbenium ion yields the α -product and the ${}^{3}H_{4}$ configured oxocarbenium ion yields the β -product. For L-configured hexoses the opposite is true.⁵²



Figure 3: Equilibrium between ${}^{3}H_{4}$ and ${}^{4}H_{3}$ oxocarbenium ions and mechanistic explanation why ${}^{3}H_{4}$ -like oxocarbenium ions are Top-face selective and why ${}^{4}H_{3}$ -like oxocarbenium are bottom face selective. Prediction for the formation of an α - or β -product from a conformation is based on D-configured carbohydrates, for L-configured carbohydrates, the opposite product is formed.

The effects of single substituents on the ${}^{4}H_{3}/{}^{3}H_{4}$ equilibrium of oxocarbenium ions, and by extension the outcome of S_N1 reactions were first experimentally investigated by Woerpel and coworkers, who found that *O*-alkyl substituents on C-3 and C-4 prefer a pseudo-axial orientation in the oxocarbenium ion half chairs, due to electrostatic stabilisation of the positive charge, while alkyl substituents on the same positions prefer a pseudo-equatorial orientation because of steric reasons.^{51, 53-55}

A more quantitative investigation of the reactivity of oxocarbenium ions was recently reported by Hansen *et al.*⁵⁶ A combination of computational chemistry, superacid NMR⁵⁷ and model glycosylations with deuterium nucleophiles was used to show that a S_N1 type glycosylation reactions with fully functionalised glycosyl donors are typically highly 1,2-cis selective.

Another technique used to characterise glycosyl cations is infrared ion spectroscopy (IRIS).^{58, 59} In this technique, glycosyl cations are generated in the gas phase, for example by ion collision. The cations are then measured using IR spectroscopy. This technique has been used to study the formation of oxocarbenium and dioxolenium ions, formed by attack of the carbonyl group of one of the protecting groups (as is well described for neighbouring group participation from C-2, *vide supra*). The structures of dioxolenium ions were characterised using IRIS by Pagel and coworkers (*Figure 4A*), showing that the glucosyl 1,2-dioxolenium ion takes up a ${}^{3}S_{1}$ conformation, the mannosyl dioxolenium ion a B_{0,3} conformation, and the galactose dioxolenium ion forms a mixture of ${}^{4}E$ and ${}^{1}S_{3}$ conformers.²¹

Acyl protecting group participation from other positions than C-2, has been less well understood than neighboring group participation by C-2-acyl groups. IRIS has been used to better understand remote participation of acyl groups on other positions than C-2.^{58, 59} Rijs, Boltje and coworkers used a combination of NMR and IRIS to investigate the mechanisms behind the stereoselectivity of 3,6-uronic acid lactone donors. The high β -selectivity of the mannuronic acid 3,6-lactone donor was explained by participation from the acetyl group on C-4 via a dioxolenium ion with a B_{1,4} conformation (*Figure 4B*).⁶⁰ To prove that the increased α -selectivity of 4-O-acetyl galactosyl donors (compared to per-benzyl donors) is due to remote participation, Marianski, Pagel and coworkers used IR spectroscopy to characterise a ¹S₅ configured dioxolenium ion that is formed when a 4-O-acetyl galactosyl donor is activated (*Figure 4C*).⁶¹

Boltje, Codée and coworkers studied the stabilisation of uronic acid glycosyl cations through participation from a C-4 acetyl protecting group or participation from the ester on C-5 using IRIS. It was concluded that stabilisation happens mainly through participation of the C-5 carboxyl, when C-2 and C-5 are *cis*, as is the case with mannuronic and taluronic acid. When C-2 and C-5 are *trans*, as is the case for glucuronic and galacturonic acid, stabilisation mainly happens trough participation from the acetyl group on C-4. (*Figure 4D*) ⁶²

Finally, through a combination of experimental glycosylations, DFT-calculations and IR-spectroscopy, it was found that remote participation is particularly strong from the C-3 position of mannose, making glycosylations with these donors highly α -selective. The order of remote participation was found to be as follows (strongest to weakest) 3-Ac-Man » 4-Ac-Gal > 3-Ac-Glu \approx 3-Ac-Gal > 4-Ac-Glu > 4-Ac-Man \approx 6-Ac-Glc/Gal/Man.⁶³



Figure 4: Selected IRIS experiments. A: structures of glucose, mannose and galactose dioxolenium ions with neighbouring group participation.²¹ B: the 3,6-mannuronic acid lactone donor is β -selective by participation of the acetyl group on C-4.⁶⁰ C: remote participation of the C-4-O-acetyl group on a galactose donor via a ¹S₅ dioxolenium ion.⁶² D: the structure of the dioxolenium ion of 4-O-acyl glucuronic acid donors is mainly determined by the stereochemistry of C-2. Mannuronic acid and taluronic acid show participation via C-5, while glucuronic acid and galacturonic acid show participation via C-4.⁶⁰

Covalent species in glycosylation reactions

On the other side of the mechanistic spectrum of glycosylation reactions, are S_N2 -like reactions, in which covalent reactive intermediates play a decisive role. Through *in-situ* anomerisation, first described by Lemieux and coworkers, a relatively stable and unreactive α -species is in equilibrium with a more reactive and less stable β -species. The equilibrium leans towards the side of the α -species, but the more reactive β -species can selectively react with an acceptor in an S_N2 reaction to form an α -glycosidic bond (*Figure 5A*).⁶⁴ Examples using this phenomenon have been described for bromides⁶⁵ and iodides⁶⁶⁻⁶⁹ using a source of X⁻ ions, for example TBABr or TBAI.

Based on this mechanism, the use of nucleophilic additives to modulate the stereochemical outcome of the glycosylation reaction has been explored (Figure 5B). West and Schuerch used dimethylsulfide, triethylamine and triphenylphosphine for the modulation of methanolysis of glucosyl bromides. They proposed that through the formation of a β -adduct with the additive, the α -product is formed through an S_N2 mechanism. Dimethylsulfide gave a 6:1 α : β ratio, where triethylamine and triphenylphosphine gave full α -selectivity.⁷⁰ Amides are also used as glycosylation modulator. Koto and coworkers introduced N,N-dimethylacetamide (DMA) as an additive for the stereoselective synthesis of α -glucosides.⁷¹⁻⁷³ More recently N,Ndimethylformamide (DMF) was introduced as a glycosylation modulator by Mong and coworkers for the synthesis of α -glucosides⁷⁴ and α -2-deoxy or 2,6-deoxy sugars.⁷⁵ DMF was, however, less successful in the modulation of less reactive 2-azido-glycosyl donors. Therefore, N-formylmorpholine (NFM) was introduced to overcome the low reactivity issues. With NFM α -2-azido-glucosides and α -2-azido-galactosides could be synthesised with good yield and selectivity.⁷⁶ Of note, the amide additives work well for stereoselectivity modulation with secondary alcohols, but not that well with more reactive primary alcohols.

Based on their success with sulfur containing chiral auxiliaries (see above) Boons and coworkers investigated phenyl ethyl sulfide (PhSEt) and thiophene as additive for 1,2cis glycosylation of α -2-azido-glucoside donors. With a disarmed donor, these additives gave good yield and selectivity. With an armed donor, significantly less selectivity was obtained.⁷⁷ Diphenyl sulfoxide was first introduced for dehydrative glycosylations by Gin and coworkers,¹³ but is was also used as an additive for the glycosylation with sialic acid donors by Crich and Li (see also chapter 7), where it was shown that the sulfoxonium adduct plays an important role in ensuring a productive outcome of the glycosylation reaction.⁷⁸ Bennett and coworkers used 2,3-bis(2,3,4-trimethoxyphenyl)-cyclopropene-1-thione for stereoselective glycosylation 2,6-dideoxy sugars with a quaternary carbon on C-3 in the total synthesis of the antibiotic saccharomicin B.⁷⁹

Like West and Schuerch, Ye and coworkers investigated phosphines for the synthesis of α -glucosides and galactosides. In a system based on urea catalysed glycosylation of chloride donors, they found tri-(2,4,6-trimethoxyphenyl)-phosphine to be the most effective.⁸⁰ The use of phosphine oxides was first described by Bogusiak and Szeja, who used HMPA as an additive for the stereoselective synthesis of α -xylofuranoses.⁸¹ Later, Mukaiyama and coworkers further investigated the effect of different phosphine oxides with glycosyl bromides, iodides and acetates for the synthesis of α -glucosides. The inherent instability of glucosyl iodides was overcome by using TMSI and phosphine oxides were also used in the synthesis of α -ribofuranosides,⁸⁵ α -2-deoxyglycosides⁸⁶ and β -3-amino-2,3,6-trideoxy sugars.⁸⁷ A representative example which shows the synthetic utility of glycosylation modulated by nucleophilic additives was published by Wang *et*

al. (*Figure 5C*). For secondary alcohols, DMF was used as an additive, while TMSI/Ph₃P=O was used in glycosylations with primary alcohols in the stereoselective synthesis of the α -glucosidic bonds using an *in-situ* anomerisation mechanism.⁸⁸⁻⁹⁰ In a similar way, methyl(phenyl)formamide was used for glucosazide donors.^{76, 91}

The extent to which in-situ anomerisation plays a role in pre-activation based glycosylations which generate triflates as reactive species remains somewhat controversial, but recently, sophisticated NMR studies have also shown that in situ anomerisation can also play a role in glycosylations which have triflates as reactive intermediates (see below)



Figure 5: A: explanation of in-situ anomerisation. B: Structures of additives used for the modulation of stereoselectivity in glycosylation reactions. C: representative synthesis of an oligosaccharide using additives by Wang et al.⁸⁸

Variable temperature NMR (VT –NMR) is a versatile technique to investigate the covalent reactive intermediates in glycosylation reactions. In this method, a donor and an activator are reacted in an NMR tube to enable the recording of NMR spectra of the reaction mixture at low temperature to characterise the reactive species that are formed. Many reactive intermediates, mostly triflates, have been characterised using this method. Frihed, Bols and Pedersen have provided an extensive review on glycosyl triflates⁹² and a few representative examples will be highlighted here.

When trichloroacetimidates (TCA) are used as donor, the reactive intermediates that are formed are determined by the nature of the activator (*Figure 6A*). By using a combination of 1-H NMR, 19-F NMR and DOSY NMR, Qiao *et al.* showed that when triflate based activators are used, α -triflates can be formed, which eventually decompose to provide a mixture of α - and β -trichloroacetamides. With BF₃-Et₂O, the β -fluorides were formed, which isomerise to the α -anomer at higher temperature. When bistriflimide activators are used, the silylated donor was found to be formed as a reactive intermediate, which decomposes by an intramolecular Friedel-Crafts type reaction of the C-2-benzyl group.⁹³

During the synthesis of mannuronic acid and 2- and 2,3-deoxy amino mannuronic acid containing bacterial oligosaccharides, Walvoort *et al.* characterised the triflates that are formed when the thio donors are activated with the Ph₂SO/Tf₂O reagent combination (*Figure 6B*). The α -triflate was formed exclusively in all cases, but two species were observed by VT-NMR, because the triflates were present as a conformational mixture of ⁴C₁ and ¹C₄ conformers.⁹⁴⁻⁹⁶

During the total synthesis of a complex oligosaccharide from *Mycobacterium marinum* by Hansen *et al*, VT-NMR was used in the optimisation of glycosylations with rare caryophyllose donors (*Figure 6C*). When the alcohols on the side-chain on C-4 were protected with benzyl groups, the glycosylation reactions were unsuccessful due to the rapid formation of a bicyclic side product. When the benzyl groups were replaced by carbonate protecting groups, the caryophyllose β -oxosulfonium triflate was found as the main reactive intermediate, which successfully react to form the glycosylation products.⁹⁷

Santana *et al.* have used VT-NMR to show that β -triflates play a role in glycosylation reactions of benzylidene protected glucosyl, mannosyl and allosyl donors, (*Figure 6D*). Normally, β -triflates are not visible in VT-NMR experiments due to their low concentration, but though a series of sophisticated 1D and 2D experiments it was possible to confirm their presence.⁹⁸

The aforementioned formation of dioxolenium ions that occurs when there is a participating protecting group on C-2 can also be observed using VT-NMR (*Figure 6E*). When a peracetylthio glucosyl donor was activated with AgOTf/p-TolSCl in CDCl₃ at -60 °C, a 1:1 mixture of anomeric triflates and dioxolenium ions was obtained. Upon warming to -20 °C, the dioxolenium ion was converted into the α -triflate. When the

mixture was recooled to -60 °C, the mixture of triflates and dioxolenium ions was formed again.⁹⁹



Figure 6: Examples of VT-NMR used to investigate reactive intermediates formed in glycosylation reactions. A: Reactive species and decomposition products from a trichloroacetimidate donor with different activators.⁹³ B: Conformational equilibrium of triflates that form upon activation of the mannuronic acid donors.⁹⁵ C: Donor optimisation in the total synthesis of a Mycobacterium marinum Lipooligosaccharide.⁹⁷ D: In-situ anomerisation studied with VT-NMR.⁹⁸ E: The equilibrium between dioxolenium ions and anomeric triflates, observed by VT-NMR.⁹⁹

Acceptor reactivity

Influence of acceptor reactivity on the glycosylation reaction

The reactivity of the acceptor plays a crucial role in the outcome of a glycosylation reaction. The extent to which the reactivity of the acceptor affects the outcome depends heavily on other factors such as the reaction conditions and the donor. To understand the influence of acceptor reactivity on the outcome of glycosylation reactions, a series of model acceptors with varying nucleophilicity was introduced, with ethanol (EtOH) being the most nucleophilic and 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) the least.¹⁰⁰ The acceptors in this set are not chiral, so that any difference in stereochemical outcome is due to differences in nucleophilicity and not due to diastereomeric effects.¹⁰¹ *Table 1* shows a few key results in recent studies.

Glucose, mannose and mannuronic acid donors (Donors 1, 2 and 4) were used by van der Vorm *et al.* to investigate the influence of acceptor nucleophilicity on the reaction mechanism of glycosylation reactions. This set of ethanol acceptors together with some carbohydrate acceptors show that more nucleophilic acceptors react via a $S_N 2$ type mechanism, while less nucleophilic acceptors react via a mechanism with more $S_N 1$ character.¹⁰² In another study, it was shown that the stereoselectivity of conformationally restricted glucosazide donors **3** strongly depends on the nucleophilicity of the acceptor. This donor is more β -selective than its glucose counterpart, because the electron withdrawing azide on C-2 stabilises the α -triflate more, making a $S_N 2$ -type glycosylation more favourable.¹⁰³

Hagen *et al.* have used the set of model acceptors to map the relation between acceptor nucleophilicity and stereoselectivity for 2-azidofucosyl donors (*e.g.* using donor **5**).¹⁰⁴ The set of fluorinated acceptors was also used by Hansen *et al.* to generate more insight into the reactivity of rare building blocks used in the synthesis of a complex oligosaccharide from *Mycobacterium marinum* (donors **6** and **7**).⁹⁷ Finally, this set of nucleophiles was also used in the aforementioned study on remote participation.⁶³

Introduction

Table 1: Model glycosylations by van a	der Vorm et al.	. (1-4) ^{102, 103} , Hagen	<i>et al.</i> $(5)^{104}$ <i>and</i>
Hansen et al. $(6 \text{ and } 7)^{97} \text{ n.d.} = \text{not dete}$	ermined		

Ph		SPh Ph O	OBn O SPh	Ph TO O BnO	SPh
	0Bn 1	ыю	2 0	3	3
MeC	D_2C OBn	707			N ₃ N ₃
BnC	SPh	BnOOBn			BnO OBn
	4	5		BnO SPh 6	7
					_ F _
\sim	DH F	∽ _{он} і	≡∽_он	F F	F F
			F	F OH	F OH
EtO	4	MFE	DFE	TFE	É
		Acco	ntor (product a	R wield)	HFIP
Donor -	FtOH	MEE	DEF	TFF	HEID
	14	1B	10	10	 1E
1	1:10	1:2.8	5:1	>20:1	>20:1
	(83%)	(70%)	(90%)	(80%)	(65%)
	2A	2B	2C	2D	2E
2	1:5	1:5	1:5	1:4	3:1
	(70%)	(86%)	(90%)	(78%)	(56%)
	3A	3B	3C	3D	3E
3	<1:20	1:6.7	2.9:1	>20:1	>20:1
	(83%)	(90%)	(64%)	(94%)	(53%)
	4A	4B	4C	4D	4 E
4	1:8	1:6	1:5	1:2.5	1:1
	(95%)	(70%)	(87%)	(85%)	(52%)
	5A	5B	5C	5D	
5	1:1	1:1	2:1	19:1	n.d.
	(88%)	(72%)	(81%)	(80%)	
-	6A	6B	6C	6D	6E
6	1:1	2:1	4:1	>20:1	>20:1
	(60%)	(76%)	(100%)	(77%)	(28%)
-	7A	УB	70	7D	7E
	1.8:1 (87%)	1:1.1 (100%)	5.5:1	> 20:1 (70%)	>20:1
	(0/70)	(100%)	(9170)	(70%)	(09%)

Reactivity of carbohydrate acceptors

The glycosylations with fluorinated model acceptors highlight the importance of acceptor reactivity on the outcome of glycosylation reactions. But in contrast to glycosyl donors, where the structure-reactivity relations are relatively well described thank to spectroscopic and computational studies (see above) as well as measurement of relative reactivity values of thioglycosides,¹⁰⁵⁻¹⁰⁷ factors influencing the reactivity of glycosyl acceptors are less well studied.¹⁰⁸ As described above, the stereochemical outcome of benzylidene glucose and glucosamine donors 1 and 3 highly depends on the nucleophilicity of the acceptor. This property was used to "measure" the reactivity of a large set of acceptors, all with systematic variations in stereochemistry and protecting group patterns. Screening of systematically varied sets of acceptors using this system shows how seemingly small changes on in the protecting group pattern of the acceptor can drastically change the reactivity of an acceptor. For example, when the C-3 protecting group of a C-4-OH glucose acceptor was changed from a benzyl to a sterically similar benzoyl group (effectively substituting a CH₂ group for a C=O group) the outcome of the glycosylation reaction changed from being unselective to fully α selective and from β -selective to α -selective (*Figure 7*).¹⁰⁹

A more systematic understanding of which factors influence the reactivity of the acceptor could also help developing a quantitative measurement system for the reactivity of acceptor reactivity, as proposed by Wong, Wang and coworkers.¹¹⁰ This can in turn be used to measure the influence of acceptor reactivity on the outcome of glycosylation reactions.



Figure 7: Seemingly small differences in the glycosyl acceptors have a detrimental outcome on the glycosylation reaction in terms of stereoselectivity. Changing a CH_2 group into a C=O group on an acceptor reverses the stereoselectivity of the glycosylation reaction.¹⁰⁹

Contents

The aim of this thesis is to increase the understanding of several aspects of the glycosylation reaction and the influence of these on the (stereochemical) outcome, and as such make rational design of a synthesis route towards a target oligosaccharide possible.

Chapter 2 describes the synthesis of glycosyl donors of all the eight diastereomers of phenyl 2,3,4,6-tetra-O-benzyl-1-thio- β -pyranosyl donors, as well as their 6-deoxy analogues and studies the behaviour in S_N 1-like reactions via computational and experimental chemistry.

Chapter 3 deals with the characterisation of reactive covalent species in $S_N 2$ like reactions with VT-NMR and the investigation of the influence of nucleophilicity of oxygen nucleophiles on the mechanism of the glycosylation reaction.

Chapter 4 reports the structure-reactivity relationships of ether and ester protected carbohydrate acceptors using the stereoselectivity of two conformational restricted donors.

Chapter 5 builds on chapter 4 and outlines the influence of azides, trifluoro- and trichloroacetamides on the reactivity of different glycosyl acceptors.

Chapter 6 presents an application of the research as described in chapter 2-5 for the synthesis of an oligosaccharide with an unusual structure found in *Acinetobacter Baumannii*, an antibiotic resistant pathogen, through the mapping of the reactivity and selectivity of 2,3-di-*N*-acetlyglucuronic acid and bacillosamine donors and acceptors using VT-NMR and model glycosylations.

Chapter 7 provides a brief summary and gives some suggestions for further research.

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Chapter 2: Stereoselectivity of S_N 1-like reactions of all eight diastereoisomeric pyranosyl and 6-deoxy pyranosyl donors with D- or C-nucleophiles

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Introduction

Despite significant progress over the last decades, the construction of a glycosidic bond in a stereoselective and high vielding way remains a challenging, time consuming and resource intensive operation for which no universal guidelines exist.¹⁻³ The outcome of a glycosylation reaction is dependent on properties inherent to the used building blocks, as well as on environmental factors, including but not limited to solvent, temperature and concentration.⁴ The reason that the outcome of a reaction between a donor and an acceptor remains hard to predict, is the continuum of reaction mechanisms that can be followed to lead to two products (Figure 1). When a glycosyl donor (I) is activated by a promotor (E-X) a variety of reactive species can form (II-VIII), including α - or β -covalent species (VIII and II respectively) which react predominantly via a $S_N 2$ mechanism and oxocarbenium ion like species (III-VII) which react in a S_N 1-type fashion. Which pathways are followed depends on the reactivity of the donor and the incoming nucleophile (NuH) and the S_N2 - and S_N1 -type pathways can yield the α -product (IX), the β -product (X) or a mixture of the two.⁵⁻⁸ In order to better understand, and eventually predict the outcome of a glycosylation reaction, it is essential to know which products can be formed by following the different mechanistic pathways. The covalent species involved in the S_N2 reactions can be studied by spectroscopic techniques and over the years multiple covalent species, such as triflates and oxosulfonium triflates, have been observed by the use of variable temperature NMR (VT-NMR).⁹⁻¹⁶ On the other hand, oxocarbenium ions are more difficult to study due to their high reactivity and short lifetime, and currently no spectroscopic method exists to observe, let alone characterise oxocarbenium ions of relevant donors, in reaction-like media.



Figure 1: Mechanistic continuum of a glycosylation reaction, II, VIII: covalent species; III, VII: contact ion pair; IV, VI: solvent separated ion pair; V: oxocarbenium ion. this work investigates V. LG: leaving group, E-X: activator, NuH: nucleophile

Over the last years, tremendous progress has been made in the understanding of glycosyl cations and their reactivity thanks to a combination of mechanistic experiments, NMR experiments in superacid media, IR spectroscopy, computational chemistry, or a combination thereof.¹⁷⁻³¹ Understanding, and predicting the (stereochemical) outcome of $S_N 1$ like glycosylation reactions remains challenging nonetheless. While it has long been clear that the conformational behaviour of oxocarbenium ions – and by extension the stereochemical outcome of S_N1 like reactions- is heavily dependent on the substitution pattern on the carbohydrate ring,^{19,} ^{31, 32} there is a need for more quantitative data on how the effects of the functional groups on C-2, C-3, C-4 and C-6 together impact the ions. In order to systematically investigate the combined effect of the ring substituents on fully decorated glycosyl oxocarbenium ions, here all 8 possible diastereoisomeric β -thiophenol 2,3,4,6-tetra-Obenzyl pyranosyl donors, as well their 6-deoxy counterparts (Figure 2) are probed in reactions that typically follow an S_N1-like pathway. To this end, the addition reactions of two nucleophiles, TES-D and allyl-TMS were studied. To investigate the conformational preferences of the involved oxocarbenium ions, conformational energy landscape (CEL) maps were generated using density functional theory (DFT) according to the recently published method by Hansen et al.²⁶ It has previously been reported that the outcome of addition reactions of TES-D to (partially stripped) glycosyl oxocarbenium ions can be rationalized using the most relevant conformers of the glycosyl oxocarbenium ions.²⁶ For some fully decorated glycosyl cations, however, the addition reactions of allyl-TMS proceeded with different selectivity that what would be expected based on the conformational preference of the intermediate glycosyl cations.
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For example, the mannosyl donor 2 reacts with TES-D to selectively gives the β product, which can be accounted for by the diastereoselective attack of the nucleophile on the β -face of the ${}^{3}H_{4}$ -half chair oxocarbenium ion,²⁶ but the reaction with allyl-TMS under the same conditions gives a $66:34 \alpha:\beta$ mixture. The systematic investigation of all possible diastereoisomeric pyranosyl oxocarbenium ions reported here reveals that the addition of TES-D to the oxocarbenium ions, in most cases, proceeds in a stereoselective fashion to provide the products derived from the most favourable oxocarbenium ions. However, when significant steric interactions develop between the incoming nucleophile and the ions and between substituents on the pyranosyl ring, additions to higher energy ions can become more favorable. The complete set of all eight possible pyranosyl diastereoisomers and the use of the two different nucleophiles has allowed to define these Curtin-Hammett kinetic scenarios, which all together detailed picture of the interplay between oxocarbenium provide a ion stability/reactivity, steric interactions in the developing transition states and nucleophile reactivity. These will be instrumental in the understanding and optimisation of the stereochemical outcome of glycosylation reactions.



Figure 2: structures of the donors (1-16) used in this study. ¹: The *D*-isomer is shown for ease of comparison, but the *L*-isomer is used in the experiments.

Results and discussion:

Donor synthesis

The glycosyl donors, derived from monosaccharides that are commercially readily available (i.e. glucose, mannose, galactose, rhamnose and fucose), was achieved using the following (well-established) reaction sequence: acetylation, installation of the anomeric thiophenol group, deacetylation and benzylation.²⁶ The synthesis of the other diastereomers is depicted in Scheme 1 (the 6-O-benzyl donors) and Scheme 2 (the 6deoxy sugars). Allose donor 4 was synthesized by the regioselective inversion of the C-3-OH of benzylidene protected glucose 17 via a Mitsunobu reaction with benzoic acid, followed by global deprotection and benzylation. Altrose 5 was synthesised by formation of 2,3-anhydro allose **22** from methyl 4,6-*O*-benzylidene-α-D-glucopyranose (20),¹² followed by sulfuric acid catalysed acetolysis.³³ The β -thiophenol moiety was installed by converting the anomeric acetyl group to a chloride using SOCl₂/SnCl₄,³⁴ followed by treatment with NaH/PhSH in DMF. Finally, the acetyl esters were replaced by benzyl ethers under standard conditions. D-Gulose donor 6 was prepared as previously described for the L-isomer,³⁵ using D-gulonic acid 1,4-lactone (27) as starting material. Idose donor 7 was synthesised by antimony(V) chloride mediated inversion of the C-1, C-2, C-3 and C-4 stereocenters of peracetylated glucose (28).³⁶ The β thiophenol moiety was installed by converting the anomeric acetyl group to the anomeric α-bromide with HBr in acetic acid, followed by treatment with NaH/PhSH in DMF. Next the acetyl groups were replaced by benzyl groups. Finally, talose donor 8 was synthesised from partially protected galactose building block 36 by inversion of C-2 via an oxidation and reduction sequence, followed by acid catalysed deprotection of the TIPS-ether and isopropylidene groups and benzylation. The 6-deoxy glucose, allose and altrose donors were synthesised by deoxygenation of the C-6-O-tosyl precursors with lithium aluminium hydride, as shown in Scheme 2. The 6-deoxy gulose donor 14 was synthesised from fucose building block 49, which was transformed into 6deoxygulose **50** in 5 steps according to literature procedure,³⁷ followed by deprotection and benzylation. Both the 6-deoxy idose and 6-deoxy talose donors were synthesised from 3,4-isopropylidene protected fucose building block 52. The C-2-OH was inverted by oxidation with Dess-Martin periodinane followed by reduction with NaBH₄ to give talose configured building block 54. The idose donor was obtained by removal of the isopropylidene, followed by regioselective benzoylation of the resulting diol, yielding compound **56**. Inversion of the free C-3-OH was then achieved by triflation followed by substitution with TBANO₂³⁸. Unfortunately, the substitution reaction was accompanied

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by the formation of elimination products leading to a low yield of compound **58**.^{*} Sufficient material could be generated nonetheless for the upcoming glycosylation studies. Debenzoylation followed by benzylation yielded donor **15**. Acidic deprotection followed by benzylation of compound **54** yielded talose donor **16**.



Scheme 1: synthesis of per-benzylated Allose (4), altrose (5), gulose (6), idose (7) and talose (8) β thiophenol donors. Reagents and conditions: a) BzOH, Ph₃P, DIAD, THF, 70 °C, 52%; b) i: pTsOH, MeOH, 50 °C, ii: NaOMe, MeOH, 81%; c) NaH, BnBr, DMF, 83 %; d) MsCl, pyridine; e) KOH, THF/MeOH 3:2, reflux, 43% over 2 steps; f) Ac₂O, H₂SO₄, 70%; g) SOCl₂, SnCl₄, DCM; h) NaH, PhSH, DMF, 49% over 2 steps; i) NaOMe, MeOH; j) BnBr, NaH, DMF, 84% over 2 steps; k) SbCl₅, DCM; l) NaOAc, H₂O; m) Ac₂O, pyridine, 38% over 3 steps; n) HBr/HOAc, DCM; o) NaH, PhSH, DMF, 56% over 2 steps; p) NaOMe, MeOH, q) BnBr, NaH, DMF, 73% r) i: TIPS-Cl, imidazole, DMF, ii: 2,2,-dimetoxypropane, pTsOH, 57% over 2 steps; s) Dess-Martin, DCM, 94%; t) NaBH₄, MeOH, 0 °C, 67%; u) pTsOH, MeOH, 50 °C; v) BnBr, NaH, DMF, 64% over 2 steps

^{*} Sanapala and Kulkarni have reported that inversion of the C-3-OH, of a very similar building block carrying a C-4-O-2,2,2-trichloroethoxycarbonyl (Troc) group, under the same conditions proceeds in 54% yield, see ref 38.



Scheme 2: synthesis of 6-deoxy donors 9, 12, 13, 14, 15 and 16. Reagents and conditions: a) pyridine, pTsCl; b) LiAlH₄, THF reflux, 47% over 2 steps; c) Ph₃P, BzOH, DIAD, THF reflux; d) NaOMe, MeOH; e) BnBr, NaH, DMF, 32% over 3 steps; f) BH₃-THF, CoCl₂, THF; g) pTsCl, pyridine; h) LiAlH₄, THF reflux, 48% over 3 steps; i) i: TIPS-Cl, imidazole, DMF, ii: BnBr, NaH, DMF, 85% over 2 steps; j) TFA, THF/H₂O 4:1, 84%; k) pTsCl, pyridine; l) LiAlH₄, THF reflux, 64% over 2 steps; m) NaOMe, MeOH; n) BnBr, NaH, DMF, 65% over 2 steps; o) Dess-Martin periodinane, DCM; p) NaBH₄, MeOH, -10 °C, 33% over 2 steps; r) BzCl, pyridine, DCM, 79%; r) i: MeOH, amberlite, reflux, ii: PhC(OMe)₃, CSA, DCM, iii: H₂O, 54% over 3 steps; s) Tf₂O, pyridine, DCM, -10 °C; t) TBANO₂, ACN, 80 °C; u) NaOMe, MeOH; v) BnBr, NaH, DMF, 9% over 4 steps; w) i: PTSA, MeOH, 50 °C; x) BnBr, NaH, DMF, 75% over 2 steps

CEL maps and stereoselectivity of glycosylations with TES-D and Allyl-TMS

The generation of the oxocarbenium ion CEL maps and the prediction of the stereochemical outcome of S_N1 reactions to these was done as previously described by Hansen et al.²⁶ In order to reduce the required calculation time, the benzyl (OBn) protecting groups were changed for smaller, electronically similar methyl (OMe) groups. The workflow is depicted in *Figure 3*. The starting conformation for the CEL map was determined by first generating a conformational library using the 'conformation distribution search' included in spartan '14³⁹ using the B3LYP as hybrid functional in the gas phase with 6-31G(d) as the basis set. Next, the found structures were re-optimised using Gaussian 09⁴⁰ using DFT/B3LYP/6-311G(d,p), including an optimisation with a polarisable continuum solvent model (PCM) to account for the solvation in dichloromethane. The structure with the lowest energy was used as starting point for the CEL map generation. In order to make sure that the entire conformational space was scanned, three dihedral angles, C1-C2-C3-C4 (D1), C3-C4-C5-O (D3) and C5-O-C1-C2 (D5) were changed from -60° to 60° in steps of 15°, giving a total of 729 structures. For donors 1-8, three different O5-C5-C6-O6 rotamers (the gg, gt and tg structures) were taken into account, as it has been shown that the stability and reactivity of the ions is significantly impacted by the orientation of the C-6-group.⁴¹ The three CEL maps were generated separately and subsequently the maps were merged using the structures that were lowest in energy.



Figure 3: Overview of the workflow to map the conformational and stereoselective preference of pyranosyl oxocarbenium ions. (1) The complete conformational space of a six-membered ring was scanned by computing 729 prefixed structures. A few canonical conformations (chair, half-chair, envelope, and boat) are depicted. (2) The associated energies were graphed on slices dividing the Cremer–Pople sphere. (3) Top- and bottom-face selective conformers lie in separate areas of the sphere. The family of the top face-selective (${}^{3}E$, ${}^{3}H_{4}$, E_{4} , and $B_{2,5}$)-like structures is found in the area contoured with the red-dashed line, while the bottom face-selective family of (${}^{4}E$, ${}^{4}H_{3}$, E_{3} , and ${}^{2,5}B$)-like conformers is found on the opposite side of the sphere, grouped within the blue-dashed line. (4) On the basis of the Boltzmann distribution of the top- and bottom-face selective structures, the stereochemical outcome of nucleophilic addition reactions to pyranosyl oxocarbenium ions can be computed. The picture and description are reprinted from ACS Central Science by T. Hansen et al.²⁶

In order to visualise the energy levels of the conformations on the Cremer-Pople sphere,⁴² the sphere was dissected in slices that combine closely associated conformers. The OriginPro software⁴³ was employed to produce the energy heat maps, contoured at 0.5 kcal/mol. The CEL maps revealed that the ³E, ³H₄, E₄, and B_{2,5} conformations together with the opposing ⁴E, ⁴H₃, E₃, and ^{2,5}B conformations are generally energetially most favourable. To predict the stereoselectivity of the oxocarbenium ions the conformations were divided in top-face (the ³E, ³H₄, E₄, and B_{2,5}-type conformations) and bottom-face (⁴E, ⁴H₃, E₃, and ^{2,5}B-type conformations) selective families, based on the most likely mode of attack by the nucleophile. The most favourable reaction path for the half chair-type structures leads to the products via a chair-like structure, while the most favourable approach of the boat-like ions is from the convex face of the structures. To calculate the theoretical α : β ratio based on a given CEL map, the Boltzmann distribution (eq. 1) was used to determine the relative population of the α -and β -selective conformations. Only the conformations with a relative energy lower than 5 kcal/mol were included in the calculations.

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

The CEL maps for the 6-deoxy pyranosyl oxocarbenium ions and the C-6-OMe ions are depicted in *Figure 4* and *Figure 5*, respectively. The collection of CEL maps clearly illustrates how changing the configuration of one, two or three stereocenters impacts the conformational preference of the ions. When comparing the structures of the 6deoxy ions to their C-6-OMe counterparts is becomes apparent that similar families of favourable conformers are found for both pyranosyl classes but that there is a difference between the relative energy of the conformations. The stability of the conformations identified by the CEL maps may be rationalised by taking into account the individual 'preferences' of the susbtituents to best stabilise (or least destabilise) the ions, as experimentally determined by Woerpel and co-workers^{19, 20, 31, 32} and computationally substantiated by Hansen et al.26 Pyranosyl oxocarbenium ions placing alkoxy groups at the C-3 and C-4 positions in a *pseudo*-axial orientation are more stable than their pseudo-equatorial counterparts. For steric reasons, the C-5 group is placed preferentially in a pseudo-equatorial orientation, just like the C-2-alkoxy group. This orientation of the C-2-group also enables stabilisation of the oxocarbenium ion by hyperconjugative stabilization by the pseudo-axial C-2-H atom. When all these preferences can be achieved in concert, as is the case for the 6-deoxy gulosyl oxocarbenium ion, the ion shows a very strong preference for a single well-defined conformation, *i.e.* the ${}^{4}H_{3}$ half chair. The structures that are capable of placing three out of the four substituents in their favorable orientation (6-deoxy mannose/galactose/allose/idose) also show a relatively strong preference for the

structure with the three substituents placed in a stereoelectronic favourable orientation. The structures where only two substituents can be placed in a favourable manner show the most 'filled' CEL maps with multiple structures being relatively close in energy.

The results of the glycosylations of the eight 6-deoxy pyranosyl and eight C-6-O-benzyl donors are summarized in Table 1, and Table 2, respectively, where they are also compared to the calculated α : β ratio based on the CEL maps of the oxocarbenium ions. It has previously been described for a large set of "stripped" pyranosyl oxocarbeniums, that the CEL maps could be used well to rationalise the stereoselectivity of reactions of these with TES-D. From the results in *Table 1* it becomes apparent that in the 6-deoxy series the theoretically predicted and experimentally observed selectivities for the addition of TES-D to the mannose-, galactose-, allose-, altrose-, gulose- and taloseconfigured ions match well. Discrepancies are found for the 6-deoxy glucose and 6deoxy idose ions. While the 6-deoxy glucose CEL-map predicts an unselective addition reaction, the experiment delivers the α -product with excellent stereoselectivity. Based on the ground-state energy of the different conformers of the 6-deoxy idose ion an α selective addition could be expected, where a β -selective addition is experimentally observed. The deviation in the selectivity predicted based on the ground-state energy of the ions and the experimentally determined stereoselectivity may be rationalded by steric interactions that develop in the transition states leading to the products, between the oxocarbenium ion and the incoming nucleophile and the interactions of the axial subtituents of the ions/products. For the 6-deoxy glucose ion, the E_4 conformer is relatively close in energy to the ${}^{4}H_{3}$ half chair ion ($\Delta G = 0.5$ kcalmol⁻¹) but attack on the top face of the E_4 conformer will lead to significant steric interactions with the *pseudo*axial C-3 and C-5 substituents. In addition, transformation from the envelope structure to a ${}^{4}C_{1}$ chair will increase the 1,3-diaxial interactions between the groups at C-2 and C-4. For the addition of TES-D to the 6-deoxy idose ion a similar analysis can be made. Even though there is a significant difference in stability between the ${}^{3}H_{4}$ half chair and the ⁴*E* envelope ($\Delta G = 3.4$ kcalmol⁻¹), attack at the latter conformer is hindered by the axial C-3-group and, in line with the analysis above, the ${}^{4}E$ to ${}^{1}C_{4}$ transformation will lead to the development of significant 1,3-diaxial interactions of the C-2 and C-4 groups.

The developing steric interactions are even more important in the additions of allyl-TMS to the oxocarbenium ions. Allyl-TMS is a weaker nucleophile than TES-D and therefore the transition state of the reactions of this nucleophile (Mayr nucleophilicity parameter 1.96 (TES-D) *vs* 3.58 (allyl-TMS)) are expected to be later on the reaction coordinate. Thus, for the 6-deoxy mannose case this leads to erosion of β -selectivity, as attack on the β -face of the ³*E* envelope generates 1,3-diaxial interactions with the substituents at the C-3 and C-5 position and a gauche interaction with the C-2substituent. Even though the ground state energy difference between the ³*E* envelope and the ⁴H₃ half chair ions is significant ($\Delta G = 3.1 \text{ kcalmol}^{-1}$), the developing steric interactions counterbalance this energy gap. For 6-deoxy altrose the ground state energy difference between the two half chairs on either side of the CEL is relatively small. With the reactive and small nucleophile TES-D the intrinsic difference between the ${}^{3}H_{4}$ and ${}^{4}H_{3}$ half chair ions ($\Delta G = 0.4$ kcalmol⁻¹) is mirrored in the stereoselectivity of the addition reaction (α : β = 12:88), while the less reactive allyl-TMS provides an α selective reaction (α : β = 89:11). The developing 1,3-diaxial interaction between the nucleophile and the C-5 methyl group and gauche interaction with the C-2-substituent raise the transition state energy for the addition on the β -face of the ³H₄ half chair ion such that addition to the α -face of the opposite half chair becomes more favorable. For 6-deoxy idose, these steric interactions also make addition to the less stable ${}^{4}E$ oxocarbenium ion less favorable than top-face addition to the ${}^{4}H_{3}$ half chair. As the addition of allyl-TMS to this ion proceeds with lower β -selectivity than the addition of the smaller and more reactive TES-D it appears that the steric interactions of the incoming allyl-TMS with the substituent at C-2 and C-5 make the transition state for the allyl-TMS addition on the top face more unfavorable leading to the formation of relatively more of the α -product. For 6-deoxy talose a complete shift in stereoselectivity is observed when comparing the TES-D and allyl-TMS additions, again indicating important steric gauche and di-axial interactions in top-face attack of the most stable ${}^{3}H_{4}$ half chair ion. As the difference in ground state energy between the 6-deoxy talose ${}^{3}H_{4}$ and ${}^{4}H_{3}$ half chair ions ($\Delta G = 1.2$ kcalmol⁻¹) is smaller than that of the 6-deoxy mannose ions ($\Delta G = 3.1$ kcalmol⁻¹) and therefore the change in stereoselectivity observed for addition to the 6-deoxy talose ion is more significant (<2:98 to >98:2 vs <2:98 to 77:23).

Donor	Calculated α:β selectivity	TES-D		Allyl-TMS				
		Product	α:β	Product	α:β			
		(Yield)		(Yield)				
9 (6-deoxy glucose)	55:45	9A (59%)	>98:2	9B (64%)	>98:2			
10 (6-deoxy mannose)	<2:98	10A (79%)	<2:98	10B (83%)	77:23			
11 (6-deoxy galactose)	>98:2	11A (74%)	>98:2	11B (76%)	>98:2			
12 (6-deoxy allose)	>98:2	12A (57%)	>98:2	12B (57%)	>98:2			
13 (6-deoxy altrose)	23:77	13A (85%)	12:88 ^a	13B (67%)	89:11			
14 (6-deoxy gulose)	>98:2	14A (86%)	>98:2	14B (75%)	>98:2			
15 (6-deoxy idose)	>98:2	15A (50%)	<2:98	15B (48%)	21:79			
16 (6-deoxy talose)	12:88	16A (68%)	<2:98 ^a	16B (55%)	>98:2			

Table 1: predicted and experimental stereoselectivities of all 8 6-deoxy pyranosyl donors

a: determined after debenzylation followed by benzoylation. Calculated $\alpha:\beta$ ratios are based on methylated oxocarbenium ions, experimental $\alpha:\beta$ values are based on benzylated donors. The CEL maps and TES-D results of donors **10** and **11** were previously reported.²⁶



Figure 4: CEL maps of all 6-deoxy pyranosyl oxocarbenium ions

Table 2 summarises the results for the reactions of the C-6-OMe/OBn pyranosyl donors. When these results are compared to the experimental results of the 6-deoxy series it becomes apparent that these are very similar and thus that in most cases the C-6-substituent has relatively little influence on the stereoselectivity of the reactions. As mentioned above, the CEL maps of the C-6-OMe and 6-deoxy pyranosyl oxocarbenium ions reveal similar conformations to be relevant and this translates into comparable stereoselectivities in the addition reactions. A notable difference can be observed for the glucopyranosyl ion, where there is a significantly larger difference in stability between the ⁴H₃ half chair ion and the $E_4/^2S_0$ ($\Delta G = 2.3$ kcalmol⁻¹) than found for the 6deoxyglucosyl ions ($\Delta G = 0.5$ kcalmol⁻¹). This however does not lead to a different stereochemical outcome of the addition reactions, as the sterically least hindered mode of attack can now take place on the most stable oxocarbenium ion conformer. For the talose ion a significant difference is observed as well, with the ${}^{3}H_{4}$ and ${}^{4}H_{3}$ half chair ions being of comparable stability, which translates to a theoretical 1:1 α : β -ratio. The TES-D addition however provides solely the β-product. This would indicate that the 1,3-diaxial interactions between the C-2 and C-4 groups, that develop in the transition state of the reaction of TES-D on the bottom face of the ⁴E envelope, are prohibitively large to favour attack of the nucleophile on the top face of the ${}^{3}H_{4}$ half chair ion. When allyl-TMS is used as a nucleophile the steric interactions of the nucleophile with the electrophile will become more important (i.e. the 1,3-diaxial type interaction with the groups at C-3 and C-5 as well as the gauche interaction with the group at C-2) making the top face attack less favourable and thus leading to the formation of an α/β -mixture. In all, the above-described analyses show that, in line with the study of Hansen *et al.*, the conformational preference of a pyranosyl oxocarbenium ion translates well into the selectivity observed in the addition of TES-D to these ions. TES-D experiences relatively little steric interactions with the substituents on the ring during the addition reaction. If, however, 1,3-diaxial interactions develop between the substituents on the ring in the transition state of the addition reaction (as in the β-face attack on the 6deoxy glucose ⁴E-ion, the α -face attack on the 6-deoxy idose ⁴E-ion and the α -face attack on the 6-deoxy talose ${}^{4}H_{3}$ -ion), these can significantly increase the hight of the transition states. Allyl-TMS, a larger and less reactive nucleophile, in contrast can experiences significant 1,3-diaxial type interactions with axial substitutions at the C-3 and C-5 position of the pyranosyl ion as well as gauche interactions with the group at C-2. These interactions can induce a Curtin-Hammett kinetic scenario, in which the higher energy oxocarbenium ion conformer becomes the most relevant product forming intermediate.

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Donor	Calculated	TES-D		Allyl-TMS				
		Product	α:β	Product	α:β			
	a:p selectivity	(Yield)		(Yield)				
1 (Glucose)	>98:2	1A (70%)	>98:2	1B (71%)	>98:2			
2 (Mannose)	3:97	2A (93%)	3:97	2B (80%)	66:34			
3 (Galactose)	>98:2	3A (86%)	>98:2	3B (80%)	>98:2			
4 (Allose)	>98:2	4A (74%)	>98:2	4B (46%)	>98:2			
5 (Altrose)	4:96	5A (55%)	20:80	5B (68%)	89:11			
6 (Gulose)	>98:2	6A (83%)	>98:2	6B (71%)	>98:2			
7 (Idose)	90:10	7A (74%)	<2:98 ^a	7 B (n.d.) ^b	13:87			
8 (Talose)	52:48	8A (51%)	<2:98 ^a	8B (67%)	57:43			

 Table 2: predicted and experimental stereoselectivities of all 8 pyranosyl donors

^{*a*} determined after debenzylation followed by benzoylation. ^{*b*} an accurate determination of the yield is not possible due to poor separation from a side product.^{*†*} Calculated α : β ratios are based on methylated oxocarbenium ions, experimental α : β values are based on benzylated donors. The CEL maps and TES-D results of donors **1-3** were previously reported.²⁶

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The side product is the 1,6-anhydro product from donor 7, compound 61. This product forms in 81% yield when donor 7 is activated, but no nucleophile is added.



Figure 5: CEL maps of all pyranosyl oxocarbenium ions

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Conclusion

In conclusion, this chapter has investigated S_N1-like glycosylation reaction mechanisms and the influence of the substitution pattern of the glycosyl donor on the conformational preference of the involved oxocarbenium ions. To fuel these studies, synthetic routes towards all 8 possible diastereoisomeric β -thiophenol 2,3,4,6-tetra-Obenzyl pyranosyl donors, and their 6-deoxy-counterparts were developed. Next, the conformational preference of the oxocarbenium ions was mapped by the generation of CEL maps and the donors were reacted with both TES-D and allyl-TMS in order to trap the oxocarbenium ions. These results show that the stereochemical outcome of C-6deoxy and C-6-OBn donors to be very similar. Even for idose and talose, where the ${}^{1}C_{4}$ conformation of the C-6-OBn oxocarbenium ions was found to be found relatively favorable, the C-6-substituents does not significantly contribute to the stereochemical outcome. Another observation is that the stereochemistry of C-2 is a very important factor for the stereochemical outcome of the reactions with TES-D, since all TES-D reactions were highly 1,2-cis selective, even when the CEL maps predict a mixture or 1,2-trans selectivity. This 1,2-cis selectivity is correctly predicted in 12 out of 16 cases by the CEL maps. A striking difference in the stereoselectivity of the reactions with TES-D and allyl-TMS were observed for the pyranosides having an axial C-2-OBn. Where the TES-D reactions are all highly β -selective, the allyl-TMS reactions are either α -selective or proceed with relatively poor β -selectivity. For the reactions in which the ground state energy of the oxocarbenium ions proved to be a poor predictor of the stereoselectivity of the glycosylation reactions, Curtin Hammett kinetic scenarios were invoked to rationalize the outcome of the reactions. When developing steric interactions between the incoming nucleophile and the electrophile, as well as interactions developing between the substituents on the pyranosyl ring become prohibitively large, reactions on less favorable oxocarbenium ions can become attractive. To better understand the steric and electronic factors at play during the transition state of the reactions, future research will have to focus on computationally studying the transition state of these reactions, in which the donor oxocarbenium ions are systematically varied and paired with C-nucleophiles, of gradually changing nucleophilicity.

Experimental

Generation of CEL-maps and calculation of the expected stereochemistry based on the CELmaps

The generation of CEL-maps and the calculation of the expected stereoselectivity of the oxocarbenium ions based on the CEL-maps was performed as previously described by T. Hansen *et al.*²⁶

General experimental procedures

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 (Tf₂O) was distilled over P₂O₅ and stored at -20°C under a nitrogen atmosphere. 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.). Thin-layer chromatography (TLC) analysis was conducted on TLC silica gel 60 plates (Kieselgel 60 F254, Merck) with UV detection by (254 nm) and by spraying with 20% sulfuric acid in ethanol or by spraying with a solution of $(NH_4)_6Mo_7O_{24}$ ·H₂O (25 g/L) and $(NH_4)_4$ Ce(SO4)₄·2H₂O (10 g/L) in 10% ag. sulfuric acid followed by charring at ±250 °C. 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. 1H and 13C NMR spectra were recorded on Bruker AV-400, Bruker DMX-400, and Bruker AV-500 NMR instruments. Chemical shifts (δ) are given in parts per million (ppm) relative to tetramethylsilane as an internal standard or the residual signal of the deuterated solvent. Coupling constants (1) are given in Hertz (Hz). All presented 13C-APT spectra are protondecoupled. NMR peak assignments were made using COSY and HSQC. When necessary, additional NOESY, HMBC and HMBC-GATED 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 1H 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.

General procedure for Ph₂SO/Tf₂O meditated glycosylations

Donor (0.1 mmol, 1 eq), Ph₂SO (0.13 mmol, 1.3 eq) and TTBP (0.25 mmol, 2.5 eq) were coevaporated twice with toluene, dissolved in 2 mL DCM and stirred for 30 min at RT with 3Å molecular sieves. The solution was cooled to -80 °C and Tf₂O (22 μ L, 0.13 mmol, 2 eq) was added. The reaction mixture was allowed to warm to -60 °C and then recooled to -78 °C, after which the acceptor (2-6 eq) was added. The reaction mixture was allowed to warm to -60 °C for

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and stirred between 1-24 hr at that temperature. The reaction was quenched with 2 mL sat aq NaHCO₃ or 0.2 mL 1M Et₃N in DCM, 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 MgSO4, filtered, and concentrated in vacuo. Purification by silica gel flash column chromatography yielded the glycosylation product as a mixture of anomers.

General procedure for debenzylation followed by benzoylation

Benzylated product was dissolved in EtOH (0.05 M) with an equal weight of 5% Pd/C. the reaction mixture was flushed with N_2 (2x) and H_2 (2x) and kept under H_2 atmosphere overnight, after which it was flushed twice with N_2 , filtered over a plug of celite and concentrated under reduced pressure. The crude tri- or tetra-ol was coevaporated 3x with toluene and dissolved in pyridine (1 mL) and treated with BzCl (2 eq per OH). After 24 hr, the reaction mixture was diluted with EA and washed with 1M HCl and bicarb. The organic phase was dried with MgSO₄ and concentrated. Silica chromatography yields the benzoylated product.

Phenyl 3-O-benzoyl-4,6-O-benzylidene-1-thio-β-D-allopyranose (18)



Phenyl 4,6-O-benzylidene-1-thio-β-D-glucopyranose⁴⁴ (17, 7.21 g, 20 mmol), benzoic acid (3.66 g, 30 mmol, 1.5 eq) and triphenylphosphine (7.87 g, 30 mmol, 1.5 eq) were dissolved in THF and heated to a gentle reflux. DIAD (5.91 mL, 30 mmol,1.5 eq) was added dropwise over 5 min, after which TLC showed full conversion of the starting material. The reaction mixture was cooled to RT and concentrated under reduced pressure. The residue was dissolved in EtOAc and washed with sat. aq. NaHCO₃. The organic phase was dried with MgSO₄ and concentrated under reduced pressure. Purification over silica ($10\% \rightarrow 25\%$ acetone in pentane) yields the title compound as offwhite foam. Yield: 4.87 g, 10.5 mmol, 52%. ¹H NMR (400 MHz, CDCl₃) & 8.09 - 8.02 (m, 2H, CHarom), 7.70 - 7.63 (m, 2H, CHarom), 7.60 - 7.51 (m, 4H, CHarom), 7.49 - 7.41 (m, 4H, CHarom), 7.39 - 7.34 (m, 5H, CH_{arom}), 7.28 (dd, J = 5.1, 1.9 Hz, 3H, CH_{arom}), 6.01 (t, J = 2.8 Hz, 1H, H-3), 5.55 (s, 1H, CHPh), 5.00 (d, J = 9.8 Hz, 1H, H-1), 4.46 (dd, J = 10.6, 5.0 Hz, 1H, H-6), 4.15 (td, J = 9.9, 5.1 Hz, 1H, H-5), 3.80 (t, J = 10.4 Hz, 1H, H-6), 3.75 (dd, J = 9.5, 2.6 Hz, 2H, H-2, H-4), 2.75 (s, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 166.5 (C=O), 136.9 (C_q), 133.6, 133.5, 132.3, 132.2 (CH_{arom}), 132.1, 132.1 (C_q), 131.1, 130.0, 129.2, 128.7, 128.7, 128.6, 128.6, 128.4, 126.2 (CH_{arom}), 101.8 (CHPh), 86.5 (C-1), 77.0 (C-4), 70.4 (C-3), 69.2 (C-6), 69.0 (C-5), 67.8 (C-2);); HRMS: [M+NH₄]⁺ calcd for C₂₆H₂₄O₆SNH₄ 482.16318, found 487.16258

Phenyl 1-thio- β -D-allopyranose (19)

Compound **18** (3.17 g, 6.82 mmol) and pTsOH hydrate (130 mg, 0.68 mmol, 0.1 eq) were dissolved in methanol and heated to 50 °C. After TLC shows full removal of the benzylidene, the reaction mixture was cooled to RT and NaOMe (184 mg, 3.41 mmol, 0.5 eq) was added. After full deprotection, the solution was neutralised with Amberlite IR-120(H), filtered over celite and

concentrated. The residue was purified over silica (50% acetone in DCM), to yield the title compound as colourless oil. Yield: 1.51 g, 5.55 mmol, 81%. ¹H NMR (400 MHz, Acetone) δ 7.55 – 7.49 (m, 2H, CH_{arom}), 7.33 – 7.27 (m, 2H, CH_{arom}), 7.27 – 7.21 (m, 1H, CH_{arom}), 4.94 (d, *J* = 9.8 Hz, 1H, H-1), 4.14 (t, *J* = 3.0 Hz, 1H, H-3), 3.88 – 3.79 (m, 1H, H-6), 3.70 – 3.60 (m, 2H, H-5, H-6), 3.53 (dd, *J* = 9.7, 3.0 Hz, 1H, H-4), 3.41 (d, *J* = 10.1 Hz, 1H, H-2); ¹³C NMR (101 MHz, Acetone) δ 135.7 (C_q), 131.7, 129.6, 127.5 (CH_{arom}), 85.6 (C-1), 77.8 (C-5), 72.4 (C-3), 70.7 (C-2), 68.6 (C-4), 63.1 (C-6); HRMS: [M+Na]⁺ calcd for C₁₂H₁₆O₅S 295.06107, found 295.06054

Phenyl 2,3,4,6-tetra-O-benzyl-1-thio-β-D-allopyranose (4)

Compound 19 (1.63 g, 6 mmol, 1 eq) was dissolved in 50 mL DMF and cooled to 0°C, after which sodium hydride (60% dispersion in mineral oil, 1.44 g, 36 mmol, 6 eq.) was added portionwise. After stirring for an additional 30 minutes, benzyl bromide (4.28 mL, 36 mmol, 6 eq) was added and the mixture was allowed to warm to RT. Upon completion of the reaction, excess sodium hydride was destroyed carefully with water. The aqueous phase was extracted with diethyl ether, the organic phase washed with distilled water and brine, dried with Na₂SO₄ and concentrated under reduced pressure. The residue was purifed over silica (5% EtOAc in pentane) to give the title compound as a colourless oil that solidifies over time. Yield: 2.80 g, 4.42 mmol, 74%. $[\alpha]_{0.5}^{25} =$ -0.6° (c = 0.85, CHCl₃); IR (thin film): 697, 737, 1050, 1089; ¹H NMR (400 MHz, CDCl₃) δ 7.64 -7.49 (m, 2H, H-Ar), 7.40 - 7.14 (m, 23H, CH_{arom}), 5.24 (d, J = 9.7 Hz, 1H, H-1), 4.83 (d, J = 11.9 Hz, 1H, CHH Bn), 4.77 (d, J = 11.9 Hz, 1H, CHH Bn), 4.62 – 4.57 (m, 2H, 2x CHH Bn), 4.55 – 4.51 (m, 2H, 2x CHH Bn), 4.49 (d, J = 7.9 Hz, 1H, CHH Bn), 4.41 (d, J = 11.6 Hz, 1H, CHH Bn), 4.13 (t, J = 2.5 Hz, 1H, H-3), 4.09 (ddd, J = 9.8, 4.5, 1.9 Hz, 1H, H-5), 3.80 (dd, J = 10.9, 1.9 Hz, 1H, H-6), 3.71 (dd, *J* = 10.9, 4.5 Hz, 1H, H-6), 3.49 (dd, *J* = 9.8, 2.4 Hz, 1H, H-4), 3.31 (dd, *J* = 9.8, 2.4 Hz, 1H, H-2); ¹³C NMR (101 MHz, CDCl₃) δ 139.0, 138.6, 138.0, 137.9, 134.1 (C_q), 131.9, 128.8, 128.6, 128.5, 128.5, 128.5, 128.4, 128.3, 128.3, 128.1, 128.1, 128.0, 128.0, 127.9, 127.9, 127.7, 127.5, 127.5, 127.2 (C-Ar), 83.9 (C-1), 78.0 (C-2), 75.6 (C-4), 75.2 (C-5), 74.4 (CH₂ Bn), 73.7 (C-3), 73.5 (CH₂ Bn), 72.5 (CH₂ Bn), 71.7 (CH₂ Bn), 69.4 (C-6); HRMS: [M+NH₄]⁺ calcd for C40H40O5SNH4 650.29347, found 650.29182

Methyl 2,3-anhydro-4,6-O-benzylidene-α-D-allopyranoside (22)



Compound 20⁴⁴ (25.7 g, 91.2 mmol) was dissolved in pyridine (150 mL) and cooled to 0°C. methane sulfonyl chloride (21,2 mL, 273 mmol, 3 eq.) was added dropwise. The mixture was diluted with EA and washed with water and twice with brine. The organic layer was dried with MgSO₄ and concentrated in vacuo to obtain the crude dimesylate 21 which was used without further purification. Crude compound 21 (\leq 91.2 mmol) was dissolved in THF/MeOH (750 mL, 2:3, v:v). KOH (15.3 g, 273 mmol, 3 eq.) was added. The reaction mixture was refluxed overnight at 70°C. The mixture was concentrated to about 20% of the volume. Water was added, and the compound was extracted with EA. The organic fraction was washed with water 3 times. The organic layer was dried with MgSO₄ and concentrated in vacuo. The crude product was

concentrated in vacuo. The residue was purified by multiple crystallizations in an EA/pentane mixture and yielded the title compound as a fluffy off-white solid. Yield: 10.5 g, 39.8 mmol, 43% over 2 steps. ¹H NMR (400 MHz, CDCl₃) δ 7.55 – 7.45 (m, 2H, CH_{arom}), 7.43 – 7.31 (m, 3H, CH_{arom}), 5.57 (s, 1H, CHPh), 4.89 (d, *J* = 2.70 Hz, 1H, H-1), 4.24 (dd, *J* = 10.3, 5.0, 1H, H-6), 4.09 (ddd, *J* = 10.3, 9.1, 5.0 Hz, 1H, H-5), 3.96 (dd, *J* = 9.1, 1.2 Hz, 1H, H-4), 3.69 (t, *J* = 10.3 Hz, 1H, H-6), 3.53 (dt, *J* = 4.2, 1.1 Hz, 1H, H-3), 3.49 (dd, *J* = 4.3, 2.8 Hz, 1H, H-2), 3.47 (s, 3H, CH₃ OMe), ¹³C NMR (101 MHz, CDCl₃) δ 137.2 (C_q), 129.4, 128.5, 126.4 (CH_{arom}), 102.9 (CHPh), 95.4 (C-1), 78.0 (C-4), 69.0 (C-6), 60.1 (C-5), 56.0 (OMe), 53.3 (C-2), 50.9 (C-3). Spectra in agreement with literature.¹²

1,2,3,4,6-penta-O-acetyl-α,β-D-altropyranoside (23)



Compound **22** (5.29 g, 20 mmol) was suspended in 30 mL Ac₂O and cooled to 0 °C. After dropwise addition of 0.6 mL H₂SO₄ in 30 mL Ac₂O, the reaction mixture was allowed to warm to RT and stirred overnight. The reaction mixture was poured in ice water and extracted twice with diethyl ether. Combined organic phases were washed with sat. aq. NaHCO₃, dried with MgSO₄ and concentrated. Purification with silica chromatography (15→25% acetone in pentane) yields the title compound as yellow oil which solidifies over time. Yield: 5.83 g, 14.9 mmol, 75%, major anomer (1): minor anomer (2) = 1 : 0.6, with traces of furanosides. ¹H NMR (400 MHz, CDCl₃) δ 6.16 (d, *J* = 2.0 Hz, 0.6H, H-1₂), 6.01 (t, *J* = 1.2 Hz, 1H, H-1₁), 5.44 (dd, *J* = 5.6, 3.3 Hz, 0.6H), 5.32 (td, *J* = 3.6, 1.0 Hz, 1H), 5.24 – 5.21 (m, 1H), 5.19 (dd, *J* = 5.7, 2.4 Hz, 1H), 4.99 (dd, *J* = 3.7, 1.5 Hz, 1H), 4.39 (td, *J* = 4.6, 2.0 Hz, 0.6H), 4.37 – 4.27 (m, 2H), 4.23 (t, *J* = 3.1 Hz, 0.6H), 4.20 (t, *J* = 2.8 Hz, 0.3H), 4.16 (dd, *J* = 12.1, 2.1 Hz, 1H), 2.21 – 2.00 (m, 24H, CH₃ Ac), ¹³C NMR (101 MHz, CDCl₃) δ 170.8, 170.7, 169.6, 169.6, 169.5, 169.3, 169.3, 169.1, 168.8, 168.4 (C=O), 90.5 (C-1₁), 90.1 (C-1₂), 72.2, 68.4, 67.4, 66.7, 66.6, 65.5, 64.6, 62.8 (C-6₂), 62.4 (C-6₁), 21.0, 20.9, 20.9, 20.8, 20.8, 20.7 (CH₃ Ac). Spectra in agreement with literature.³³

Phenyl 2,3,4,6-tetra-O-acetyl-1-thio-β-D-altropyranoside (25)



Compound **23** (5.80 g, 14.9 mmol) was dissolved in DCM and cooled to 0 °C. SOCl₂ (2.10 mL, 29.7 mmol, 2 eq) was added, followed by SnCl₄ (1M in DCM, 14.9 mL, 14.9 mmol, 1 eq). After TLC shows full conversion, the reaction mixture was quenched with ice water and extracted twice with DCM. Combined organic phases were washed with sat. aq. NaHCO₃, dried with MgSO₄ and concentrated, yielding chloride **24**, which was immediately dissolved in DMF. The solution was cooled to 0 °C, and thiophenol (2.12 mL, 20.8 mmol, 1.4 eq) and sodium hydride (60% dispersion in mineral oil, 713 mg, 17.8 mmol, 1.2 eq) were added. After full conversion, the reaction mixture was diluted with water and extracted twice with diethyl ether. The organic phases were dried with MgSO₄ and concentrated, yielding crude **25** as an α , β -mixture from which the desired β -anomer was isolated as white solid by silica chromatography (10 \rightarrow 20% acetone in pentane), followed by recrystallization from the same solvents. Yield: 3.78 g, 8.58 mmol, 58%. ¹H

NMR (400 MHz, CDCl₃) δ 7.58 – 7.53 (m, 2H, CH_{arom}), 7.36 – 7.30 (m, 3H, CH_{arom}), 5.41 (t, J = 3.4 Hz, 1H, H-3), 5.22 (dd, J = 3.7, 1.5 Hz, 1H, H-2), 5.19 (d, J = 1.5 Hz, 1H, H-1), 5.12 (dd, J = 10.4, 3.2 Hz, 1H, H-4), 4.28 – 4.20 (m, 2H, 2x H-6), 4.09 (ddd, J = 10.4, 5.5, 3.5 Hz, 1H, H-5), 2.22 (s, 3H, CH₃ Ac), 2.12 (s, 3H, CH₃ Ac), 2.11 (s, 3H, CH₃ Ac), 1.99 (s, 3H, CH₃ Ac); ¹³C NMR (101 MHz, CDCl₃) δ 170.8, 169.6, 169.6, 169.0 (C=O), 133.9 (C_q), 131.7, 129.1, 128.0 (CH_{arom}), 83.9 (C-1), 72.8 (C-5), 71.2 (C-2), 67.2 (C-3), 65.5 (C-4), 63.3 (C-6), 20.9, 20.9, 20.8, 20.7 (CH₃ Ac); ¹³C HMBC-GATED NMR (101 MHz, CDCl₃): δ 83.9 ($J_{H1-C1} = 157$ Hz, β); HRMS: [M+NH₄]⁺ calcd for C₂₀H₂₄O₉SNH₄ 458.14793, found 458.14698

Phenyl 2,3,4,6-tetra-O-benzyl-1-thio-β-D-altropyranoside (5)



Compound 25 (1.50 g, 3.41 mmol) was dissolved in methanol with NaOMe (46 mg, 0.85 mmol, 0.25 eq). After TLC shows full deacetylation, the reaction mixture was neutralised with amberlite IR-120(H), filtered and concentrated under reduced pressure to yield crude tetra-ol 26, which was used without further purification. Compound 26 was dissolved in DMF, and NaH (60% dispersion in mineral oil, 0.681 g, 17.03 mmol, 5 eq) and benzyl bromide (2.02 mL, 17.03 mmol, 5 eq) were added. After completion, the reaction was quenched with water and extracted with diethyl ether. The organic phase was dried with Na₂SO₄ and concentrated under reduced pressure. The residue was purified over silica (5% EtOAc in pentane), obtaing the title compound as colourless oil. Yield: 1.82 g, 2.88 mmol, 84% over 2 steps. $[\alpha]_D^{25} = -12.2^\circ$ (c = 0.88, CHCl₃); IR (thin film): 698, 750, 1027, 1070, 1454; ¹H NMR (400 MHz, CDCl₃) & 7.55 - 7.50 (m, 2H, CH_{arom}), 7.36 - 7.25 (m, 16H, CH_{arom}), 7.24 - 7.16 (m, 7H, CH_{arom}), 5.23 (d, J = 1.4 Hz, 1H, H-1), 4.65 - 7.25 (m, 16H, CH_{arom}), 7.24 - 7.16 (m, 7H, CH_{arom}), 7.23 (d, J = 1.4 Hz, 1H, H-1), 4.65 - 7.25 (m, 16H, CH_{arom}), 7.24 - 7.16 (m, 7H, CH_{arom}), 7.23 (d, J = 1.4 Hz, 1H, H-1), 4.65 - 7.25 (m, 16H, CH_{arom}), 7.24 - 7.16 (m, 7H, CH_{arom}), 7.16 - 7.16 (m, 7H, 4.59 (m, 2H, 2x CHH Bn), 4.56 (d, J = 11.6 Hz, 2H, CHH Bn ,CHH Bn), 4.47 - 4.41 (m, 2H, 2x CH*H* Bn), 4.34 (s, 2H, CH₂ Bn), 4.12 (ddd, *J* = 10.1, 6.6, 1.9 Hz, 1H, H-5), 3.87 (dd, *J* = 11.0, 1.9 Hz, 1H, H-6), 3.79 (dd, J = 10.1, 2.7 Hz, 1H, H-4), 3.73 (dd, J = 3.7, 1.4 Hz, 1H, H-2), 3.72 - 3.67 (m, 2H, H-3, H-6); 13 C NMR (101 MHz, CDCl₃) δ 138.8, 138.2, 138.0, 137.9, 136.0 (C_q), 130.5, 128.9, 128.6, 128.5, 128.5, 128.5, 128.3, 128.3, 128.2, 128.0, 128.0, 127.9, 127.9, 127.5, 126.8 (CH_{aron}), 85.0 (C-1), 78.8 (C-2), 75.8 (C-5), 73.7, 73.6 (CH₂ Bn), 73.1 (C-4), 73.1 (CH₂ Bn), 72.6 (C-3), 71.8 (CH₂ Bn), 70.3 (C-6); HRMS: [M+NH₄]⁺ calcd for C₄₀H₄₀O₅SNH₄ 650.29347, found 650.29153

Phenyl-2,3,4,6-tetra-O-benzyl-1-thio-β-D-gulopyranoside (6)



The title compound was synthesised in 8 steps as previously described for the L-isomer from L-gulonolactone,³⁵ but with D-gulonolactone **27** as starting material. $[\alpha]_D^{25} = -9.2^{\circ}$ (c = 0.20, CHCl₃); IR (thin film): 741, 1001, 1028, 1076, 1101, 1207, 1360, 1439, 1454, 1497; ¹H NMR (400 MHz, CDCl₃) δ 7.67 – 7.60 (m, 2H, CH_{arom}), 7.41 – 7.25 (m, 21H, CH_{arom}), 7.18 – 7.12 (m, 2H, CH_{arom}), 5.30 (d, *J* = 9.9 Hz, 1H, H-1), 4.72 (d, *J* = 12.1 Hz, 1H, CHH Bn), 4.65 (d, *J* = 11.7 Hz, 1H, CHH Bn), 4.58 – 4.52 (m, 2H, CHH Bn, CHH Bn), 4.49 (d, *J* = 11.9 Hz, 1H, CHH Bn), 4.45 (d, *J* =

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11.8 Hz, 1H, CH*H* Bn), 4.37 (d, *J* = 12.0 Hz, 1H, C*H*H Bn), 4.32 (d, *J* = 12.0 Hz, 1H, CH*H* Bn), 4.20 (td, *J* = 6.4, 1.5 Hz, 1H, H-5), 3.82 (dd, *J* = 9.9, 2.9 Hz, 1H, H-2), 3.77 (t, *J* = 3.4 Hz, 1H, H-3), 3.72 (dd, *J* = 9.8, 6.3 Hz, 1H, H-6), 3.66 (dd, *J* = 9.8, 6.5 Hz, 1H, H-6), 3.57 (dd, *J* = 3.8, 1.4 Hz, 1H, H-4); ¹³C NMR (101 MHz, CDCl₃) δ 138.3, 138.3, 138.0, 138.0, 134.5 (C_q), 131.5, 128.7, 128.4, 128.4, 128.4, 128.0, 127.9, 127.9, 127.9, 127.8, 127.8, 127.6, 126.9 (CH_{arom}), 84.4 (C-1), 74.9, 74.8 (C-2, C-4), 74.5 (C-5), 73.4, 73.3 (CH₂ Bn), 73.1 (C-3), 72.8, 72.5 (CH₂ Bn), 69.0 (C-6); HRMS: calcd for C₄₀H₄₀O₅SNH₄ 650.29347, found 650.29166

1,2,3,4,6-Penta-O-acetyl-a-D-idopyranoside (31)



1,2,3,4,6-Penta-O-acetyl-B-D-glucopyranoside (28, 39.0 g, 100 mmol) was dissolved in 200 mL DCM and cooled to 0 °C after which SbCl₅ (15.4 mL, 120 mmol, 1.2 eq) was added. When dioxolenium ion 29 precipitated, the reaction mixture was warmed to RT and stirred for a further 15 minutes. The solids were filtered off, washed 3x with diethyl ether and suspended in 500 mL water with NaOAc (98 g, 1.2 mol, 12 eq). After 1 hr, the reaction mixture was extracted 3x with DCM. Combined organic phases were washed twice with sat. aq. NaHCO₃ and once with brine. After drying with MgSO4 and concentration under reduced pressure, a mixture of tetra-acetates 30a and 30b was obtained. The residue was dissolved in 60 mL pyridine and 20 mL Ac₂O and stirred overnight. The reaction mixture was diluted with DCM and washed with 1M HCl and sat. aq. NaHCO₃. Drying and concentration of the organic phase yields the pure title compound as yellowish oil. Yield: 13 g, 33 mmol, 33%. ¹H NMR (400 MHz, CDCl₃) δ 6.05 (d, J = 1.6 Hz, 1H, H-1), 5.06 (td, *J* = 3.8, 1.1 Hz, 1H, H-3), 4.93 (dd, *J* = 3.8, 2.4 Hz, 1H, H-4), 4.87 (ddd, *J* = 3.9, 2.2, 0.8 Hz, 1H, H-2), 4.47 (td, J = 6.3, 2.3 Hz, 1H, H-5), 4.25 - 4.13 (m, 2H, H-6), 2.13 - 2.11 (m, 9H, 3x CH₃ Ac), 2.11 (s, 3H, CH₃ Ac), 2.07 (s, 3H, CH₃ Ac); ¹³C NMR (101 MHz, CDCl₃) δ 170.5, 169.7, 169.1, 168.8, 168.5 (C=O), 90.6 (C-1), 66.6 (C-3), 66.3, 66.1, 66.1 (C-2, C-4, C-5), 61.8 (C-6), 20.8, 20.7, 20.7, 20.6 (CH₃ Ac). Spectra in agreement with literature.³⁶

Phenyl 2,3,4,6-tetra-O-acetyl-1-thio-β-D-idopyranoside (33)



Compound **31** (13 g, 33.3 mmol) was dissolved in 100 mL DCM, after which HBr (33% in AcOH, 29 mL, 167 mmol, 5 eq) was added. After full conversion, as indicated by TLC, the reaction mixture was diluted with DCM and washed twice with cold water. The organic phase was dried with MgSO₄ and concentrated under reduced pressure. The residue was coevaporated twice with toluene to yield crude bromide **32**, which was immediately dissolved in DMF. The solution was cooled to 0 °C and PhSH (5.10 mL, 50 mmol, 1.5 eq) and NaH (60% dispersion in mineral oil, 1.87g, 46.6 mmol, 1.4 eq) were added. The reaction mixture was allowed to warm to RT and stirred for a further 2 hr, after which the reaction was quenched with water and extracted with diethyl ether. The organic phase was dried with MgSO₄ and concentrated under reduced pressure

and the residue purified over silica (10%→20% acetone) to obtain the title compound as yellow oil. Yield: 8.16 g, 18.5 mmol, 56%. ¹H NMR (400 MHz, CDCl₃) δ 7.61 – 7.54 (m, 2H, CH_{arom}), 7.38 – 7.29 (m, 3H, CH_{arom}), 5.14 (d, *J* = 1.7 Hz, 1H, H-1), 5.12 (t, *J* = 2.7 Hz, 1H, H-3) 5.08 (ddd, *J* = 2.6, 1.7, 1.0 Hz, 1H, H-2), 4.86 (ddd, *J* = 2.8, 1.6, 1.0 Hz, 1H, H-4), 4.31 – 4.21 (m, 2H, H-6), 4.18 (ddd, *J* = 7.9, 4.8, 1.6 Hz, 1H, H-5), 2.20 (s, 3H, CH₃ Ac), 2.16 (s, 3H, CH₃ Ac), 2.14 (s, 3H, CH₃ Ac), 2.09 (s, 3H, CH₃ Ac); ¹³C NMR (101 MHz, CDCl₃) δ 170.5, 169.6, 169.4, 168.0 (C=O), 134.0 (C_q), 131.7, 131.5, 129.0, 127.9 (CH_{arom}), 84.4 (C-1), 73.5 (C-5), 68.2 (C-4), 66.7 (C-3), 64.8 (C-2), 62.6 (C-6), 20.8, 20.7, 20.7, 20.6 (CH₃ Ac); ¹³C-HMBC-GATED NMR (101 MHz, CDCl₃): δ 84.4 (*J*_{H1-C1} = 157 Hz, β); HRMS: [M+NH₄]⁺ calcd for C₂₀H₂₄O₉SNH₄ 458.14793, found 458.14678

Phenyl 2,3,4,6-tetra-O-benzyl-1-thio-β-D-idopyranoside (7)



Compound **33** was deactylated and benzylated as described for compound **5**, yielding the title compound as colourless oil. Yield: 3.40 g, 5.37 mmol, 73%; $[\alpha]_{D}^{25} = -42.7^{\circ}$ (c = 0.54, CHCl₃); IR (thin film): 698, 753, 1027, 1049 ; ¹H NMR (400 MHz, CDCl₃) δ 7.60 – 7.55 (m, 2H, CH_{arom}), 7.45 – 7.32 (m, 16H, CH_{arom}), 7.30 – 7.21 (m, 5H, CH_{arom}), 7.20 – 7.16 (m, 2H, CH_{arom}), 5.19 (d, *J* = 1.7 Hz, 1H, H-1), 4.68 (s, 2H, CH₂ Bn), 4.62 – 4.56 (m, 2H, 2x CHH Bn), 4.52 (d, *J* = 11.6 Hz, 1H, CHH Bn), 4.41 (d, *J* = 12.2 Hz, 1H, CHH Bn), 4.32 (d, *J* = 2.4 Hz, 2H, CH₂ Bn), 4.10 (ddd, *J* = 6.9, 5.3, 1.8 Hz, 1H, H-5), 3.89 (dd, *J* = 10.1, 6.8 Hz, 1H, H-6), 3.73 (dd, *J* = 10.2, 5.3 Hz, 1H, H-6), 3.71 – 3.67 (m, 2H, H-2, H-3), 3.40 (dt, *J* = 2.9, 1.4 Hz, 1H, H-4); ¹³C NMR (101 MHz, CDCl₃) δ 138.5 138.0, 137.8, 137.5, 136.5 (C_q), 130.3, 128.8, 128.7, 128.5, 128.4, 128.4, 128.1, 128.0, 127.9, 127.8, 127.6, 126.6 (CH_{arom}), 86.5 (C-1), 76.4 (C-5), 75.8 (C-2/C-3), 73.6, 73.4, 72.2, 72.1 (CH₂ Bn), 71.7 (C-4), 71.1 (C-2/C-3), 70.1 (C-6); HRMS: calcd for C₄₀H₄₀O₅SNH₄ 650.29347, found 650.29149

Phenyl 3,4-O-isopropylidene-6-O-triisopropylsilyl-1-thio-β-D-galactopyranoside (36)



Phenyl 1-thio-β-D-galactopyranoside (**35**, 8.17 g, 30 mmol) was dissolved in DMF with imidazole (5.11 g, 75 mmol, 2.5 eq) and TIPS-Cl (8.35 mL, 39 mmol, 1.3 eq). After 3 hr, the reaction mixture was quenched with 10 mL methanol and concentrated under reduced pressure. The residue was dissolved in DCM and washed with 1M HCl and with sat. aq. NaHCO₃. The organic phase was dried with MgSO₄ and concentrated under reduced pressure. The residue was dissolved in 150 mL 2,2-dimethoxypropane with PTSA-H₂O (0.57 g, 3 mmol, 0.1 eq). After full conversion, triethylamine (0.82 mL, 6 mmol, 0.2 eq) was added and solvent removed *in vacuo*. Silica chromatography (15% EtOAc in pentane) yield the title compound as colourless oil. Yield: 8.00 g, 17.0 mmol, 57% over 2 steps. ¹H NMR (400 MHz, CDCl₃) δ 7.57 – 7.53 (m, 2H, CH_{arom}), 7.30 (dd, *J* = 5.1, 2.0 Hz, 3H, CH_{arom}), 4.46 (d, *J* = 10.3 Hz, 1H, H-1), 4.28 (dd, *J* = 5.4, 2.0 Hz, 1H, H-4), 4.08 (dd, *J* = 6.9, 5.3 Hz, 1H, H-3), 4.00 – 3.95 (m, 2H, 2x H-6), 3.85 (ddd, *J* = 6.9, 5.9, 2.1

Hz, 1H, H-5), 3.57 (ddd, J = 10.3, 6.9, 1.8 Hz, 1H, H-2), 2.50 (d, J = 2.0 Hz, 1H, OH), 1.43 (s, 3H, CH₃ isopropylidene), 1.33 (s, 3H, CH₃ isopropylidene), 1.17 – 1.03 (m, 21H, 6x CH₃ TIPS, 3x CH TIPS); ¹³C NMR (101 MHz, CDCl₃) δ 132.6 (C_q), 132.4, 129.1, 129.1, 128.1 (CH_{arom}), 110.2 (C_q isopropylidene), 88.5 (C-1), 79.0 (C-3), 77.6 (C-5), 73.3 (C-4), 71.8 (C-2), 62.6 (C-6), 28.3, 26.4 (CH₃ isopropylidene), 18.1, 18.1, 12.0 (CH₃ TIPS, CH TIPS); HRMS: [M+NH₄]⁺ calcd for C₂₄H₄₀O₅SSiNH₄ 486.27040, found 486.26949

Phenyl 3,4-O-isopropylidene-6-O-triisopropylsilyl-1-thio-β-D-talopyranoside (38)



Compound 36 (8.00 g, 17.0 mmol) was dissolved in DCM and Dess-Martin periodiane (10.9g, 25.6 mmol, 1.5 eq) was added. After full conversion, the reaction mixture was diluted with DCM and washed with sat. aq. Na₂S₂O₃. The organic phase was dried with MgSO₄ and concentrated to obain crude ketone 37 (94% yield) which was used without further purification. The ketone was dissolved in 1:1 THF/MeOH and cooled to 0 °C, after which NaBH₄ (1.21 g, 31.9 mmol, 2 eq) was added. After full conversion, the reaction mixture was concentrated. The residue was dissolved in ethyl acetate and washed with water. The organic phase was dried with MgSO4 and concentrated under reduced pressure. Silica chromatography (10% EtOAc in pentane) yields the title compound as colourless oil that solidifies upon standing. Yield: 5.02g, 10.7 mmol, 67% based on ketone 37. ¹H NMR (400 MHz, CDCl₃) δ 7.54 - 7.46 (m, 2H, CH_{arom}), 7.34 - 7.17 (m, 3H, CH_{arom}), 4.77 (d, J = 1.4 Hz, 1H, H-1), 4.30 - 4.18 (m, 2H, H-3, H-4), 4.05 - 3.96 (m, 3H, H-2, 2x H-6), 3.89 – 3.82 (m, 1H, H-5), 2.57 (d, J = 9.0 Hz, 1H, OH), 1.62 (s, 3H, CH₃ isopropylidene), 1.38 (s, 3H, CH₃ isopropylidene), 1.16 - 0.98 (m, 21H, 6x CH₃ TIPS, 3x CH TIPS); ¹³C NMR (101 MHz, CDCl₃) δ 135.8 (C_q), 130.8, 129.0, 127.2 (CH_{arom}), 110.1(C_q isopropylidene), 88.0 (C-1), 77.3 (C-5), 74.0 (C-3), 71.0 (C-4), 68.1 (C-2), 62.7 (C-6), 25.9, 25.5(CH₃ isopropylidene), 18.1, 18.1, 12.0 (CH₃ TIPS, CH TIPS); HRMS: [M+NH₄]⁺ calcd for C₂₄H₄₀O₅SSiNH₄ 486.27040, found 486.26972

Phenyl 2,3,4,6-tetra-O-benzyl-1-thio-β-D-talopyranoside (8)

BnO BnO BnO SPh

Compound **38** (4.90 g, 10.5 mmol) and PTSA-H₂O (0.40 g, 2.10 mmol, 0.2 eq) were dissolved in methanol and heated to a reflux. After TLC shows full deprotection, triethylamine (0.43 mL, 3.14 mmol, 0.3 eq) was added and the reaction mixture was concentrated under reduced pressure, yielding crude tetra-ol **39**, which was coevaporated twice with toluene, dissolved in DMF and treated with benzyl bromide (6.8 mL, 57.5 mmol, 5.5 eq) and sodium hydride (60% dispersion in mineral oil, 2.30 g, 57.5 mmol, 5.5 eq). After full conversion, the reaction mixture was quenched with water and extracted with diethyl ether. The organic phase was dried with MgSO₄ and concentrated. Recrystallization from EtOAc/pentane yields the title compound as white powder. Yield: 4.20 g, 6.64 mmol, 64% over 2 steps. $[\alpha]_D^{25} = -38.7^\circ$ (c = 0.30, CHCl₃); IR (thin film): 695, 737, 1027, 1069, 1362, 1454; ¹H NMR (400 MHz, CDCl₃) δ 7.49 (ddt, *J* = 11.0, 7.7, 1.6 Hz, 4H, CH_{arom}), 7.38 – 7.16 (m, 21H, CH_{arom}), 5.06 (d, *J* = 11.7 Hz, 1H, CHH Bn), 5.01 – 4.91 (m, 2H,

CHH Bn, CHH Bn), 4.80 – 4.71 (m, 2H, H-1, CHH Bn), 4.59 (d, J = 1.5 Hz, 2H, CH₂ Bn), 4.51 (d, J = 11.5 Hz, 1H, CHH Bn), 4.44 (d, J = 11.5 Hz, 1H, CHH Bn), 4.12 (dt, J = 2.9, 1.3 Hz, 1H, H-2), 3.91 (dt, J = 3.0, 1.4 Hz, 1H, H-4), 3.84 (dd, J = 9.8, 6.2 Hz, 1H, H-6), 3.76 (dd, J = 9.8, 5.8 Hz, 1H, H-6), 3.60 (td, J = 6.1, 1.5 Hz, 1H, H-5), 3.50 (t, J = 3.0 Hz, 1H, H-3); ¹³C NMR (101 MHz, CDCl₃) δ 139.0, 138.7, 138.2, 137.8, 136.3 (C_q), 130.7, 128.8, 128.6, 128.4, 128.4, 128.3, 128.1, 128.0, 127.9, 127.8, 127.7, 127.4, 127.3, 127.3, 126.9 (CH_{arom}), 89.0 (C-1), 81.0 (C-3), 79.1 (C-5), 76.3 (C-2), 74.8, 74.0, 73.7 (CH₂ Bn), 72.1 (C-4), 71.0 (CH₂ Bn), 69.9 (C-6); HRMS: calcd for C₄₀H₄₀O₅SNH₄ 650.29347, found 650.29169

Phenyl 6-deoxy-2,3,4-tri-O-benzyl-1-thio-β-D-glucopyranoside (9)

Phenyl 2,3,4-tri-O-benzyl-1-thio-β-D-glucopyranoside⁴⁵ (40, 0.95 g, 1.75 mmol) was dissolved in 5 mL pyridine with p-TsCl (0.50 g, 2.63 mmol, 1.5 eq). After full conversion, the reaction mixture was diluted with EtOAc and washed with 1M HCl and sat. aq. NaHCO3. The organic phase was dried with MgSO₄ and concentrated under reduced pressure, yielding the crude tosylate 41, which was dissolved in THF with LiAlH₄ (1M sln in THF, 7 mL, 7 mmol, 4 eq) and heated to 70 °C. After full conversion, the reaction mixture was cooled to 0 °C and carefully quenched with 1M HCl, after which the reaction mixture was extracted with EtOAc. The organic phase was washed with sat. aq. NaHCO₃, dried with MgSO₄ and concentrated under reduced pressure. Silica chromatography (10% Et₂O in pentane) yields the title compound as white solid. Yield: 0.43 g, 0.82 mmol, 47% over 2 steps. ¹H NMR (400 MHz, CDCl₃) δ 7.56 - 7.52 (m, 2H, CH_{arom}), 7.39 (dd, J = 8.0, 1.5 Hz, 2H, CH_{arom}), 7.36 - 7.25 (m, 16H, CH_{arom}), 4.93 - 4.82 (m, 4H, 3x CHH Bn, CHH Bn), 4.75 (d, J = 10.2 Hz, 1H, CHH Bn), 4.68 – 4.63 (m, 2H, H-1, CHH Bn), 3.67 (t, J = 8.9 Hz, 1H, H-3), 3.49 (dd, J = 9.7, 9.0 Hz, 1H, H-2), 3.42 (dq, J = 9.5, 6.1 Hz, 1H, H-5), 3.23 (t, J = 9.2 Hz, 1H, H-4), 1.35 (d, J = 6.1 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 138.5, 138.2, 134.0 (C_a), 132.0, 129.0, 128.6, 128.5, 128.3, 128.1, 128.0, 128.0, 128.0, 127.9, 127.6 (CH_{arom}), 87.6 (C-1), 86.7 (C-3), 83.4 (C-4), 81.4 (C-2), 75.9 (CH₂ Bn), 75.7 (C-5), 75.6, 75.5 (CH₂ Bn), 18.3 (C-6). Spectra in agreement with literature.46

Phenyl 2,3-di-O-benzyl-4,6-O-benzylidene-1-thio-β-D-allopyranose (43)

Phenyl 4,6-O-benzylidene-1-thio- β -D-glucopyranose (17, 2.74 g, 7.60 mmol), benzoic acid (1.39 g, 11.4 mmol, 1.5 eq) and triphenylphosphine (2.99 g, 11.4 mmol,1.5 eq) were dissolved in THF and heated to a gentle reflux. DIAD (2.25 mL, 11.4 mmol,1.5 eq) was added dropwise over 5 min, after which TLC showed full conversion of the starting material. The reaction mixture was cooled to RT and concentrated under reduced pressure. The residue was filtered over a short plug of silica (25% EA) to remove triphenylphosphine oxide, yielding impure product **18**. This was then dissolved in methanol and treated with NaOMe (0.5g). After debenzoylation, the reaction mixture was dissolved in DMF and NaH (60% dispersion in mineral oil, 1.21 g, 30.1 mmol, 4 eq) and benzyl bromide (3.58 mL, 30.1 mmol 4 eq) were added. After 4 hr, the reaction was quenched

with water and extracted with diethyl ether. The organic phase was dried with MgSO₄ and concentrated. The residue was purified over silica (100% toluene) to give the title compound as colourless oil. Yield: 1.30 g, 2.40 mmol, 32% over 3 steps. ¹H NMR (400 MHz, CDCl₃) δ 7.55 – 7.25 (m, 20H, CH_{arom}), 5.47 (s, 1CHPh), 5.25 (d, *J* = 9.8 Hz, 1H, H-1), 4.89 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.78 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.54 (d, *J* = 2.5 Hz, 2H, CH₂ Bn), 4.38 (dd, *J* = 10.4, 5.2 Hz, 1H, H-6), 4.21 – 4.12 (m, 2H, H-3, H-5), 3.72 (t, *J* = 10.4 Hz, 1H, H-6), 3.52 (dd, *J* = 9.5, 2.1 Hz, 1H, H-4), 3.38 (dd, *J* = 9.8, 2.7 Hz, 1H, H-2); ¹³C NMR (101 MHz, CDCl₃) δ 138.7, 137.6, 137.5 (C_q), 133.3, 132.2, 129.3, 128.9, 128.6, 128.5, 128.3, 128.2, 128.2, 128.0, 127.6, 126.3 (CH_{arom}), 102.1 (CHPh), 84.7 (C-1), 79.9 (C-4), 77.1 (C-2), 74.1 (CH₂ Bn), 73.8 (C-3), 72.1 (CH₂ Bn), 69.4 (C-6), 66.4 (C-5); HRMS: [M+NH₄]⁺ calcd for C₃₃H₃₂O₅SNH₄ 558.23087, found 558.22995

Phenyl 6-deoxy-2,3,4-tri-O-benzyl-1-thio-β-D-allopyranose (12)

Phenyl 2,3-di-O-benzyl-4,6-O-benzylidene-1-thio-β-D-allopyranose (43, 1.25 g, 2.31 mmol) was dissolved in 7 mL of a 1M BH₃-THF solution in THF (7 mL, 6.94 mmol, 3 eq) and CoCl₂ (900 mg, 6.94 mmol, 3 eq) was added. After TLC shows full conversion of the stm, the reaction was diluted with ethyl acetate and filtered over celite. Water was added, and under vigorous stirring, excess CoCl₂ was reduced with NaBH₄. Solids were filtered off and the phases were separated. The organic phase was dried with MgSO4 and concentrated, yielding crude Phenyl 2,3,4-tri-Obenzyl-1-thio- β -D-allopyranose (44) which was used without further purification. This compound was dissolved in DCM with DMAP (1.13 g, 9.25 mmol, 4 eq) and p-TsCl (881 mg, 4.62 mmol, 2 eq). After full conversion, the reaction mixture was diluted with EtOAc and washed with 1M HCl and sat. aq. NaHCO3. The organic phase was dried with MgSO4 and concentrated under reduced pressure, vielding the crude tosylate, which was dissolved in THF with LiAlH₄ (1M sln in THF, 9.3 mL, 9.3 mmol, 4 eq) and heated to 70 °C. After full conversion, the reaction mixture was cooled to 0 °C and carefully quenched with 1M HCl, after which the reaction mixture was extracted with EtOAc. The organic phase was washed with sat. aq. NaHCO₃, dried with MgSO4 and concentrated under reduced pressure. Silica chromatography (10% Et2O in pentane) yields the title compound as colourless oil. Yield: 588 mg, 1.12 mmol, 48% over 3 steps. $[\alpha]_D^{25} = 21.2^\circ$ (c = 1.44, CHCl₃); IR (thin film): 697, 750, 1049, 1089, 1454; ¹H NMR (400 MHz, CDCl₃) δ 7.55 - 7.50 (m, 2H, CH_{arom}), 7.39 - 7.21 (m, 18H, CH_{arom}), 5.24 (d, J = 9.8 Hz, 1H, H-1), 4.84 (d, J = 11.9 Hz, 1H, CHH Bn), 4.77 (d, J = 11.9 Hz, 1H, CHH Bn), 4.63 (d, J = 11.6 Hz, 1H, CHH Bn), 4.56 (d, J = 11.6 Hz, 1H, CHH Bn), 4.52 (d, J = 11.7 Hz, 1H, CHH Bn), 4.39 (d, J = 11.7 Hz, 1H, CHH Bn), 4.13 (t, J = 2.4 Hz, 1H, H-3), 4.01 (dq, J = 9.5, 6.2 Hz, 1H, H-5), 3.30 (dd, J = 9.8, 2.5 Hz, 1H, H-2), 3.02 (dd, J = 9.5, 2.3 Hz, 1H, H-4), 1.28 (d, J = 6.2 Hz, 3H, H-6); ¹³C NMR $(101 \text{ MHz}, \text{CDCl}_3) \delta 139.0, 137.9, 134.2 \text{ (C}_q), 131.6, 128.8, 128.5, 128.3, 128.1, 128.0, 128.0, 127.9, 128.0$ 127.5, 127.2 (CHarom), 83.8 (C-1), 80.9 (C-4), 78.5 (C-2), 74.4 (CH2 Bn), 73.2 (C-3), 72.6 (CH2 Bn), 71.6 (C-5), 71.6 (CH₂ Bn), 18.3 (C-6); HRMS: [M+NH₄]⁺ calcd for C₃₃H₃₄O₄SNH₄ 544.25161, found 544.25045

Phenyl 2,3,4-tri-O-benzyl-6-O-triisopropylsilyl-1-thio-β-D-altropyranoside (46)

TIPSO Bno Bno Bno SPh

Compound 26 (1.47 g, 5.39 mmol) was dissolved in dry DMF (15 mL). Imidazole (917 mg, 13.5 mmol, 2.5 eq.) and then TIPS-Cl (1.49 mL, 7.01 mmol, 1.3 eq.) where added to the mixture. The reaction was stirred until TLC showed full conversion. The mixture was then guenched with methanol (743 µL, 18.4 mmol, 10 eq.) and diluted in water. The aqueous laver was then 3 times extracted with DCM. The combined organic layers where then washed with 0.1 M aq. HCl and sat. aq. bicarb. The organic layer was diluted dried with MgSO4 and concentrated in vacuo. This yielded a crude TIPS compound which was not characterized and immediately used in the next reaction. The TIPS compound was dissolved in dry DMF (20 mL) and cooled to 0°C. NaH (60% dispersion in mineral oil, 1.08 g, 26.6 mmol, 5 eq.) was added in portions. The mixture was stirred for 30 minutes. Benzyl Bromide (3.20 mL, 26.6 mmol, 5 eq.) was added. The mixture was stirred for 30 minutes before being allowed to warm to room temperature. The reaction was stirred until TLC showed full conversion. The mixture was slowly quenched with water and extracted with a diethyl ether/pentane (1:1) mixture. The organic layer was washed with water and brine. After which it was dried using MgSO4 and concentrated in vacuo. The residue was purified over silica (1% EA in pentane) to yield the title compound as a colourless oil. Yield: 3.13 g, 4.57 mmol, 85%. ¹H NMR (400 MHz, CDCl₃) δ 7.55 - 7.49 (m, 2H,CH_{arom}), 7.39 - 7.14 (m, 18H, CH_{arom}), 5.22 (d, J = 1.4 Hz, 1H, H-1), 4.64 (d, J = 12.2 Hz, 1H, CHH Bn), 4.58 (d, J = 12.2 Hz, 1H, CHH Bn), 4.56 (s, 2H, CH2 Bn), 4.46 (d, J = 12.3 Hz, 1H, CHH Bn), 4.43 (d, J = 12.2 Hz, 1H, CH*H* Bn), 4.36 (d, *J* = 1.6 Hz, 2H, CH₂ Bn), 4.03 (dd, *J* = 10.7, 1.8 Hz, 1H, H-6), 3.96 (ddd, *J* = 9.8, 6.1, 1.8 Hz, 1H, H-5), 3.83 (dd, J = 10.8, 6.1 Hz, 1H, H-6), 3.77 - 3.69 (m, 3H, H-2, H-3, H-4), 1.15 – 1.01 (m, 21H, CH₃ TIPS, CH TIPS); ¹³C NMR (101 MHz, CDCl₃) δ 138.3, 138.2, 138.1, 136.6 (C_q), 130.2, 128.8, 128.5, 128.2, 128.2, 128.1, 128.0, 127.9, 126.6 (CH_{arom}), 85.1 (C-1), 79.3 (C-2), 77.2 (C-5), 73.7, 73.1 (CH₂ Bn), 73.0, 72.8 (C-3, C-4), 71.8 (CH₂ Bn), 63.8 (C-6), 18.2, 18.2 (CH₃ TIPS), 12.1 (CH TIPS).

Phenyl 2,3,4-tri-O-benzyl-1-thio-β-D-altropyranoside (47)



Compound **46** (3.13 g, 4.57 mmol) was dissolved in THF (30 mL). A mixture of TFA/H₂O (1:1, 20 mL) was then added. The reaction was allowed to stir until the TLC showed full conversion. It was quenched with bicarb, extracted with EA and washed with brine. The organic layer was dried using MgSO₄ and concentrated in vacuo. The residue was purified over silica (20% EA in pentane) to yield the title compound as a colourless oil. Yield: 1.66 g, 3.05 mmol, 84%. ¹H NMR (400 MHz, CDCl₃) δ 7.45 (dd, *J* = 7.2, 1.8 Hz, 2H, CH_{arom}), 7.38 – 7.19 (m, 18H, CH_{arom}), 5.25 (d, *J* = 1.3 Hz, 1H, H-1), 4.58 (dd, *J* = 12.1, 4.2 Hz, 2H, CH₂ Bn), 4.45 (t, *J* = 11.7 Hz, 2H, CH₂ Bn), 4.39 (s, 2H, CH₂ Bn), 3.95 (ddd, *J* = 9.8, 5.4, 3.1 Hz, 1H, H-3), 3.89 (ddd, *J* = 11.8, 6.3, 3.1 Hz, 1H, H-6), 3.81 (dd, *J* = 9.8, 2.5 Hz, 1H, H-4), 3.78 – 3.68 (m, 3H, H-2, H-5, H-6), 2.16 (t, *J* = 6.7 Hz, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 138.1, 137.8, 137.6, 135.3 (C_q), 130.5, 129.1, 128.6, 128.6, 128.5, 128.5, 128.3, 128.1, 128.1, 128.0, 127.1 (CH_{arom}), 84.9 (C-1), 78.7 (C-5), 75.5 (C-3),

73.7, 73.2 (CH₂ Bn), 73.0 (C-4), 72.5 (C-2), 71.8 (CH₂ Bn), 63.0 (C-6); HRMS: [M+NH₄]⁺ calcd for C₃₃H₃₄O₅SNH₄ 560.24652, found 560.24545

Phenyl 6-deoxy-2,3,4-tri-O-benzyl-1-thio-β-D-altropyranoside (13)

Compound 47 (1.66 g, 3.05 mmol) was dissolved in pyridine (5 mL) and cooled to 0°C. Tosylchloride (871 mg, 4.57 mmol, 1.5 eq.) was added after which the mixture was allowed to warm to room temperature. The reaction was stirred till the TLC showed full conversion. The reaction was quenched with 0.1 M aq. HCl and extracted with diethyl ether. The organic layer was then washed with bicarb and brine. The organic layer was then dried using MgSO4 and concentrated in vacuo. This yielded a crude tosylate 48 which was immediately used in the next reaction. The tosylate was dissolved in THF (30 mL) and LiAlH4 (2.3 M in 2-methylhydrofuran, 5.30 mL, 12.2 mmol, 4 eq.) was added. The mixture was heated to reflux temperature and stirred till TLC showed full conversion. After which the mixture was cooled to 0°C and quenched with 1 M aq. HCl. The aqueous phase was then extracted twice with EA. The combined organic layers where then washed with bicarb and brine. The organic phase was then dried using MgSO4 and concentrated in vacuo. The residue was purified over silica (5% EA in pentane) to yield the title compound as a colourless oil. Yield: 1.03 g, 1.94mmol, 64%. $[\alpha]_D^{25} = 14.1^{\circ}$ (c = 0.35, CHCl₃); IR (thin film): 697, 748, 1027, 1088, 1454; ¹H NMR (400 MHz, CDCl₃) δ 7.51 - 7.45 (m, 2H, CH_{arom}), 7.38 – 7.19 (m, 18H, CH_{arom}), 5.19 (d, J = 1.5 Hz, 1H, H-1), 4.63 (d, J = 12.1 Hz, 1H, CHH Bn), 4.55 (d, J = 12.2 Hz, 1H, CHH Bn), 4.51 – 4.40 (m, 2H, CHH Bn, CHH Bn), 4.37 (s, 2H, CH₂Bn), 3.95 (dq, J = 9.7, 6.2 Hz, 1H, H-5), 3.73 (dd, J = 3.7, 1.5 Hz, 1H, H-2), 3.68 (t, J = 3.2 Hz, 1H, H-3), 3.51 (dd, J = 9.6, 2.7 Hz, 1H, H-4), 1.33 (d, J = 6.2 Hz, 3H, H-6), ¹³C NMR (101 MHz, CDCl₃) δ 130.6, 128.9, 128.6, 128.6, 128.5, 128.3, 128.2, 128.1, 128.0, 128.0, 127.0 (CH_{arom}), 84.9 (C-1), 78.9 (C-2), 77.8 (C-4), 73.8, 73.1 (CH₂Bn), 72.5 (C-3), 72.0 (CH₂Bn), 71.8 (C-5), 18.4 (C-6); HRMS: [M+NH4]⁺ calcd for C33H34O4SNH4 544.25161, found 544.25007

Phenyl 6-deoxy-3-O-acetyl-2,4-di-O-benzoyl-1-thio-\beta-L-gulopyranoside(50)

The title compound was synthesises in 5 steps from fucose building block **49** according to literature procedure.³⁷ ¹H NMR (400 MHz, CDCl₃) δ 8.01 – 7.93 (m, 4H, CH_{arom}), 7.65 – 7.53 (m, 4H, CH_{arom}), 7.50 – 7.42 (m, 4H, CH_{arom}), 7.41 – 7.30 (m, 3H, CH_{arom}), 5.60 (dd, *J* = 2.5, 1.4 Hz, 1H, H-3), 5.28 – 5.23 (m, 2H, H-1, H-2), 5.18 (dd, *J* = 3.8, 1.3 Hz, 1H, H-4), 4.33 (qd, *J* = 6.3, 1.2 Hz, 1H, H-5), 2.13 (s, 3H, CH₃ Ac), 1.30 (d, *J* = 6.5 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 169.0, 165.3, 164.9 (C=O), 134.0, 133.7, 133.4 (CH_{arom}), 131.3 (C_q), 130.1, 129.8 (CH_{arom}), 129.6, 129.1 (C_q), 128.9, 128.7, 128.6, 128.4 (CH_{arom}), 82.3 (C-1), 71.7 (C-5), 70.9 (C-4), 68.1 (C-3), 67.0 (C-2), 20.9 (CH₃ Ac), 16.5 (C-6).

Phenyl 6-deoxy-2,3,4-tri-O-benzyl-1-thio-β-L-gulopyranoside(14)

Compound 50 (1.60 g, 3.16 mmol) was dissolved in methanol with NaOMe (171 mg, 3.16 mmol, 1 eq) and stirred until TLC shows full deprotection. The reaction mixture was neutralised with amberlite, filtered and concentrated. The crude triol (51) was coevaporated twice with toluene and dissolved in DMF, after which NaH (60% dispersion in mineral oil, 505 mg, 12.6 mmol, 4 eq) and benzyl bromide (1.50 mL, 12.6 mmol, 4 eq) were added. After full conversion, the reaction was quenched with water and extracted with diethyl ether. The organic phase was dried with MgSO₄ and concentrated. Silica chromatography (5% to 10% diethyl ether in pentane) yields the title compound as colourless oil. Yield: 1.08 g, 2.05 mmol, 65%. $[\alpha]_D^{25} = -0.4^{\circ}$ (c = 0.48, CHCl₃); IR (thin film): 698, 753, 1042, 1454; ¹H NMR (400 MHz, CDCl₃) δ 7.62 – 7.55 (m, 2H, CH_{arom}), 7.36 - 7.21 (m, 16H, CHarom), 7.14 (dd, J = 7.0, 2.6 Hz, 2H, CHarom), 5.19 (d, J = 9.6 Hz, 1H, H-1), 4.70 (d, J = 12.1 Hz, 1H, CHH Bn), 4.60 (d, J = 11.7 Hz, 1H, CHH Bn), 4.48 (d, J = 12.2 Hz, 1H, CHH Bn), 4.39 (d, J = 11.7 Hz, 1H, CHH Bn), 4.33 (s, 2H, CH₂ Bn), 4.03 (qd, J = 6.5, 1.2 Hz, 1H, H-5), 3.78 - 3.68 (m, 2H, H-2, H-3), 3.20 (dd, J = 3.4, 1.4 Hz, 1H, H-4), 1.20 (d, J = 6.6 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 138.5, 138.2, 138.2, 134.8 (C_q), 131.6, 128.7, 128.5, 128.5, 128.4, 128.0, 127.9, 127.9, 127.9, 126.9 (CH_{arom}), 84.4 (C-1), 77.7 (C-4), 74.8 (C-2), 73.6 (C-3), 73.5, 73.0, 72.7 (CH₂ Bn), 71.5 (C-5), 16.5 (C-6); HRMS: [M+NH₄]⁺ calcd for C₃₃H₃₄O₄SNH₄ 544.25161, found 544.25079

Phenyl 6-deoxy-3,4-O-isopropylidene-1-thio-β-L-talopyranoside(54)



Known fucose intermediate 5247 (5.93 g, 20 mmol) was dissolved in DCM with Dess-Martin periodinane (12.7 g, 30 mmol, 1.5 eq) and NaHCO₃ (8.40 g, 100 mmol, 5 eq) were dissolved in dichloromethane. After TLC shows full conversion, the reaction mixture was washed with sat. aq. Na₂S₂O₃, dried with MgSO₄ and concentrated, yielding the crude ketone (53) which was used without further purification. The ketone was dissolved in 1:1 MeOH/THF and cooled to -10 °C, after which NaBH₄ (2.27 g, 60 mmol, 3 eq) was added in portions. After full conversion, the reaction mixture was concentrated, dissolved in ethyl acetate and washed with water. The organic phase was dried with MgSO4 and concentrated. The residue was purified with silica chromatography, yielding the title compound as colourless oil. Yield: 1.97 g, 6.65 mmol, 33%. ¹H NMR (400 MHz, CDCl₃) δ 7.54 – 7.47 (m, 2H, CH_{arom}), 7.34 – 7.22 (m, 3H, CH_{arom}), 4.73 (d, J = 1.4 Hz, 1H, H-1), 4.20 (dd, *J* = 5.8, 5.0 Hz, 1H, H-3), 4.02 (dd, *J* = 5.8, 2.6 Hz, 1H, H-4), 3.96 (ddd, *J* = 9.1, 4.7, 1.2 Hz, 1H, H-2), 3.86 (qd, *J* = 6.6, 2.7 Hz, 1H, H-5), 2.57 (d, *J* = 9.1 Hz, 1H, OH), 1.63 (s, 3H, CH₃ isopropylidene), 1.45 (d, J = 6.6 Hz, 3H, H-6), 1.40 (s, 3H, CH₃ isopropylidene); ¹³C NMR (101 MHz, CDCl₃) δ 135.5 (C_q), 131.2, 129.1, 127.4 (CH_{arom}), 109.8 (C_q isopropylidene), 87.6 (C-1), 74.2 (C-3), 73.9 (C-4), 72.5 (C-5), 67.8 (C-2), 25.9, 25.6 (CH₃ isopropylidene), 17.0 (C-6);); HRMS: [M+NH4]⁺ calcd for C15H20O4SNH4 314.14206, found 314.14148.

Phenyl 6-deoxy-2-O-benzoyl-3,4-O-isopropylidene-1-thio-β-L-talopyranoside(55)



Product **54** (1.95 g, 6.58 mmol) was dissolved in 20 mL 1:1 DCM/pyridine and BzCl (1.15 mL, 9.87 mmol, 1.5 eq) was added. After TLC shows full conversion, the reaction mixture was diluted with DCM and washed twice with a 1 M CuSO₄ sln. The organic phase was dried with MgSO₄ and concentrated. Silica chromatography (10 to 15% acetone in pentane) yields the title compound as white solid. Yield: 2.08 g, 5.19 mmol, 79%. ¹H NMR (400 MHz, CDCl₃) δ 8.27 – 8.19 (m, 2H, CH_{arom}), 7.65 – 7.56 (m, 1H, CH_{arom}), 7.49 (ddd, *J* = 8.0, 5.4, 1.5 Hz, 4H, CH_{arom}), 7.36 – 7.22 (m, 3H, CH_{arom}), 5.60 (dd, *J* = 5.7, 1.9 Hz, 1H, H-2), 4.94 (d, *J* = 1.9 Hz, 1H, H-1), 4.49 (t, *J* = 5.9 Hz, 1H, H-3), 4.10 (dd, *J* = 6.1, 2.7 Hz, 1H, H-4), 3.98 (qd, *J* = 6.5, 2.7 Hz, 1H, H-5), 1.57 (d, *J* = 6.6 Hz, 3H, H-6), 1.34 (s, 3H, CH₃ isopropylidene), 1.27 (s, 3H, CH₃ isopropylidene); ¹³C NMR (101 MHz, CDCl₃) δ 166.1 (C=O), 135.2, 133.3 (C_q), 131.0, 130.4, 129.9, 129.1, 128.5, 127.5 (CH_{arom}), 110.2 (C_q isopropylidene), 85.8 (C-1), 73.2 (C-4), 72.9 (C-5), 72.5 (C-3), 68.2 (C-2), 26.0, 25.5 (CH₃ isopropylidene), 17.2 (C-6); HRMS: [M+Na]⁺ calcd for C₂₂H₂₄O₅SNa 423.12367, found 423.12293.

Phenyl 6-deoxy-2,4-di-O-benzoyl -1-thio-β-L-talopyranoside(56)

BZO^{OH} OBZ

SPh

Product 55 (2.00 g, 4.99 mmol) was dissolved in methanol with 400 mg amberlite and heated to a gentle reflux. After isopropylidene removal, the reaction mixture was cooled to RT and filtered over celite. The filtrate was concentrated, coevaporated twice with toluene and dissolved in DCM. CSA (116 mg, 0.50 mmol, 0.1 eq) and trimethylorthobenzoate (1.29 mL, 7.49 mmol, 1.5 eq) were added and the reaction mixture was stirred for 24 hr, after which 10 mL of water was added. After vigorously stirring for another 24 hr, the reaction mixture was washed with sat. aq. NaHCO₃. The organic phase was dried with MgSO₄ and concentrated. Silica chromatography (25% EtOAc in pentane) yields the title compound as white solid. Yield: 1.24 g, 2.67 mmol 54%. ¹H NMR (400 MHz, CDCl₃) δ 8.21 - 8.16 (m, 2H, CH_{arom}), 8.05 - 8.00 (m, 2H, CH_{arom}), 7.61 -7.56 (m, 1H, CH_{arom}), 7.55 - 7.50 (m, 2H, CH_{arom}), 7.45 (tt, J = 7.7, 1.3 Hz, 1H, CH_{arom}), 7.41 -7.35 (m, 2H, CH_{arom}), 7.34 – 7.26 (m, 3H, CH_{arom}), 7.19 – 7.12 (m, 2H, CH_{arom}), 5.73 (ddd, J = 3.8, 1.3, 0.8 Hz, 1H, H-2), 5.41 (dd, J = 2.8, 1.1 Hz, 1H, H-4), 5.04 (d, J = 1.5 Hz, 1H, H-1), 4.24 (q, J = 3.9 Hz, 1H, H-3), 3.92 (qd, J = 6.3, 1.2 Hz, 1H, H-5), 3.32 (d, J = 5.1 Hz, 1H, OH), 1.41 (d, J = 6.5 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 167.7, 167.2 (C=O), 134.4 (C_q), 133.6, 133.3, 131.2, 130.5, 130.2 (CHarom), 129.4, 129.2 (Cq), 128.5, 128.2, 127.8 (CHarom), 86.5 (C-1), 74.4 (C-5), 72.3 (C-2), 70.9 (C-3), 70.2 (C-2), 17.2 (C-6); HRMS: [M+Na]⁺ calcd for C₂₆H₂₄O₆SNa 487.11858, found 487.11790.

Phenyl 6-deoxy-2,3,4-tri-O-benzyl -1-thio-β-L-idopyranoside(15)

OBn ·Ο SPh ÓBn BnO

Compound 56 (1.20 g, 2.58 mmol) was dissolved in DCM and cooled to -10 °C, after which pyridine (0.63 mL, 7.75 mmol, 3 eq) and Tf₂O (0.65 mL, 3.87 mmol, 1.5 eq) were added. After full conversion, the reaction mixture was washed with 1M HCl and sat. aq. NaHCO₃, dried with MgSO4 and concentrated at 25 °C. The triflate 57 was then dissolved in ACN and treated with TBANO₂ (1.49 g, 5.17 mmol, 2 eq) and heated to 80 °C. After 24 hr, the reaction mixture was cooled to RT and concentrated. Silica chromatography yields ca 0.4 g of very impure inverted product 58. This was then treated with 50 mg NaOMe in MeOH. After debenzoylation, the reaction mixture was quenched with amberlite, filtered and concentrated under reduced pressure. The crude triol was coevaporated 3x with toluene and dissolved in DMF, after which BnBr and NaH, both 4 eq based on pure compound 58, were added. After 4 hr, the reaction was quenched with water and extracted twice with Et₂O. Silica chromatography (5% Et₂O in pentane) yields the title compound as yellowish oil. Yield: 122 mg, 0.232 mmol, 9% over 4 steps. $[\alpha]_D^{25} =$ 20.8° (c = 0.07, CHCl₃); IR (thin film): 697, 1050, 1076, 1076, 1088, 1455; ¹H NMR (400 MHz, CDCl₃) δ 7.50 – 7.09 (m, 20H, CH_{arom}), 5.10 (d, J = 1.8 Hz, 1H, H-1), 4.64 (d, J = 1.8 Hz, 2H, CH₂ Bn), 4.58 (d, I = 12.4 Hz, 1H, CHH Bn), 4.38 (d, I = 12.4 Hz, 1H, CHH Bn), 4.31 (d, I = 12.1 Hz, 1H, CHH Bn), 4.23 (d, J = 12.1 Hz, 1H, CHH Bn), 3.88 (qd, J = 6.5, 1.7 Hz, 1H, H-5), 3.65 (t, J = 2.6 Hz, 1H, H-3), 3.61 (d, J = 2.7 Hz, 1H, H-2), 3.08 (s, 1H, H-4), 1.29 (d, J = 6.6 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 138.2, 138.0, 137.6, 136.8 (C_q), 130.4, 128.8, 128.7, 128.6, 128.4, 128.4, 128.1, 128.0, 127.9, 127.9, 126.6 (CH_{arom}), 86.4 (C-1), 75.5 (C-2), 74.0 (C-4), 73.4 (CH₂ Bn), 72.8 (C-5), 72.4, 72.1 (CH₂ Bn), 71.6 (C-3), 17.0 (C-6); HRMS: [M+NH₄]⁺ calcd for C₃₃H₃₄O₄S 544.25161, found 544.25040.

Phenyl 6-deoxy-2,3,4-tri-O-benzyl-1-thio-β-L-talopyranoside(16)



Compound 54 (0.60 g, 2.02 mmol) and PTSA-H₂O (0.04 g, 0.20 mmol, 0.1 eq) were dissolved in methanol and heated to 50 °c. After TLC shows full deprotection, the reaction mixture was concentrated under reduced pressure, yielding crude tri-ol nr, which was coevaporated twice with toluene, dissolved in DMF and treated with benzyl bromide (0.96 mL, 8.10 mmol, 4 eq) and sodium hydride (60% dispersion in mineral oil, 0.32 g, 8.10 mmol, 4 eq). After full conversion, the reaction mixture was quenched with water and extracted with diethyl ether. The organic phase was dried with MgSO₄ and concentrated under reduced pressure. Silica chromatography (5 to 10% acetone) yields the title compound as colourless oil. Yield: 800 mg, 1.52 mmol, 75%. $[\alpha]_D^{25}$ = 35.6° (c = 0.92, CHCl₃); IR (thin film): 695, 738, 1066, 1362, 1454; ¹H NMR (400 MHz, CDCl₃) δ 7.51 - 7.45 (m, 4H, CH_{arom}), 7.41 - 7.18 (m, 16H, CH_{arom}), 5.07 (d, J = 11.8 Hz, 1H, CHH Bn), 5.00 (d, J = 12.1 Hz, 1H, CHH Bn), 4.95 (d, J = 11.8 Hz, 1H, CHH Bn), 4.83 (d, J = 12.0 Hz, 1H, CHH Bn), 4.69 (d, J = 1.5 Hz, 1H, H-1), 4.59 (s, 2H, CH₂ Bn), 4.09 (dt, J = 2.8, 1.3 Hz, 1H, H-2), 3.64 - 3.60 (m, 1H, H-4), 3.52 - 3.44 (m, 2H, H-3, H-5), 1.34 (d, J = 6.4 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 139.2, 138.9, 138.0, 136.5 (C_q), 130.9, 128.8, 128.6, 128.5, 128.4, 128.1, 128.1, 127.9, 127.4, 127.4, 126.9 (CH_{arom}), 88.8 (C-1), 81.6 (C-3), 76.0 (C-5), 75.8 (C-2), 74.8 (CH₂ Bn), 74.6 (C-4), 74.3, 71.0 (CH₂ Bn), 17.6 (C-6); HRMS: [M+NH₄]⁺ calcd for C₃₃H₃₄O₄SNH₄ 544.25161, found 544.25024.

1,6-anhydro-2,3,4-tri-O-benzyl-D-idopyranoside (61)

Title compound was formed as side product in reactions 7A and 7B. When the idose donor 7 was reacted according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations, but no nucleophile was added, the product was formed in 81% yield after quenching after 24 hr. ¹H NMR (500 MHz, CDCl₃) δ 7.36 – 7.26 (m, 15H, CH_{arom}), 5.30 (d, *J* = 1.8 Hz, 1H, H-1), 4.84 (d, *J* = 2.2 Hz, 2H, CH₂ Bn), 4.73 – 4.70 (m, 2H, 2x CHH Bn), 4.68 (d, *J* = 11.9 Hz, 1H, CHH Bn), 4.62 (d, *J* = 11.8 Hz, 1H, CHH Bn), 4.39 (t, *J* = 4.6 Hz, 1H, H-5), 4.13 (dd, *J* = 7.7, 0.9 Hz, 1H, H-6), 3.78 (t, *J* = 8.1 Hz, 1H, H-3), 3.72 – 3.66 (m, 2H, H-4, H-6), 3.47 (dd, *J* = 7.9, 1.8 Hz, 1H, H-2);¹³C NMR (126 MHz, CDCl₃) δ 138.8, 138.2, 138.1 (C_q), 128.7, 128.6, 128.5, 128.1, 128.1, 128.0, 128.0, 127.8, 127.8 (CH_{arom}), 99.8 (C-1), 82.6 (C-2), 82.0 (C-3), 79.5 (C-4), 75.6 (CH₂ Bn), 73.4 (C-5), 73.2, 73.2 (CH₂ Bn), 65.6 (C-6). Spectra in agreement with literature.⁴⁸

1-deutero-1-deoxy-2,3,4,6-tetra-O-benzyl-a-D-allopyranoside (4A)



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **4** and TES-D, yielding compound **4A** (39 mg, 74 µmol, 74%, colourless oil, $\alpha:\beta > 98:2$) ¹H NMR (400 MHz, CDCl₃) δ 7.42 – 7.17 (m, 20H, CH_{arom}), 4.88 (d, *J* = 12.1 Hz, 1H, CHH Bn), 4.82 (d, *J* = 12.1 Hz, 1H, CHH Bn), 4.59 (d, *J* = 12.3 Hz, 1H, CHH Bn), 4.55 (d, *J* = 12.2 Hz, 1H, CHH Bn), 4.53 – 4.47 (m, 3H, CHH Bn, CH₂ Bn), 4.37 (d, *J* = 11.5 Hz, 1H, CHH Bn), 4.21 (t, *J* = 2.5 Hz, 1H, H-3), 3.89 (ddd, *J* = 9.8, 4.0, 2.1 Hz, 1H, H-5), 3.84 – 3.81 (m, 1H, H-1), 3.70 (dd, *J* = 10.5, 2.2 Hz, 1H, H-6), 3.65 (dd, *J* = 10.5, 4.1 Hz, 1H, H-6), 3.51 (dd, *J* = 5.1, 2.3 Hz, 1H, H-2), 3.46 (dd, *J* = 9.8, 2.4 Hz, 1H, H-4); ¹³C NMR (101 MHz, CDCl₃) δ 139.3, 138.3, 138.2, 138.1 (C_q), 128.6, 128.5, 128.4, 128.3, 128.1, 127.9, 127.8, 127.7, 127.5, 127.4 (CH_{arom}), 75.9, 75.8 (C-2, C-4), 74.0 (CH₂ Bn), 73.9 (C-5), 73.7 (CH₂ Bn), 73.1 (C-3), 71.4, 71.3 (CH₂ Bn), 69.4 (C-6), 64.0 (t, *J* = 22.0 Hz, C-1); HRMS: [M+NH₄]⁺ calcd for C₃₄H₃₅DO₅NH₄ 543.29638, found 543.29537.

1-deutero-1-deoxy-2,3,4,6-tetra-O-benzyl-α,β-D-altropyranoside (5A)



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **5** and TES-D, yielding compound **5A** (29 mg, 55 µmol, 55%, colourless oil, $\alpha:\beta = 20:80$) ¹H NMR (500 MHz, CDCl₃) δ 7.37 – 7.17 (m, 20H, CH_{arom}), 4.66 – 4.61 (m, 2H, 2x CHH Bn), 4.57 (d, *J* = 9.4 Hz, 1H, CHH Bn), 4.55 (d, *J* = 9.4 Hz, 1H, CHH Bn), 4.52 (d, *J* = 12.2 Hz, 1H, CHH Bn), 4.44 (d, *J* = 11.6 Hz, 1H, CHH Bn), 4.42 – 4.36 (m, 2H, 2x CHH Bn), 3.96 (ddd, *J* = 9.7, 5.7, 2.0 Hz, 1H, H-5), 3.88 (d, *J* = 1.5 Hz, 0.2H, H-1 α), 3.86 – 3.81 (m, 1H, H-3), 3.80 (dd, *J* = 9.8, 2.9 Hz, 1H, H-4), 3.79 (d, *J* = 1.4 Hz, 0.8H, H-1 β), 3.76 (dd, *J* = 10.6, 2.0 Hz, 1H, H-6), 3.66 (dd, *J* = 10.6, 5.7 Hz, 1H, H-6), 3.50 (dd, *J* = 3.8, 1.5 Hz, 1H, H-2); ¹³C

NMR (126 MHz, CDCl₃) δ 138.5, 138.5, 138.3, 138.3 (C_q), 128.5, 128.5, 128.4, 128.4, 128.1, 128.0, 127.9, 127.8, 127.8, 127.6 (CH_{arom}), 74.8 (C-2), 74.7 (C-5), 73.9 (C-4), 73.7, 72.9 (CH₂ Bn), 72.7 (C-3), 71.8, 71.0 (CH₂ Bn), 70.3 (C-6), 64.5 (t, *J* = 22.0 Hz, C-1); HRMS: [M+NH₄]⁺ calcd for C₃₄H₃₅DO₅NH₄ 543.29638, found 543.29526.

<u>1-deutero-1-deoxy-2,3,4,6-tetra-O-benzyl-a-D-gulopyranoside (6A)</u>



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **6** and TES-D, yielding compound **6A** (44 mg, 83 µmol, 83%, colourless oil, $\alpha:\beta > 98:2$); ¹H NMR (500 MHz, CDCl₃) δ 7.35 – 7.25 (m, 18H, CH_{arom}), 7.15 – 7.11 (m, 2H, CH_{arom}), 4.70 (d, *J* = 12.2 Hz, 1H, CHH Bn), 4.56 – 4.50 (m, 3H, 2x CHH Bn, CHH Bn), 4.47 (d, *J* = 12.1 Hz, 1H, CHH Bn), 4.43 (d, *J* = 12.1 Hz, 1H, CHH Bn), 4.39 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.35 (d, *J* = 12.0 Hz, 1H, CHH Bn), 3.96 (ddd, *J* = 7.1, 5.8, 1.6 Hz, 1H, H-5), 3.86 (dd, *J* = 5.1, 2.7 Hz, 1H, H-2), 3.83 (dd, *J* = 5.1, 1.2 Hz, 1H, H-1), 3.80 (ddd, *J* = 4.0, 2.6, 1.3 Hz, 1H, H-3), 3.56 (dd, *J* = 9.7, 6.8 Hz, 1H, H-6), 3.50 (dd, *J* = 3.9, 1.6 Hz, 1H, H-4), 3.42 (dd, *J* = 9.8, 5.9 Hz, 1H); ¹³C NMR (126 MHz, CDCl₃) δ 138.7, 138.5, 138.2, 138.0 (C_q), 128.6, 128.5, 128.5, 128.3, 128.0, 128.0, 127.9, 127.8, 127.7 (CH_{arom}), 75.3 (C-4), 73.6 (CH₂ Bn), 73.6 (C-5), 73.0 (CH₂ Bn), 73.0 (C-2), 72.9 (CH₂ Bn), 72.4 (C-3), 71.5 (CH₂ Bn), 69.5 (C-6), 64.1 (t, *J* = 22.0 Hz, C-1); HRMS: [M+NH₄]⁺ calcd for C₃₄H₃₅DO₅NH₄ 543.29638, found 543.29537.

1-deutero-1-deoxy-2,3,4,6-tetra-O-benzyl-β-D-idopyranoside (7A)



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor 7 and TES-D, yielding compound 7**A**. (39 mg, 74 μmol, 74%, colourless oil, α:β <2:98); ¹H NMR (500 MHz, CDCl₃) δ 7.38 – 7.22 (m, 20H, CH_{arom}), 4.66 – 4.59 (m, 4H, 4x CHH Bn), 4.55 – 4.47 (m, 4H, CHH Bn), 4.01 (ddd, *J* = 7.6, 4.6, 3.1 Hz, 1H, H-5), 3.82 – 3.76 (m, 2H, H-1, H-6), 3.71 (t, *J* = 4.6 Hz, 1H, H-3), 3.62 (dd, *J* = 10.3, 4.6 Hz, 1H, H-6), 3.52 (dd, *J* = 4.8, 3.2 Hz, 1H, H-4), 3.42 (t, *J* = 3.9 Hz, 1H, H-2); ¹³C NMR (126 MHz, CDCl₃) δ 138.4, 138.3, 138.3, 138.2 (C_q), 128.5, 128.5, 128.5, 128.4, 128.3, 128.0, 127.9, 127.9, 127.9, 127.8, 127.7 (CH_{arom}), 74.9 (C-4), 74.6 (C-5), 74.2 (C-2), 74.0 (C-3), 73.6, 73.1, 72.7, 71.9 (CH₂ Bn), 68.6 (C-6), 65.2 (t, *J* = 22.0 Hz, C-1); HRMS: [M+NH₄]⁺ calcd for C₃₄H₃₅DO₅NH₄ 543.29638, found 543.29518. Comparison with **7A-H** confirms the formation of a single diastereomer, which is characterised as the β-anomer from the benzoylated derivative **7A-Bz**

1-deoxy-2,3,4,6-tetra-O-benzyl-D-idopyranoside (7A-H)



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor 7 and TES-H, yielding compound 7**A**. (45 mg, 86 µmol, 86%, colourless oil). ¹H NMR (400 MHz, CDCl₃) δ 7.41 – 7.24 (m, 20H, CH_{arom}), 4.67 – 4.61 (m, 4H, CHH Bn), 4.58 – 4.48 (m, 4H, CHH Bn), 4.04 (ddd, *J* = 7.6, 4.6, 3.1 Hz, 1H, H-5), 3.96 – 3.90 (m, 1H, H-1eq), 3.87 – 3.79 (m, 2H, H-1ax, H-6), 3.73 (t, *J* = 4.6 Hz, 1H, H-3), 3.64 (dd, *J* = 10.3, 4.6 Hz, 1H, H-6), 3.54 (ddd, *J* = 4.6, 3.2, 0.8 Hz, 1H, H-4), 3.45 (tdd, *J* = 4.2, 3.1, 0.8 Hz, 1H, H-2); ¹³C NMR (101 MHz, CDCl₃) δ 138.4, 138.3, 138.2, 138.2 (C_q), 128.5, 128.5, 128.4, 128.3, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7 (CH_{arom}, 74.9 (C-4), 74.6 (C-5), 74.2 (C-2), 73.9 (C-3), 73.6, 73.0, 72.7, 71.9 (CH₂ Bn), 68.6 (C-6), 65.5 (C-1); HRMS: [M+NH₄]⁺ calcd for C₃₄H₃₆O₅NH₄ 542.29010, found 542.28852.

1-deutero-1-deoxy-2,3,4,6-tetra-O-benzoyl-β-D-idopyranoside (7A-Bz)



Title compound was prepared according to the general procedure for debenzylation and benzoylation of glycosylated products with **8A** in 60% yield. ¹H NMR (500 MHz, CDCl₃) δ 8.16 – 8.13 (m, 2H, CH_{arom}), 8.12 – 8.09 (m, 2H, CH_{arom}), 8.06 – 8.02 (m, 2H, CH_{arom}), 7.95 – 7.91 (m, 2H, CH_{arom}), 7.65 – 7.58 (m, 2H, CH_{arom}), 7.58 – 7.54 (m, 1H, CH_{arom}), 7.53 – 7.46 (m, 3H, CH_{arom}), 7.45 – 7.37 (m, 4H, CH_{arom}), 7.22 – 7.16 (m, 2H, CH_{arom}), 5.70 (t, *J* = 3.1 Hz, 1H, H-3), 5.40 (ddd, *J* = 3.2, 2.0, 1.0 Hz, 1H, H-4), 5.16 (ddd, *J* = 3.1, 2.1, 1.0 Hz, 1H, H-2), 4.70 (dd, *J* = 11.6, 7.5 Hz, 1H, H-6), 4.53 (dd, *J* = 11.6, 4.9 Hz, 1H, H-6), 4.46 (ddd, *J* = 7.2, 4.9, 2.0 Hz, 1H, H-5), 4.17 (d, *J* = 2.1 Hz, 1H, H-1); ¹³C NMR (126 MHz, CDCl₃) δ 166.4, 165.7, 165.5, 164.3 (C=O), 133.9, 133.7, 133.4, 130.3, 130.1, 129.9 (CH_{arom}), 129.7, 129.4, 129.3, 129.1 (C_q), 128.8, 128.7, 128.6, 128.4 (CH_{arom}), 7.31 (C-5), 67.3, 67.2 (C-2, C-4), 66.6 (C-3), 63.5 (C-6). C-1 is invisible in the 13C-spectrum, but shows a cross-peak at 66.1 in the HSQC spectrum; HRMS: [M+Na]⁺ calcd for C₃₄H₂₇DO₉Na 604.16883, found 604.16860.

1-deutero-1-deoxy-2,3,4,6-tetra-O-benzyl-β-D-talopyranoside (8A)



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **8** and TES-D, yielding compound **8A**. (27 mg, 51 µmol, 51%, colourless oil, α: β <2:98); ¹H NMR (400 MHz, CDCl₃) δ 7.41 – 7.16 (m, 20H, CH_{arom}), 4.81 (d, *J* = 11.9 Hz, 1H, CHH Bn), 4.74 (d, *J* = 12.5 Hz, 1H, CHH Bn), 4.69 – 4.54 (m, 5H, 2x CHH Bn, 3x CHH Bn), 4.48 (d, *J* = 12.0 Hz, 1H, CHH Bn), 3.91 (dd, *J* = 10.4, 7.2 Hz, 1H, H-6), 3.75 (tdt, *J* = 8.9, 6.2, 3.1 Hz, 3H, H-3, H-4, H-5), 3.70 – 3.60 (m, 2H, H-2, H-6), 3.48 (d, *J* = 3.0 Hz, 1H, H-1); ¹³C NMR (101 MHz, CDCl₃) δ 138.8, 138.7, 138.6, 138.4 (C_q), 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.1, 127.9, 127.7, 127.6, 127.6, 127.5 (CH_{arom}), 77.3, 74.6 (C-3, C-4, C-5), 73.6 (CH₂ Bn), 73.4 (C-2), 72.9, 72.0, 71.8 (CH₂ Bn), 68.4 (C-6); C-1 is invisible in the 13C-spectrum, but shows a cross-peak at 64.6 in the HSQC spectrum; HRMS: [M+NH₄]⁺ calcd for C₃₄H₃₅DO₅NH₄ 543.29638, found 543.29541. Comparison with **8A-H** shows that one diastereomer is selectively formed, which is characterised as the β-anomer from the benzoylated derivative **8A-Bz**

1-deoxy-2,3,4,6-tetra-O-benzyl-β-D-talopyranoside (8A-H)



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **8** and TES-H, yielding compound **8A.** (28 mg, 53 µmol, 53%, colourless oil) ¹H NMR (500 MHz, CDCl₃) δ 7.52 – 6.88 (m, 20H, CH_{arom}), 4.81 (d, *J* = 11.9 Hz, 1H, CHH Bn), 4.74 (d, *J* = 12.4 Hz, 1H, CHH Bn), 4.68 – 4.54 (m, 5H, 2x CHH Bn, 3x CHH Bn), 4.48 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.04 (dd, *J* = 12.0, 5.4 Hz, 1H, H-1), 3.92 (dd, *J* = 10.6, 7.4 Hz, 1H, H-6), 3.83 – 3.72 (m, 3H, H-3, H-4, H-5), 3.69 – 3.60 (m, 2H, H-2, H-6), 3.50 (dd, *J* = 12.0, 3.1 Hz, 1H, H-1); ¹³C NMR (126 MHz, CDCl₃) δ 138.8, 138.7, 138.6, 138.4 (C_q), 128.5, 128.4, 128.4, 128.3, 128.3, 128.1, 127.9, 127.7, 127.6, 127.6, 127.5 (CH_{arom}), 77.3, 74.6 (C-3, C-4, C-5), 73.6 (CH₂ Bn), 73.4 (C-2), 72.9, 72.0, 71.8 (CH₂ Bn), 68.4 (C-6); C-1 is invisible in the 13C-spectrum, but shows a cross-peak at 64.6 in the HSQC spectrum; HRMS: [M+NH₄]⁺ calcd for C₃₄H₃₆O₅NH₄ 542.29010, found 542.28886.

1-deutero-1-deoxy-2,3,4,6-tetra-O-benzoyl-β-D-talopyranoside (8A-Bz)

Title compound was prepared according to the general procedure for debenzylation and benzoylation of glycosylated products with **8A** in 36% yield. ¹H NMR (400 MHz, CDCl₃) δ 8.14 (ddd, *J* = 8.3, 6.6, 1.3 Hz, 4H, CH_{arom}), 8.07 – 8.04 (m, 2H, CH_{arom}), 8.03 – 7.99 (m, 2H, CH_{arom}), 7.85 – 7.80 (m, 2H, CH_{arom}), 7.68 – 7.55 (m, 4H, CH_{arom}), 7.54 – 7.44 (m, 6H, CH_{arom}), 7.42 – 7.37 (m, 2H, CH_{arom}), 7.33 – 7.22 (m, 6H, CH_{arom}), 5.96 (dt, *J* = 3.9, 1.2 Hz, 1H, H-4), 5.65 (t, *J* = 4.0 Hz, 1H, H-3), 5.62 (dt, *J* = 4.4, 1.2 Hz, 1H, H-2), 4.74 (dd, *J* = 11.5, 7.1 Hz, 1H, H-6), 4.49 (dd, *J* = 11.5, 5.8 Hz, 1H, H-6), 4.27 (ddd, *J* = 7.2, 5.8, 1.6 Hz, 1H, H-5), 4.02 (d, *J* = 1.6 Hz, 1H, H-1); ¹³C NMR (101 MHz, CDCl₃) δ 166.3, 166.2, 166.0, 165.2 (C=O), 133.8, 133.3, 133.1, 130.2, 130.1, 129.9, 129.8, 129.8 (CH_{arom}), 129.5, 129.3, 129.1, 128.5 (C_q), 128.5, 128.5, 128.3, 128.3 (CH_{arom}), 75.6 (C-5), 68.6 (C-1, C-3), 67.6 (C-2), 66.9 (C-4), 62.9 (C-6); HRMS: [M+NH4]⁺ calcd for C₃₄H₂₇DO₉NH₄ 599.21343, found 599.21225.

1-deutero-1,6-dideoxy-2,3,4-tri-O-benzyl-a-D-glucopyranoside (9A)

Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **9** and TES-D, yielding compound **9A** (25 mg, 59 µmol, 59%, colourless oil, $\alpha:\beta > 98:2$); ¹H NMR (500 MHz, CDCl₃) δ 7.40 – 7.24 (m, 15H, CH_{arom}), 4.97 (d, *J* = 11.0 Hz, 1H, CHH Bn), 4.89 (d, *J* = 10.8 Hz, 1H, CHH Bn), 4.85 (d, *J* = 11.0 Hz, 1H, CHH Bn), 4.72 (d, *J* = 11.5 Hz, 1H, CHH Bn), 4.66 – 4.58 (m, 2H, 2x CHH Bn), 3.93 (d, *J* = 4.5 Hz, 1H, H-1), 3.64 – 3.55 (m, 2H, H-2, H-3), 3.31 (dq, *J* = 9.4, 6.1 Hz, 1H, H-5), 3.16 – 3.07 (m, 1H, H-4), 1.26 (d, *J* = 6.1 Hz, 3H, H-6); ¹³C NMR (126 MHz, CDCl₃) δ 138.9, 138.4, 138.3 (C_q), 128.6, 128.6,

128.5, 128.1, 128.1, 128.0, 127.9, 127.8 (CH_{arom}), 86.3 (C-4), 83.8 (C-3), 79.0 (C-2), 76.2 (C-5), 75.7, 75.6, 73.4 (CH₂ Bn), 67.7 (t, J = 22.0 Hz, C-1) 18.4 (C-1); HRMS: [M+NH₄]⁺ calcd for C₂₇H₂₉DO₄NH₄ 437.25451, found 437.25374.

1-deutero-1,6-dideoxy-2,3,4-tri-O-benzyl-a-D-allopyranoside (12A)

Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **12A** and TES-D, yielding compound **12A** (24 mg, 57 μmol, 57%, colourless oil, α:β >98:2); ¹H NMR (500 MHz, CDCl₃) δ 7.42 – 7.25 (m, 15H, CH_{arom}), 4.89 (d, J = 12.0 Hz, 1H, CHH Bn), 4.83 (d, J = 12.0 Hz, 1H, CHH Bn), 4.59 – 4.52 (m, 3H, 2x CHH Bn, CHH Bn), 4.40 (d, J = 11.7 Hz, 1H, CHH Bn), 4.21 (bs, 1H, H-3), 3.83 (dq, J = 9.4, 6.2 Hz, 1H, H-5), 3.74 (d, J = 4.8 Hz, 1H, H-1), 3.47 (dd, J = 4.9, 2.2 Hz, 1H, H-2), 2.97 (dd, J = 9.4, 2.4 Hz, 1H, H-4), 1.21 (d, J = 6.2 Hz, 3H, H-6); ¹³C NMR (126 MHz, CDCl₃) δ 139.3, 138.4, 138.1 (C_q), 128.6, 128.5, 128.3, 128.1, 128.0, 127.9, 127.9, 127.9, 127.5, 127.4 (CH_{arom}), 81.3 (C-4), 76.4 (C-2), 74.0 (CH₂ Bn), 72.7 (C-3), 71.3 (2x CH₂ Bn), 70.7 (C-5), 63.82 (t, J = 22.0 Hz, C-1), 18.3 (C-6); HRMS: [M+NH₄]⁺ calcd for C₂₇H₂₉DO₄NH₄ 437.25451, found 437.25365.

<u>1-deutero-1,6-dideoxy-2,3,4-tri-O-benzyl-α,β-D-allopyranoside (13A)</u>



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **12A** and TES-D, yielding compound **12A** (36 mg, 85 µmol, 85%, colourless oil, $\alpha:\beta = 12:88$) ¹H NMR (500 MHz, CDCl₃) δ 7.59 – 6.76 (m, 15H, CH_{arom}), 4.67 (d, *J* = 12.2 Hz, 1H, CHH Bn), 4.58 (t, *J* = 12.8 Hz, 2H, CHH Bn, CHH Bn), 4.53 (d, *J* = 11.7 Hz, 1H, CHH Bn), 4.49 (d, *J* = 11.7 Hz, 1H, CHH Bn), 4.45 (d, *J* = 12.4 Hz, 1H, CHH Bn), 3.91 – 3.86 (m, 1H, H-5), 3.85 (t, *J* = 3.3 Hz, 1H, H-3), 3.82 – 3.79 (m, 1H, H-1αβ), 3.53 (dd, *J* = 3.8, 1.5 Hz, 1H, H-2), 3.49 (dd, *J* = 9.4, 2.8 Hz, 1H, H-4), 1.32 (d, *J* = 6.2 Hz, 3H, H-6); ¹³C NMR (126 MHz, CDCl₃) δ 138.6, 138.4, 138.3 (C_q), 128.5, 128.5, 128.5, 128.1, 127.9, 127.9, 127.8, 127.8, 127.8 (CH_{arom}), 79.0 (C-4), 75.0 (C-2), 72.8 (CH₂ Bn), 72.4 (C-3), 71.9, 71.2 (CH₂ Bn), 71.2 (C-5), 64.6 (t, *J* = 22.0 Hz, C-1), 18.3 (C-6); HRMS: [M+NH₄]⁺ calcd for C₂₇H₂₉DO₄NH₄ 437.25451, found 437.25365. Because of overlap of H-1α and H-1β, the ratio was determined from the benzoylated derivate **13A-Bz**

1-deutero-1,6-dideoxy-2,3,4-tri-O-benzoyl-α,β-D-allopyranoside (13A-Bz)



Title compound was prepared according to the general procedure for debenzylation and benzoylation of glycosylated products with **13A** in 80% yield. ¹H NMR (850 MHz, CDCl₃) δ 8.14 (dd, *J* = 8.3, 1.2 Hz, 2H, CH_{arom}), 8.06 (dd, *J* = 8.3, 1.2 Hz, 2H, CH_{arom}), 7.91 (dd, *J* = 8.4, 1.3 Hz, 2H, CH_{arom}), 7.64 – 7.59 (m, 2H, CH_{arom}), 7.52 (tt, *J* = 7.4, 1.3 Hz, 1H, CH_{arom}), 7.51 – 7.47 (m, 4H,

CH_{arom}), 7.38 – 7.33 (m, 2H, CH_{arom}), 5.86 (t, *J* = 3.6 Hz, 1H, H-3), 5.42 (dd, *J* = 9.4, 3.2 Hz, 1H, H-4), 5.32 (dd, *J* = 4.1, 1.7 Hz, 1H, H-2), 4.18 (dq, *J* = 9.4, 6.3 Hz, 1H, H-5), 4.15 (s, 0.12Hα), 4.13 (d, *J* = 1.6 Hz, 0.88H, H-1β), 1.36 (d, *J* = 6.3 Hz, 3H, H-6); ¹³C NMR (126 MHz, CDCl₃) δ 165.6, 165.5, 165.1 (C=O), 133.7, 133.6, 133.4, 130.1, 129.9, 129.8 (CH_{arom}), 129.6, 129.5 (C_q), 128.8, 128.7, 128.5 (CH_{arom}), 71.7 (C-4), 71.0 (C-3), 70.2 (C-2), 68.0 (C-3), 65.4 (t, *J* = 22.0 Hz, C-1), 18.0 (C-6); HRMS: [M+NH₄]⁺ calcd for C₂₇H₂₃DO₇NH₄ 479.19231, found 479.19118.

<u>1-deutero-1,6-dideoxy-2,3,4-tri-O-benzyl-a-L-gulopyranoside (14A)</u>

Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **14A** and TES-D, yielding compound **14A** (36 mg, 86 µmol, 86%, colourless oil, α : β >98:2); ¹H NMR (400 MHz, CDCl₃) δ 7.37 – 7.26 (m, 13H, CH_{arom}), 7.22 – 7.18 (m, 2H, CH_{arom}), 4.74 (d, *J* = 12.2 Hz, 1H, CHH Bn), 4.56 – 4.52 (m, 2H, CHH Bn, CHH Bn), 4.49 (d, *J* = 10.3 Hz, 1H, CHH Bn), 4.46 (d, *J* = 10.3 Hz, 1H, CHH Bn), 4.41 (d, *J* = 12.1 Hz, 1H, CHH

(m, 2H, CH_{arom}), 4.74 (d, J = 12.2 Hz, 1H, CHH Bn), 4.56 – 4.52 (m, 2H, CHH Bn, CHH Bn), 4.49 (d, J = 10.3 Hz, 1H, CHH Bn), 4.46 (d, J = 10.3 Hz, 1H, CHH Bn), 4.41 (d, J = 12.1 Hz, 1H, CHH Bn), 3.89 – 3.83 (m, 2H, H-2, H-5), 3.82 (dd, J = 4.6, 2.0 Hz, 1H, H-2), 3.79 (d, J = 4.9 Hz, 1H, H-1), 3.25 (dd, J = 3.8, 1.4 Hz, 1H, H-4), 1.12 (d, J = 6.6 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 138.7, 138.5, 138.1 (C_q), 128.5, 128.5, 128.5, 128.3, 128.0, 127.9, 127.8, 127.8, 127.7 (CH_{arom}), 77.8 (C-4), 73.1 (2x CH₂ Bn), 73.0 (C-2), 72.7 (C-3), 71.5 (CH₂ Bn), 70.5 (C-5), 64.1 (t, J = 22.0 Hz, C-1) 16.4 (C-6); HRMS: [M+NH₄]⁺ calcd for C₂₇H₂₉DO₄NH₄ 437.25451, found 437.25364.

1-deutero-1,6-dideoxy-2,3,4-tri-O-benzyl-β-L-idopyranoside (15A)

Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **15** and TES-D on 50 µmol scale, yielding compound **15A**. (11 mg, 25 µmol, 50%, colourless oil, α : β <2:98); ¹H NMR (500 MHz, CDCl₃) δ 7.40 – 7.08 (m, 15H, CH_{arom}), 4.68 – 4.62 (m, 4H, 2x CHH Bn, CH₂ Bn), 4.60 (d, *J* = 12.1 Hz, 1H, CHH Bn), 4.55 (d, *J* = 11.9 Hz, 1H, CHH Bn), 3.96 (qd, *J* = 6.7, 3.9 Hz, 1H, H-5), 3.73 – 3.69 (m, 2H, H-1, H-3), 3.42 (dd, *J* = 5.7, 4.1 Hz, 1H, H-2), 3.39 (dd, *J* = 6.2, 3.9 Hz, 1H, H-4), 1.26 (d, *J* = 6.8 Hz, 3H, H-6); ¹³C NMR (126 MHz, CDCl₃) δ 138.5, 138.5, 138.5 (C_q), 128.6, 128.5, 128.5, 128.2, 128.0, 128.0, 127.9, 127.8 (CH_{arom}), 77.8 (C-4), 76.4 (C-3), 75.5 (C-2), 73.9, 72.9, 72.5 (CH₂ Bn), 71.0 (C-5), 63.7 (t, *J* = 22.0 Hz, C-1), 14.4 (C-6); HRMS: [M+NH₄]⁺ calcd for C₂₇H₂₉DO₄NH₄ 437.25451, found 437.25369

1-deutero-1,6-dideoxy-2,3,4-tri-O-benzyl-β-L-talopyranoside (16A)

BnO^{OBn} OBn

Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **16** and TES-D, yielding compound **16A**. (29 mg, 68 µmol, 68%, colourless oil, α : β <2:98); ¹H NMR (500 MHz, CDCl₃) δ 7.60 – 6.99 (m, 15H, CH_{arom}), 4.90 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.80 (d, *J* = 12.6 Hz, 1H, CHH Bn), 4.75 (d, *J* = 12.0 Hz, 1H, CHH Bn),

4.68 – 4.63 (m, 2H, CHH Bn, CHH Bn), 4.59 (d, J = 12.1 Hz, 1H, CHH Bn), 3.70 (bs, 1H, H-4), 3.65 (t, J = 2.5 Hz, 1H, H-2), 3.63 – 3.55 (m, 2H, H-3, H-5), 3.41 (d, J = 2.4 Hz, 1H, H-1), 1.34 (d, J = 6.5 Hz, 3H, H-6); ¹³C NMR (126 MHz, CDCl₃) δ 139.1, 138.9, 138.7 (C_q), 128.4, 128.3, 128.2, 128.2, 127.9, 127.6, 127.5, 127.5, 127.4 (CH_{arom}), 78.7 (C-4), 76.2 (C-3), 73.2 (CH₂ Bn), 72.9 (C-2), 71.8, 71.6 (CH₂ Bn), 16.4 (C-6), C-3 and C-1 are invisible in the 13C spectrum, but show crosspeaks at 74.1 and 65.4 respectively in the HSQC spectrum. HRMS: [M+NH₄]⁺ calcd for $C_{27}H_{29}DO_4NH_4$ 437.25451, found 437.25372. The product is characterised as the β-anomer form **16A-Bz**

1-deutero-1,6-dideoxy-2,3,4-tri-O-benzoyl-β-L-talopyranoside (16A-Bz)

BZO^{OBZ} OBZ

Title compound was prepared according to the general procedure for debenzylation and benzoylation of glycosylated products with **16A** in 91% yield. ¹H NMR (850 MHz, CDCl₃) δ 8.12 (dd, *J* = 8.4, 1.2 Hz, 2H, CH_{arom}), 8.01 – 7.97 (m, 2H, CH_{arom}), 7.81 – 7.75 (m, 2H, CH_{arom}), 7.58 (tt, *J* = 7.4, 1.3 Hz, 1H, CH_{arom}), 7.50 (tt, *J* = 7.5, 1.3 Hz, 1H, CH_{arom}), 7.46 (ddt, *J* = 8.7, 7.4, 1.5 Hz, 1H, CH_{arom}), 7.37 – 7.33 (m, 2H, CH_{arom}), 7.28 – 7.24 (m, 2H, CH_{arom}), 7.24 – 7.20 (m, 2H, CH_{arom}), 5.65 (dt, *J* = 3.9, 1.1 Hz, 2H, H-4), 5.57 (t, *J* = 4.1 Hz, 1H, H-3), 5.55 (dt, *J* = 4.1, 1.2 Hz, 2H, H-2), 3.95 (qd, *J* = 6.4, 1.3 Hz, 1H, H-5), 3.93 (d, *J* = 1.2 Hz, 1H, H-1), 1.37 (d, *J* = 6.5 Hz, 3H, H-6); ¹³C NMR (126 MHz, CDCl₃) δ 166.6, 166.5, 165.5 (C=O), 133.8, 133.3, 133.1, 130.3, 130.2, 130.1 (CH_{arom}), 130.1, 129.9 (Cq), 129.9 (CH_{arom}), 129.4 (Cq), 128.6, 128.5, 128.4, 128.3 (CH_{arom}), 74.2 (C-5), 69.8 (C-4), 69.2 (C-3), 68.8 (t, *J* = 22.0 Hz, C-1), 67.5 (C-2), 17.1 (C-6); HRMS: [M+NH₄]⁺ calcd for C₂₇H₂₃DO₇NH₄ 479.19231, found 479.19112.

1-allyl-1-deoxy-2,3,4,6-tetra-O-benzyl-α-D-glucopyranoside (1B)



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **1** and Allyl-TMS, yielding compound **1B** (40 mg, 71 µmol, 71%, colourless oil, $\alpha:\beta > 98:2$); ¹H NMR (500 MHz, CDCl₃) δ 7.38 – 7.13 (m, 20H, CH_{arom}), 5.81 (dddd, J = 16.6, 10.2, 7.4, 6.3 Hz, 1H, CH₂-CH=CH₂), 5.17 – 4.98 (m, 2H, CH₂-CH=CH₂), 4.93 (d, J = 11.0 Hz, 1H, CHH Bn), 4.84 – 4.76 (m, 2H, CHH Bn, CHH Bn), 4.69 (d, J = 11.6 Hz, 1H, CHH Bn), 4.84 – 4.76 (m, 2H, CHH Bn), 4.69 (d, J = 11.6 Hz, 1H, CHH Bn), 4.67 – 4.58 (m, 2H, CHH Bn, CHH Bn), 4.50 – 4.44 (m, 2H, 2x CHH Bn), 4.13 (dt, J = 10.4, 5.0 Hz, 1H, H-1), 3.80 (dd, J = 9.4, 7.5 Hz, 1H, H-3), 3.76 (dd, J = 9.4, 5.5 Hz, 1H, H-2) 3.70 (dd, J = 10.6, 3.4 Hz, 1H, H-6), 3.67 – 3.59 (m, 3H, H-4, H-5, H-6), 2.56 – 2.44 (m, 2H, CH₂-CH=CH₂); ¹³C NMR (126 MHz, CDCl₃) δ 138.9, 138.4, 138.3, 138.2 (C_q), 134.9 (CH₂-CH=CH₂), 128.6, 128.5, 128.1, 128.1, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7 (CH_{arom}), 117.6(CH₂-CH=CH₂), 82.6 (C-2), 79.8 (C-3), 78.2 (C-4), 75.6, 75.2 (CH₂ Bn), 73.8 (C-1), 73.6, 73.2 (CH₂ Bn), 71.2 (C-5), 69.0 (C-6), 29.9 (CH₂-CH=CH₂); HRMS: [M+Na]⁺ calcd for C₃₇H₄₀NaO₅ 587.2768, found 587.2770

1-allyl-1-deoxy-2,3,4,6-tetra-O-benzyl-α,β-D-mannopyranoside (2B)



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor 2 and Allyl-TMS, yielding compound 2B (45 mg, 80 µmol, 80%, colourless oil, α : β >66:34); data of the α -anomer: ¹H NMR (500 MHz, CDCl₃): δ 7.41 – 7.23 (m, 20H, CH_{arom}), 5.81 - 5.69 (m, 1H, CH₂-CH=CH₂), 5.06 - 4.98 (m, 2H, CH₂-CH=CH₂), 4.74 - 4.65 (m, 2H, CHH Bn, CHH Bn), 4.61 - 4.48 (m, 6H, 3x CHH Bn, 3x CHH), 4.04 (ddd, J = 7.8, 6.1, 4.7 Hz, 1H, H-1), 3.88 – 3.81 (m, 2H, H-4, H-5), 3.80 – 3.74 (m, 2H, H-3, H-6), 3.71 (dd, J = 10.3, 3.5 Hz, 1H, H-6), 3.62 (dd, J = 4.9, 2.9 Hz, 1H, H-2), 2.39 – 2.27 (m, 2H, CH₂-CH=CH₂); 13C NMR (126 MHz, CDCl3, HSQC): δ 138.6, 138.4, 138.4, 138.3 (C_q), 134.0 (CH₂-CH-CH₂), 128.5, 128.4, 128.4, 128.4, 128.3, 128.2, 128.2, 128.1, 128.1, 128.1, 128.0, 127.8, 127.7, 127.7, 127.6 (CH_{arom}), 117.3 (CH₂-CH=CH₂), 77.0 (C-3), 75.3 (C-2), 75.0, 74.0 (CH₂ Bn), 73.9 (C-5), 73.4 (CH₂ Bn), 72.5 (C-1), 72.2, 71.7 (CH₂ Bn), 69.3 (C-6), 33.9 (CH₂-CH=CH₂); diagnostic signals of the βanomer: 1H NMR (500 MHz, CDCl₃): δ 4.87 (d, J = 10.8 Hz, 1H, CHH Bn), 4.78 (d, J = 11.7 Hz, 1H, CHH Bn), 3.46 (ddd, J = 9.7, 5.8, 1.8 Hz, 1H, H-5), 3.36 – 3.30 (m, 1H, H-1), 2.50 (dtt, J = 12.7, 6.4, 1.6 Hz, 1H, CHH-CH=CH₂); 13C NMR (126 MHz, CDCl3): δ 134.8 (CH₂-CH=CH₂), 117.4 (CH₂-CH=CH₂), 80.0 (C-5), 78.4 (C-1), 75.4, 74.5, 73.6, 72.6 (CH₂ Bn), 69.9 (C-6). HRMS: [M+Na]+ calcd for C₃₇H₄₀NaO₅ 587.2768, found 587.2781.

1-allyl-1-deoxy-2,3,4,6-tetra-O-benzyl-a-D-galactopyranoside (3B)



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **3** and Allyl-TMS, yielding compound **3B** (46 mg, 80 µmol, 80%, colourless oil, α:β >98:2); ¹H NMR (500 MHz, CDCl₃) δ 7.91 – 6.50 (m, 20H, CH_{arom}), 5.75 (ddt, *J* = 17.1, 10.2, 6.9 Hz, 1H, CH₂-CH=CH₂), 5.13 – 4.98 (m, 2H, CH₂-CH=CH₂), 4.80 – 4.63 (m, 2H, 2x CHH Bn), 4.65 – 4.39 (m, 6H, 2x CHH Bn, 4x CHH Bn), 4.05 (bs, 1H, H-5), 4.03 – 3.97 (m, 1H, H-3), 4.00 (dd, J = 4.0, 2.6 Hz, 1H, H-1), 3.88 – 3.81 (m, 1H, H-6), 3.75 (s, 1H, H-4), 3.72 (dd, *J* = 6.9, 2.8 Hz, 1H, H-2), 3.66 (dd, *J* = 10.6, 4.7 Hz, 1H, H-6), 2.47 – 2.38 (m, 1H, CHH-CH=CH₂), 2.38 – 2.29 (m, 1H, CHH-CH=CH₂), 128.6, 128.6, 128.6, 128.5, 128.2, 128.1, 128.0, 128.0, 127.8, 127.7 (CH_{arom}), 117.0 (CH₂-CH=CH₂), 76.7 (C-2), 76.7 (C-4), 74.5 (C-3), 73.4, 73.3, 73.3, 73.2 (CH₂ Bn), 73.0 (C-5), 70.8 (C-1), 67.5 (C-6), 33.9 (CH₂-CH=CH₂); HRMS: [M+Na]⁺ calcd for C₃₇H₄₀NaO₅ 587.2768, found 587.2776.

1-allyl-1-deoxy-2,3,4,6-tetra-O-benzyl-a-D-allopyranoside (4B)

BnO BnO BnÒ BnÓ
Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **4** and Allyl-TMS, yielding compound **4B** (26 mg, 46 µmol, 46%, colourless oil, $\alpha:\beta > 98:2$); ¹H NMR (400 MHz, CDCl₃) δ 7.38 – 7.18 (m, 20H, CH_{arom}), 5.93 – 5.81 (m, 1H, CH₂-CH-CH₂), 5.07 (dq, *J* = 17.2, 1.6 Hz, 1H, CH₂-CH=CHH), 5.02 (ddt, *J* = 10.2, 2.3, 1.1 Hz, 1H, CH₂-CH=CHH), 4.82 (d, *J* = 3.4 Hz, 2H, CH₂ Bn), 4.62 (d, *J* = 12.2 Hz, 1H, CHH Bn), 4.56 (s, 2H, CH₂ Bn), 4.50 (d, *J* = 6.9 Hz, 1H, CHH Bn), 4.47 (d, *J* = 8.3 Hz, 1H, CHH Bn), 4.38 (d, *J* = 11.4 Hz, 1H, CHH Bn), 4.21 (t, *J* = 2.8 Hz, 1H, H-3), 4.11 (ddd, *J* = 11.3, 6.1, 3.1 Hz, 1H, H-1), 4.00 (ddd, *J* = 9.7, 3.6, 2.1 Hz, 1H, H-5), 3.76 (dd, *J* = 10.4, 3.4 Hz, 1H, H-6), 3.67 (dd, *J* = 10.4, 2.1 Hz, 1H, H-6), 3.62 (dd, *J* = 6.0, 2.6 Hz, 1H, H-2), 3.56 (dd, *J* = 9.7, 2.8 Hz, 1H, H-4), 3.13 – 2.94 (m, 1H, CHH-CH=CH₂), 2.54 (dddt, *J* = 15.4, 6.2, 2.8, 1.4 Hz, 1H, CHH-CH=CH₂); ¹³C NMR (101 MHz, CDCl₃) δ 139.3, 138.4, 138.2 (Cq), 136.8 (CH₂-CH=CH₂), 128.6, 128.4, 128.4, 128.4, 128.3, 128.0, 127.9, 127.9, 127.8, 127.6, 127.5, 127.4 (CH_{arom}), 116.3 (CH₂-CH=CH₂), 77.2 (C-4), 75.1 (C-2), 74.5 (C-1), 74.2 (C-3), 74.1, 73.7, 71.4, 71.3 (CH₂ Bn), 69.4 (C-6), 67.2 (C-5), 31.5 (CH₂-CH=CH₂); HRMS: [M+NH₄]⁺ calcd for C₃₇H₄₀O₅NH₄ 582.32140, found 582.32030.

1-allyl-1-deoxy-2,3,4,6-tetra-O-benzyl-α,β-D-altropyranoside (5B)



The title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor 5 and Allyl-TMS, yielding compound 5B (38 mg, 68 µmol, 68%, colourless oil, $\alpha:\beta = 89:11$) Data for the α -anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.35 – 7.22 (m, 20H, CH_{arom}), 5.85 (ddt, J = 17.1, 10.2, 6.9 Hz, 1H, CH₂-CH=CH₂), 5.12 - 5.00 (m, 2H, CH₂-CH=CH₂), 4.68 (d, J = 11.3 Hz, 1H, CHH Bn), 4.59 - 4.53 (m, 3H, 3x CHH Bn), 4.53 - 4.47 (m, 4H, 4x CH*H* Bn), 4.17 (q, *J* = 5.2 Hz, 1H, H-5), 3.86 (dd, *J* = 5.3, 3.1 Hz, 1H, H-4), 3.77 - 3.71 (m, 2H, H-1, H-3), 3.66 - 3.61 (m, 2H, H-2, H-6), 3.57 (dd, J = 10.3, 4.8 Hz, 1H, H-6), 2.63 - 2.43 (m, 2H, CH₂-CH=CH₂); ¹³C NMR (101 MHz, CDCl₃) δ 138.4, 138.4, 138.3 (C_q), 135.3 (CH₂=CH=CH₂), 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.1, 128.0, 128.0, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7 (CHarom), 117.0 (CH2-CH=CH2), 77.3, 77.2 (C-2, C-3), 74.8 (C-1), 73.7, 73.4 (CH₂ Bn), 73.4 (C-4), 72.2, 71.7 (CH₂ Bn), 71.7 (C-5), 69.1 (C-6), 35.9 (CH₂-CH=CH₂); diagnostic peaks for the β -anomer: ¹H NMR (400 MHz, CDCl₃) δ 5.68 (dddd, J = 16.4, 10.1, 7.9, 6.1 Hz, 1H, CH₂-CH=CH₂), 4.02 - 3.94 (m, 2H), 3.32 (dd, J = 3.5, 1.5 Hz, 1H), 2.31 -2.21 (m, 2H, CH₂-CH=CH₂); ¹³C NMR (101 MHz, CDCl₃) δ 135.1 (CH₂-CH=CH₂), 75.9, 75.2, 74.3, 73.0, 72.7, 71.8, 70.2 (C-6), 35.2 (CH₂-CH=CH₂); HRMS: [M+NH₄]⁺ calcd for C₃₇H₄₀O₅NH₄ 582.32140, found 582.31959.

1-allyl-1-deoxy-2,3,4,6-tetra-O-benzyl-a-D-gulopyranoside (6B)



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **6** and Allyl-TMS, yielding compound **6B** (40 mg, 71 µmol, 71%, colourless oil, α : β >98:2); ¹H NMR (400 MHz, CDCl₃) δ 7.36 – 7.19 (m, 20H, CH_{arom}), 5.78 (ddt, *J*

= 17.1, 10.2, 7.0 Hz, 1H, CH₂-CH=CH₂), 5.07 (dq, J = 17.2, 1.6 Hz, 1H, CH₂-CH=CHH), 5.01 (ddt, J = 10.2, 2.2, 1.2 Hz, 1H, CH₂-CH=CHH), 4.74 (d, J = 11.8 Hz, 1H, CHH Bn), 4.69 (d, J = 12.1 Hz, 1H, CHH Bn), 4.64 (d, J = 12.1 Hz, 1H, CHH Bn), 4.61 – 4.55 (m, 2H, 2x CHH Bn), 4.54 – 4.47 (m, 3H, 3x CHH Bn), 4.22 (dt, J = 6.6, 4.7 Hz, 1H, H-5), 3.94 – 3.87 (m, 2H, H-1, H-4), 3.85 (t, J = 3.4 Hz, 1H, H-3), 3.79 (dd, J = 6.8, 3.0 Hz, 1H, H-2), 3.69 (dd, J = 10.3, 6.6 Hz, 1H, H-6), 3.64 (dd, J = 10.3, 5.1 Hz, 1H, H-6), 2.73 (dt, J = 15.6, 8.0 Hz, 1H, CHH-CH=CH₂), 2.36 (dddt, J = 14.9, 7.4, 4.9, 1.3 Hz, 1H, CHH-CH=CH₂); ¹³C NMR (101 MHz, CDCl₃) δ 138.8, 138.7, 138.5, 138.4 (Cq), 135.9 (CH₂=CH=CH₂), 128.5, 128.4, 128.4, 128.1, 128.0, 127.8, 127.8, 127.7, 127.6, 127.6 (CH_{arom}), 116.7 (CH₂-CH=CH₂), 75.9 (C-4), 75.1 (C-3), 73.7 (C-1), 73.4, 73.3, 73.1, 73.1 (CH₂ Bn), 68.2 (C-6), 33.4 (CH₂-CH=CH₂); C-2 and C-5 are invisible in the 13C-spectrum, but show cross-peaks at 77.0 and 69.9 respectively in the HSQC spectrum; HRMS: [M+NH₄]⁺ calcd for C₃₇H₄₀O₅NH₄ 582.32140, found 582.32010

1-allyl-1-deoxy-2,3,4,6-tetra-O-benzyl-a-D-idopyranoside (7B-a)



An analytical amount was isolated as the minor product from reaction between donor 7 and allyl-TMS according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations. ¹H NMR (400 MHz, CDCl₃) δ 7.37 – 7.22 (m, 20H, CH_{arom}), 5.89 (dddd, *J* = 17.6, 10.3, 7.4, 6.1 Hz, 1H, CH₂-CH=CH₂), 5.16 – 5.02 (m, 2H, CH₂-CH=CH₂), 4.90 – 4.83 (m, 2H, 2x CHH Bn), 4.74 (d, *J* = 10.9 Hz, 1H, CHH Bn), 4.66 (d, *J* = 11.5 Hz, 1H, CHH Bn), 4.63 – 4.55 (m, 4H, 2x CHH Bn, CH₂ Bn), 4.24 (ddd, *J* = 8.5, 5.6, 3.3 Hz, 1H, H-5), 3.84 (dd, *J* = 11.0, 8.2 Hz, 1H, H-6), 3.80 – 3.69 (m, 4H, H-1, H-3, H-4, H-6), 3.27 (dd, *J* = 9.4, 7.8 Hz, 1H, H-2), 2.58 (dddt, *J* = 14.7, 6.3, 3.3, 1.5 Hz, 1H, CHH-CH=CH₂), 138.4, 138.3, 138.2 (C_q), 134.8 (CH₂-CH=CH₂), 128.6, 128.5, 128.5, 128.0, 127.9, 127.9, 127.8, 127.7 (CH_{arom}), 117.2 (CH₂-CH=CH₂), 82.7 (C-3/C-4), 81.3 (C-2), 79.5 (C-3/C-4), 75.4, 75.0 (CH₂ Bn), 73.4 (C-5), 73.4, 73.3 (CH₂ Bn), 72.2 (C-1), 66.0 (CH₂ Bn), 36.3 (CH₂-CH=CH₂); HRMS: [M+NH₄]⁺ calcd for C₃₇H₄₀O₅NH₄ 582.32140, found 582.31962.

1-allyl-1-deoxy-2,3,4,6-tetra-O-benzyl-β-D-idopyranoside (7B-β)



An analytical amount was isolated as the major product from reaction between donor 7 and allyl-TMS according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations. ¹H NMR (400 MHz, CDCl₃) δ 7.46 – 7.32 (m, 18H, CH_{arom}), 7.27 – 7.23 (m, 2H, CH_{arom}), 5.82 (dddd, *J* = 16.7, 10.2, 7.7, 6.3 Hz, 1H, CH₂-CH=CH₂), 5.13 (dq, *J* = 17.1, 1.6 Hz, 1H, CH₂-CH=CHH), 5.08 (ddt, *J* = 10.2, 2.2, 1.1 Hz, 1H, CH₂-CH=CHH), 4.69 – 4.64 (m, 2H, 2x CHH Bn), 4.62 (d, *J* = 12.3 Hz, 1H, CHH Bn), 4.57 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.52 – 4.46 (m, 2H, 2x CHH Bn), 4.43 (d, *J* = 12.3 Hz, 1H, CHH Bn), 4.36 (d, *J* = 12.3 Hz, 1H, CHH Bn), 4.04 (td, *J* = 6.2, 1.8 Hz, 1H, H-5), 3.84 – 3.77 (m, 2H, H-1, H-6), 3.75 – 3.70 (m, 2H, H-3, H-6), 3.49 (dt, *J* = 2.8, 1.4 Hz, 1H, H-4), 3.30 (dt, *J* = 2.9, 1.5 Hz, 1H, H-2), 2.68 (dddt, *J* = 14.0, 7.8, 6.3, 1.5 Hz, 1H, CHH-CH=CH₂), 2.36

(dddt, *J* = 14.2, 7.6, 6.4, 1.2 Hz, 1H, CH*H*-CH=CH₂); ¹³C NMR (101 MHz, CDCl₃) δ 138.5, 138.2, 138.1, 137.9 (C_q), 135.2 (CH₂-CH=CH₂), 128.7, 128.7, 128.5, 128.5, 128.4, 128.3, 128.3, 127.9, 127.8, 127.8, 127.7, 127.7, 127.5 (CH_{arom}), 116.7 (CH₂-CH=CH), 76.0 (C-1), 75.7 (C-5), 73.5 (CH₂ Bn), 73.4 (C-2), 72.4 (CH₂ Bn), 72.2 (C-4), 72.2 (CH₂ Bn, 71.8 (CH₂ Bn), 70.0 (C-3), 69.9 (C-6), 35.4 (CH₂-CH=CH₂); HRMS: [M+NH₄]⁺ calcd for C₃₇H₄₀O₅NH₄ 582.32140, found 582.31991.

1-allyl-1-deoxy-2,3,4,6-tetra-O-benzyl-α,β-D-talopyranoside (8B)



The title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor 8 and Allyl-TMS, yielding compound 8B (38 mg, 68 µmol, 68%, colourless oil, $\alpha:\beta$ = 57:43). Data reported for a 1:1 mixture: ¹H NMR (400 MHz, CDCl₃) δ 7.41 – 7.16 (m, 40H, CH_{arom}), 5.89 (dddd, J = 17.7, 10.2, 7.6, 6.2 Hz, 1H, CH₂-CH=CH₂), 5.71 (dddd, J = 16.7, 10.2, 7.7, 6.4 Hz, 1H, CH₂-CH=CH₂), 5.10 (dt, J = 17.2, 1.7 Hz, 1H, CH₂-CH=CHH), 5.07 -4.96 (m, 4H, CH₂-CH=CHH, 2x CH₂-CH=CHH, CHH Bn), 4.94 (d, J = 12.0 Hz, 1H, CHH Bn), 4.85 – 4.77 (m, 2H, CH₂ Bn), 4.75 (d, J = 12.0 Hz, 1H, CHH Bn), 4.71 (d, J = 12.0 Hz, 1H, CHH Bn), 4.61 – 4.53 (m, 6H, 4x CHH Bn, 2x CHH Bn), 4.53 – 4.48 (m, 2H, 2x CHH Bn), 4.45 (d, J = 11.7 Hz, 1H, CHH Bn), 4.39 – 4.30 (m, 2H, H-5a, CHH Bn), 4.17 (dd, J = 11.9, 8.8 Hz, 1H, H-6a), 4.12 (t, J = 2.5 Hz, 1H, H-3 α), 3.95 – 3.89 (m, 2H, H-1 α , H-2 β), 3.80 (dd, J = 12.0, 2.0 Hz, 1H, H-2.3 Hz, 1H, H-4α), 3.52 (td, *J* = 6.2, 1.5 Hz, 1H, H-3β), 3.47 (t, *J* = 3.0 Hz, 1H, H-1β), 3.29 (ddd, *J* = 7.5, 6.4, 1.4 Hz, 1H, H-5β), 3.12 (dd, J = 9.4, 2.6 Hz, 1H, H-2α), 2.66 – 2.51 (m, 2H, 2x CHH-CH=CH₂), 2.36 – 2.27 (m, 1H, CHH-CH=CH₂), 2.27 – 2.18 (m, 1H, CHH-CH=CH₂); ¹³C NMR (101 MHz, CDCl₃) δ 139.2, 138.9, 138.8, 138.3, 138.3, 138.1, 137.9 (C_q), 135.1, 135.0 (CH₂-CH=CH₂), 128.7, 128.6, 128.6, 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 128.2, 128.2, 128.2, 128.1, 128.0, 127.9, 127.9, 127.8, 127.8, 127.8, 127.7, 127.6, 127.5, 127.5, 127.5, 127.4, 127.3 (CH_{arom}), 117.1, 117.1 (CH₂-CH=CH₂), 82.3 (C-1β), 80.0 (C-5β), 79.0 (C-3β), 78.1 (C-2α), 76.8 (C-4α), 75.2 (C-5α), 74.3, 74.2, 74.0 (CH₂ Bn), 74.0 (C-4β), 73.7, 73.2 (CH₂ Bn), 73.1 (C-3α), 72.7 (C-2β), 71.4, 71.1, 71.0 (CH₂ Bn), 69.9 (C-6β), 67.4 (C-1α), 66.4 (C-6α), 35.9, 35.8 (CH₂-CH=CH₂); HRMS: [M+NH₄]⁺ calcd for C₃₇H₄₀O₅NH₄ 582.32140, found 582.31986.

1-allyl-1,6-dideoxy-2,3,4-tri-O-benzyl-a-D-glucopyranoside (9B)



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **9** and Allyl-TMS, yielding compound **9B** (29 mg, 64 µmol, 64%, colourless oil, α : β >98:2); ¹H NMR (400 MHz, CDCl₃) δ 7.36 – 7.27 (m, 15H, CH_{arom}), 5.86 – 5.70 (m, 1H, CH₂-CH=CH₂), 5.15 – 5.04 (m, 2H, CH₂-CH=CH₂), 4.93 (d, *J* = 10.9 Hz, 1H, CHH Bn), 4.89 (d, *J* = 10.7 Hz, 1H, CHH Bn), 4.81 (d, *J* = 10.9 Hz, 1H, CHH Bn), 4.70 (d, *J* = 11.6 Hz, 1H, CHH Bn), 4.65 – 4.60 (m, 2H, 2x CHH Bn), 4.06 – 3.97 (m, 1H, H-1), 3.81 – 3.69 (m, 2H, H-2, H-3), 3.63 – 3.55 (m, 1H, H-5), 3.16 – 3.09 (m, 1H, H-4), 2.56 – 2.40 (m, 2H, CH₂-CH=CH₂), 1.23 (d, *J* = 6.1 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 138.9, 138.4 (C_q), 134.9 (CH₂-CH=CH₂),

131.2, 129.5, 129.3, 128.6, 128.6, 128.5, 128.2, 128.1, 127.9, 127.8, 124.9 (CH_{arom}), 117.0 (CH₂-CH=CH₂), 84.4 (C-4), 82.4, 80.6 (C-2, C-3), 75.6, 75.6 (CH₂ Bn), 73.8 (C-1), 73.2 (CH₂ Bn), 67.6 (C-5), 30.1 (CH₂-CH=CH₂), 18.5 (C-6); HRMS: $[M+NH_4]^+$ calcd for C₃₀H₃₄O₄NH₄ 476.27954, found 476.27873.

1-allyl-1-deoxy-2,3,4-tri-O-benzyl-α,β-L-rhamnopyranoside (10B)

Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor 10 and Allyl-TMS, yielding compound 10B (38 mg, 83 µmol, 83%, colourless oil, α : β 77:23); Data for the α -anomer: ¹H NMR (500 MHz, CDCl₃): δ 7.48 – 7.13 (m, 15H, CH_{arom}), 5.77 – 5.58 (m, 1H, CH₂-CH=CH₂), 5.05 – 4.91 (m, 2H, CH₂-CH=CH₂), 4.84 (d, J = 11.1 Hz, 1H, CHH Bn), 4.81 – 4.55 (m, 5H, 2x CHH Bn, 3x CHH Bn,), 4.01 (ddd, J = 8.2, 6.6, 3.4 Hz, 1H, H-1), 3.74 (dd, J = 7.9, 3.1 Hz, 1H, H-3), 3.67 (dd, J = 7.7, 6.1 Hz, 1H, H-5), 3.66 - 3.59 (m, 1H, H-2), 3.58 (t, J = 7.8 Hz, 1H, H-4), 2.34 (tdd, J = 8.2, 6.5, 1.4 Hz, 1H, CHH-CH=CH₂), 2.23 (dqd, J = 14.2, 6.9, 1.6 Hz, 1H, CHH-CH=CH₂), 1.33 (d, J = 6.2 Hz, 3H, H-6); ${}^{13}C$ NMR (126 MHz, CDCl3): δ 138.9, 138.6, 138.4 (C_q), 134.4 (CH₂-CH=CH₂), 128.6, 128.6, 128.5, 128.5, 128.2, 128.2, 128.0, 127.9, 127.8, 127.8, 127.7, 127.6 (CH_{arom}), 117.9 (CH₂-CH=CH₂), 80.3 (C-4), 78.1 (C-3), 75.3 (C-2), 74.8 (CH₂ Bn), 73.2 (C-1), 72.1, 71.8 (CH₂ Bn), 69.8 (C-5), 34.1 (CH₂-CH=CH₂), 18.2 (C-6); diagnostic signals for the β -anomer: 1H NMR (500 MHz, CDCl₃): δ 3.78 (dd, J = 2.7, 1.0 Hz, 1H, H-2), 3.36 - 3.28 (m, 2H, H-1, H-5), 2.50 - 2.39 (m, 1H, CHH-CH=CH₂); 13C NMR (126 MHz, CDCl3): § 134.9 (CH2-CH=CH2), 117.3 (CH2-CH=CH2), 78.3 (C-1), 76.1 (C-5), 74.9 (C-2), 35.9 (CH₂-CH=CH₂), 19.6 (C-6); HRMS: [M+Na]⁺ calcd for C₃₀H₃₄NaO₄ 481.2349, found 481.2355.

1-allyl-1-deoxy-2,3,4-tri-O-benzyl-α-L-fucopyranoside (11B)



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **11** and Allyl-TMS, yielding compound **11B** (35 mg, 76 µmol, 76%, colourless oil, $\alpha:\beta > 98:2$); ¹H NMR (500 MHz, CDCl₃): δ 8.06 – 6.84 (m, 15H, CH_{arom}), 5.76 (ddt, J = 17.1, 10.2, 6.9 Hz, 1H, CH₂-CH=CH₂), 5.14 – 4.93 (m, 2H, CH₂-CH=CH₂), 4.80 – 4.53 (m, 5H, 3x CHH Bn, 2x CHH Bn), 4.52 (d, J = 11.8 Hz, 1H, CHH Bn), 4.06 (ddd, J = 8.5, 5.2, 2.4 Hz, 1H, H-1), 3.95 (dd, J = 6.7, 3.8 Hz, 1H, H-5), 3.82 – 3.70 (m, 3H, H-2, H-3, H-4), 2.40 (dddt, J = 14.7, 9.4, 6.8, 1.4 Hz, 1H, CHH-CH=CH₂), 2.31 (dddd, J = 13.4, 6.9, 4.1, 1.4 Hz, 1H, CHH-CH=CH₂), 1.29 (d, J = 6.7 Hz, 3H, H-6); 13C NMR (126 MHz, CDCl₃): δ 139.0, 138.7, 138.5 (C_q), 135.5 (CH₂-CH=CH₂), 128.5, 128.4, 128.3, 128.1, 127.9, 127.7, 127.7, 127.7, 127.6 (CH_{arom}), 117.9 (CH₂-CH=CH₂), 76.9 (C-3), 76.7 (C-4), 76.0 (C-2), 73.2, 73.1, 73.1(CH₂ Bn), 70.3, (C-1), 68.8 (C-5), 31.2 (CH₂-CH=CH₂), 14.5 (C-6); HRMS: [M+Na]⁺ calcd for C₃₀H₃₄NaO₄ 481.2349, found 481.2347.

1-allyl-1,6-dideoxy-2,3,4-tri-O-benzyl-α-D-allopyranoside (12B)

Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **12** and Allyl-TMS, yielding compound **12B** (26 mg, 57 µmol, 57%, colourless oil, $\alpha:\beta > 98:2$); ¹H NMR (400 MHz, CDCl₃) δ 7.40 – 7.25 (m, 15H, CH_{arom}), 5.92 – 5.78 (m, 1H, CH₂-CH=CH₂), 5.14 – 4.99 (m, 2H, CH₂-CH=CH₂), 4.86 (d, *J* = 11.7 Hz, 1H, CHH Bn), 4.82 (d, *J* = 12.1 Hz, 1H, CHH Bn), 4.58 (s, 2H, CH₂ Bn), 4.55 (d, *J* = 11.7 Hz, 1H, CHH Bn), 4.40 (d, *J* = 11.7 Hz, 1H, CHH Bn), 4.19 (t, *J* = 2.6 Hz, 1H, H-3), 4.05 – 3.94 (m, 2H, H-1, H-5), 3.59 (dd, *J* = 6.0, 2.7 Hz, 1H, H-2), 3.11 – 2.99 (m, 2H, H-4, CHH-CH=CH₂), 2.58 – 2.48 (m, 1H, CHH-CH=CH₂), 1.22 (d, *J* = 6.2 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 139.2, 138.4, 138.1 (C_q), 136.8 (CH₂-CH=CH₂), 128.6, 128.5, 128.3, 128.3, 128.1, 127.9, 127.8, 127.5, 127.4 (CH_{arom}), 116.4 (CH₂-CH=CH₂), 80.6 (C-4), 77.6 (C-2), 74.3 (C-1), 74.0 (CH₂ Bn), 73.7 (C-3), 71.4, 71.2 (CH₂ Bn), 63.6 (C-5), 31.8 (CH₂-CH=CH₂), 18.2 (C-6); HRMS: [M+NH₄]⁺ calcd for C₃₀H₃₄O₄NH₄ 476.27954, found 476.27879.

1-allyl-1,6-dideoxy-2,3,4-tri-O-benzyl-α,β-D-altropyranoside (13B)



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **12** and Allyl-TMS, yielding compound **13B**. (31 mg, 67 μmol, 67%, colourless oil, α:β 89:11) Data for the α-anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.37 – 7.26 (m, 15H, CH_{arom}), 5.84 (ddt, J = 17.1, 10.2, 6.9 Hz, 1H, CH₂-CH=CH₂), 5.13 – 5.02 (m, 2H, CH₂-CH=CH₂), 4.74 (d, J = 11.3 Hz, 1H, CHH Bn), 4.62 – 4.55 (m, 5H, 2x CHH Bn, 3x CHH Bn), 4.21 – 4.11 (m, 1H, H-5), 3.79 (dd, J = 6.8, 3.1 Hz, 1H, H-3), 3.72 – 3.62 (m, 2H, H-1, H-2), 3.52 (dd, J = 4.8, 3.1 Hz, 1H, H-4), 2.62 – 2.45 (m, 2H, CH₂-CH=CH₂), 1.19 (d, J = 6.8 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 138.5, 138.5, 138.4 (Cq), 135.4 (CH₂-CH=CH₂), 128.5, 128.5, 128.1, 128.0, 128.0, 127.9, 127.8, 127.7 (CH_{arom}), 116.9 (CH₂-CH=CH₂), 77.6 (C-2), 77.3 (C-4), 77.3 (C-3), 74.0 (CH₂ Bn), 73.4 (C-1), 72.3, 71.7 (CH₂ Bn), 68.4 (C-5), 36.9 (CH₂-CH=CH₂), 13.1 (C-6); diagnostic peaks for the β-anomer: ¹H NMR (400 MHz, CDCl₃) δ 5.74 – 5.61 (m, 1H, CH₂-CH=CH₂), 2.39 (dt, J = 13.1, 6.9 Hz, 1H, CHH-CH=CH₂), 127.0 (CH₂-CH=CH₂), 34.1 (CH₂-CH=CH₂), 18.3 (C-6); HRMS: [M+NH₄]⁺ calcd for C₃₀H₃₄O₄NH₄ 476.27954, found 476.27867.

<u>1-allyl-1,6-dideoxy-2,3,4-tri-O-benzyl-a-L-gulopyranoside (14B)</u>

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Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **14** and Allyl-TMS, yielding compound **14B** (35 mg, 75 μ mol, 75%, colourless oil, α : β >98:2); ¹H NMR (400 MHz, CDCl₃) δ 7.38 – 7.26 (m, 15H, CH_{arom}), 5.73 (ddt, *J*

= 17.1, 10.2, 7.0 Hz, 1H, CH₂-CH=CH₂), 5.08 – 4.97 (m, 2H, CH₂-CH=CH₂), 4.86 (d, J = 11.6 Hz, 1H, CHH Bn), 4.74 (s, 2H, CH₂ Bn), 4.67 (d, J = 11.8 Hz, 1H, CHH Bn), 4.61 (d, J = 11.7 Hz, 1H, CHH Bn), 4.58 (d, J = 11.8 Hz, 1H, CHH Bn), 4.28 – 4.20 (m, 1H, H-5), 3.91 (bs, 1H, H-4), 3.81 (t, J = 2.7 Hz, 1H, H-3), 3.78 – 3.67 (m, 2H, H-1, H-2), 2.57 (dt, J = 14.6, 7.5 Hz, 1H, CHH-CH=CH₂), 2.28 (dt, J = 14.1, 6.3 Hz, 1H, CHH-CH=CH₂), 1.20 (d, J = 6.8 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 138.9, 138.7, 138.6 (Cq), 135.6 (CH₂-CH=CH₂), 128.5, 128.4, 128.4, 128.2, 128.0, 127.8, 127.7, 127.6, 127.6 (CH_{arom}), 116.8 (CH₂-CH=CH₂), 78.1 (C-2), 77.2 (C-4), 75.7 (C-3) 73.7, 73.2, 73.2 (CH₂ Bn), 72.1 (C-1), 34.4 (CH₂-CH=CH₂), 13.5 (C-6), C-5 is invisible in the 13C-spectrum, but shows a cross-peak at 68.0 in the HSQC-spectrum; HRMS: [M+NH₄]⁺ calcd for C₃₀H₃₄O₄NH₄ 476.27954, found 476.27877

<u>1-allyl-1,6-dideoxy-2,3,4-tri-O-benzyl-α,β-L-idopyranoside (15B)</u>



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor 15 and Allyl-TMS on 50 µmol scale, yielding compound 15B. (11 mg, 24 µmol, 48%, colourless oil, α : β 21:79) Data for the β -anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.66 - 7.02 (m, 15H, CH_{arom}), 5.79 - 5.65 (m, 1H, CH₂-CH=CH₂), 5.06 - 4.94 (m, 2H, CH₂-CH=CH₂), 4.61 – 4.53 (m, 2H, 2x CHH Bn), 4.41 (d, J = 12.3 Hz, 2H, 2x CHH Bn), 4.32 (s, 2H, CH₂ Bn), 3.77 (qd, J = 6.6, 1.7 Hz, 1H, H-5), 3.70 – 3.60 (m, 2H, H-1, H-3), 3.19 (q, J = 2.7, 2.2) Hz, 1H, H-2), 3.10 (t, J = 2.8 Hz, 1H, H-4), 2.57 – 2.48 (m, 1H, CHH-CH=CH₂), 2.33 – 2.24 (m, 1H, CH*H*-CH=CH₂), 1.21 (d, *J* = 6.6 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 138.4, 138.4, 138.1 (C_q), 135.5 (CH₂-CH=CH₂), 128.8, 128.7, 128.6, 128.4, 128.4, 128.1, 128.0, 127.9, 127.9, 127.8 (CH_{arom}), 116.7 (CH₂-CH=CH₂), 76.1 (C-1), 74.8 (C-4), 73.2 (C-2), 72.5, 72.3 (CH₂ Bn), 72.2 (C-5), 71.9 (CH₂ Bn), 70.5 (C-3), 35.6 (CH₂-CH=CH₂), 17.0 (C-6); diagnostic peaks for the α-anomer: ¹H NMR (400 MHz, CDCl₃) δ 5.88 – 5.79 (m, 1H, CH₂-CH=CH₂), 4.90 (d, J = 10.8 Hz, 1H, CHH Bn), 4.80 (d, J = 10.8 Hz, 1H, CHH Bn), 4.68 (d, J = 11.6 Hz, 1H, CHH Bn), 4.19 (p, J = 6.5 Hz, 1H, H-5), 3.24 (dd, J = 9.7, 8.7 Hz, 1H), 1.27 (d, J = 7.0 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) & 134.7 (CH₂-CH=CH₂), 117.5 (CH₂-CH=CH₂), 81.9, 80.6, 75.3, 73.2, 70.8, 70.0, 11.0 (C-6); HRMS: [M+NH₄]⁺ calcd for C₃₀H₃₄O₄NH₄ 476.27954, found 476.27867.

1-allyl-1,6-dideoxy-2,3,4-tri-O-benzyl-a-L-talopyranoside (16B)



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor 16 and Allyl-TMS, yielding compound 16B (25 mg, 55 μ mol, 55%, colourless oil, $\alpha:\beta > 98:2$); ¹H NMR (500 MHz, CDCl₃) δ 7.40 – 7.23 (m, 15H, CH_{arom}), 5.90 – 5.77 (m, 1H, CH₂-CH=CH₂), 5.09 (dq, *J* = 17.2, 1.6 Hz, 1H, CH₂-CH=CHH), 5.06 – 5.02 (m, 1H, CH₂-CH=CHH), 4.87 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.80 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.58 (s, 2H, CH₂ Bn), 4.54 (d, *J* = 11.5 Hz, 1H, CHH Bn), 4.38 (d, *J* = 11.5 Hz, 1H, CHH Bn), 4.22 (t, *J* = 2.6 Hz, 1H, H-3), 4.18 (p, *J* = 6.9 Hz, 1H, H-5), 4.07 – 4.00 (m, 1H, H-1), 3.51 (dd, *J* = 6.0, 2.7 Hz, 1H, H-4), 3.13 (dd, *J* = 9.4, 2.8 Hz, 1H, H-2), 2.61 (dddd, *J* = 13.1, 6.0, 3.2, 1.6 Hz, 1H, CHH=CH=CH₂CH₂CH₂CH₂CH₂CH₂(d, *J* = 14.9, 7.8 Hz, 1H, CHH-CH=CH₂), 1.49 (d, *J* = 7.0 Hz, 3H, H-6);

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 $\label{eq:constraint} \begin{array}{l} ^{13}C\ NMR\ (126\ MHz,\ CDCl_3)\ \delta\ 139.3,\ 138.5,\ 138.1\ (C_q),\ 135.2\ (CH_2-CH=CH_2),\ 128.5,\ 128.5,\ 128.3, \\ 128.0,\ 127.9,\ 127.9,\ 127.9,\ 127.5,\ 127.4\ (CH_{arom}),\ 116.8\ (CH_2-CH=CH_2),\ 78.5\ (C-2),\ 77.5\ (C-4), \\ 74.0\ (CH_2\ Bn),\ 73.8\ (C-3),\ 71.3,\ 71.0\ (CH_2\ Bn),\ 70.5\ (C-5),\ 66.7\ (C-1),\ 36.1\ (CH_2-CH=CH_2),\ 14.1\ (C-6);\ HRMS:\ [M+NH_4]^+\ calcd\ for\ C_{30}H_{34}O_4NH_4\ 476.27954,\ found\ 476.27866. \end{array}$

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Chapter 3: Acceptor nucleophilicity – Glycosylation stereoselectivity mapping for all eight diastereomeric pyranosyl donors

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Chapter 3

Introduction

Upon activation of a glycosyl donor in a glycosylation reaction, a mixture of different reactive intermediates is formed (Figure 1). Depending on the glycosyl donor, the activator, the acceptor (NuH) and external factors, the α -product, the β -product or a mixture thereof can be formed, through a $S_N 2$ mechanism, featuring a covalent reactive intermediate or a S_N 1-like mechanism, operating via an oxocarbenium ion intermediate.¹⁻⁴ Insight into the "extremes of the mechanistic spectrum" can help to better understand and eventually predict the stereochemical outcome of glycosylation reactions taking place somewhere along the mechanism continuum. The previous Chapter deals with the S_N side of the spectrum by determining the influence of the substitution pattern of the sugar ring on the conformational preference and reactivity of the intermediate oxocarbenium ions, using a combination of computational chemistry and glycosylation experiments with C- and D-nucleophiles. This Chapter will focus on the other end of the mechanistic spectrum by investigating the covalent intermediates and the influence of the reactivity of the acceptor on the S_N mechanism. For S_N reactions and the associated oxocarbenium ions, it is clear that the functional groups on C-2, C-3, C-4 and C-6 heavily influence the outcome,⁵⁻⁷ with the stereochemistry of C-2 playing an all important role (this thesis, Chapter 2). To systematically map the influence of the ring substitution pattern of the donor in S_N 2type glycosylations, in the study of this Chapter all eight diastereomeric pyranosyl thiophenol donors^{*} were used (*Figure 2A*) while the reactive intermediates, formed upon activation were characterised using variable temperature (VT)-NMR. While VT-NMR has been used to detect many covalent species for the usual monosaccharides (predominantly triflates and oxosulfonium triflates)⁸⁻¹⁵ the reactive intermediates for the more rare diastereomers have not yet been identified.



Figure 1: Equilibrium of reactive species in a glycosylation reaction,

[‡] For the synthesis of the allose, altrose, gulose, idose and talose donor, see Chapter 2

After establishing of the structure of the species formed upon activation of the eight diastereomeric pyranosyl donors, the effect of the nucleophilicity of the acceptor on the stereoselectivity of the glycosylations was mapped. To this end the well-established set of fluorinated model alcohols (*Figure 2B*) was used. Of these, the most reactive acceptor -ethanol- has been shown to react with relatively stable covalent intermediates (generally the axially oriented α -triflates), while the weaker nucleophiles (such as trifluorethanol) require a more potent electrophile, such as a β -triflate or more dissociated oxocarbenium ion-triflate ion pair.^{9, 10, 14, 16-19}



Figure 2: A: Donors (1-8) divided by configuration and *B*: model acceptors (EtOH, MFE, DFE, TFE and HFIP) used in this study.

Results and discussion

Characterisation of reactive intermediates

To study the glycosylating properties of the glycosyl donors **1-8** their activation and the formation of reactive intermediates was studied by VT-NMR (*Figure* **3-6**). To this end, a mixture of the donor (1 eq) and Ph₂SO (1.3 eq) in CD₂Cl₂ (50 mM) was cooled to -80 °C, after which Tf₂O (1.3 eq) added. The reaction mixture was then allowed to warm to -60 °C after which the reactive species were characterized. To aid in the identification some experiments were repeated using 3 eq. Ph₂SO, promoting the formation of sulfoxonium triflate species. The results of the VT-NMR are summarized in *Table* **1**.

When glucose donor 1 was activated, a mixture of two species was formed (*Figure* 3), which were identified as the α -triflate (**A**, H-1: 6.15 (d, *J* = 3.1 Hz)), previously reported in literature,^{20, 21} and the α -oxosulfonium triflate (C, H-1: 6.51 (d, J = 3.4 Hz)). Galactose 2 gave three species upon activation: the α -triflate (A, H-1: 6.19 (d, J = 3.3Hz)), the α -oxosulfonium triflate (C, H-1: 6.43 (d, I = 3.5 Hz)) and the β -oxosulfonium triflate (D, H-1: 5.50 (d, J = 7.9 Hz)), of which the α -triflate has previously been described.²¹ Both allose (3) and gulose donor (4, Figure 4) gave the α - and β oxosulfonium triflates upon activation (for allose: C, H-1: 6.13 (d, I = 3.7 Hz) and D, H-1: 5.79 (d, I = 7.8 Hz); for gulose: C, H-1: 6.21 (d, I = 3.6 Hz) and (D, H-1: 5.80 (d, I =8.1 Hz)). The latter two donors provide significantly more of the β -oriented covalent species, which can be directly related to the axial C-3-substituent that destabilizes the α oriented triflate and oxosulfonium triflate through 1,3-diaxial interactions. Activation of mannose donor (5, *Figure 5*), led to three species: the α -triflate (A, H-1: 6.10 (s)), the α -oxosulfonium triflate (C, H-1: 6.44 (s)) and the β -oxosulfonium triflate (D, H-1: 5.86 (s)). It has been argued that mannosyl β -triflates cannot be formed because of their instability, that results from the unfavourable orientation with respect to the ring oxygen and the C-2-substituent (the so called Δ 2-effect). The formation of the β oxosulfonium triflate however indicates that a role for these species in the glycosylation manifold should not a priori be ruled out. Of note, for a conformationally restricted mannose-type donor a β -oxosulfonium triflate has also been reported.²² The α -triflate and a-oxosulfonium triflate have previously been characterised for the tetra-O-methyl donor.^{23, 24} Talose (6, *Figure 5*), forms the α -triflate upon activation (A, H-1: 6.17 (s)) as well as an α -oxosulfonium triflate (C, H-1: 6.28 (s)). No β -oriented species could be identified from the mixture of this active donor. Altrose (7, *Figure 6*) also gave two α oriented species upon activation: the α -triflate (A, H-1: 5.96 (s)) and the α oxosulfonium triflate (C, H-1: 6.26 (s)). The activation of Idose (8, Figure 6) under the standard conditions led to the formation of a side product, which unfortunately could not be characterized. This may be due to the relatively high reactivity of the idose donor, resulting from the three axial ring substituents.²⁵ When three equivalents of Ph₂SO were used for the activation the α -triflate (A, H-1: 6.17 (s)) as well as the α oxosulfonium triflate (C, H-1: 6.28 (s)) were formed



Figure 3: Activated donors 1 and 2 at -60 °C in CD₂Cl₂

1H-NMR of activated donor 3



Figure 4: Activated donors 3 and 4 at -60 °C in CD₂Cl₂





Figure 5: Activated donors 5 and 6 at -60 °C in CD₂Cl₂

1H-NMR of activated donor 7



Figure 6: Activated donors 7 and 8 at -60 C in CD₂Cl₂

	H-1 : δ (multiplicity, <i>J_{H1-H2}</i>)						
Donor	α-OTf	β-OTf	α -OSPh ₂ ⁺	β -OSPh ₂ ⁺	ratio		
	(A)	(B)	(C)	(D)			
Glucose (1)	6.15		6.51	d	A:C		
	(d, J = 3.1 Hz)	11 . α.	(d, J = 3.4 Hz)	11. a .	49:51		
Galactose (2)	6.19		6.43	5.50	A:C:D		
	(d, <i>J</i> = 3.3 Hz)	n.a.	(d, J = 3.5 Hz)	(d, J = 7.9 Hz)	37:55:7		
Allose (3)	n.d.	n.d.	6.13	5.79	C:D		
			(d, J = 3.7 Hz)	(d, J = 7.8 Hz)	70:30		
Gulose (4)		n.d.	6.21	5.80	C:D		
	n.a.		(d, J = 3.6 Hz)	(d, J = 8.1 Hz)	41:59		
Mannose (5)	6.10	nd	6.44	5.86	A:C:D		
	(s)	11 . α.	(s)	(s)	71:18:11		
Talose (6)	6.17	nd	6.28	nd	A:C		
	(s)	11 . α.	(s)	n.a	91:9		
Altrose (7)	5.96	nd	6.26	nd	A:C		
	(s)	n.a.	(s)	n.a	35:65		
Idose (8) ^a	6.00	nd	6.21	nd	A:C		
	(s)	11 . α.	(s)	11. u	19:81		

Table 1: Reactive species observed with VT-NMR at -60 °C. n.d. = not detected

a: 3 eq. of Ph_2SO were used, in VT-NMR with 1.3 eq. Ph_2SO only an yet unidentified decomposition product was found.

Chapter 3

Reactions with O-nucleophiles

Next, all eight pyranosyl donors were glycosylated with five different acceptors of different nucleophilicity (EtOH, MFE, DFE, TFE and HFIP) to probe the relation between stereoselectivity of the glycosylation reaction and reactivity of the acceptor.^{9, 10,} ^{17, 18} The results of these glycosylations are summarized in *Table 2*, together with the results of the glycosylation of the donors with the S_N1 model nucleophile TES-D (*This* thesis, chapter 2). In Table 2, the donors are organized by configuration of their C-2 and C-3 substituents to highlight the correlation between the orientation of these substituents and the reactivity-stereoselectivity trends. Of note, the selectivity of HFIP, the weakest O-nucleophile, differs significantly form the selectivity obtained with TES-D. TES-D gives *cis* selectivity with respect to the C-2-OBn (α when C-2-OBn is equatorial and β when C-2-OBn is axial), while the glycosylations of HFIP selectively provide the α -products, regardless of the stereochemistry of C-2. The differences between the results of the "S_N1 nucleophile" TES-D and HFIP suggest that reactions between a glycosyl donor and a weak O-nucleophile follow a different pathway than nucleophilic addition to an oxocarbenium ion. Another clear trend when looking at the stereoselectivity trends going from ethanol (EtOH) to 2,2,2-trifloroethanol (TFE) is observed for the donors having an equatorial C-3-OBn group (*i.e.* glucose, galactose, mannose and talose, 1, 2, 5 and 6 respectively): the stereoselectivity observed for these donors gradually changes as a function of acceptor nucleophilicity with the more nucleophilic acceptors giving more β -product and the less nucleophilic acceptors providing more α -product. When the C-3-OBn group is axial (as in the allose, gulose, altrose and idose donors 3, 4, 7 and 8) no clear acceptor reactivity-stereoselectivity relationship was found. A potential mechanistic rationale for these observations is depicted in *Figure 7*. For the donors with an equatorial C-3-OBn, the α -triflate or α oxosulfonium triflate are more stable than the β -species, as revealed by the VT-NMR experiments. The α -species can be in equilibrium with the more reactive β intermediates, that can form, as indicated by the observation of the galactose and mannose β -oxosulfonium triflates. The most reactive acceptors can substitute the α triflate or α -oxosulfonium triflates to provide the β -product. With gradually decreasing acceptor reactivity, substitution of the more reactive β -intermediates will become more important, leading to the formation of more α -product (*Figure 7A*). In the donors having a C-3-OBn is axial, the difference in stability between the α -species and the β species is smaller because of the 1,3-diaxial interactions between the α -(oxosulfonium) triflate on C-1 and the OBn-group on C-3.²⁶ However, in the S_N2-type substitution on the β-species, the trajectory for the incoming nucleophile is also hindered by the C-3-OBn group (Figure 7B). Thus, the 'conflicting' steric interactions lead to overall poor stereoselectivity in the glycosylation reactions.

Donor	C-2	C-3	TES-D	HFIP	TFE	DFE	MFE	EtOH
1	-		1A	1F	1E	1D	1C	1B
Glc	Eq	Eq	>98:2	>98:2	75:25	48:52	36:64	15:85
			(70%)	(41%)	(80%)	(58%)	(75%)	(70%)
2			2A	2F	2 E	2D	2C	2B
Gal	Eq	Eq	>98:2	>98:2	87:13	66:34	31:69	17:83
			(86%)	(33%)	(79%)	(69%)	(84%)	(73%)
3 All	Eq	Ax	3A	3F	3E	3D	3C	3B
			>98:2	>98:2	50:50	58:42	55:45	46:54
			(74%)	(30%)	(68%)	(60%)	(n.d.) ^a	(45%)
			4A	4F	4 E	4D	4C	4B
4	Eq	Ax	>98:2	>98:2	60:40	69:31	83:17	78:22
Gul	-		(83%)	(39%)	(85%)	(83%)	(85%)	(94%)
_			5A	5F	5E	5D	5C	5B
5 M	Ax	Eq	3:97	>98:2	>98:2	80:20	60:40	33:67
Man			(93%)	(39%)	(84%)	(65%)	(75%)	(70%)
6			6A	6F	6 E	6D	6C	6B
0 T-1	Ax	Eq	<2:98	>98:2	90:10	86:14	80:20	68:32
1 ai			(51%)	(14%)	(69%)	(73%)	(74%)	(70%)
-			7A	7 F	7E	7D	7C	7B
/	Ax	Ax	20:80	>98:2	85:15	69:31	58:42	75:25
Alt			(55%)	(16%)	(73%)	(64%)	(60%)	(79%)
0			8A	8F	8E	8D	8C	8B
Ğ LL	Ax	Ax	<2:98	>98:2	69:31	55:45	57:43	57:43
100			(74%)	(22%)	(66%)	(72%)	(72%)	(76%)

Table 2: Stereoselectivity of all eight pyranosyl donors with O-nucleophiles and TES-D. Selectivity is given as the α : β ratio in the glycosylation product. Eq = equatorial, Ax = axial n.d. = not determined

For reactions with TES-D, see chapter 2. The stereoselectivity of donors **1**, **2** and **5** was previously published.¹⁹ a: an accurate yield can't be determined because of poor separation of the glycosylated product from the hydrolysed donor



Figure 7: The impact of the orientation of the C-3-OBn on the acceptor reactivity-stereoselectivity trends. A: For donors having an equatorial C-3-OBn the α -oriented intermediates are more stable, and the β -intermediates are more reactive. The most nucleophilic acceptors can react with the more prevalent former species, while less reactive acceptors need a stronger electrophile. Through a Curtin-Hammett type scenario, the reaction of the poor nucleophiles will shift to the substitution of the β -configured intermediates. B: The axial C-3-OBn destabilizes the α -triflate and oxosulfonium triflate, favoring the formation of the corresponding β -species, but also hinders nucleophilic attack of the incoming nucleophile on the β -species.

Conclusion

After the investigation of the S_N side of the glycosylation as outlined in Chapter 2, the research of this chapter has characterized the covalent reactive species of all eight pyranosyl donors that play a role on the S_N2 -side of the glycosylation reaction mechanism continuum. VT-NMR was used to characterise the reactive intermediates. In general, activation of the glycosyl donors leads to the preferential formation of α triflates and α -oxosulfonium triflates. The galactose and mannose donors do provide a minor amount of the β -oxosulfonium triflate, while activation of the allose and especially the gulose donor, both having an axial C-3-group, leads to the generation of a significant amount of the equatorially oriented oxosulfonium species. Even though only minor amounts of the β -oxosulfonium triflates are formed, the existence of these species indicates that they may play a role in the glycosylation reactions of the different donors. Next, the eight pyranosyl donors were reacted with a set of model acceptors of gradually changing nucleophilicity. From the glycosylation with fluorinated acceptors, it becomes clear that, while S_N1 reactions are typically 1,2-cis selective as observed by glycosylation with TES-D and supported by CEL-maps of the oxocarbenium ions, glycosylation of (very) weak O-nucleophiles always provide the α -product, regardless of the stereochemistry at C-2. This shows that the reactions of weak C/D or Onucleophiles do not proceed via the same pathway. This discrepancy can be explained by the different nature of the nucleophiles and stereoelectronic effects that play a role in the transition states of the addition reactions to the oxocarbenium ions. The development of a stabilizing anomeric effect may promote the formation of the α products and H-bonding effects between the nucleophile and donor species will also play a role in shaping the trajectory of the incoming O-nucleophiles. However, the acceptor reactivity-stereoselectivity trends observed here, can also be accounted for

with S_N2 -type product forming reaction pathways. For the donors having an equatorially oriented C-3-OBn group, a clear shift from β - to α -selectivity was observed with decreasing nucleophilicity of the acceptor. Through a Curtin-Hammett kinetic scenario, in which the weaker nucleophiles preferentially react with the less available but more reactive intermediates, the acceptor reactivity-stereoselectivity trends can be explained. The donors that carry an axial C-3-OBn group typically provide mixtures of anomers in a ratio that shows no clear correlation with the nucleophilicity of the acceptor. To better understand the stereochemical outcome of the glycosylations studied here, systematic computational studies into the nature of the different transition states as well as kinetic studies, supplemented by the establishment of kinetic isotope effects will prove valuable.

Chapter 3

Experimental

Procedure for VT-NMR experiments of glycosyl donors

A mixture of donor (30 μ mol) and Ph₂SO (39 μ mol or 90 μ mol) was coevaporated with toluene, dissolved in 0.6 mL of CD₂Cl₂ under nitrogen atmosphere and transferred to an oven-dried NMR tube flushed with nitrogen gas and sealed with an NMR tube septum. The magnet was cooled to -80 °C, locked, and shimmed and the sample was measured prior to activation. In a separate cold bath (-80 °C) the sample was treated with Tf₂O (39 μ mol) and shaken and recooled 3x. 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 of equilibration time for every temperature.

General procedure for Ph₂SO/Tf₂O mediated glycosylations

Donor (0.1 mmol, 1 eq), Ph₂SO (0.13 mmol, 1.3 eq) and TTBP (0.25 mmol, 2.5 eq) were coevaporated twice with toluene, dissolved in 2 mL DCM and stirred for 30 min at RT with 3 Å molecular sieves. The solution was cooled to -80 °C and Tf₂O (22 μ L, 0.13 mmol, 2 eq) was added. The reaction mixture was allowed to warm to -60 °C and then recooled to -80 °C, after which the acceptor (0.2 mmol, 2 eq) in DCM (0.4 mL, 0.5 M) was added. The reaction mixture was allowed to warm to -60 °C and then recooled to -80 °C, after which the acceptor (0.2 mmol, 2 eq) in DCM (0.4 mL, 0.5 M) was added. The reaction mixture was allowed to warm to -60 °C for and stirred for 2 hr at that temperature. The reaction was quenched with 2 mL sat aq NaHCO₃, 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 MgSO4, filtered, and concentrated in vacuo. Purification by silica gel flash column chromatography and/or sephadex LH-20 size-exclusion chromatography yielded the glycosylation product as a mixture of anomers.

Ethyl-2,3,4,6-tetra-O-benzyl-α,β-D-allopyranoside (3B)

Bno O Bno Bno no

Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **3** and ethanol, yielding compound **3B** (25 mg, 45 µmol, 45%, colourless oil, $\alpha:\beta = 46:54$). An analytical amount was separated of both anomers was separated for characterisation. α -anomer: ¹H NMR (400 MHz, CDCl₃) δ , 7.35 – 7.15 (m, 20H, CH_{arom}), 4.97 (d, *J* = 12.3 Hz, 1H, CHH Bn), 4.92 (d, *J* = 4.0 Hz, 1H, H-1), 4.83 (d, *J* = 12.3 Hz, 1H, CHH Bn), 4.92 (d, *J* = 4.0 Hz, 1H, H-1), 4.83 (d, *J* = 12.3 Hz, 1H, CHH Bn), 4.64 – 4.56 (m, 3H, CHH Bn, CH₂ Bn), 4.52 – 4.45 (m, 2H, CHH Bn, CHH Bn), 4.37 (d, *J* = 11.6 Hz, 1H, CHH Bn), 4.27 (dt, *J* = 10.1, 2.5 Hz, 1H, H-5), 4.18 (t, *J* = 2.8 Hz, 1H, H-3), 3.85 – 3.74 (m, 2H, CHH Et, H-6), 3.67 (dd, *J* = 10.5, 2.1 Hz, 1H, H-6), 3.60 – 3.49 (m, 2H, CHH Et, H-4), 3.43 (dd, *J* = 4.1, 2.8 Hz, 1H, H-2), 1.28 (t, *J* = 7.1 Hz, 3H, CH₃ Et) ¹³C NMR (101 MHz, CDCl₃) δ 145.7, 139.7, 138.3, 138.2 (C_q), 131.2, 129.5, 128.5, 128.4, 128.4, 128.0, 128.0, 127.9, 127.8, 127.8, 127.7, 127.1, 124.9 (CH_{arom}), 97.0 (C-1), 76.7 (C-2), 74.9 (C-4), 73.7, 73.5 (CH₂ Bn), 72.6 (C-3), 71.2, 71.2 (CH₂ Bn), 69.0 (C-6), 66.2 (C-5), 63.9 (CH₂ Et), 15.4 (CH₃ Et); β -anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.52 – 7.04 (m, 20H, CH_{arom}), 4.93 – 4.84 (m, 3H, 2x CHH Bn, H-1), 4.79 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.68 – 4.57 (m, 2H, CHH Bn, CHH Bn), 4.54 (d, *J* = 12.3 Hz,

1H, CH*H* Bn), 4.47 (d, *J* = 11.5 Hz, 1H, C*H*H Bn), 4.35 (d, *J* = 11.5 Hz, 1H, CH*H* Bn), 4.10 (t, *J* = 2.6 Hz, 1H, H-3), 4.06 (ddd, *J* = 9.8, 4.8, 1.9 Hz, 1H, H-5), 3.99 (dq, *J* = 9.5, 7.1 Hz, 1H, C*H*H Et), 3.76 (dd, *J* = 10.7, 1.9 Hz, 1H, H-6), 3.70 – 3.55 (m, 2H, CH*H* Et, H-6), 3.45 (dd, *J* = 9.8, 2.5 Hz, 1H, H-4), 3.24 (dd, *J* = 7.9, 2.7 Hz, 1H, H-2), 1.27 (t, *J* = 7.0 Hz, 3H, CH₃ Et) ¹³C NMR (101 MHz, CDCl₃) δ 139.2, 139.0, 138.6, 138.0 (C_q), 128.5, 128.4, 128.4, 128.3, 128.0, 127.9, 127.9, 127.8, 127.7, 127.6, 127.6, 127.4 (CH_{arom}), 101.1 (C-1), 79.1 (C-2), 75.9 (C-4), 74.9 (C-3), 74.5, 73.6, 73.2 (CH₂ Bn), 72.5 (C-5), 71.6 9, CH₂ Bn), 69.6 (C-6), 65.5 (CH₂ Et), 15.6 (CH₃ Et); HRMS: [M+NH₄]⁺ calcd for C₃₆H₄₀O₆NH₄ 586.31631, found 586.31478.

2-Fluoroethyl-2,3,4,6-tetra-O-benzyl-α,β-D-allopyranoside (3C)



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor 3 and 2-fluoroethanol, yielding compound 3C (colourless oil, $\alpha:\beta$ = 55:45, contaminated with hydrolysed donor). Data reported for a 1:1 mixture: ¹H NMR (500 MHz, CDCl₃) δ 7.44 – 7.16 (m, 40H, CH_{arom}), 4.98 – 4.94 (m, 2H, H-1a, CHH Bn), 4.93 (d, J = 7.9 Hz, 1H, H-1β), 4.90 – 4.86 (m, 2H, 2x CHH Bn), 4.84 – 4.77 (m, 2H, 2x CHH Bn), 4.66 – 4.58 (m, 6H, 2x CH₂-CHHF, 4x CHH Bn/CHH Bn), 4.56 – 4.44 (m, 7H, 2x CH₂-CHHF, 5x CHH Bn/CHH Bn), 4.38 (d, J = 11.6 Hz, 1H, CHH Bn), 4.35 (d, J = 11.5 Hz, 1H, CHH Bn), 4.32 - 4.28 (m, 1H, H-5a), 4.18 (t, J = 2.8 Hz, 1H, H-3a), 4.14 – 4.03 (m, 3H, H-3β, H-5β, CHH-CH₂F), 3.97 – 3.87 (m, 1H, CHH-CH₂F), 3.86 – 3.71 (m, 4H, H-6a, H-6β, 2x CHH-CH₂F), 3.70 – 3.64 (m, 2H, H-6a, H-6β), 3.55 (dd, J = 9.9, 2.7 Hz, 1H, H-4α), 3.48 - 3.43 (m, 2H, H-2α, H-4β), 3.27 (dd, J = 7.9, 2.6 Hz, 1H, H-2β); ¹³C NMR (126 MHz, CDCl₃) δ 139.6, 139.1, 138.9, 138.5, 138.2, 138.1, 138.0, 137.9, 137.8, 137.8 (C_q), 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.4, 128.3, 128.3, 128.1, 128.1, 128.1, 128.1, 128.0, 128.0, 128.0, 128.0, 127.9, 127.9, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 127.6, 127.5, 127.1 (CH_{arom}), 101.5 (C-1β), 97.6 (C-1α), 83.0 (d, J = 169.4 Hz, CH₂- CH_2F), 82.9 (d, J = 169.4 Hz, CH_2-CH_2F) 78.9 (C-2 β), 76.6 (C-2 α), 75.7 (C-4 β), 74.9 (C-3 β), 74.8 (C-4α), 74.5, 73.7, 73.6, 73.6, 73.2 (CH₂ Bn), 72.6, 72.6 (C-3α, C-5β), 71.7, 71.3, 71.2 (CH₂ Bn), 69.4 (C-6β), 68.9 (C-6α, CH₂-CH₂F), 67.5 (d, J = 20.6 Hz, CH₂-CH₂F) 66.4 (C-5α); HRMS: [M+NH₄]⁺ calcd for C₃₆₃H₃₉FO₆NH₄ 604.30689, found 604.30531.

2,2-difluoroethyl-2,3,4,6-tetra-O-benzyl-α,β-D-allopyranoside (3D)

Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **3** and 2,2-difluoroethanol, yielding compound **3D** (36 mg, 60 µmol, 60%, colourless oil, $\alpha:\beta = 58:42$) Data reported for a 1:1 mixture: ¹H NMR (400 MHz, CDCl₃) δ 7.60 – 6.88 (m, 40H, CH_{arom}), 5.96 (tddd, *J* = 55.6, 7.4, 5.0, 3.6 Hz, 2H, 2x CH₂-CHF₂), 4.96 – 4.88 (m, 3H, H-1 α , H-1 β , CHH Bn), 4.86 – 4.76 (m, 3H, 2x CHH Bn, CHH Bn), 4.62 – 4.53 (m, 6H, 6x CHH Bn/CHH Bn), 4.52 – 4.44 (m, 4H, 4x CHH Bn/CHH Bn), 4.38 (d, *J* = 8.4 Hz, 1H, CHHBn), 4.35 (d, *J* = 8.4 Hz, 1H, CHHBn), 4.28 (ddd, *J* = 9.8, 3.4, 2.1 Hz, 1H, H-5 α), 4.17 (t, *J* = 2.7 Hz, 1H, H-3 α), 4.09 (t, *J* = 2.6 Hz, 1H, H-3 β), 4.05 (ddd, *J* = 9.8, 4.5, 2.0 Hz, 1H, H-5 β), 4.03 – 3.92 (m,

1H, CHH-CHF₂), 3.90 – 3.71 (m, 5H, H-6 α , H-6 β , CHH-CHF₂, 2x CHH-CHF₂), 3.70 – 3.63 (m, 2H, H-6 α , H-6 β), 3.55 (dd, *J* = 9.9, 2.7 Hz, 1H, H-4 α), 3.47 (dd, *J* = 9.8, 2.5 Hz, 1H, H-4 β), 3.44 (dd, *J* = 4.0, 2.8 Hz, 1H, H-2 α), 3.26 (dd, *J* = 7.9, 2.6 Hz, 1H, H-2 β); ¹³C NMR (101 MHz, CDCl₃) δ 139.4, 139.0, 138.6, 138.3, 138.1, 137.9, 137.9 (C_q), 128.6, 128.5, 128.5, 128.3, 128.1, 128.1, 128.1, 128.0, 127.9, 127.9, 127.9, 127.9, 127.8, 127.7, 127.6, 127.2 (CH_{arom}), 117.3 – 111.7 (m, 2x CH₂-CHF₂) 101.8 (C-1 β), 98.1 (C-1 α), 78.8 (C-2 β), 76.5 (C-2 α), 75.5 (C-4 β), 74.7 (C-4 α), 74.6 (C-3 β), 74.6, 73.7, 73.6, 73.6, 73.2 (CH₂ Bn), 72.6 (C-5 β), 72.4 (C-3 α), 71.7, 71.5, 71.3 (CH₂ Bn), 69.2 (C-6 β), 68.7 (C-6 α), 68.9 – 67.4 (m, 2x CH₂-CHF₂), 66.7 (C-5 α); HRMS: [M+NH₄]⁺ calcd for C₃₆H₃₈F₂O₆NH₄ 622.29747, found 622.29587.

2,2,2-trifluoroethyl-2,3,4,6-tetra-O-benzyl-α,β-D-allopyranoside (3E)



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor 3 and 2,2,2-trifluoroethanol, yielding compound 3E (43 mg, 68 µmol, 68%, colourless oil, $\alpha:\beta$ = 50:50). Data reported for a 1:1 mixture: ¹H NMR (400 MHz, CDCl₃) δ 7.63 – 7.08 (m, 40H, CH_{arom}), 5.04 – 4.97 (m, 3H, H-1a, H-1β, CHH Bn), 4.96 – 4.80 (m, 4H, 3x CHH Bn, CHHBn), 4.68 – 4.49 (m, 9H, 4x CHH Bn, 5x CHH Bn), 4.42 (dd, J = 13.4, 11.5 Hz, 2H, 2x CHH Bn), 4.33 (dt, J = 10.4, 2.7 Hz, 1H, H-5a), 4.31 – 4.19 (m, 2H, H-3a, CHH-CF₃), 4.15 (t, J = 2.6 Hz, 1H, H-3β), 4.12 - 4.02 (m, 2H, H-5β, CHH-CF₃), 4.01 - 3.89 (m, 2H 2x CHH-CF₃), 3.84 (dd, *J* = 10.6, 3.3 Hz, 1H, H-6α), 3.78 (dd, *J* = 10.8, 2.0 Hz, 1H, H-6β), 3.72 (ddd, *J* = 10.6, 3.3, 2.2 Hz, 2H, H-6α, H-6β), 3.63 (dd, J = 9.9, 2.7 Hz, 1H, H-4α), 3.57 – 3.49 (m, 2H, H-2α, H-4β), 3.33 (dd, J = 7.9, 2.6 Hz, 1H, H-2β); ¹³C NMR (101 MHz, CDCl₃) δ 139.4, 138.9, 138.6, 138.3, 138.1, 138.0, 137.9 (Cq), 128.6, 128.5, 128.5, 128.3, 128.1, 128.0, 128.0, 127.9, 127.9, 127.9, 127.8, 127.8, 127.8, 127.8, 127.7, 127.6, 127.1 (CH_{arom}), 101.6 (C-1β), 97.9 (C-1α), 78.6 (C-2β), 76.7 (C-2α), 75.4 (C-4β), 74.7(C-3β), 74.6 (CH₂ Bn), 74.3 (C-4α), 73.7, 73.6, 73.6, 73.2 (CH₂ Bn), 72.7(C-5β), 72.5 (C-3α), 71.7, 71.5, 71.2 (CH₂ Bn), 69.0 (C-6β), 68.6 (C-6α), 67.0 (C-5α), 66.3 (q, J = 34.8 Hz, CH₂-CF₃), 65.3 (q, J = 34.8 Hz, CH₂-CF₃); HRMS: [M+NH₄]⁺ calcd for C₃₆H₃₇F₃O₆NH₄ 640.28805, found 640.28621.

<u>1,1,1,3,3,3-hexafluoro-2-propyl-2,3,4,6-tetra-O-benzyl-a-D-allopyranoside (3F)</u>



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **3** and 1,1,1,3,3,3-hexafluoropropan-2-ol, yielding compound **3F** (21 mg, 30 µmol, 30%, colourless oil, $\alpha:\beta = >98:2$) ¹H NMR (400 MHz, CDCl₃) δ 7.40 – 7.18 (m, 20H, CH_{arom}), 5.22 (d, *J* = 4.0 Hz, 1H, H-1), 4.94 (d, *J* = 12.1 Hz, 1H, CHH Bn), 4.80 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.64 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.60 (d, *J* = 12.1 Hz, 1H, CHH Bn), 4.55 – 4.44 (m, 4H, CH(CF₃)₂, CHH Bn, 2x CHH Bn), 4.42 – 4.32 (m, 2H, H-5, CHH Bn), 4.18 (t, *J* = 2.6 Hz, 1H, H-3), 3.82 (dd, *J* = 10.7, 2.9 Hz, 1H, H-6), 3.65 (dd, *J* = 10.7, 2.1 Hz, 1H, H-6), 3.61 (dd, *J* = 10.0,

2.6 Hz, 1H, H-4), 3.50 (dd, J = 4.1, 2.6 Hz, 1H, H-2); ¹³C NMR (101 MHz, CDCl₃) δ 139.2, 138.0, 137.9, 137.7 (C_q), 128.6, 128.5, 128.4, 128.4, 128.2, 128.2, 128.1, 128.0, 128.0, 127.9, 127.9, 127.9, 127.9, 127.8, 127.6, 127.2 (CH_{arom}), 99.0 (C-1), 76.5 (C-2), 73.9 (C-4), 73.8, 73.5 (CH₂ Bn), 72.0 (C-3), 71.4, 71.2 (CH₂ Bn), 68.2 (C-6), 67.9 (C-5); HRMS: [M+NH₄]⁺ calcd for C₃₇H₃₆F₆O₆ 708.27543, found 708.27395.

Ethyl-2,3,4,6-tetra-O-benzyl-a-D-gulopyranoside (4B)

Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor 4 and ethanol, yielding compound 4B (54 mg, 94 µmol, 94%, colourless oil, α : β = 78:22). Data for the α -anomer: ¹H NMR (500 MHz, CDCl₃) δ 7.38 – 7.22 (m, 18H, CHarom), 7.14 – 7.08 (m, 2H, CHarom), 4.90 (d, J = 3.3 Hz, 1H, H-1), 4.82 (d, J = 12.5 Hz, 1H, CHH Bn), 4.59 (d, J = 9.6 Hz, 1H, CHH Bn), 4.56 (d, J = 12.5 Hz, 1H, CHH Bn), 4.54 – 4.46 (m, 2H, CHH Bn, CHH Bn), 4.41 (d, J = 12.0 Hz, 1H, CHH Bn), 4.39 – 4.33 (m, 2H, H-5, CHH Bn), 4.29 (d, J = 11.9 Hz, 1H, CHH Bn), 3.85 – 3.77 (m, 1H, CHH Et), 3.77 (td, J = 3.6, 2.4 Hz, 2H, H-2, H-3), 3.64 – 3.53 (m, 2H, H-6, CHH Et), 3.52 (dd, J = 3.5, 1.4 Hz, 1H, H-4), 3.49 (dd, J = 9.7, 6.6 Hz, 1H, H-6), 1.29 (t, J = 7.1 Hz, 3H, CH₃ Et); ¹³C NMR (126 MHz, CDCl₃) δ 139.1, 138.4, 138.1 (C_q), 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 128.0, 128.0, 128.0, 127.9, 127.9, 127.9, 127.8, 127.7, 127.7, 127.7, 127.6, 127.5 (CH_{aron}), 97.0 (C-1), 75.3 (C-4), 73.5 (C-2, C-3), 73.4, 72.9, 72.8, 71.6 (CH₂ Bn), 69.2 (C-6), 65.5 (C-5), 64.0 (CH₂ Et), 15.3 (CH₃ Et); diagnostic peaks for the β-anomer: ¹H NMR (500 MHz, CDCl₃) δ 4.10 (td, J = 6.4, 1.5 Hz, 1H, H-5), 3.97 (dq, J = 9.4, 7.1 Hz, 1H, CHH Et), 3.73 (t, J = 3.5 Hz, 1H), 3.44 (dd, J = 3.7, 1.5 Hz, 1H), 1.25 (t, J = 7.1 Hz, 3H, CH₃ Et) ¹³C NMR (126 MHz, CDCl₃) δ 100.9 (C-1), 76.4, 75.2, 74.8, 73.6, 72.6, 72.0 (C-5), 69.1 (C-6), 65.2 (CH₂ Et), 15.5 (CH₃ Et); HRMS: [M+NH₄]⁺ calcd for C₃₆H₄₀O₆NH₄ 586.31631, found 586.31510.

2-fluoroethyl-2,3,4,6-tetra-O-benzyl-α-D-gulopyranoside (4C)



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **4** and 2-fluoroethanol, yielding compound **4C** (50 mg, 85 µmol, 85%, colourless oil, $\alpha:\beta = 83:17$). Data for the α -anomer: ¹H NMR (500 MHz, CDCl₃) δ 7.37 – 7.08 (m, 20H, CH_{arom}), 4.94 (d, *J* = 3.9 Hz, 1H, H-1), 4.83 (d, *J* = 12.4 Hz, 1H, CHH Bn), 4.67 (ddd, *J* = 5.3, 4.7, 2.6 Hz, 1H, CH₂-CHHF), 4.63 – 4.55 (m, 3H, CH₂-CHHF, CHH Bn, CHH Bn), 4.53 – 4.46 (m, 2H, CHH Bn, CHH Bn), 4.44 – 4.39 (m, 2H, H-5, CHH Bn), 4.37 (d, *J* = 11.9 Hz, 1H, CHH Bn), 4.31 (d, *J* = 12.0 Hz, 1H, CHH Bn), 3.92 (dddd, *J* = 29.9, 12.3, 4.9, 3.5 Hz, 1H, CHH-CH₂F), 3.86 – 3.76 (m, 3H, H-2, H-3, CHH-CH₂F), 3.59 – 3.52 (m, 2H, H-4, H-6), 3.48 (dd, *J* = 9.8, 6.5 Hz, 1H, H-6); ¹³C NMR (126 MHz, CDCl₃) δ 139.0, 138.4, 138.3, 138.0 (C_q), 128.6, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.1, 128.1, 128.0, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7, 127.6, 127.6 (CH_{arom}), 97.7 (C-1), 83.1 (d, *J* = 169.0 Hz, CH₂-CH₂F) 75.2

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(C-4), 73.5 (C-2/C-3), 73.3, 73.0 (CH₂ Bn), 72.9 (C-2/C-3), 72.9, 71.7 (CH₂ Bn), 69.1 (C-6), 67.5 (d, J = 20.6 Hz, CH₂-CH₂F), 65.6 (C-5); diagnostic peaks for the β-anomer: ¹H NMR (500 MHz, CDCl₃) δ 4.88 – 4.85 (m, 2H, H-1, CHH Bn), 4.10 (ddd, J = 6.3, 5.3, 1.4 Hz, 1H, H-5), 3.74 (t, J = 3.4 Hz, 1H), 3.44 (dd, J = 3.7, 1.5 Hz, 1H); ¹³C NMR (126 MHz, CDCl₃) δ 101.3 (C-1), 82.8 (d, J = 169.3 Hz, CH₂-CH₂F), 76.2, 75.0, 74.7, 72.1, 69.0, 68.5 (d, J = 20.3 Hz, CH₂-CH₂F); HRMS: [M+NH₄]⁺ calcd for C₃₆₃H₃₉FO₆NH₄ 604.30689, found 604.30571.

2,2-difluoroethyl-2,3,4,6-tetra-O-benzyl-a-D-gulopyranoside (4D)



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **4** and 2,2-difluoroethanol, yielding compound **4D** (50 mg, 83 μmol, 83%, colourless oil, $\alpha:\beta = 69:31$) Data for the α-anomer: ¹H NMR (500 MHz, CDCl₃) δ 7.38 – 7.20 (m, 20H, CH_{arom}), 6.05 (tt, *J* = 55.8, 4.6 Hz, 1H, CH₂-CHF₂), 4.89 (d, *J* = 3.9 Hz, 1H, H-1), 4.80 (d, *J* = 12.4 Hz, 1H, CHH Bn), 4.56 (s, 2H, CH₂ Bn), 4.50 – 4.45 (m, 2H, CHH Bn, CHH Bn), 4.42 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.38 – 4.34 (m, 2H, H-5, CHH Bn), 4.32 – 4.28 (m, 1H, CHH Bn), 3.82 – 3.76 (m, 4H, H-2, H-3, CH₂-CHF₂), 3.55 – 3.51 (m, 2H, H-4, H-6), 3.45 (dd, *J* = 9.8, 6.1 Hz, 1H, H-6); ¹³C NMR (126 MHz, CDCl₃) δ 138.8, 138.2, 138.1, 137.8 (C_q), 128.6, 128.5, 128.5, 128.4, 128.4, 128.2, 128.1, 128.1, 127.8, 127.7 (CH_{arom}), 114.7 (t, *J* = 241.0 Hz, CH₂-CHF₂), 98.4 (C-1), 75.1 (C-4), 73.4 (CH₂ Bn), 73.3 (C-3), 73.0, 72.9 (CH₂ Bn), 72.7 (C-5), 71.8 (C-6), 68.2 (t, *J* = 29.1 Hz, CH₂-CHF₂), 66.0 (C-5); diagnostic peaks for the β-anomer: ¹H NMR (500 MHz, CDCl₃) δ 4.90 (d, *J* = 8.1 Hz, 1H, H-1), 4.72 (d, *J* = 12.2 Hz, 1H, CHH Bn), 4.15 (td, *J* = 6.4, 1.5 Hz, 1H, H-5), 4.05 (dddd, *J* = 20.0, 11.6, 10.2, 3.3 Hz, 1H, CHH-CH₂F), 3.88 (dd, *J* = 4.5, 1.7 Hz, 1H), 3.77 (t, *J* = 3.4 Hz, 1H); ¹³C NMR (126 MHz, CDCl₃) δ 101.7 (C-1), 76.1, 74.9, 74.6, 72.8, 72.7, 72.3, 68.9 – 68.4 (m, CH₂-CHF₂); HRMS: [M+NH₄]⁺ calcd for C₃₆H₃₈F₂O₆NH₄ 622.29747, found 622.29587.

2,2,2-trifluoroethyl-2,3,4,6-tetra-O-benzyl-α-D-gulopyranoside (4E)



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **4** and 2,2,2-trifluoroethanol, yielding compound **4E** (53 mg, 85 µmol, 85%, colourless oil, $\alpha:\beta = 60:40$). Data reported for a 1:1 mixture: ¹H NMR (500 MHz, CDCl₃) δ 7.57 – 6.96 (m, 40H, CH_{arom}), 4.99 (d, *J* = 3.8 Hz, 1H, H-1 α), 4.95 (d, *J* = 8.0 Hz, 1H, H-1 β), 4.92 – 4.84 (m, 2H, 2x CHH Bn), 4.74 (d, *J* = 12.2 Hz, 1H, CHH Bn), 4.65 (d, *J* = 12.3 Hz, 1H, CHH Bn), 4.62 – 4.39 (m, 11H, H-5 α , 3x CHH Bn, 7x CHH Bn), 4.34 (d, *J* = 2.1 Hz, 1H, CH₂ Bn), 4.23 (dq, *J* = 12.0, 8.7 Hz, 1H, CHH-CF₃), 4.14 (td, *J* = 6.4, 1.5 Hz, 1H, H-5 β), 4.07 (dq, *J* = 12.4, 9.0 Hz, 1H, H-3 α), 3.77 (t, *J* = 3.5 Hz, 1H, H-3 β), 3.66 – 3.57 (m, 5H, H-2 β , H-4 α , H-6 α , 2x H-6 β), 3.53 (dd, *J* = 9.8, 6.4 Hz, 1H, H-6 α), 3.48 (dd, *J* = 3.8, 1.5 Hz, 1H, H-4 β); ¹³C NMR (126 MHz, CDCl₃) δ 138.9, 138.7, 138.3, 138.2, 138.2, 137.9, 137.8 (C_q), 128.6, 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, 127.8, 127.7, 127.5 (CH_{arom}), 125.3, 125.0, 123.1, 122.8 (CH₂-CF₃), 101.5 (C-1 β), 97.9 (C-1 α), 75.9 (C-2 β), 75.4 (C-4 α), 74.9 (C-3 β), 74.6 (C-4 β), 73.6 (CH₂ Bn), 73.6 (C-2 α), 73.5, 73.4, 73.1, 73.0 (CH₂ Bn), 72.9 (C-3 α), 72.8 (CH₂ Bn), 72.4 (C-5 β), 71.8 (CH₂ Bn), 68.9 (C-6 α , C-6 β), 66.3 (C-5 α), 66.2 (q, *J* = 34.8 Hz, CH₂-CF₃), 65.2 (q, *J* = 34.7 Hz, CH₂-CF₃); HRMS: [M+NH₄]⁺ calcd for C₃₆H₃₇F₃O₆NH₄ 640.28805, found 640.28617

1,1,1,3,3,3-hexafluoro-2-propyl-2,3,4,6-tetra-O-benzyl-α-D-gulopyranoside (4F)



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor 4 and 1,1,1,3,3,3-hexafluoropropan-2-ol, yielding compound 4F (27 mg, 39 µmol, 39%, colourless oil, $\alpha:\beta = >98:2$) ¹H NMR (400 MHz, CDCl₃) δ 7.35 – 7.26 (m, 18H, CH_{arom}), 7.18 – 7.12 (m, 2H, CH_{arom}), 5.19 (d, *J* = 4.0 Hz, 1H, H-1), 4.89 (d, *J* = 11.9 Hz, 1H, CHH Bn), 4.65 (d, *J* = 12.1 Hz, 1H, CHH Bn), 4.56 – 4.38 (m, 8H, H-5, CH(CF₃)₂, 2x CHH Bn, 4x CHH Bn), 3.89 (dd, *J* = 4.0, 3.0 Hz, 1H, H-2), 3.86 – 3.80 (m, 1H, H-3), 3.66 (dd, *J* = 4.1, 1.6 Hz, 1H, H-4), 3.58 – 3.46 (m, 2H, 2x H-6); ¹³C NMR (101 MHz, CDCl₃) δ 138.9, 138.2, 137.9, 137.8 (C_q), 128.6, 128.5, 128.3, 128.2, 128.0, 127.8, 127.7, 127.7, 127.5 (CH_{arom}), 98.9 (C-1), 75.5 (C-4), 73.4 (CH₂ Bn), 73.3 (C-2), 73.2, 73.2 (CH₂ Bn), 73.0 – 71.9 (m, C-3, CH(CF₃)₂) 71.6 (CH₂ Bn), 68.5 (C-6), 67.0 (C-5); HRMS: [M+NH₄]⁺ calcd for C₃₇H₃₆F₆O₆ 708.27543, found 708.27274.

Ethyl-2,3,4,6-tetra-O-benzyl-α,β-D-altropyranoside (6B)



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **6** and ethanol, yielding compound **6B** (45 mg, 79 μmol, 79%, colourless oil, $\alpha:\beta = 75:25$). Data for the α-anomer: ¹H NMR (500 MHz, CDCl₃) δ 7.42 – 7.12 (m, 20H, CH_{arom}), 4.83 (d, J = 2.0 Hz, 1H, H-1), 4.64 – 4.57 (m, 3H, 3x CHH Bn), 4.53 – 4.47 (m, 4H, CHH Bn, 3x CHH Bn), 4.44 (d, J = 11.8 Hz, 1H, CHH Bn), 4.27 (ddd, J = 8.0, 4.4, 3.0 Hz, 1H, H-5), 3.87 (dd, J = 8.5, 3.3 Hz, 1H, H-4), 3.84 – 3.78 (m, 1H, CHH Et), 3.77 (t, J = 4.0 Hz, 1H, H-3), 3.74 (dd, J = 4.7, 2.0 Hz, 1H, H-2), 3.69 (t, J = 3.8 Hz, 2H, 2x H-6), 3.50 – 3.45 (m, 1H, CHH Et), 1.22 (t, J = 7.1 Hz, 3H, CH₃ Et); ¹³C NMR (126 MHz, CDCl₃) δ 138.7, 138.5, 138.3, 138.2 (Cq), 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.0, 127.9, 127.8, 127.8, 127.6, 127.5 (CH_{arom}), 99.2 (C-1), 76.0 (C-4), 74.0 (C-3), 73.5 (CH₂ Bn), 72.9 (C-2), 72.7, 72.0, 71.7 (CH₂ Bn), 69.8 (C-6), 68.3 (C-5), 63.4 (CH₂ Et), 15.2 (CH₃ Et); ¹³C-HMBC-GATED NMR (126 MHz, CDCl₃) δ 4.82 – 4.77 (m, 2H, H-1, CHH Bn), 4.07 (ddd, J = 8.9, 5.9, 2.8 Hz, 1H, H-5), 3.97 (dq, J = 9.5, 7.1 Hz, 1H, CHH Et), 1.24 (t, J = 7.1 Hz, 3H, CH₃ Et); ¹³C NMR (126 MHz, CDCl₃) δ 9.00 (C-1), 75.5, 73.9, 73.8, 73.6, 73.6, 73.4, 72.8, 71.8, 70.4, 65.1 (CH₂ Et), 15.4 (CH₃ Et); ¹³C-HMBC-GATED NMR

(126 MHz, CDCl₃): δ 99.0 ($J_{\text{H1-C1}}$ = 155 Hz, β); HRMS: [M+NH₄]⁺ calcd for C₃₆H₄₀O₆NH₄ 586.31631, found 586.31503.

2-Fluoroethyl-2,3,4,6-tetra-O-benzyl-α,β-D-altropyranoside (6C)

Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor 6 and 2-fluoroethanol, yielding compound 6C (35 mg, 60 μ mol, 60%, colourless oil, $\alpha:\beta = 58:42$). Data reported for a 1:1 mixture: ¹H NMR (500 MHz, CDCl₃) δ 7.58 – 6.94 (m, 40H, CH_{arom}), 4.93 – 4.90 (m, 2H, H-1α, H-1β), 4.85 (d, J = 12.6 Hz, 1H, CHH Bn), 4.67 - 4.59 (m, 7H, , 2x CH2-CHHF, 5x CHH Bn/CHH Bn), 4.59 - 4.49 (m, 9H, 2x CH2-CHHF, 7x CHH Bn/CHH Bn), 4.46 (d, J = 11.8 Hz, 1H, CHH Bn), 4.43 (d, J = 11.7 Hz, 1H, CHH Bn), 4.39 $(d, J = 11.7 \text{ Hz}, 1\text{H}, \text{CH} H \text{Bn}), 4.31 (dt, J = 8.1, 3.8 \text{ Hz}, 1\text{H}, \text{H}-5\alpha), 4.18 - 4.06 (m, 2\text{H}, \text{H}-5\beta)$ CHH-CH₂F), 4.02 – 3.88 (m, 2H, H-4a, CHH-CH₂F), 3.86 – 3.69 (m, 11H, H-2a, H-2β, H-3a, H-3β, H-4β, 2x H-6α, 2x H-6β, 2x CHH-CH₂F); ¹³C NMR (126 MHz, CDCl₃) δ 138.7, 138.6, 138.4, 138.4, 138.1, 138.1 (C_q), 128.5, 128.5, 128.4, 128.4, 128.3, 128.1, 128.1, 128.0, 127.9, 127.9, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 127.6 (CH_{arom}), 99.6 (C-1α), 99.5 (C-1β), 83.0 (d, *J* = 168.9 Hz, CH₂-CH₂F), 82.9 (d, J = 169.1 Hz, CH₂-CH₂F), 75.5 (C-2α), 75.1 (C-2β, 73.9 (CH₂ Bn), 73.7 (C-3α), 73.6, 73.5 (CH₂ Bn), 73.4, 73.4 (C-3β, C-4β, C-5β), 72.9 (CH₂ Bn), 72.7 (C-4α), 72.7, 72.0, 71.8, 71.7 (CH₂ Bn), 70.2 (C-6 β), 69.7 (C-6 α), 68.6 (d, *J* = 19.8 Hz, CH₂-CH₂F), 68.4 (C-5 α), 66.84 (d, J = 20.0 Hz, CH₂-CH₂F); ¹³C-HMBC-GATED NMR (126 MHz, CDCl₃): δ 99.6 ($J_{H1-C1} = 168$ Hz, α), 99.5 (*J*_{H1-C1} = 161 Hz, β); HRMS: [M+NH₄]⁺ calcd for C₃₆₃H₃₉FO₆NH₄ 604.30689, found 604.30606.

2,2-difluoroethyl-2,3,4,6-tetra-O-benzyl-α,β-D-altropyranoside (6D)



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **6** and 2,2-difluoroethanol, yielding compound **6D** (39 mg, 64 μmol, 64%, colourless oil, $\alpha:\beta = 69:31$) Data for the α-anomer: ¹H NMR (500 MHz, CDCl₃) δ 7.42 – 6.98 (m, 20H, CH_{arom}), 5.91 (dddd, *J* = 56.1, 55.2, 5.2, 3.3 Hz, 1H, CH₂-CHF₂), 4.85 (d, *J* = 1.4 Hz, 1H, H-1), 4.63 – 4.50 (m, 4H, 4x CHH Bn/ CHH Bn), 4.50 – 4.37 (m, 4H, 4x CHH Bn/ CHH Bn), 4.26 (dt, *J* = 8.8, 3.7 Hz, 1H, H-5), 3.91 – 3.83 (m, 2H, H-4, CHH-CHF₂), 3.77 – 3.74 (m, 2H, H-2, H-3), 3.70 – 3.64 (m, 3H, 2x H-6, CHH-CHF₂); ¹³C NMR (126 MHz, CDCl₃) δ 138.5, 138.5, 138.3, 138.3, 137.9 (C_q), 128.6, 128.5, 128.4, 128.4, 128.0, 127.9, 127.9, 127.8 (CH_{arom}), 117.0 – 112.1 (m, CH₂-CHF₂) 100.1 (C-1), 75.4, 73.6 (C-2, C-3), 73.6, 72.8 (CH₂ Bn), 72.6 (C-4), 72.2, 71.8 (CH₂ Bn), 69.6 (C-6), 68.6 (C-5), 67.1 (dd, *J* = 29.6, 27.2 Hz, CH₂-CHF₂); ¹³C-HMBC-GATED NMR (126 MHz, CDCl₃) δ 5.98 (dddd, *J* = 56.3, 55.0, 5.5, 3.0 Hz, 1H, CH₂-CHF₂), 4.90 (d, *J* = 1.4 Hz, 1H, H-1), 4.81 (d, *J* = 12.5 Hz, 1H, CHH Bn), 4.10 (ddd, *J* = 9.4, 5.8, 2.5 Hz, 1H, H-5), 4.08 – 4.00 (m, 1H, CHH-CHF₂); ¹³C NMR (126 MHz, CDCl₃); ⁵O NMR (126 MHz, CDCl₃) δ 9.99 (C-1), 74.9, 73.9, 73.8, 73.5, 73.2, 73.0, 71.9,

70.0 (C-6); ¹³C-HMBC-GATED NMR (126 MHz, CDCl₃): δ 99.9 ($J_{H_1-C_1} = 160$ Hz, β); HRMS: [M+NH₄]⁺ calcd for C₃₆H₃₈F₂O₆NH₄ 622.29747, found 622.29581.

2,2,2-trifluoroethyl-2,3,4,6-tetra-O-benzyl-α,β-D-altropyranoside (6E)

Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor 6 and 2,2,2-trifluoroethanol, yielding compound 6E (46 mg, 73 µmol, 73%, colourless oil, $\alpha:\beta$ = 85:15). Data for the α -anomer: ¹H NMR (500 MHz, CDCl₃) δ 7.38 – 7.25 (m, 20H, CH_{arom}), 4.94 (s, 1H, H-1), 4.67 - 4.59 (m, 3H, 3x CHH Bn), 4.58 - 4.50 (m, 4H, CHH Bn, 3x CHH Bn), 4.47 (d, J = 11.8 Hz, 1H, CHH Bn), 4.30 (ddd, J = 8.9, 4.3, 2.8 Hz, 1H, H-5), 4.06 (dq, J = 12.3, 9.0 Hz, 1H, CHH-CF₃), 3.95 - 3.86 (m, 2H, H-4, CHH-CF₃), 3.83 - 3.79 (m, 2H, H-2, H-3), 3.76 - 3.70 (m, 2H, 2x H-6); ¹³C NMR (126 MHz, CDCl₃) & 138.4, 138.3, 138.3, 137.8 (C_q), 128.6, 128.4, 128.4, 128.1, 128.0, 127.9, 127.8, 127.8, 127.7 (CH_{arom}), 124.1 (q, J = 278.3 Hz, CH₂-CF₃), 99.7 (C-1), 75.1 (C-2/C-3), 73.6 (CH₂ Bn), 73.6 (C-2/C-3), 72.8 (CH₂ Bn), 72.5 (C-4), 72.2, 71.8 (CH₂ Bn), 69.4 (C-6), 68.7 (C-5), 64.36 (q, J = 34.5 Hz, CH₂-CF₃); ¹³C-HMBC-GATED NMR (126 MHz, CDCl₃): δ 99.7 (*J*_{H1-C1} = 169 Hz, α); diagnostic peaks for the β -anomer: ¹H NMR (500 MHz, CDCl₃) δ 4.96 (d, *J* = 1.4 Hz, 1H, H-1), 4.82 (d, *J* = 12.5 Hz, 1H, CHH Bn), 4.42 (d, J = 11.7 Hz, 1H, CHH Bn), 4.24 (dq, J = 12.4, 8.9 Hz, 1H, CHH-CF₃); ¹³C NMR (126 MHz, CDCl₃) δ 99.6 (C-1), 74.6, 73.8, 73.8, 73.7, 73.6, 73.1, 73.0, 72.0, 70.0 (C-6); ¹³C-HMBC-GATED NMR (126 MHz, CDCl₃): δ 99.7 (J_{H1-C1} = 162 Hz, β); HRMS: [M+NH₄]⁺ calcd for C₃₆-H₃₇F₃O₆NH₄ 640.28805, found 640.28612

1,1,1,3,3,3-hexafluoro-2-propyl-2,3,4,6-tetra-O-benzyl-α-D-altropyranoside (6F)



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **6** and 1,1,1,3,3,3-hexafluoropropan-2-ol, yielding compound **6F** (11 mg, 16 µmol, 16%, colourless oil, $\alpha:\beta = >98:2$) ¹H NMR (400 MHz, CDCl₃) δ 7.36 – 7.27 (m, 18H, CH_{arom}), 7.21 (ddt, *J* = 8.4, 5.3, 2.2 Hz, 2H, CH_{arom}), 5.05 (s, 1H, H-1), 4.64 (d, *J* = 12.1 Hz, 1H, CHH Bn), 4.58 – 4.49 (m, 4H, CH(CF₃)₂, 3x CHH Bn), 4.48 – 4.39 (m, 3H, 3x CHH Bn), 4.35 – 4.29 (m, 2H, H-5, CHH Bn), 3.96 (dd, *J* = 9.4, 3.1 Hz, 1H, H-4), 3.80 (dd, *J* = 4.3, 1.6 Hz, 1H, H-2), 3.78 – 3.73 (m, 2H, H-3, H-6), 3.66 (dd, *J* = 10.9, 2.3 Hz, 1H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 138.2 (Cq), 130.5, 128.9, 128.7, 128.6, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.3, 128.2, 128.2, 128.0, 128.0, 127.9, 127.9, 127.9, 127.7 (CH_{arom}), 100.7 (C-1), 74.3 (C-2), 73.6 (CH₂ Bn), 73.1 (C-3), 72.9, 72.3, 72.0 (CH₂ Bn), 72.0 (C-4), 69.1 (C-5), 69.0 (C-6); ¹³C-HMBC-GATED NMR (101 MHz, CDCl₃): δ 100.7 (*J*_{H1-C1} = 173 Hz, α); HRMS: [M+NH₄]⁺ calcd for C₃₇H₃₆F₆O₆ 708.27543, found 708.27387.

Ethyl-2,3,4,6-tetra-O-benzyl-α,β-D-talopyranoside (7B)



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor 7 and ethanol, yielding compound 7B (40 mg, 70 µmol, 70%, colourless oil, $\alpha:\beta = 68:32$) Data for the α -anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.44 – 7.23 (m, 20H, CH_{arom}), 5.04 – 4.99 (m, 2H, H-1, CHH Bn), 4.92 (d, J = 12.6 Hz, 1H, CHH Bn), 4.85 – 4.76 (m, 2H, 2x CHH Bn), 4.62 - 4.57 (m, 3H, CHH Bn, CH2 Bn), 4.54 - 4.51 (m, 1H, CHH Bn), 4.02 (td, J = 6.3, 1.9 Hz, 1H, H-5), 3.96 (p, J = 1.4 Hz, 1H, H-3), 3.83 - 3.72 (m, 5H, H-2, H-4, 2x H-6, CHH Et), 3.50 (dq, J = 9.8, 6.9 Hz, 1H, CHH Et), 1.21 (t, J = 7.1 Hz, 3H, CH₃ Et); ¹³C NMR (101 MHz, CDCl₃) δ 139.2, 138.9, 138.6, 138.4 (C_q), 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 127.9, 127.2 (CH_{aron}), 99.0 (C-1), 77.6, 74.6 (C-2, C-4), 73.8, 73.7 (CH₂ Bn), 73.5 (C-3), 73.2, 71.3 (CH₂ Bn), 70.8 (C-5), 69.6 (C-6), 63.2 (CH₂ Et), 15.1 (CH₃ Et); ¹³C-HMBC-GATED NMR (101 MHz, CDCl₃): δ 99.0 ($J_{\text{H1-C1}}$ = 169 Hz, α); diagnostic peaks for the β -anomer: ¹H NMR (400 MHz, CDCl₃) δ 4.45 (d, *J* = 12.2 Hz, 1H, CH*H* Bn), 4.42 (d, *J* = 1.3 Hz, 1H, H-1), 4.08 (dt, *J* = 9.3, 7.1 Hz, 1H, CHH Et), 3.93 (dt, J = 3.1, 1.2 Hz, 1H), 3.59 (td, J = 5.4, 4.7, 2.2 Hz, 1H, H-5), 3.44 (t, J = 3.1 Hz, 1H), 1.30 (t, I = 7.1 Hz, 3H, CH₃ Et); ¹³C NMR (101 MHz, CDCl₃) δ 102.4 (C-1), 79.0, 75.3, 74.8, 74.6, 72.6, 70.8, 69.8 (C-6), 64.9 (CH2 Et), 15.3 (CH3 Et); ¹³C-HMBC-GATED NMR (101 MHz, CDCl₃): δ 102.4 (J_{H1-C1} = 154 Hz, β) HRMS: [M+NH₄]⁺ calcd for C₃₆H₄₀O₆NH₄ 586.31631, found 586.31493.

<u>2-fluoroethyl-2,3,4,6-tetra-O-benzyl-α,β-D-talopyranoside (7C)</u>

Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor 7 and 2-fluoroethanol, yielding compound 7C (43 mg, 74 µmol, 74%, colourless oil, $\alpha:\beta = 80:20$) Data for the α -anomer: ¹H NMR (500 MHz, CDCl₃) δ 7.45 – 6.98 (m, 20H, CH_{arom}), 5.01 (d, J = 1.8 Hz, 1H, H-1), 4.96 (d, J = 11.9 Hz, 1H, CHH Bn), 4.86 (d, J = 12.5 Hz, 1H, CHH Bn), 4.78 - 4.70 (m, 2H, 2x CHH Bn), 4.57 - 4.51 (m, 4H, CHH Bn, CH₂ Bn, CH₂-CHHF), 4.49 – 4.44 (m, 2H, CHH Bn, CH₂-CHHF), 3.98 (td, J = 6.2, 1.9 Hz, 1H, H-5), 3.91 (dt, J = 2.7, 1.4 Hz, 1H, H-3), 3.89 - 3.79 (m, 2H, H-2, CHH-CH₂F), 3.79 - 3.76 (m, 1H, H-4), 3.75 -3.62 (m, 3H, 2x H-6, CHH-CH₂F); ¹³C NMR (126 MHz, CDCl₃) δ 139.1, 138.7, 138.4, 138.3 (C_q), 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.1, 128.1, 128.0, 127.9, 127.8, 127.8, 127.7, 127.6, 127.6, 127.5, 127.4, 127.3, 127.2, 127.2 (CH_{arom}), 99.5 (C-1), 82.6 (d, J = 169.6 Hz, CH₂-CH2F), 77.4 (C-4), 74.3 (C-2), 73.8, 73.6 (CH2 Bn), 73.3 (C-3), 73.3, 71.3 (CH2 Bn), 70.9 (C-5), 69.6 (C-6), 66.6 (d, J = 19.7 Hz, CH₂-CH₂F); ¹³C-HMBC-GATED NMR (126 MHz, CDCl₃): δ 99.5 $(J_{\text{H1-C1}} = 170 \text{ Hz}, \alpha)$; diagnostic peaks for the β -anomer: ¹H NMR (500 MHz, CDCl₃) δ 5.06 (d, J =12.8 Hz, 1H, CHH Bn), 4.16 – 4.02 (m, 1H, CHH-CF₂), 3.55 (t, J = 5.7 Hz, 1H), 3.39 (t, J = 3.1 Hz, 1H); ¹³C NMR (126 MHz, CDCl₃) δ 102.1 (C-1), 83.0 (d, J = 169.0 Hz, CH₂-CH₂F), 81.4, 79.2, 75.3, 74.4, 72.4, 68.21 (d, J = 19.8 Hz, CH₂-CH₂F); HRMS: [M+NH₄]⁺ calcd for C₃₆₃H₃₉FO₆NH₄ 604.30689, found 604.30540.

2,2-difluoroethyl-2,3,4,6-tetra-O-benzyl-α,β-D-talopyranoside (7D)



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor 7 and 2,2-fluoroethanol, yielding compound 7D (44 mg, 73 µmol, 73%, colourless oil, $\alpha:\beta = 86:14$) Data for the α -anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.60 – 6.98 (m, 20H, CH_{arom}), 5.88 (tdd, J = 55.4, 4.8, 3.5 Hz, 1H, CH₂-CHF₂), 4.99 (d, J = 1.9 Hz, 1H, H-1), 4.95 (d, J = 11.9 Hz, 1H, CHH Bn), 4.85 (d, J = 12.4 Hz, 1H, CHH Bn), 4.77 – 4.67 (m, 2H, 2x CHH Bn), 4.55 – 4.43 (m, 4H, 2x CH₂ Bn), 3.95 (td, J = 6.1, 1.9 Hz, 1H, H-5), 3.89 (p, J = 1.4 Hz, 1H, H-3), 3.82 - 3.72 (m, 4H, H-2, H-3, H-6, CHH-CHF2), 3.72 - 3.64 (m, 2H, H-6, CHH-CHF2); ¹³C NMR (101 MHz, CDCl₃) δ 139.0, 138.6, 138.3, 138.2 (C_a), 128.5, 128.5, 128.3, 128.2, 128.2, 128.2, 127.9, 127.8, 127.7, 127.6, 127.5, 127.3 (CH_{arom}), 114.1 (t, J = 240.9 Hz, CH₂-CHF₂) 100.1 (C-1), 77.1, 74.0 (C-2, C-3), 73.8, 73.6, 73.4 (CH₂ Bn), 73.2 (C-4), 71.4 (C-5), 71.4 (CH₂ Bn), 69.5 (C-6), 66.9 (t, J = 28.1 Hz, CH_2 -CHF₂); ¹³C-HMBC-GATED NMR (101 MHz, CDCl₃): δ 100.1 ($J_{\text{H1-C1}} =$ 171 Hz, α); diagnostic peaks for the β-anomer: ¹H NMR (400 MHz, CDCl₃) δ 6.10 – 5.78 (m, 1H, CH_2 - CHF_2), 4.45 – 4.42 (m, 2H, H-1, CHH Bn), 4.39 (d, J = 12.2 Hz, 1H), 4.07 (dddd, J = 23.5, 11.8, 9.3, 2.7 Hz, 1H, CHH-CHF₂), 3.56 (dt, J = 6.9, 3.5 Hz, 1H), 3.39 (t, J = 3.1 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 102.1 (C-1), 75.5, 74.6, 74.2, 72.3, 70.8; ¹³C-HMBC-GATED NMR (101 MHz, CDCl₃): δ 102.1 (J_{H1-C1} = 156 Hz, β); HRMS: [M+NH₄]⁺ calcd for C₃₆H₃₈F₂O₆NH₄ 622.29747, found 622.29554.

2,2,2-trifluoroethyl-2,3,4,6-tetra-O-benzyl-α,β-D-talopyranoside (7E)



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor 7 and 2,2,2-fluoroethanol, yielding compound 7E (43 mg, 43 μmol, 43%, colourless oil, $\alpha:\beta = 90:10$) Data for the α-anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.55 – 6.96 (m, 20H, CH_{arom}), 5.04 (d, *J* = 1.9 Hz, 1H, H-1), 4.95 (d, *J* = 11.8 Hz, 1H, CHH Bn), 4.85 (d, *J* = 12.4 Hz, 1H, CHH Bn), 4.77 – 4.69 (m, 2H, 2x CHH Bn), 4.55 – 4.50 (m, 3H, CHH Bn, CH₂ Bn), 4.47 (d, *J* = 11.9 Hz, 1H, CHH Bn), 4.01 – 3.90 (m, 3H, H-3, H-5, CHH-CF₃), 3.88 – 3.78 (m, 2H, H-2, CHH-CF₃), 3.76 – 3.66 (m, 3H, H-4, 2x H-6); ¹³C NMR (101 MHz, CDCl₃) δ 138.9, 138.4, 138.2, 138.2 (C_q), 128.5, 128.5, 128.5, 128.4, 128.3, 128.2, 128.2, 128.2, 127.9, 127.8, 127.7, 127.5, 127.4, 127.3 (CH_{arom}), 99.7 (C-1), 76.9 (c-4), 73.8(C-2, CH₂ Bn), 73.6, 73.5(CH₂ Bn), 73.0(C-3), 71.6 (C-5), 71.4 (CH₂ Bn), 69.4 (C-6), 64.2 (q, *J* = 34.8 Hz, CH₂-CF₃); ¹³C-HMBC-GATED NMR (101 MHz, CDCl₃) δ 4.38 (d, *J* = 12.1 Hz, 1H, CHH Bn), 4.21 (dq, *J* = 12.4, 8.9 Hz, 1H, CHH-CF₃), 3.57 (dt, *J* = 6.5, 3.2 Hz, 1H), 3.42 – 3.38 (m, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 75.6, 70.9, 69.5, a cross-peak for (H-1, C-1) is visible at (4.50, 101.4) in the HSQC spectrum; ¹³C-

HMBC-GATED NMR (101 MHz, CDCl₃): δ 101.4 (J_{H1-C1} = 157 Hz, β); HRMS: [M+NH₄]⁺ calcd for C₃₆H₃₇F₃O₆NH₄ 640.28805, found 640.28619.

1,1,1,3,3,3-hexafluoro-2-propyl-2,3,4,6-tetra-O-benzyl-α-D-talopyranoside (7F)



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor 7 and 1,1,1,3,3,3-hexafluoropropan-2-ol, yielding compound 7F (10 mg, 14 µmol, 14%, colourless oil, α : β = >98:2) ¹H NMR (500 MHz, CDCl₃) δ 7.39 – 7.20 (m, 20H, CH_{arom}), 5.22 (d, *J* = 1.7 Hz, 1H, H-1), 4.96 (d, *J* = 11.8 Hz, 1H, CHH Bn), 4.81 (d, *J* = 12.4 Hz, 1H, CHH Bn), 4.76 – 4.70 (m, 2H, 2x CHH Bn), 4.54 (s, 2H, CH₂ Bn), 4.52 – 4.44 (m, 3H, CH(CF₃)₂), 4.03 (td, *J* = 6.2, 1.8 Hz, 1H, H-5), 3.95 (p, *J* = 1.4 Hz, 1H, H-4), 3.85 (dt, *J* = 3.0, 1.3 Hz, 1H, H-2), 3.74 – 3.65 (m, 3H, H-3, 2x H-6); ¹³C NMR (126 MHz, CDCl₃) δ 138.8, 138.2, 138.0, 138.0 (Cq), 128.6, 128.5, 128.4, 128.3, 127.9, 127.8, 127.7, 127.6, 127.4 (CH_{arom}), 101.2 (C-1), 76.5 (C-3), 73.8, 73.7, 73.6 (CH₂ Bn), 73.4 (C-2), 72.6 (C-4), 72.4 (C-5), 71.5 (CH₂ Bn), 69.0 (C-6); ¹³C-HMBC-GATED NMR (126 MHz, CDCl₃): δ 101.2 (*J*_{H1-C1} = 175 Hz, a); HRMS: [M+NH₄]⁺ calcd for C₃₇H₃₆F₆O₆ 708.27543, found 708.27354.

Ethyl-2,3,4,6-tetra-O-benzyl-α,β-D-idopyranoside (8B)



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **8** and ethanol, yielding compound **8B** (44 mg, 76 μmol, 76%, colourless oil, $\alpha:\beta = 57:43$). Data reported for a 1:1 mixture: ¹H NMR (400 MHz, CDCl₃) δ 7.43 – 7.13 (m, 40H, CH_{arom}), 4.85 (d, J = 5.4 Hz, 1H, H-1α), 4.79 (d, J = 11.5 Hz, 1H, CHH Bn), 4.77 – 4.70 (m, 3H, H-1 β , CHH Bn, CHH Bn), 4.68 – 4.60 (m, 5H, 5x CHH Bn/CHH Bn), 4.58 – 4.46 (m, 8H, 8x CHH Bn/CHH Bn), 4.21 (dt, J = 7.0, 4.6 Hz, 1H, H-5α), 4.13 (dt, J = 7.4, 4.8 Hz, 1H, H-5 β), 3.97 (dq, J = 9.5, 7.0 Hz, 1H, CHH Et), 3.91 – 3.84 (m, 2H, CHH Et, H-6 β), 3.83 – 3.77 (m, 3H), 3.77 – 3.72 (m, 1H, H-6 α), 3.71 – 3.65 (m, 2H), 3.60 – 3.51 (m, 2H), 3.51 – 3.44 (m, 3H), 1.23 (t, J = 7.1 Hz, 6H, 2x CH₃ Et); ¹³C NMR (101 MHz, CDCl₃) δ 138.7, 138.5, 138.3, 138.3 (C_q), 128.5, 128.4, 128.2, 128.1, 128.1, 128.1, 128.0, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7 (CH_{arom}), 100.1 (C-1 α), 98.9 (C-1 β), 80.1, 79.2, 77.8, 75.8, 75.6, 74.3, 74.1 (C-5 β), 73.9, 73.8, 73.7, 73.5, 73.4, 73.2, 72.7, 70.0 (C-5 α), 69.9 (C-6 β), 68.4 (C-6 α), 64.4, 64.3 (2x CH₂ Et), 15.4, 15.1 (2x CH₃ Et); ¹³C-HMBC-GATED NMR (101 MHz, CDCl₃): δ 100.1 ($J_{\text{H-C1}} = 165$ Hz, α), 98.9 ($J_{\text{H-C1}} = 161$ Hz, β); HRMS: [M+NH₄]⁺ calcd for C₃₆H₄₀O₆NH₄ 586.31631, found 586.31458.

2-fluoroethy-2,3,4,6-tetra-O-benzyl-α,β-D-idopyranoside (8C)

Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor 8 and 2-fluoroethanol, yielding compound 8C (42 mg, 72 µmol, 72%, colourless oil, α : β = 57:43). Data reported for a 1:1 mixture: ¹H NMR (400 MHz, CDCl₃) δ 7.57 – 6.84 (m, 40H, CH_{arom}), 4.95 (d, J = 5.0 Hz, 1H, H-1a), 4.87 – 4.78 (m, 5H, H-1 β , 4x CHH Bn/CHH Bn), 4.76 - 4.61 (m, 8H, 6x CHH Bn/CHH Bn, 2x CH₂-CHHF), 4.61 - 4.47 (m, 8H, 6x CHH Bn/CHH Bn, 2x CH₂-CHHF), 4.26 (dt, *J* = 7.1, 4.4 Hz, 1H, H-5α), 4.22 – 4.08 (m, 2H, H-5β, CHH-CH₂F), 4.07 – 3.95 (m, 1H, CHH-CH₂F), 3.92 (dd, *J* = 10.1, 7.8 Hz, 1H, H-6β), 3.88 – 3.75 (m, 6H,, H-3a, H-3β, H-6a, H-6β, 2x CHH-CH₂F), 3.76 – 3.67 (m, 2H, H-4a, H-6β), 3.63 – 3.54 (m, 2H, H-2α, H-2β), 3.54 (dd, J = 5.4, 3.9 Hz, 1H, H-4β); ¹³C NMR (101 MHz, CDCl₃) δ 138.7, 138.5, 138.4, 138.3, 138.3, 138.2, 138.2, (C_q), 128.5, 128.5, 128.4, 128.3, 128.2, 128.2, 128.1, 128.0, 127.9, 127.9, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7, 127.7, (CH_{arom}), 100.8 (C-1α), 99.7 (C-1α), 83.0 (d, J = 169.0 Hz, CH₂-CH₂F), 82.8 (d, J = 169.4 Hz, CH₂-CH₂F), 79.4 (C-2 β), 78.8 (C-3 β), 77.5 (C-4α), 75.9 (C-2α), 75.2 (C-3α, C-4β), 74.2 (C-5β), 74.1, 73.8, 73.7, 73.6, 73.5, 73.4, 73.2, 72.7 (CH₂ Bn), 69.9 (C-5 α), 69.7 (C-6 β), 68.6 (C-6 α), 68.0 (d, J = 19.8 Hz, CH₂-CH₂F), 67.5 (d, J = 10.8 Hz, CH₂-CH 19.9 Hz, CH₂-CH₂F); ¹³C-HMBC-GATED NMR (101 MHz, CDCl₃): δ 100.8 (J_{H1-C1} = 167 Hz, α), 99.7 ($J_{H1-C1} = 162$ Hz, β); HRMS: [M+NH₄]⁺ calcd for C₃₆₃H₃₉FO₆NH₄ 604.30689, found 604.30571.

2,2-difluoroethy-2,3,4,6-tetra-O-benzyl-α,β-D-idopyranoside (8D)



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **8** and 2,2-difluoroethanol, yielding compound **8D** (44 mg, 72 μmol, 72%, colourless oil, $\alpha:\beta = 55:45$) Data reported for a 1:1 mixture: ¹H NMR (500 MHz, CDCl₃) δ 7.53 – 7.06 (m, 40H, CH_{arom}), 6.11 – 5.84 (m, 2H, 2x CH₂-CHF₂), 4.93 (d, *J* = 4.7 Hz, 1H, H-1α), 4.82 (d, *J* = 2.4 Hz, 1H, H-1β), 4.80 – 4.45 (m, 16H, 8x CH₂ Bn), 4.24 (dt, *J* = 7.2, 4.2 Hz, 1H, H-5α), 4.14 (ddd, *J* = 8.1, 4.8, 3.4 Hz, 1H, H-5β), 4.12 – 4.02 (m, 1H, CHH-CHF₂), 3.99 – 3.85 (m, 2H, H-6β, CHH-CHF₂), 3.85 – 3.83 (m, 1H, H-3α), 3.82 – 3.72 (m, 5H, H-3β, H-6α, H-6β, 2x CH*H*-CHF₂), 3.70 – 3.67 (m, 2H, H-4α, H-6α), 3.58 – 3.54 (m, 2H, H-2αβ), 3.51 (dd, *J* = 5.0, 3.6 Hz, 1H, H-4β); ¹³C NMR (126 MHz, CDCl₃) δ 138.5, 138.4, 138.1, 138.1, 138.0, 138.0 (Cq), 128.5, 128.5, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7 (CH_{arom}), 116.8 – 112.1 (m, 2x CH₂-CHF₂) 101.4 (C-1α), 100.0 (C-1β), 78.9 (C-2α), 78.5 (C-3α), 77.3 (C-4α), 75.4 (C-2β), 74.9 (C-3β), 74.7 (C-4β), 74.3 (C-5β), 74.0, 73.8, 73.8, 73.5, 73.5, 73.4, 73.1, 72.6 (CH₂ Bn), 69.9 (C-6β), 69.5 (C-6α), 68.6 (C-5α); ¹³C-HMBC-GATED NMR (101 MHz, CDCl₃): δ 101.4 (*J*_{H1-C1} = 168 Hz, α), 100.0 (*J*_{H1-C1} = 162 Hz, β); HRMS: [M+NH₄]⁺ calcd for C₃₆H₃₈E₂O₆NH₄ 622.29747, found 622.29604.
2,2,2-trifluoroethy-2,3,4,6-tetra-O-benzyl-α,β-D-idopyranoside (8E)



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **8** and 2,2,2-trifluoroethanol, yielding compound **8E** (41 mg, 66 μmol, 66%, $\alpha:\beta = 69:31$) Data for the α-anomer: ¹H NMR (500 MHz, CDCl₃) δ 7.40 – 7.24 (m, 20H, CH_{arom}), 4.99 (d, J = 4.6 Hz, 1H, H-1), 4.79 (dd, J = 11.5, 10.0 Hz, 2H, CH₂ Bn), 4.71 – 4.60 (m, 3H, 3x CHH Bn), 4.59 – 4.51 (m, 3H, 3x CHH Bn), 4.23 (dt, J = 7.1, 4.2 Hz, 1H, H-5), 4.13 – 4.05 (m, 1H, CHH-CF₃), 3.98 – 3.89 (m, 1H, CHH-CF₃), 3.84 (dd, J = 7.2, 5.7 Hz, 1H, H-3), 3.78 – 3.73 (m, 1H, H-6), 3.70 – 3.65 (m, 2H, H-4, H-6), 3.59 (dd, J = 7.2, 4.7 Hz, 1H, H-2); ¹³C NMR (126 MHz, CDCl₃) δ 138.4, 138.1, 138.1, 138.0 (C_q), 128.6, 128.5, 128.5, 128.5, 128.3, 128.1, 128.0, 128.0, 127.9, 127.7 (CH_{arom}), 101.0 (C-1), 78.4, 78.3 (C-2, C-3), 77.2 (C-4), 74.0, 73.8, 73.5, 73.2 (CH₂ Bn), 70.0 (C-5), 68.6 (C-6), 64.6 (q, J = 34.5 Hz, CH-CF₃); ¹³C-HMBC-GATED NMR (126 MHz, CDCl₃) δ 101.0 ($J_{H1-C1} = 169$ Hz, α); diagnostic peaks for the β-anomer: ¹H NMR (500 MHz, CDCl₃) δ 4.89 (d, J = 2.5 Hz, 1H, H-1), 3.51 (dd, J = 5.2, 3.7 Hz, 1H); ¹³C NMR (126 MHz, CDCl₃) δ 99.7 (C-1), 74.4, 73.6, 72.7, 69.4 (C-6), 68.2 – 67.3 (m, 2x CH₂-CHF₂); ¹³C-HMBC-GATED NMR (126 MHz, CDCl₃): δ 99.7 ($J_{H1-C1} = 163$ Hz, β); HRMS: [M+NH₄]⁺ calcd for C₃₆-H₃₇F₃O₆NH₄ 640.28805, found 640.28690.

1,1,1,3,3,3-hexafluoro-2-propyl-2,3,4,6-tetra-O-benzyl-α-D-idopyranoside (8F)



Title compound was prepared according to the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **8** and 1,1,1,3,3,3-hexafluoropropan-2-ol, yielding compound **8F** (15 mg, 22 µmol, 22%, colourless oil, $\alpha:\beta = >98:2$) ¹H NMR (500 MHz, CDCl₃) δ 7.40 – 7.20 (m, 20H, CH_{arom}), 5.16 (d, *J* = 4.2 Hz, 1H, H-1), 4.76 (t, *J* = 11.4 Hz, 2H, CH₂ Bn), 4.67 (d, *J* = 11.7 Hz, 1H, CHH Bn), 4.65 – 4.59 (m, 2H, CH(CF₃)₂, CHH Bn), 4.57 (d, *J* = 11.5 Hz, 1H, CHH Bn), 4.52 (d, *J* = 3.1 Hz, 2H, CH₂ Bn), 4.26 (td, *J* = 6.2, 3.6 Hz, 1H, H-5), 3.81 (dd, *J* = 7.1, 5.1 Hz, 1H, H-3), 3.72 – 3.68 (m, 3H, H-4, 2x H-6), 3.65 (dd, *J* = 7.1, 4.2 Hz, 1H, H-2); ¹³C NMR (126 MHz, CDCl₃) δ 138.3, 138.1, 138.1, 137.6 (Cq), 129.6, 129.3, 128.9, 128.7, 128.6, 128.6, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.8, 127.7, 127.7 (CH_{arom}), 101.6 (C-1), 78.1 (C-3), 77.6 (C-2), 73.8, 73.8, 73.6, 73.3 (CH₂ Bn), 70.1 (C-5), 68.2 (C-6), a cross-peak for (H-4, C-4) is visible at (3.70, 76.2) in the HSQC spectrum; ¹³C-HMBC-GATED NMR (126 MHz, CDCl₃): δ 101.6 (*J*_{H1-C1} = 173 Hz, a); HRMS: [M+NH₄]⁺ calcd for C₃₇H₃₆F₆O₆ 708.27543, found 708.27396.

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4

Chapter 4: How configuration and protecting group pattern influence glycosyl acceptor reactivity

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Results from this chapter are published in

Chemical Science, 2023, 14, 1532-1542

Introduction

Typically, the optimization of glycosylation reactions in the context of oligosaccharide total synthesis is done in a target-oriented approach and despite decades of research no universal guidelines exist to ensure general stereoselective and high yielding glycosylations.¹⁻⁵ Many different protocols for the synthesis of oligosaccharides have been developed, with most of them taking the same approach (*Figure 1*). First, a donor with a latent leaving group (LG) is activated with an activator (E-X) to form an activated donor. This electrophile then reacts with a nucleophile, the acceptor, in the glycosylation reaction, forming a glycosidic bond.⁶ Not surprisingly, the outcome of a glycosylation reaction, in terms of both stereoselectivity and yield, is dependent on many variables. Both external factors such as temperature, solvent, concentration and activator as well as inherent properties of the donor and the acceptor play a determining role.⁷



Two important parameters are the reactivity of the donor,⁸⁻¹⁰ as well as the nucleophilicity of the acceptor.^{8, 11-14} Donor reactivity has been thoroughly investigated: countless relative reactivity values of thioglycosides have been determined,¹⁵⁻¹⁷ various reactive species have been observed and characterized by variable temperature NMR,¹⁸ and the reactivity of oxocarbenium-like intermediates has been probed via a combination of experiments, computational chemistry and spectroscopy.^{14, 19, 20} Thanks to systematic mechanistic studies, the effect of both stereochemistry and protecting group pattern on the reactivity of the donor is relatively well understood. On the other hand, factors influencing the reactivity of the acceptor are less well understood, because systematic studies regarding the reactivity of the acceptor in the glycosylation reaction are much more scarce. Quite often acceptors with multiple variations are compared, making it unclear which structural modification is responsible for the difference in reactivity.²¹ By carefully choosing a set of acceptors and changing the structure in a systematic way, it is possible to determine the effect of a single variation in the stereochemistry or protecting group pattern on the reactivity of the acceptor. This work investigates the reactivity of glycosyl acceptors of C-2, C-3, or C-4 hydroxyls of Dglucose, D-mannose, D-galactose, L-rhamnose and L-fucose acceptors, having different protecting group patterns of ether and ester groups. In order to limit steric effects when comparing different ether/ester protecting groups, sterically similar benzyl and benzoyl groups were used.

Model "stripped" carbohydrate-like acceptors and glycerol alcohols are probed for comparison. The glycerol acceptors in this series resemble typical carbohydrate acceptors as they are cyclic and secondary alcohols, flanked by protected alcohols. However, unlike carbohydrate acceptors, they are not chiral, eliminating the effect of double stereodifferentiation in the glycosylation reaction.

The method used for measuring the reactivity of the acceptors is based on the stereoselective outcome in a glycosylation reaction with the acceptors and two donors: phenyl 2,3-di-O-benzyl-4,6-O-benzylidene-1-thio-β-D-glucopyranoside (Donor A) and 2-deoxy-2-azido-3-O-benzyl-4,6-O-benzylidene-1-thio-β-D-glucopyranoside phenyl (Donor B). Recently the stereoselectivity of glycosylation reactions of these donors was reported to be a measure for the reactivity of the acceptor.¹³ More nucleophilic acceptors, provide β -selective glycosylations, while less nucleophilic acceptors lead to α -selectivity. The mechanism to explain the change in stereoselectivity is shown in *Figure 2*. Both thioglycoside donors form an α -triflate upon activation with Ph₂SO and Tf_2O . More nucleophilic acceptors react with this triflate in an S_N2 like mechanism, while less nucleophilic acceptors react with the corresponding \beta-triflate or an oxocarbenium ion-like species to form the α -product.¹² Donor B shows higher β selectivity with the same acceptor than **Donor A** because the electron-withdrawing azide on C-2 stabilises the anomeric triflate rendering the $S_N 2$ substitution of the α triflate more predominant.8



Figure 2: Glycosylation mechanisms and the relation between stereoselectivity of *donor A* and *Donor B* and nucleophilicity of the acceptor

Results and discussion

Stereoselectivity

In this study, 60 acceptors were reacted with **Donor A** and **Donor B**. The acceptors can be divided in six groups based on their configuration. The results of the glucose series (acceptors 1-12), are reported in Table 1, the mannose series (13-23) in Table 2, the galactose series (24-35) in Table 3, the rhamnose series (36-42) in Table 4, the fucose series (43-50) in Table 5 and the model acceptors (51-60) in Table 6. When analysing these results, several trends became clear. In the previous study,¹³ the reactivity of glucosyl C-4-hydroxy groups was thoroughly investigated (*Table 1*). It was found that the protecting groups on the C-6-position and on the C-3-position have an effect on the reactivity, with the protecting group on the C-3-position having a larger influence, due to the closer proximity. When both positions are changed from benzyl ethers to benzoyl esters, the deactivating effects work in concert leading the following order of reactivity of the glucosyl C-4-OH acceptors: 1 > 2 > 3 > 4. A similar effect is found for the mannosyl C-4-OH (Table 2 acceptors 13-16). Also, in this series the protecting group on the C-3-position has a larger influence on the reactivity of the acceptor than the protecting group on the 6-position, and again the effects of the C-3/C-6 benzyl/benzoyl groups are additive, leading to the order of reactivity for the mannosyl C-4-OH acceptors 13 > 14 > 15 > 16. Of note, the mannosyl C-4-OH acceptors are all more reactive than their glucosyl C-4-OH equivalents.

The axial galactosyl C-4-OH is significantly less reactive (*Table 3* acceptor 24). When the protection groups on the C-6-position or the C-3-position of the galactose acceptors are changed from benzyl ethers to benzoyl esters (acceptors 25 and 26 respectively) the reactivity does not change significantly. Only when all protecting groups are changed to benzoyl esters, a significant effect is found and the reactivity decreases to provide highly α -selective glycosylations (acceptor 27). The C-4-hydroxyls of D- and L-rhamnose and D- and L-fucose (acceptors 36, 37, 43, 44, *Table 4* and *Table* 5) were used to investigate double stereodifferention effects in this glycosylation system. Although there are minor differences in stereoselectivity between the D- and Lisomers, the configuration of the acceptor seems to be more important than the absolute stereochemistry. The D-rhamnose and fucose acceptors have similar reactivity as their mannose and galactose counterparts, which is in line with what was previously found for C-4-OH glucose and C-4-OH 6-deoxyglucose acceptors.¹³ Regarding the reactivity of the C-3-hydroxyls, it is remarkable that the glycosylation with the glucose C-3-OH (acceptor 5) is much more β -selective than the mannosyl, galactosyl, rhamnosyl and fucosyl C-3-OH (acceptor 17, 28, 38, and 45 respectively), which all provide similar stereoselectivity. The main structural difference that distinguishes the glucosyl C-3-OH from the other alcohols, is that this alcohol has two equatorially oriented neighboring groups, while in mannose, galactose, rhamnose and fucose one of the neighboringing groups is axial, suggesting that this is important for the reactivity of the acceptor. Another difference is that benzoylation of the 2- and 4position of glucose (acceptors 6 and 7) has a similar effect on the reactivity and that the effects are additive (acceptor 8). While the glycosylation of all per-benzovlated acceptors (acceptors 20, 31, 41 and 48) show great α -selectivity, the effects of single benzoyl group (as in mannosyl acceptors 18 and 19, galactosyl acceptors 29 and 30, rhamnosyl acceptors 39 and 40 and fucosyl acceptors 46 and 47), depends strongly on which position it is placed. In mannose and rhamnose, benzoylation of the equatorial C-4-OH significantly diminishes the reactivity (acceptors 18 and 39) while benzoylation of the axial C-2-alcohol has little effect on the reactivity (acceptors 19 and 40). This effect was also observed for the galactosyl and fucosyl acceptors were benzovlation of the axial C-4-OH (acceptors 29 and 46) has a lower effect on the reactivity of the free alcohol than benzoylation of the equatorial C-2-OH (acceptors 30 and 47). These results show that the electron withdrawing effect of the benzoate esters critically depends on the orientation of this protecting group relative to the free OHgroup.

The results of the glycosylations with the C-2-OH acceptors show the same trend. The reactivity of the equatorial alcohols (acceptors 9, 12, 32, 35, 49, 50) is higher than that of the axial alcohols (acceptors 21 and 42). Substitution of benzyl groups for benzoyl groups also decreases the reactivity of the glucosyl, mannosyl and galactosyl C-2-OH (acceptors 9-11, 21-23 and 32-34). When regarding the reactivity of α -OMe vs β -OMe acceptors (9 vs 12, 32 vs 35 and 49 vs 50) it becomes clear that alcohols next to equatorial ethers are more reactive than those next to one axial ether, in line with the reactivity trend revealed above for the C-3-OH acceptors. Furthermore, the β -OMe acceptors 12, 35 and 50 have a similar reactivity as the other acceptors having the free alcohol next to two equatorial ethers (acceptors 1, 5, 13, 36, 37, 50) and the α -OMe acceptors 9 and 32 react in a similar fashion to the other acceptors having one axial and one equatorial ether (acceptors 17, 28, 38 and 45), again showing that the configuration of functional groups next to the alcohol is important for the reactivity with acceptors alcohols next to only equatorial benzyl ethers being more nucleophilic than those next to an axial benzyl ethers. From all the tested acceptors, only acceptor 49 shows a higher β -selectivity than what could be expected based on the above-described configurationreactivity trends between.

Finally, two sets of model acceptors were introduced to 'isolate' the effect of the different neighboring groups and serve as benchmark to aid in (future) calculations to get more quantitative grip on the relative reactivity of the tested acceptors and provide a mechanistic explanation for the reactivity differences between acceptors. The first set consists of 'stripped' carbohydrate acceptors with a single substituent next to the alcohol. The experimental data obtained with these nucleophiles show that the same reactivity trends found for the carbohydrate acceptors above: equatorial acceptors are more reactive than axial acceptors (51, 53 and 55 vs 56), alcohols next to equatorial benzyl ethers are more nucleophilic than those next to axial benzyl ethers (51 and 55 vs 53) and equatorial esters decrease the nucleophilicity much more than axial esters as compared to corresponding ethers (51 vs 52 and 53 vs 54). The second set of model acceptors consist of four glycerol C-2-OH acceptors, which were designed to investigate the effect of different protecting groups on non-chiral cyclic acceptors containing a secondary alcohol next to two protected oxygen atoms. Not surprisingly, the reactivity of the glyceroyl alcohols in the acceptors is heavily dependent on the protecting groups. The isopropylidene protected acceptor (59) is the most reactive, followed by the *cis*benzylidene protected acceptor (58), the trans-benzylidene protected acceptor (57) and finally the carbonate protected acceptor (60)

	Donor A		A	Donor B	
Acceptor	structure	Product (yield)	α:β	Product (yield)	α:β
1ª	BnO HO BnO BnO BnO OMe	1A (82%)	1:1	1B (88%)	1:7
2ª	BRO BNO BNO BNO BNO OMe	2A (92%)	4:1	2B (67%)	1:1.1
3ª	BnO HO BzO BnO OMe	3A (95%)	>20:1	3B (77%)	6.7:1
4ª	BZO HO BZO BZO OMe	4A (91%)	>20:1	4 B (69%)	>20:1
5ª	BnO HO BnO BnO OMe	5A (78%)	1:2.7	5 B (70%)	<1:20
6	Bno HO Bno OMe	6A (98%)	2.6:1	6B (99%)	1:5
7	Bno HO Bzo OMe	7 A (99%)	1.8:1	7 B (93%)	1:4
8ª	BZO HO BZO BZO BZO OMe	8A (100%)	>20:1	8B (83%)	>20:1
9ª	Bno Bno Ho OMe	9A (76%)	9:1	9B (66%)	1.6:1
10	Bno Bzo Ho OMe	10A (78%)	>20:1	10B (82%)	6:1
11ª	BZO BZO HO Mo Me	11A (85%)	>20:1	11B (92%)	13:1
12	BnO BnO HO	12A (96%)	1:1.9	12B (78%)	1:6

 Table 1: Glucose acceptors and their stereoselectivities with donor A and donor B. a: results are taken from ref 13

		Donor A		Donor	В
Acceptor	structure	Product		Product	arß
		(yield)	u:p	(yield)	a:p
13ª	BnO HO BnO OMe	13A (76%)	1:2	13B (72%)	<1:20
14	BZO HO BNO OMe	14A (76%)	1.3:1	14B (92%)	1:8
15	Bno Ho Bzo OMe	15A (62%)	9:1	15B (93%)	1.5:1
16	BZO HO BZO OMe	16A (66%)	>20:1	16B (98%)	10:1
17ª	BnO HO HO OMe	17A (82%)	8:1	17B (70%)	1.1:1
18	Bno Bzo Ho OMe	18A (87%)	>20:1	18B (87%)	>20:1
19	BnO HO HO OMe	19A (82%)	10:1	19B (93%)	1:1
20 ª	BZO HO HO OMe	20A (100%)	>20:1	20B (100%)	>20:1
21 ^a	BnO BnO OMe	21A (95%)	>20:1	21B (65%)	7:1
22	Bno OH Bzo OMe	22A (76%)	>20:1	22B (51%)	7:1
23	BZO BZO OMe	23A (77%)	>20:1	23B (51%)	>20:1

Table 2: Mannose acceptors and their stereoselectivities with donor A and donor B. a: results are taken from ref 13

		Donor A		Donor B	
Acceptor	structure	Product		Product	
		(yield)	a:p	(yield)	a:p
24ª	HO OBn BnO BnO OMe	24A (72%)	12:1	24B (86%)	3:1
25		25A (85%)	>20:1	25B (100%)	3:1
26	HO OBn BZO BnO OMe	26A (78%)	11:1	26B (67%)	3:1
27	HO OBZ BZO BZO OMe	27A (70%)	>20:1	27B (100)	>20:1
28ª	BnO OBn HO BnO OMe	28A (85%)	6:1	28B (88%)	1:1.3
29	BzO HO BnO _{OMe}	29A (76%)	16:1	29B (60%)	1.3:1
30	BnO OBn HO BZO OMe	30A (84%)	>20:1	30B (82%)	13:1
31ª	BZO OBZ HO BZO OMe	31A (83%)	>20:1	31B (90%)	11:1
32ª	BnO OBn BnO HO HOOMe	32A (87%)	10:1	32B (73%)	1:1.3
33	Bro OBn BzO HOOMe	33A (89%)	>20:1	33B (51%)	3:1
34	BZO BZO HOOMe	34A (88%)	>20:1	34B (87%)	6:1

Table 3: Galactose acceptors and their stereoselectivities with **donor A** and **donor B**.a: results aretaken from ref 13

35	BnO OBn BnO OMe HO	35A (83%)	1.5:1	35B (86%)	1:10

		Donor A		Donor B		
Acceptor	structure	Product (yield)	α:β	Product (yield)	α:β	
36		36A (89%)	1:2.4	36B (75%)	<1:20	
37	HO BnO OBn	37A (90%)	1.7:1	37B (99%)	1:10	
38	BnO HO OBn	38A (100%)	7:1	38B (68%)	1.4:1	
39	BzO HO OBn	39A (69%)	>20:1	39B (50%)	12:1	
40	BnO HO OBz	40A (66%)	6:1	40B (55%)	1:1	
41	BzO HO OBz	41A (83%)	>20:1	41B (100%)	12:1	
42	Bno Bno OH	42A (59%)	>20:1	42A (77%)	3:1	

Table 4: Rhamnose acceptors and their stereoselectivities with donor A and donor B

		Donor A		Donor B	
Acceptor	structure	Product (yield)	α:β	Product (yield)	α:β
43	HO BnO BnO BnO OMe	43A (98%)	>20:1	43B (100%)	1.3:1
44	OMe OBn HO	44A (85%)	14:1	44B (100%)	3:1
45	OMe OMe BnOOH	45A (100%)	3.2:1	45B (88%)	1:2
46	OMe OMe BzOOH	46A (100%)	>20:1	46B (100%)	2:1
47	OMe OT OBz BnO ^{OH}	47A (100%)	>20:1	47B (92%)	9:1
48	OMe OT OBz BZO	48A (100%)	>20:1	48B (100%)	>20:1
49	ОМе Тотон BnO	49A (55%)	1:1	49B (95%)	1:5.5
50	OBn BnO	50A (86%)	1:1.2	50B (93%)	<1:20

 Table 5: Fucose acceptors and their stereoselectivities with donor A and donor B

	1	Donor	A	Donor B	
Acceptor	structure	Product (yield)	α:β	Product (yield)	α:β
51	BnO to	51A (81%)	1:1.6	51B (85%)	1:13
52	BZO HO	52A (53%)	5:1	52B (60%)	1.4:1
53	BnO HO	53A (97%)	4:1	53B (60%)	1:1.4
54	HO HO	54A (100%)	8:1	54B (100%)	1.5:1
55	HOTO	55 A (98%)	1:1.6	55B (97%)	1:16
56	HO BnO	56A (100%)	11:1	56B (93%)	1.4:1
57	HO COLPh	57A (100%)	6:1	57B (100%)	2.9:1
58	OH COCPh	58A (79%)	1.6:1	58B (31%)	1:3
59	OH CO	59A (96%)	1:1	59B (100%)	1:10
60	OH COLO	60A (97%)	>20:1	60B (99%)	>20:1

Table 6: Model acceptors and their stereoselectivities with donor A and donor B

Structure-reactivity relationships

In order to reveal structure-reactivity relationships for the large collection of acceptors, they were divided in groups based on their configuration and protecting group pattern and their reactivity of acceptors plotted as percentage β -product formed with both **donor A** and **donor B**.

Figure 3 shows the importance of configuration on the reactivity of the acceptor. Equatorial acceptors are generally more reactive than axial acceptors (light blue circles and blue squares bar vs black triangles). Furthermore, the orientation of the group next to the alcohol is important for the reactivity of the acceptor. When the nucleophilic alcohol only has equatorial neighbours (light blue circles) the acceptor is more nucleophilic than an acceptor with an axial neighbour (blue squares)



Figure 3: Configuration vs reactivity (measured as percentage β -product for **Donor A** and **Donor B**) of glycosyl acceptors. Light blue circles: equatorial alcohol acceptors with only equatorial neighboring OBn and OMe groups, i.e. acceptors **1**, **5**, **12**, **13**, **35**, **36**, **37**, **50**, **51** and **55**. Blue squares: equatorial alcohol with one axial neighboring OBn or OMe group, i.e. acceptors **9**, **17**, **28**, **32**, **38**, **45**, **49** and **53**. Black triangles: axial alcohols, i.e. acceptors **21**, **24**, **42**, **43**, **44** and **56**.

Figure 4 shows the effect of the orientation of a benzoyl group on the reactivity of the acceptors. When the neighboring benzoyl is axial (red diamonds) the effect on the reactivity is smaller than that of an equatorial benzoyl (yellow triangles). Benzyl protected acceptors with one axial neighboring OBn or OMe group (blue circles) and acceptors with one axial and one equatorial benzoyl group (green inverted triagles) are provided as a reference.



Figure 4: Protecting group pattern vs reactivity (measured as percentage β -product for **Donor A** and **Donor B**) of glycosyl acceptors. Blue circles: equatorial alcohol acceptors with one axial neighboring OBn or OMe group, i.e. acceptors **9**, **17**, **28**, **32**, **38**, **45**, **49** and **53**. Red diamonds: equatorial alcohol acceptors with one axial neighboring OBz group, i.e. acceptors **9**, **17**, **28**, **32**, **38**, **45**, **49** and **53**. Red diamonds: equatorial alcohol acceptors with one axial neighboring OBz group, i.e. acceptors **19**, **29**, **40**, **46** and **54**. Yellow triangles: equatorial alcohol acceptors with one axial neighboring OBz group and one equatorial neighboring OBz group, i.e. acceptors **10**, **18**, **30**, **34**, **40** and **47**. Green triangles: equatorial alcohol acceptors with one axial and one equatorial neighboring OBz group, i.e. acceptors **20**, **31**, **41** and **48**.

Proton affinity

Next, a method was sought to establish acceptor reactivity in a more quantitiative manner. To this end the proton affinity of the model acceptors **59-68** and partially fluorinated ethanols was calculated. The computed proton affinity (ΔH_{PA}) is defined as the enthalpy for the reaction described in *equation 1* in the gas phase.

$$ROH \rightarrow RO^- + H^+(1)$$

The proton affinity of a given alcohol serves as a measure for the electron density of the alcohol, and thus relates to the nucleophilicity of the acceptor alcohols. First the proton affinities were computed for ethanol, 2-fluoroethanol, 2,2-difluoroethanol and 2,2,2-

trifluoroethanol and compared to experimental values from literature.²³⁻²⁵ For each acceptor and the corresponding alkoxide the enthalpy of the lowest energy conformer was computed at DLPNO-CCSD(T)/CBS(3/4,def2)²⁶⁻²⁹ //DLPNO-MP2/def2-TZVP^{26-28, 30, 31} at T=298.15K using ORCA5.0.1.³² This general purpose method³³ has recently been shown to provide energies similar to the 'golden standard', canonical CCSD(T) calculations, for carbohydrate conformations.³⁴ First the ΔH_{PA} of the fluorinated ethanol derivates were computed at both DLPNO-CCSD(T) and canonical CCSD(T) level, and compared to the experimental value to gauge the accuracy of the method. The DLPNO-CCSD(T) computations provided excellent agreement with both computed canonical CCDT(T) calculations and experimental values (*Table 7*).

Jrom merature			
Acceptor	Calculated ΔH_{PA} DLNPO-CCDS(T)	Calculated ΔH_{PA} CCDS(T)	experimental ΔH_{PA}
	(Kcal/mol)	(Kcal/mol)	(Kcal/mol)
Ethanol	379.1	379.4	379.1 ± 1.0^{23}
MFE	372.1	372.5	370.9 ± 2.9^{24}
DFE	366.6	367.0	366.2 ± 2.2^{25}
TFE	361.4	361.7	361.4 ± 2.4^{25}

Table 7: calculated proton affinities of ethanol acceptors compared to their experimental values from literature

Next the proton affinities for the other acceptors were calculated. In these computations, the relatively large benzyl, benzoyl and benzylidene protecting groups were replaced for smaller but electronically similar methyl, acetyl and ethylidene groups. For ease of comparison, the proton affinities are shown as the relative proton affinity to triflic acid ($\Delta\Delta$ H_{PA}), which can be defined by *equation 2*. The results of these calculations are depicted in *Table 8* and listed in order of increasing relative proton affinity.

$$\Delta \Delta H_{PA} (ROH) = \Delta H_{PA} (ROH) - \Delta H_{PA} (TfOH) (2)$$

A		$\Delta\Delta H_{PA}$	Percentage β	Percentage β
Acceptor	structure	(Kcal/mol)	Donor A	Donor B
TfOH	О F ₃ C-S-ОН О	0	0 ^b	0 ^b
60	OH O	58.3	0	0
TFE	F₃C∕OH	64.4	0	0
61	HOTO	68.0	14 ^a	26ª
62	AcO HO	68.7	11ª	40 ª
DFE	F₂HC OH	69.4	17	26
63	AcO 10	69.5	17 ^a	42ª
64	HOTO	69.6	62 ^a	94ª
65	MeOO	70.5	62 ^a	93ª
66	HOHO	70.9	20ª	58ª
67	HO MeO	71.4	8 ^a	42ª
68	OH	76.0	38ª	75 ^a
59	OH CO	76.2	50	91
MFE	FH ₂ C OH	74.9	74	87
EtOH	Н₃С́ОН	81.9	91	100

Table 8: Proton affinity vs stereoselectivity for the studied model acceptors.

 a Stereoselectivity based on experimental data from benzyl, benzoyl or benzylidene protected analogues, see above. b Determined by NMR at – 40 $^\circ C$

The correlation between proton-affinity and reactivity of the acceptor (as measured by the percentage of β -product in a glycosylation reaction with **Donor A** or **Donor B**) is plotted in *Figure 5A-C*. When the proton affinity of all acceptors is plotted agains the β -selectivity of the acceptors, a coefficient of determination (R²) of 0.57 was obtained for the reactions with both **Donor A** and **Donor B** (*Figure 5A*). When only the data was used obtained for the simpler non-chiral alcohols (i.e. 59, 60, 61, 68, EtOH, MFE, DFE and TFE) the value for R^2 was much higher (0.85 for **Donor A** and 0.92 for **Donor** B), indicating a good correlation between the calculated proton affinity and the reactivity of the acceptor (Figure 5B). There is no correlation between the proton affinity of the chiral 'stripped carbohydrate' acceptors and the stereoselectivity of the reactions ($R^2 < 0.01$, Figure 5C), showing that reactivity of these acceptors in the glycosylations with donors A and B is not solely determined by the electron density of the alcohol, as determined by the ΔH_{PA} , but rather by the more complex interplay of both steric and electronic factors. Although the computations listed in Table 8 show that the method used to compute the proton affinity can accurately reconstitute this parameter for simple alcohols in the gas phase, it is not surprising that there is poorer correlation with the reactivity of the more complex alcohols in solution.

Another recent study has attempted to describe acceptor reactivity with a parameter (Aka) relating to the reaction rate of acceptors with 3,4-dihydropyran (DHP) under acidic conditions.²² The authors found relatively good correlations between this parameter, the reactivity of the donor and the outcome of the glycosylation reaction. So for future research it would be interesting to measure the Aka of this set of acceptors and investigate if the same trends can be found as described in this work.

Chapter 4



Figure 5: Calculated proton affinity vs experimental stereoselectivity with R^2 displayed for A: all acceptors for which proton affinity was calculated; B: for the set of non-chiral acceptors and C: 'stripped carbohydrate-like' acceptors. Acceptor **60** was excluded for the calculation of R^2 because of non-linearity of the graph in that area, since the amount of β -product can not be lower than 0%, and acceptors with a higher proton affinity already show full α -selectivity. Experimental values of β -selectivity are based on benzyl, benzoyl and benzylidene protected acceptors, the calculated proton affinity is based on methyl, acetyl and ethylidene protected analogues.

Conclusions

In conclusion, structure-reactivity relationships for a large set of glycosyl acceptors have been established, based on the stereoselectivity of these acceptors in glycosylations with two conformationally restricted glucosyl donors. The reactivity-stereoselectivity correlation is based on the premise that reactive acceptors predominantly provide the β-product via an $S_N 2$ like mechanism in which a covalent anomeric α-triflate is displaced, while less reactive acceptors give more α -product via a glycosylation proceeding with more S_N like character. In total, 60 acceptors were tested, and this systematic series of nucleophiles has revealed several factors that influence the reactivity of the acceptor. With regards to configuration, equatorial acceptors are more reactive than axial alcohols. Also, the configuration of the protected alcohols next to the OH-group are important, and acceptors in which the neighboring protected alcohols take up an equatorial position, are more reactive than acceptors in which one of the flanking protected alcohols is axial. The protecting group pattern also plays an important role, since switching benzyl ethers to sterically similar benzoyl esters decreases the reactivity of the acceptor. However, it is important to note that the configuration of the ester is also important, and substituting an axial ether for an ester has significantly less effect on the reactivity of the acceptor than substituting an equatorial ether for an ester. To better understand the stereoelectronic effects of exerted by the different configuration and protecting group patterns, a set of model acceptors was introduced to serve as a benchmark for computational studies. Proton affinities were calculated in an attempt to explain differences in reactivity, and for simple nonchiral alcohol nucleophiles relatively good correlation was found between calculated proton affinity and reactivity. For the more complex, chiral carbohydrate-like acceptors, the differences in proton affinity proved to be relatively small, and these could not fully account for the experimentally observed differences in reactivity. Overall, this has shown that proton affinity is important for the reactivity of acceptors, but other factors may also contribute and future research efforts will focus on the investigation of steric and hydrogen bonding effects.

Experimental

Calculation of proton affinities

Spartan'14³⁵ was used to construct a conformer library of the neutral acceptor by a Monte-Carlo search. Each conformation was optimzed and evaluated using the MMFF³⁶ force field, and the 100 lowest energy structures were included in the conformer library. The conformer library of the corresponding anion was constructed by converting all hydroxyl conformers in the neutral conformer library to the corresponding alkoxide conformer. All conformers in both libraries were optimized using ORCA5.0.1³² by DFT at B3LYP-D3(BJ)/def2-TZVP(-f)^{26, 37-40} level of theory, utilizing the TighSCF and Defgrid2 keywords. All conformers with a $\Delta E < 1$ kcal mol⁻¹ were re-optimized by WFT at DLPNO-MP2/def2-TZVP^{26-28, 30, 31} level of theory. Final single point energies of all re-optimized structures were computed by WFT at DLPNO-CCSD(T)/CBS(3/4,def2)²⁶⁻³¹ level of theory, utilizing the TighSCF, Defgrid2 and NormalPNO keywords. This method has been shown to provide energies similar to canonical CCSD(T) for diverse systems,³⁴ aswell as for carbohydrate conformations specifically.³³ The final enthalpy of each conformer was constructed as DLPNO-MP2/def2-TZVP//DLPNO-CCSD(T)/CBS(3/4,def2) at T=298.15K. ΔH_{PA} was derived by equation 1.

$$\Delta H_{PA} = H_{alkoxide} - H_{alcohol} (1)$$

The ΔH_{PA} was expressed as $\Delta \Delta H_{PA}$, relative to the lowest computed ΔH_{PA} in this study; triflic acid.

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 (Tf₂O) was distilled over P₂O₅ and stored at -20°C under a nitrogen atmosphere. 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 F254, Merck) with UV detection by (254 nm) and by spraying with 20% sulfuric acid in ethanol or by spraying with a solution of (NH₄)₆Mo₇O₂₄·H₂O (25 g/L) and (NH₄)₄Ce(SO4)₄·2H₂O (10 g/L) in 10% aq. sulfuric acid followed by charring at ±250 °C. 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. 1H and 13C NMR spectra were recorded on Bruker AV-400, Bruker DMX-400, and Bruker AV-500 NMR instruments. Chemical shifts (δ) are given in parts per million (ppm) relative to tetramethylsilane as an internal standard or the residual signal

of the deuterated solvent. Coupling constants (*J*) are given in Hertz (Hz). All presented 13C-APT spectra are proton-decoupled. NMR peak assignments were made using COSY and HSQC. When necessary, additional NOESY, HMBC and HMBC-GATED 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 1H 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.

Acceptor **58** was purchased from Sigma Aldrich and used without further purification. Acceptors **26**,⁴¹ **44**,⁴² **57**,⁴³ **59**⁴³ and **60**⁴⁴ and donors A^{12} and B^8 were synthesized according to literature procedures

General procedure for Ph₂SO/Tf₂O meditated glycosylations

Donor (0.1 mmol, 1 eq), Ph₂SO (0.13 mmol, 1.3 eq) and TTBP (0.25 mmol, 2.5 eq) were coevaporated twice with toluene, dissolved in 2 mL DCM and stirred for 30 min at RT with 3A molecular sieves. The solution was cooled to -80 °C and Tf₂O (22 μ L, 0.13 mmol, 2 eq) 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 eq) in DCM (0.4 mL, 0.5 M) was added. The reaction mixture was allowed to warm to -40 °C for and stirred between 1-24 hr at that temperature. The reaction was quenched with 2 mL sat aq NaHCO₃ or 0.3 mL 1M Et₃N in DCM, and the mixture was added, the layers were separated, and the water phase was extracted once more with DCM. The combined organic layers were dried over MgSO4, filtered, and concentrated in vacuo. Purification by silica gel flash column chromatography and/or sephadex LH-20 size-exclusion chromatography yielded the glycosylation product as a mixture of anomers.

Preparations of acceptors

Glucose acceptors



Scheme S1: preparation of acceptor (6): reagents and conditions: a) NapBr, NaH, DMF 100%; b) TES-H, TFA, DCM, 0°C 84% c) BzCl, pyridine, 76% d) DDQ, DCM/H₂O (9:1), 90%

Methyl 2-O-benzyl-4,6-O-benzylidene-3-O-(2-naphthyl)methyl-a-D-glucopyranoside (S2)

methyl 2-O-benzyl-4.6-O-benzylidene-3-O-(2-naphthyl)methyl-α-D-glucopyranoside⁴⁵ (S1, 1.50 g, 4.03 mmol) was dissolved in DMF and cooled to 0 °C. NaH (60% dispersion in mineral oil, 241 mg, 6.04 mmol, 1.5 eq) was added and after 15 minutes 2-(Bromomethyl)naphthalene (1.11 g, 5.03 mmol, 1.25 eq) was added. The reaction mixture was allowed to warm to room temperature. When TLC showed full conversion, the reaction mixture was guenched with 0.1 M HCl, diluted with EtOAc and washed with sat. aq. NaHCO3 and brine. The organic phase is dried with MgSO4 and concentrated under reduced pressure. The residue is purified over silica (10%>40% EtOAc in pentane) yielding the product as a white wax in quantitative yield. ¹H NMR (400 MHz, CDCl₃) δ 7.84 - 7.74 (m, 3H, CH_{arom}), 7.72 - 7.66 (m, 1H, CH_{arom}), 7.53 - 7.46 (m, 3H, CH_{arom}), 7.46 -7.42 (m, 2H, CH_{arom}), 7.39 - 7.27 (m, 8H, CH_{arom}), 5.57 (s, 1H, CHPh), 5.07 (d, J = 11.7 Hz, 1H, CHH Bn/Nap), 5.00 (d, J = 11.6 Hz, 1H, CHH Bn/Nap), 4.87 (d, J = 12.1 Hz, 1H, CHH Bn/Nap), 4.72 (d, J = 12.2 Hz, 1H, CHH Bn/Nap), 4.61 (d, J = 3.7 Hz, 1H, H-1), 4.27 (dd, J = 10.1, 4.7 Hz, 1H, H-6), 4.10 (t, *J* = 9.3 Hz, 1H, H-3), 3.84 (td, *J* = 9.9, 4.7 Hz, 1H, H-5), 3.71 (t, *J* = 10.2 Hz, 1H, H-6), 3.66 - 3.56 (m, 2H, H-2, H-4), 3.40 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 138.2, 137.5, 136.3, 133.4, 133.1 (C_q), 129.1, 128.6, 128.4, 128.2, 128.1, 128.1, 128.1, 127.7, 126.8, 126.3, 126.2, 126.0, 125.8 (CHarom), 101.5 (CHPh), 99.3 (C-1), 82.2 (C-4), 79.4 (C-2), 78.7 (C-3), 75.5, 73.9 (CH2 Bn/Nap), 69.2 (C-6), 62.5 (C-5), 55.5 (CH3 OMe); HRMS: [M+NH4]⁺ calcd for C₃₂H₃₂O₆NH₄ 530.25371, found 530.25279.

Methyl 2,6-di-O-benzyl-3-O-(2-naphthyl)methyl-a-D-glucopyranoside (S3)

methyl 2-O-benzyl-4,6-O-benzylidene-3-O-(2-naphthyl)methyl-a-D-glucopyranoside (S2, 1.48 g, 2.89 mmol) and TES-H (2.15 mL, 28.9 mmol, 10 eq) were dissolved in DCM and cooled to 0 °C. After 15 min of stirring TFA (4.60 mL 28.9 mmol, 10 eq) was added dropwise. When TLC showed full conversion, the reaction was quenched with sat. aq. NaHCO₃. The organic phase was dried with Na₂SO₄ and concentrated under reduced pressure. The residue was purified over silica (25% EtOAc in pentane) to obtain the title compound as colourless oil Yield: 1.25 g, 2.43 mmol, 84%. ¹H NMR (400 MHz, CDCl₃) δ 7.86 – 7.79 (m, 4H, CH_{arom}), 7.48 (ddd, J = 9.3, 6.1, 1.6 Hz, 3H, CH_{arom}), 7.39 – 7.25 (m, 10H, CH_{arom}), 5.15 (d, J = 11.7 Hz, 1H, CHH Bn/Nap), 4.91 (d, J = 11.7 Hz, 1H, CHH Bn/Nap), 4.78 (d, J = 12.1 Hz, 1H, CHH Bn/Nap), 4.68 (d, J = 12.1 Hz, 1H, CH*H* Bn/Nap), 4.65 (d, *J* = 3.6 Hz, 1H, H-1), 4.59 (d, *J* = 12.2 Hz, 1H, C*H*H Bn/Nap), 4.53 (d, *J* = 12.2 Hz, 1H, CHH Bn/Nap), 3.84 (dd, J = 9.6, 8.5 Hz, 1H, H-3), 3.73 – 3.62 (m, 4H, H-4, H-5, H-6, H-6), 3.57 (dd, J = 9.5, 3.6 Hz, 1H, H-2), 3.39 (s, 3H, CH₃ OMe), 2.37 (d, J = 2.3 Hz, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 138.2, 138.1, 136.3, 133.5, 133.1 (C_q), 128.6, 128.5, 128.5, 128.3, 128.1, 127.8, 127.8, 127.8, 126.9, 126.3, 126.1, 126.0 (CHarom), 98.3 (C-1), 81.5 (C-3), 79.7 (C-2), 75.6, 73.7, 73.3 (CH₂ Bn/Nap), 70.9, 70.0 (C-4, C-5), 69.6 (C-6), 55.4 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₃₂H₃₄O₆NH₄ 532.26936, found 532.26839.

Methyl 4-O-benzoyl-2,6-di-O-benzyl-3-O-(2-naphthyl)methyl-α-D-glucopyranoside (S4)



Methyl 2,6-di-O-benzyl-3-O-(2-naphthyl)methyl-a-D-glucopyranoside (\$3, 1.20 g, 2.33 mmol) was dissolved in 5 mL pyridine, after which benzovl chloride (0.406 mL, 3.50 mmol, 1.5 eq) was added. When TLC indicated full conversion, the reaction mixture was diluted with diethyl ether, washed with 1M aq. HCl, sat. aq. NaHCO₃ and brine. The organic phase was dried with sodium sulfate and concentrated under reduced pressure. The residue was purified with silica chromatography (15% EtOAc in pentane) to yield the title compound as colourless oil. Yield: 1.10 g, 1.78 mmol, 76%. ¹H NMR (400 MHz, CDCl₃) δ 7.88 - 7.81 (m, 2H, CH_{arom}), 7.66 - 7.62 (m, 1H, CH_{arom}), 7.60 – 7.57 (m, 2H, CH_{arom}), 7.50 (ddt, J = 8.7, 7.3, 1.3 Hz, 1H, CH_{arom}), 7.45 (d, J = 8.4 Hz, 1H, CH_{arom}), 7.41 - 7.28 (m, 9H, CH_{arom}), 7.24 - 7.12 (m, 6H, CH_{arom}), 5.33 (dd, J = 10.3, 9.2 Hz, 1H, H-4), 4.99 (d, J = 11.6 Hz, 1H, CHH Bn/Nap), 4.85 (d, J = 12.1 Hz, 1H, CHH Bn/Nap), 4.79 (d, J = 11.7 Hz, 1H, CHH Bn/Nap), 4.71 (d, J = 12.1 Hz, 1H, CHH Bn/Nap), 4.68 (d, J = 3.6 Hz, 1H, H-1), 4.46 (s, 2H, CH₂ Bn/Nap), 4.11 (t, J = 9.4 Hz, 1H, H-3), 3.96 (ddd, J =10.2, 5.1, 2.7 Hz, 1H, H-5), 3.71 (dd, J = 9.6, 3.6 Hz, 1H, H-2), 3.55 (dd, J = 10.8, 2.7 Hz, 1H, H-6), 3.49 (dd, J = 10.8, 5.1 Hz, 1H, H-6), 3.44 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 165.4 (C=O), 138.1, 137.9, 135.8, 133.2 (Cq, 133.2 (CHarom), 132.9, 129.8(Cq), 129.8, 128.6, 128.4, 128.3, 128.3, 128.1, 128.1, 128.0, 127.8, 127.7, 127.6, 126.9, 126.3, 125.9, 125.7 (CH_{arom}), 98.4 (C-1), 79.8 (C-2), 79.1 (C-3), 75.5 (CH₂ Bn/Nap), 73.7 (2xCH₂ Bn/Nap), 71.0 (C-4), 69.1 (C-6), 69.1 (C-5), 55.6 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₃₉H₃₈O₇NH₄ 636.29558, found 636.29453.

Methyl 4-O-benzoyl-2,6-di-O-benzyl-a-D-glucopyranoside (6)

Methyl 4-O-benzoyl-2,6-di-O-benzyl-3-O-(2-naphthyl)methyl-α-D-glucopyranoside (S4, 1.05 g, 1.70 mmol) was dissolved in 20 mL 19:1 DCM/water, after which DDQ (770 mg, 3.39 mmol, 2 eq) was added. When TLC indicated full conversion, the organic phase was diluted with DCM, washed twice with sat. aq. NaHCO₃, dried with sodium sulfate and concentrated under reduced pressure. The residue was purified with silica chromatography (15%→25% EtOAc in pentane) to yield the title compound as a colourless oil. Yield: 731 mg, 1,53 mmol, 90%. $[\alpha]_D^{25} = 55.6^\circ$ (c = 0.73, CHCl₃); IR (thin film): 698, 713, 1027, 1043, 1097, 1269, 1452, 1724; ¹H NMR (400 MHz, CDCl₃) δ 8.03 - 7.96 (m, 2H, CHarom), 7.59 - 7.53 (m, 1H, CHarom), 7.45 - 7.28 (m, 7H, CHarom), 7.24 – 7.10 (m, 5H, CH_{arom}), 5.24 (dd, J = 10.2, 9.3 Hz, 1H, H-4), 4.77 (d, J = 12.2 Hz, 1H, CHH Bn), 4.70 (d, J = 12.2 Hz, 1H, CHH Bn), 4.67 (d, J = 3.5 Hz, 1H, H-1), 4.52 (d, J = 12.1 Hz, 1H, CHH Bn), 4.45 (d, J = 12.1 Hz, 1H, CHH Bn), 4.17 (td, J = 9.4, 2.8 Hz, 1H, H-3), 3.99 (ddd, J = 10.2, 4.6, 2.7 Hz, 1H, H-5), 3.61 - 3.50 (m, 3H, H-2, H-6, H-6), 3.40 (s, 3H, CH₃ OMe), 2.59 (d, J = 3.2 Hz, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 166.2 (C=O), 138.0, 137.7 (C_q), 133.4, 130.0 (CH_{arom}), 129.7 (C_q), 128.7, 128.5, 128.3, 128.3, 128.2, 127.8, 127.6 (CH_{arom}), 97.9 (C-1), 79.5 (C-2), 73.7, 73.5 (CH₂ Bn), 71.7, 71.7 (C-3, C-4), 68.7 (C-6), 68.6 (C-5), 55.6 (CH₃ OMe); HRMS: [M+Na]⁺ calcd for C₂₈H₃₀O₇Na 501.18837, found 501.18733.



Scheme S2: preparation of acceptor 7: reagents and conditions: a) AllylBr, NaH, DMF, 94%; b) $pTsOH+H_2O$, MeOH, 50 °C, quant.; c) BnBr, NaH, DMF, 95%; d) DDQ, DCM/H2O (9:1), 80%; e) BzCl, pyridine, 87%; f) Pd(PPh₃)₄, DMBA, MeOH, 40 °C, 90%.

Methyl 3-O-allyl-4,6-O-benzylidene-2-O-(2-naphtyl)methyl-a-D-glucopyranoside (S6)

Methyl 4,6-O-benzylidene-2-O-(2-naphtyl)methyl-a-D-glucopyranoside⁴⁶ (**\$5**, 9.3 g, 22.0 mmol, 1 eq) was dissolved in 75 ml DMF and stirred at 0 °C until the sugar was fully dissolved. To the solution was added NaH (60 % dispersion in mineral oil, 0.48 g, 33 mmol, 1.5 eq) and the mixture was stirred for another 15 min before slowly adding AllylBr (2.9 ml, 33 mmol, 1.5 eq) and the reaction was stirred at RT until TLC indicated full conversion. The reaction mixture was quenched with H₂O and extracted with Et₂O. The organic layer was washed twice with H₂O. The organic layer was dried over MgSO4, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (10% EtOAc in pentane) to provide the title compound as an oil. Yield: 9.58 g, 20.7 mmol, 94%. ¹H NMR (400 MHz, CDCl₃) δ 7.89 - 7.77 (m, 4H, CHarom), 7.60 - 7.46 (m, 5H, CHarom), 7.41 - 7.31 (m, 3H, CHarom), 6.01 (ddt, J = 17.2, 10.4, 5.7 Hz, 1H, CH₂-CH=CH₂), 5.52 (s, 1H, CHPh), 5.34 (dq, J = 17.2, 1.7 Hz, 1H, CH₂-CH=CHH), 5.19 (dq, J = 10.4, 1.3 Hz, 1H, CH₂-CH=CHH), 5.02 (d, J = 12.0 Hz, 1H, CHH Nap), 4.87 (d, J = 12.4 Hz, 1H, CHH Nap), 4.57 (d, J = 3.7 Hz, 1H, H-1), 4.43 (ddt, J = 12.7, 5.8, 1.4 Hz, 1H, CHH-CH=CH₂), 4.34 (ddt, J = 12.6, 5.7, 1.4 Hz, 1H, CHH-CH=CH₂), 4.24 (dd, J = 10.1, 4.8 Hz, 1H, H-6), 3.96 (t, J = 9.2 Hz, 1H, H-3), 3.80 (td, J = 9.9, 4.7 Hz, 1H, H-5), 3.67 (t, J = 10.3 Hz, 1H, H-6), 3.57 – 3.50 (m, 2H, H-2, H-4), 3.40 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) & 137.5, 135.8 (C_q), 135.4 (CH₂-CH=CH₂), 133.3, 133.2 (C_q), 129.0, 128.4, 128.4, 128.1, 127.9, 127.2, 126.3, 126.2 (CHarom), 117.0 (CH2-CH=CH2), 101.4 (CHPh), 99.4 (C-1), 82.2 (C-4), 78.9 (C-2), 78.2 (C-3), 74.2 (CH₂-CH=CH₂), 74.1 (CH₂ Nap), 69.2 (C-6), 62.4 (C-5), 55.5 (CH₃ OMe); HRMS: [M+Na]⁺ calcd for C₂₈H₃₀O₆Na 485.19346, found 485.19269.

Methyl 3-O-allyl-2-O-(2-naphtyl)methyl-a-D-glucopyranoside (S7)

Methyl 3-O-allyl-4,6-O-benzylidene-2-O-(2-naphtyl)methyl- α -D-glucopyranoside (**S6**, 9.57 g, 20.7 mmol, 1 eq) was dissolved in 100 ml MeOH and stirred at RT for 15 min. To the solution was added pTsOH·H₂O (0.39 g, 2.07 mmol, 0.1 eq) and the mixture was stirred for 1 h at 50 °C after which TLC indicated full conversion. The reaction mixture was set to cool down to RT and

was quenched with TEA (2.3 ml, 6.18 mmol, 0.25 eq). Solvents were evaporated under reduced pressure and purification was performed on flash column chromatography (3/2 pentane/EtOAc) to provide the title compound as a solid. Yield: 7.8 g, 20.7 mmol, quant. ¹H NMR (400 MHz, CDCl₃) δ 7.86 – 7.76 (m, 4H, CH_{arom}), 7.53 – 7.43 (m, 3H, CH_{arom}), 5.99 (ddt, *J* = 17.3, 10.4, 5.8 Hz, 1H, CH₂-CH=CH₂), 5.31 (dq, *J* = 17.2, 1.6 Hz, 1H, CH₂-CH=CHH), 5.19 (dq, *J* = 10.4, 1.4 Hz, 1H, CH₂-CH=CHH), 4.89 (d, *J* = 12.3 Hz, 1H, CHH Nap), 4.78 (d, *J* = 12.3 Hz, 1H, CHH Nap), 4.57 (d, *J* = 3.5 Hz, 1H, H-1), 4.50 (ddt, *J* = 12.6, 5.5, 1.5 Hz, 1H, CHH-CH=CH₂), 4.28 (ddt, *J* = 12.6, 5.9, 1.3 Hz, 1H, CHH-CH=CH₂), 3.80 – 3.75 (m, 2H, H-6, H-6), 3.71 (dd, *J* = 9.5, 8.7 Hz, 1H, H-3), 3.60 (dt, *J* = 9.8, 3.7 Hz, 1H, H-5), 3.52 (ddd, *J* = 9.9, 8.7, 3.0 Hz, 1H, H-4), 3.47 (dd, *J* = 9.5, 3.5 Hz, 1H, H-2), 3.35 (s, 3H, CH₃ OMe), 3.07 (d, *J* = 3.2 Hz, 1H, 4-OH), 2.36 (t, *J* = 6.2 Hz, 1H, 6-OH); ¹³C NMR (101 MHz, CDCl₃) δ 135.5 (Cq), 135.2 (CH₂-CH=CH₂), 98.3 (C-1), 81.0 (C-3), 79.6 (C-2), 74.3 (CH₂-CH=CH₂), 73.3 (CH₂ Nap), 70.8 (C-5), 70.2 (C-4), 62.2 (C-6), 55.3 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₂₁H₂₆O₆NH₄ 392.20676, found 392.20584.

Methyl 3-O-allyl-4,6-di-O-benzyl-2-O-(2-naphtyl)methyl-a-D-glucopyranoside (S8)



Methyl 3-O-allyl-2-O-(2-naphtyl)methyl-α-D-glucopyranoside (S7, 7.7 g, 20.56 mmol, 1 eq) was dissolved in 75 ml DMF and stirred at 0 °C until the sugar was fully dissolved. To the solution was added NaH (60% dispersion in mineral oil, 2.47 g, 61.69 mmol, 3 eq) and the reaction was stirred for 30 min at 0 °C after which BnBr (7.33 ml, 61.69 mmol, 3 eq) was slowly added. After 30 min the temperature was increased to RT. Once TLC indicated full conversion the reaction mixture was quenched with water and extracted twice with Et₂O. The combined organic layers were dried over MgSO4, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (9/1 pentane/EtOAc) to provide the title compound as an oil. Yield: 10.85 g, 19.55 mmol, 95%. ¹H NMR (400 MHz, CDCl₃) δ 7.85 - 7.78 (m, 4H, CHarom), 7.55 - 7.42 (m, 3H, CHarom), 7.35 - 7.23 (m, 8H, CHarom), 7.21 - 7.15 (m, 2H, CHarom), 6.03 (ddt, J = 17.3, 10.4, 5.6 Hz, 1H, CH₂-CH=CH₂), 5.33 (dq, J = 17.2, 1.7 Hz, 1H, CH₂-CH=CHH), 5.18 (dq, J = 10.4, 1.3 Hz, 1H, CH₂-CH=CHH), 4.94 (d, J = 12.3 Hz, 1H, CHH Bn), 4.84 (d, J = 8.2 Hz, 1H, CHH Nap), 4.81 (d, J = 9.9 Hz, 1H, CHH Bn), 4.62 – 4.56 (m, 2H, H-1, CHH Bn), 4.53 – 4.42 (m, 3H, CHH Bn, CHH Nap, CHH-CH=CH₂), 4.34 (ddt, J = 12.4, 5.7, 1.4 Hz, 1H, CHH-CH=CH₂), 3.86 (t, J = 9.3 Hz, 1H, H-3), 3.77 – 3.65 (m, 2H, H-5, H-6), 3.64 – 3.52 (m, 3H, H-2, H-4, H-6), 3.35 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 138.4, 138.0, 135.8 (C_q), 135.4 (CH₂-CH=CH₂), 133.3, 133.2 (C_q), 128.4, 128.4, 128.3, 128.1, 128.0, 127.8, 127.8, 127.1, 126.2, 126.1, 126.1 (CH_{arom}), 116.7 (CH₂-CH=CH₂), 98.3 (C-1), 81.8 (C-3), 79.6 (C-2), 77.7 (C-4), 75.2 (CH₂ Nap), 74.5 (CH₂-CH=CH₂), 73.6, 73.6 (CH₂ Bn), 70.1 (C-5), 68.5 (C-6), 55.2 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₃₅H₃₈O₆NH₄ 572.30066, found 572.29941.

Methyl 3-O-allyl-4,6-di-O-benzyl-a-D-glucopyranoside (S9)

Methyl 3-O-allyl-4.6-di-O-benzyl-2-O-(2-naphtyl)methyl-α-D-glucopyranoside (S8, 2.77 g, 5.0 mmol, 1 eq) was dissolved in 40 ml 9/1 DCM/H2O and stirred at RT until the sugar was fully dissolved. To the solution was added DDQ (2.27 g, 10.0 mmol, 2 eq) and the reaction was stirred for 60 min at RT after which TLC indicated full conversion. The reaction mixture was quenched with aq. Bicarb solution and extracted with DCM. The organic layer was washed twice with aq. Bicarb solution. The organic layer was dried over MgSO₄, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (7/3 pentane/EtOAc) to provide the title compound as an oil. Yield: 1.67 g, 4.01 mmol, 80%. ¹H NMR (400 MHz, CDCl₃) δ 7.37 – 7.26 (m, 8H, CH_{arom}), 7.18 (dd, J = 7.6, 1.9 Hz, 2H, CH_{arom}), 5.98 (ddt, I = 17.3, 10.4, 5.7 Hz, 1H, CH₂-CH=CH₂), 5.30 (dg, I = 17.3, 1.7 Hz, 1H, CH₂-CH=CHH), 5.17 (dt, J = 10.3, 1.5 Hz, 1H, CH₂-CH=CHH), 4.83 - 4.78 (m, 2H, H-1, CHH Bn), 4.64 (d, J = 12.2 Hz, 1H, CHH Bn), 4.56 - 4.45 (m, 2H, 2x CHH Bn), 4.41 - 4.29 (m, 2H, CH₂-CH=CH₂), 3.76 -3.70 (m, 2H, H-5, H-6), 3.69 - 3.63 (m, 2H, H-2, H-6), 3.63 - 3.54 (m, 2H, H-3, H-4), 3.41 (s, 3H, CH₃ OMe), 2.14 (d, J = 7.7 Hz, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 138.3, 138.0 (C_q), 135.3 (CH₂-CH=CH₂), 128.5, 128.0, 127.8, 127.8 (CH_{arom}), 117.1 (CH₂-CH=CH₂), 99.5 (C-1), 82.9 (C-3), 77.5 (C-4), 75.0 (CH₂ Bn), 74.3 (CH₂-CH=CH₂), 73.7 (CH₂ Bn), 72.8 (C-2), 70.2 (C-5), 68.6 (C-6), 55.3 (CH₃ OMe). Data is in agreement with literature.⁴⁷

Methyl 3-O-allyl-2-O-benzoyl-4,6-di-O-benzyl-a-D-glucopyranoside (S10)

Methyl 3-O-allyl-4,6-di-O-benzyl-α-D-glucopyranoside (S9, 1.60 g, 3.86 mmol, 1 eq) was dissolved in 30 ml pyridine and stirred at 0 °C until the sugar was fully dissolved. To the solution was added BzCl (0.58 ml, 5.02 mmol, 1.3 eq) and the reaction was stirred for 30 min at 0 °C after which the temperature was increased to RT. Once TLC indicated full conversion the reaction mixture was diluted with DCM and washed twice with 1M HCl and with sat. aq. NaHCO₃. The organic layer was dried over MgSO4, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (9/1 pentane/EtOAc) to provide the title compound as a light-yellow oil. Yield: 1.74 g, 3.36 mmol, 87%. ¹H NMR (400 MHz, CDCl₃) δ 8.15 - 8.07 (m, 2H, CH_{arom}), 7.63 - 7.53 (m, 1H, CH_{arom}), 7.46 (dd, J = 8.4, 7.1 Hz, 2H, CH_{arom}), 7.40 - 7.18 (m, 10H, CH_{arom}), 5.84 (ddt, J = 17.2, 10.3, 5.7 Hz, 1H, CH₂-CH=CH₂), 5.18 (dq, J = 17.2, 1.6 Hz, 1H, CH₂-CH=CHH), 5.10 - 5.02 (m, 3H, H-1, H-2, CH₂-CH=CHH), 4.85 (d, J = 10.8 Hz, 1H, CHH Bn), 4.66 (d, J = 12.1 Hz, 1H, CHH Bn), 4.56 – 4.51 (m, 2H, 2x CHH Bn), 4.28 (dd, J = 5.8, 1.4 Hz, 2H, CH₂-CH=CH₂), 4.03 (t, J = 9.1 Hz, 1H, H-3), 3.85 - 3.79 (m, 1H, H-5), 3.79 - 3.68 (m, 3H, H-4, 2x H-6), 3.35 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 166.0 (C=O), 138.3, 138.1, 134.9 (C_q), 133.3 (CH₂-CH=CH₂), 129.9, 128.5, 128.5, 128.1, 128.0, 127.9, 127.8 (CH_{arom}), 117.0 (CH₂-CH=CH₂), 97.3 (C-1), 79.9 (C-3), 77.9 (C-4), 75.2 (CH₂ Bn), 74.4 (CH₂-CH=CH₂), 74.2 (C-2), 73.6 (CH₂ Bn), 70.3 (C-5), 68.5 (C-6), 55.3 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₃₁H₃₄O₇NH₄ 536.26428, found 536.26337.

Methyl 2-O-benzoyl-4,6-di-O-benzyl-a-D-glucopyranoside (7)

Methyl 2-O-benzoyl-3-O-allyl-4,6-di-O-benzyl-a-D-glucopyranoside (S10, 1.65 g, 3.18 mmol, 1 eq) and DMBA (1.00 g, 6.36 mmol, 2 eq) were dissolved in 20 ml MeOH and flushed for 30 min with N₂. To the solution was added Pd(PPh₃)₄ (0.18 g, 0.16 mmol, 0.05 eq) and the mixture was heated for 1h at 40 °C, after which TLC indicated full conversion. The mixture was diluted in EtOAc and washed with saturated Bicarb sol. The aqueous layer was extracted three times with EtOAc. The combined organic layers were dried over MgSO4, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (8/2 pentane/EtOAc) to provide the title compound as a yellow oil. Yield: 1.27 g, 2.66 mmol, 84%. ¹H NMR (400 MHz, CDCl₃) δ 8.12 - 8.03 (m, 2H, CH_{arom}), 7.61 - 7.52 (m, 1H, CH_{arom}), 7.50 - 7.20 (m, 12H, CH_{arom}), 5.05 (d, J = 3.7 Hz, 1H, H-1), 4.98 (dd, J = 10.0, 3.7 Hz, 1H, H-2), 4.79 (d, J = 11.3 Hz, 1H, CHH Bn), 4.69 (d, J = 12.1 Hz, 1H, CHH Bn), 4.61 (d, J = 11.2 Hz, 1H, CHH Bn), 4.55 (d, J = 12.1 Hz, 1H, CHH Bn), 4.25 (ddd, J = 9.7, 8.5, 2.8 Hz, 1H, H-3), 3.87 - 3.76 (m, 2H, H-5, H-6), 3.77 – 3.69 (m, 1H, H-6), 3.68 (dd, J = 9.9, 8.8 Hz, 1H, H-4), 3.37 (s, 3H,CH₃ OMe), 2.30 (d, J = 3.5 Hz, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 166.4 (C=O), 138.3, 138.0, 133.4 (C₀), 130.0, 129.7, 128.6, 128.5, 128.5, 128.0, 128.0, 128.0, 127.8 (CHarom), 97.2 (C-1), 78.1 (C-4), 74.9 (CH₂ Bn), 74.1 (C-2), 73.7 (CH₂ Bn), 72.3 (C-3), 70.0 (C-5), 68.5 (C-6), 55.4 (CH₃ OMe). Data is in agreement with literature.48





Scheme S3: preparation of acceptor 10: reagents and conditions: a) Pd(PPh₃)₄, DMBA, MeOH, 40 °C, 83%; b) BzCl, pyridine, 86%; c) DDQ, DCM/H2O (9:1), 68%.

Methyl 4,6-di-O-benzyl-2-O-(2-naphtyl)methyl-a-D-glucopyranoside (S11)



Methyl 3-O-allyl-4,6-O-benzyl-2-O-(2-naphtyl)methyl- α -D-glucopyranoside (**S8**, 2.77 g, 5.0 mmol, 1 eq) and DMBA (1.57 g, 10.0 mmol, 2 eq) were dissolved in 20 ml MeOH and flushed for 30 min with N₂. To the solution was added Pd(PPh₃)₄ (0.29 g, 0.25 mmol, 0.05 eq) and the mixture was heated for 1h at 40 °C, after which TLC indicated full conversion. The mixture was diluted with EtOAc and washed with saturated Bicarb sol. The aqueous layer was extracted three times with EtOAc. The combined organic layers were dried over MgSO₄, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (8/2 pentane/EtOAc) to provide the title compound as a yellow oil. Yield: 2.12 g, 4.13 mmol, 83%. ¹H NMR (400 MHz, CDCl₃) δ 7.87 – 7.75 (m, 4H, CH_{arom}), 7.55 – 7.43 (m, 3H, CH_{arom}), 7.34 – 7.22 (m, 8H, CH_{arom}), 7.20 (dd, *J* = 7.8, 1.8 Hz, 2H, CH_{arom}), 4.87 (d, *J* = 12.3 Hz, 1H, CHH Bn/Nap), 4.86 – 4.76 (m, 2H, CHH Bn/Nap, CHH Bn/Nap), 4.64 (d, *J* = 3.5 Hz, 1H, H-1), 4.59 (d, *J* = 12.1 Hz, 1H, CHH Bn/Nap), 4.51 (d, *J* = 11.2 Hz, 1H, CHH Bn/Nap), 4.46 (d, *J* = 12.2 Hz, 1H, CHH Bn/Nap), 4.10 (td, *J* = 9.2, 2.1 Hz, 1H, H-3), 3.75 – 3.66 (m, 2H, H-5, H-6), 3.67 – 3.58 (m, 1H, H-6), 3.55 (dd, *J* = 10.2, 8.2 Hz, 1H, H-4), 3.45 (t, *J* = 9.6, 3.5 Hz, 1H, H-2), 3.32 (s, 3H, CH₃ OMe), 2.51 (d, *J* = 2.2 Hz, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 138.5, 137.9,

135.4, 133.2, 133.2 (C_q), 128.5, 128.4, 128.4, 128.0, 127.9, 127.8, 127.7, 127.1, 126.3, 126.2, 125.9 (CH_{arom}), 97.6 (C-1), 79.5 (C-2), 77.5 (C-4), 74.6 (CH₂ Bn/Nap), 73.7 (C-3), 73.5, 73.3 (CH₂ Bn/Nap), 69.7 (C-5), 68.5 (C-6), 55.3 (CH₃ OMe); HRMS: $[M+NH_4]^+$ calcd for $C_{32}H_{34}O_6NH_4$ 532.26936, found 532.843.

Methyl 3-O-benzoyl-4,6-di-O-benzyl-2-O-(2-naphtyl)methyl-a-D-glucopyranoside (S12)



Methyl 4,6-di-O-benzyl-2-O-(2-naphtyl)methyl-a-D-glucopyranoside (S11, 2.00 g, 3.9 mmol, 1 eq) was dissolved in 30 ml pyridine and stirred at 0 °C until the sugar was fully dissolved. To the solution was added BzCl (0.59 ml, 5.10 mmol, 1.3 eq) and the reaction was stirred for 30 min at 0 °C after which the temperature was increased to RT. Once TLC indicated full conversion the reaction mixture was diluted with EtOAc and washed twice with 1M HCl and once with sat. aq. NaHCO3. The organic layer was dried over MgSO4, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (9/1 pentane/EtOAc) to provide the title compound as a light-yellow oil. Yield: 2.06 g, 3.35 mmol, 86%. ¹H NMR (400 MHz, CDCl₃) δ 8.03 - 7.94 (m, 2H, CH_{arom}), 7.76 - 7.70 (m, 1H, CH_{arom}), 7.67 - 7.60 (m, 2H, CH_{arom}), 7.60 - 7.52 (m, 2H, CH_{arom}), 7.46 - 7.35 (m, 4H, CH_{arom}), 7.35 - 7.25 (m, 6H, CH_{arom}), 7.14 - 7.08 (m, 3H, CH_{arom}), 7.01 - 6.96 (m, 2H, CH_{arom}), 5.83 (dd, J = 10.0, 8.8 Hz, 1H, H-3), 4.80 (d, J = 3.5 Hz, 1H), 4.75 (d, J = 12.7 Hz, 1H, CHH Bn/Nap), 4.68 (d, J = 12.4 Hz, 1H, CHH Bn/Nap), 4.63 (d, J = 12.1 Hz, 1H, CHH Bn/Nap), 4.51 - 4.43 (m, 2H, CHH Bn/Nap, CHH Bn/Nap), 4.35 (d, J = 10.7 Hz, 1H, CHH Bn/Nap), 3.89 – 3.73 (m, 3H, H-4, H-5, H-6), 3.70 – 3.62 (m, 2H, H-2, H-6), 3.41 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 165.5 (C=O), 137.8, 137.6, 135.2, 133.1, 133.1 (Cq), 133.0 (CH_{arom}), 130.4 (Cq), 129.8, 128.5, 128.4, 128.3, 128.3, 128.2, 128.1, 127.9, 127.9, 127.7, 126.9, 126.1, 126.0 (CH_{arom}), 97.9 (C-1), 77.1 (C-2), 76.1 (C-4), 74.5 (CH₂ Bn/Nap), 74.3 (C-3), 73.7, 72.8 (CH₂ Bn/Nap), 69.8 (C-5), 68.3 (C-6), 55.4 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₃₉H₃₈O₇NH₄ 636.29558, found 636.29410.

Methyl 3-O-benzoyl-4,6-di-O-benzyl-a-D-glucopyranoside (10)



Methyl 3-O-benzoyl-4,6-di-O-benzyl-2-O-(2-naphtyl)methyl- α -D-glucopyranoside (**S11**, 2.0 g, 3.23 mmol, 1 eq) was dissolved in 30 ml 9/1 DCM/H₂O and stirred at RT until the sugar was fully dissolved. To the solution was added DDQ (1.47 g, 6.46 mmol, 2 eq) and the reaction was stirred for 60 min at RT after which TLC indicated full conversion. The reaction mixture was quenched with aq. Bicarb solution and extracted with DCM. The organic layer was washed twice with aq. Bicarb solution. The organic layer was dried over MgSO₄, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (7/3 pentane/EtOAc) to provide the title compound as an oil. Yield: 0.901 g, 1.88 mmol, 68%. ¹H NMR (400 MHz, CDCl₃) δ 8.10 – 8.02 (m, 2H, CH_{arom}), 7.62 – 7.52 (m, 1H, CH_{arom}), 7.48 – 7.27 (m, 8H, CH_{arom}), 7.14 (dd, *J* = 5.0, 2.0 Hz, 3H, CH_{arom}), 7.14 (dd, *J* = 5.0, 2.0 Hz, 3H, CH_{arom}), 7.14 (dd, *J* = 12.1 Hz, 1H, CHH Bn), 4.57 (d, *J* = 10.8 Hz, 1H, CHH Bn), 4.53 (d, *J* = 12.1 Hz, 1H, CHH Bn),

4.44 (d, J = 10.8 Hz, 1H, CHH Bn), 3.90 – 3.83 (m, 2H, H-4, H-5), 3.83 – 3.73 (m, 2H, H-2, H-6), 3.71 (dd, J = 10.4, 1.2 Hz, 1H, H-6), 3.45 (s, 3H, CH₃ OMe), 2.21 (d, J = 11.3 Hz, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 166.9 (C=O), 137.9, 137.7(C_q), 133.2 (CH_{arom}), 130.1 (C_q), 129.9, 128.6, 128.5, 128.4, 128.2, 128.0, 127.9, 127.8 (CH_{arom}), 99.7 (C-1), 76.7 (C-3), 75.6 (C-4), 74.8, 73.8 (CH₂ Bn), 71.8 (C-2), 70.4 (C-5), 68.3 (C-6), 55.6 (CH₃ OMe). Data is in agreement with literature.⁴⁹





Scheme S4: preparation of acceptor 12: reagents and conditions: a) i: DBTO, toluene, reflux, ii: CsF, BnBr, DMF, 58% over 2 steps; b) NapBr, NaH, DMF, 96%; c) i: PTSA, MeOH, 60 °C, ii: BnBr, NaH, DMF, 91% over 2 steps; d) DDQ, DCM/H2O (9:1), 75%.

Methyl 3-O-benzyl-4,6-O-benzylidene-β-D-glucopyranoside (S14)



Methyl 4,6-O-benzylidene- β -D-glucopyranoside⁵⁰ (**S13**, 1.60 g, 5.67 mmol) and di-n-butyltin oxide (1.83 g, 7.37 mmol, 1.3 eq) were refluxed in a Dean-Stark setup for 2 hr, after which the solvent was removed under reduced pressure. The residue was dissolved in DMF. Benzyl bromide (0.88 mL, 7.37 mmol, 1.3 eq) and CsF (1.12 g, 7.37 mmol) were added and the reaction mixture was stirred overnight, after which it was diluted with water and extracted twice with diethyl ether. Combined organic phases were dried and concentrated under reduced pressure. The residue was recrystallized from EA/pentane, yielding the title compound as white solid. Yield: 1.22 g, 3.28 mmol, 58%. ¹H NMR (400 MHz, CDCl₃) δ 7.52 – 7.46 (m, 2H, CH_{arom}), 7.42 – 7.26 (m, 8H, CH_{arom}), 5.58 (s, 1H, CHPh), 4.98 (d, *J* = 11.6 Hz, 1H, CHH Bn), 4.79 (d, *J* = 11.6 Hz, 1H, CHH Bn), 4.37 (dd, *J* = 10.5, 5.0 Hz, 1H, H-6), 4.33 (d, *J* = 7.7 Hz, 1H, H-1), 3.81 (t, *J* = 10.3 Hz, 1H, H-6), 3.75 – 3.64 (m, 2H, H-3, H-4), 3.57 (s, 4H, H-2, CH₃ OMe), 3.50 – 3.42 (m, 1H, H-5), 2.49 (d, *J* = 2.2 Hz, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 138.4, 137.3 (C_q), 129.2, 128.6, 128.4, 128.2, 128.0, 126.1 (CH_{arom}), 104.3 (C-1), 101.4 (CHPh), 81.6 (C-4), 80.3 (C-3), 74.8 (CH₂ Bn, 74.3 (C-2), 68.8 (C-6), 66.5 (C-5), 57.6 (CH₃ OMe). Spectra in agreement with literature.⁵¹

$\frac{\text{Methyl 3-O-benzyl-4,6-O-benzylidene-2-O-(2-naphtyl)methyl-\beta-D-glucopyranoside (S15)}}{\text{Phr} O - \text{O} - \text{O}$

Methyl 3-O-benzyl-4,6-O-benzylidene- β -D-glucopyranoside (**S14**, 1.20 g, 3.22 mmol) and NapBr (1.07 g, 4.83 mmol, 1.5 eq) were dissolved in DMF, after which NaH (60% dispersion in mineral oil, 193 mg, 4.83 mmol, 1.5 eq) was added. After completion of the reaction, water was added to quench the excess reagent. The formed precipitate was collected by filtration, washed with water

and with pentane and dried under vacuum, yielding the title compound as white solid. Yield: 1.59 g, 3.10 mmol, 96%. ¹H NMR (400 MHz, CDCl₃) δ 7.84 (dtd, *J* = 11.7, 6.3, 3.3 Hz, 4H, CH_{arom}), 7.52 (dtd, *J* = 10.9, 6.9, 6.3, 3.0 Hz, 5H, CH_{arom}), 7.46 – 7.35 (m, 5H, CH_{arom}), 7.33 – 7.26 (m, 4H, CH_{arom}), 5.62 (s, 1H, CHPh), 5.08 (d, *J* = 11.2 Hz, 1H, CHH Bn/Nap), 5.01 – 4.93 (m, 2H, CHH Bn/Nap, CHH Bn/Nap), 4.86 (d, *J* = 11.4 Hz, 1H, CHH Bn/Nap), 4.51 (d, *J* = 7.7 Hz, 1H, H-1), 4.42 (dd, *J* = 10.5, 5.0 Hz, 1H, H-6), 3.88 – 3.80 (m, 2H, H-4, H-6), 3.74 (t, *J* = 9.2 Hz, 1H, H-3), 3.55 (dd, *J* = 8.6, 7.7 Hz, 1H, H-2), 3.48 (td, *J* = 9.6, 5.0 Hz, 1H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 138.5, 137.3, 135.9, 133.3, 133.0 (C_q), 129.0, 128.3, 128.3, 128.1, 128.1, 128.0, 127.7, 127.7, 126.8, 126.2, 126.0, 125.9 (CH_{arom}), 105.3 (C-1), 101.2 (CHPh), 82.2 (C-2), 81.6 (C-3), 80.8 (C-4), 75.3, 75.2 (CH₂ Bn, CH₂ Nap), 68.8 (C-6), 66.0 (C-5), 57.5 (CH₃ OMe). Spectra in agreement with literature.⁵²

Methyl 3,4,6-tri-O-benzyl-2-O-(2-naphtyl)methyl-β-D-glucopyranoside (S16)

Methyl 3-O-benzyl-4,6-O-benzylidene-2-O-(2-naphtyl)methyl-β-D-glucopyranoside (S15, 1.55 g, 3.02 mmol) was dissolved with PTSA-H2O (58 mg, 0.30 mmol, 0.1 eq) and heated to 50 °C. After TLC indicates full conversion, the reaction mixture was quenched with triethylamine (0.06 mL, 0.45 mmol, 0.15 eq) and concentrated under reduced pressure. The residue was dissolved in DMF and treated with benzyl bromide (1.08 mL, 9.07 mmol, 3 eq) and sodium hydride (60% dispersion in mineral oil, 0.36 g, 9.07 mmol, 3 eq). After 1 hr, the reaction was quenched with water and extracted twice with diethyl ether. Combined organic phases were dried with MgSO4 and concentrated. The residue was purified over silica (10% EtOAc in pentane) to obtain the title compound as colourless oil that slowly solidifies. Yield: 1.66 g, 2.74 mmol, 91%. ¹H NMR (400 MHz, CDCl3) & 7.90 - 7.79 (m, 4H, CHaron), 7.57 - 7.48 (m, 3H, CHaron), 7.44 - 7.38 (m, 4H, CH_{arom}), 7.38 - 7.30 (m, 10H, CH_{arom}), 7.25 - 7.20 (m, 2H, CH_{arom}), 5.15 (d, J = 11.2 Hz, 1H, CHH Bn/Nap), 5.02 (d, J = 11.0 Hz, 1H, CHH Bn/Nap), 4.94 (d, J = 11.2 Hz, 1H, CHH Bn/Nap), 4.91 -4.85 (m, 2H, CHH Bn/Nap, CHH Bn/Nap), 4.70 (d, J = 12.2 Hz, 1H, CHH Bn/Nap), 4.65 - 4.57 (m, 2H, 2x CHH Bn/Nap), 4.42 (d, J = 7.8 Hz, 1H, H-1), 3.83 (dd, J = 10.7, 2.0 Hz, 1H, H-6), 3.79 - 3.75 (m, 1H, H-6), 3.75 - 3.65 (m, 5H, H-3, H-4, CH₃ OMe), 3.60 - 3.52 (m, 2H, H-2, H-5); ¹³C NMR (101 MHz, CDCl₃) δ 138.7, 138.3, 138.2, 136.1, 133.4, 133.1 (C_q), 128.5, 128.5, 128.2, 128.1, 128.1, 127.9, 127.9, 127.9, 127.8, 127.7, 127.7, 126.9, 126.4, 126.1, 125.9 (CH_{arom}), 104.9 (C-1), 84.8 (C-4), 82.4 (C-2), 78.0 (C-3), 75.8, 75.1 (CH₂ Bn/Nap), 75.0 (C-5), 74.9, 73.6 (CH₂ Bn/Nap), 69.0 (C-6), 57.3 (CH₃ Me); HRMS: [M+NH₄]⁺ calcd for C₃₉H₄₀O₆NH₄ 622.31631, found 622.31478.

Methyl 3,4,6-tri-O-benzyl-β-D-glucopyranoside (12)



Methyl 3,4,6-tri-O-benzyl-2-O-(2-naphtyl)methyl- β -D-glucopyranoside (**S16**, 1.63 g, 2.70 mmol) and DDQ (1.23 g, 5.40 mmol, 2 eq) were dissolved in 30 mL 9:1 DCM/H₂O and vigorously stirred. When TLC showed full conversion, the reaction mixture was diluted with DCM and washed twice with sat. aq. NaHCO₃. The organic phase was dried with MgSO₄ and concentrated under reduced pressure. The residue was purified over silica (20% EtOAc in pentane) to give the titel compound as white solid. Yield: 945 mg, 2.03 mmol, 75%. ¹H NMR (400 MHz, CDCl₃) δ 7.45

-7.30 (m, 13H, CH_{arom}), 7.25 -7.17 (m, 2H, CH_{arom}), 4.97 (d, *J* = 11.3 Hz, 1H, CHH Bn), 4.93 -4.84 (m, 2H, CHH Bn, CHH Bn), 4.68 (d, *J* = 12.2 Hz, 1H, CHH Bn), 4.64 -4.53 (m, 2H, CHH Bn), 4.23 (d, *J* = 7.3 Hz, 1H, H-1), 3.81 (dd, *J* = 10.8, 2.2 Hz, 1H, H-6), 3.76 (dd, *J* = 10.8, 4.5 Hz, 1H, H-6), 3.71 -3.58 (m, 6H, H-2, H-3, H-4, CH₃ OMe), 3.54 (ddt, *J* = 9.4, 4.6, 2.4 Hz, 1H, H-5), 2.49 (d, *J* = 2.1 Hz, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 138.6, 138.1, 138.1 (C_q), 128.5, 128.5, 128.4, 128.0, 128.0, 127.9, 127.8, 127.8, 127.7 (CH_{arom}), 103.7 (C-1), 84.5 (C-4), 77.6 (C-3), 75.2 (CH₂ Bn), 75.2 (C-2), 75.1 (CH₂ Bn), 74.6 (C-5), 73.6 (CH₂ Bn), 68.8 (C-6), 57.2 (CH₃ OMe). Spectra in agreement with literature.⁵³

Mannose acceptors

Preparation of acceptor 14



Scheme S5: preparation of acceptor 14: reagents and conditions a) BzCl, pyridine, DCM, 0 °C, 83%

methyl 6-O-benzoyl-2,3-di-O-benzyl-a-D-mannopyranoside (14)



methyl 2,3-di-*O*-benzyl-α-D-mannopyranoside⁵⁴ (**S17**, 1.51 g, 4.03 mmol) and pyridine (1.63 mL, 20.2 mmol, 5 eq) were dissolved in 12 mL DCM and cooled to 0°C, after which benzoyl chloride (0.492 mL, 4.23 mmol, 1.05 eq) was added dropwise as a 1.6 M solution in DCM. The reaction was allowed to warm to RT overnight and diluted with DCM, washed with 1M aq. HCl and sat. aq. NaHCO₃. The organic phase was sodium sulfate and concentrated under reduced pressure. The residue was purified with silica chromatography (20% EA in pentane) to yield the title compound (1.60 g, 3.34 mmol, 83%) as a colourless oil. ¹H NMR (400 MHz, CDCl₃) δ 8.08 – 8.00 (m, 2H, CH_{arom}), 7.53 (ddt, *J* = 8.7, 7.0, 1.3 Hz, 1H, CH_{arom}), 7.40 – 7.25 (m, 12H, CH_{arom}), 4.82 (d, *J* = 1.7 Hz, 1H, H-1), 4.70 – 4.59 (m, 5H, H-6, H-6, CHH Bn, CH₂ Bn), 4.51 (d, *J* = 11.7 Hz, 1H, CHH Bn), 4.11 (t, *J* = 9.7 Hz, 1H, H-4), 3.86 (dt, *J* = 9.8, 3.6 Hz, 1H, H-5), 3.81 (dd, *J* = 3.1, 1.8 Hz, 1H, H-2), 3.75 (dd, *J* = 9.5, 3.1 Hz, 1H, H-3), 3.37 (s, 3H, CH₃ OMe), 2.61 (s, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 166.8 (C=O), 138.2 (Cq), 138.1 (CH_{arom}), 133.1 (Cq), 130.1, 129.9, 128.6, 128.5, 128.4, 128.0, 127.9, 127.8, 127.8 (CH_{arom}), 99.1 (C-1), 79.6 (C-3), 74.1 (C-2), 72.7, 71.9 (CH₂ Bn), 70.8 (C-5), 66.6 (C-4), 64.2 (C-6), 55.0 (CH₃ OMe); Spectra in agreement with literature.⁵⁵
Chapter 4

Preparation of acceptor 15



Scheme S6: preparation of acceptor 15: reagents and conditions: a) $PhCH(OMe)_2$, $HBF_4 \bullet Et_2O$, DMF 96%; b) i) Bu_2SnO , toluene, reflux 3h; ii) NapBr, CsF, DMF, 79%; c) BnBr, NaH, DMF, 90%; d) DDQ, DCM/H2O (9:1), 80%; e) BzCl, pyridine 83%; f) TES-H, TFA, DCM, 0 °C, 92%.

Methyl 4,6-O-benzylidene-a-D-mannopyranoside (S19)



Methyl- α -D-mannopyranoside (**S18**, 3.88 g, 20.0 mmol, 1 eq) was dissolved in 20 ml DMF and stirred until the sugar was fully dissolved. To the solution was added benzaldehyde dimethyl acetal (3.22 ml, 21.4 mmol, 1.07 eq) and HBF₄·Et₂O (32.74 ml, 20.0 mmol, 1 eq), the mixture was stirred for 4h at RT after which TLC indicated full conversion. The reaction mixture was quenched with TEA. Solvents were evaporated under reduced pressure and purification was performed on flash column chromatography (3/2pentane/EtOAc) to provide the title compound as a solid. Yield: 5.00 g, 17.8 mmol, 89%. ¹H NMR (400 MHz, CDCl₃) δ 7.52 – 7.46 (m, 2H, CH_{arom}), 7.40 – 7.35 (m, 3H, CH_{arom}), 5.56 (s, 1H, CHPh), 4.73 (d, *J* = 1.4 Hz, 1H, H-1), 4.31 – 4.25 (m, 1H, H-6), 4.04 (dd, *J* = 9.4, 3.6 Hz, 1H, H-3), 4.00 (dd, *J* = 3.5, 1.5 Hz, 1H, H-2), 3.91 (t, *J* = 9.2 Hz, 1H, H-4), 3.84 – 3.77 (m, 2H, H-5, H-6), 3.39 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 137.3 (Cq), 129.4, 128.6, 128.5, 128.5, 126.7, 126.4, 126.2 (CH_{arom}), 102.4 (CHPh), 101.4 (C-1), 79.0 (C-4), 70.9 (C-2), 68.9 (C-6), 68.8 (C-3), 63.0 (C-5), 55.2 (OMe). Data in agreement with literature.⁵⁶

Methyl 4,6-O-benzylidene-3-O-(2-naphtyl)methyl-a-D-mannopyranoside (S20)



Methyl 4,6-O-benzylidene- α -D-mannopyranoside (**S19**, 5.44 g, 19.3 mmol) and di-nbutyltin(IV) oxide (6.24 g, 25.06 mmol, 1.3 eq) were dissolved in 100 ml toluene and refluxed for 3 hours, after which solvents where evaporated under reduced pressure. To the crude mixture was added NapBr (5.54 g, 25.06 mmol, 1.3 eq) and CsF (3.81 g, 25.06 mmol, 1.3 eq) and dissolved in 100 ml DMF. The reaction was stirred overnight at RT. The reaction mixture was diluted in Et₂O and washed twice with H₂O. The organic layer was dried over MgSO₄, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (3/1 pentane/EtOAc) to provide the title compound as a light-yellow oil. Yield: 6.47 g, 15.2 mmol, 79%.¹H NMR (400 MHz, CDCl₃) δ 7.85 – 7.78 (m, 3H, CH_{arom}), 7.75 – 7.70 (m, 1H, CH_{arom}), 7.55 – 7.44 (m, 5H, CH_{arom}), 7.42 – 7.35 (m, 3H, CH_{arom}), 5.63 (s, 1H, CHPh), 4.98 (d, J = 12.1 Hz, 1H, CHH Nap), 4.88 (d, J = 12.2 Hz, 1H, CHH Nap), 4.75 (d, J = 1.5 Hz, 1H, H-1), 4.28 (dd, J = 9.7, 4.3 Hz, 1H, H-6), 4.13 (t, J = 9.3 Hz, 1H, H-4), 4.07 (dt, J = 3.3, 1.6 Hz, 1H, H-2), 3.94 (dd, J = 9.6, 3.4 Hz, 1H, H-3), 3.90 – 3.84 (m, 1H, H-6), 3.81 (ddd, J = 10.3, 9.0, 4.2 Hz, 1H, H-5), 3.35 (s, 3H, CH₃ OMe), 2.78 (d, J = 1.6 Hz, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 137.6, 135.4, 133.2, 133.1 (C_q), 129.0, 128.3, 128.3, 128.0, 127.7, 126.6, 126.2, 126.2, 126.0, 125.8 (CH_{arom}), 101.7 (CHPh), 101.2 (C-1), 78.9 (C-4), 75.6 (C-3), 72.9 (CH₂ Nap), 69.9 (C-2), 68.9 (C-6), 63.3 (C-5), 54.9 (CH₃ OMe). Data in agreement with literature.⁵⁷

Methyl 2-O-benzyl-4,6-O-benzylidene-3-O-(2-naphtyl)methyl-a-D-mannopyranoside (S21)



Methyl 4,6-O-benzylidene-3-O-(2-naphtyl)methyl- α -D-mannopyranoside (**S20**, 5.09 g, 15.2 mmol) was dissolved in 75 ml DMF and stirred at 0 °C until the sugar was fully dissolved. To the solution was added NaH (60% dispersion in mineral oil, 0.92 g, 23.0 mmol, 1.5 eq) and the reaction was stirred for 30 min at 0 °C after which BnBr (2.73 ml, 23.0 mmol, 1.5 eq) was slowly added. After 30 min the temperature was increased to RT. Once TLC indicated full conversion, the reaction mixture was quenched with water and extracted twice with Et₂O. The combined organic layers were dried over MgSO₄, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (8/2 pentane/EtOAc) to provide the title compound as an oil. Yield: 5.55 g, 13.77 mmol, 90%. ¹H NMR (400 MHz, CDCl₃) δ 7.85 - 7.75 (m, 3H, CHarom), 7.74 - 7.64 (m, 1H), 7.59 - 7.27 (m, 14H, CHarom), 5.67 (s, 1H, CHPh), 4.93 (d, J = 12.3 Hz, 1H, CHH Bn/Nap), 4.87 – 4.75 (m, 3H, CHH Bn/Nap, CH₂ Bn/Nap), 4.70 (d, J = 1.7 Hz, 1H, H-1), 4.31 - 4.24 (m, 2H, H-4, H-6), 3.99 (dd, J = 10.0, 3.3 Hz, 1H, H-3), 3.90 (t, J = 1.0, 3.3 = 10.3 Hz, 1H, H-6), 3.86 (dd, *J* = 3.3, 1.7 Hz, 1H, H-2), 3.77 (ddd, *J* = 10.4, 9.1, 4.7 Hz, 1H, H-5), 3.30 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 138.2, 137.8, 136.2, 133.4, 133.0 (C_q), 129.0, 128.5, 128.3, 128.2, 128.1, 128.0, 127.9, 127.7, 126.2, 126.2, 126.1, 125.8, 125.7 (CHarom), 101.7 (CHPh), 100.5 (C-1), 79.2 (C-4), 76.3 (C-3), 76.2 (C-2), 73.7, 72.9 (CH₂ Bn, CH₂ Nap), 69.0 (C-6), 64.1 (C-5), 54.9 (CH₃ OMe).

Methyl 2-O-benzyl-4,6-O-benzylidene-a-D-mannopyranoside (S22)



Methyl 2-*O*-benzyl-4,6-*O*-benzylidene-3-*O*-(2-naphtyl)methyl- α -D-mannopyranoside. (**S21**, 1.72 g, 3.36 mmol) was dissolved in 25 ml 9/1 DCM/H₂O and stirred at RT until the sugar was fully dissolved. To the solution was added DDQ (1.52 g, 6.71 mmol, 2 eq) and the reaction was stirred for 60 min at RT after which TLC indicated full conversion. The reaction mixture was quenched with sat. aq. Bicarb solution and extracted with DCM. The organic layer was washed twice with sat. aq. Bicarb solution, dried over MgSO₄, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (8/2 pentane/EtOAc) to provide the title compound as an oil. Yield: 1.00 g, 2.69 mmol, 80%. ¹H NMR (400 MHz, CDCl₃) δ 7.53 – 7.45 (m, 2H, CH_{arom}), 7.41 – 7.28 (m, 8H, CH_{arom}), 5.56 (s, 1H, CHPh), 4.77 – 4.72 (m, 2H, H-1, CHH Bn), 4.68 (d, *J* = 11.7 Hz, 1H, CHH Bn), 4.26 (dd, *J* = 9.3, 3.9 Hz, 1H, H-6), 4.07 (ddd, *J* =

9.9, 7.9, 3.7 Hz, 1H, H-5), 3.90 (t, J = 9.4 Hz, 1H, H-4), 3.86 – 3.82 (m, 2H, H-2, H-6), 3.81 – 3.72 (m, 1H, H-3), 3.36 (s, 3H, CH₃ OMe), 2.39 (d, J = 8.0 Hz, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 137.7, 137.4 (C_q), 129.2, 128.7, 128.3, 128.2, 128.0, 126.4 (CH_{arom}), 102.2 (CHPh), 99.5 (C-1), 79.6 (C-4), 78.5 (C-2), 73.8 (CH₂ Bn), 68.9 (C-6), 68.8 (C-5), 63.4 (C-3), 55.1 (CH₃ OMe). Data in agreement with literature⁵⁸

Methyl 3-O-benzoyl-2-O-benzyl-4,6-O-benzylidene-a-D-mannopyranoside (S23)



Methyl 2-*O*-benzyl-4,6-*O*-benzylidene- α -D-mannopyranoside (**S22**, 0.95 g, 2.55 mmol) was dissolved in 10 ml pyridine and stirred at 0 °C until the sugar was fully dissolved. To the solution was added BzCl (0.39 ml, 3.32 mmol, 1.3 eq) and the reaction was stirred at RT until TLC indicated full conversion. The reaction mixture was diluted in DCM and washed twice with aq. 1M HCl and twice with aq. Bicarb solution. The organic layer was dried over MgSO₄, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (8/2 pentane/EtOAc) to provide the title compound as an oil. Yield: 1.28 g, 2.54 mmol, 63%. ¹H NMR (400 MHz, CDCl₃) δ 8.10 – 8.03 (m, 2H, CH_{arom}), 7.60 – 7.52 (m, 1H, CH_{arom}), 7.47 – 7.40 (m, 4H, CH_{arom}), 7.23 – 7.17 (m, 3H, CH_{arom}) 7.35 – 7.26 (m, 5H, CH_{arom}), 5.62 (s, 1H, CHPh), 5.55 (dd, *J* = 10.4, 3.4 Hz, 1H, H-3), 4.77 (d, *J* = 1.6 Hz, 1H, H-1), 4.64 (s, 2H, CH₂ Bn), 4.35 (dd, *J* = 10.6, 9.1 Hz, 1H, H-4), 4.32 – 4.28 (m, 1H, H-6), 4.09 (dd, *J* = 3.5, 1.6 Hz, 1H, H-2), 4.00 – 3.89 (m, 2H, H-5, H-6), 3.40 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 165.9 (C=O), 137.6, 137.4 (Cq), 133.2 (CH_{arom}), 130.1 (Cq), 129.9, 129.0, 128.5, 128.5, 128.3, 128.0, 126.3 (CH_{arom}), 101.8 (CHPh), 100.2 (C-1), 76.5 (C-2, C-4), 73.9 (CH₂ Bn), 71.3 (C-3), 69.0 (C-6), 64.1 (C-5), 55.2 (CH₃ OMe). Data in agreement with literature.⁵⁹

Methyl 3-O-benzoyl-2,6-di-O-benzyl-a-D-mannopyranoside (15)



Methyl 3-O-benzoyl-2-O-benzyl-4,6-O-benzylidene- α -D-mannopyranoside (**S23**, 0.54 g, 1.13 mmol) was dissolved in 20 ml anhydrous DCM and stirred at 0 °C until the sugar was fully dissolved. To the solution was added TES-H (1.8 ml, 11.3 mmol, 10 eq) and the mixture was stirred for another 15 min before slowly adding TFA (0.84 ml, 11.3 mmol, 10 eq) and the reaction was stirred at 0 °C until TLC indicated full conversion. The reaction mixture was quenched with aq. Bicarb solution and extracted with DCM. The organic layer was washed twice with aq. Bicarb solution. The organic layer was dried over MgSO₄, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (8/2 pentane/EtOAc) to provide the title compound as an oil. Yield: 0.49 g, 1.03 mmol, 92 %. ¹H NMR (400 MHz, CDCl₃) δ 8.09 – 8.02 (m, 2H, CH_{arom}), 7.61 – 7.55 (m, 1H, CH_{arom}), 7.47 – 7.41 (m, 2H, CH_{arom}), 7.38 – 7.32 (m, 4H, CH_{arom}), 7.32 – 7.26 (m, 3H, CH_{arom}), 7.20 (tt, *J* = 3.9, 2.4 Hz, 3H, CH_{arom}), 5.36 (dd, *J* = 9.9, 3.3 Hz, 1H, H-3), 4.79 (d, *J* = 1.7 Hz, 1H, H-1), 4.70 – 4.64 (m, 3H, CHH Bn, CH₂ Bn), 4.60 (d, *J* = 11.9 Hz, 1H, CHH Bn), 4.26 (t, *J* = 9.0 Hz, 1H, H-4), 3.94 (dd, *J* = 3.3, 1.8 Hz, 1H, H-2), 3.90 – 3.74 (m, 3H, H-5, 2x H-6), 3.40 (s, 3H, CH₃ OMe), 2.67 (s, 1H, OH); ¹³C NMR (101 MHz,

CDCl₃) δ 166.7 (C=O), 138.1, 137.9 (C_q), 133.3 , 130.0 (CH_{arom}), 129.9 (C_q), 128.5, 128.4, 127.8 (CH_{arom}), 99.2 (C-1), 75.9 (C-2), 74.8 (C-3), 73.8, 73.3 (CH₂ Bn), 71.3 (C-5), 70.7 (C-6), 67.8 (C-4), 55.1 (CH₃OMe). Data in agreement with literature⁶⁰



Scheme S7: preparation of acceptor 16: reagents and conditions: a) BzCl, pyridine, 95%; b) $pTsOH \cdot H_2O$, MeOH, 50 °C, 62%; c) BzCl, pyridine, DCM, 0 °C, 38%.

Methyl 2,3-di-O-benzoyl-4,6-O-benzylidene-a-D-mannopyranoside (S24)



Methyl 4,6-*O*-benzylidene- α -D-mannopyranoside (**S19**, 1.04 g, 3.68 mmol) was dissolved in 20 ml pyridine and stirred at 0 °C until the sugar was fully dissolved. To the solution was added BzCl (1.28 ml, 11.04 mmol, 3.0 eq) and the reaction was stirred for 30 min at 0 °C after which the temperature was increased to RT. Once TLC indicated full conversion the reaction mixture was diluted with EtOAc and washed twice with sat. aq. NaHCO₃. The organic layer was dried over MgSO₄, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (9/1 pentane/EtOAc) to provide the title compound as a light-yellow oil. Yield: 1.73 g, 3.51 mmol, 95%. ¹H NMR (400 MHz, CDCl₃) δ 8.13 – 8.07 (m, 2H, CH_{arom}), 7.94 – 7.88 (m, 2H, CH_{arom}), 7.61 – 7.55 (m, 1H, CH_{arom}), 7.50 – 7.40 (m, 5H, CH_{arom}), 7.32 – 7.24 (m, 5H, CH_{arom}), 5.83 (dd, *J* = 10.3, 3.6 Hz, 1H, H-3), 5.72 (dd, *J* = 3.6, 1.6 Hz, 1H, H-2), 5.67 (s, 1H, CHPh), 4.88 (d, *J* = 1.6 Hz, 1H, H-1), 4.42 – 4.32 (m, 2H, H-4), 4.10 (td, *J* = 9.8, 4.7 Hz, 1H, H-5), 3.96 (t, *J* = 10.3 Hz, 1H, H-6), 3.42 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 165.4 (C=O), 137.1 (C_q), 133.5, 133.0, 129.8, 129.7 (CH_{arom}), 129.7, 129.4, 129.0, 128.6, 128.5, 128.4, 128.4, 128.2, 128.2, 126.2, 126.2 (CH_{arom}), 101.9 (CH Ph), 9.9.6 (C-1), 76.8 (C-4), 70.9 (C-2), 69.0 (C-3), 68.8 (C-6), 63.8 (C-5), 55.3 (CH₃ OMe). Data in agreement with literature.⁶¹

Methyl 2,3-di-O-benzoyl-a-D-mannopyranoside (S25)



Methyl 2,3-di-O-benzoyl-4,6-O-benzylidene- α -D-mannopyranoside (**S24**, 1.65 g, 3.36 mmol, 1 eq) was dissolved in 25 ml MeOH and stirred at RT for 15 min. To the solution was added pTsOH·H₂O (64.0 mg, 0.34 mmol, 0.1 eq) and the mixture was stirred for 1h at 50 °C after which TLC indicated full conversion. The reaction mixture was set to cool down to RT and was quenched with TEA (0.25 ml, 0.8 mmol, 0.25 eq). Solvents were evaporated under reduced pressure and purification was performed on flash column chromatography (3/2 pentane/EtOAc) to provide the title compound as a solid. Yield: 0.842 g, 2.10 mmol, 62%. ¹H NMR (400 MHz, CDCl₃) δ 8.07 (dd, *J* = 8.4, 1.4 Hz, 2H, CH_{arom}), 7.91 (dd, *J* = 8.4, 1.4 Hz, 2H, CH_{arom}), 7.55 – 7.58

(m, 1H, CH_{arom}), 7.55 – 7.45 (m, 3H, CH_{arom}) 7.38 – 7.31 (m, 2H, CH_{arom}), 5.64 – 5.49 (m, 2H, H-2, H-3), 4.90 (d, J = 1.4 Hz, 1H, H-1), 4.33 (t, J = 9.4 Hz, 1H, H-4), 3.98 (dd, J = 3.8, 1.1 Hz, 2H, 2x H-6), 3.85 (dt, J = 9.7, 3.7 Hz, 1H, H-5), 3.47 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 167.0, 165.6 (C=O), 133.7, 133.6, 129.9, 129.9 (CH_{arom}), 129.5, 129.3 (C_q), 128.7, 128.5 (CH_{arom}), 98.8 (C-1), 73.2 (C-3), 72.4 (C-5), 70.67 (C-2), 67.0 (C-4), 62.4 (C-6), 55.4 (CH₃ OMe). Data in agreement with literature.⁶²

Methyl 2,3,6-tri-O-benzoyl-a-D-mannopyranoside (16)



Methyl 2,3-di-O-benzoyl-a-D-mannopyranoside (S25, 800 mg, 1.99 mmol) and pyridine (0.80 mL, 9.94 mmol, 5 eq) were dissolved in 7 mL DCM and cooled to 0 °C. Benzoyl chloride (0.24 mL, 2.09 mmol, 1.05 eq) was added over 15 minutes, after which the reaction mixture was allowed to warm to RT. After 16 hr stirring, the reaction mixture was diluted with dichloromethane and washed twice with 1M HCl and with sat. aq. NaHCO₃. The organic phase was dried with MgSO₄ and concentrated under reduced pressure. The residue was purified by silica chromatography (5% EtOAc in pentane), yielding the title compound as colourless oil. Yield: 0.38 g, 0.76 mmol, 38 %. ¹H NMR (400 MHz, CDCl₃) δ 8.14 (dd, J = 8.4, 1.3 Hz, 2H, CH_{arom}), 7.98 (dd, J = 8.3, 1.3 Hz, 2H, CH_{arom}), 7.92 (dd, J = 8.4, 1.3 Hz, 2H, CH_{arom}), 7.65 - 7.60 (m, 1H, CH_{arom}), 7.59 - 7.54 (m, 1H, CH_{arom}), 7.53 - 7.49 (m, 1H, CH_{arom}), 7.48 - 7.44 (m, 2H, CH_{arom}), 7.39 - 7.30 (m, 4H, CH_{arom}), 5.70 - 5.58 (m, 2H, H-2, H-3), 4.93 (s, 1H, H-1), 4.91 (dd, J = 12.2, 4.0 Hz, 1H, H-6), 4.65 (dd, *J* = 12.0, 2.2 Hz, 1H, H-6), 4.28 (dd, *J* = 10.7, 8.5 Hz, 1H, H-4), 4.10 (ddd, J = 9.9, 3.9, 2.2 Hz, 1H, H-5), 3.50 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 167.1, 166.9, 165.5 (C=O), 133.5, 133.5, 133.4, 130.0, 129.9, 129.9 (CH_{arom}), 129.6, 129.4 (C_q), 128.7, 128.6, 128.5 (CH_{arom}), 98.8 (C-1), 72.8 (C-2), 71.3 (C-5), 70.6 (C-3), 66.5 (C-4), 63.5 (C-6), 55.5 (CH₃OMe). Data in agreement with literature.⁶³



Scheme S8: preparation of acceptor *18*: reagents and conditions: *a*) TES-H TFA, DCM, 0 °C, 92%; *b*) *BzCl*, pyridine, 55%; *c*) DDQ, DCM/H₂O 9:1, 77%

Methyl 2,6-di-O-benzyl-3-O-(2-naphtyl)methyl-a-D-mannopyranoside (S26)



Methyl 2-O-benzyl-4,6-O-benzylidene-3-O-(2-naphtyl)methyl- α -D-mannopyranoside (**S21**, 3.33 g, 6.50 mmol) was dissolved in 40 ml anhydrous DCM and stirred at 0 °C until the sugar was fully dissolved. To the solution was added TES-H (10.38 ml, 65 mmol, 10 eq) and the mixture was stirred for another 15 min before slowly adding TFA (4.84 ml, 65 mmol, 10 eq). The reaction was

kept at 0 °C until TLC indicated full conversion. The reaction mixture was quenched with sat. aq. NaHCO₃ and extracted with DCM. The organic layer was washed twice with sat. aq. NaHCO₃. The organic layer was dried over MgSO₄, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (7/3 pentane/EtOAc) to provide the title compound as an oil. Yield: 2.42 g, 4.70z mmol, 72%. ¹H NMR (400 MHz, CDCl₃) δ 7.87 – 7.75 (m, 4H, CH_{arom}), 7.51 – 7.42 (m, 3H, CH_{arom}), 7.38 – 7.25 (m, 12H, CH_{arom}), 4.79 (d, *J* = 1.7 Hz, 1H, H-1), 4.75 – 4.69 (m, 2H, 2x CHH Bn/Nap), 4.67 – 4.61 (m, 3H, CHH Bn/Nap, 2x CHH Bn/Nap), 4.59 (d, *J* = 12.1 Hz, 1H, CHH Bn/Nap), 4.15 – 4.04 (m, 1H, H-4), 3.83 – 3.76 (m, 3H, H-2, 2x H-6) 3.76 – 3.70 (m, 2H, H-3, H-5), 3.34 (s, 3H,CH₃ OMe), 2.63 – 2.58 (m, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 138.3, 138.2, 135.8, 133.3, 133.0 (C_q), 128.4, 128.4, 128.3, 128.0, 127.9, 127.8, 127.7, 127.6, 126.5, 126.3, 126.0, 125.8 (CH_{arom}), 99.2 (C-1), 79.7 (C-3), 73.9 (C-2), 73.6, 72.7, 71.9 (CH₂ Bn, CH₂ Nap), 71.4 (C-5), 70.5 (C-6), 68.0 (C-4), 54.9 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₃₂H₃₄O₆NH₄ 532.26936, found 532.26887.

Methyl 4-O-benzoyl-2,6-di-O-benzyl-3-O-(2-naphtyl)methyl-a-D-mannopyranoside (S27)



Methyl 2,6-di-O-benzyl-3-O-(2-naphtyl)methyl-a-D-mannopyranoside (**S27**, 2.30 g, 4.47 mmol) was dissolved in 25 ml pyridine and stirred at 0 °C until the sugar was fully dissolved. To the solution was added BzCl (0.70 ml, 5.81 mmol, 1.3 eq) and the reaction was stirred for 30 min at 0 °C after which the temperature was increased to RT. Once TLC indicated full conversion the reaction mixture was diluted with EtOAc and washed twice with 1M HCl and with sat. aq. NaHCO₃. The organic layer was dried over MgSO₄, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (9/1 pentane/EtOAc) to provide the title compound as a light-yellow oil. Yield: 1.53 g, 2.46 mmol, 55%. ¹H NMR (400 MHz, CDCl₃) δ 7.97 - 7.91 (m, 2H, CH_{aron}), 7.77 - 7.71 (m, 1H, CH_{aron}), 7.56 (dd, J = 16.2, 7.5 Hz, 4H, CHarom), 7.47 - 7.34 (m, 6H, CHarom), 7.34 - 7.27 (m, 3H, CHarom), 7.26 - 7.14 (m, 7H, CH_{arom}), 5.66 (t, J = 9.8 Hz, 1H, H-4), 4.86 - 4.80 (m, 2H, H-1, CHH Bn/Nap), 4.76 (d, J = 12.5 Hz, 1H, CHH Bn/Nap), 4.71 (d, J = 12.5 Hz, 1H, CHH Bn/Nap), 4.55 (d, J = 12.5 Hz, 1H, CHH Bn/Nap), 4.51 (d, J = 2.7 Hz, 2H, CH₂ Bn/Nap), 4.01 – 3.91 (m, 2H, H-3, H-6), 3.88 (dd, J = 3.3, 1.8 Hz, 1H, H-2), 3.68 (dd, J = 10.8, 6.2 Hz, 1H, H-6), 3.62 (dd, J = 10.8, 2.9 Hz, 1H, H-5), 3.37 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 165.7 (C=O), 138.3, 138.2, 135.6, 133.2 (C_q), 133.1 (CH_{arom}), 133.0, 130.1 (C_q), 129.9, 128.5, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.7, 127.7, 127.4, 126.5, 126.1, 125.9, 125.9 (CH_{arom}), 99.5 (C-1), 76.8 (C-3), 74.0 (C-2), 73.6, 73.0, 71.8 (CH₂ Bn, CH₂ Nap), 70.7 (C-5), 70.1 (C-6), 69.5 (C-4), 55.1 (OMe); HRMS: [M+NH₄]⁺ calcd for C₃₉H₃₈O₇NH₄ 636.29461, found 636.29461.

Methyl 4-O-benzoyl-2,6-di-O-benzyl-a-D-mannopyranoside (18)



Methyl 4-O-benzoyl-2,6-di-O-benzyl-3-O-(2-naphtyl)methyl- α -D-mannopyranoside (**S27**, 1.45 g, 2.34 mmol) was dissolved in 20 ml 9/1 DCM/H₂O and stirred at RT until the sugar was fully

dissolved. To the solution was added DDQ (1.06 g, 4.69 mmol, 2 eq) and the reaction was stirred for 60 min at RT after which TLC indicated full conversion. The reaction mixture was diluted with DCM and washed twice with sat. aq. NaHCO₃. The organic layer was dried over MgSO₄, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (9/1 pentane/EtOAc) to provide the title compound as an oil. Yield: 0.86 g, 1.80 mmol, 77%. $[\alpha]_D^{25} = +22.9^{\circ}$ (c = 0.6, CHCl₃); IR (thin film): 416, 699, 716, 750, 1037, 1060, 1106, 1270, 1731, 2350; ¹H NMR (400 MHz, CDCl₃) δ 8.02 – 7.95 (m, 2H, CH_{arom}), 7.59 – 7.49 (m, 1H, CH_{arom}), 7.46 – 7.29 (m, 7H, CH_{arom}), 7.24 – 7.10 (m, 5H, CH_{arom}), 5.38 (t, J = 9.9 Hz, 1H, H-4), 4.87 (d, J = 1.5 Hz, 1H, H-1), 4.77 (d, J = 11.8 Hz, 1H, CHH Bn), 4.61 (d, J = 11.8 Hz, 1H, CHH Bn), 4.57 (d, J = 12.1 Hz, 1H, CHH Bn), 4.50 (d, J = 12.1 Hz, 1H, CHH Bn), 4.07-3.95 (m, 2H, H-3, H-5), 3.79 (dd, J = 3.7, 1.6 Hz, 1H, H-2), 3.70 – 3.58 (m, 2H, 2x H-6), 3.41 (s, 3H, CH₃ OMe), 2.45 (d, J = 10.6 Hz, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 166.6 (C=O), 138.0, 137.6 (C_q), 133.2, 129.9 (CH_{arom}), 129.8 (C_q), 128.6, 128.4, 128.3, 128.1, 128.0, 127.6, 127.54 (CH_{arom}), 98.2 (C-1), 78.2 (C-2), 73.6, 73.2 (CH₂ Bn), 71.0 (C-4), 70.1, 69.8 (C-3, C-5), 69.4 (C-6), 55.2(CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₂₈H₃₀O₇NH₄ 496.23298, found 496.23176.





Scheme S9: preparation of acceptor 19: reagents and conditions: a) 2,2-dimethoxypropane, PTSA, acetone, water, 54%; b) BnBr, NaH, DMF, 64%; c) TFA, H₂O, CHCl₃, quant; d) i: Bu₂SnO, toluene reflux, ii: NapBr, CsF, DMF, 74%; e) BzCl, pyridine, 94%; f) DDQ, DCM/H₂O (9:1), 74%

Methyl 2,3-O-isopropylidene-a-D-mannopyranoside (S28)



Methyl α-D-mannopyranoside (**S18**, 3.88 g, 20.0 mmol), 2,2-dimethoxypropane (36.8 ml, 300 mmol, 15 eq) and pTsOH·H₂O (0.38 g, 2 mmol, 0.1 eq) were dissolved in 40 ml Acetone and stirred at RT for 15 min. To the solution was added 80 ml H₂O and the mixture was stirred for 4h at RT. The reaction mixture was quenched with aq. Bicarb sol. Solvents were evaporated under reduced pressure and purification was performed on flash column chromatography (1/1 pentane/EtOAc) to provide the title compound as a solid. Yield: 2.48 g, 10.59 mmol, 53 %. ¹H NMR (400 MHz, CDCl₃) δ 4.92 (s, 1H, H-1), 4.21-4.09 (m, 2H, H-2, H-3), 3.86 (t, *J* = 3.2 Hz, 2H, 2x H-6), 3.74 (dd, *J* = 9.6, 5.9 Hz, 1H, H-4), 3.60 (dt, *J* = 9.5, 4.0 Hz, 1H, H-5), 3.39 (s, 3H, CH₃ isopropylidene); ¹³C NMR (101 MHz, CDCl₃) δ 109.5 (C_q isopropylidene), 98.2 (C-1), 78.5, 75.6 (C-2, C-3), 69.6 (C-5), 68.8 (C-4), 61.7 (C-6), 54.9 (CH₃ OMe), 27.9 (CH₃ isopropylidene), 26.1 (CH₃ isopropylidene). Data in agreement with literature.⁶⁴

Methyl 4,6-di-O-benzyl-2,3-O-isopropylidene-α-D-mannopyranoside (S29)



Methyl 2,3-O-isopropylidene-α-D-mannopyranoside (**S28**, 0.50 g, 2.13 mmol) was dissolved in 20 ml DMF and stirred at 0 °C until the sugar was fully dissolved. To the solution was added NaH (60% dispersion in mineral oil, 0.26 g, 6.40 mmol, 3 eq) and the reaction was stirred for 30 min at 0 °C after which BnBr (0.76 ml, 6.40 mmol, 3 eq) was slowly added. After 30 min the temperature was increased to RT. Once TLC indicated full conversion the reaction mixture was quenched with water and extracted twice with Et₂O. The combined organic layers were dried over MgSO₄, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (19/1 pentane/EtOAc) to provide the title compound as an oil. Yield: 0.62 g, 1.49 mmol, 70%. ¹H NMR (400 MHz, CDCl₃) δ 7.39 – 7.22 (m, 10H, CH_{arom}), 4.95 (d, J = 0.8 Hz, 1H, H-1), 4.86 (d, J = 11.5 Hz, 1H, CHH Bn), 4.63 (d, J = 12.2 Hz, 1H, CHH Bn), 4.58 – 4.52 (m, 2H, 2x CHH Bn), 4.30 (dd, J = 6.9, 5.9 Hz, 1H, H-3), 4.13 (dd, J = 5.8, 0.9 Hz, 1H, H-2), 3.79 -3.65 (m, 3H, H-5, 2x H-6), 3.56 (dd, *J* = 9.9, 6.9 Hz, 1H, H-4), 3.39 (s, 3H, CH₃ OMe), 1.51 (s, 3H, CH₃ isopropylidene)), 1.37 (s, 3H, CH₃ isopropylidene); 13 C NMR (101 MHz, CDCl₃) δ 138.4, 138.3 (C_q), 128.3, 128.2, 127.9, 127.6, 127.6, 127.5 (CH_{arom}), 109.4 (C_q isopropylidene), 98.3 (C-1), 78.9 (C-3), 75.8 (C-2), 75.8 (C-4), 73.5, 72.8 (CH₂ Bn), 69.3 (C-6), 68.3 (C-5), 54.9 (CH₃ OMe), 27.9 (CH₃ isopropylidene), 26.3 (CH₃ isopropylidene). Data in agreement with literature⁶⁵

Methyl 4,6-di-O-benzyl-α-D-mannopyranoside (S30)



Methyl 2,3-*O*-isopropylidene-4,6-di-*O*-benzyl- α -D-mannopyranoside (**S29**, 0.55 g, 1.33 mmol) was dissolved in 10 ml CHCl₃ and stirred until the sugar was fully dissolved. To the solution was added TFA (0.82 ml, 10.62 mmol, 8.0 eq) and H₂O (0.07 ml, 3.58 mmol, 2.7 eq), the reaction was stirred for 4h at RT. Once TLC indicated full conversion the reaction mixture was quenched with TEA, the reaction mixture was concentrated under reduced pressure. Purification was performed on flash column chromatography (1/1 pentane/EtOAc) to provide the title compound as a solid. Yield: 0.50 g, 1.33 mmol, quant. ¹H NMR (400 MHz, CDCl₃) δ 7.43 – 7.23 (m, 10H, CH_{arom}), 4.75 (s, *J* = 1.1 Hz, 1H, H-1), 4.74 – 4.65 (m, 2H, 2x CHH Bn), 4.59 – 4.52 (m, 2H, 2x CHH Bn), 3.97 – 3.87 (m, 2H, H-2, H-5), 3.78 (dd, 1H, H-6), 3.75 – 3.69 (m, 3H, H-3, H-4, H-6), 3.36 (s, 3H, CH₃ OMe), 2.37 (s, 2H, 2-OH, 3-OH); ¹³C NMR (101 MHz, CDCl₃) δ 138.4, 138.1 (C_q), 128.7, 128.5, 128.1, 128.1, 127.9 (CH_{arom}), 100.7 (C-1), 75.9 (C-4), 74.7, 73.7 (CH₂ Bn), 71.9 (C-5), 71.1 (C-2), 70.7 (C-3), 68.9 (C-6), 55.1 (CH₃ OMe). Data in agreement with literature.⁶⁶

Methyl 4,6-di-O-benzyl-3-O-(2-naphtyl)methyl-α-D-mannopyranoside (S31)



Methyl 4,6-di-O-benzyl-a-D-mannopyranoside (S30, 1.94 g, 5.18 mmol) and dibutyltin(IV) oxide (1.68 g, 6.74 mmol, 1.3 eq) were dissolved in 75 ml toluene and refluxed for 3 hours, after which solvents where evaporated under reduced pressure. The residue was dissolved in DMF and NapBr (1.49 g, 6.74 mmol, 1.3 eq) and CsF (1.02 g, 6.74 mmol, 1.3 eq) were added. The reaction was stirred overnight at RT. The reaction mixture was diluted with Et₂O and washed twice with H₂O. The organic layer was dried over MgSO₄, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (3/1 pentane/EtOAc) to provide the title compound as a light-yellow oil. Yield: 1.98 g, 3.85 mmol, 74%. ¹H NMR (400 MHz, CDCl₃) δ 7.86 - 7.70 (m, 4H, CH_{arom}), 7.51 - 7.42 (m, 3H, CH_{arom}), 7.38 - 7.26 (m, 8H, CH_{arom}), 7.19 - 7.13 (m, 2H, CH_{arom}), 4.89 - 4.79 (m, 4H, H-1, 2x CHH Bn/Nap, CHH Bn/Nap), 4.66 (d, J = 12.1 Hz, 1H, CHH Bn/Nap), 4.55 (d, J = 9.6 Hz, 1H, CHH Bn/Nap), 4.52 (d, J = 8.3 Hz, 1H, CH*H* Bn/Nap), 4.07 (t, *J* = 1.7 Hz, 1H, H-2), 3.92 (dd, *J* = 9.1, 3.1 Hz, 1H, H-3), 3.87 (t, *J* = 8.9 Hz, 1H, H-4), 3.80 - 3.67 (m, 3H, H-5, 2x H-6), 3.36 (s, 3H, CH₃ OMe), 2.50 (d, J = 2.2 Hz, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 138.4, 138.3, 135.4, 133.3, 133.1 (C_q), 128.4, 128.4, 128.0, 127.9, 127.8, 127.7, 127.7, 126.7, 126.3, 126.1, 125.9 (CH_{arom}), 100.4 (C-1), 80.3 (C-3), 75.2 (CH₂ Bn/Nap), 74.4 (C-4), 73.6, 72.1 (CH₂ Bn/Nap), 71.1 (C-5), 69.1 (C-6), 68.5 (C-5), 55.0 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₃₂H₃₄O₆ 532.26936, found 532.26888.

Methyl 2-O-benzoyl-4,6-di-O-benzyl-3-O-(2-naphtyl)methyl-a-D-mannopyranoside (S32)



Methyl 4,6-di-O-benzyl-3-O-(2-naphtyl)methyl-a-D-mannopyranoside (S31, 1.90 g, 3.69 mmol) was dissolved in 20 ml pyridine and stirred at 0 °C until the sugar was fully dissolved. To the solution was added BzCl (0.56 ml, 4.8 mmol, 1.3 eq) and the reaction was stirred for 30 min at 0 °C after which the temperature was increased to RT. Once TLC indicated full conversion the reaction mixture was diluted with EtOAc and washed twice with 1M HCl and once with sat. aq. NaHCO₃. The organic layer was dried over MgSO₄, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (9/1 pentane/EtOAc) to provide the title compound as a light-yellow oil. Yield: 2.15 g, 3.47 mmol, 94%. ¹H NMR (400 MHz, CDCl₃) δ 8.13 - 8.06 (m, 2H, CH_{arom}), 7.83 - 7.74 (m, 2H, CH_{arom}), 7.71 (d, J = 8.4 Hz, 1H, CHarom), 7.65 - 7.60 (m, 1H, CHarom), 7.59 - 7.52 (m, 1H, CHarom), 7.46 - 7.23 (m, 14H, CHarom), 7.18 (ddd, J = 6.0, 2.5, 1.5 Hz, 2H, CH_{arom}), 5.67 (dd, J = 2.9, 2.0 Hz, 1H, H-2), 4.95 - 4.89 (m, 2H, 2x CHH Bn/Nap), 4.88 (d, J = 1.9 Hz, 1H, H-1) 4.77 - 4.69 (m, 2H, CHH Bn/Nap, CHH Bn/Nap), 4.60 – 4.48 (m, 2H, 2x CH*H* Bn/Nap), 4.15 (dd, *J* = 9.2, 2.9 Hz, 1H, H-3), 4.10 (t, *J* = 9.2 Hz, 1H, H-4), 3.90 (dd, *J* = 10.5, 3.9 Hz, 1H, H-6), 3.85 (dt, *J* = 9.2, 2.8 Hz, 1H, H-5), 3.80 (dd, *J* = 10.5, 1.7 Hz, 1H, H-6), 3.39 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 165.8 (C=O), 138.5, 138.4, 135.5, 133.3 (CHarom), 133.2 (Cq), 132.9 (CHarom), 130.0 (Cq), 129.9, 128.4, 128.4, 128.3, 128.0, 127.9, 127.9, 127.6, 127.5, 127.5, 126.7, 126.0, 125.9, 125.8 (CH_{arom}), 98.9 (C-1), 78.2 (C-3), 75.3 (CH₂ Bn/Nap), 74.3 (C-4), 73.5, 71.5(CH₂ Bn/Nap), 71.5 (C-5), 69.1 (C-6), 68.9 (C-2), 55.0 (CH₃ OMe); HRMS: [M+Na]⁺ calcd for C₃₉H₃₈O₇NH₄ 636.29558, found 636.29475.

Methyl 2-O-benzoyl-4,6-di-O-benzyl-a-D-mannopyranoside (19)



Methyl 2-O-benzoyl-4,6-di-O-benzyl-3-O-(2-naphtyl)methyl-a-D-mannopyranoside. (S32, 2.05 g, 3.31 mmol) was dissolved in 25 ml 9/1 DCM/H2O and stirred at RT until the sugar was fully dissolved. To the solution was added DDQ (1.50 g, 6.63 mmol, 2 eq) and the reaction was stirred for 60 min at RT after which TLC indicated full conversion. The reaction mixture was quenched with aq. Bicarb solution and extracted with DCM. The organic layer was washed twice with aq. Bicarb solution. The organic layer was dried over MgSO4, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (9/1 pentane/EtOAc) to provide the title compound as an oil. Yield: 1.17 g, 2.44 mmol, 74%. ¹H NMR (400 MHz, CDCl₃) δ 8.03 (dd, J = 8.3, 1.3 Hz, 2H, CH_{arom}), 7.60 - 7.52 (m, 1H, CH_{arom}), 7.44 -7.18 (m, 12H, CH_{arom}), 5.35 (dd, J = 3.4, 1.8 Hz, 1H, H-2), 4.85 (d, J = 1.8 Hz, 1H, H-1), 4.80 (d, J = 11.1 Hz, 1H, CHH Bn), 4.75 (d, J = 12.0 Hz, 1H, CHH Bn), 4.63 (d, J = 11.1 Hz, 1H, CHH Bn), 4.56 (d, J = 11.9 Hz, 1H, CHH Bn), 4.24 (dd, J = 9.4, 3.4 Hz, 1H, H-3), 3.99 (t, J = 9.6 Hz, 1H, H-4), 3.91 (dd, J = 10.9, 3.9 Hz, 1H, H-6), 3.85 - 3.74 (m, 2H, H-5, H-6), 3.39 (s, 3H, CH₃ OMe) 2.24 (s, 1H, OH);¹³C NMR (101 MHz, CDCl₃) δ 166.3 (C=O), 138.4, 138.3 (C_q), 133.3, 130.0 (CH_{arom}), 129.7 (C_q), 128.5, 128.5, 128.4, 128.1, 127.9, 127.6, 127.6 (CH_{arom}), 98.6 (C-1), 75.8 (C-4), 74.9, 73.6 (CH₂ Bn), 72.9 (C-2), 71.3 (C-5), 70.6 (C-3), 69.1 (C-6), 55.2 (CH₃ OMe). Data in agreement with literature.67





Scheme **S10**: preparation of acceptor **22**: reagents and conditions: a) BzCl, 2-aminoethyl diphenylborinate, Dipea, ACN, 61%

Methyl 3-O-benzoyl-4,6-di-O-benzyl-a-D-mannopyranoside (22)



Methyl 4,6-di-O-benzyl- α -D-mannopyranoside (**S30**, 0.51 g, 1.27 mmol) and 2-aminoethyl diphenylborinate (0.03 g, 0.12 mmol, 0.1 eq) where dissolved in 10 ml anhydrous CH₃CN. To the solution was added DIPEA (0.31 ml, 1.80 mmol, 1.5 eq) and BzCl (0.21 ml, 1.80 mmol, 1.5 eq) the mixture was stirred for 4 hours, after which TLC indicated full conversion. The mixture was diluted in EtOAc and washed with H₂O. The aqueous layer was extracted twice with EtOAc. The combined organic layers were dried over MgSO₄, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (9/1 pentane/EtOAc) to provide the title compound as a yellow oil. Yield: 0.35 g, 0.74 mmol, 61%. ¹H NMR (400 MHz, CDCl₃) δ 8.11 – 8.00 (m, 2H, CH_{arom}), 7.64 – 7.54 (m, 1H, CH_{arom}), 7.50 – 7.42 (m, 3H, CH_{arom}), 7.39 – 7.28 (m, 5H, CH_{arom}), 7.20 – 7.12 (m, 3H, CH_{arom}), 7.09 – 6.99 (m, 2H, CH_{arom}), 5.50 (dd, *J*

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= 9.6, 3.1 Hz, 1H, H-3), 4.79 (d, J = 1.9 Hz, 1H, H-1), 4.70 (d, J = 12.1 Hz, 1H, CHH Bn), 4.64 (d, J = 10.9 Hz, 1H, CHH Bn), 4.55 (d, J = 12.1 Hz, 1H, CHH Bn), 4.48 (d, J = 10.9 Hz, 1H, CHH Bn), 4.21 – 4.12 (m, 2H, H-2, H-4), 3.88 (ddt, J = 10.5, 4.4, 2.1 Hz, 1H, H-5), 3.82 (dd, J = 10.7, 3.9 Hz, 1H, H-6), 3.73 (dd, J = 10.6, 2.0 Hz, 1H, H-6), 3.42 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 165.7 (C=O), 138.1, 137.8 (Cq), 133.3 (CH_{arom}), 130.0 (Cq), 129.8, 129.8, 128.7, 128.6, 128.5, 128.4, 128.1, 128.0, 127.8, 127.8, 127.1 (CH_{arom}), 100.9 (C-1), 75.1 (C-3), 74.9, 73.7 (CH₂ Bn), 73.0 (C-4), 71.2 (C-5), 69.7 (C-2), 68.6 (C-6), 55.2 (CH₃ OMe). Data in agreement with literature.⁶⁷

Preparation of acceptor 23



Scheme S11: preparation of acceptor *23*: reagents and conditions: *a*) *BzCl*, pyridine, 96%; *b*) acetic acid, reflux, 85%; *c*) *BzCl*, 2-aminoethyl diphenylborinate, Dipea, ACN, 55%

Methyl 4,6-di-O-benzoyl-2,3-O-isopropylidene-α-D-mannopyranoside (S33)



Methyl 2,3-O-isopropylidene-α-D-mannopyranoside (**S28**, 0.43 g, 1.84 mmol) was dissolved in 20 ml pyridine and stirred at 0 °C until the sugar was fully dissolved. To the solution was added BzCl (0.75 ml, 6.40 mmol, 3.0 eq) and the reaction was stirred for 30 min at 0 °C after which the temperature was increased to RT. Once TLC indicated full conversion the reaction mixture was diluted with EtOAc and washed twice with 1M HCl and with sat. aq. NaHCO₃. The organic layer was dried over MgSO₄, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (9/1 pentane/EtOAc) to provide the title compound as a light-yellow oil. Yield: 0.78 g, 1.77 mmol, 96%. ¹H NMR (400 MHz, CDCl₃) 8.07 - 7.97 (m, 4H, CH_{arom}), 7.58 - 7.49 (m, 2H, CH_{arom}), 7.45 - 7.34 (m, 4H, CH_{arom}), 5.42 (dd, J = 10.3, 7.6 Hz, 1H, H-4), 5.03 (s, 1H, H-1), 4.54 (dd, J = 12.0, 3.1 Hz, 1H, H-6), 4.47 - 4.34 (m, 2H, H-3, H-6), 4.23 (dd, J = 5.5, 0.8 Hz, 1H, H-2), 4.18 - 4.09 (m, 1H, H-5), 3.44 (s, 3H, CH₃ OMe), 1.64 (s, 3H, CH₃ isopropylidene), 1.37 (s, 3H, CH₃ isopropylidene). ¹³C NMR (101 MHz, CDCl₃) δ 166.3, 165.7 (C=O), 133.4, 133.1, 130.0 (CH_{arom}), 129.9 (C_q), 129.7 (CH_{arom}), 129.5 C_q), 128.5, 128.5 (CH_{aron}), 110.3 (Cq isopropylidene), 98.3 (C-1), 76.1 (C-3), 75.9 (C-2), 70.7 (C-4), 66.4 (C-5), 63.8 (C-6), 55.3 (CH₃ OMe), 27.9 (CH₃ isopropylidene), 26.5 (CH₃ isopropylidene). Data in agreement with literature.68

Methyl 4,6-di-O-benzoyl-a-D-mannopyranoside (S34)



ÓМе

Methyl 2,3-O-isopropylidene-4,6-di-O-benzoyl- α -D-mannopyranoside (**S33**, 0.73 g, 1.65mmol) was dissolved in 10 ml Acetic acid and refluxed for 1 h. Once TLC indicated full conversion the

reaction mixture was cooled down to RT and concentrated under reduced pressure. Purification was performed on flash column chromatography (3/2 pentane/EtOAc) to provide the title compound as a solid. Yield: 0.56 g, 1.40 mmol, 85 %. ¹H NMR (400 MHz, CDCl₃) δ 8.09 – 7.95 (m, 4H, CH_{arom}), 7.62 – 7.49 (m, 2H, CH_{arom}), 7.48 – 7.35 (m, 4H, CH_{arom}), 5.39 (dd, *J* = 10.1, 9.3 Hz, 1H, H-4), 4.86 (d, *J* = 1.6 Hz, 1H, H-1), 4.60 (dd, *J* = 11.9, 2.7 Hz, 1H, H-6), 4.46 (dd, *J* = 11.9, 5.9 Hz, 1H, H-6), 4.22 (ddd, *J* = 10.2, 5.9, 2.7 Hz, 1H, H-5), 4.11 (dd, *J* = 9.4, 3.6 Hz, 1H, H-3), 4.03 (dd, *J* = 3.5, 1.7 Hz, 1H, H-2), 3.44 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 167.4, 166.4 (C=O), 133.8, 133.2, 130.1 (CH_{arom}), 129.8 (Cq), 129.8 (CH_{arom}), 129.2 (Cq), 128.7, 128.5 (CH_{arom}), 100.6 (C-1), 71.5 (C-4), 70.7 (C-2), 70.6 (C-3), 67.9 (C-5), 63.9 (C-6), 55.4 (CH₃ OMe). Data in agreement with literature.⁶⁸

Methyl 3,4,6-tri-O-benzoyl-a-D-mannopyranoside (23)



Methyl 4,6-di-*O*-benzoyl- α -D-mannopyranoside (**S34**, 0.45 g, 1.20 mmol) and 2-aminoethyl diphenylborinate (0.03 g, 0.13 mmol, 0.1 eq) where dissolved in 10 ml anhydrous CH₃CN. To the solution was added DIPEA (0.27 ml, 1.52 mmol, 1.2 eq) and BzCl (0.18 ml, 1.52 mmol, 1.2 eq) the mixture was stirred for 4 hours, after which TLC indicated full conversion. The mixture was diluted in EtOAc and washed with H₂O. The aqueous layer was extracted twice with EtOAc. The combined organic layers were dried over MgSO₄, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (9/1 pentane/EtOAc) to provide the title compound as a yellow oil. Yield: 0.35 g, 0.70 mmol, 55%. ¹H NMR (400 MHz, CDCl₃) δ 8.11 – 8.00 (m, 2H, CH_{arom}), 7.95 (ddt, *J* = 11.8, 7.0, 1.4 Hz, 4H, CH_{arom}), 7.61 – 7.45 (m, 3H, CH_{arom}), 7.43 – 7.31 (m, 6H, CH_{arom}), 5.93 (t, *J* = 10.0 Hz, 1H, H-4), 5.67 (dd, *J* = 10.0, 3.2 Hz, 1H, H-3), 4.89 (d, *J* = 1.8 Hz, 1H, H-1), 4.60 (dd, *J* = 12.0, 3.0 Hz, 1H, H-6), 4.49 (dd, *J* = 12.0, 5.5 Hz, 1H, H-6), 4.44 – 4.28 (m, 2H, H-2, H-5), 3.50 (s, 3H, CH₃ OMe), 2.35 (s, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 166.3, 165.7, 165.6 (C=O), 133.5, 133.2, (C_q), 129.9, 129.9, 129.9, 129.8, 129.3, 129.2, 128.6, 128.5, 128.5 (CH_{arom}), 100.8 (C-1), 72.7 (C-3), 69.5 (C-2), 68.7 (C-5), 67.1 (C-4), 63.7 (C-6), 55.5 (CH₃ OMe). Data in agreement with literature.⁶⁷

Chapter 4

Galactose acceptors

Preparation of acceptor 25



Scheme S12: preparation of acceptor **25**: reagents and conditions: a) PhCH(OMe)₂, HBF₄-Et₂O, DMF, 89%; b) BnBr, NaH, DMF, 65%; c) PTSA, MeOH, 50 °C, 94%; d) BzCl, pyridine, DCM, 0 °C, 48%

Methyl 4,6-O-benzylidene-a-D-galactopyranoside (\$36)



Methyl- α -D-galactopyranoside (**S35**, 4.85 g, 25.0 mmol) was dissolved in 25 ml DMF and stirred until the sugar was fully dissolved. To the solution was added benzaldehyde dimethyl acetal (4.03 ml, 26.75 mmol, 1.07 eq) and HBF₄-Et₂O (3.43 ml, 25.0 mmol, 1 eq), the mixture was stirred for 4h at RT after which TLC indicated full conversion. The reaction mixture was quenched with TEA (4.2 ml, 50.0 mmol, 2 eq). Solvents were evaporated under reduced pressure and purification was performed on flash column chromatography (3/2pentane/EtOAc) to provide the title compound as a solid. Yield: 6.3 g, 22.3 mmol, 89%. ¹H NMR (400 MHz, CDCl₃) δ 8.01 – 7.33 (m, 5H, CH_{arom}), 5.55 (s, 1H, CHPh), 4.91 (d, *J* = 3.2 Hz, 1H, H-1), 4.31 – 4.22 (m, 2H, H-2, H-6), 4.06 (d, *J* = 1.8 Hz, 1H, H-6), 3.99 – 3.88 (m, 2H, H-3, H-5), 3.68 (d, *J* = 1.6 Hz, 1H, H-4), 3.45 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 137.7 (Cq), 129.1, 128.2, 126.3 (CH_{arom}), 101.2 (CHPh), 100.4 (C-1), 76.0 (C-2), 69.7 (C-3), 69.6 (C-5), 69.4 (C-6), 62.7 (C-4), 55.7 (OMe). Data in agreement with literature.⁶⁹

Methyl 2,3-di-O-benzyl-4,6-O-benzylidene-a-D-galactopyranoside (S37)



Methyl 4,6-di-O-benzylidene- α -D-galactopyranoside. (**S36**, 7.0 g, 24.8 mmol) was dissolved in 75 ml DMF and stirred at 0 °C until the sugar was fully dissolved. To the solution was added NaH

(60% dispersion in mineral oil, 2.98 g, 74.39 mmol, 3 eq) and the reaction was stirred for 30 min at 0 °C after which BnBr (8.84 ml, 74.39 mmol, 3 eq) was slowly added. After 30 min the temperature was increased to RT. Once TLC indicated full conversion the reaction mixture was quenched with water and extracted twice with Et₂O. The combined organic layers were dried over MgSO₄, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (8/2 pentane/EtOAc) to provide the title compound as an oil. Yield: 11.47 g, 16.12 mmol, 65%. ¹H NMR (400 MHz, CDCl₃) δ 7.56 – 7.22 (m, 15H, CH_{arom}), 5.48 (s, 1H, CHPh), 4.88 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.84 (d, *J* = 12.4 Hz, 1H, CHH Bn), 4.78 – 4.72 (m, 2H, CHH Bn, H-1), 4.68 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.21 (dd, *J* = 12.4, 1.6 Hz, 1H, H-6), 4.18 (dd, *J* = 3.5, 1.2 Hz, 1H, H-4), 4.06 (dd, *J* = 10.1, 3.5 Hz, 1H, H-3), 4.03 – 3.99 (m, 1H, H-6), 3.99 – 3.94 (m, 1H, H-2), 3.58 (q, *J* = 1.6 Hz, 1H, H-5), 3.38 (s, 3H, CH₃ OMe);¹³C NMR (101 MHz, CDCl₃) δ 138.9, 138.7, 137.9 (C_q), 129.0, 128.5, 128.2, 128.2, 127.8, 127.8, 127.7, 126.5 (CH_{arom}), 101.2 (CHPh), 99.6 (C-1), 76.2 (C-2), 75.6 (C-3), 74.9 (C-4), 73.9 (CH₂ Bn), 72.3 (CH₂ Bn), 69.5 (C-6), 62.5 (C-5), 55.6 (CH₃ OMe). Data in agreement with literature.⁷⁰

Methyl 2,3-di-O-benzyl-a-D-galactopyranoside (S38)



Methyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene- α -D-galactopyranoside (**S37**, 2.31 g, 5.0 mmol) was dissolved in 30 ml MeOH and stirred at RT for 15 min. To the solution was added pTsOH·H₂O (95.1 mg, 0.50 mmol, 0.1 eq) and the mixture was stirred for 1h at 50 °C after which TLC indicated full conversion. The reaction mixture was set to cool down to RT and was quenched with TEA. Solvents were evaporated under reduced pressure and purification was performed on flash column chromatography (3/2pentane/EtOAc) to provide the title compound as a solid. Yield: 1.75 g, 4.70 mmol, 94%. ¹H NMR (400 MHz, CDCl₃) δ 7.38 – 7.27 (m, 10H, CH_{arom}), 4.80 (dd, *J* = 11.8, 2.8 Hz, 2H, 2x CHH Bn), 4.72 – 4.63 (m, 3H, H-1, 2x CHH Bn), 4.03 (s, 1H, H-4), 3.90 – 3.84 (m, 3H, H-2, H-3, H-6), 3.79 – 3.71 (m, 2H, H-5, H-6), 3.37 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 138.3, 138.1 (Cq), 128.6, 128.5, 128.1, 128.0, °127.9 (CH_{arom}), 98.7 (C-1), 77.4 (C-2), 75.7 (C-3), 73.6, 73.0 (CH₂ Bn), 69.1 (C-4), 69.0 (C-5), 63.0 (C-6), 55.4 (CH₃ OMe). Data in agreement with literature.⁷¹

Methyl 6-O-benzoyl-2,3-di-O-benzyl-a-D-galactopyranoside (25)



Methyl 2,3-di-O-benzyl- α -D-galactopyranoside (**S38**, 0.75 g, 2.00 mmol) and pyridine (0.81 mL, 10.0 mmol, 5 eq) were dissolved in 6 mL DCM and cooled to 0 °C, after which BzCl (0.25 mL, 2.10 mmol, 1.05 eq) was added over 15 min. The reaction mixture was allowed to warm to RT overnight, before being diluted with DCM and washed with 1M HCl and sat. aq. NaHCO₃. The organic phase was dried with MgSO₄ and concentrated under reduced pressure. The residue was purified over silica (10% EtOAc in pentane) to yield the title compound as colourless oil. Yield:

468 mg, 0.96 mmol, 48% ¹H NMR (400 MHz, CDCl₃) δ 8.05 – 8.00 (m, 2H, CH_{arom}), 7.59 – 7.54 (m, 1H, CH_{arom}), 7.43 (dd, J = 8.3, 7.1 Hz, 2H, CH_{arom}), 7.39 – 7.27 (m, 10H, CH_{arom}), 4.87 – 4.78 (m, 2H, 2x CHH Bn), 4.71 (d, J = 11.6 Hz, 1H, CHH Bn), 4.69 – 4.65 (m, 2H, H-1, CHH Bn), 4.55 (dd, J = 11.5, 5.0 Hz, 1H, H-6), 4.49 (dd, J = 11.5, 7.4 Hz, 1H, H-6), 4.10 – 4.01 (m, 2H, H-4, H-5), 3.91 (dd, J = 9.7, 3.0 Hz, 1H, H-3), 3.86 (dd, J = 9.8, 3.3 Hz, 1H, H-2), 3.37 (s, 3H, CH₃ OMe), 2.55 (s, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 166.5 (C=O), 138.4, 138.1 (Cq), 133.2 (CH_{arom}), 130.0 (Cq), 129.8, 128.7, 128.6, 128.5, 128.2, 128.1, 128.0, 128.0 (CH_{arom}), 98.6 (C-1), 77.5 (C-3), 75.7 (C-2), 73.7, 73.2 (CH₂ Bn), 68.0, 67.6 (C-4, C-5), 64.1 (C-6), 55.4 (CH₃ OMe). Spectra in agreement with literature.⁷²

Preparation of acceptor 27



Scheme S13: preparation of acceptor 27: reagents and conditions: a) BzCl, pyridine, 63%

Methyl 2,3,6-tri-O-benzoyl-a-D-galactopyranoside (27)



Methyl-a-D-galactopyranoside (S35, 0.78 g, 4.0 mmol) was dissolved in 20 ml pyridine and stirred at 0 °C until the sugar was fully dissolved. To the solution was added BzCl (2.14 ml, 18.4 mmol, 4.6 eq) over a 30 min time frame and the reaction was stirred for 4 h at RT after which TLC indicated full conversion. The reaction mixture was quenched with H₂O and extracted with Toluene. The organic layer was washed twice with aq. 1M HCl solution and once with aq. Bicarb solution. The organic layer was dried over MgSO4, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (9/1 pentane/EtOAc \rightarrow 8/2 pentane/EtOAc) to provide the title compound as an oil. Yield: 1.28 g, 2.54 mmol, 63%. ¹H NMR (400 MHz, CDCl₃) δ 8.16 - 7.88 (m, 6H, CH_{arom}), 7.58 (ddt, J = 8.8, 6.9, 1.3 Hz, 1H, CHarom), 7.54 - 7.48 (m, 2H, CHarom), 7.47 - 7.42 (m, 2H, CHarom), 7.37 (td, J = 7.8, 1.6 Hz, 4H, CH_{arom}) 5.76 (dd, J = 10.7, 3.0 Hz, 1H, H-3), 5.69 (dd, J = 10.7, 3.5 Hz, 1H, H-2), 5.22 (d, J = 3.6 Hz, 1H, H-1), 4.68 (dd, *J* = 11.5, 5.8 Hz, 1H, H-6), 4.57 (dd, *J* = 11.4, 6.9 Hz, 1H, H-6), 4.41 (d, *J* = 1.8 Hz, 1H, H-4), 4.36 (t, J = 6.3 Hz, 1H, H-5), 3.45 (s, 3H, CH₃ OMe), 2.68 (s, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) & 166.6, 166.2, 165.9 (C=O), 133.6, 133.4, 133.4, 129.9, 129.9, 129.8 (CH_{arom}), 129.7, 129.5, 129.4 (C_q), 128.6, 128.5 (CH_{arom}), 97.7 (C-1), 70.9 (C-3), 69.0 (C-2), 68.3 (C-4), 67.8 (C-5), 63.5 (C-6), 55.6 (CH₃ OMe). Data in agreement with literature.⁷³





Scheme S14: preparation of acceptor 29: reagents and conditions: a) Benzoyl cyanide, DMAP, DCM, - 78 °C, 65%

Methyl 4-O-benzoyl-2,6-di-O-benzyl-a-D-galactopyranoside (29)



Methyl 2,6-di-O-benzyl-α-D-galactopyranoside⁷⁴ (S39, 1.30 g, 3.47 mmol) was dissolved in 20 ml anhydrous DCM. The solution was cooled down to -78 °C and BzCN (0.46 g, 3.47 mmol, 1 eq) and DMAP (43.4 mg, 0.35 mmol, 0.1 eq) were added. After 4 h TLC indicated full conversion and the reaction was guenched with aq. NH₄Cl, filtered over a celite pad and extracted with DCM. The organic phase was washed twice with aq. Na₂S₂O₃. The organic layer was dried over MgSO4, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (3/1 pentane/EtOAc) to provide the title compound as an oil. Yield: 1.08 g, 2.26 mmol, 65%. $[\alpha]_D^{25} = +46.5^{\circ}$ (c = 0.60, CHCl₃); IR (thin film): 412, 699, 714, 738, 985, 1027, 1046, 1097, 1177, 1193, 1272, 1313, 1349, 1452, 1720; ¹H NMR (400 MHz, CDCl₃) δ 8.09 -7.98 (m, 2H, CH_{arom}), 7.65 - 7.51 (m, 1H, CH_{arom}), 7.48 - 7.40 (m, 2H, CH_{arom}), 7.42 - 7.25 (m, 5H, CH_{arom}), 7.26 - 7.13 (m, 4H, CH_{arom}), 5.66 (dd, J = 3.6, 1.3 Hz, 1H, H-4), 4.81 (d, J = 3.5 Hz, 1H, H-1), 4.74 (d, J = 12.0 Hz, 1H, CHH Bn), 4.68 (d, J = 12.0 Hz, 1H, CHH Bn), 4.50 (d, J = 11.8 Hz, 1H, CHH Bn), 4.40 (d, J = 11.8 Hz, 1H, CHH Bn), 4.27 (dt, J = 10.0, 3.2 Hz, 1H, H-3), 4.17 (td, *J* = 6.1, 1.3 Hz, 1H, H-5), 3.82 (dd, *J* = 10.0, 3.5 Hz, 1H, H-2), 3.55 (d, *J* = 6.2 Hz, 2H, 2x H-6), 3.40 (s, 3H, CH₃ OMe), 2.41 (d, J = 3.0 Hz, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 166.4 (C=O), 138.0, 137.8 (Cq), 133.3, 130.0 (CHarom), 129.9 (Cq), 128.6, 128.5, 128.4, 128.3, 128.2, 127.7 (CHarom), 98.2 (C-1), 76.8 (C-2), 73.6 73.2 (CH2 Bn), 71.4 (C-4), 68.9 (C-6), 68.5 (C-3), 68.2 (C-5), 55.6 (CH₃ OMe); HRMS: [M+Na]⁺ calcd for C₂₈H₃₀O₇ 501.18837, found 501.18754.

Chapter 4

Preparation of acceptor 30



Scheme S15: preparation of acceptor 30: reagents and conditions: a) i: DBTO, toluene reflux, ii: allyl bromide, TBAI, toluene, 75 °C, iii: PhCH(OCH₃)₂, PTSA, acetonitrile, 60 °C, 300 mbar, 27% over 3 steps; b) NapBr, NaH, DMF, 81%; c) PTSA, MeOH, 50 °C, 82%; d) BnBr, NaH, DMF, 86%; e) DDQ, DCM/H₂O (9:1), 79%; f) BzCl, pyridine, 90%; g) Pd(Ph₃P)₄, DMBA, MeOH, 40 °C, quant

Methyl 3-O-allyl-4,6-O-benzylidene-a-D-galactopyranoside (S40)



Methyl a-D-galactopyranoside (S35, 9.71 g, 50 mmol) and di-n-butyltin oxide (13.7 g, 55 mmol, 1.1 eq) were refluxed in toluene for 3 hr, while water was removed with a Dean-Stark trap. After this, the reaction mixture was cooled to 60 °C and TBAI (20.3 g, 55 mmol, 1.1 eq) and allyl bromide (5.18 mL, 60 mmol, 1.2 eq) were added. The reaction mixture was stirred overnight at this temperature and subsequently concentrated under reduced pressure. Silica chromatography (4% MeOH in DCM) yields impure Methyl 3-O-allyl-α-D-galactopyranoside (9.9 g, max. 42.3 mmol, 85%) as red oil. This was dissolved in acetonitrile with PTSA-H₂O (0.80 g, 4.23 mmol, ca. 0.1 eq) and benzaldehyde dimethyl acetal (8.92 mL, 59.2 mmol, ca. 1.4 eq). The reaction mixture was heated to 60 °C at 300 mbar until TLC showed full conversion. The reaction was then concentrated under reduced pressure. The residue was dissolved in EtOAc and washed with sat. aq. NaHCO3. The organic phase was dried with MgSO4 and concentrated under reduced pressure. Recrystallisation from EA/pentane yields the title compound as yellowish solid. Yield: 4.3 g, 13.3 mmol, 27% based on S35. ¹H NMR (400 MHz, CDCl₃) δ 7.59 - 7.48 (m, 2H, CH_{arom}), 7.45 - 7.30 (m, 3H, CH_{aron}), 5.99 (ddt, J = 17.3, 10.3, 5.8 Hz, 1H, CH₂-CH=CH₂), 5.57 (s, 1H, CHPh), 5.35 (dq, J = 17.3, 1.6 Hz, 1H, CH₂-CH=CHH), 5.23 (dq, J = 10.3, 1.3 Hz, 1H, CH₂-CH=CH*H*), 4.97 (d, *J* = 3.7 Hz, 1H, H-1), 4.34 (dd, *J* = 3.5, 1.2 Hz, 1H, H-4), 4.30 (dd, *J* = 12.5, 1.6 Hz, 1H, H-6), 4.30 - 4.21 (m, 1H, CHH-CH=CH₂), 4.24 - 4.14 (m, 2H, H-2, CHH-CHCH₂), 4.10 (dd, *J* = 12.5, 1.8 Hz, 1H, H-6), 3.76 (dd, *J* = 10.1, 3.5 Hz, 1H, H-3), 3.68 (q, *J* = 1.6 Hz, 1H, H-5), 3.48 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 137.8 (C_q), 135.0(CH₂-CH=CH₂), 129.0, 128.2, 126.4 (CH_{arom}), 117.7 CH₂-CH=CH₂), 101.1 (CHPh), 100.2 (C-1), 76.1 (C-3), 73.7 (C-4), 70.6 (CH₂-CH=CH₂), 69.6 (C-6), 68.0 (C-2), 62.9 (C-5), 55.7 (CH₃ OMe). Spectra in agreement with literature.75

Methyl 3-O-allyl-4,6-O-benzylidene-2-O-(2-naphtyl)methyl-a-D-galactopyranoside (S41)



Methyl 3-O-allyl-4,6-O-benzylidene- α -D-galactopyranoside (**S40**, 4.25 g, 13.18 mmol) was dissolved in 50 ml DMF and stirred at 0 °C until the sugar was fully dissolved. To the solution was added NaH (60 % dispersion in mineral oil, 0.69 g, 17.14 mmol, 1.3 eq) and the mixture was stirred for another 15 min before slowly adding NapBr (3.79 g, 17.14 mmol, 1.3 eq) and the reaction was stirred at RT until TLC indicated full conversion. The reaction mixture was guenched with H_2O and extracted with Et_2O . The organic layer was washed twice with H_2O . The organic laver was dried over MgSO₄, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (8/2 pentane/EtOAc) to provide the title compound as an oil. Yield: 4.85 g, 10.48 mmol, 81%. ¹H NMR (400 MHz, CDCl₃) δ 7.85 – 7.77 (m, 4H, CHaron), 7.55 - 7.43 (m, 5H, CHaron), 7.35 - 7.28 (m, 3H, CHaron), 6.07 - 5.92 (m, 1H, CH₂-CH=CH₂), 5.53 (s, 1H, CHPh), 5.36 (dq, J = 17.2, 1.6 Hz, 1H, CH₂-CH=CHH), 5.20 (dq, J = 10.4, 1.4 Hz, 1H, CH₂-CH=CHH), 5.06 - 4.97 (m, 1H, CHH Nap), 4.82 (d, J = 12.2 Hz, 1H, CHH Nap), 4.77 (d, J = 3.5 Hz, 1H, H-1), 4.35 – 4.24 (m, 2H, H-4, CH₂-CH=CH₂), 4.21 (dd, J = 12.5, 1.6 Hz, 1H, H-6), 4.08 (dd, J = 10.1, 3.6 Hz, 1H, H-2), 4.03 (dd, J = 12.5, 1.8 Hz, 1H, H-6), 3.95 (dd, J = 10.2, 3.4 Hz, 1H, H-3), 3.62 (d, J = 1.5 Hz, 1H, H-5), 3.39 (s, 3H, CH_3 OMe); ${}^{13}C$ NMR (101 MHz, CDCl₃) δ 137.9, 136.1 (C_q), 135.4 (CH₂-CH=CH₂), 133.3, 133.1 (C_q), 129.0, 128.2, 128.0, 127.8, 127.0, 126.5, 126.2, 126.1, 126.0 (CH_{arom}), 117.2 (CH₂-CH=CH₂), 101.3 (CHPh), 99.6 (C-1), 75.6 (C-3), 75.5 (C-2), 75.1 (C-4), 74.0 (CH₂ Nap), 71.6 (CH₂-CH=CH₂), 69.5 (C-6), 62.7 (C-5), 55.7 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₂₈H₃₀O₆NH₄ 480.23806, found 480.23749.

Methyl 3-O-allyl-2-O-(2-naphtyl)methyl-a-D-galactopyranoside (S42)



Methyl 3-O-allyl-4,6-di-O-benzylidene-2-O-(2-naphtyl)methyl- α -D-galactopyranoside (**S41**, 4.76 g, 10.3 mmol) was dissolved in 50 ml MeOH and stirred at RT for 15 min. To the solution was added pTsOH·H₂O (0.20 g, 1.03 mmol, 0.1 eq) and the mixture was stirred for 1h at 50 °C after which TLC indicated full conversion. The reaction mixture was set to cool down to RT and was quenched with TEA. Solvents were evaporated under reduced pressure and purification was performed on flash column chromatography (1/1 pentane/EtOAc) to provide the title compound as a solid. Yield: 3.17 g, 8.46 mmol, 82 %. ¹H NMR (400 MHz, CDCl₃) δ 7.86 – 7.77 (m, 4H, CH_{arom}), 7.54 – 7.43 (m, 3H, CH_{arom}), 5.96 (ddt, *J* = 17.3, 10.4, 5.7 Hz, 1H, CH₂-CH=CH₂), 5.33 (dq, *J* = 17.2, 1.6 Hz, 1H, CH₂-CH=CHH), 5.22 (dq, *J* = 10.3, 1.3 Hz, 1H, CH₂-CH=CH*H*), 4.95 (d, *J* = 12.3, 1H, CHH Nap), 4.81 (d, *J* = 12.3 Hz, 1H, CHH Nap), 4.69 (d, *J* = 3.3 Hz, 1H, H-1), 4.29 (ddt, *J* = 12.7, 5.4, 1.5 Hz, 1H, CHH-CH=CH₂), 4.20 (ddt, *J* = 12.7, 6.9 Hz, 1H, H-6), 3.87 – 3.80 (m,

2H, H-2, H-3), 3.80 – 3.76 (m, 2H, H-5, H-6), 3.38 (s, 3H, CH₃ OMe), 2.72 (s, 1H, OH), 2.37 (s, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 135.9 (C_q), 134.7(CH₂-CH=CH₂), 133.3, 133.2 (C_q), 128.3, 128.0, 127.8, 126.9, 126.3, 126.1, 126.1 (CH_{arom}), 117.6 (CH₂-CH=CH₂), 98.7 (C-1), 76.9 (C-3), 75.5 (C-2), 73.8 (CH₂ Nap), 71.8 (CH₂-CH=CH₂), 69.2 (C-4), 69.0 (C-5), 63.2 (C-6), 55.5 (CH₃ OMe); HRMS: [M+Na]⁺ calcd for C₂₁H₂₆O₆Na 397.16216, found 397.16144.

Methyl 3-O-allyl-4,6-di-O-benzyl-2-O-(2-naphtyl)methyl-a-D-galactopyranoside (S43)



Methyl 3-O-allyl-2-O-(2-naphtyl)methyl-a-D-galactopyranoside (S42, 2.62 g, 7.0 mmol, 1 eq) was dissolved in 40 ml DMF and stirred at 0 °C until the sugar was fully dissolved. To the solution was added NaH (60% dispersion in mineral oil, 0.84 g, 21.0 mmol, 3 eq) and the reaction was stirred for 30 min at 0 °C after which BnBr (2.49 ml, 21.0 mmol, 3 eq) was slowly added. After 30 min the temperature was increased to RT. Once TLC indicated full conversion the reaction mixture was quenched with water and extracted twice with Et₂O. The combined organic layers were dried over MgSO₄, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (9/1 pentane/EtOAc) to provide the title compound as an oil. Yield: 3.35 g, 6.02 mmol, 86%. ¹H NMR (400 MHz, CDCl₃) δ 7.85 - 7.76 (m, 4H, CH_{arom}), 7.55 – 7.42 (m, 3H, CH_{arom}), 7.38 – 7.21 (m, 10H, CH_{arom}), 5.99 (ddt, J = 17.3, 10.5, 5.3 Hz, 1H, CH₂-CH=CH₂), 5.37 (dq, J = 17.2, 1.8 Hz, 1H, CH₂-CH=CHH), 5.20 (dq, J = 10.4, 1.5 Hz, 1H, CH₂-CH=CHH), 4.98 (d, J = 12.3 Hz, 1H, CHH Bn), 4.94 (d, J = 11.4 Hz, 1H, CHH Nap), 4.84 (d, J = 12.3 Hz, 1H, CHH Bn), 4.67 (d, J = 3.6 Hz, 1H, H-1), 4.56 (d, J = 11.4 Hz, 1H, CHH Nap), 4.47 (d, *J* = 11.8 Hz, 1H, CHH Bn), 4.39 (d, *J* = 11.8 Hz, 1H, CHH Bn), 4.32 (ddt, *J* = 13.0, 5.1, 1.6 Hz, 1H, CHH-CH=CH₂), 4.23 (ddt, J = 13.0, 5.4, 1.6 Hz, 1H, CHH-CH=CH₂), 4.03 (dd, J = 10.1, 3.7 Hz, 1H, H-2), 3.93 (d, J = 2.8 Hz, 1H, H-4), 3.89 (t, J = 6.5 Hz, 1H, H-5), 3.84 (dd, J = 10.1, 2.9 Hz, 1H, H-3), 3.51 (d, J = 6.5 Hz, 2H, 2x H-6), 3.36 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 138.8, 138.1, 136.2 (C_q), 135.3 (CH₂-CH=CH₂), 133.4, 133.2 (C_q), 128.5, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.8, 127.7, 126.9, 126.2, 126.1, 125.9 (CH_{arom}), 116.6 (CH₂-CH=CH₂), 98.9 (C-1), 78.7 (C-3), 76.4 (C-2), 75.0 (C-4), 74.8 (CH₂ Nap), 73.8 (CH₂ Bn), 73.6 (CH₂ Bn), 72.0 (CH₂-CH=CH₂), 69.3 (C-5), 69.2 (C-6), 55.5 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C35H38O6 572.30066, found 572.29988.

Methyl 3-O-allyl-4,6-di-O-benzyl-a-D-galactopyranoside (S44)

OBn BnO AllvIO

Methyl 3-O-allyl-4,6-di-O-benzyl-2-O-(2-naphtyl)methyl- α -D-galactopyranoside (**S43**, 1.66 g, 3.0 mmol) was dissolved in 30 ml 9/1 DCM/H₂O and stirred at RT until the sugar was fully dissolved. To the solution was added DDQ (1.36 g, 3.0 mmol, 2 eq) and the reaction was stirred for 60 min at RT after which TLC indicated full conversion. The reaction mixture was quenched with aq. Bicarb solution and extracted with DCM. The organic layer was washed twice with aq.

Bicarb solution. The organic layer was dried over MgSO₄, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (7/3 pentane/EtOAc) to provide the title compound as an oil. Yield: 0.973 g, 2.36 mmol, 79%. ¹H NMR (400 MHz, CDCl₃) δ 7.41 – 7.17 (m, 10H, CH_{arom}), 5.94 (ddt, *J* = 17.2, 10.4, 5.6 Hz, 1H, CH₂-CH=CH₂), 5.32 (dq, *J* = 17.2, 1.6 Hz, 1H, CH₂-CH=CHH), 5.20 (dq, *J* = 10.4, 1.4 Hz, 1H, CH₂-CH=CHH), 4.87 (d, *J* = 11.4 Hz, 1H, CHH Bn), 4.84 (d, *J* = 3.9 Hz, 1H, H-1), 4.56 (d, *J* = 11.4 Hz, 1H, CHH Bn), 4.52 (d, *J* = 11.7 Hz, 1H, CHH Bn), 4.44 (d, *J* = 11.7 Hz, 1H, CHH Bn), 4.18 (ddt, *J* = 12.7, 5.5, 1.5 Hz, 1H, CHH-CH=CH₂), 4.17 – 4.07 (m, 2H, H-2, CHH-CH=CH₂), 3.95 (dd, *J* = 2.9, 1.3 Hz, 1H, H-4), 3.90 (t, *J* = 2.7 Hz, 1H, H-5), 3.64 – 3.52 (m, 3H, H-3, 2x H-6), 3.42 (s, 3H, CH₃ OMe), 2.22 (d, *J* = 7.1 Hz, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 138.6, 138.0 (C_q), 134.7 (CH₂-CH=CH₂), 128.6, 128.4, 128.3, 127.9, 127.9, 127.8 (CH_{arom}), 117.4 (CH₂-CH=CH₂), 99.7 (C-1), 79.1 (C-3), 74.7 (CH₂ Bn), 73.7 (C-4), 73.7 (CH₂ Bn), 71.2 (CH₂-CH=CH₂), 69.7 (C-5), 69.1 (C-6), 68.9 (C-2), 55.6 (OMe); HRMS: [M+Na]⁺ calcd for C₂₄H₃₀O₆Na 437.19346, found 437.19295.

Methyl 3-O-allyl-2-O-benzoyl-4,6-di-O-benzyl-a-D-galactopyranoside (\$45)

Allylo

Methyl 3-O-allyl-4,6-di-O-benzyl-a-D-galactopyranoside (S44, 0.92 g, 2.22 mmol) was dissolved in 25 ml pyridine and stirred at 0 °C until the sugar was fully dissolved. To the solution was added BzCl (0.35 ml, 2.89 mmol, 1.3 eq) and the reaction was stirred for 30 min at 0 °C after which the temperature was increased to RT. Once TLC indicated full conversion the reaction mixture was diluted with EtOAc and washed twice with 1M HCl and once with sat. aq. NaHCO3. The organic layer was dried over MgSO₄, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (9/1 pentane/EtOAc) to provide the title compound as a light-yellow oil. Yield: 1.04 g, 2.0 mmol, 90%. ¹H NMR (400 MHz, CDCl₃) δ 8.12 - 8.05 (m, 2H, CHarom), 7.61 - 7.52 (m, 1H, CHarom), 7.49 - 7.40 (m, 2H, CHarom), 7.39 - 7.24 (m, 10H, CH_{arom}), 5.94 - 5.79 (m, 1H, CH₂-CH=CH₂), 5.49 (dd, J = 10.2, 3.7 Hz, 1H, H-2), 5.28 (dq, J = 17.2, 1.7 Hz, 1H, CH₂-CH=CHH), 5.14 (dq, J = 10.4, 1.4 Hz, 1H, CH₂-CH=CH*H*), 5.10 (d, *J* = 3.7 Hz, 1H, H-1), 4.97 (d, *J* = 11.5 Hz, 1H, C*H*H Bn), 4.60 (d, *J* = 11.5 Hz, 1H, CH*H* Bn), 4.52 (d, *J* = 11.7 Hz, 1H, CHH Bn), 4.44 (d, *J* = 11.7 Hz, 1H, CHH Bn), 4.17 (d, *J* = 5.5 Hz, 1H, CH₂-CH=CH₂), 4.06 - 3.95 (m, 3H, H-3, H-4, H-5), 3.68 - 3.57 (m, 2H, 2x H-6), 3.35 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 166.2 (C=O), 138.6, 138.1 (C_q), 134.8 (CH₂-CH=CH₂), 133.1 (CH_{arom}), 130.3 (C_q), 129.9, 128.6, 128.5, 128.4, 128.4, 128.0, 127.9, 127.8 (CH_{arom}), 117.2 (CH₂-CH=CH₂), 97.7 (C-1), 76.6 (C-4), 74.9 (CH₂ Bn), 74.7 (C-3), 73.7 (CH₂ Bn), 71.9 (CH₂-CH=CH₂) 71.9 (C-2), 69.4 (C-5), 69.1 (C-6), 55.5 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₃₁H₃₄O₇NH₄ 536.26428, found 536.26380.





Methyl 2-O-benzoyl-3-O-allyl-4,6-di-O-benzyl-α-D-galactopyranoside (S45, 0.95 g, 1.83 mmol) and DMBA (0.57 g, 3.66 mmol, 2 eq) were dissolved in 20 ml MeOH and flushed for 30 min with N_2 . To the solution was added Pd(PPh₃)₄ (0.11 g, 0.09 mmol, 0.05 eq) and the mixture was heated for 1h at 40 °C, after which TLC indicated full conversion. The mixture was diluted in EtOAc and washed with saturated Bicarb sol. The aqueous laver was extracted three times with EtOAc. The combined organic layers were dried over MgSO4, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (8/2 pentane/EtOAc) to provide the title compound as a yellow oil. Yield: 0.88 g, 1.83 mmol, quant. $[\alpha]_{25}^{25} = +168.6^{\circ}$ (c = 0.6, CHCl₃); IR (thin film): 698, 714, 1048, 1103, 1280, 1717; ¹H NMR (400 MHz, CDCl₃) δ 8.10 -8.05 (m, 2H, CHarom), 7.59 - 7.53 (m, 1H, CHarom), 7.46 - 7.39 (m, 2H, CHarom), 7.39 - 7.27 (m, 10H, CH_{arom}), 5.25 (dd, J = 10.3, 3.7 Hz, 1H, H-2), 5.02 (d, J = 3.7 Hz, 1H, H-1), 4.73 (s, 1H, CH₂ Bn), 4.58 (d, J = 11.7 Hz, 1H, CHH Bn), 4.50 (d, J = 11.7 Hz, 1H, CHH Bn), 4.17 (ddd, J = 10.3, 9.3, 3.5 Hz, 1H, H-3), 4.10 – 4.04 (m, 1H, H-5), 4.02 (dd, J = 3.6, 1.2 Hz, 1H, H-4), 3.75 – 3.59 (m, 2H, 2x H-6), 3.38 (s, 3H, CH₃ OMe), 2.17 (d, J = 9.4 Hz, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 167.0 (C=O), 138.2, 137.9 (C_a), 133.4, 130.1 (CH_{arom}), 129.9 (C_a), 128.7, 128.6, 128.5, 128.2, 128.1, 128.0, 128.0 (CHarom), 97.8 (C-1), 77.7 (C-4), 75.6 (CH₂ Bn), 73.7 (CH₂ Bn), 72.9 (C-2), 69.0, 68.9 (C-3, C-5), 68.7 (C-6), 55.6 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₂₈H₃₀O₇NH₄ 496.23298, found 496.23242.





Scheme S16: preparation of acceptor 33: reagents and conditions: a) Pd(Ph₃P)₄, DMBA, methanol, 40 °C, 95%; b) BzCl, pyridine, 97%; c) DDQ, DCM/H₂O (9:1), 84%

Methyl 4,6-di-O-benzyl-2-O-(2-naphtyl)methyl-a-D-galactopyranoside (S46)



3-O-allyl-4,6-di-O-benzyl-2-O-(2-naphtyl)methyl- α -D-galactopyranoside (**S43** 1.59 g, 2.87 mmol) and DMBA (0.90 g, 5.73 mmol, 2 eq) where dissolved in 50 ml MeOH and flushed for 30 min with N₂. To the solution was added Pd(PPh₃)₄ (0.17 g, 0.14 mmol, 0.05 eq) and the mixture was heated for 1h at 40 °C, after which TLC indicated full conversion. The mixture was diluted in EtOAc and washed with saturated aq. Bicarb sol. The aqueous layer was extracted three times with EtOAc. The combined organic layers were dried over MgSO₄, filtered and concentrated

under reduced pressure. Purification was performed on flash column chromatography (17/3 pentane/EtOAc) to provide the title compound as a yellow oil. Yield: 1.40 g, 2.72 mmol, 95%. ¹H NMR (400 MHz, CDCl₃) δ 7.86 – 7.78 (m, 4H, CH_{arom}), 7.53 – 7.46 (m, 3H, CH_{arom}), 7.35 – 7.22 (m, 5H, CH_{arom}), 4.88 (d, *J* = 12.2 Hz, 1H, CHH Bn/Nap), 4.85 – 4.76 (m, 2H, CHH Bn/Nap, CHH Bn/Nap), 4.69 (d, *J* = 3.5 Hz, 1H, H-1), 4.60 (d, *J* = 11.5 Hz, 1H, CHH Bn/Nap), 4.51 (d, *J* = 11.8 Hz, 1H, CHH Bn/Nap), 4.69 (d, *J* = 3.5 Hz, 1H, H-1), 3.384 (dd, *J* = 10.0, 3.5 Hz, 1H, H-2), 3.55 (d, *J* = 6.4 Hz, 2H, 2x H-6), 3.32 (s, 3H, CH₃ OMe), 2.26 (d, *J* = 4.9 Hz, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 138.5, 138.0, 135.7, 133.3, 133.3 (C_q), 128.5, 128.5, 128.3, 128.1, 127.9, 127.8, 127.2, 126.3, 126.2, 126.1 (CH_{arom}), 98.1 (C-1), 77.5 (C-2), 76.8 (C-4), 75.3, 73.6, 73.3 (CH₂ Bn, CH₂ Nap), 70.4 (C-3), 69.2 (C-5), 69.1 (C-6), 55.5 (CH₃ OMe). HRMS: [M+Na]⁺ calcd for C₃₂H₃₄O₆Na 537.22531, found 537.22250.

Methyl 3-O-benzoyl-4,6-di-O-benzyl-2-O-(2-naphtyl)methyl-a-D-galactopyranoside (S47)



Methyl 4,6-di-O-benzyl-2-O-(2-naphtyl)methyl-a-D-galactopyranoside (**S46**, 1.30 g, 2.53 mmol) was dissolved in 25 ml pyridine and stirred at 0 °C until the sugar was fully dissolved. To the solution was added BzCl (0.38 ml, 3.28 mmol, 1.3 eq) and the reaction was stirred for 30 min at 0 °C after which the temperature was increased to RT. Once TLC indicated full conversion the reaction mixture was diluted with EtOAc and washed twice with 1M HCl. The organic layer was dried over MgSO₄, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (9/1 pentane/EtOAc) to provide the title compound as a lightyellow oil. Yield: 1.51 g, 2.45 mmol, 97%. ¹H NMR (400 MHz, CDCl₃) δ 7.96 (dd, J = 8.3, 1.4 Hz, 2H, CH_{arom}), 7.82 – 7.75 (m, 1H, CH_{arom}), 7.75 – 7.65 (m, 3H, CH_{arom}), 7.55 (ddt, J = 8.7, 7.1, 1.3 Hz, 1H, CH_{arom}), 7.49 - 7.41 (m, 2H, CH_{arom}), 7.41 - 7.37 (m, 3H, CH_{arom}), 7.36 - 7.24 (m, 5H, CH_{arom}), 7.20 – 7.08 (m, 5H, CH_{arom}), 5.59 (dd, *J* = 10.6, 3.1 Hz, 1H, H-3), 4.83 (d, *J* = 3.7 Hz, 2H, H-1, CH₂ Bn/Nap), 4.62 (d, J = 11.4 Hz, 1H, CHH Bn/Nap), 4.51 (d, J = 11.9 Hz, 1H, CHH Bn/Nap), 4.45 – 4.36 (m, 2H, 2x CHH Bn/Nap), 4.24 (dd, J = 10.5, 3.6 Hz, 1H, H-2), 4.16 (dd, J = 3.1, 1.3 Hz, 1H, H-4), 4.12 (t, *J* = 6.5, 1.3 Hz, 1H, H-5), 3.55 (dd, *J* = 6.6, 1.2 Hz, 2H, 2x H-6), 3.43 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 165.9 (C=O), 138.0, 138.0, 135.7, 133.3 (C_q), 133.2 (CH_{arom}), 133.2, 130.0 (C_g), 129.9, 128.5, 128.4, 128.3, 128.1, 128.1, 127.8, 127.8, 127.0, 126.2, 126.1, 126.0 (CH_{arom}), 98.6 (C-1), 75.7 (C-4), 75.3 (CH₂ Bn/Nap), 74.3 (C-2), 73.5, 73.4 (CH₂ Bn/Nap), 73.0 (C-3), 68.9 (C-5), 68.7 (C-6), 55.6 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₃₉H₃₈O₇NH₄ 636.29558, found 636.29474.

Methyl 3-O-benzoyl-4,6-di-O-benzyl-a-D-galactopyranoside (33)



Chapter 4

Methyl 3-O-benzoyl-4,6-di-O-benzyl-2-O-(2-naphtyl)methyl-a-D-galactopyranoside (**\$47**, 1.45 g, 2.34 mmol) was dissolved in 25 ml 9/1 DCM/H₂O and stirred at RT until the sugar was fully dissolved. To the solution was added DDQ (1.06 g, 4.69 mmol, 2 eq) and the reaction was stirred for 60 min at RT after which TLC indicated full conversion. The reaction mixture was guenched with aq. Bicarb solution and extracted with DCM. The organic layer was washed twice with aq. Bicarb solution. The organic layer was dried over MgSO4, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (3/1 pentane/EtOAc) to provide the title compound as a solid. Yield: 0.94 g, 1.96 mmol, 84%. $[\alpha]_{2}^{25} =$ +97.9° (c = 0.60, CHCl₃); IR (thin film): 698, 738, 1027, 1056, 1070, 1094, 1124, 1149, 1273, 1315, 1352, 1452, 1717; ¹H NMR (400 MHz, CDCl₃) δ 8.10 – 8.03 (m, 2H, CH_{arom}), 7.57 (ddt, J = 8.7, 7.1, 1.3 Hz, 1H, CHarom), 7.48 - 7.38 (m, 2H, CHarom), 7.39 - 7.18 (m, 10H, CHarom), 5.39 (dd, J = 10.4, 3.0 Hz, 1H, H-3), 4.89 (d, J = 3.9 Hz, 1H, H-1), 4.77 (d, J = 11.4 Hz, 1H, CHH Bn), 4.54 (d, J = 9.1 Hz, 1H, CHH Bn), 4.51 (d, *J* = 8.7 Hz, 1H, CHH Bn), 4.44 (d, *J* = 11.8 Hz, 1H, CHH Bn), 4.27 (ddd, J = 11.3, 10.4, 3.9 Hz, 1H, H-2), 4.13 – 4.04 (m, 2H, H-4, H-5), 3.60 (d, J = 6.6 Hz, 2H, 2x H-6), 3.46 (s, 3H, CH₃ OMe), 2.03 (d, J = 11.2 Hz, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 166.7 (C=O), 138.12, 137.9 (Cq), 133.4, 130.0 (CH_{arom}), 129.9 (Cq), 128.6, 128.6, 128.5, 128.1, 127.9, 127.9 (CHarom), 99.9 (C-1), 75.6 (C-4), 75.3 (CH2 Bn), 74.4 (C-3), 73.6 (CH2 Bn), 69.5 (C-5), 68.7 (C-6), 68.1 (C-2), 55.7 (CH₃ OMe); HRMS: [M+Na]⁺ calcd for 501.18837, found 501.18772.

Preparation of acceptor 34



Scheme S17: preparation of acceptor **34**: reagents and conditions: *a*) *i*) Pd(Ph₃P)₄, DMBA, methanol, 40 °C, ii: BzCl, pyridine, 89% over 2 steps; b) DDQ, DCM/H₂O (9:1), 61%

Methyl 3,4,6-tri-O-benzoyl-2-O-(2-naphtyl)methyl-a-D-galactopyranoside (S48)



Methyl 3-O-allyl-2-O-(2-naphtyl)methyl- α -D-galactopyranoside (**S42**, 0.5 g, 1.34 mmol) and DMBA (0.42 g, 2.67 mmol, 2 eq) were dissolved in 25 ml MeOH and flushed for 30 min with N₂. To the solution was added Pd(PPh₃)₄ (0.08 g, 0.07 mmol, 0.05 eq) and the mixture was heated for 1h at 40 °C, after which TLC indicated full conversion. The mixture conventrated under reduced pressure and the crude intermediate was dissolved in 25 ml pyridine and stirred at 0 °C until it was dissolved. To the solution was added BzCl (0.63 ml, 5.36 mmol, 4 eq) and stirred for 30 min at 0 °C, after which the temperature was increased to RT. The reaction was stirred overnight and diluted in DCM, once TLC indicated full conversion. The organic layer was washed three times with 1M aq. HCl and once with sat. aq. Bicarb. The combined organic layers were dried over MgSO₄, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (4/1 pentane/EtOAc) to provide the slightly impure title compound as a yellow oil. Yield: 0.772 g, 1.19 mmol, 89% over 2 steps. ¹H NMR (400 MHz, CDCl₃) δ 8.02 –

7.95 (m, 2H), 7.90 – 7.84 (m, 2H), 7.82 – 7.76 (m, 3H), 7.72 – 7.66 (m, 3H), 7.60 – 7.51 (m, 3H), 7.50 – 7.45 (m, 3H), 7.40 (dd, J = 8.7, 7.0 Hz, 3H), 7.35 – 7.26 (m, 7H), 5.92 (d, J = 3.4 Hz, 1H, H-4), 5.81 (dd, J = 10.4, 3.4 Hz, 1H, H-3), 4.96 (d, J = 3.6 Hz, 1H, H-1), 4.86 (d, J = 12.5 Hz, 1H, CHH Nap), 4.59 – 4.46 (m, 2H, H-5, H-6), 4.35 – 4.24 (m, 1H, H-6), 4.22 (dd, J = 10.5, 3.4 Hz, 1H, H-2), 3.50 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 166.2, 165.6, 165.5 (C=O), 135.4, 135.2, 134.4, 133.5, 133.3, 133.2, 133.2 (C_q), 130.8, 130.7, 130.3, 129.9, 129.8, 129.7, 129.6, 129.5, 129.3, 129.0, 128.6, 128.6, 128.5, 128.4, 128.0, 127.9, 127.2, 126.3, 126.2, 126.1 (CH_{arom}), 98.7 (C-1), 73.4 (CH₂ Nap), 73.4 (C-2), 70.3 (C-3), 69.7 (C-4), 66.9 (C-5), 62.8 (C-6), 55.8 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₃₉H₃₄O₉NH₄ 664.25411, found 664.25339.

Methyl 3,4,6-tri-O-benzoyl-a-D-galactopyranoside (34)



Methyl 3,4,6-tri-O-benzyl-2-O-(2-naphtyl)methyl-α-D-galactopyranoside (0.82 g, 1.27 mmol) was dissolved in 25 ml 9/1 DCM/H₂O and stirred at RT until the sugar was fully dissolved. To the solution was added DDQ (0.58 g, 2.54 mmol, 2 eq) and the reaction was stirred for 60 min at RT after which TLC indicated full conversion. The reaction mixture was quenched with aq. Bicarb solution and extracted with DCM. The organic layer was washed twice with aq. Bicarb solution. The organic layer was dried over MgSO₄, filtered and concentrated under reduced pressure. Purification was performed on flash column chromatography (4/1 pentane/EtOAc) to provide the title compound as a solid. Yield: 0.39 g, 0.78 mmol, 62%. ¹H NMR (400 MHz, CDCl₃) δ 8.12 – 8.04 (m, 2H, CH_{arom}), 8.05 - 7.98 (m, 2H, CH_{arom}), 7.90 - 7.83 (m, 2H, CH_{arom}), 7.62 (ddt, J = 8.7, 7.1, 1.3 Hz, 1H, CHarom), 7.60 - 7.51 (m, 1H, CHarom), 7.53 - 7.44 (m, 3H, CHarom), 7.46 - 7.37 (m, 2H, CH_{arom}), 7.35 - 7.26 (m, 2H, CH_{arom}), 5.91 (dd, J = 3.4, 1.3 Hz, 1H, H-4), 5.59 (dd, J = 10.3, 3.4 Hz, 1H, H-3), 5.05 (d, *J* = 3.8 Hz, 1H, H-1), 4.58 (dd, *J* = 11.0, 7.0 Hz, 1H, H-6), 4.50 (ddd, *J* = 6.8, 5.4, 1.3 Hz, 1H, H-5), 4.36 (dd, J = 11.0, 5.6 Hz, 1H, H-6), 4.28 (td, J = 10.7, 3.8 Hz, 1H, H-2), 3.54 (s, 3H, CH₃ OMe), 2.19 (d, J = 11.0 Hz, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 166.4, 166.2, 165.7 (C=O), 133.7, 133.4, 133.3, 130.0, 129.9 (CH_{arom}), 129.8 (C_q), 129.5, 128.7, 128.6, 128.4 (CH_{arom}), 99.9 (C-1), 71.5 (C-3), 69.4 (C-4), 68.1 (C-2), 67.3 (C-5), 62.7 (C-6), 55.9 (CH₃ OMe). Data in agreement with literature.76

Chapter 4

Preparation of acceptor 35



Scheme S18: preparation of acceptor **35**: reagents and conditions: a) 2,2-dimethoxypropane, PTSA, 78%; b) allyl bromide, NaH, DMF, 71%; c) i: PTSA, MeOH, 50 °C, ii: BnBr, NaH, DMF, 76% over 2 steps; d) Pd(Ph₃P)₄, DMBA, MeOH, 85%

Methyl 3,4-O-isopropylidene-6-(1'-methoxy-1'-methyl)ethyl-β-D-galactopyranoside (S50)



Methyl β-D-galactopyranoside (**S49**, 3.88 g, 20 mmol) was suspended in 2,2-dimethoxypropane (49 mL, 400 mmol, 20 eq) and PTSA-H₂O (380 mg, 2 mmol, 0.1 eq) was added. The reaction mixture was stirred for 72 hr before being quenched with triethylamine (0.42 mL, 3 mmol, 0.15 eq) and concentrated under reduced pressure. The residue was purified over silica (20% \rightarrow 40% acetone in pentane with 1% triethylamine), to provide the title compound as colourless oil. Yield: 4.79 g, 15.6 mmol, 78%. ¹H NMR (400 MHz, CDCl₃) δ 4.18 (dd, *J* = 5.5, 2.2 Hz, 1H, H-4), 4.11 (d, *J* = 8.2 Hz, 1H, H-1), 4.07 (dd, *J* = 7.3, 5.4 Hz, 1H, H-3), 3.87 (td, *J* = 6.1, 2.1 Hz, 1H, H-5), 3.72 (d, *J* = 6.1 Hz, 2H, 2x H-6), 3.60 – 3.50 (m, 4H, H-2, CH₃ OMe), 3.24 (s, 3H, CH₃ OMe), 2.80 (d, *J* = 2.3 Hz, 1H, OH), 1.52 (s, 3H, CH₃ isopropylidene), 1.38 – 1.36 (m, 6H, 2x CH₃ isopropylidene), 1.34 (s, 3H, CH₃ isopropylidene) ¹³C NMR (101 MHz, CDCl₃) δ 110.2 (C_q isopropylidene), 78.9 (C-3), 73.8 (C-2, C-4), 72.6 (C-5), 60.4 (C-6), 56.9, 48.6 (CH₃ OMe), 28.2, 26.3, 24.5, 24.5 (CH₃ isopropylidene). Spectra in agreement with literature⁷⁷



Methyl 3,4-*O*-isopropylidene-6-(1'-methoxy-1'-methyl)ethyl-β-D-galactopyranoside (**S50**) 4.75 g, 15.5 mmol) was dissolved in DMF and allyl bromide (2 mL, 23.3 mmol, 1.5 eq) and sodium hydride (60% dispersion in mineral oil, 0.93 g, 23.3 mmol, 1.5 eq) were added. When TLC shows

full conversion, the reaction was quenched with water. The aquatic phase was extracted twice with diethyl ether. Combined organic phases were dried with MgSO₄ and concentrated under reduced pressure. The residue was purified over silica (10% acetone in pentane with 1% triethylamine) to provide the title compound as colourless oil. Yield: 3.79g, 10.9 mmol, 71%. ¹H NMR (400 MHz, CDCl₃) δ 5.94 (ddt, *J* = 17.3, 10.4, 5.8 Hz, 1H, CH₂-CH=CH₂), 5.30 (dq, *J* = 17.2, 1.7 Hz, 1H, CH₂-CH=CHH), 5.18 (dq, *J* = 10.4, 1.3 Hz, 1H, CH₂-CH=CHH), 4.33 – 4.21 (m, 2H, CH₂-CH=CH₂), 4.18 (d, *J* = 8.1 Hz, 1H, H-1), 4.17 – 4.15 (m, 1H, H-4), 4.11 (dd, *J* = 6.8, 5.5 Hz, 1H, H-3), 3.82 (td, *J* = 6.2, 2.0 Hz, 1H, H-5), 3.70 (dd, *J* = 6.0, 0.9 Hz, 2H, 2x H-6), 3.53 (s, 3H, CH₃ OMe), 3.34 (dd, *J* = 8.0, 6.8 Hz, 1H, H-2), 3.24 (s, 3H, CH₃ isopropylidene), 1.37 (s, 3H, CH₃ isopropylidene), 1.36 (s, 3H, CH₃ isopropylidene) ¹³C NMR (101 MHz, CDCl₃) δ 134.9 (CH₂-CH=CH₂), 117.3 (CH₂-CH=CH₂), 109.8 (Cq isopropylidene), 103.6 (C-1), 100.1 (Cq isopropylidene), 79.6 (C-2), 79.1 (C-3), 73.9 (C-4), 72.5 (CH₂-CH=CH₂), 72.1 (C-5), 60.4 (C-6), 56.6, 48.5 (CH₃ OMe), 27.9, 26.3, 24.4, 24.4 (CH₃ isopropylidene). Spectra in agreement with literature.⁷⁸

Methyl 2-O-allyl-3,4,6-tri-O-benzyl-β-D-galactopyranoside (S52)

BnO OBn BnO OAllyl

2-O-allyl-3,4-O-isopropylidene-6-(1'-methoxy-1'-methyl)ethyl-β-D-galactopyranoside Methyl (S51, 1.5 g, 4.33 mmol) and PTSA-H₂O (82 mg, 0.43 mmol, 0.1 eq) were dissolved in methanol and heated to 50 °C. When TLC shows full removal of isopropylidenes, the reaction is guenched with Et₃N (0.12 mL, 0.87 mmol, 0.2 eg) and concentrated under reduced pressure. After residual methanol and water were removed by azeotropic distillation with toluene, the residue was dissolved in DMF. Benzyl bromide (2.31 mL, 19.5 mmol, 4.5 eq) and NaH (60% dispersion in mineral oil, 779 mg, 19.5 mmol, 4.5 eq) were added. When TLC shows full conversion, the reaction was quenched with water and extracted with diethyl ether. The organic phase was dried with Na₂SO₄ and concentrated under reduced pressure. The residue was purified over silica (10% EtOAc in pentane), yielding the title compound as colourless oil. Yield: 1.67 g, 3.30 mmol, 76% over 2 steps. ¹H NMR (400 MHz, CDCl₃) δ 7.41 - 7.21 (m, 15H, CH_{aron}), 5.97 (ddt, J = 17.3, 10.4, 5.8 Hz, 1H, CH₂-CH=CH₂), 5.28 (dt, J = 17.3, 1.7 Hz, 1H, CH₂-CH=CHH), 5.15 (dq, J = 10.3, 1.3 Hz, 1H, CH₂-CH-CHH), 4.92 (d, J = 11.7 Hz, 1H, CHH Bn), 4.76 (d, J = 11.9 Hz, 1H, CHH Bn), 4.70 (d, J = 11.9 Hz, 1H, CHH Bn), 4.61 (d, J = 11.7 Hz, 1H, CHH Bn), 4.44 (d, J = 11.8 Hz, 1H, CHH Bn), 4.43 - 4.33 (m, 2H, CHH-CH=CH2, CHH Bn), 4.28 - 4.18 (m, 2H, H-1, CHH-CH=CH₂), 3.86 (dd, *J* = 3.0, 1.0 Hz, 1H, H-4), 3.67 (dd, *J* = 9.7, 7.6 Hz, 1H, H-2), 3.60 – 3.56 (m, 2H, 2x H-6), 3.55 – 3.49 (m, 4H, H-5, CH₃ OMe), 3.46 (dd, *J* = 9.8, 2.9 Hz, 1H, H-3); ¹³C NMR (101 MHz, CDCl₃) & 138.8, 138.7, 138.1 (C_q), 135.5 (CH₂-CH=CH₂), 128.6, 128.5, 128.4, 128.3, 128.0, 127.9, 127.7, 127.7, 127.6 (CH_{arom}), 116.8 (CH₂-CH=CH₂), 104.9 (C-1), 82.2 (C-3), 79.4 (C-2), 74.5, 74.1 (CH₂ Bn), 73.7 (CH₂-CH=CH₂), 73.6 (C-4), 73.5 (C-5), 73.2 (CH₂ Bn), 69.0 (C-6), 57.1 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₃₁H₃₆O₆NH₄ 522.28501, found 522.28412.

Methyl 3,4,6-tri-O-benzyl-β-D-galactopyranoside (35)

Methyl 2-O-allyl-3,4,6-tri-O-benzyl-β-D-galactopyranoside (**S52**, 1.6 g, 3.17 mmol) and DMBA (990 mg, 6.34 mmol, 2 eq) were dissolved in methanol and heated to 40 °C. After degassing with N₂ for 30 min, Pd(Ph₃P)₄ (183 mg, 0.159 mmol, 0.05 eq) was added. When TLC shows full conversion, the reaction mixture concentrated under reduced pressure. The residue was dissolved in diethyl ether and washed twice with sat. aq. NaHCO₃. The organic phase was dried with Na₂SO₄ and concentrated under reduced pressure. The residue was purified over silica (30% EA in pentane), yielding the title compound as yellowish powder. Yield: 1.25 g, 2.69 mmol, 85%. ¹H NMR (400 MHz, CDCl₃) δ 7.69 – 6.98 (m, 15H, CH_{arom}), 4.88 (d, *J* = 11.6 Hz, 1H, CHH Bn) 4.72 (d, *J* = 11.9 Hz, 1H, CHH Bn), 4.66 – 4.57 (m, 2H, 2x CHH Bn), 4.48 (d, *J* = 11.7 Hz, 1H, CHH Bn), 4.43 (d, *J* = 11.8 Hz, 1H, CHH Bn), 4.18 (d, *J* = 7.6 Hz, 1H, H-1), 4.00 – 3.89 (m, 2H, H-2, H-4), 3.66 – 3.56 (m, 3H, H-5, 2x H-6), 3.52 (s, 3H, CH₃ OMe), 3.43 (dd, *J* = 9.8, 2.8 Hz, 1H, H-3), 2.50 (d, *J* = 2.0 Hz, 1H, OH) ¹³C NMR (101 MHz, CDCl₃) δ 138.6, 138.1, 137.9 (C_q), 128.6, 128.5, 128.3, 128.3, 128.0, 127.9, 127.8, 127.7 (CH_{arom}), 104.2 (C-1), 82.1 (C-3), 74.6 (CH₂ Bn), 73.8 (C-5), 73.7 (CH₂ Bn), 72.8 (C-4), 72.4 (CH₂ Bn), 71.3 (C-4), 68.8 (C-6), 57.1 (CH₃ OMe); spectra in agreement with literature.⁷⁹

Rhamnose acceptors



Scheme S19: preparation of acceptor **36**: reagents and conditions: *a*) *i*: TsCl, pyridine, *ii*: LiAlH₄, THF, reflux, 52% over 2 steps

Methyl 2,3-di-O-benzyl-a-D-rhamnopyranoside (36)



Methyl 2,3-di-O-benzyl- α -D-mannopyranoside (**S17**, 1.80 g, 4.81 mmol, 1 eq) and TsCl (1.1 g, 5.77 mmol, 1.2 eq) were dissolved in 30 ml pyridine and stirred at RT overnight. The reaction mixture was diluted in EtOAc and washed three times with 1M aq. HCl. The organic layer was dried over MgSO₄, filtered and concentrated under reduced pressure to obtain crude intermediate. The crude intermediate was dissolved in 30 ml THF and a solution of LiAlH₄ (2.4 M in THF, 8.01 ml, 19.22 mmol, 4 eq) was slowly added. The reaction mixture was refluxed for 10 min, set to cool down to RT and quenched with 1M aq. HCl and extracted with EtOAc. The organic layer was washed once with 1M aq. HCl and twice aq. Bicarb solution. The organic layer was dried over MgSO₄, filtered and concentrated under reduced pressure. The Purification was

performed on flash column chromatography (8/2 pentane/EtOAc) to provide the title compound as an oil. Yield: 0.88 g, 2.50 mmol, 52%. $[\alpha]_D^{25} = -10.9^{\circ}$ (c = 0.34, CHCl₃); IR (thin film): 698, 738, 1027, 1059, 1268, 1367, 1454; ¹H NMR (400 MHz, CDCl₃) δ 7.40 – 7.23 (m, 10H, CH_{arom}), 4.74 – 4.66 (m, 2H, H-1, CHH Bn), 4.63 (d, *J* = 12.3 Hz, 1H, CHH Bn), 4.56 (d, *J* = 11.7 Hz, 1H, CHH Bn), 4.41 (d, *J* = 11.7 Hz, 1H, CHH Bn), 3.79 (dd, *J* = 3.1, 1.8 Hz, 1H, H-2), 3.77 – 3.68 (m, 1H, H-4), 3.67 – 3.56 (m, 2H, H-3, H-5), 3.32 (s, 3H, CH₃ OMe), 2.33 (s, 1H, OH), 1.33 (d, *J* = 6.1 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 138.2, 138.2 (C_q), 128.6, 128.5, 128.0, 127.9, 127.8, 127.8, 127.8 (CH₃rom), 99.2 (C-1), 79.9 (C-3), 73.8 (C-2), 72.7 (CH₂ Bn), 71.7 (C-4), 71.5 (CH₂ Bn), 68.3 (C-5), 54.8 (CH₃ OMe), 17.9 (C-6); HRMS: [M+Na]⁺ calcd for C₂₁H₂₆O₅Na 381.16725, found 381.16640.

Preparation of acceptor 37



Scheme S20: preparation of acceptor *37*: reagents and conditions: a) NapBr, NaH, DMF, 71%; b) i: PTSA, methanol, 60 °C, ii: BnBr, NaH, DMF, 70% over 2 steps; DDQ, DCM/H₂O (9:1), 79%

Methyl 2,3-O-isopropylidene-4-O-(2-naphthyl)methyl-α-L-rhamnopyranoside (S54)



Methyl 2,3-O-isopropylidene- α -L-rhamnopyranoside⁸⁰ (S53, 4.00 g, 18.3 mmol) was dissolved in DMF and cooled to 0 °C after which NaH (60% dispersion in mineral oil, 953 mg, 23.8 mmol, 1.3 eq) was added. After stirring for 10 minutes, 2-(Bromomethyl)naphthalene (5.27 g, 23.8 mmol, 1.3 eq) was added. The reaction mixture was allowed to warm to RT and upon completion (as indicated by TLC) quenched with water. The aqueous phase was extracted twice with diethyl ether, the combined organic phases were dried with MgSO4 and concentrated. The residue is purified over silica (3% EtOAc in pentane), yielding the desired product as yellow oil. Yield: 4.68 g, 13.1 mmol, 71%. ¹H NMR (400 MHz, CDCl₃) δ 7.85 – 7.76 (m, 4H, CH_{arom}), 7.53 – 7.35 (m, 3H, CH_{arom}), 5.05 (d, J = 11.8 Hz, 1H, CHH Nap), 4.85 (app. s, 1H, H-1), 4.79 (d, J = 11.8 Hz, 1H, CH*H* Nap), 4.29 (dd, *J* = 7.1, 5.8 Hz, 1H, H-3), 4.14 (d, *J* = 5.8 Hz, 1H, H-2), 3.69 (dq, *J* = 9.7, 6.2 Hz, 1H, H-5), 3.35 (s, 3H, CH₃ OMe), 3.25 (dd, J = 9.8, 7.1 Hz, 1H, H-4), 1.50 (s, 3H, CH₃ isopropylidene), 1.38 (s, 3H, CH₃ isopropylidene), 1.31 (d, J = 6.2 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 135.9, 133.3, 133.1 (C_q), 128.7, 128.5, 128.1, 128.0, 127.8, 127.6, 127.5, 126.9, 126.2, 126.1, 126.0, 125.9, 125.6 (CH_{arom}), 109.3 (C_q isopropylidene), 98.1 (C-1), 81.1 (C-4), 78.8 (C-3), 76.1 (C-2), 73.0 (CH₂ Nap), 64.5 (C-5), 54.9 (CH₃ OMe), 28.1, 26.4 (CH₃ isopropylidene), 18.0 (C-6); HRMS: [M+Na]⁺ calcd for C₂₁H₂₆O₅NH₄ 381.16725, found 381.16670.

Methyl 2,3-di-O-benzyl-4-O-(2-naphtyl)mehtyl-a-L-rhamnopyranoside (S55)



Methyl 2,3-O-isopropylidene-4-O-(2-naphthyl)methyl-a-L-rhamnopyranoside (S54, 1.40 g, 3.91 mmol) was dissolved in methanol with PTSA-H₂O (74 mg, 0.39 mmol, 0.1 eq) and heated to 60 °C. When TLC shows full removal of the isopropylidene, the reaction is guenched with triethylamine (0.13 mL, 0.98 mmol, 0.2 eq) and concentrated under reduced pressure. The residue is coevaporated with toluene and dissolved in DMF. The resulting solution is cooled to 0 °C, after which NaH (60% dispersion in mineral oil, 469 mg, 11.7 mmol, 3 eq) was added. After stirring for 10 minutes, benzyl bromide (1.93 mL, 11.7 mmol, 3 eq) was added. The reaction mixture was allowed to warm to RT and upon completion (as indicated by TLC) quenched with water. The aqueous phase was extracted twice with diethyl ether, the combined organic phases were dried with MgSO₄ and concentrated. The residue is purified over silica (5→10% EtOAc in pentane), yielding the desired product as yellowish oil. Yield: 1.365 g, 2.74 mmol, 70% over 2 steps.¹H NMR (400 MHz, CDCl₃) δ 7.85 - 7.72 (m, 4H, CH_{arom}), 7.47 - 7.41 (m, 3H, CH_{arom}), 7.40 - 7.25 (m, 10H, CH_{arom}), 5.10 (d, J = 11.1 Hz, 1H, CHH Bn/Nap), 4.81 (d, J = 11.2 Hz, 1H, CHH Bn/Nap), 4.77 - 4.70 (m, 2H, CH₂ Bn/Nap), 4.67 (d, J = 1.8 Hz, 1H, H-1), 4.62 (s, 2H, CH₂ Bn/Nap), 3.88 (dd, J = 9.0, 3.1 Hz, 1H, H-3), 3.80 (dd, J = 3.2, 1.9 Hz, 1H, H-2), 3.72 - 3.67 (m, 2H, H-4, H-5), 3.29 (s, 3H, CH₃ OMe), 1.37 (d, J = 5.7 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 138.7, 138.4, 136.3, 133.4, 133.0 (C_a), 128.5, 128.1, 128.1, 128.0, 127.8, 127.7, 127.6, 126.6, 126.2, 126.1, 125.9 (CH_{arom}), 99.2 (C-1), 80.6 (C-4), 80.3 (C-3), 75.5 (CH₂ Bn/Nap), 74.8 (C-2), 72.9, 72.2 (CH₂ Bn/Nap), 68.0 (C-5), 54.7 (CH₃ OMe), 18.2 (C-6); HRMS: [M+NH₄]⁺ calcd for C₃₂H₃₄O₅NH₄ 516.27445, found 516.27370.

Methyl 2,3-di-O-benzyl-4-O-(2-naphtyl)mehtyl-α-L-rhamnopyranoside (37)



Methyl 2,3-di-O-benzyl-4-O-(2-naphtyl)mehtyl- α -L-rhamnopyranoside (**S55**, 1.30 g, 2.61 mmol) was dissolved in 20 mL 9:1 DCM/water, after which DDQ (1.184 g, 5.21 mmol, 2 eq) was added. When TLC shows full conversion, the reaction mixture is diluted with DCM and washed twice with sat. aq. NaHCO₃. The organic phase was dried with MgSO₄ and concentrated under reduced pressure. The residue is purified over silica, yielding the title compound as colourless oil. Yield: 740 mg, 2.07 mmol, 79%. ¹H NMR (400 MHz, CDCl₃) δ 7.39 – 7.24 (m, 10H, CH_{arom}), 4.74 – 4.68 (m, 2H, H-1, CHH Bn), 4.64 (d, *J* = 12.3 Hz, 1H, CHH Bn), 4.56 (d, *J* = 11.6 Hz, 1H, CHH Bn), 4.41 (d, *J* = 11.7 Hz, 1H, CHH Bn), 3.79 (dd, *J* = 3.1, 1.8 Hz, 1H, H-2), 3.72 (td, *J* = 9.3, 1.6 Hz, 1H, H-4), 3.66 – 3.59 (m, 2H, H-3, H-5), 3.33 (s, 3H, CH₃ OMe), 2.31 (d, *J* = 1.9 Hz, 1H, OH), 1.33 (d, *J* = 6.1 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 138.3, 138.2 (C_q), 128.7, 128.5, 128.0, 128.0, 127.9, 127.9 (CH₃ OMe), 17.9 (C-6). spectra in agreement with literature.⁸¹



Scheme S21: preparation of acceptor 38: reagents and conditions: a) BnBr, NaH, DMF 81%; b) MeOH, PTSA, 50 °C ,93%; c) i: DBTO, toluene, reflux, ii: CsF, allyl bromide, DMF, 93% over 2 steps; d) BnBr, NaH, DMF, 80%; e) Pd(Ph₃P)₄, DMBA, MeOH, 40 °C, 84%

Methyl 4-O-benzyl-2,3-O-ispropylidene-a-L-rhamnopyranoside (S56)



S53 (2.62 g, 12 mmol) was dissolved in DMF and cooled to 0 °C, after which NaH (60% dispersion in mineral oil, 720 mg, 18 mmol, 1.5 eq) was added. The solution was stirred for 10 minutes at 0 °C, benzyl bromide (2.14 mL, 18 mmol, 1.5 eq) was added and the reaction mixture was allowed to warm to RT. When TLC shows full conversion of the starting material, the reaction is quenched with water and extracted with diethyl ether. The organic phase was dried with MgSO₄ and concentrated under reduced pressure. The residue was purified over silica (10% diethyl ether in pentane), yielding the desired product as colourless oil. Yield: 2.99 g, 9.69 mmol, 81%. ¹H NMR (400 MHz, CDCl₃) δ 7.38 – 7.23 (m, 5H, CH_{arom}), 4.90 (d, *J* = 11.6 Hz, 1H, *CH*H Bn), 4.85 (app. s, 1H, H-1), 4.62 (d, *J* = 11.6 Hz, 1H, CH*H* Bn), 4.25 (dd, *J* = 7.1, 5.8 Hz, 1H, H-3), 4.12 (dd, *J* = 5.8, 0.7 Hz, 1H, H-2), 3.66 (dq, *J* = 9.8, 6.2 Hz, 1H, H-5), 3.35 (s, 3H, CH₃ isopropylidene), 1.29 (d, *J* = 6.2 Hz, 3H, H-6) ¹³C NMR (101 MHz, CDCl₃) δ 138.4 (C_q), 128.3, 128.0, 127.6 (CH_{arom}), 109.2 (C_q isopropylidene), 98.1 (C-1), 81.1 (C-4), 78.7 (C-3), 76.0 (C-2), 72.9 (CH₂ Bn), 64.4 (C-5), 54.8 (CH₃ OMe), 28.0 (CH₃ isopropylidene), 26.3 (CH₃ isopropylidene), 17.9 (C-6). Spectra in agreement with literature.⁸²

Methyl 4-O-benzyl-a-L-rhamnopyranoside (S57)



S56 (2.90 g, 9.40 mmol) was dissolved in methanol with PTSA-H₂O (179 mg, 0.94 mmol, 0.1 eq) and heated to 50 °C. When TLC shows full conversion, the reaction is quenched with triethylamine (0.26 mL, 1.88 mmol, 0.2 eq) and concentrated under reduced pressure. The residue is purified over silica (25% acetone in pentane) yielding the title compound as white powder. Yield: 2.437 g, 8.75 mmol, 93%. ¹H NMR (400 MHz, CDCl₃) δ 7.46 – 7.14 (m, 5H,

CH_{arom}), 4.76 (d, J = 11.3 Hz, 1H, CHH Bn), 4.71 (d, J = 11.3 Hz, 1H, CHH Bn), 4.63 (d, J = 1.4 Hz, 1H, H-1), 3.93 – 3.84 (m, 2H, H-2, H-3), 3.69 (dq, J = 9.5, 6.3 Hz, 1H, H-5), 3.39 – 3.29 (m, 4H, CH₃ OMe, H-4), 2.84 (d, J = 3.8 Hz, 1H, OH), 2.67 (d, J = 5.2 Hz, 1H, OH), 1.35 (d, J = 6.3 Hz, 3H, H-6) ¹³C NMR (101 MHz, CDCl₃) δ 138.4 (C_q), 128.7, 128.1, 128.0 (CH_{arom}), 100.5 (C-1), 81.7 (C-4), 75.1 (CH₂ Bn), 71.6, 71.2 (C-2 and C-3), 67.1 (C-5), 54.9 (CH₃ OMe), 18.1 (C-6). Spectra in agreement with literature.⁸²

Methyl 3-O-allyl-4-O-benzyl-a-L-rhamnopyranoside (S58)



\$57 (1.43 g, 5 mmol) and dibutyltin oxide (1.618 g, 6.5 mmol, 1.3 eq) were refluxed in toluene for 2 hr with a Dean-Stark setup. The reaction mixture was concentrated under reduced pressure and the residue dissolved in DMF, after which Caesium fluoride (987 mg, 6.5 mmol, 1.3 eq) and allyl bromide (0.56 mL, 6.5 mmol, 1.3 eq) were added. The reaction mixture was stirred overnight, diluted with water and extracted twice with diethyl ether. Combined organic phases were dried and concentrated under reduced pressure. The residue was purified using flash chromatography (20% EtOAc in pentane) yielding the product as colourless oil. Yield: 1.428 g, 4.63 mmol, 93%. ¹H NMR (400 MHz, CDCl₃) δ 7.37 - 7.27 (m, 5H, CH_{arom}), 5.95 (ddt, J = 17.2, 10.4, 5.6 Hz, 1H, CH₂-CH=CH₂), 5.32 (dq, J = 17.2, 1.6 Hz, 1H, CH₂-CH=CHH), 5.20 (dq, J = 17.2, 1H 10.4, 1.4 Hz, 1H, CH₂-CH=CHH), 4.87 (d, J = 10.9 Hz, 1H, CHH Bn), 4.70 (d, J = 1.6 Hz, 1H, H-1), 4.63 (d, *J* = 10.9 Hz, 1H, CH*H* Bn), 4.19 (ddt, *J* = 12.7, 5.8, 1.4 Hz, 1H, C*H*H-CH=CH₂), 4.13 (ddt, J = 12.6, 5.5, 1.5 Hz, 1H, CHH-CH=CH₂), 4.00 (dt, J = 3.6, 1.8 Hz, 1H, H-2), 3.74 - 3.63 (m, 2H, H-3, H-5), 3.41 (t, J = 9.3 Hz, 1H, H-4), 3.34 (s, 3H, CH₃ OMe), 2.53 (d, J = 2.0 Hz, 1H, OH), 1.31 (d, J = 6.2 Hz, 3H, H-6), ¹³C NMR (101 MHz, CDCl₃) δ 138.5 (C₄), 134.6 (CH₂-CH=CH₂), 128.4, 128.0, 127.7 (CH_{arom}), 117.4 (CH₂-CH=CH₂), 100.0 (C-1), 79.9 (C-4), 79.6 (C-3), 75.3 (CH₂ Bn), 70.9 (CH2-CH=CH2), 68.6 (C-2), 67.1 (C-5), 54.8 (CH3 OMe), 17.9 (C-6). Spectra in agreement with literature.83

Methyl 3-O-allyl-2,4-di-O-benzyl-a-L-rhamnopyranoside (S59)



S58 (1.40 g, 4.54 mmol) was dissolved in DMF and cooled to 0 °C, after which NaH (60% dispersion in mineral oil, 272 mg, 6.81 mmol, 1.5 eq) was added. The solution was stirred for 10 minutes at 0 °C, benzyl bromide (0.81 mL, 6.81 mmol, 1.5 eq) was added and the reaction mixture was allowed to warm to RT. When TLC shows full conversion of the starting material, the reaction is quenched with water and extracted with diethyl ether. The organic phase was dried with MgSO₄ and concentrated under reduced pressure. The residue was purified over silica (10% diethyl ether in pentane), yielding the desired product as colourless oil. Yield: 1.454 g, 3.65 mmol, 80%. ¹H NMR (400 MHz, CDCl₃) δ 7.43 – 7.25 (m, 10H, CH_{arom}), 5.93 (ddt, *J* = 17.3, 10.6, 5.4 Hz, 1H, CH₂-CH=CH₂), 5.32 (dq, *J* = 17.2, 1.7 Hz, 1H, CH₂-CH=CHH), 5.17 (dq, *J* = 10.5, 1.5 Hz, 1H, CH₂-CH=CHH), 4.94 (d, *J* = 10.8 Hz, 1H, CHH Bn), 4.79 (d, *J* = 12.6 Hz, 1H, CHH Bn), 4.74 (d, *J* = 12.5 Hz, 1H, CHH Bn), 4.67 – 4.59 (m, 2H, CHH Bn, H-1), 4.08 (dq, *J* = 5.4, 1.4 Hz,

2H, CH₂-CH=CH₂), 3.77 – 3.69 (m, 2H, H-2, H-3), 3.68 – 3.60 (m, 1H, H-5), 3.59 – 3.54 (m, 1H, H-4), 3.29 (s, 3H, CH₃ OMe), 1.33 (d, J = 6.1 Hz, 3H, H-6) ¹³C NMR (101 MHz, CDCl₃) δ 138.8, 138.5 (C_q), 135.1 (CH₂-CH=CH₂), 128.5, 128.5, 128.1, 128.0, 127.8, 127.7 (CH_{arom}), 116.7 (CH₂-CH=CH₂), 99.2 (C-1), 80.5 (C-4), 79.9 (C-3), 75.5 (CH₂ Bn), 74.8 (C-2), 72.9 (CH₂ Bn), 71.1 (CH₂-CH=CH₂), 67.9 (C-5), 54.7 (CH₃ OMe), 18.1 (C-6). Spectra in agreement with literature.⁸⁴

Methyl 2,4-di-O-benzyl-a-L-rhamnopyranoside (38)



\$59 (1.40 g, 3.51 mmol) and 1,3-dimethylbarbituric acid (1.097 g, 7.03 mmol, 2 eq) were dissolved in methanol, flushed with nitrogen and heated to 40 °C. Tetrakis(triphenylphosphine)palladium(0) (203 mg, 0.176 mmol, 0.05 eq) was added under a flow of nitrogen. When TLC shows full conversion, the reaction mixture was concentrated to ca. 20% of the original volume, diluted with ethyl acetate and wash twice with sat. aq. NaHCO₃. The organic phase was dried with MgSO4 and concentrated under reduced pressure. The residue was purified over silica (15% acetone in pentane) yielding the title compound as colourless oil. Yield: 1.06 g, 2.96 mmol, 84 %. ¹H NMR (400 MHz, CDCl₃) δ 7.41 – 7.25 (m, 10H, CH_{arom}), 4.90 (d, J = 11.1 Hz, 1H, CHH Bn), 4.74 (d, J = 11.8 Hz, 1H, CHH Bn), 4.71 (d, J = 1.5 Hz, 1H, H-1), 4.65 (d, J = 11.1 Hz, 1H, CHH Bn), 4.58 (d, J = 11.7 Hz, 1H, CHH Bn), 3.92 (td, J = 9.2, 3.8 Hz, 1H, H-3), 3.71 (dd, J = 3.9, 1.6 Hz, 1H, H-2), 3.65 (dq, J = 9.5, 6.2 Hz, 1H, H-5), 3.37 - 3.25 (m, 4H, CH₃ OMe, H-4), 2.33 (d, J = 9.3 Hz, 1H, OH), 1.34 (d, J = 6.2 Hz, 3H, H-6) ¹³C NMR (101 MHz, CDCl₃) δ 138.7, 137.8 (C_q), 128.7, 128.5, 128.2, 128.1, 128.0, 127.8 (CH_{arom}), 98.0 (C-1), 82.4 (C-4), 78.7 (C-2), 75.1 (CH₂ Bn), 73.1 (CH₂ Bn), 71.7 (C-3), 67.1 (C-5), 54.8 (CH₃ OMe), 18.1 (C-6). Spectra in agreement with literature.84



Scheme S22: preparation of acceptor *39*: reagents and conditions: a) PTSA, MeOH, 50 °C, 77%; b) *i*: DBTO, toluene, reflux, *ii*: allyl bromide, CsF, DMF, 100% over 2 steps; c) BnBr, NaH, DMF, 78%; d) DDQ, DCM/H₂O (9:1), 92%; e) BzCl, pyridine 87%; f) Pd(Ph₃P)₄, DMBA, MeOH, 40 °C, 100%





2,3-O-isopropylidene-4-O-(2-naphthyl)methyl- α -L-rhamnopyranoside (**S54**, 2.56 g, 7.14 mmol) and PTSA-H₂O (136 mg, 0.71 mmol, 0.1 eq) were dissolved in MeOH and heated to 50 °C. When TLC showed full conversion, the reaction was quenched with trimethylamine (0.2 mL, 1.43 mmol, 0.2 eq) and concentrated under reduced pressure. The residue is purified over silica (50% EA/pentane), yielding the title compound as white powder. Yield: 1.76 g, 5.53 mmol, 77%. ¹H NMR (400 MHz, DMSO) δ 7.92 – 7.78 (m, 4H, CH_{arom}), 7.50 (td, *J* = 5.9, 3.0 Hz, 3H, CH_{arom}), 5.02 (d, *J* = 11.8 Hz, 1H, CHH Nap), 4.99 (d, *J* = 4.4 Hz, 1H, OH), 4.88 (d, *J* = 6.9 Hz, 1H, OH), 4.75 (d, *J* = 11.8 Hz, 1H, CHH Nap), 4.46 (d, *J* = 1.4 Hz, 1H, H-1), 3.68 – 3.62 (m, 2H, H-2, H-3), 3.48 (dq, *J* = 9.5, 6.2 Hz, 1H, H-5), 3.31 (t, *J* = 9.2 Hz, 1H, H-4), 3.23 (s, 3H, CH₃ OMe), 1.17 (d, *J* = 6.3 Hz, 3H, H-6); ¹³C NMR (101 MHz, DMSO) δ 136.8, 132.8, 132.4 (Cq), 127.7, 127.6, 127.6, 126.2, 126.1, 125.9, 125.8 (CH_{arom}), 101.0 (C-1), 80.8 (C-4), 73.8 (CH₂ Nap), 71.1, 70.8 (C-2, C-3), 66.9 (C-5), 54.1 (CH₃ OMe), 18.1 (C-6); HRMS: [M+Na]⁺ calcd for C₁₈H₂₂O₅Na 341.13594, found 341.13544.

Methyl 3-O-allyl-4-O-(2-naphthyl)methyl-a-L-rhamnopyranoside (S61)



Methyl 4-O-(2-naphthyl)methyl-a-L-rhamnopyranoside (S60, 1.59 g, 5 mmol) and dibutyltin oxide (1.49 g, 6 mmol, 1.2 eq) are suspended in toluene and heated to reflux in a Dean-Stark setup for 2 hr, after which the reaction mixture was concentrated under reduced pressure. The residue is dissolved in DMF after which caesium fluoride (911 mg, 6 mmol, 1.2 eq) and allyl bromide (0.52 mL, 6 mmol, 1.2 eq) were added. After overnight stirring at room temperature, the reaction mixture was diluted with water and extracted with diethyl ether. The organic phase was dried with MgSO4 and concentrated under reduced pressure. Silica chromatography (20% EtOAc in pentane) yields the title compound in quantitative yield as colourless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.84 - 7.77 (m, 4H, CH_{arom}), 7.49 - 7.44 (m, 3H, CH_{arom}), 5.95 (ddt, J = 17.2, 10.3, 5.6 Hz, 1H, CH₂-CH=CH₂), 5.32 (dq, J = 17.2, 1.6 Hz, 1H, CH₂-CH=CHH), 5.20 (dq, J = 10.4, 1.4 Hz, 1H, CH₂-CH=CHH), 5.02 (d, J = 11.0 Hz, 1H, CHH Nap), 4.79 (d, J = 11.2 Hz, 1H, CHH Nap), 4.71 (d, J = 1.7 Hz, 1H, H-1), 4.21 (ddt, J = 12.7, 5.7, 1.4 Hz, 1H, CHH-CH=CH₂), 4.15 (ddt, J = 12.7, 5.6, 1.5 Hz, 1H, CHH-CH=CH₂), 4.01 (dt, J = 3.6, 1.9 Hz, 1H, H-2), 3.80 - 3.66 (m, 2H, H-3, H-5), 3.47 (t, J = 9.4 Hz, 1H, H-4), 3.35 (s, 3H, CH₃ OMe), 2.59 (d, J = 2.1 Hz, 1H, OH), 1.34 (d, J = 6.2 Hz, 3H, H-5); 13 C NMR (101 MHz, CDCl₃) δ 136.1 (C_q), 134.7 (CH₂-CH=CH₂), 133.4, 133.1 (Cq), 128.2, 128.0, 127.8, 126.7, 126.1, 126.1, 126.0 (CHarom), 117.5 (CH2-CH=CH2), 100.2 (C-1), 80.0 (C-4), 79.7 (C-3), 75.5 (CH₂ Nap), 71.0 (CH₂-CH=CH₂), 68.7 (C-2), 67.2 (C-5), 54.9 (CH₃ OMe), 18.1 (C-6); HRMS: [M+Na]+ calcd for C₂₁H₂₆O₅Na 381.16725, found 381.166652

Methyl 3-O-allyl-2-O-benzyl-4-O-(2-naphthyl)methyl-α-L-rhamnopyranoside (S62)



S61 (1.70 g, 4.74 mmol) was dissolved in DMF and cooled to 0 °C after which NaH (60% dispersion in mineral oil, 285 mg, 7.11 mmol, 1.5 eq) was added. After stirring for 10 minutes, benzyl bromide (0.84 mL, 7.11 mmol, 1.5 eq) was added. The reaction mixture was allowed to

warm to RT and upon completion (as indicated by TLC) quenched with water. The aqueous phase was extracted twice with diethyl ether, the combined organic phases were dried with MgSO₄ and concentrated. The residue is purified over silica (10% diethyl ether in pentane), yielding the desired product as colourless oil. Yield: 1.67 g, 3.72 mmol, 78%. ¹H NMR (400 MHz, CDCl₃) δ 7.90 – 7.72 (m, 4H, CH_{arom}), 7.53 – 7.25 (m, 8H, CH_{arom}), 5.95 (ddt, *J* = 17.2, 10.6, 5.4 Hz, 1H, CH₂-CH=CH₂), 5.33 (dq, *J* = 17.2, 1.7 Hz, 1H, CH₂-CH=CHH), 5.18 (dq, *J* = 10.4, 1.5 Hz, 1H, CH₂-CH=CHH), 5.10 (d, *J* = 11.2 Hz, 1H, CHH Bn/Nap), 4.86 – 4.71 (m, 3H, CHH Bn/Nap, CH₂ Bn/Nap), 4.65 (d, *J* = 1.5 Hz, 1H, H-1), 4.10 (dq, *J* = 5.3, 1.3 Hz, 2H, CH₂-CH=CH₂), 3.82 – 3.73 (m, 2H, H-2, H-3), 3.73 – 3.59 (m, 2H, H-4, H-5), 3.29 (s, 3H, CH₃ OMe), 1.36 (d, *J* = 5.9 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 138.5, 136.4 (C_q), 135.1 (CH₂-CH=CH₂), 133.4, 133.1 (C_q), 128.5, 128.2, 128.0, 127.8, 126.6, 126.2, 126.1, 125.9 (CH_{arom}), 116.7 (CH₂-CH=CH₂), 99.2 (C-1), 80.6 (C-4), 80.0 (C-3), 75.5 (CH₂ Bn/Nap), 74.8 (C-2), 72.9 (CH₂ Bn/Nap), 71.1 (CH₂-CH=CH₂), 67.9 (C-5), 54.7 (CH₃ OMe), 18.2 (C-6); HRMS: [M+NH₄]⁺ calcd for C₂₈H₃₂O₅NH₄ 466.25880, found 466.25794.

Methyl 3-O-allyl-2-O-benzyl-a-L-rhamnopyranoside (S63)



S62 (1.6 g, 3.57 mmol) was dissolved in 20 mL 9:1 DCM/H₂O, after which DDQ (1.62 g, 7.13 mmol, 2 eq) was added. When TLC shows full conversion, the reaction mixture was diluted with DCM and washed twice with sat. aq. Bicarb. The organic phase was dried and concentrated under reduced pressure. Silica chromatography (10% acetone in pentane) yield the title compound as yellowish oil. Yield: 1.01 g, 3.28 mmol, 92%. ¹H NMR (400 MHz, CDCl₃) δ 7.40 – 7.27 (m, 5H), 5.90 (ddt, *J* = 17.1, 10.3, 5.6 Hz, 1H), 5.28 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.19 (dq, *J* = 10.4, 1.4 Hz, 1H), 4.76 – 4.58 (m, 3H), 4.01 (ddt, *J* = 12.5, 5.5, 1.5 Hz, 1H), 3.60 (ddt, *J* = 12.6, 5.8, 1.4 Hz, 1H), 3.75 (dd, *J* = 3.1, 1.8 Hz, 1H), 3.69 (td, *J* = 9.3, 2.0 Hz, 1H), 3.63 (dq, *J* = 9.3, 6.0 Hz, 1H), 3.53 (dd, *J* = 9.2, 3.1 Hz, 1H), 2.43 (d, *J* = 2.0 Hz, 1H), 1.34 (d, *J* = 6.0 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 138.1, 134.5, 128.4, 128.0, 127.8, 117.5, 99.2, 79.4, 73.4, 72.6, 71.6, 70.3, 68.2, 54.8, 17.8; HRMS: [M+Na]⁺ calcd for C₁₇H₂₄O₅Na 331.15160, found 331.15103.

Methyl 3-O-allyl-4-O-benzoyl-2-O-benzyl-a-L-rhamnopyranoside (S64)



S63 (975 mg, 3.16 mmol) is dissolved in 5 mL pyridine after which benzoyl chloride (0.55 mL, 4.74 mmol, 1.5 eq) was added slowly. When TLC shows that the reaction is complete, the mixture is diluted with ethyl acetate and washed with 2 x 100 mL 1M aq. HCl and with 100 mL sat. aq. NaHCO₃. The organic phase was dried and concentrated under reduced pressure. The residue is purified with silica chromatography (5% \rightarrow 10% ethyl acetate in pentane) to yield the desired compound as a colourless oil. Yield: 1.13 g, 2.74 mmol, 87%. ¹H NMR (400 MHz, CDCl₃) δ 8.09 – 8.04 (m, 2H, CH_{arom}), 7.60 – 7.54 (m, 1H, CH_{arom}), 7.45 (dd, *J* = 8.4, 7.1 Hz, 2H, CH_{arom}), 7.42 – 7.38 (m, 2H, CH_{arom}), 7.30 – 7.26 (m, 1H, CH_{arom}), 5.72 (ddt, *J* = 17.2, 10.3, 5.5 Hz, 1H, CH₂-CH=CH₂), 5.44 (t, *J* = 9.7 Hz, 1H, H-4), 5.16 (dq, *J* = 17.2, 1.7 Hz, 1H, CH₂-

Chapter 4

CH=CHH), 5.04 (dq, J = 10.4, 1.4 Hz, 1H, CH₂-CH=CHH), 4.85 (d, J = 12.5 Hz, 1H, CHH Bn), 4.75 (d, J = 12.5 Hz, 1H, CHH Bn), 4.71 (d, J = 1.8 Hz, 1H, H-1), 4.03 (ddt, J = 13.0, 5.4, 1.5 Hz, 1H, CHH-CH=CH₂), 3.92 (ddt, J = 13.1, 5.7, 1.5 Hz, 1H, CHH-CH=CH₂), 3.89 – 3.82 (m, 2H, H-3, H-5), 3.81 (dd, J = 3.2, 1.9 Hz, 1H, H-2), 3.36 (s, 3H, CH₃ OMe), 1.27 (d, J = 6.3 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 165.8 (C=O), 138.4 (C_q), 134.8 (CH₂-CH=CH₂), 133.1 (CH_{arom}), 130.3 (C_q), 129.8, 128.5, 128.4, 128.1, 127.7 (CH_{arom}), 117.1 (CH₂-CH=CH₂), 99.8 (C-1), 77.2 (C-3), 74.6 (C-2), 73.8 (C-4), 73.2 (CH₂ Bn), 71.3 (CH₂-CH=CH₂), 67.0 (C-5), 55.0 (CH₃ OMe), 17.8 (C-6); HRMS: [M+NH₄]⁺ calcd for C₂₄H₂₈O₆NH₄ 430.22241, found 430.22153.

Methyl 4-O-benzoyl-2-O-benzyl-a-L-rhamnopyranoside (39)



Nr. (1.10 g, 2.67 mmol) and 1,3-Dimethylbarbituric acid (833 mg, 5.33 mmol, 2 eq) were dissolved in methanol. The solution was flushed with nitrogen and heated to 40 °C, after which Pd(PPh₃)₄ (154 mg, 0.133 mmol, 0.05 eq) was added under a flow of nitrogen. When TLC shows full conversion, the reaction mixture is cooled to RT, diluted with ethyl acetate and washed with sat. aq. NaHCO₃. The aqueous phase was extracted with ethyl acetate, combined organic phases were dried with MgSO4 and concentrated under reduced pressure. The residue is purified over silica (30% diethyl ether in pentane), yielding the title compound in quantitative yield as a yellowish oil that solidifies over a few days. $\left[\alpha\right]_{D}^{25} = -0.29^{\circ}$ (c = 0.34, CHCl₃); IR (thin film): 711, 1069, 1269, 1316, 1452, 1724; ¹H NMR (400 MHz, CDCl₃) δ 8.13 - 8.00 (m, 2H, CH_{arom}), 7.56 (ddt, J = 8.7, 7.0, 1.3 Hz, 1H, CHarom), 7.47 - 7.41 (m, 2H, CHarom), 7.39 - 7.29 (m, 5H, CHarom), 5.14 (t, J = 9.8 Hz, 1H, H-4), 4.83 – 4.70 (m, 2H, H-1, CHH Bn), 4.62 (d, J = 11.7 Hz, 1H, CHH Bn), 3.98 (ddd, *J* = 11.0, 9.8, 3.7 Hz, 1H, H-3), 3.89 (dq, *J* = 9.7, 6.3 Hz, 1H, H-5), 3.78 (dd, *J* = 3.8, 1.6 Hz, 1H, H-2), 3.38 (s, 3H, CH₃ OMe), 2.40 (d, *J* = 11.0 Hz, 1H, OH), 1.27 (d, *J* = 6.3 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 166.7 (C=O), 137.6 (C_q), 133.3 (CH_{arom}), 130.0 (C_q), 129.9, 128.7, 128.5, 128.2, 128.0 (CHarom), 98.3 (C-1), 78.5 (C-2), 75.6 (C-3), 73.3 (CH2 Bn, 69.9 (C-3), 66.1 (C-5), 55.1 (CH₃ OMe), 17.7 (C-6); HRMS: [M+Na]⁺ calcd for C₂₁H₂₄O₆Na 395.14651, found 395.14590

Preparation of acceptor 40



Scheme S23: preparation of acceptor **40**: reagents and conditions: *a*) BzCN, DMAP, DCM, -78 °C, 81%

Methyl 2-O-benzoyl-4-O-benzyl-a-L-rhamnopyranoside (40)



Nr. (805 mg, 3 mmol) and benzovl cyanide (433 mg, 3.30 mmol, 1.1 eq) were dissolved in dichloromethane. 3A molecular sieves were added, the solution was stirred for 30 min at room temperature and subsequently cooled to -78 °C. DMAP (37 mg, 0.30 mmol, 0.1 eq) was added and the reaction mixture kept at that temperature for 2 hr after which it was slowly allowed to warm to RT. When TLC showed full conversion, the reaction was guenched with MeOH and sat aq. NH₄Cl, diluted with dichloromethane, washed with sat aq. NH₄Cl and sat aq. NaHCO₃. The organic phase was dried with MgSO4 and concentrated under reduced pressure. The residue was purified over silica (15% EA in pentane) yielding the title compound as colourless oil. Yield: 900 mg, 2.42 mmol, 81%. ¹H NMR (400 MHz, CDCl₃) δ 8.15 - 7.97 (m, 2H, CH_{arom}), 7.59 (ddt, J = 8.7, 6.9, 1.3 Hz, 1H, CHarom), 7.53 - 7.43 (m, 2H, CHarom), 7.40 - 7.28 (m, 5H, CHarom), 5.33 (dd, J = 3.6, 1.7 Hz, 1H, H-2), 4.86 (d, J = 11.1 Hz, 1H, CHH Bn), 4.77 - 4.71 (m, 2H, CHH Bn, H-1), 4.20 (ddd, *J* = 9.0, 5.1, 3.5 Hz, 1H, H-3), 3.79 (dq, *J* = 9.5, 6.2 Hz, 1H, H-5), 3.46 (t, *J* = 9.4 Hz, 1H, H-4), 3.37 (s, 3H, CH₃ OMe), 2.28 (d, J = 5.1 Hz, 1H, OH), 1.40 (d, J = 6.3 Hz, 3H, H-6) ¹³C NMR (101 MHz, CDCl₃) δ 166.4 (C=O), 138.3 (C_q), 133.5, 130.0 (CH_{arom}), 129.8 (C_q), 128.6, 128.6, 128.1, 128.0 (CH_{arom}), 98.5 (C-1), 81.8 (C-4), 75.2 (CH₂ Bn), 73.3 (C-2), 70.6 (C-3), 67.4 (C-5), 55.1 (CH₃ OMe), 18.3 (C-6). Spectra in agreement with literature.⁸³

Preparation of acceptor 41



Scheme S24: preparation of acceptor *41*: reagents and conditions: *a*) *BzCl*, pyridine, 100%; PTSA, *MeOH*, 50 °C, 78%; *c*) *BzCN*, *DMAP*, *DCM*, -78 °C, 44%

Methyl 4-O-benzoyl-2,3-isopropylidene-a-L-rhamnopyranoside (S65)



S53 (2.18 g, 10 mmol) was dissolved in 10 mL pyridine, after which benzoyl chloride (1.74 mL, 15 mmol, 1.5 eq) was added dropwise. When TLC shows full consumption of the starting material, the reaction mixture is diluted with ethyl acetate and washed twice with water. The organic phase is dried with MgSO₄ and concentrated under reduced pressure. Residual pyridine was removed by coevaporation with toluene. The residue was purified over silica (10% EtOAc in pentane) yielding the title compound in quantitative yield as colourless oil that slowly solidifies. ¹H NMR (400 MHz, CDCl₃) δ 8.10 – 8.03 (m, 2H, CH_{arom}), 7.60 – 7.50 (m, 1H, CH_{arom}), 7.44 (dd, *J* = 8.4, 7.1 Hz, 2H, CH_{arom}), 5.13 (dd, *J* = 10.1, 7.8 Hz, 1H, H-4), 4.96 (app. s, 1H, H-1), 4.34 (dd, *J* = 7.8, 5.4 Hz, 1H, H-3), 4.20 (dd, *J* = 5.4, 0.7 Hz, 1H, H-2), 3.87 (dq, *J* = 10.1, 6.3 Hz, 1H, H-5), 3.42 (s, 3H, CH₃ OMe), 1.63 (s, 3H, CH₃ isopropylidene), 1.36 (s, 3H, s, 3H, CH₃ isopropylidene), 1.23 (d, *J* = 6.4 Hz, 3H, H-6) ¹³C NMR (101 MHz, CDCl₃) δ 165.9 (C=O), 133.3, 129.9, 128.5 (CH_{arom}), 110.0 (C_q isopropylidene), 98.2 (C-1), 76.1 (C-2), 76.0 (C-3), 75.1 (C-4), 64.1 (C-5), 55.1 (CH₃
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OMe), 27.9 (CH₃ isopropylidene), 26.5 (CH₃ isopropylidene), 17.2 (C-6). Spectra in agreement with literature.⁸⁵

Methyl 4-O-benzoyl-a-L-rhamnopyranoside (S66)

S65 (3.5 g, 10.9 mmol) was dissolved in methanol with PTSA-H₂O (207 mg, 1.09 mmol, 0.1 eq) and heated to 50 °C. When TLC shows full conversion, the reaction is quenched with triethylamine (0.31 mL, 2.17 mmol, 0.2 eq) and concentrated under reduced pressure. The residue is purified over silica (20% acetone in pentane) yielding the title compound as viscous colourless oil. Yield: 2.38 g, 8.43 mmol, 78%. ¹H NMR (400 MHz, CDCl₃) δ 8.16 – 7.91 (m, 2H, CH_{arom}), 7.63 – 7.53 (m, 1H, CH_{arom}), 7.44 (dd, *J* = 8.6, 7.0 Hz, 2H, CH_{arom}), 5.09 (t, *J* = 9.3 Hz, 1H, H-4) 4.76 (d, *J* = 1.2 Hz, 1H, H-1), 4.04 – 3.99 (m, 2H, H-2, H-3), 3.94 (dq, *J* = 9.8, 6.3 Hz, 1H, H-5), 3.40 (s, 3H, CH₃ OMe), 1.28 (d, *J* = 6.3 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 167.5 (C=O), 133.5, 130.0 (CH_{arom}), 129.6 (Cq), 128.6 (CH_{arom}), 100.7 (C-1), 76.1 (C-4), 71.0, 70.4 (C-2, C-3), 65.8 (C-5), 55.2 (CH₃ OMe), 17.7 (C-6). Spectra in agreement with literature.⁸⁶

Methyl 2,4-di-O-benzoyl-a-L-rhamnopyranoside (41)



S66 (1.129g, 4 mmol) and benzoyl cyanide (557 mg, 4.40 mmol, 1.1 eq) were dissolved in dichloromethane. 3 Å molecular sieves were added, the solution was stirred for 30 min at room temperature and subsequently cooled to -78 °C. DMAP (49 mg, 0.40 mmol, 0.1 eq) was added and the reaction mixture kept at that temperature for 2 hr after which it was slowly allowed to warm to RT. When TLC showed full conversion, the reaction was quenched with MeOH and sat aq. NH₄Cl, diluted with dichloromethane, washed with sat aq. NH₄Cl and sat aq. NaHCO₃. The organic phase was dried with MgSO₄ and concentrated under reduced pressure. The residue was purified over silica (15% EA in pentane) yielding the title compound as colourless oil. Yield: 672 mg, 1.74 mmol, 44% ¹H NMR (400 MHz, CDCl₃) δ 8.14 – 8.05 (m, 4H, CH_{arom}), 7.64 – 7.57 (m, 2H, CH_{arom}), 7.52 – 7.44 (m, 4H, CH_{arom}), 5.38 (dd, *J* = 3.5, 1.7 Hz, 1H, H-2), 5.26 (t, *J* = 9.8 Hz, 1H, H-4), 4.87 (d, *J* = 1.6 Hz, 1H, H-1), 4.30 (ddd, *J* = 9.9, 8.1, 3.5 Hz, 1H, H-3), 4.11 – 3.99 (m, 1H, H-5), 3.45 (s, 3H, CH₃ OMe), 2.44 (d, *J* = 8.2 Hz, 1H, OH), 1.33 (d, *J* = 6.2 Hz, 3H, H-6) ¹³C NMR (101 MHz, CDCl₃) δ 167.2, 166.2 (C=O), 133.7, 133.6, 130.0, 130.0 (CH_{arom}), 129.6, 129.5 (Cq), 128.7, 128.6 (CH_{arom}), 98.5 (C-1), 75.7 (C-4), 73.3 (C-2), 69.1 (C-3), 66.2 (C-5), 55.4 (CH₃ OMe), 17.8 (C-6). Spectra in agreement with literature.⁸⁷





Scheme S25: preparation of acceptor 42: reagents and conditions: *a*) i: PTSA, MeOH, 50 °C, ii: DBTO, toluene, reflux, iii: CsF, BnBr, DMF, 77% over 3 steps

Methyl 3,4-di-O-benzyl-a-L-rhamnopyranoside (42)



Methyl 4-O-benzyl-2,3-O-ispropylidene-a-L-rhamnopyranoside (\$56, 1.12 g, 3.63 mmol) and PTSA-H₂O (69 mg, 0.36 mmol, 0.1 eq) were dissolved in methanol. The reaction mixture was heated to 50 °C. When TLC shows full removal of the isopropylidene, triethylamine (0.1 mL, 0.73 mmol, 0.2 eq) was added and the mixture was concentrated under reduced pressure. The residue was dissolved in toluene with dibutyltin oxide (1.18 g, 4.72 mmol, 1.3 eq) and refluxed for 2.5 hr in a Dean-Stark setup. The reaction mixture was cooled to RT and concentrated under reduced pressure. The residue was dissolved in DMF and caesium fluoride (717 mg, 4.72 mmol, 1.3 eq) and benzyl bromide (0.56 mL, 4.72 mmol, 1.3 eq) were added. After 72 hr stirring, the reaction mixture was diluted with water and extracted twice with diethyl ether. Combined organic phases were dried with MgSO4 and concentrated. The residue was purified over silica (10% Et2O in pentane) yielding the title compound as colourless oil. Yield: 1.00 g, 2.79 mmol, 77%. ¹H NMR (400 MHz, CDCl₃) δ 7.42 - 7.26 (m, 10H, CH_{arom}), 4.88 (d, J = 10.9 Hz, 1H, CHH Bn), 4.70 (d, J = 1.7 Hz, 1H, H-1), 4.68 (s, 2H, CH₂ Bn), 4.64 (d, J = 10.9 Hz, 1H, CHH Bn), 4.02 (dt, J = 3.6, 1.8 Hz, 1H, H-2), 3.82 (dd, J = 9.1, 3.4 Hz, 1H, H-3), 3.70 (dq, J = 9.6, 6.2 Hz, 1H, H-5), 3.45 (t, J = 9.4 Hz, 1H, H-4), 3.34 (s, 3H, CH₃ OMe), 2.53 (d, J = 1.9 Hz, 1H, OH), 1.32 (d, J = 6.3 Hz, 3H, H-6), ¹³C NMR (101 MHz, CDCl₃) δ 138.5, 138.0 (C_a), 128.7, 128.5, 128.1, 128.0, 127.8 (CH_{arom}), 100.1 (C-1), 80.2, 80.0 (C-3, C-4), 75.5, 72.1 (CH₂ Bn), 68.6 (C-2), 67.2 (C-5), 54.9 (CH₃ OMe), 18.0 (C-6). Spectra in agreement with literature.88

Fucose acceptors

Preparation of acceptor 43



Scheme S26: preparation of acceptor **43**: reagents and conditions: *a*) *i*: TsCl, pyridine, *ii*: LiAlH₄, THF, reflux, 52% over 2 steps

Methyl 2,3-di-O-benzyl-a-D-fucopyranoside (43)



Methyl 2,3,-di-O-benzyl-a-D-galactopyranoside (\$38, 0.75 g, 2 mmol) was dissolved in pyridine (3.3 mL, 40 mmol, 20 eq.) and cooled to 0 °C. Tosyl chloride (0.458 g, 2.4 mmol, 1.2 eq) was added and the reaction mixture was allowed to warm to RT overnight, diluted with ethyl acetate and washed with 1 M HCl and sat. aq. NaHCO3. The organic phase was dried with MgSO4 and concentrated under reduced pressure to yield the crude tosylate which was used without further purification. The tosylate was dissolved in THF, LiAlH₄ (2.50 mL of a 2.4M solution in 2methyltetrahydrofuran, 6 mmol, 3 eq) was added and the reaction mixture was heated to a gentle reflux. When TLC shows full conversion, the reaction mixture was cooled to 0 °C and carefully quenched with sat. aq. NaHCO₃. Solids were filtered off over celite and the filtrate was extracted with ethyl acetate. The organic phase was washed with 1M HCl, sat. aq. NaHCO3 and brine, dried with MgSO₄ and concentrated. The residue was purified over silica (30%→50% EA in pentane) to give the title compound as colourless oil. Yield: 373 mg, 1.04 mmol, 52%. ¹H NMR (400 MHz, CDCl₃) δ 7.45 - 7.21 (m, 10H, CH_{arom}), 4.80 (d, J = 11.9 Hz, 2H, 2x CHH Bn), 4.68 (dd, J = 13.6, 11.9 Hz, 2H, 2x CHH Bn), 4.62 (d, J = 3.4 Hz, 1H, H-1), 3.91 – 3.75 (m, 4H, H-2, H-3, H-4, H-5), 3.36 (s, 3H, CH₃ OMe), 2.49 (s, 1H, OH), 1.26 (d, I = 6.6 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 138.5, 138.3 (C_q), 128.6, 128.4, 128.1, 127.9, 127.9, 127.8 (CH_{arom}), 98.6 (C-1), 78.0 (C-3), 75.6 (C-2), 73.5, 72.8 (CH₂ Bn), 70.4 (C-4), 65.1 (C-5), 55.4 (CH₃ OMe), 16.2 (C-6). Spectra in agreement with literature.89

Preparation of isopropylidene intermediates of fucose acceptors



Scheme S27: preparation of isopropylidene intermediates: reagents and conditions: a) i: MeOH, amberlite-H⁺, reflux, ii: Ac₂O, pyridine, 52% over 2 steps; b) i: NaOMe, MeOH, ii: PTSA, 2,2-dimethoxypropane, 76% over 2 steps; c) Benzyl bromide, NaH, DMF, 82%; d) allyl bromide, NaH, DMF, 97%; e) NapBr, NaH, DMF, 77%

Methyl 2,3,4-tri-O-acetyl-a-L-fucopyranoside (S68)

Fucose (**S67**, 5.0 g, 30.5 mmol) was dissolved in methanol, after which 8 g Amberlite IR-120 Hform was added. The mixture was refluxed for 24 hr, cooled to RT and filtered to remove the Amberlite. The filtrate was concentrated under reduced pressure, coevaporated with toluene and dissolved in 30 mL pyridine. Ac₂O (17.3 mL, 183 mmol, 6 eq) was added and the mixture was reacted overnight, after which it was diluted with ethyl acetate and washed with 1 M HCl and sat. aq. NaHCO₃. The organic phase was dried with MgSO₄ and concentrated under reduced pressure, yielding a mixture of both anomers. The desired α -anomer was isolated via silica chromatography (20% diethyl ether in pentane, first eluting product) as a colourless oil. Yield: 4.92 g, 16.2 mmol, 53%.¹H NMR (300 MHz, CDCl₃) δ 5.36 (dd, *J* = 10.8, 3.4 Hz, 1H, H-3), 5.30 (dd, *J* = 3.4, 1.3 Hz, 1H, H-4), 5.15 (dd, *J* = 10.8, 3.7 Hz, 1H, H-2), 4.94 (d, *J* = 3.7 Hz, 1H, H-1), 4.18 – 4.10 (m, 1H, H-5), 3.40 (s, 3H, CH₃ OMe), 2.18 (s, 3H, CH₃ Ac), 2.09 (s, 3H, CH₃ Ac), 1.99 (s, 3H, CH₃ Ac), 1.16 (d, *J* = 6.5 Hz, 3H, H-6). Spectra in agreement with literature.⁹⁰

Methyl 3,4-O-isopropylidene-a-L-fucopyranoside (S69)



Methyl 2,3,4-tri-*O*-acetyl- α -L-fucopyranoside (**S68**, 9.95 g, 32.7 mmol) and sodium methoxide (353 mg, 6.54 mmol, 0.2 eq) were dissolved in methanol. When TLC shows full deprotection, the solution was acidified with Amberlite IR-120 H-form to a pH of 5 and filtered over a short path of celite. The filtrate was concentrated under reduced pressure and residual water and methanol were removed by azeotropic distillation with toluene. The residue was suspended in 2,2-dimehtoxypropane (40 mL, 327 mmol, 10 eq) and PTSA-H₂O (622 mg, 3.27 mmol, 0.1 eq) was added. After overnight stirring, triethylamine (0.92 mL, 6.54 mmol, 0.2 eq) was added and the mixture was concentrated under reduced pressure. Silica chromatography (10% acetone in pentane) yields the title compound as colourless oil. Yield: 5.40 g, 24.7 mmol, 76%. ¹H NMR (400 MHz, CDCl₃) δ 4.72 (d, *J* = 3.9 Hz, 1H, H-1), 4.19 (t, *J* = 6.3 Hz, 1H, H-3), 4.11 (qd, *J* = 6.7, 2.4 Hz, 1H, H-5), 4.05 (dd, *J* = 5.9, 2.4 Hz, 1H, H-4), 3.79 (td, *J* = 6.7, 3.8 Hz, 1H, H-2), 3.44 (s, 3H, CH₃ OMe), 2.43 (d, *J* = 6.7 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 109.3 (C_q isopropylidene), 1.33 (d, *J* = 6.7 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 109.3 (C_q isopropylidene), 16.4 (C-6). Spectra in agreement with literature.⁹¹

Methyl 2-O-benzyl-3,4-O-isopropylidene-α-L-fucopyranoside (S70)



Methyl 3,4-O-isopropylidene- α -L-fucopyranoside (**S69**, 1.5 g, 6.87 mmol), benzyl bromide (1.22 mL, 10.3 mmol, 1.5 eq) and sodium hydride (60% dispersion in mineral oil, 412 mg, 10.3 mmol, 1.5 eq) were dissolved in dimethylformamide. When TLC shows full conversion, the reaction was quenched with water and extracted with diethyl ether. The organic phase was dried with MgSO₄ and concentrated under reduced pressure. The residue was purified over silica (10% diethyl ether in pentane), yielding the title compound as colourless oil. Yield: 1.74 g, 5.65 mmol, 82%. ¹H NMR (400 MHz, CDCl₃) δ 7.41 – 7.24 (m, 5H, CH_{arom}), 4.82 (d, *J* = 12.6 Hz, 1H, CHH Bn), 4.72 (d, *J* =

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12.7 Hz, 1H, CH*H* Bn), 4.61 (d, J = 3.5 Hz, 1H, H-1), 4.32 (dd, J = 7.9, 5.4 Hz, 1H, H-3), 4.11 – 4.01 (m, 2H, H-4, H-5), 3.50 (dd, J = 7.9, 3.6 Hz, 1H, H-2), 3.38 (s, 3H, CH₃ OMe), 1.40 (s, 3H, CH₃ isopropylidene), 1.35 (s, 3H, CH₃ isopropylidene), 1.32 (d, J = 6.7 Hz, 3H, H-6), ¹³C NMR (101 MHz, CDCl₃) δ 138.3 (C_q), 128.5, 128.1, 127.9 (CH_{arom}), 108.9 (C_q isopropylidene), 98.5 (C-1), 76.3, 76.2, 76.2 (C-2, C-3, C-4), 72.4 (CH₂ Bn), 62.9 (C-5), 55.6 (CH₃ OMe), 28.3, 26.6 (CH₃ isopropylidene), 16.4 (C-6). Spectra in agreement with literature.⁹²

Methyl 2-O-allyl-3,4-O-isopropylidene-α-L-fucopyranoside (S71)



Methyl 3,4-O-isopropylidene-a-L-fucopyranoside (**S69**, 1.5 g, 6.87 mmol), allyl bromide (0.89 mL, 10.3 mmol, 1.5 eq) and sodium hydride (60% dispersion in mineral oil, 247 mg, 10.3 mmol, 1.5 eq) were dissolved in DMF. After full conversion, the reaction was quenched with water and extracted with diethyl ether. The organic phase was dried with MgSO₄ and concentrated under reduced pressure. Silica chromatography (10% acetone in pentane) yields the title compound as colourless oil. Yield: 1.71 g, 6.64 mmol, 97%. ¹H NMR (400 MHz, CDCl₃) δ 5.93 (dddd, *J* = 17.3, 10.3, 6.3, 5.5 Hz, 1H, CH₂-CH=CH₂), 5.28 (dq, *J* = 17.3, 1.6 Hz, 1H, CH₂-CH=CHH), 5.19 (dq, *J* = 10.3, 1.3 Hz, 1H, CH₂-CH=CHH), 4.73 (d, *J* = 3.5 Hz, 1H, H-1), 4.32 – 4.23 (m, 2H, H-3, CHH-CH=CH₂), 4.18 (ddt, *J* = 13.0, 6.3, 1.3 Hz, 1H, CH₃-CH=CH₂), 4.12 – 4.02 (m, 2H, H-4, H-5), 3.52 (dd, *J* = 7.9, 3.6 Hz, 1H, H-2), 3.41 (s, 3H, CH₃ OMe), 1.53 (s, 3H, CH₃ isopropylidene), 1.39 – 1.30 (m, 6H, H-6, CH₃ isopropylidene), ¹³C NMR (101 MHz, CDCl₃) δ 135.0 (CH₂-CH=CH₂), 117.8 (CH₂-CH=CH₂), 108.9 (Cq isopropylidene), 98.5 (C-1), 76.5, 76.3, 76.1 (C-2, C-3, C-4), 71.9 (CH₂-CH=CH₂), 62.9 (C-5), 55.6 (CH₃ OMe), 28.4, 26.5 (CH₃ isopropylidene), 16.4 (C-6). Spectra in agreement with literature.⁹³

Methyl 3,4-O-isopropylidene-2-O-(2-naphthyl)methyl-a-L-fucopyranoside (S72)



Methyl 3,4-O-isopropylidene-α-L-fucopyranoside (1 g, 4.58 mmol), 2-(Bromomethyl)naphthalene (1.52 g, 6.87 mmol, 1.5 eq) and sodium hydride (60% dispersion in mineral oil, 275 mg, 6.87 mmol, 1.5 eq) were dissolved in DMF. When TLC shows full conversion, the reaction was quenched with water and extracted with diethyl ether. The organic phase was dried with MgSO4 and concentrated under reduced pressure. The residue was purified over silica (10% diethyl ether in pentane) to yield the title compound as colourless oil. Yield: 1.27 g, 3.54 mmol, 77%. ¹H NMR (400 MHz, CDCl₃) δ 7.91 – 7.79 (m, 4H, CH_{arom}), 7.55 (dd, J = 8.4, 1.7 Hz, 1H, CH_{arom}), 7.52 – 7.45 (m, 2H, CH_{arom}), 5.01 (d, J = 12.2 Hz, 1H, CHH Nap), 4.91 (d, J = 12.7 Hz, 1H, CHH Nap), 4.66 (d, J = 3.6 Hz, 1H, H-1), 4.39 (dd, J = 7.9, 5.5 Hz, 1H, H-3), 4.17 -4.05 (m, 2H, H-4, H-5), 3.58 (dd, J = 7.9, 3.5 Hz, 1H, H-2), 3.41 (s, 3H, CH₃ OMe), 1.41 (s, 3H, CH₃ isopropylidene), 1.38 (s, 3H, CH₃ isopropylidene), 1.34 (d, J = 6.7 Hz, 3H, H-6), ¹³C NMR (101 MHz, CDCl₃) δ 135.8, 133.3, 133.2 (C_q), 128.3, 128.0, 127.8, 127.0, 126.2, 126.1, 126.0 (CH_{arom}), 108.9 (C_q isopropylidene), 98.5 (C-1), 76.3, 76.2, 76.2 (C-2, C-3, C-4), 72.6 (CH₂ Nap), 62.9 (C-5), 55.6 (CH₃ OMe, 28.3, 26.5 (CH₃ isopropylidene), 16.4 (C-6). Spectra in agreement with literature.⁹⁴



Scheme **S28**: preparation of acceptor **45**: reagents and conditions: a) PTSA, MeOH, 91%; b) i: DBTO, toluene reflux, ii: allyl bromide, CsF, DMF, 58%; c) BnBr, NaH, DMF, %; d) DMBA, $Pd(Ph_3P)_4$, MeOH, 40 °C, 96%

Methyl 2-O-benzyl-a-L-fucopyranoside (S73)



Methyl 2-O-benzyl-3,4-O-isopropylidene- α -L-fucopyranoside (**S70**, 1.40 g, 4.54 mmol) and PTSA-H₂O (86 mg, 0.45 mmol, 0.1 eq) were dissolved in methanol and stirred until TLC showed full conversion of the starting material. 0.19 mL triethylamine was added and the reaction mixture was concentrated under reduced pressure. The residue was purified over silica (30% EtOAc in pentane) to give the title compound as colourless oil. Yield: 1.11 g, 4.14 mmol, 91%. ¹H NMR (400 MHz, CDCl₃) δ 7.38 – 7.28 (m, 5H, CH_{arom}), 4.68 – 4.63 (m, 3H, H-1, CH₂ Bn), 3.97 (dt, *J* = 9.8, 3.1 Hz, 1H, H-3), 3.94 – 3.88 (m, 1H, H-5), 3.81 – 3.75 (m, 1H, H-4), 3.69 (dd, *J* = 9.9, 3.5 Hz, 1H, H-2), 3.34 (s, 3H, CH₃ OMe), 2.79 (d, *J* = 3.2 Hz, 1H, 3-OH), 2.63 (d, *J* = 2.7 Hz, 1H, 4-OH), 1.27 (d, *J* = 6.6 Hz, 3H, H-6), ¹³C NMR (101 MHz, CDCl₃) δ 138.0 Cq), 128.6, 128.2, 128.1 (CH_{arom}), 97.7 (C-1), 76.5 (C-2), 72.8 (CH₂ Bn), 71.6 (C-4), 69.5 (C-3), 65.3 (C-5), 55.3 (CH₃ OMe), 16.1 (C-6). Spectra in agreement with literature.⁹⁵

Methyl 3-O-allyl-2-O-benzyl-a-L-fucopyranoside (S74)



Methyl 2-O-benzyl- α -L-fucopyranoside (**S73**, 671 mg, 2.5 mmol) and dibutyltin oxide (809 mg, 3.25 mmol, 1.3 eq) were refluxed in toluene for 2 hr, while water was removed using a Dean-Stark trap. The reaction mixture was cooled to RT and concentrated under reduced pressure. The residue was dissolved in DMF, after which CsF (494 mg, 3.25 mmol, 1.3 eq) and allyl bromide (0.28 mL, 3.25 mmol, 1.3 eq) were added. The reaction mixture was stirred overnight, after which

it was diluted with water and extracted with diethyl ether. The organic phase was dried with MgSO₄ and concentrated under reduced pressure. Silica chromatography (30% diethyl ether in pentane) yield the title compound as colourless oil. Yield: 446 mg, 1.45 mmol, 58%. ¹H NMR (400 MHz, CDCl₃) δ 7.42 – 7.19 (m, 5H, CH_{arom}), 5.95 (ddt, *J* = 17.2, 10.4, 5.6 Hz, 1H, CH₂-CH=CH₂), 5.32 (dq, *J* = 17.2, 1.7 Hz, 1H, CH₂-CH=CHH), 5.20 (dt, *J* = 10.3, 1.5 Hz, 1H, CH₂-CH=CHH), 4.78 (d, *J* = 12.1 Hz, 1H, CHH Bn), 4.64 (d, *J* = 12.1 Hz, 1H, CHH Bn), 4.61 (d, *J* = 2.7 Hz, 1H, H-1), 4.29 – 4.16 (m, 2H, CH₂-CH=CH₂), 3.89 (q, *J* = 6.6 Hz, 1H, H-5), 3.83 (q, *J* = 1.5 Hz, 1H, H-4), 3.79 – 3.72 (m, 2H, H-2, H-3), 3.36 (s, 3H, CH₃ OMe), 2.60 – 2.31 (m, 1H, OH), 1.28 (d, *J* = 6.6 Hz, 3H, H-6), ¹³C NMR (101 MHz, CDCl₃) δ 138.5 (C_q), 134.9 (CH₂-CH=CH₂), 128.5, 128.1, 127.9 (CH_{arom}), 117.4 (CH₂-CH=CH₂), 98.7 (C-1), 77.5, 75.3 (C-2, C-3), 73.5 (CH₂ Bn), 71.6 (CH₂-CH=CH₂), 70.4 (C-4), 65.1 (C-5), 55.4 (CH₃ OMe), 16.2 (C-6); HRMS: [M+H]⁺ calcd for C₁₇H₂₄O₅H 309.16965, found 309.14832.

Methyl 3-O-allyl-2,4-di-O-benzyl-a-L-fucopyranoside (S75)

Methyl 3-O-allyl-2-O-benzyl-a-L-fucopyranoside (S74, 425 mg, 1.38 mmol), benzyl bromide (0.33 mL, 2.76 mmol, 1.5 eq) and sodium hydride (60% dispersion in mineral oil, 110 mg, 2.76 mmol, 1.5 eq) were dissolved in DMF. After full conversion of the starting material, the reaction was quenched with water and extracted with diethyl ether. The organic phase was dried with MgSO4 and concentrated under reduced pressure. Silica chromatography (25% diethyl ether in pentane) yield the title compound as colourless oil. Yield: 438 mg, 1.10 mmol, 80%). ¹H NMR (400 MHz, CDCl₃) δ 7.41 - 7.25 (m, 10H, CH_{arom}), 5.98 (ddt, J = 17.2, 10.5, 5.2 Hz, 1H, CH₂-CH=CH₂), 5.36 (dq, J = 17.2, 1.8 Hz, 1H, CH₂-CH=CHH), 5.19 (dq, J = 10.5, 1.5 Hz, 1H, CH₂-CH=CHH), 4.98 (d, J = 11.6 Hz, 1H, CHH Bn), 4.82 (d, J = 12.1 Hz, 1H, CHH Bn), 4.70 - 4.62 (m, 3H, H-1, 2x CHH Bn), 4.31 (ddt, J = 13.0, 5.0, 1.6 Hz, 1H, CHH-CH=CH₂), 4.20 (ddt, J = 13.1, 5.5, 1.5 Hz, 1H, CHH-CH=CH₂), 3.97 (dd, J = 10.1, 3.7 Hz, 1H, H-2), 3.88 - 3.77 (m, 2H, H-3, H-5), 3.63 (dd, J = 2.9, 1.3 Hz, 1H, H-4), 3.34 (s, 3H, CH₃ OMe), 1.12 (d, J = 6.5 Hz, 3H, H-6), ¹³C NMR (101 MHz, CDCl₃) δ 138.8 (C_α), 135.4 (CH₂-CH=CH₂), 128.6, 128.4, 128.3, 128.2, 127.7, 127.7 (CHarom), 116.4 (CH2-CH=CH2), 99.0 (C-1), 79.1 (C-3), 77.6 (C-4), 76.1 (C-2), 74.8, 73.6 (CH₂ Bn), 72.0 (CH₂-CH=CH₂), 66.1 (C-5), 55.4 (CH₃ OMe), 16.7 (C-6); HRMS: [M+Na]⁺ calcd for C₂₄H₃₀O₅Na 421.19909, found 421.19662.

Methyl 2,4-di-O-benzyl-a-L-fucopyranoside (45)

OMe -OBn

Methyl 3-O-allyl-2,4-di-O-benzyl- α -L-fucopyranoside (**S75**, 418 mg, 1.05 mmol) and DMBA (328 mg, 2.10 mmol, 2 eq) were dissolved in methanol. The reaction mixture was flushed with N₂ for 30 min and heated to 40 °C, after which Pd(Ph₃P)₄ (61 mg, 0.05 mmol, 0.05 eq) was added under a flow of N₂. Upon completion, the reaction mixture was concentrated under reduced pressure and the residue was purified by silica chromatography (15% acetone in pentane), yielding the title compound as colourless oil. Yield: 361 mg, 1.01 mmol, 96%. ¹H NMR (400 MHz, CDCl₃) δ 7.52 –

7.14 (m, 10H, CH_{arom}), 4.84 (d, J = 11.6 Hz, 1H, CHH Bn), 4.73 – 4.63 (m, 4H, H-1, CHH Bn, CH₂ Bn), 4.06 (ddd, J = 10.0, 4.7, 3.2 Hz, 1H, H-3), 3.92 – 3.86 (m, 1H, H-5), 3.78 (dd, J = 10.1, 3.5 Hz, 1H, H-2), 3.64 (dd, J = 3.4, 1.3 Hz, 1H, H-5), 3.32 (s, 3H, CH₃ OMe), 2.28 (d, J = 4.7 Hz, 1H, OH), 1.17 (d, J = 6.6 Hz, 3H, H-6), ¹³C NMR (101 MHz, CDCl₃) δ 138.5, 138.3 (C_q), 128.6, 128.5, 128.4, 128.3, 128.1, 127.9 (CH_{arom}), 98.1 (C-1), 79.5 (C-4), 77.2 (C-2), 75.6, 73.0 (CH₂ Bn), 70.6 (C-3), 66.1 (C-5), 55.4 (CH₃ OMe), 16.8 (C-6). Spectra in agreement with literature.⁹⁵

Preparation of acceptor 46



Scheme S29: preparation of acceptor **46**: reagents and conditions: a) i: PTSA, MeOH, 50 °C, ii: DBTO, toluene reflux, iii: NapBr, CsF, DMF, 76%; b) BzCl, pyridine, 98%; c) DDQ, DCM/H₂O (9:1), 84%

Methyl 2-O-benzyl-3-O-(2-naphthyl)methyl-a-L-fucopyranoside (S76)

Methyl 2-O-benzyl-3,4-O-isopropylidene-a-L-fucopyranoside (S70, 1.72 g, 5.58 mmol) and PTSA-H₂O (106 mg, 0.56 mmol, 0.1 eq) were dissolved in methanol and stirred until TLC showed full conversion of the starting material. 0.16 mL triethylamine was added and the reaction mixture was concentrated under reduced pressure. The residue was dissolved in toluene with dibutyltin oxide (1.81 g, 7.25 mmol, 1.3 eq) and heated to a reflux while removing water with a Dean-Stark trap. After 2 hr, the reaction mixture was cooled to RT and concentrated under reduced pressure. The residue was dissolved in DMF and NapBr (1.60 g, 7.25 mmol, 1.3 eq) and CsF (1.10 g, 7.25 mmol, 1.3 eq) were added. After stirring overnight, the reaction mixture was diluted with water and extracted with diethyl ether. The organic phase was dried with MgSO4 and concentrated under reduced pressure. Silica chromatography (10% acetone in pentane) yields the title compound as colourless oil. Yield: 1.72 g, 4.22 mmol, 76%. ¹H NMR (400 MHz, CDCl₃) δ 7.91 - 7.81 (m, 5H, CH_{arom}), 7.56 - 7.49 (m, 4H, CH_{arom}), 7.45 - 7.30 (m, 5H, CH_{arom}), 5.00 (d, *J* = 12.6 Hz, 1H, CHH Bn/Nap), 4.91 (d, *J* = 11.8 Hz, 1H, CHH Bn/Nap), 4.86 (d, *J* = 12.2 Hz, 1H, CHH Bn/Nap), 4.74 (d, J = 12.1 Hz, 1H, CHH Bn/Nap), 4.68 (d, J = 3.5 Hz, 1H, H-1), 3.95 (dd, J = 9.8, 3.2 Hz, 1H, H-3), 3.92 - 3.87 (m, 2H, H-2, H-5), 3.85 (dt, J = 3.1, 1.5 Hz, 1H, H-4), 3.41 (s, 3H, CH₃ OMe), 2.55 (t, I = 1.5 Hz, 1H, OH), 1.30 (d, I = 6.6 Hz, 3H, H-6), ¹³C NMR (101 MHz, CDCl₃) δ 138.5, 135.7, 133.3, 133.2 (C_a), 128.5, 128.4, 128.4, 128.2, 128.0, 127.9, 127.8, 126.8, 126.3, 126.3, 126.1, 126.0, 125.9 (CH_{arom}), 98.6 (C-1), 77.8 (C-3), 75.7 (C-2), 73.5, 73.0 (CH₂ Bn, CH₂ Nap), 70.6 (C-4), 65.1 (C-5), 55.4 (CH₃ OMe), 16.2 (C-6); HRMS: [M+NH₄]⁺ calcd for C25H28O5NH4 426.22750, found 426.22659.

Methyl 4-O-benzoyl-2-O-benzyl-3-O-(2-naphthyl)methyl-a-L-fucopyranoside (S77)

Methyl 2-O-benzyl-3-O-(2-naphthyl)methyl-α-L-fucopyranoside (S76, 1.67 g, 4.09 mmol) was dissolved in 5 mL pyridine, after which benzoyl chloride (0.71 mL, 6.13 mmol, 1.5 eq) was added. Upon full conversion of the starting material, the reaction mixture was diluted with ethyl acetate and washed with 1M HCl and with sat. aq. NaHCO3. The organic phase was dried and concentrated under reduced pressure. Silica chromatography (25% diethyl ether in pentane) yields the title compound as colourless oil. Yield: 2.06 g, 4.09 mmol, 98%. ¹H NMR (400 MHz, CDCl₃) δ 8.17 - 8.10 (m, 2H, CH_{arom}), 7.87 - 7.78 (m, 3H, CH_{arom}), 7.75 - 7.71 (m, 1H, CH_{arom}), 7.66 - 7.60 (m, 1H, CH_{arom}), 7.53 - 7.43 (m, 5H, CH_{arom}), 7.42 - 7.32 (m, 5H, CH_{arom}), 5.69 (dd, J = 3.4, 1.3 Hz, 1H, H-4), 5.00 (d, J = 11.7 Hz, 1H, CHH Bn/Nap), 4.91 (d, J = 12.1 Hz, 1H, CHH Bn/Nap), 4.83 (d, J = 11.7 Hz, 1H, CHH Bn/Nap), 4.79 – 4.73 (m, 2H, H-1, CHH Bn/Nap), 4.19 – 4.11 (m, 2H, H-3, H-5), 4.00 (dd, J = 10.1, 3.6 Hz, 1H, H-2), 3.46 (s, 3H, CH₃ OMe), 1.23 (d, J = 6.5 Hz, 3H, H-6), ¹³C NMR (101 MHz, CDCl₃) δ 166.4 (C=O), 138.5, 135.9, 133.4 (C_q), 133.2 (CH_{arom}), 133.0, 130.2 (C_q), 130.2, 130.1, 128.5, 128.5, 128.4, 128.2, 128.1, 128.1, 127.9, 127.7, 126.7, 126.0, 126.0, 125.8 (CH_{arom}), 99.2 (C-1), 76.4 (C-3), 75.0 (C-2), 73.7, 72.1 (CH₂ Bn, CH₂ Nap), 71.8 (C-4), 64.9 (C-5), 55.6 (CH₃ OMe), 16.4 (C-6); HRMS: [M+NH₄]⁺ calcd for C₃₂H₃₂O₆NH₄ 530.25371, found 530.25291.

Methyl 4-O-benzoyl-2-O-benzyl-a-L-fucopyranoside (46)

OMe OBn

Methyl 4-*O*-benzoyl-2-*O*-benzyl-α-L-fucopyranoside (2.00 g, 3.90 mmol) and DDQ (1.77 g, 7.80 mmol, 2 eq) were dissolved in DCM/H₂O (9:1). After full conversion, the reaction mixture was diluted with DCM and washed twice with sat. aq. NaHCO₃. The organic phase was dried with MgSO₄ and concentrated under reduced pressure. The residue was purified over silica (15% acetone in pentane) to give the title compound as colourless oil. Yield: 1.22 g, 3.28 mmol, 84%. $[\alpha]_D^{25} = -99.0^{\circ}$ (c = 0.60, CHCl₃); IR (thin film): 668, 713, 751, 1050, 1274, 1452, 1721; ¹H NMR (400 MHz, CDCl₃) δ 8.13 – 8.05 (m, 2H, CH_{arom}), 7.65 – 7.58 (m, 1H, CH_{arom}), 7.48 (dd, *J* = 8.4, 7.1 Hz, 2H, CH_{arom}), 7.44 – 7.31 (m, 5H, CH_{arom}), 5.50 (dd, *J* = 3.6, 1.3 Hz, 1H, H-4), 4.80 (d, *J* = 3.5 Hz, 1H, H-1), 4.77 (d, *J* = 12.0 Hz, 1H, CH_H Bn), 4.73 (d, *J* = 12.0 Hz, 1H, CH_H Bn), 4.30 (dt, *J* = 10.0, 3.3 Hz, 1H, H-3), 4.14 (qd, *J* = 6.5, 1.3 Hz, 1H, H-5), 3.85 (dd, *J* = 10.1, 3.5 Hz, 1H, H-2), 3.42 (s, 3H, CH₃ OMe), 2.45 (d, *J* = 3.2 Hz, 1H, OH), 1.20 (d, *J* = 6.6 Hz, 3H, H-6), ¹³C NMR (101 MHz, CDCl₃) δ 166.6 (C=O), 137.9 (Cq), 133.2, 129.9 (CH_{arom}), 129.8 (Cq), 128.6, 128.4, 128.2, 128.1 (CH_{arom}), 98.1 (C-1), 76.5 (C-2), 73.8 (C-4), 72.9 (CH₂ Bn), 68.3 (C-3), 64.9 (C-5), 55.5 (CH₃ OMe), 16.2 (C-6); HRMS: [M+Na]⁺ calcd for C₂₁H₂₄O₆Na 395.14651, found 395.14616.



Scheme S30: preparation of acceptor 47: reagents and conditions: a) i: PTSA, MeOH, 50 °C, ii: DBTO, toluene reflux, iii: NapBr, CsF, DMF, 98%; b) BnBr, NaH, DMF, 65%; c) $Pd(Ph_3P)_4$, DMBA, MeOH, 40 °C, 71%; d) BzCl, pyridine, 100%; e) DDQ, DCM/H₂O (9:1), 84%

Methyl 2-O-allyl-3-O-(2-naphthyl)methyl-a-L-fucopyranoside (S78)



Methyl 2-O-allyl-3,4-O-isopropylidene-a-L-fucopyranoside (S71, 1.7 g, 6.58 mmol) and PTSA-H₂O (125 mg, 0.66 mmol, 0.1 eq) were dissolved in methanol and heated to 50 °C. After full conversion, 0.2 mL triethylamine was added and the reaction mixture was concentrated under reduced pressure. The residue was dissolved in toluene with dibutyltin oxide (2.1 g, 8.45 mmol, 1.3 eq) and heated to a reflux for 2 hr, while removing water with a Dean-Stark trap. The reaction mixture was then cooled to RT and concentrated under reduced pressure. The residue was dissolved in DMF and NapBr (1.87 g, 8.45 mmol, 1.3 eq), CsF (1.28 g, 8.45 mmol, 1.3 eq) were added. After overnight stirring, the reaction mixture was diluted with water and extracted with diethyl ether. The organic phase was dried with MgSO4 and concentrated under reduced pressure. The residue was purified over silica (10% acetone in pentane) yielding the slightly impure title compound as yellowish oil. Yield: 2.27 g, 6.34 mmol, 98%. ¹H NMR (400 MHz, CDCl₃) δ 7.93 – 7.78 (m, 4H, CH_{arom}), 7.55 – 7.45 (m, 3H, CH_{arom}), 6.00 (dddd, *J* = 17.2, 10.3, 6.3, 5.4 Hz, 1H, CH₂-CH=CH₂), 5.34 (dq, J = 17.2, 1.6 Hz, 1H, CH₂-CH=CHH), 5.23 (dq, J = 10.3, 1.3 Hz, 1H, CH₂-CH=CHH), 4.98 (d, J = 11.8 Hz, 1H, CHH Nap), 4.88 (d, J = 11.9 Hz, 1H, CHH Nap), 4.83 (d, J = 3.4 Hz, 1H, H-1), 4.31 (ddt, J = 12.8, 5.4, 1.4 Hz, 1H, CHH-CH=CH₂), 4.23 (ddt, J = 12.8, 6.3, 1.3 Hz, 1H, CHH-CH=CH₂), 3.95 - 3.80 (m, 4H, H-2, H-3, H-4, H-5), 3.43 (s, 3H, CH₃ OMe), 2.54 (t, J = 1.5 Hz, 1H, OH), 1.31 (d, J = 6.7 Hz, 3H, H-6), ¹³C NMR (101 MHz, CDCl₃) δ 135.8 (C_q), 135.0 (CH₂-CH=CH₂), 133.3, 133.2 (C_q), 128.4, 128.0, 127.8, 126.8, 126.3, 126.1, 125.9 (CH_{arom}), 117.7 (CH₂-CH=CH₂), 98.6 (C-1), 77.7 (C-3), 75.6 (C-2), 73.1 (CH₂ Nap), 72.7 (CH2-CH=CH2), 70.7 (C-4), 65.2 (C-5), 55.4 (CH3 OMe), 16.2 (C-6); HRMS: [M+Na]⁺ calcd for C₂₁H₂₆O₅Na 381.16725, found 381.16656.

Methyl 2-O-allyl-4-O-benzyl-3-O-(2-naphthyl)methyl-a-L-fucopyranoside (S79)

Methyl 2-O-allyl-3-O-(2-naphthyl)methyl-a-L-fucopyranoside (S78, 1.26 g, 3.50 mmol) was dissolved in DMF after which benzyl bromide (0.62 mL, 5.25 mmol, 1.5 eq) and sodium hydride (60% dispersion in mineral oil, 210 mg, 5.25 mmol, 1.5 eq) were added. After full conversion, the reaction was quenched with water and extracted with diethyl ether. The organic phase was dried with MgSO₄ and concentrated under reduced pressure. The residue was purified over silica (10% diethyl ehter in pentane) yielding the title compound as colourless oil. Yield: 1.02 g, 2.26 mmol, 65%. ¹H NMR (400 MHz, CDCl₃) δ 7.87 – 7.78 (m, 4H, CH_{arom}), 7.57 – 7.44 (m, 3H, CH_{arom}), 7.37 (ddt, J = 5.2, 3.8, 1.5 Hz, 2H, CH_{arom}), 7.35 - 7.26 (m, 3H, CH_{arom}), 5.97 (dddd, J = 17.0, 10.3, 6.3, 5.4 Hz, 1H, CH₂-CH=CH₂), 5.31 (dq, J = 17.2, 1.6 Hz, 1H, CH₂-CH=CHH), 5.18 (dq, J = 10.4, 1.3 Hz, 1H, CH₂-CH=CHH), 5.09 - 4.97 (m, 2H, CHH Bn, CHH Nap), 4.86 (d, J = 12.1 Hz, 1H, CH*H* Nap), 4.82 (d, *J* = 3.6 Hz, 1H, H-1), 4.71 (d, *J* = 11.6 Hz, 1H, CH*H* Bn), 4.31 (ddt, *J* = 12.7, 5.4, 1.5 Hz, 1H, CHH-CH=CH₂), 4.22 (ddt, J = 12.8, 6.3, 1.3 Hz, 1H, CHH-CH=CH₂), 4.02 (dd, J = 10.1, 3.6 Hz, 1H, H-2), 3.92 (dd, J = 10.1, 2.9 Hz, 1H, H-3), 3.82 (qd, J = 6.4, 1.2 Hz, 1H, H-5), 3.63 (dd, J = 2.9, 1.3 Hz, 1H, H-4), 3.39 (s, 3H, CH₃ OMe), 1.12 (d, J = 6.5 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 138.7, 136.6 (C_q), 135.2 (CH₂-CH=CH₂), 133.4, 133.0 (C_q), 128.6, 128.3, 128.2, 128.0, 127.8, 127.7, 126.3, 126.2, 125.9, 125.9 (CH_{arom}), 117.6 (CH₂-CH-CH₂), 98.9 (C-1), 79.3 (C-3), 78.2 (C-2), 76.5 (C-4), 75.0 (CH₂ Bn), 73.6 (CH₂ Nap), 72.8 (CH₂-CH=CH₂), 66.2 (C-5), 55.4 (CH₃ OMe), 16.7 (C-6); HRMS: [M+NH₄]⁺ calcd for C₂₈H₃₂O₅NH₄ 466.25880, found 466.25832.

Methyl 4-O-benzyl-3-O-(2-naphthyl)methyl-a-L-fucopyranoside (S80)

Methyl 2-O-allyl-4-O-benzyl-3-O-(2-naphthyl)methyl-α-L-fucopyranoside (S79, 1.00 g, 2.23 mmol) and DMBA (696 mg, 4.46 mmol, 2eq) were dissolved in methanol, heated to 40 °C and flushed with N₂ for 30 minutes after which Pd(Ph₃P)₄ was added under a flow of N₂. After full conversion, as indicated by TLC, the reaction mixture was concentrated under reduced pressure. The residue was dissolved in ethyl acetate and washed twice with sat aq. NaHCO₃. The organic phase was dried with MgSO4 and concentrated under reduced pressure. The residue was purified over silica (15% acetone in pentane) yielding the title compound as off-white powder. Yield: 650 mg, 1.59 mmol, 71%. ¹H NMR (400 MHz, CDCl₃) δ 7.90 – 7.79 (m, 4H, CH_{arom}), 7.54 – 7.45 (m, 3H, CH_{arom}), 7.41 - 7.36 (m, 2H, CH_{arom}), 7.34 - 7.26 (m, 3H, CH_{arom}), 4.97 (d, J = 11.6 Hz, 1H, CHH Bn/Nap), 4.89 (s, 2H, CH₂ Bn/Nap), 4.82 (d, J = 3.9 Hz, 1H, H-1), 4.70 (d, J = 11.6 Hz, 1H, CH*H* Bn/Nap), 4.21 (ddd, *J* = 9.9, 7.6, 4.0 Hz, 1H, H-2), 3.84 (qd, *J* = 6.3, 1.4 Hz, 1H, H-5), 3.73 (dd, J = 9.9, 2.8 Hz, 1H, H-3), 3.68 (dd, J = 2.9, 1.2 Hz, 1H, H-4), 3.39 (s, 3H, CH₃ OMe), 2.19 (d, J = 7.7 Hz, 1H, OH), 1.19 (d, J = 6.5 Hz, 3H, H-6), ¹³C NMR (101 MHz, CDCl₃) δ 138.6, 135.9, 133.4, 133.1 (Cq), 128.4, 128.4, 128.4, 128.0, 127.9, 127.8, 126.5, 126.3, 126.1, 125.8 (CH_{arom}), 99.9 (C-1), 80.0 (C-3), 76.9 (C-4), 74.4, 73.4 (CH₂ Bn, CH₂ Nap), 69.1 (C-2), 66.7 (C-5), 55.5 (CH₃ OMe), 16.9 (C-6); HRMS: [M+NH₄]⁺ calcd for C₂₅H₂₈O₅ 426.22750, found 426.22664.

Methyl 2-O-benzoyl-4-O-benzyl-3-O-(2-naphthyl)methyl-α-L-fucopyranoside (S81)

Methyl 4-O-benzyl-3-O-(2-naphthyl)methyl-a-L-fucopyranoside (S80, 625 mg, 1.53 mmol) was dissolved in 5 mL pyridine, after which benzovl chloride (0.27 mL, 2.30 mol, 1.5 eq) was added. After full conversion of the starting material (TLC), the reaction mixture was diluted with ethyl acetate and washed with 1M HCl and sat. aq. NaHCO₃. The organic phase was dried with MgSO₄ and concentrated under reduced pressure. The residue was purified over silica ($5\% \rightarrow 10\%$ acetone in pentane) yielding the title compound as oil that solidifies upon standing. Yield: 784 mg, 1.53 mmol, 100%. ¹H NMR (400 MHz, CDCl₃) & 8.09 - 8.04 (m, 2H, CH_{arom}), 7.82 - 7.78 (m, 1H, CHarom), 7.73 (d, J = 8.8 Hz, 2H, CHarom), 7.71 - 7.67 (m, 1H, CHarom), 7.59 - 7.53 (m, 1H, CHarom), 7.48 - 7.38 (m, 7H, CH_{aron}), 7.34 - 7.26 (m, 3H, CH_{aron}), 5.60 (dd, J = 10.5, 3.8 Hz, 1H, H-2), 5.07 (d, J = 3.8 Hz, 1H, H-1), 5.04 (d, J = 11.7 Hz, 1H, CHH Bn/Nap), 4.86 (s, 2H, CH₂ Bn/Nap), 4.72 (d, J = 11.7 Hz, 1H, CHH Bn/Nap), 4.14 (dd, J = 10.5, 2.9 Hz, 1H, H-3), 3.91 (q, J = 6.3 Hz, 1H, H-5), 3.75 (dd, *J* = 2.9, 1.3 Hz, 1H, H-4), 3.32 (s, 3H, CH₃ OMe), 1.20 (d, *J* = 6.5 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 166.3 (C=O), 138.5, 135.9, 133.3 (C_q), 133.1 (CH_{arom}), 133.1, 130.3 (C_a), 130.0, 128.6, 128.5, 128.4, 128.3, 128.0, 127.8, 126.5, 126.2, 126.0, 125.9 (CH_{arom}), 97.8 (C-1), 77.3 (C-3, C-4), 75.0, 73.0 (CH₂ Bn, CH₂ Nap), 71.8 (C-2), 66.3 (C-5), 55.5 (CH₃ OMe), 16.8 (C-6); HRMS: [M+NH₄]⁺ calcd for C₃₂H₃₂O₆NH₄ 530.25371, found 530.25265.

Methyl 2-O-benzoyl-4-O-benzyl-a-L-fucopyranoside (47)

Methyl 2-*O*-benzoyl-4-*O*-benzyl-3-*O*-(2-naphthyl)methyl- α -L-fucopyranoside (**S81**, 750 mg, 1.46 mmol) and DDQ (664 mg, 2.93 mmol, 2eq) were dissolved in DCM/H₂O (9:1). After full conversion, indicated by TLC, the reaction mixture was diluted with DCM and washed twice with sat. aq. NaHCO₃. The organic phase was dried with MgSO₄ and concentrated under reduced pressure, The residue was purified over silica (5% \rightarrow 10% acetone in pentane) yielding the title compound as oil that solidifies upon standing. Yield: 455 mg, 1.22 mmol, 84%. [α]_D²⁵ = -126.0° (c = 0.35, CHCl₃); IR (thin film): 711, 756, 1049, 1279, 1452, 1720; ¹H NMR (400 MHz, CDCl₃) δ 8.16 – 8.02 (m, 2H, CH_{arom}), 7.65 – 7.53 (m, 1H, CH_{arom}), 7.49 – 7.28 (m, 8H, CH_{arom}), 5.25 (dd, *J* = 10.4, 3.7 Hz, 1H, H-2), 4.99 (d, *J* = 3.7 Hz, 1H, H-1), 4.83 (d, *J* = 11.6 Hz, 1H, CHH Bn), 4.76 (d, *J* = 11.6 Hz, 1H, CHH Bn), 4.19 (ddd, *J* = 10.5, 9.4, 3.5 Hz, 1H, H-3), 4.01 (qd, *J* = 6.6, 1.5 Hz, 1H, H-5), 3.73 (dd, *J* = 3.7, 1.3 Hz, 1H, H-4), 3.38 (s, 3H, CH₃ OMe), 2.23 (d, *J* = 9.4 Hz, 1H, OH), 1.30 (d, *J* = 6.6 Hz, 3H, H-6), ¹³C NMR (101 MHz, CDCl₃) δ 167.0 (C=O), 138.1, 133.3 (CH_{arom}), 130.0 (C_q), 129.9, 128.7, 128.5, 128.2, 128.2 (CH_{arom}), 97.8 (C-1), 80.9 (C-4), 76.3 (CH₂ Bn), 72.7 (C-2), 69.3 (C-3), 66.2 (C-5), 55.6 (CH₃ OMe), 16.9 (C-6); HRMS: [M+NH₄]⁺ calcd for C₂₁H₂₄O₆NH₄ 390.19111, found 390.19054.



Scheme **S31**: preparation of acceptor **48**: reagents and conditions: a) i: DMBA, Pd(Ph₃P)₄, methanol, 40 °C, ii: BzCl, pyridine, 73%; b) DDQ, DCM/H₂O (9:1), 58%

Methyl 2,4-di-O-benzoyl-3-O-(2-naphthyl)methyl-α-L-fucopyranoside (S82)

Methyl 2-O-allyl-3-O-(2-naphthyl)methyl-α-L-fucopyranoside (**S78**, 896 mg, 2.50 mmol) and DMBA (781 mg, 5.00 mmol, 2 eq) were dissolved in methanol, heated to 40 °C and flushed with N_2 for 30 minutes after which Pd(Ph₃P)₄ (144 mg, 0.125 mmol, 0.05 eq) was added under a flow of N2. After full conversion, as indicated by TLC, the reaction mixture was concentrated under reduced pressure. The residue was dissolved in 7.5 mL pyridine and benzoyl chloride (0.87 mL, 7.50 mmol, 3 eq) was added. After overnight reaction, the reaction mixture was diluted with ethyl acetate and washed with 1M HCl and sat. aq. NaHCO₃. The organic phase was dried with MgSO₄ and concentrated under reduced pressure. The residue was purified over silica to give the title compound. Yield: 632 mg, 1.20 mmol, 48%. Further elution gave methyl 2-O-benzoyl-3-O-(2naphthyl)methyl-α-L-fucopyranoside. Yield: 323 mg, 0.77 mmol, 31%. The latter was converted to the title compound with BzCl/pyridine in 89%, to give a total yield of 73%. ¹H NMR (400 MHz, CDCl₃) δ 8.29 - 8.19 (m, 2H, CH_{arom}), 8.08 - 8.02 (m, 2H, CH_{arom}), 7.85 - 7.79 (m, 1H, CH_{arom}), 7.74 - 7.68 (m, 2H, CH_{arom}), 7.67 - 7.58 (m, 3H, CH_{arom}), 7.56 - 7.36 (m, 7H, CH_{arom}), 5.79 (dd, *J* = 3.5, 1.3 Hz, 1H, H-4), 5.52 (dd, *J* = 10.4, 3.8 Hz, 1H, H-2), 5.17 (d, *J* = 3.7 Hz, 1H, H-1), 4.92 (d, J = 12.6 Hz, 1H, CHH Nap), 4.77 (d, J = 12.6 Hz, 1H, CHH Nap), 4.26 (dd, J = 10.4, $3.5 \text{ Hz}, 1\text{H}, \text{H-3}, 4.21 \text{ (qd, } I = 6.6, 1.2 \text{ Hz}, 1\text{H}, \text{H-5}, 3.40 \text{ (s, 3H, CH}_3 \text{ OMe}, 1.30 \text{ (d, } I = 6.6 \text{ Hz}, 1.2 \text{ Hz$ 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 166.6, 166.3 (C=O), 135.5 (C_q), 133.4, 133.3 (CH_{arom}), 133.1 (C_q), 130.2, 130.0 (CH_{arom}), 130.0, 129.9 (C_q), 128.6, 128.6, 128.5, 128.2, 128.0, 127.7, 126.7, 126.1, 125.9 (CH_{arom}), 97.8 (C-1), 73.2 (C-3), 71.4 (CH₂ Nap), 71.0, 71.0 (C-2, C-4), 64.9 (C-5), 55.6 (CH3 OMe), 16.5 (C-6); HRMS: [M+NH4]+ calcd for C32H30O7NH4 544.23298, found 544.23201.

Methyl 2,4-di-O-benzoyl-a-L-fucopyranoside (48)

OMe OBz

Methyl 2,4-di-O-benzoyl-3-O-(2-naphthyl)methyl- α -L-fucopyranoside (**S82**, 950 mg, 1.80 mmol) and DDQ (819 mg, 3.61 mmol, 2 eq) were dissolved in 9:1 DCM/H₂O. After full conversion, the reaction mixture was diluted with DCM and washed twice with sat. aq. NaHCO₃. The organic phase was dried with MgSO₄ and concentrated under reduced pressure. The residue was purified over silica (10% acetone in pentane) to give the title compound as white solid. Yield: 403 mg, 1.04

mmol, 58%. ¹H NMR (400 MHz, CDCl₃) δ 8.19 – 8.12 (m, 2H, CH_{arom}), 8.11 – 8.04 (m, 2H, CH_{arom}), 7.64 – 7.53 (m, 2H, CH_{arom}), 7.52 – 7.39 (m, 4H, CH_{arom}), 5.56 (dd, *J* = 3.6, 1.3 Hz, 1H, H-4), 5.35 (dd, *J* = 10.5, 3.6 Hz, 1H, H-2), 5.11 (d, *J* = 3.7 Hz, 1H, H-1), 4.48 (dd, *J* = 10.4, 3.5 Hz, 1H, H-3), 4.22 (qd, *J* = 6.5, 1.4 Hz, 1H, H-5), 3.43 (s, 3H, CH₃ OMe), 2.39 (s, 1H, OH), 1.25 (d, *J* = 6.6 Hz, 3H, H-6), ¹³C NMR (101 MHz, CDCl₃) δ 167.0, 166.9 (C=O), 133.6, 133.5, 130.1, 130.0 (CH_{arom}), 129.7, 129.5 (C_q), 128.7, 128.6 (CH_{arom}), 97.8 (C-1), 74.5 (C-4), 72.4 (C-2), 67.6 (C-3), 65.1 (C-5), 55.7 (CH₃ OMe), 16.4 (C-6). Spectra in agreement with literature.⁹⁶

Preparation of acceptor 49



Scheme S32: preparation of acceptor **49**: reagents and conditions: a) i: PTSA, MeOH, 50 °C, ii: BnBr, NaH, DMF, 72%; b) DDQ, DCM/H₂O (9:1), 82%

Methyl 3,4-di-O-benzyl-2-O-(2-naphthyl)methyl-a-L-fucopyranoside (S83)



Methyl 3,4-O-isopropylidene-2-O-(2-naphthyl)methyl- α -L-fucopyranoside (**S72**, 1.25 g, 3.49 mmol) and PTSA-H₂O (66 mg, 0.35 mmol, 0.1 eq) were dissolved in methanol and heated to 50 °C. After full conversion, 0.1 mL of triethylamine was added and the mixture was concentrated under reduced pressure. The residue was dissolved in DMF and benzyl bromide (1.24 mL, 10.5 mmol, 3 eq) and sodium hydride (60% dispersion in mineral oil, 418 mg, 10.5 mmol, 3 eq) were added. After stirring for 2.5 hr, the reaction was quenched with water and extracted with diethyl ether. The organic phase was dried with MgSO4 and concentrated under reduced pressure. The residue was purified over silica (5% acetone in pentane) to give the title compound as colourless oil. Yield: 1.25 g, 2.51 mmol, 72%. ¹H NMR (400 MHz, CDCl₃) δ 7.84 – 7.73 (m, 4H, CH_{arom}), 7.50 (dd, J = 8.4, 1.7 Hz, 1H, CHarom), 7.48 - 7.39 (m, 4H, CHarom), 7.38 - 7.25 (m, 7H, CHarom), 5.01 -4.96 (m, 2H, 2x CHH Bn/Nap), 4.91 (d, J = 11.8 Hz, 1H, CHH Bn/Nap), 4.86 (d, J = 12.3 Hz, 1H, CHH Bn/Nap), 4.77 (d, J = 11.8 Hz, 1H, CHH Bn/Nap), 4.68 – 4.62 (m, 2H, H-1, CHH Bn/Nap), 4.09 (dd, J = 10.1, 3.6 Hz, 1H, H-2), 3.96 (dd, J = 10.1, 2.9 Hz, 1H, H-3), 3.88 - 3.79 (m, 1H, H-5), 3.65 (dd, J = 2.9, 1.2 Hz, 1H, H-4), 3.36 (s, 3H, CH₃ OMe), 1.10 (d, J = 6.5 Hz, 3H, H-6), ¹³C NMR (101 MHz, CDCl₃) δ 139.1, 138.7, 136.1, 133.4, 133.2 (C_q), 128.6, 128.5, 128.3, 128.2, 128.1, 127.8, 127.7, 127.6, 127.0, 126.2, 126.1, 125.9 (CH_{arom}), 98.9 (C-1), 79.5 (C-3), 78.0 (C-4), 75.8 (C-2), 75.0, 73.7, 73.5 (CH₂ Bn, CH₂ Nap), 66.2 (C-5), 55.5 (CH₃ OMe), 16.7 (C-6); HRMS: [M+NH₄]⁺ calcd for C₃₂H₃₄O₅NH₄ 516.27445, found 516.27365.

Methyl 2,3-di-O-benzyl-a-L-fucopyranoside (49)

Methyl 3,4-di-O-benzyl-2-O-(2-naphthyl)methyl- α -L-fucopyranoside (**S83**, 1.12 g, 2.25 mmol) and DDQ (1.02 g, 4.50 mmol, 2 eq) were dissolved in DCM/H₂O 9:1. After full conversion of the starting material, the reaction mixture was diluted with dichloromethane and washed twice with sat. aq. NaHCO₃. The organic phase was dried with MgSO₄ and concentrated under reduced pressure. The residue was purified over silica (10% \rightarrow 15% acetone in pentane) to give the title compound as white solid. Yield: 665 mg, 1.86 mmol, 82%. ¹H NMR (400 MHz, CDCl₃) δ 7.42 – 7.23 (m, 10H, CH_{arom}), 4.94 (d, *J* = 11.5 Hz, 1H, CHH Bn), 4.81 (d, *J* = 3.9 Hz, 1H, H-1), 4.75 (d, *J* = 11.9 Hz, 1H, CHH Bn), 4.72 (d, *J* = 11.8 Hz, 1H, CHH Bn), 4.65 (d, *J* = 11.6 Hz, 1H, CHH Bn), 4.17 (ddd, *J* = 9.8, 7.3, 3.9 Hz, 1H, H-2), 3.88 – 3.81 (m, 1H, H-5), 3.70 (dd, *J* = 9.9, 2.8 Hz, 1H, H-3), 3.67 (dd, *J* = 2.9, 1.1 Hz, 1H, H-4), 3.40 (s, 3H, CH₃ OMe), 2.17 (d, *J* = 7.3 Hz, 1H, OH), 1.19 (d, *J* = 6.5 Hz, 3H, H-6), ¹³C NMR (101 MHz, CDCl₃) δ 138.5, 138.3 (Cq), 128.5, 128.3, 127.8, 127.7 (CH_{arom}), 99.7 (C-1), 80.0 (C-3), 76.7 (C-4), 74.0, 72.1 (CH₂ Bn), 68.9 (C-2), 66.1 (C-5), 54.9 (CH₃ OMe), 15.7 (C-6). Spectra in agreement with literature.⁹⁷





Scheme S33: preparation of acceptor 50: reagents and conditions: a) i: NaOMe, MeOH, ii: 2,2dimethoxypropane, PTSA, 76%; b) NapBr, NaH, DMF, 92%; c) i: PTSA, MeOH, 50 °C, ii: BnBr, NaH, DMF, 79%; d) DDQ, DCM/H₂O (9:1), 77%

Methyl 2,3,4-tri-O-acetyl-β-L-fucopyranoside (S84)

Title compound was isolated as a side product during multiple preparations of the α-anomer (**S68**). ¹H NMR (400 MHz, CDCl₃) δ 5.24 (dd, *J* = 3.5, 1.2 Hz, 1H, H-4), 5.18 (dd, *J* = 10.4, 7.9 Hz, 1H, H-2), 5.02 (dd, *J* = 10.4, 3.4 Hz, 1H, H-3), 4.38 (d, *J* = 7.9 Hz, 1H, H-1), 3.82 (qd, *J* = 6.4, 1.1 Hz, 1H, H-5), 3.52 (s, 3H, CH₃ OMe), 2.18 (s, 3H, CH₃ Ac), 2.06 (s, 3H, CH₃ Ac), 1.99 (s, 3H, CH₃ Ac), 1.24 (d, *J* = 6.5 Hz, 3H, H-6); Spectra in agreement with literature.⁹⁰

Methyl 3,4-O-isopropylidene-β-L-fucopyranoside (S85)

Methyl 2,3,4-tri-*O*-acetyl- β -L-fucopyranoside (**S84**, 3.00 g, 9.86 mmol) and NaOMe (53 mg, 0.99 mmol, 0.1 eq) were dissolved in methanol. After full deprotection, the pH of the reaction mixture was adjusted to 5 with amberlite. The solution was filtered over a short path of celite and concentrated under reduced pressure. Residual methanol and water were removed by coevaporation with toluene. The residue was suspended in 2,2-dimethoxypropane (30.2 mL, 246 mmol, 25 eq), after which PTSA-H₂O (188 mg, 0.99 mmol, 0.1 eq) was added. After 16 hr, triethylamine (0.28 mL, 1.97 mmol, 0.2 eq) was added and the reaction mixture was concentrated under reduced pressure. The residue was purified over silica (35% ethyl acetate in pentane) yields the title compound as colourless oil that slowly solidifies. Yield: 1.63 g, 7.47 mmol, 76%. ¹H NMR (400 MHz, CDCl₃) δ 4.10 – 4.01 (m, 2H, H-1, H-2), 4.01 (dd, *J* = 5.5, 2.2 Hz, 1H, H-4), 3.87 (qd, *J* = 6.6, 2.1 Hz, 1H, H-5), 3.56 – 3.47 (m, 4H, H-3, CH₃ OMe), 2.79 (d, *J* = 2.5 Hz, 1H, OH), 1.53 (s, 3H, CH₃ isopropylidene), 1.43 (d, *J* = 6.6 Hz, 3H, H-6), 1.36 (s, 3H, CH₃ isopropylidene), ¹³C NMR (101 MHz, CDCl₃) δ 109.9 (C_q isopropylidene), 103.2 (C-1), 78.9 (C-2), 76.4 (C-4), 73.7 (C-3), 69.2 (C-5), 56.9 (CH₃ OMe), 28.3, 26.4, (CH₃ isopropylidene) 16.6 (C-6). Spectra in agreement with literature.⁹¹

Methyl 3,4-O-isopropylidene-2-O-(2-naphthyl)methyl-β-L-fucopyranoside (S86)



Methyl 3,4-*O*-isopropylidene-β-L-fucopyranoside (**S85**, 1.25 g, 5.73 mmol) was dissolved in DMF, after which NapBr (1.90 g, 8.59 mmol, 1.5 eq) and NaH (60% dispersion in mineral oil, 344 mg, 8.59 mmol, 1.5 eq) were added. Upon full conversion, the reaction was quenched with water and extracted with diethyl ether. The organic phase was dried with MgSO₄ and concentrated under reduced pressure. The residue was purified over silica (15% diethyl ether in pentane) to give the title compound as yellowish oil. Yield: 1.89 g, 5.27 mmol, 92%. ¹H NMR (400 MHz, CDCl₃) δ 7.86 – 7.77 (m, 4H, CH_{arom}), 7.52 (dd, *J* = 8.6, 1.7 Hz, 1H, CH_{arom}), 7.48 – 7.41 (m, 2H, CH_{arom}), 4.99 (d, *J* = 12.0 Hz, 1H, CHH Nap), 4.95 (d, *J* = 12.0 Hz, 1H, CH*H* Nap), 4.22 (d, *J* = 8.0 Hz, 1H, H-1), 4.16 (dd, *J* = 7.0, 5.5 Hz, 1H, H-3), 3.98 (dd, *J* = 5.5, 2.1 Hz, 1H, H-4), 3.82 (qd, *J* = 6.6, 2.1 Hz, 1H, H-5), 3.56 (s, 3H, CH₃ OMe), 3.42 (dd, *J* = 8.1, 7.1 Hz, 1H, H-2), 1.40 (d, *J* = 6.6 Hz, 3H, H-6), 1.33 (s, 3H, CH₃ isopropylidene), 1.29 (s, 3H, CH₃ isopropylidene); HRMS: [M+NH₄]⁺ calcd for C₂₁H₂₆O₅NH₄ 376.21185, found 376.21136.

Methyl 3,4-di-O-benzyl-2-O-(2-naphthyl)methyl-β-L-fucopyranoside (S87)

Methyl 3,4-O-isopropylidene-2-O-(2-naphthyl)methyl- β -L-fucopyranoside (**S86**, 1.85 g, 5.16 mmol) and PTSA-H₂O (98 mg, 0.52 mmol, 0.1 eq) were dissolved in methanol and heated to 50 °C. After full conversion, triethylamine (0.15 mL, 1.03 mmol, 0.2 eq) was added and the mixture was concentrated under reduced pressure. Residual methanol and water were removed by coevaporation with toluene. The residue was dissolved in DMF, after which benzyl bromide (1.84 mL, 15.5 mmol, 3 eq) and sodium hydride (60% dispersion in mineral oil, 619 mg, 15.5 mmol, 3 eq) were added. After full conversion, the reaction was quenched with water and extracted with diethyl ether. The organic phase was dried with MgSO₄ and concentrated under reduced

pressure. The residue was purified over silica (25% diethyl ether in pentane) to give the title compound as white solid. Yield: 2.03 g, 4.07 mmol, 79%. ¹H NMR (400 MHz, CDCl₃) δ 7.83 – 7.73 (m, 4H, CH_{arom}), 7.50 (dd, *J* = 8.4, 1.6 Hz, 1H, CH_{arom}), 7.48 – 7.43 (m, 2H, CH_{arom}), 7.39 – 7.25 (m, 10H, CH_{arom}), 5.07 (d, *J* = 11.2 Hz, 1H, CHH Bn/Nap), 4.98 (d, *J* = 11.7 Hz, 1H, CHH Bn/Nap), 4.92 (d, *J* = 11.2 Hz, 1H, CHH Bn/Nap), 4.81 (d, *J* = 11.9 Hz, 1H, CHH Bn/Nap), 4.92 (d, *J* = 7.6 Hz, 1H, H-1), 3.86 (dd, *J* = 9.7, 7.7 Hz, 1H, H-2), 3.58 – 3.52 (m, 5H, H-3, H-4, CH₃ OMe), 3.47 (qd, *J* = 6.3, 1.1 Hz, 1H, H-5), 1.20 (d, *J* = 6.4 Hz, 3H, H-6), ¹³C NMR (101 MHz, CDCl₃) δ 138.8, 138.7, 136.6, 133.5, 133.1 (C_q), 128.6, 128.5, 128.2, 128.1, 128.0, 127.8, 127.7, 127.7, 127.6, 126.8, 126.5, 126.0, 125.8 (CH_{arom}), 105.0 (C-1), 82.2 (C-3), 79.7 (C-2), 76.4 (C-4), 75.2, 74.7, 73.3 (CH₂ Bn, CH₂ Nap), 69.8 (C-5), 55.6 (CH₃ OMe), 15.1 (C-6); HRMS: [M+NH₄]⁺ calcd for C₃₂H₃₄O₅NH₄ 516.27445, found 516.27379.

Methyl 3,4-di-O-benzyl-β-L-fucopyranoside (50)

Methyl 3,4-di-O-benzyl-2-O-(2-naphthyl)methyl- β -L-fucopyranoside (**S87**, 1.10 g, 2.21 mmol) and DDQ (1.00 g, 4.41 mmol, 2 eq) were dissolved in DCM/H₂O 9:1. After full conversion of the starting material, the reaction mixture was diluted with dichloromethane and washed twice with sat. aq. NaHCO₃. The organic phase was dried with MgSO₄ and concentrated under reduced pressure. The residue was purified over silica (15% acetone in pentane) to give the title compound as white solid. Yield: 607 mg, 1.69 mmol, 77%. $[\alpha]_D^{25} = 2.76^\circ$ (c = 0.25, CHCl₃); IR (thin film): ¹H NMR (400 MHz, CDCl₃) δ 7.43 – 7.24 (m, 10H, CH_{arom}), 4.93 (d, *J* = 11.7 Hz, 1H, CHH Bn), 4.75 (d, *J* = 11.9 Hz, 1H, CHH Bn), 4.72 – 4.66 (m, 2H, 2x CHH Bn), 4.14 (d, *J* = 7.6 Hz, 1H, H-1), 3.93 (ddd, *J* = 9.7, 7.6, 1.9 Hz, 1H, H-2), 3.61 (dd, *J* = 2.9, 1.1 Hz, 1H, H-4), 3.55 – 3.48 (m, 4H, H-5, CH₃ OMe), 3.44 (dd, *J* = 9.8, 2.9 Hz, 1H, H-3), 2.41 (d, *J* = 2.0 Hz, 1H, OH), 1.24 (d, *J* = 6.4 Hz, 3H, H-6), ¹³C NMR (101 MHz, CDCl₃) δ 138.6, 138.2 (C_q), 128.7, 128.5, 128.3, 128.0, 127.8, 127.7 (CH_{arom}), 104.1 (C-1), 82.5 (C-3), 75.7 (C-4), 74.8, 73.1 (CH₂ Bn), 71.3 (C-2), 70.8 (C-5), 58.0 (CH₃ OMe), 10.8 (C-6); HRMS: [M+NH₄]⁺ calcd for C₂₁H₂₆O₅NH₄ 376.21185, found 376.21140.

Model acceptors

Preparation of acceptors 51 and 52



Scheme S34: preparation of acceptors 51 and 52: reagents and conditions: a) Pd/C, H₂, EtOAc; b) NaOMe/MeOH; c) PhCH(OMe)₂, PTSA, 85% over 3 steps; d) TBSCl, imidazole, DMF, 98%; e) NBS, BaCO₃, cyclohexane, reflux, 75%; f) Bu₃SnH, cat AIBN, toluene, reflux 94%; g) PTSA, MeOH, 95%; h) BH₃-NH(CH₃)₂, BF₃-Et₂O, 89%; i) TsCl, pyridine; j) LAH, THF, reflux, 79% over 2 steps; k) PTSA, MeOH, 91%

1,2-di-deoxy-4,6-O-benzylidene-D-glucopyranose (S91)

commercially available tri-O-acetly-D-glucal (S88, 20 g, 73.5 mmol) and Pd/C (10%, 500 mg) were dissolved in ethyl acetate and flushed with nitrogen gas, flushed with hydrogen gas and kept under hydrogen atmosphere overnight. The reaction mixture was flushed with nitrogen, filtered over celite and concentrated, yielding \$89. The residue was dissolved in methanol and NaOMe (794 mg, 14.7 mmol, 0.2 eq) was added. When TLC shows full conversion, the reaction was quenched with amberlite, concentrated under reduced pressure and residual methanol and water were removed by azeotroping with toluene. The crude triol (S90) was then dissolved in acetonitrile with PTSA-H₂O (1.40 g, 7.35 mmol, 0.1 eq) and benzaldehyde dimethyl acetal (15.5 mL, 103 mmol, 1.4 eq). The reaction was heated to 60 °C at 275 mbar. After 45 min, the reaction was concentrated under reduced pressure. The residue was dissolved in ethyl acetate and washed with sat aq. NaHCO₃. The organic phase was dried with MgSO₄ and concentrated. The residue was purified by precipitation form EA/pentane yielding the title compound white solid. Yield: 14.7 g, 62.2 mmol, 85% over 3 steps. ¹H NMR (400 MHz, CDCl₃) δ 7.49 (dq, *J* = 4.9, 2.7 Hz, 2H, CH_{arom}), 7.38 (qd, J = 4.7, 1.7 Hz, 3H, CH_{arom}), 5.55 (s, 1H, CHPh), 4.28 (dd, J = 10.4, 4.9 Hz, 1H, H-6), 3.98 (ddd, J = 11.8, 5.3, 1.6 Hz, 1H, H-1_{eq}), 3.86 (tdt, J = 11.4, 5.9, 2.9 Hz, 1H, H-3), 3.69 (td, J = 10.3, 3.9 Hz, 1H, H-6), 3.55 (tt, J = 11.9, 2.9 Hz, 1H, H-1_{ax}), 3.43 (t, J = 9.0 Hz, 1H, H-4), 3.33 (td, J = 9.6, 4.9 Hz, 1H, H-5), 2.65 (t, J = 2.8 Hz, 1H, OH), 2.09 – 1.92 (m, 1H, H-2_{eq}), 1.80 (tdd, J = 13.1, 11.0, 5.2 Hz, 1H, H-2ax). Spectra in agreement with literature.98

1,2-di-deoxy-4,6-O-benzylidene-3-O-dimethyltertbutylsilyl-D-glucopyranose (S92)

Ph O O TBSO

S91 (2 g, 8.46 mmol) was dissolved in DMF and imidazole (1.15 g, 16.9 mmol, 2 eq) and TBSCl (1.91 g, 12.7 mmol, 1.5 eq) were added. When TLC shows full conversion, the reaction is quenched with 5 mL methanol, diluted with water and extracted with diethyl ether. The organic phase was dried with MgSO₄, concentrated and the residue was purified over silica (10% diethyl ether in pentane) yielding the product as colourless oil. Yield: 2.90 g, 8.27 mmol, 98%. ¹H NMR (400 MHz, CDCl₃) δ 7.54 – 7.46 (m, 2H, CH_{arom}), 7.41 – 7.30 (m, 3H, CH_{arom}), 5.56 (s, 1H, CHPh), 4.27 (dd, *J* = 10.3, 4.9 Hz, 1H, H-6), 3.95 (ddd, *J* = 11.8, 5.1, 1.6 Hz, 1H, H-1_{eq}), 3.87 (ddd, *J* = 10.6, 8.6, 5.4 Hz, 1H, H-3), 3.70 (t, *J* = 10.2 Hz, 1H, H-6), 3.55 (td, *J* = 12.2, 2.6 Hz, 1H, H-1_{ax}), 3.44 (t, *J* = 8.9 Hz, 1H, H-4), 3.31 (td, *J* = 9.6, 4.9 Hz, 1H, H-5), 1.97 – 1.76 (m, 2H, H-2_{ax}, H-2_{eq}), 0.87 (s, 9H, C(CH₃) TBS), 0.08 (s, 3H, CH₃ TBS), 0.04 (s, 3H, CH₃ TBS) ¹³C NMR (101 MHz, CDCl₃) δ 137.8 (Cq), 128.9, 128.2, 126.2 (CH_{arom}), 101.6 (CHPh), 84.0 (C-4), 71.9 (C-5), 70.4 (C-3), 69.1 (C-6), 66.6 (C-1), 35.6 (C-2), 25.9 (C(CH₃)₃ TBS), 18.4 (C(CH₃)₃ TBS), -4.3 (CH₃ TBS), -4.7 (CH₃ TBS). spectra in agreement with literature.⁹⁹

1,2,6-tri-deoxy-6-bromo-4-O-benzoyl-3-O-dimethyltertbutylsilyl-D-glucopyranose (S93)

S92 (1.4 g, 3.99 mmol), N-bromosuccinimide (782 mg, 4.39 mmol, 1.1 eq) and barium carbonate (1.58 g, 7.99 mmol, 2 eq) were suspended in cyclohexane and heated to a reflux, after which the reaction mixture turns red. After the red colour fades, the progress was checked with TLC. Since some starting material was still present, another 0.2 eq of NBS was added and the reaction progress was checked again after the red colour faded again. TLC showed full consumption of the starting material, so the solids in the reaction mixture were removed by filtration and washed with ethyl acetate. The filtrate was washed with sat. aq. Na₂S₂O₃, dried with MgSO₄ and concentrated under reduced pressure. The residue was purified over silica (3% EA in pentane) yielding the title compound as colourless oil. Yield: 1.29 g, 3 mmol, 75%. ¹H NMR (400 MHz, CDCl₃) δ 8.13 – 7.96 (m, 2H, CH_{arom}), 7.66 – 7.54 (m, 1H, CH_{arom}), 7.52 – 7.40 (m, 2H, CH_{arom}), 5.01 (dd, *J* = 9.3, 8.5 Hz, 1H, H-4), 4.07 (ddd, *J* = 11.9, 4.7, 2.2 Hz, 1H, H-1_{eq}), 3.91 (ddd, *J* = 10.7, 8.5, 5.2 Hz, 1H, H-3), 3.62 (ddd, J = 9.4, 7.5, 2.7 Hz, 1H, H-5), 3.54 (td, J = 11.6, 11.1, 2.1 Hz, 1H, H-1ax), 3.51 – 3.47 (m, 1H, H-6), 3.41 (dd, J = 11.1, 7.5 Hz, 1H, H-6), 2.01 – 1.80 (m, 2H, H-2ax), H-2eq), 0.74 (s, 9H C(CH₃)₃ TBS), 0.01 (s, 3H, CH₃ TBS), -0.14 (s, 3H, CH₃ TBS) ¹³C NMR (101 MHz, CDCl₃) δ 165.5 (C=O), 133.4, 129.9 (CH_{arom}), 129.8 (C_q), 128.5 (CH_{arom}), 78.2 (C-5), 75.3 (C-4), 71.5 (C-3), 65.4 (C-1), 34.9 (C-2), 32.4 (C-6), 25.6 (C(CH₃)₃ TBS), 17.8 (C(CH₃)₃ TBS), -4.3 (CH₃ TBS), -4.8 (CH₃ TBS). spectra in agreement with literature.⁹⁹

1,2,6-tri-deoxy-4-O-benzoyl-3-O-dimethyltertbutylsilyl-D-glucopyranose (S94)

BZO TBSO

S93 (1.25 g, 2.91 mmol), AIBN (0.2 M solution in toluene, 1.46 mL, 0.29 mmol, 0.1 eq) and tri-nbutyltin hydride (1,10 mL, 4.08 mmol, 1.4 eq) were dissolved in toluene and heated to a reflux. When TLC shows full conversion, the reaction mixture was concentrated and the residue was purified over silica ($3\rightarrow6\%$ diethyl ether in pentane) yielding the slightly impure title compound as colourless oil. Yield: 974 mg, 2.75 mmol, 94%. ¹H NMR (400 MHz, CDCl₃) δ 8.05 (dt, *J* = 7.1, 1.4 Hz, 2H, CH_{arom}), 7.61 – 7.52 (m, 1H, CH_{arom}), 7.51 – 7.38 (m, 2H, CH_{arom}), 4.88 (t, *J* = 9.1 Hz, 1H, H-4), 3.96 (ddd, *J* = 11.8, 4.8, 1.9 Hz, 1H, H-1_{eq}), 3.85 (ddd, *J* = 10.7, 8.7, 5.5 Hz, 1H, H-3), 3.55 – 3.33 (m, 2H, H-1_{ax}, H-5), 1.98 – 1.77 (m, 2H, H-2), 1.21 (d, *J* = 6.2 Hz, 3H, H-6), 0.74 (s, 9H, C(CH₃)₃ TBS), 0.01 (s, 3H, CH₃ TBS), -0.14 (s, 3H, CH₃ TBS) ¹³C NMR (101 MHz, CDCl₃) δ 165.8 (C=O), 133.1 (CH_{arom}), 130.4 (C_q), 129.8, 128.4 (CH_{arom}), 78.3 (C-4), 75.0 (C-5), 71.8 (C-3), 65.6 (C-1), 35.5 (C-2), 25.6 (C(CH₃)₃ TBS), 18.2 (C-6), 17.9 (C(CH₃)₃ TBS), -4.3 (CH₃ TBS), -4.8 (CH₃ TBS); HRMS: [M+H]⁺ calcd for C₁₉H₃₀O₄SiH 351.19861, found 351.19794.

1,2,6-tri-deoxy-4-O-benzoyl-D-glucopyranose (52)

S94 (925 mg, 2.64 mmol) and PTSA-H₂O (50 mg, 0.26 mmol, 0.1 eq) were dissolved in methanol. When TLC indicates full conversion, the reaction was quenched with triethylamine (0.08 mL, 0.53 mmol, 0.2 eq) and concentrated. The residue was purified over silica (25% EtOAc in pentane) to give the title compound as a colourless oil that slowly solidifies. Yield: 595 mg, 2.52 mmol, 95%. $[\alpha]_D^{25} = 33.4^{\circ}$ (c = 0.39, CHCl₃); IR (thin film): 711, 1069, 1118, 1271, 1721; ¹H NMR (400 MHz, CDCl₃) δ 8.14 – 7.97 (m, 2H, CH_{arom}), 7.59 (ddt, *J* = 8.7, 6.9, 1.3 Hz, 1H, CH_{arom}), 7.52 – 7.42 (m, 2H, CH_{arom}), 4.71 (t, *J* = 9.2 Hz, 1H, H-4), 3.98 (ddd, *J* = 11.8, 5.0, 1.7 Hz, 1H, H-1eq), 3.84 (ddt, *J* = 11.3, 8.9, 5.1 Hz, 1H, H-3), 3.57 – 3.41 (m, 2H, H-1ax, H-5), 2.71 (d, *J* = 5.0 Hz, 1H, OH), 2.10 (ddt, *J* = 13.2, 5.3, 1.9 Hz, 1H, H-2eq), 1.83 (tdd, *J* = 12.9, 11.3, 5.0 Hz, 1H, H-2ax), 1.26 (d, *J* = 6.2 Hz, 3H, H-6) ¹³C NMR (101 MHz, CDCl₃) δ 167.4 (C=O), 133.6, 129.9 (CH_{arom}), 129.7 (Cq), 128.6 (CH_{arom}), 7.9.9 (C-4), 74.6 (C-5), 71.8 (C-3), 65.7 (C-1), 34.6 (C-2), 18.3 (C-6); HRMS: [M+Na]⁺ calcd for C₁₃H₁₆O₄Na 259.09408, found 259.09365.

1,2-di-deoxy-4-O-benzyl-3-O-dimethyltertbutylsilyl-D-glucopyranose (\$95)

BnO TBSO

S92 (1.4 g, 3.99 mmol) was dissolved in dichloromethane and cooled to 0 °C, after which borane dimethylamine complex (1.18 g, 20.0 mmol, 5 eq) and BF₃-etherate (2.47 mL, 20.0 mmol, 5 eq) were added. When TLC shows full conversion of the starting material, the reaction was quenched with sat. aq. NaHCO₃, diluted and extracted twice with DCM. Combined organic phases were washed with sat. aq. NaHCO₃, dried with MgSO₄ and concentrated. The residue was purified over silica (20% EA in pentane) to yield the title compound as colourless oil. Yield: 1.25 g, 3.55 mmol, 89% ¹H NMR (400 MHz, CDCl₃) δ 7.37 – 7.26 (m, 5H, CH_{arom}), 4.91 (d, *J* = 11.1 Hz, 1H, CHH Bn), 4.61 (d, *J* = 11.2 Hz, 1H, CHH Bn), 3.91 (ddd, *J* = 11.7, 4.9, 1.8 Hz, 1H, H-1_{eq}), 3.84 – 3.75 (m, 2H, H-3, H-6), 3.63 (ddd, *J* = 11.6, 6.8, 4.7 Hz, 1H, H-6), 3.41 (ddd, *J* = 12.7, 11.7, 2.2 Hz, 1H, H-1_{ax}), 3.28 (dd, *J* = 9.6, 8.1 Hz, 1H, H-4), 3.21 (ddd, *J* = 9.5, 4.8, 2.7 Hz, 1H, H-5), 1.92 (dd, *J* = 6.9, 6.0 Hz, 1H, OH), 1.86 (ddt, *J* = 13.3, 5.2, 2.0 Hz, 1H, H-2_{eq}), 1.77 – 1.64 (m, 1H, H-2_{ax}), 0.93 (s, 9H, C(CH₃)₃ TBS) 0.11 (s, 3H, CH₃ TBS), 0.10 (s, 3H, CH₃ TBS) ¹³C NMR (101 MHz, CDCl₃) δ 138.5 (C_q), 128.5, 128.1, 127.8 (CH_{arom}), 79.9, 79.8 (C-4/C-5), 75.2 (CH₂ Bn), 74.6 (C-3), 65.5 (C-1), 62.8 (C-6), 35.6 (C-2), 26.0 (C(CH₃)₃ TBS)), 18.1 (*C*(CH₃)₃ TBS), -4.2 (CH₃ TBS), -4.4 (CH₃ TBS). spectra in agreement with literature.⁹⁹

1,2,6-tri-deoxy-4-O-benzyl-3-O-dimethyltertbutylsilyl-D-glucopyranose (S97)

BnO TBSO

\$95 (1.20 g, 3.40 mmol) was dissolved in 5.5 mL pyridine, after which *p*-toluenesulfonyl chloride (1.30 g, 6.81 mmol, 2 eq) was added. When TLC shows full conversion, the reaction mixture is diluted with ethyl acetate and washed with 2x 100 mL 1M HCl and with sat. aq. NaHCO₃. The organic phase was dried with MgSO4 and concentrated under reduced pressure, yielding the crude tosylate (S96) which was used without further purification. The tosylate was dissolved in THF, lithium aluminium hydride (2.4 M in 2-methyltetrahydrofuran, 5.67 mL, 13.6 mmol, 4 eq) was added and the mixture was heated to reflux. When TLC shows full conversion, the reaction mixture was cooled to 0 °C and excess reagent was very carefully quenched with 1M aq HCl and extracted twice with ethyl acetate. Combined organic phases were washed with sat. aq. NaHCO₃, dried with MgSO4 and concentrated under reduced pressure. The residue was purified over silica $(3 \rightarrow 6\%$ diethyl ether in pentane), yielding the title compound as colourless oil. Yield: 906 mg, 2.69 mmol, 79% over 2 steps. ¹H NMR (400 MHz, CDCl₃) δ 7.40 - 7.24 (m, 5H, CH_{arom}), 4.93 (d, J = 11.0 Hz, 1H, CHH Bn), 4.61 (d, J = 11.1 Hz, 1H, CHH Bn), 3.85 (ddd, J = 11.7, 4.8, 1.8 Hz, 1H, H-1_{eq}), 3.74 (ddd, J = 11.0, 8.3, 5.2 Hz, 1H, H-3), 3.37 (td, J = 12.2, 2.2 Hz, 1H, H-1_{ax}), 3.24 (dq, J = 9.2, 6.2 Hz, 1H, H-5), 2.95 (t, J = 8.8 Hz, 1H, H-4), 1.85 (ddt, J = 13.2, 5.2, 2.0 Hz, 1H, H-2_{eq}), 1.72 (tdd, J = 12.9, 11.0, 4.9 Hz, 1H, H-2_{ea}), 1.25 (d, J = 6.2 Hz, 3H, H-6), 0.92 (s, 9H, C(CH₃)₃) TBS), 0.16 - 0.06 (m, 6H, 2x CH₃ TBS) ¹³C NMR (101 MHz, CDCl₃) δ 138.7 (C_q), 128.4, 128.0, 127.7 (CH_{arom}), 85.7 (C-4), 76.1 (C-5), 75.5 (CH₂ Bn), 74.6 (C-3), 65.4 (C-1), 35.9 (C-2), 26.0 (C(CH₃)₃ TBS), 18.7 (C-6), 18.1 (C(CH₃)₃ TBS), -4.2 (CH₃ TBS), -4.3 (CH₃ TBS); HRMS: [M+Na]⁺ calcd for C₁₉H₃₂O₃SiNa 359.20129, found 359.20078.

1,2,6-tri-deoxy-4-O-benzyl-D-glucopyranose (51)

S97 (875 mg, 2.60 mmol) and PTSA-H₂O (50 mg, 0.26 mmol, 0.1 eq) were dissolved in methanol. When TLC shows full conversion, the reaction was quenched with triethylamine (0.07 mL, 0.52 mmol, 0.2 eq) and concentrated under reduced pressure. The residue was purified over silica (25% EtOAc in pentane) to give the desired compound as white solid. Yield: 528 mg, 2.38 mmol, 91%. $[\alpha]_D^{25} = -13.0^{\circ}$ (c = 0.35, CHCl₃); IR (thin film): 689, 839, 1070, 1090, 1105, 1454; ¹H NMR (400 MHz, CDCl₃) δ 7.43 – 7.29 (m, 5H, CH_{arom}), 4.79 (d, *J* = 11.2 Hz, 1H, CH*H* Bn), 4.70 (d, *J* = 11.3 Hz, 1H, CH*H* Bn), 3.90 (ddd, *J* = 11.7, 5.0, 1.6 Hz, 1H, H-1_{eq}), 3.67 (tdt, *J* = 8.4, 5.1, 2.9 Hz, 1H, H-3), 3.41 (ddd, *J* = 12.6, 11.7, 2.2 Hz, 1H, OH), 1.94 (ddt, *J* = 13.0, 5.2, 1.9 Hz, 1H, H-2_{eq}), 1.69 (tdd, *J* = 12.9, 11.4, 5.0 Hz, 1H, H-2_{ax}), 1.35 (d, *J* = 6.2 Hz, 3H, H-6) ¹³C NMR (101 MHz, CDCl₃) δ 138.4 (C_q), 128.8, 128.2, 128.0 (CH_{arom}), 86.7 (C-4), 76.0 (C-5), 75.4 (CH₂ Bn), 72.9 (C-3), 65.7 (C-1), 33.8 (C-2), 18.8 (C-6). HRMS: [M+Na]⁺ calcd for C₁₃H₁₈O₃Na 245.11482, found 245.11489.

Preparation of acceptors 53 and 54



Scheme S35: preparation of acceptors 53 and 54: reagents and conditions: a) Pd/C, H₂, EtOAc; b) NaOMe/MeOH; c) PhCH(OMe)₂, PTSA, 55% over 3 steps; d) TBSCl, imidazole, DMF, 73%; e) NBS, BaCO₃, cyclohexane, reflux, 70%; f) Bu₃SnH, cat AIBN, toluene, reflux 89%; g) PTSA, MeOH, 91%; h) BH₃-NH(CH₃)₂, BF₃-Et₂O, 62%; i) TsCl, pyridine; j) LAH, THF, reflux, 39% over 2 steps; k) PTSA, MeOH, 67%

1,2-di-deoxy-4,6-O-benzylidene-D-galactopyranose (S101)



commercially available tri-O-acetly-D-galactal (S98, 10 g, 36.5 mmol) and Pd/C (5%, 500 mg) were dissolved in ethyl acetate and flushed with nitrogen gas, flushed with hydrogen gas and kept under hydrogen atmosphere overnight. The reaction mixture was flushed with nitrogen, filtered over celite, concentrated, yielding \$99. The residue was dissolved in methanol and NaOMe (394 mg, 7.29 mmol, 0.2 eq) was added. When TLC shlows full conversion, the reaction was quenched with Amberilte IR-120 H-form to a pH of ~5, concentrated under reduced pressure and residual methanol and water were removed by azeotroping with toluene. The crude triol (\$100) was then dissolved in acetonitrile with PTSA-H₂O (694 mg, 3.65 mmol, 0.1 eq) and benzaldehyde dimethyl acetal (7.7 mL, 51 mmol, 1.4 eq). The reaction was heated to 60 °C at 275 mbar. After 60 min, the reaction was concentrated under reduced pressure. The residue was dissolved in ethyl acetate and washed with sat. aq. NaHCO₃. The organic phase was dried with MgSO₄ and concentrated. The residue was recrystallized from EA/pentane to yield the title compound as fluffy white solid. Yield: 4.72 g, 20 mmol, 55% over 3 steps. ¹H NMR (400 MHz, CDCl₃) δ 7.58 - 7.52 (m, 2H, CHarom), 7.44 - 7.37 (m, 3H, CHarom), 5.62 (s, 1H, CHPh), 4.30 (dd, J = 12.4, 1.6 Hz, 1H, H-6), 4.16 - 4.10 (m, 2H, H-1_{eq}, H-4), 4.04 (dd, J = 12.5, 1.8 Hz, 1H, H-6), 3.78 (dddd, J = 11.8, 10.8, 5.1, 3.5 Hz, 1H, H-3), 3.48 (td, J = 12.2, 2.0 Hz, 1H, H-1ax), 3.33 (q, J = 1.6 Hz, 1H, H-5), 2.52 (d, J = 10.8 Hz, 1H, OH), 2.02 (qd, J = 12.4, 4.6 Hz, 1H, H-2_{ax}), 1.81 - 1.74 (m, 1H, H-2_{eq}); ¹³C NMR (101 MHz, CDCl₃) δ 137.8 (C_q), 129.1, 128.2, 126.4 (CH_{arom}), 101.2 (CHPh), 75.3 (C-4), 70.3 (C-5), 70.1 (C-6), 68.8 (C-3), 65.8 (C-1), 30.2 (C-2). Spectra in agreement with literature.¹⁰⁰

1,2-di-deoxy-4,6-O-benzylidene-3-O-dimethyltertbutylsilyl-D-galactopyranose (S102)



1,2-di-deoxy-4,6-*O*-benzylidene-D-galactopyranose (**S101**, 4.70 g, 19.9 mmol) was dissolved in DMF with imidazole (3.39 g, 49.8 mmol, 2.5 eq). TBSCl (3.90 g, 25.9 mmol, 1.3 eq) was added and the mixture was stirred at room temperature. When TLC shows full conversion, the reaction mixture was diluted with water and extracted twice with diethyl ether. Combined organic phases were dried with MgSO₄ and concentrated under reduced pressure. The residue was purified over silica (10% acetone in pentane) yielding the title compound as white powder. Yield: 5.12 g, 14.6 mmol, 73% ¹H NMR (400 MHz, CDCl₃) δ 7.57 – 7.52 (m, 2H, CH_{arom}), 7.37 – 7.28 (m, 3H, CH_{arom}), 5.57 (s, 1H, CHPh), 4.27 (dd, *J* = 12.4, 1.6 Hz, 1H, H-6), 4.10 (ddd, *J* = 11.7, 4.6, 1.8 Hz, 1H, H-1_{eq}), 4.01 (dd, *J* = 12.3, 1.8 Hz, 1H, H-6), 3.96 (d, *J* = 3.2 Hz, 1H, H-4), 3.84 (ddd, *J* = 11.7, 4.8, 3.4 Hz, 1H, H-3), 3.49 (ddd, *J* = 12.6, 11.6, 2.0 Hz, 1H, H-1_{ax}), 3.26 (q, *J* = 1.5 Hz, 1H, H-5), 2.21 (tdd, *J* = 12.8, 11.6, 4.6 Hz, 1H, H-2_{ax}), 1.55 (ddq, *J* = 12.8, 4.7, 1.7 Hz, 1H, H-1_{eq}), 0.91 (s, 9H, C(CH₃)₃ TBS), 0.20 – 0.00 (m, 6H, 2x CH₃ TBS), ¹³C NMR (101 MHz, CDCl₃) δ 138.3 (C_q), 128.6, 128.0, 126.3 (CH_{arom}), 100.7 (CHPh), 76.5 (C-4), 70.7 (C-3), 70.6 (C-6), 70.4 (C-5), 66.2 (C-1), 30.0 (C-2), 25.9 (C(CH₃)₃ TBS), 18.3 (C(CH₃)₃ TBS), -4.2, -4.3 (CH₃ TBS); HRMS: [M+Na]⁺ calcd for C₁₉H₃₀O₄SiNa 373.18056, found 373.17989.

1,2,6-tri-deoxy-6-bromo-4-O-benzoyl-3-O-dimethyltertbutylsilyl-D-galactopyranose (S103)



1,2-di-deoxy-4,6-O-benzylidene-3-O-dimethyltertbutylsilyl-D-galactopyranose (S102, 2.28 g, 6.50 mmol), barium carbonate (2.57 g, 13.0 mmol, 2 eq) and N-bromosuccinimide (1.27g, 7.15 mmol, 1.1 eq) were suspended in cyclohexane and heated to a reflux. Upon heating, the solution becomes red and then colourless after a few minutes. After the fading of the red colour, TLC showed full conversion. Solids were filtered off and washed with ethyl acetate. The organic phase was washed with sat. aq. Na₂S₂O₃, dried with MgSO₄ and concentrated under reduced pressure. The residue was purified over silica (5% diethyl ether in pentane) to obtain the title compound as colourless oil. ¹H NMR (400 MHz, CDCl₃) δ 8.14 - 8.04 (m, 2H, CH_{arom}), 7.61 - 7.54 (m, 1H, CHarom), 7.48 - 7.41 (m, 2H, CHarom), 5.51 - 5.46 (m, 1H, H-4), 4.14 (ddd, J = 11.9, 4.7, 2.2 Hz, 1H, H-1_{eq}), 3.95 (ddd, *J* = 10.9, 4.8, 3.2 Hz, 1H, H-3), 3.77 (ddd, *J* = 7.3, 5.7, 1.5 Hz, 1H, H-5), 3.57 $(td, J = 12.1, 2.3 Hz, 1H, H-1_{ax}), 3.47 - 3.36 (m, 2H, 2x H-6), 2.10 (qd, J = 12.4, 4.7 Hz, 1H, H-2_{ax}), 3.47 - 3.46 (m, 2H, 2x H-6), 2.10 (qd, J = 12.4, 4.7 Hz, 1H, H-2_{ax}), 3.47 - 3.46 (m, 2H, 2x H-6), 2.10 (qd, J = 12.4, 4.7 Hz, 1H, H-2_{ax}), 3.47 - 3.46 (m, 2H, 2x H-6), 2.10 (qd, J = 12.4, 4.7 Hz, 1H, H-2_{ax}), 3.47 - 3.46 (m, 2H, 2x H-6), 2.10 (qd, J = 12.4, 4.7 Hz, 1H, H-2_{ax}), 3.47 - 3.46 (m, 2H, 2x H-6), 3.46 (m, 2H, 2x H-6), 3.47 - 3.46 (m, 2H, 2x H-6),$ 1.69 (dddt, J = 13.0, 4.8, 2.5, 1.2 Hz, 1H, H-2_{eq}), 0.77 (s, 9H, C(CH₃)₃ TBS), 0.06 (s, 3H, CH₃ TBS), 0.05 (s, 3H, CH₃ TBS), ¹³C NMR (101 MHz, CDCl₃) δ 166.1 (C=O), 133.2 (CH_{arom}), 130.2 (C_q), 130.0, 128.5 (CH_{arom}), 79.7 (C-5), 72.9 (C-4), 68.6 (C-3), 65.3 (C-1), 30.8, 30.7 (C-2, C-6), 25.7 (C(CH₃)₃ TBS), 18.0 (C(CH₃)₃ TBS), -4.7, -4.8 (CH₃ TBS); HRMS: [M+H]⁺ calcd for C19H29BrO4SiH 429.10913; 431.10708, found 429.10855; 431.10647.

1,2-di-deoxy-4-O-benzoyl-3-O-dimethyltertbutylsilyl-D-fucopyranose (S104)



1,2,6-tri-deoxy-6-bromo-4-*O*-benzoyl-3-*O*-dimethyltertbutylsilyl-D-galactopyranose (**S103**, 1.90 g, 4.42 mmol), tributyltin hydride (1.67 mL, 6.19 mmol, 1.4 eq) and AIBN (0.2 M in toluene, 2.21 mL, 0.44 mmol, 0.1 eq) were dissolved in toluene and heated to a reflux. After 4 hr, the reaction was incomplete and showed no further conversion, so an extra 0.5 eq tributyltin hydride and 0.05 eq AIBN were added. After completion, the reaction mixture was concentrated under reduced pressure. The residue was purified over silica (5% diethyl ether in pentane) to give the title compound as colourless oil. Yield: 1.38 g, 3.93 mmol, 89%. ¹H NMR (400 MHz, CDCl₃) δ 8.18 – 8.11 (m, 2H, CH_{arom}), 7.63 – 7.55 (m, 1H, CH_{arom}), 7.51 – 7.42 (m, 2H, CH_{arom}), 5.27 (dd, *J* = 3.1, 1.4 Hz, 1H, H-4), 4.10 (ddd, *J* = 11.8, 4.8, 1.8 Hz, 1H, H-1_{eq}), 3.94 (ddd, *J* = 11.5, 5.0, 3.3 Hz, 1H, H-3), 3.68 (qd, *J* = 6.4, 1.2 Hz, 1H, H-5), 3.56 (ddd, *J* = 12.8, 11.8, 2.1 Hz, 1H, H-1_{ax}), 2.12 (tdd, *J* = 12.8, 11.4, 4.8 Hz, 1H, H-2_{ax}), 1.72 – 1.64 (m, 1H, H-2_{eq}), 1.23 (d, *J* = 6.4 Hz, 3H, H-6), 0.79 (s, 9H, C(CH₃)₃ TBS), 0.08 (s, 3H, CH₃ TBS), 0.07 (s, 3H, CH₃ TBS), ¹³C NMR (101 MHz, CDCl₃) δ 166.6 (C=O), 132.9 (CH_{arom}), 130.7 (C_q), 129.9, 128.4 (CH_{arom}), 73.8 (C-5), 73.4 (C-4), 69.7 (C-3), 66.0 (C-1), 30.8 (C-2), 25.7 (C(CH₃)₃ TBS), 18.1 (*C*(CH₃)₃ TBS), 17.5 (C-6), -4.6, -4.8 (CH₃ TBS); HRMS [M+H]⁺ calcd for C₁₉H₃₀O₄SiH 351.19861, found 351.19802.

1,2-di-deoxy-4-O-benzoyl-D-fucopyranose (54)



1,2-di-deoxy-4-O-benzoyl-3-O-dimethyltertbutylsilyl-D-fucopyranose (**S104**, 1.30 g, 3.71 mmol) and PTSA-H₂O (71 mg, 0.37 mmol, 0.1 eq) were dissolved in methanol. After full conversion, triethylamine (0.10 mL, 0.74 mmol, 0.2 eq) was added and the reaction mixture was concentrated under reduced pressure. Silica chromatography (25% EtOAc in pentane) yields the title compound as colourless oil. Yield: 800 mg, 3.39 mmol, 91%. $[\alpha]_D^{25} = 30.8^{\circ}$ (c = 1.12, CHCl₃); IR (thin film): 713, 1086, 1115, 1274, 1717; ¹H NMR (400 MHz, CDCl₃) δ 8.20 – 8.08 (m, 2H, CH_{arom}), 7.65 – 7.55 (m, 1H, CH_{arom}), 7.53 – 7.41 (m, 2H, CH_{arom}), 5.37 – 5.18 (m, 1H, H-4), 4.09 (ddd, *J* = 11.8, 4.8, 1.8 Hz, 1H, H-1_{eq}), 3.99 (dtd, *J* = 11.7, 4.9, 3.2 Hz, 1H, H-3), 3.64 (qd, *J* = 6.5, 1.2 Hz, 1H, H-5), 3.53 (ddd, *J* = 12.6, 11.8, 2.3 Hz, 1H, H-1_{ax}), 2.42 (d, *J* = 4.9 Hz, 1H, OH), 2.08 – 1.91 (m, 1H, H-2_{ax}), 1.83 – 1.72 (m, 1H, H-2_{eq}), 1.22 (d, *J* = 6.4 Hz, 3H, H-6), ¹³C NMR (101 MHz, CDCl₃) δ 167.6 (C=O), 133.5, 130.0 (CH_{arom}), 129.8 (C_q), 128.6 (CH_{arom}), 7.38 (C-4), 73.5 (C-5), 69.6 (C-3), 66.1 (C-1), 29.6 (C-2), 17.6 (C-6); HRMS [M+H]⁺ calcd for C₁₃H₁₆O₄H 237.11214, found 237.11150.

1,2-di-deoxy-4-O-benzyl-3-O-dimethyltertbutylsilyl-D-galactopyranose (S105)



1,2-di-deoxy-4,6-O-benzylidene-3-O-dimethyltertbutylsilyl-D-galactopyranose (S102, 2.28 g, 6.50 mmol) and BH₃-NH(CH₃)₂ (1.92 g, 32.5 mmol, 5 eq) were dissolved in DCM and cooled to 0 $^{\circ}$ C

after which BF₃-Et₂O (4.0 mL, 32.5 mol, 5 eq) was added dropwise. After full conversion, the reaction was quenched with sat. aq. NaHCO₃. The aquatic phase was extracted twice with dichloromethane. Organic phases were combined, washed with sat. aq. NaHCO₃, dried with MgSO₄ and concentrated under reduced pressure. Silica chromatography (15% acetone in pentane) yields the title compound as colourless oil. Yield: 1.41 g, 4.00 mmol, 62%.¹H NMR (400 MHz, CDCl₃) δ 7.40 – 7.27 (m, 5H, CH_{arom}), 4.99 (d, *J* = 11.7 Hz, 1H, CHH Bn), 4.64 (d, *J* = 11.7 Hz, 1H, CHH Bn), 4.03 (ddd, *J* = 11.6, 4.8, 2.1 Hz, 1H, H-1_{eq}), 3.84 (ddd, *J* = 11.3, 4.6, 2.7 Hz, 1H, H-3), 3.78 (ddd, *J* = 11.2, 7.0, 3.0 Hz, 1H, H-6), 3.59 (dt, *J* = 2.6, 1.3 Hz, 1H, H-4), 3.49 – 3.40 (m, 2H, H-1_{ax}, H-6), 3.34 (ddd, *J* = 7.1, 4.7, 1.4 Hz, 1H, H-5), 2.19 (tdd, *J* = 14.1, 11.8, 4.8 Hz, 1H, H-2_{ax}), 1.82 (dd, *J* = 8.8, 3.5 Hz, 1H, OH), 1.58 (ddtd, *J* = 12.9, 4.6, 2.3, 1.4 Hz, 1H, H-2_{eq}), 0.94 (s, 9H, C(CH₃)₃ TBS), 0.14 (s, 3H, CH₃ TBS), 0.12 (s, 3H, CH₃ TBS), ¹³C NMR (101 MHz, CDCl₃) δ 138.8 (Cq), 128.6, 128.5, 127.9 (CH_{arom}), 79.1 (C-5), 76.1 (C-4), 74.5 (CH₂ Bn), 72.8 (C-3), 66.0 (C-1), 63.2 (C-6), 30.8 (C-2), 26.0 (C(CH₃)₃ TBS), 18.2 (C(CH₃)₃ TBS), -4.3, -4.5 (CH₃ TBS); HRMS: [M+Na]⁺ calcd for C₁₉H₃₂O₄SiNa 375.19621, found 375.19571

1,2-di-deoxy-4-O-benzyl-3-O-dimethyltertbutylsilyl-D-fucopyranose (S107)



1,2-di-deoxy-4-O-benzyl-3-O-dimethyltertbutylsilyl-D-galactopyranose (1.35 g, 3.83 mmol) and tosyl chloride (1.46 g, 7.66 mmol, 2 eq) were dissolved in pyridine and reacted for 4 hr, after which the reaction mixture was diluted with ethyl acetate and washed with 1M HCl and sat. aq. NaHCO₃. The organic phase was dried with MgSO₄ and concentrated under reduced pressure, vielding **S106**. The residue was dissolved in THF and lithium aluminium hydride (4 M in Et_2O_1) 3.83 mL, 15.3 mmol, 4 eq) was added dropwise. The reaction mixture was refluxed overnight, before being cooled to 0 °C. Excess reagent was carefully quenched with 1M HCl. The aquatic phase was extracted twice with ethyl acetate. Combined organic phases were washed with sat. aq. NaHCO₃, dried with MgSO₄ and concentrated under reduced pressure. Silica chromatography (10% diethyl ether in pentane) gives the title compound as colourless oil. Yield: 506 mg, 1.50 mmol, 39%. Further elution also gave 29% of recovered starting material. ¹H NMR (400 MHz, CDCl₃) δ 7.42 - 7.38 (m, 2H, CH_{arom}), 7.34 - 7.30 (m, 2H, CH_{arom}), 7.28 - 7.24 (m, 1H, CH_{arom}), 5.01 (d, *J* = 11.6 Hz, 1H, CHH Bn), 4.64 (d, *J* = 11.6 Hz, 1H, CHH Bn), 3.97 (ddd, *J* = 11.6, 4.9, 1.8 Hz, 1H, H-1_{eq}), 3.82 (ddd, J = 11.5, 4.7, 2.6 Hz, 1H, H-3), 3.49 – 3.32 (m, 3H, H-1_{ax}, H-4, H-5), 2.16 (tdd, J = 12.7, 11.5, 4.9 Hz, 1H, H-2_{ax}), 1.58 – 1.48 (m, 1H, H-2_{eq}), 1.16 (d, J = 6.3 Hz, 3H, H-6), 0.94 (s, 9H, C(CH₃)₃ TBS), 0.12 (s, 3H, CH₃ TBS), 0.11 (s, 3H, CH₃ TBS), ¹³C NMR (101 MHz, CDCl₃) δ 139.3 (C₄), 128.5, 128.2, 127.5 (CH_{arom}), 79.2 (C-4), 75.0 (CH₂ Bn), 75.0 (C-5), 73.4 (C-3), 66.0 (C-1), 30.4 (C-2), 26.0 (C(CH₃)₃ TBS), 18.2 (C(CH₃)₃ TBS), 17.9 (C-6), -4.3, -4.5 (C-6); HRMS: [M+NH₄]⁺ calcd for C₁₉H₃₂O₃SiNH₄ 354.24590, found 354.24526

1,2-di-deoxy-4-O-benzyl-D-fucopyranose (53)



1,2-di-deoxy-4-O-benzyl-3-O-dimethyltertbutylsilyl-D-fucopyranose (**S107**, 450 mg, 1.34 mmol) and PTSA-H₂O (25 mg, 0.13 mmol, 0.1 eq) were dissolved in methanol. After full conversion,

triethylamine (38 µL, 0.27 mmol, 0.2 eq) was added and the reaction mixture was concentrated under reduced pressure. Silica chromatography (25% ethyl acetate in pentane) yield the title compound as colourless oil. Yield: 200 mg, 0.90 mmol, 67%. $[\alpha]_D^{25} = 54.4^{\circ}$ (c = 0.33, CHCl₃); IR (thin film): 714, 1027, 1086, 1275, 1454; ¹H NMR (400 MHz, CDCl₃) δ 7.41 – 7.29 (m, 5H, CH_{arom}), 4.85 (d, *J* = 11.6 Hz, 1H, CHH Bn), 4.64 (d, *J* = 11.7 Hz, 1H, CHH Bn), 3.98 (ddd, *J* = 11.7, 4.8, 2.0 Hz, 1H, H-1_{eq}), 3.68 (dddd, *J* = 11.5, 10.1, 5.1, 3.4 Hz, 1H, H-3), 3.51 – 3.49 (m, 1H, H-4), 3.48 – 3.35 (m, 2H, H-1_{ax}, H-5), 1.91 – 1.78 (m, 2H, H-2_{ax}, OH), 1.69 (ddtd, *J* = 12.7, 5.3, 2.2, 1.0 Hz, 1H, H-2_{eq}), 1.30 (d, *J* = 6.5 Hz, 3H, H-6), ¹³C NMR (101 MHz, CDCl₃) δ 138.4 (Cq), 128.8, 128.2, 128.2 (CH_{arom}), 80.1 (C-4), 76.1 (CH₂ Bn), 75.0 (C-5), 70.1 (C-3), 65.8 (C-1), 30.7 (C-2), 17.9 (C-6); HRMS: [M+Na]⁺ calcd for C₁₃H₁₈O₃Na 245.11482, found 245.11441.

Preparation of acceptor 55



Scheme **S36**: preparation of acceptor **55**: reagents and conditions: a) BnBr, NaH, DMF, 86%; b) MeOH, 60 °C, 100%; c) i: TsCl, pyridine, ii: LiAlH₄, THF, reflux, 68% over 2 steps

1,2-di-deoxy-3-O-benzyl-4,6-O-benzylidene-D-glucopyranose (S108)

1,2-di-deoxy-4,6-O-benzylidene-D-glucopyranose (**S91**, 1.18 g, 5 mmol), benzyl bromide (0.89 mL, 7.50 mmol, 1.5 eq) and sodium hydride (60% dispersion in mineral oil, 300 mg, 7.50 mmol, 1.5 eq) were dissolved in DMF. When TLC shows full conversion, the reaction is quenched with water and extracted with diethyl ether. The organic phase was dried with MgSO₄ and concentrated under reduced pressure. The residue was purified over silica (15% diethyl ether in pentane), yielding the title compound as white solid. Yield: 1.41 g, 4.30 mmol, 86%. ¹H NMR (400 MHz, CDCl₃) δ 7.54 – 7.49 (m, 2H, CH_{arom}), 7.43 – 7.25 (m, 8H, CH_{arom}), 5.62 (s, 1H, CHPh), 4.84 (d, *J* = 12.1 Hz, 1H, CHH Bn), 4.72 (d, *J* = 12.1 Hz, 1H, CHH Bn), 4.29 (dd, *J* = 10.4, 4.9 Hz, 1H, H-6), 3.98 (ddd, *J* = 11.8, 5.3, 1.5 Hz, 1H, H-1_{eq}), 3.77 – 3.64 (m, 3H, H-3, H-4, H-6), 3.52 (ddd, *J* = 12.8, 11.8, 2.4 Hz, 1H, H-1_{ax}), 3.34 (ddd, *J* = 10.1, 8.7, 4.9 Hz, 1H, H-5), 2.06 (dddd, *J* = 13.5, 5.0, 2.3, 1.5 Hz, 1H, H-2_{eq}), 1.82 (tdd, *J* = 13.1, 10.6, 5.3 Hz, 1H, H-2_{ax}), ¹³C NMR (101 MHz, CDCl₃) δ 138.8, 137.8 (Cq), 129.0, 128.5, 128.3, 127.8, 127.7, 126.2 (CH_{arom}), 101.4 (CHPh), 84.0 (C-4), 76.0 (C-3), 72.7 (CH₂ Bn), 71.8 (C-5), 69.1 (C-6), 66.6 (C-1), 32.5 (C-2); HRMS: [M+Na]⁺ calcd for C₂₀H₂₂O₄Na 349.14103, found 349.14054.

1,2-di-deoxy-3-O-benzyl-D-glucopyranose (S109)



1,2-di-deoxy-3-O-benzyl-4,6-O-benzylidene-D-glucopyranose (**S108**, 1.40 g, 4.3 mmol) and PTSA-H₂O (82 mg, 0.43 mmol, 0.1 eq) were dissolved in methanol and heated to 60 °C. When TLC shows full conversion, triethylamine (0.12 mL, 0.86 mmol, 0.2 eq) was added and the reaction mixture was concentrated under reduced pressure. The residue was purified over silica (15% acetone in DCM) yielding the title compound as colourless oil in quantitative yield. ¹H

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NMR (400 MHz, CDCl₃) δ 7.40 – 7.28 (m, 5H, CH_{arom}), 4.71 (d, J = 11.6 Hz, 1H, CHH Bn), 4.52 (d, J = 11.6 Hz, 1H, CHH Bn), 4.00 (ddd, J = 11.8, 4.9, 1.7 Hz, 1H, H-1_{eq}), 3.87 (ddd, J = 11.7, 6.0, 3.5 Hz, 1H, H-6), 3.74 (ddd, J = 11.7, 6.6, 5.2 Hz, 1H, H-6), 3.56 – 3.37 (m, 3H, H-1_{ax}, H-3, H-4), 3.24 (ddd, J = 8.9, 5.2, 3.4 Hz, 1H, H-5), 2.79 (d, J = 2.2 Hz, 1H, 4-OH), 2.27 (t, J = 6.3 Hz, 1H, 6-OH), 2.07 (ddt, J = 12.8, 4.0, 1.9 Hz, 1H, H-2_{eq}), 1.62 (tdd, J = 12.7, 10.7, 4.9 Hz, 1H, H-2_{ax}), ¹³C NMR (101 MHz, CDCl₃) δ 138.2 (C_q), 128.6, 127.9, 127.8 (CH_{arom}), 80.5 (C-3), 79.7 (C-5), 71.6 (C-4), 70.9 (CH₂ Bn), 65.7 (C-1), 63.1 (C-6), 30.5 (C-2). Spectra in agreement with literature.¹⁰¹

1,2,6-tri-deoxy-3-O-benzyl-D-glucopyranose (55)

HO BnO

1,2-di-deoxy-3-O-benzyl-D-glucopyranose (S109, 1.03 g, 4.30 mmol) was dissolved in 25 mL pyridine, after which para-toluenesulfonyl chloride (1.23 g, 6.45 mmol, 1.5 eq) was added. The reaction mixture was stirred overnight, diluted with ethyl acetate and washed with 1M HCl and sat. aq. NaHCO₃. The organic phase was dried with MgSO₄ and concentrated under reduced pressure. The crude tosylate was dissolved in THF and lithium aluminiumhydride (2.4 M in THF, 7.2 mL, 17.2 mmol, 4 eq) was added. The reaction mixture was heated to a reflux. When complete, the reaction mixture was cooled to 0 °C, carefully quenched with 1M HCl and extracted twice with ethyl acetate. The combined organic phases were washed with sat. aq. NaHCO₃, dried with MgSO₄ and concentrated under reduced pressure. The residue was purified by silica chromatography (10% acetone in pentane) to give the title compound as colourless oil. Yield: 645 mg, 2.90 mmol, 68% over 2 steps. $[\alpha]_{25}^{25} = -65.0^{\circ}$ (c = 0.10, CHCl₃); IR (thin film): 668, 699, 1093, 1276, 1455; ¹H NMR (400 MHz, CDCl₃) δ 7.41 – 7.27 (m, 5H, CH_{arom}), 4.71 (d, J = 11.6 Hz, 1H, CHH Bn), 4.50 (d, J = 11.6 Hz, 1H, CHH Bn), 3.95 (ddd, J = 11.9, 4.9, 1.7 Hz, 1H, H-1_{eq}), 3.47 - 3.35 (m, 2H, H-1ax, H-3), 3.28 - 3.15 (m, 2H, H-4, H-5), 2.53 (d, J = 1.7 Hz, 1H, OH), 2.07 (ddt, J = 12.8, 4.4, 2.0 Hz, 1H, H-2_{eq}), 1.64 (tdd, J = 12.7, 11.1, 4.9 Hz, 1H, H-2_{ax}), 1.30 (d, J = 5.5 Hz, 3H, H-6), ¹³C NMR (101 MHz, CDCl₃) δ 138.2 (C_q), 128.6, 127.9, 127.8 (CH_{arom}), 80.6 (C-3), 76.2, 76.2 (C-4, C-5), 70.7 (CH₂ Bn), 65.5 (C-1), 30.7 (C-2), 18.3 (C-6); HRMS: [M+Na]⁺ calcd for C13H18O3Na 245.11482, found 245.11450.

Preparation of acceptor 56



Scheme **\$37**: preparation of acceptor **56**: reagents and conditions: a) BnBr, NaH, DMF, 89%; b) MeOH, 60 °C, 97%; c) i: TsCl, pyridine, ii: LiAlH₄, THF, reflux, 70% over 2 steps

1,2-di-deoxy-3-O-benzyl-4,6-O-benzylidene-D-galactopyranose (\$110)



1,2-di-deoxy-4,6-O-benzylidene-D-galactopyranose (**S101**, 1.18 g, 5 mmol), benzyl bromide (0.89 mL, 7.50 mmol, 1.5 eq) and sodium hydride (60% dispersion in mineral oil, 300 mg, 7.50 mmol, 1.5 eq) were dissolved in DMF. When TLC shows full conversion, the reaction is quenched with water and extracted with diethyl ether. The organic phase was dried with MgSO₄ and concentrated under reduced pressure. The residue was purified over silica (10% \rightarrow 15% acetone in pentane), yielding the title compound as white powder. Yield: 1.45 g, 4.43 mmol, 89%. ¹H NMR (400 MHz, CDCl₃) δ 7.60 – 7.53 (m, 2H, CH_{arom}), 7.41 – 7.26 (m, 8H, CH_{arom}), 5.58 (s, 1H, CHPh), 4.67 (s, 2H, CH₂ Bn), 4.26 (dd, *J* = 12.3, 1.6 Hz, 1H, H-2), 4.20 – 4.12 (m, 2H, H-1_{eq}, H-4), 4.01 (dd, *J* = 12.4, 1.8 Hz, 1H, H-6), 3.57 (ddd, *J* = 11.9, 4.7, 3.1 Hz, 1H, H-3), 3.47 (ddd, *J* = 12.6, 11.7, 2.0 Hz, 1H, H-1_{ax}), 3.23 (q, *J* = 1.6 Hz, 1H, H-5), 2.25 (qd, *J* = 12.5, 4.6 Hz, 1H, H-2_{ax}), 1.74 (dddd, *J* = 12.4, 4.6, 2.8, 1.3 Hz, 1H, H-2_{eq}), ¹³C NMR (101 MHz, CDCl₃) δ 138.4, 138.1 (C_q), 128.9, 128.6, 128.2, 127.8, 126.5 (CH_{arom}), 101.1 (CHPh), 75.5 (C-3), 73.4 (C-4), 70.6 (C-6), 70.2 (C-5), 69.6 (C-1), 66.2 (CH₂ Bn), 26.9 (C-2); HRMS: [M+Na]⁺ calcd for C₂₀H₂₂O₄Na 349.14103, found 349.14066.

1,2-di-deoxy-3-O-benzyl-D-galactopyranose (S111)

1,2-di-deoxy-3-O-benzyl-4,6-O-benzylidene-D-galactopyranose (**S110**) 1.63 g, 5 mmol) and PTSA-H₂O (95 mg, 0.5 mmol, 0.1 eq) were dissolved in methanol and heated to 60 °C. When TLC shows full conversion, triethylamine (0.14 mL, 1 mmol, 0.2 eq) was added and the reaction mixture was concentrated under reduced pressure. The residue was purified over silica (25% acetone in DCM) yielding the title compound as white powder. Yield: 1.16 g, 4.85 mmol, 97%. ¹H NMR (400 MHz, CDCl₃) δ 7.41 – 7.28 (m, 5H, CH_{arom}), 4.61 (d, *J* = 1.7 Hz, 2H, CH₂ Bn), 4.07 (ddd, *J* = 11.7, 5.1, 1.7 Hz, 1H, H-1_{eq}), 4.03 – 3.98 (m, 1H, H-4), 3.92 (ddd, *J* = 11.7, 6.7, 3.7 Hz, 1H, H-6), 3.75 (ddd, *J* = 11.7, 8.5, 4.3 Hz, 1H, H-6), 3.53 (ddd, *J* = 11.6, 5.0, 3.0 Hz, 1H, H-3), 3.41 (ddd, *J* = 12.7, 11.7, 2.3 Hz, 1H, H-1_{ax}), 3.33 (ddt, *J* = 6.6, 4.2, 1.2 Hz, 1H, H-5), 2.61 (dd, *J* = 2.5, 1.2 Hz, 1H, 4-OH), 2.54 (dd, *J* = 8.5, 3.8 Hz, 1H, 6-OH), 2.01 (tdd, *J* = 12.8, 11.5, 5.0 Hz, 1H, H- $_{2ax}$), 1.75 (ddq, *J* = 13.0, 5.0, 1.9 Hz, 1H, H- $_{2eq}$), ¹³C NMR (101 MHz, CDCl₃) δ 137.9 (C_q), 128.7, 128.1, 127.8 (CH_{arom}), 78.5 (C-5), 75.9 (C-3), 69.8 (CH₂ Bn), 67.0 (C-4), 66.0 (C-6), 63.6 (C-1), 26.5 (C-2). HRMS [M+Na]⁺ calcd for C₁₃H₁₈O₄Na 261.10973, found 261.10949.

1,2-di-deoxy-3-O-benzyl-D-fucopyranose (56)



1,2-di-deoxy-3-O-benzyl-D-galactopyranose (S111, 1.13 g, 4.74 mmol) was dissolved in 25 mL pyridine, after which para-toluenesulfonyl chloride (1.36 g, 7.11 mmol, 1.5 eq) was added. The reaction mixture was stirred overnight, diluted with ethyl acetate and washed with 1M HCl and sat. aq. NaHCO₃. The organic phase was dried with MgSO₄ and concentrated under reduced pressure. The crude tosylate was dissolved in THF and lithium aluminiumhydride (2.4 M in THF, 7.9 mL, 19 mmol, 4 eq) was added. The reaction mixture was heated to a reflux. When complete, the reaction mixture was cooled to 0 °C, carefully quenched with 1M HCl and extracted twice with ethyl acetate. The combined organic phases were washed with sat. aq.

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NaHCO₃, dried with MgSO₄ and concentrated under reduced pressure. The residue was purified by silica chromatography (10% acetone in pentane) to give the title compound as colourless oil. Yield: 740 mg, 3.33 mmol, 70% over 2 steps. $[\alpha]_D^{25} = 33.9^{\circ}$ (c = 0.43, CHCl₃); IR (thin film): 668, 700, 980, 1027, 1086, 1183; ¹H NMR (400 MHz, CDCl₃) δ 7.39 – 7.28 (m, 5H, CH_{arom}), 4.64 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.60 (d, *J* = 11.9 Hz, 1H, CHH Bn), 4.00 (ddd, *J* = 11.7, 5.1, 1.7 Hz, 1H, H-1_{eq}), 3.82 – 3.74 (m, 1H, H-4), 3.52 (ddd, *J* = 11.6, 5.1, 3.0 Hz, 1H, H-3), 3.43 – 3.34 (m, 2H, H-1_{ax}, H-5), 2.22 (dd, *J* = 3.3, 1.0 Hz, 1H, OH), 1.94 (tdd, *J* = 12.9, 11.6, 5.1 Hz, 1H, H-2_{ax}), 1.73 (dddd, *J* = 11.8, 6.3, 2.4, 1.3 Hz, 1H, H-2_{eq}), 1.31 (d, *J* = 6.5 Hz, 3H, H-6), ¹³C NMR (101 MHz, CDCl₃) δ 138.1 (C_q), 128.7, 128.0, 127.8 (CH_{arom}), 76.5 (C-3), 74.6 (C-5), 69.7 (CH₂ Bn), 68.8 (C-4), 65.9 (C-1), 26.3 (C-2), 17.5 (C-6); HRMS [M+Na]⁺ calcd for C₁₃H₁₈O₃Na 245.11482, found 245.11451.

Characterisation of glycosylation products



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor A and acceptor 6. Yield: 93 mg, 98 μ mol, 98%, α : β = 2.6:1. Data reported for a 1:0.4 mixture of anomers: ¹H NMR (500 MHz, CDCl₃) & 8.06 - 8.00 (m, 1H), 7.98 - 7.93 (m, 2H), 7.60 - 7.00 (m, 38H), 5.49 - 5.41 (m, 2H, H-4a, CHPha), 5.30 (dd, J = 10.3, 9.1 Hz, 0.4H, H-4 β), 5.24 (s, 0.4H, CHPh β), 5.19 (d, J = 3.5 Hz, 1H, H-1'a), 4.97 (d, J = 11.5 Hz, 0.4H), 4.89 – 4.85 (m, 0.8H, H-1'β, CHH Bnβ), 4.82 (d, J = 10.9 Hz, 1H), 4.79 – 4.73 (m, 2H), 4.66 (d, J = 12.0 Hz, 0.4 H), 4.59 - 4.50 (m, 5H), 4.48 - 4.41 (m, 2H), 4.40 - 4.26 (m, 4H), 4.18 (d, J = 1.0 Hz)12.1 Hz, 1H), 4.04 – 3.93 (m, 3H), 3.68 – 3.47 (m, 7H), 3.37 (d, J = 2.9 Hz, 4H, CH₃ Meaβ), 3.35 – 3.30 (m, 1H), 3.28 (t, J = 9.3 Hz, 0.4H, H-3' β), 3.20 (td, J = 9.7, 5.0 Hz, 0.4H, H-5' β), 2.90 (t, J = 9.7, 5.0 Hz, 0.4H, H-5' β), 3.90 (t, J = 9.7, 5.0 Hz, 0.4H, H-5' β), 3.90 (t, J = 9.7, 5.0 Hz, 0.4H, H-5' β), 3.90 (t, J = 9.7, 5.0 Hz, 0.4H, H-5' β), 3.90 (t, J = 9.7, 5.0 Hz, 0.4H, H-5' β), 3.90 (t, J = 9.7, 5.0 Hz, 0.4H, H-5' β), 5.0 10.1 Hz, 0.4H, H-6' β); ¹³C NMR (126 MHz, CDCl₃) δ 165.3, 165.2, 138.8, 138.7, 138.2, 138.0, 137.9, 137.8, 137.8, 137.7, 137.4, 133.2, 133.1, 130.6, 129.9, 129.9, 129.9, 129.0, 128.8, 128.8, 128.6, 128.6, 128.4, 128.4, 128.3, 128.3, 128.3, 128.2, 128.2, 128.2, 128.0, 128.0, 127.9, 127.9, 127.8, 127.8, 127.8, 127.6, 127.6, 127.5, 127.5, 127.5, 126.2, 126.0, 102.9 (C-1'β), 101.3 (CHPha), 100.9 (CHPhβ), 98.6 (C-1'a), 98.1 (C-1β), 97.7 (C-1a), 82.7, 82.3, 81.5, 81.0, 80.3, 78.8, 78.6, 78.6, 77.4, 77.2, 76.9, 76.2, 75.5, 75.3, 75.0, 73.9, 73.7, 73.7, 73.6, 72.9, 72.2, 69.6, 69.4, 69.1, 68.8, 68.6, 68.5, 65.5, 63.0, 55.5, 55.4, HRMS: [M+NH₄]⁺ calcd for C₅₅H₅₆O₁₂NH₄ 926.41100, found 926.40958.

Disaccharide 6B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor **6**. Yield: 86 mg, 99 µmol, 99%, $\alpha:\beta = 1:5$. IR (thin film): 696, 711, 749, 998, 1027, 1043, 1070, 1091, 1174, 1269, 1452, 1727, 2109; Data for β -anomer: ¹H NMR (500 MHz, CDCl₃) δ 8.04 – 7.14 (m, 25H, CH_{arom}), 5.27 (dd, *J* = 10.3, 9.1 Hz, 1H, H-4), 5.23 (s, 1H, CH Ph), 4.89 (d, *J* = 11.9 Hz, 1H, CHH Bn), 4.83 (d, *J* = 11.4 Hz, 1H, CHH Bn), 4.73 (d, *J* = 11.4 Hz, 1H, CHH Bn), 4.67 (d, *J* = 8.0 Hz, 1H, H-1'), 4.60 (d, *J* = 11.8 Hz, 1H,

CH*H* Bn), 4.56 (d, *J* = 3.6 Hz, 1H, H-1), 4.53 – 4.47 (m, 2H, C*H*H Bn, CH*H* Bn), 4.26 (t, *J* = 9.3 Hz, 1H, H-3), 4.02 – 3.92 (m, 1H, H-5), 3.85 (dd, *J* = 10.5, 5.0 Hz, 1H, H-6'), 3.72 (dd, *J* = 9.7, 3.6 Hz, 1H, H-2), 3.63 – 3.51 (m, 2H, H-6 x2), 3.47 – 3.42 (m, 1H, H-3'), 3.37 (d, *J* = 4.2 Hz, 4H, CH₃ OMe, H-2'), 3.34 – 3.28 (m, 1H, H-4'), 3.17 – 3.11 (m, 1H, H-5'), 2.76 (t, *J* = 10.3 Hz, 1H, H-6'). ¹³C NMR (126 MHz, CDCl₃) δ 165.1 (C=O), 138.1, 138.0, 137.8, 137.2, 133.1, 130.5, 129.9, 129.7, 129.1, 128.9, 128.7, 128.6, 128.6, 128.4, 128.4, 128.3, 128.3, 128.3, 128.3, 128.3, 128.2, 128.1, 127.8, 127.8, 127.8, 127.6, 127.6, 126.1, 126.0 (CH_{arom}), 102.2 (C-1'), 101.1 (CH Ph), 97.8 (C-1), 81.4 (C-4'), 79.8 (C-2), 79.2 (C-3'), 77.7 (C-3), 74.9 (CH₂ Bn), 73.8 (CH₂ Bn), 73.7 (CH₂ Bn), 69.5 (C-4), 68.9 (C-6), 68.7 (C-5), 68.1 (C-6'), 66.2 (C-2'), 65.6 (C-5'), 55.5 (CH₃ OMe). Diagnostic peaks for α-anomer: ¹H NMR (500 MHz, CDCl₃) δ 5.50 (s, 1H, CH Ph), 5.36 (dd, *J* = 10.3, 9.2 Hz, 1H, H-4), 5.04 (d, *J* = 3.8 Hz, 1H, H-1'), 4.65 – 4.63 (m, 1H, H-1), 4.15 (dd, *J* = 10.2, 4.9 Hz, 1H, H-5), 3.37 (s, 3H, CH₃ OMe). ¹³C NMR (126 MHz, CDCl₃) δ 165.3 (C=O), 137.5, 137.5, 133.3, 131.8, 131.2, 129.7, 124.8, 124.5 (CH_{arom}), 101.3 (CHPh), 99.5 (C-1'), 97.5 (C-1), 82.7 (C-4'), 78.0, 77.6, 76.7, 75.1 (CH₂ Bn), 73.3 (CH₂ Bn), 72.1 (C-4), 69.3 (C-6'), 68.8 (C-6), 63.3, 63.0, 55.4 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₄₈H₄₉N_{3O₁₁NH₄ 861.37053, found 861.36976.}

Disaccharide 7A



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor A and acceptor 7. Yield: 94 mg, 99 μ mol, 99%, α : β = 1.8:1. Data reported for a 2:1 mixture of anomers: ¹H NMR (500 MHz, CDCl₃) δ 8.04 – 7.99 (m, 4H), 7.95 (dd, J = 8.3, 1.4 Hz, 2H), 7.53 (t, J = 7.4 Hz, 1H), 7.50 - 7.45 (m, 4H), 7.41 - 7.15 (m, 66H), 7.10 (ddt, *J* = 7.8, 4.8, 2.2 Hz, 6H), 5.50 (s, 1H, CHPhβ), 5.39 (s, 2H, CHPhα), 5.21 (dd, *J* = 9.7, 3.8 Hz, 2H, H-2a), 5.14 (dd, J = 9.9, 3.6 Hz, 3H, H-1'a, H-2 β), 5.10 – 5.06 (m, 3H, H-1 β , CHH Bna)), $4.95 (d, J = 10.5 Hz, 1H), 4.92 (d, J = 3.8 Hz, 2H, H-1\alpha), 4.90 (d, J = 7.7 Hz, 1H, H-1'\beta), 4.82 (d, J = 10.5 Hz, 1H), 4.92 (d,$ = 11.4 Hz, 2H), 4.77 - 4.70 (m, 6H), 4.67 (d, J = 12.1 Hz, 1H), 4.65 - 4.57 (m, 5H), 4.57 - 4.50 (m, 4H), 4.48 – 4.40 (m, 3H), 4.39 – 4.31 (m, 3H), 4.14 (dd, J = 10.2, 4.9 Hz, 2H), 3.99 (t, J = 9.4 Hz, 2H), 3.94 (td, J = 10.0, 4.9 Hz, 2H), 3.89 - 3.79 (m, 6H), 3.78 - 3.73 (m, 2H), 3.70 (td, J = 10.6, 1.8 Hz, 3H), 3.63 – 3.55 (m, 2H), 3.53 (t, J = 8.9 Hz, 1H), 3.48 – 3.42 (m, 4H), 3.40 – 3.33 (m, 12H); ¹³C NMR (126 MHz, CDCl₃) δ 166.0 (C=Oα), 165.9 (C=Oβ), 138.7, 138.6, 138.5, 138.5, 138.3, 138.3, 138.1, 138.1, 137.6, 137.4, 133.2, 133.1, 130.1, 129.9, 129.8, 129.7, 129.0, 128.8, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.3, 128.2, 128.1, 128.1, 128.0, 128.0, 128.0, 127.9, 127.8, 127.8, 127.6, 127.5, 127.4, 126.2, 126.1, 103.9 (C-1'β), 101.2 (CHPha), 101.1 (CHPhβ), 98.9 (C-1'a), 97.2 (C-1'a), 1a), 97.0 (C-1β), 82.3, 82.3, 81.7, 81.2, 79.6, 79.5, 78.1, 77.8, 77.7, 77.4, 77.2, 76.9, 76.0, 75.2, 75.1, 75.1, 75.0, 74.9, 74.7, 73.7, 73.7, 73.7, 73.0, 70.1, 69.8, 68.9, 68.7, 68.6, 68.6, 66.1, 63.2, 55.3, 55.3; HRMS: [M+NH₄]⁺ calcd for C₅₅H₅₆O₁₂NH₄ 926.41100, found 926.40981

Disaccharide 7B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor 7. Yield: 81 mg, 93 μ mol, 93%, α : β = 1:4. Data for the β-anomer: ¹H NMR (500 MHz, CDCl₃) δ 8.08 (dd, J = 8.4, 1.3 Hz, 2H, CH_{arom}), 7.62 – 7.56 (m, 1H, CH_{aron}), 7.49 - 7.43 (m, 4H, CH_{aron}), 7.41 - 7.20 (m, 18H, CH_{aron}), 5.51 (s, 1H, CHPh), 5.23 (dd, J = 10.0, 3.7 Hz, 1H, H-2), 5.05 (d, J = 3.6 Hz, 1H, H-1), 4.94 (d, J = 10.6 Hz, 1H, CHH Bn), 4.75 (d, J = 11.3 Hz, 1H, CHH Bn), 4.71 (d, J = 8.0 Hz, 1H, H-1'), 4.66 (d, J = 12.0 Hz, 1H, , CHH Bn), 4.60 (d, J = 11.2 Hz, 1H, CHH Bn), 4.54 (d, J = 12.2 Hz, 1H, CHH Bn), 4.49 – 4.43 (m, 2H, H-3, CH*H* Bn), 4.26 (dd, *J* = 10.5, 5.0 Hz, 1H, H-6'), 3.84 (ddd, *J* = 10.0, 3.7, 1.9 Hz, 1H, H-5), 3.80 - 3.73 (m, 2H, H-4, H-6), 3.70 (dd, J = 10.7, 1.9 Hz, 1H, H-6), 3.61 (t, J = 9.2 Hz, 1H, H-4'), 3.55 (t, J = 10.2 Hz, 1H, H-6'), 3.38 - 3.32 (m, 5H, H-2', H-5', CH₃ OMe), 3.29 (t, J = 9.2 Hz, 1H, H-3'); ¹³C NMR (126 MHz, CDCl₃) δ 165.8 (C=O), 138.5, 138.1, 137.8, 137.1 (C_q), 133.3 (CH_{arom}), 129.9 (C_q), 129.8, 129.8, 129.2, 128.6, 128.6, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.1, 128.1, 128.0, 127.9, 127.9, 127.9, 127.8, 127.8, 127.8, 127.7, 126.2, 126.0 (CH_{arom}), 102.9 (C-1'), 101.3 (CHPh), 97.1 (C-1), 81.6 (C-4'), 79.4 (C-3), 79.2 (C-3'), 76.0 (C-4), 75.0, 74.9 (CH₂ Bn), 74.2 (C-2), 73.7 (CH₂ Bn), 70.2 (C-5), 68.6, 68.5 (C-6, C-6'), 66.5, 66.3 (C-2', C-5'), 55.3 (CH₃ OMe); diagnostic peaks for the α -anomer: ¹H NMR (500 MHz, CDCl₃) δ 5.41 (d, J = 3.8 Hz, 1H, H-1'), 5.35 (s, 1H, CHPh), 4.82 (d, J = 11.0 Hz, 1H, CHH Bn), 4.38 (dd, J = 10.0, 8.4 Hz, 1H, H-3), 4.08 (dd, J = 10.2, 4.8 Hz, 1H, H-6'), 3.94 (dd, J = 10.0, 9.1 Hz, 1H), 3.46 (t, J = 10.3 Hz, 1H); ¹³C NMR (126 MHz, CDCl₃) δ 166.1 (C=O), 98.4 (C-1'), 97.2 (C-1), 82.8, 78.8, 76.6, 76.2, 75.0, 74.5, 73.8, 72.3, 70.1, 68.3, 63.4, 63.0, 55.3 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₄₈H₄₉N₃O₁₁NH₄ 861.37053, found 861.36933.

Disaccharide 10A



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **A** and acceptor **10**. Yield: 75 mg, 78 µmol, 78%, $\alpha:\beta > 20:1$. ¹H NMR (500 MHz, CDCl₃) δ 8.07 – 7.98 (m, 2H, CH_{arom}), 7.41 – 7.17 (m, 23H, CH_{arom}), 7.13 – 7.08 (m, 3H, CH_{arom}), 7.01 – 6.97 (m, 2H, CH_{arom}), 5.88 (dd, *J* = 10.1, 8.9 Hz, 1H, H-3), 5.30 (s, 1H, CHPh), 4.92 (d, *J* = 3.4 Hz, 1H, H-1), 4.84 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.80 – 4.76 (m, 2H, H-1', CHH Bn), 4.71 (d, *J* = 11.2 Hz, 1H, CHH Bn), 4.67 (d, *J* = 8.7 Hz, 1H, CHH Bn), 4.64 (d, *J* = 8.6 Hz, 1H, CHH Bn), 4.52 (d, *J* = 9.0 Hz, 1H, CHH Bn), 4.50 (d, *J* = 7.8 Hz, 1H, CHH Bn), 4.40 (d, *J* = 10.8 Hz, 1H, CHH Bn), 3.95 – 3.86 (m, 4H, H-2, H-3', H-4, H-5), 3.84 – 3.78 (m, 2H, H-6'), 3.72 – 3.66 (m, 2H, H-5', H-6), 3.44 (dd, *J* = 9.3, 3.5 Hz, 1H, H-2'), 3.41 – 3.38 (m, 4H, H-4', CH₃ OMe), 3.37 – 3.33 (m, 1H, H-6'); ¹³C NMR (126 MHz, CDCl₃) δ 165.5 (C=O), 138.8, 138.6, 137.8, 137.6, 137.5, 133.0 (C_q), 130.1, 129.7, 128.8, 128.6, 128.5, 128.3, 128.3, 128.3, 128.3, 128.2, 128.1, 128.0, 128.0, 127.9, 127.8, 127.6, 126.3 (CH_{arom}), 101.2 (CHPh), 98.0 (C-1'), 97.3 (C-1), 82.1 (C-4'), 78.7 (C-3'), 78.2 (C-2'), 76.5 (C-4), 76.2 (C-2), 75.2 (CH₂ Bn), 74.5 (CH₂ Bn), 73.8 (CH₂ Bn), 73.7 (C-3), 73.5 (CH₂ Bn), 69.9 (C-5), 68.6 (C-6'), 68.3 (C-6), 63.0 (C-5'), 55.4 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₅₅H₅₆O₁₂NH₄ 926.41100, found 926.40995.

Disaccharide 10B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor 10. Yield: 69 mg, 82 μ mol, 82%, α : β = 6:1. Data for α-anomer: ¹H NMR (400 MHz, CDCl₃) δ 8.06 - 8.01 (m, 2H, CH_{arom}), 7.47 - 7.19 (m, 18H, CHarom), 7.15 – 7.08 (m, 3H, CHarom), 7.01 (dt, J = 4.6, 3.4 Hz, 2H, CHarom), 5.86 (dd, J = 10.0, 8.9 Hz, 1H, H-3), 5.33 (s, 1H, CHPh), 4.98 (d, J = 3.5 Hz, 1H, H-1), 4.88 (d, J = 3.6 Hz, 1H, H-1'), 4.80 (d, J = 10.9 Hz, 1H, CHH Bn), 4.68 (d, J = 5.9 Hz, 1H, CHH Bn), 4.65 (d, J = 4.7 Hz, 1H, CHH Bn), 4.53 (d, J = 8.9 Hz, 1H, CHH Bn), 4.50 (d, J = 7.7 Hz, 1H, CHH Bn), 4.42 (d, J = 10.8 Hz, 1H, CHH Bn), 3.97 - 3.87 (m, 4H, H-2, H-3', H-4, H-5), 3.84 - 3.77 (m, 2H, H-6, H-6'), 3.75 - 3.65 (m, 2H, H-5', H-6), 3.52 - 3.46 (m, 4H, H-4', CH₃ OMe), 3.39 (t, J = 10.2 Hz, 1H, H-6'), 3.27 (dd, I = 10.0, 3.6 Hz, 1H, H-2'); ¹³C NMR (101 MHz, CDCl₃) δ 165.5 (C=O), 138.0, 137.9, 137.6, 137.3, 133.15 (C_q), 130.0, 129.7, 129.7, 129.0, 128.6, 128.6, 128.5, 128.4, 128.4, 128.3, 128.2, 128.2, 128.1, 128.1, 128.0, 127.9, 127.9, 127.8, 127.8, 126.3, 126.0 (CH_{arom}), 101.3 (CHPh), 98.1 (C-1'), 97.3 (C-1), 82.6 (C-4'), 76.9 (C-2), 76.1 (C-4), 75.7 (C-3'), 75.1 (CH₂ Bn), 74.6 (CH₂ Bn), 73.8 (CH₂ Bn), 73.6 (C-3), 70.0 (C-5), 68.5 (C-6'), 68.3 (C-6), 63.4 (C-5'), 63.0 (C-2'), 55.6 (CH₃ OMe); Diagnostic peaks for β -anomer: ¹H NMR (400 MHz, CDCl₃) δ 5.52 (s, 1H, CHPh), 4.95 (d, J = 3.5 Hz, 1H, H-1), 4.28 – 4.21 (m, 2H, H-1', H-6); ¹³C NMR (101 MHz, CDCl₃) δ 103.9 (C-1'), 101.3 (CHPh), 99.5 (C-1), 81.2, 80.1, 79.7, 76.2, 74.9, 73.3, 68.5, 66.2 (C-6), 65.7, 55.5 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₄₈H₄₉N₃O₁₁NH₄ 861.37053, found 861.36950.

Disaccharide 12A



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **A** and acceptor **12**. Yield: 86 mg, 96 μmol, 96%, $\alpha:\beta = 1:1.9$. Data reported for a 1:2 mixture: ¹H NMR (500 MHz, CDCl₃) δ 7.56 – 7.08 (m, 90H, CH_{arom}), 5.68 (d, *J* = 3.8 Hz, 1H, H-1'a), 5.61 (s, 2H, CHPhβ), 5.53 (s, 1H, CHPhα), 5.11 (d, *J* = 7.6 Hz, 2H, H-1'β), 5.01 (d, *J* = 11.0 Hz, 1H, CHH Bnα), 4.97 – 4.86 (m, 9H), 4.86 – 4.82 (m, 8H), 4.77 (d, *J* = 11.2 Hz, 2H), 4.68 (dd, *J* = 12.2, 3.9 Hz, 3H), 4.64 – 4.56 (m, 6H), 4.49 (dd, *J* = 5.4, 2.2 Hz, 1H, H-1α), 4.41 (d, *J* = 7.5 Hz, 2H, H-1β), 4.37 (dd, *J* = 10.4, 5.0 Hz, 2H, H-6'β), 4.26 – 4.19 (m, 2H), 4.08 (t, *J* = 9.4 Hz, 1H), 3.90 – 3.85 (m, 3H), 3.84 – 3.71 (m, 14H), 3.66 – 3.61 (m, 3H), 3.60 (s, 6H, CH₃ OMeβ), 3.59 (s, 3H, CH₃ OMeα), 3.56 (t, *J* = 7.9 Hz, 3H), 3.41 (td, *J* = 9.8, 5.0 Hz, 2H, H-5'β); ¹³C NMR (126 MHz, CDCl₃) δ 138.8, 138.6, 138.5, 138.3, 138.2, 138.2, 138.1, 138.0, 137.9, 137.8, 137.4, 135.4, 131.7, 131.4, 130.4, 129.0, 128.7, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 128.1, 128.1, 128.0, 128.0, 127.9, 127.9, 127.8, 127.7, 127.7, 127.7, 127.6, 127.5, 126.4, 126.1, 104.6 (C-1α), 102.7 (C-1β), 102.5 (C-1'β), 101.2 (CHPha), 101.1 (CHPhβ), 96.2 (C-1'a), 85.3, 83.0, 82.5, 82.4, 81.5, 81.1, 78.9, 78.7, 78.6, 78.3, 78.2, 76.2, 75.5, 75.4, 75.3, 75.2, 75.1, 75.0, 74.9, 73.6, 73.0, 69.0, 68.9, 68.8, 68.7, 66.0 (C-5'β), 62.5 (C-5'a),

56.8 (CH₃ OMea), 56.5 (CH₃ OMe β); HRMS: [M+NH₄]⁺ calcd for C₅₅H₅₈O₁₁NH₄ 912.43174, found 912.43016.

Disaccharide 12B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor **12**. Yield: 65 mg, 78 μ mol, 78%, α : β = 1:6. Data for the β-anomer: ¹H NMR (500 MHz, CDCl₃) δ 7.41 – 7.24 (m, 25H, CH_{arom}), 5.56 (s, 1H. CHPh), 4.95 (d, J = 10.6 Hz, 1H, CHH Bn), 4.92 (d, J = 11.2 Hz, 1H, CHH Bn), 4.88 (d, J = 10.6 Hz, 1H, CHH Bn), 4.82 – 4.77 (m, 3H, H-1', CHH Bn, CHH Bn), 4.62 (d, J = 12.2 Hz, 1H, CHH Bn), 4.58 – 4.51 (m, 2H, CHH Bn), 4.32 (d, J = 7.2 Hz, 1H, H-1), 4.29 (dd, J = 10.5, 5.1 Hz, 1H, H-6'), 3.81 (t, J = 10.3 Hz, 1H, H-6'), 3.77 - 3.69 (m, 5H, H-2, H-4, H-4', 2x H-6), 3.68 - 3.64 (m, 1H, H-3), 3.56 (t, J = 9.2 Hz, 1H, H-3'), 3.53 (s, 3H, CH₃ OMe), 3.51 - 3.46 (m, 2H, H-2', H-5), 3.30 (td, J = 9.7, 5.0 Hz, 1H, H-5'); ¹³C NMR (126 MHz, CDCl₃) δ 138.3, 138.2, 138.0, 137.8, 137.2 (C_q), 129.2, 128.6, 128.5, 128.5, 128.5, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 128.0, 127.9, 127.9, 127.9, 127.9, 127.8, 127.7, 126.3, 126.1 (CHarom), 102.6 (C-1), 101.5 (C-1'), 101.3 (CHPh), 84.9 (C-4), 81.6 (C-4'), 79.7, 79.6 (C-2, C-3'), 78.3 (C-3), 75.6, 75.0 (CH₂ Bn), 74.9 (C-2'), 74.9, 73.6 (CH₂ Bn), 68.8, 68.7 (C-6, C-6'), 66.3, 66.3 (C-5, C-5'), 56.7 (CH₃ OMe); diagnostic peaks for the α anomer: ¹H NMR (500 MHz, CDCl₃) δ 5.59 (d, J = 3.8 Hz, 1H, H-1'), 5.52 (s, 1H, CHPh), 4.37 (d, *J* = 7.1 Hz, 1H, H-1), 3.98 (dd, *J* = 10.0, 9.1 Hz, 1H); ¹³C NMR (126 MHz, CDCl₃) δ 104.6 (C-1), 101.4 (CHPh), 97.1 (C-1'), 83.0, 78.6, 76.2, 76.1, 75.6, 63.0, 62.8, 57.2 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₄₈H₅₁N₃O₁₀NH₄ 847.39127, found 847.38954.

Disaccharide 14A



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **A** and acceptor **14**. Yield: 75 mg, 79 µmol, 79%, $\alpha:\beta = 1.3:1$. Data reported for a 1:1 mixture of anomers: ¹H NMR (500 MHz, CDCl₃) δ 8.10 – 8.06 (m, 2H), 8.02 – 7.94 (m, 2H), 7.54 – 7.10 (m, 56H), 5.73 (d, *J* = 4.0 Hz, 1H, H-1'a), 5.48 (s, 1H, *CH*Ph β), 5.47 (s, 1H, *CH*Ph α), 4.90 – 4.83 (m, 4H), 4.82 – 4.71 (m, 9H), 4.70 – 4.62 (m, 4H), 4.62 – 4.56 (m, 8H), 4.55 – 4.46 (m, 4H), 4.30 (t, *J* = 9.2 Hz, 1H, H-4 β), 4.17 (dd, *J* = 10.5, 5.0 Hz, 1H, H-6' β), 4.11 – 3.97 (m, 6H), 3.86 (ddd, *J* = 14.7, 9.2, 4.1 Hz, 3H), 3.82 – 3.77 (m, 2H, H-2 $\alpha\beta$), 3.74 (t, *J* = 9.0 Hz, 1H), 3.62 (t, *J* = 9.3 Hz, 1H), 3.58 – 3.53 (m, 2H), 3.51 (dd, *J* = 9.5, 4.0 Hz, 1H, H-2' α), 3.45 (t, *J* = 8.2 Hz, 1H, H-2' β), 3.37 (s, 3H, CH₃ OMe α), 3.36 (s, 3H, CH₃ OMe β), 3.24 (td, *J* = 9.7, 5.0 Hz, 1H, H-5' β); ¹³C NMR (126 MHz, CDCl₃) δ 166.3, 166.2, 139.1, 138.8, 138.5, 138.5, 138.3, 138.3, 138.1, 137.5, 137.4, 133.0, 133.0, 130.2, 130.1, 129.9, 129.9, 129.8, 129.7, 129.0, 128.9, 128.9, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.2, 128.1, 128.1, 128.0, 127.9, 127.8, 127.7, 127.7, 127.6, 127.6, 127.6, 127.5, 127.2, 126.9, 126.3, 126.1, 103.5 (C-1' β), 101.3 (CHPha), 101.2 (CHPh β), 99.1 (C-1 β), 98.6 (C-1 α), 98.4 (C-1' α), 82.7, 82.3, 81.7, 81.5, 80.3, 78.8, 78.6, 77.9, 75.9, 75.7, 75.6, 75.4, 75.2, 74.2, 73.3, 73.0, 72.7, 72.6, 71.7, 71.0,

70.2, 69.4, 68.9, 66.0, 64.2, 63.6, 63.6, 55.1;); HRMS: $[M+NH_4]^+$ calcd for $C_{55}H_{56}O_{12}NH_4$ 926.41100, found 926.40949

Disaccharide 14B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor 14. Yield: 78 mg, 92 μ mol, 92%, α : β = 1:8. Data for β-anomer: ¹H NMR (500 MHz, CDCl₃) δ 8.07 (dd, J = 8.3, 1.4 Hz, 2H, CH_{arom}), 7.54 (ddt, J = 8.7, 7.3, 1.3 Hz, 1H, CHarom), 7.44 - 7.22 (m, 22H, CHarom), 5.47 (s, 1H, CHPh), 4.89 (d, J = 11.0 Hz, 1H, CHH Bn), 4.79 - 4.76 (m, 2H, H-1, H-6), 4.75 - 4.70 (m, 3H, 2x CHH Bn, CHH Bn), 4.66 – 4.60 (m, 3H, H-6, 2x CHH Bn), 4.52 (d, J = 8.1 Hz, 1H, H-1'), 4.35 (t, J = 9.4 Hz, 1H, H-4), 4.01 – 3.94 (m, 2H, H-5, H-6'), 3.91 (dd, J = 9.1, 3.2 Hz, 1H, H-3), 3.78 (dd, J = 3.2, 2.0 Hz, 1H, H-2), 3.64 – 3.57 (m, 2H, H-3', H-4'), 3.52 (t, J = 10.3 Hz, 1H, H-6'), 3.41 (dd, J = 9.3, 8.1 Hz, 1H, H-2'), 3.36 (s, 3H, CH₃ OMe), 3.18 – 3.11 (m, 1H, H-5'); ¹³C NMR (126 MHz, CDCl₃) δ 166.4 (C=O), 138.8, 138.4, 137.7, 137.2 (C_a), 133.1 (CH_{arom}), 129.8 (C_a), 129.1, 128.5, 128.4, 128.4, 128.4, 128.3, 128.0, 127.7, 127.6, 127.0, 126.1 (CHarom), 102.2 (C-1'), 101.3 (CHPh), 98.9 (C-1), 81.7 (C-4'), 79.7 (C-3'), 78.4 (C-3), 76.0 (C-4), 75.2 (C-2), 75.0, 72.9, 72.4 (CH₂ Bn), 69.7 (C-5), 68.6 (C-6'), 67.0 (C-2'), 66.2 (C-5'), 63.6 (C-6), 55.1 (CH₃ OMe); diagnostic peaks for the α-anomer: ¹H NMR (500 MHz, CDCl₃) δ 5.67 (d, J = 4.1 Hz, 1H, H-1'), 5.51 (s, 1H, CHPh), 3.83 (dd, J = 3.1, 2.0 Hz, 1H, H-2); ¹³C NMR (126 MHz, CDCl₃) δ 101.4 (CHPh), 99.2 (C-1), 98.7 (C-1'), 82.7, 80.6, 77.4, 76.3, 63.0, 56.1 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₄₈H₄₉N₃O₁₁NH₄ 861.37053, found 861.36936.

Disaccharide 15A



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **A** and acceptor **15**. Yield: 59 mg, 62 µmol, 62%, $\alpha:\beta = 9:1$. Data for α -anomer: ¹H NMR (500 MHz, CDCl₃) δ 8.03 (dd, J = 8.3, 1.4 Hz, 2H, CH_{arom}), 7.57 – 7.52 (m, 1H, CH_{arom}), 7.49 – 7.45 (m, 2H, CH_{arom}), 7.41 – 7.33 (m, 7H, CH_{arom}), 7.31 – 7.22 (m, 10H, CH_{arom}), 7.19 – 7.05 (m, 8H, CH_{arom}), 5.65 (dd, J = 8.7, 3.3 Hz, 1H, H-3), 5.49 (s, 1H, CHPh), 5.35 (d, J = 3.8 Hz, 1H, H-1'), 4.85 (d, J = 2.3 Hz, 1H, H-1), 4.78 (d, J = 11.1 Hz, 1H, CHH Bn), 4.68 (d, J = 12.0 Hz, 1H, CHH Bn), 4.64 – 4.57 (m, 4H, H-4, CHH Bn, 2x CHH Bn), 4.55 (d, J = 11.9 Hz, 1H, CHH Bn), 4.38 (d, J = 11.9 Hz, 1H, CHH Bn), 4.30 (d, J = 11.9 Hz, 1H, CHH Bn), 4.07 (dd, J = 10.2, 4.9 Hz, 1H, H-6'), 4.00 (dd, J = 3.3, 2.3 Hz, 1H, H-2), 3.98 – 3.92 (m, 2H, H-5, H-6), 3.90 (t, J = 9.4 Hz, 1H, H-3'), 3.84 (dt, J = 10.0, 5.1 Hz, 1H, H-5'), 3.80 – 3.76 (m, 1H, H-6), 3.57 (t, J = 10.2 Hz, 1H, H-6'), 3.52 (t, J = 9.5 Hz, 1H, H-4'), 3.41 (s, 3H, CH₃ OMe), 3.40 – 3.36 (m, 1H, H-2'); ¹³C NMR (126 MHz, CDCl₃) δ 165.6 (C=O), 138.8, 138.5, 138.0, 137.8, 137.6 (C_q), 133.2 (CH_{arom}), 130.2 (C_q), 129.9, 128.9, 128.6, 128.4, 128.4, 128.3, 128.3, 128.1, 127.9, 127.8, 127.7, 127.6, 127.5, 126.2 (CH_{arom}), 101.2 (CHPh), 99.0 (C-1), 97.8 (C-1'), 82.1 (C-4'), 79.0

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(C-2'), 78.5 (C-3'), 76.0 (C-2), 75.4 (CH₂ Bn), 74.5 (C-3), 73.6, 73.3, 72.9 (CH₂ Bn), 71.1 (C-4), 70.9 (C-5), 69.4 (C-6), 69.0 (C-6'), 63.6 (C-5'), 55.1 (CH₃ OMe); ¹H NMR (500 MHz, CDCl₃) δ 5.31 (s, 1H, CHPh), 3.25 (dd, *J* = 8.9, 7.8 Hz, 1H, H-2'), 3.12 – 3.02 (m, 2H); ¹³C NMR (126 MHz, CDCl₃) δ 165.6 (C=O), 103.3 (C-1'), 101.0 (CHPh), 99.1 (C-1), 82.5, 81.5, 81.0, 76.2, 75.6, 74.9, 73.4, 73.2, 72.0, 71.5, 68.6, 68.2, 65.7, 55.1 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₅₅H₅₆O₁₂NH₄ 926.41100, found 926.40924.

Disaccharide 15B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor 15. Yield: 83 mg, 87 μ mol, 87%, α : β = 1.5:1. Data reported for a 1:1 mixture of anomers: ¹H NMR (500 MHz, CDCl₃) δ 8.11 – 8.01 (m, 4H), 7.60 - 7.54 (m, 2H), 7.47 - 7.13 (m, 34H), 5.60 (dd, J = 9.0, 3.3 Hz, 1H, H-3a), 5.53 - 5.47 (m, 2H, H-3β, CHPha), 5.31 – 5.27 (m, 2H, H-1'a, CHPhβ), 4.88 – 4.76 (m, 4H, H-1aβ, 2x CHH Bn), 4.73 - 4.61 (m, 8H), 4.58 (d, J = 12.2 Hz, 1H, CHH Bn), 4.51 (d, J = 12.0 Hz, 1H, CHH Bn), 4.45 - 4.36 = 11.0, 3.7 Hz, 1H, H-6'β), 3.95 (dd, *J* = 3.3, 2.1 Hz, 1H), 3.96 – 3.82 (m, 6H), 3.80 (ddd, *J* = 11.0, 6.6, 1.8 Hz, 2H), 3.66 - 3.57 (m, 2H), 3.42 (s, 3H, CH₃ OMea), 3.39 (s, 3H, CH₃ OMeβ), 3.39 -3.29 (m, 2H), 3.27 – 3.19 (m, 2H), 3.03 – 2.93 (m, 2H); 13 C NMR (126 MHz, CDCl₃) δ 165.6, 165.5 (C=O), 138.4, 138.3, 138.1, 138.0, 137.9, 137.9, 137.3, 137.3, 133.2, 133.1, 131.3, 130.7, 130.1, 130.0, 129.7, 129.2, 129.1, 128.6, 128.6, 128.6, 128.5, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.2, 127.9, 127.9, 127.8, 127.8, 127.7, 127.6, 127.6, 126.2, 126.1, 126.1, 125.4, 121.9, 121.9, 101.7 (C-1'β), 101.4 (CHPha), 101.2 (CHPhβ), 99.1, 99.1, 99.0 (C-1aβ, C-1'a), 82.6, 81.4, 79.2, 76.6, 76.3, 76.1, 75.2, 74.7, 74.2, 73.9, 73.8, 73.7, 73.4, 73.2, 73.1, 71.9, 71.2, 70.9, 69.8, 68.7, 68.4, 68.3, 66.3, 65.8, 63.6, 63.3, 55.2, 55.1; HRMS: [M+NH₄]⁺ calcd for C₄₈H₄₉N₃O₁₁NH₄ 861.37053, found 861.36906.

Disaccharide 16A



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **A** and acceptor **16**. Yield: 62 mg, 66 µmol, 66%, $\alpha:\beta > 20$: 1. Data for the α -anomer: ¹H NMR (500 MHz, CDCl₃) δ 8.13 (dd, J = 8.3, 1.4 Hz, 2H, CH_{arom}), 8.00 (dd, J = 8.3, 1.4 Hz, 2H, CH_{arom}), 7.89 (dd, J = 8.3, 1.3 Hz, 2H, CH_{arom}), 7.63 – 7.56 (m, 2H, CH_{arom}), 7.49 – 7.40 (m, 5H, CH_{arom}), 7.37 – 7.21 (m, 13H, CH_{arom}), 7.15 – 7.05 (m, 3H, CH_{arom}), 7.02 – 6.96 (m, 2H, CH_{arom}), 5.94 (dd, J = 9.5, 3.3 Hz, 1H, H-3), 5.69 (dd, J = 3.3, 1.9 Hz, 1H, H-2), 5.46 (s, 1H, CHPh), 5.25 (d, J = 3.9 Hz, 1H, H-1'), 4.94 – 4.88 (m, 2H, H-1, H-6), 4.82 (d, J = 11.1 Hz, 1H, CHH Bn), 4.71 – 4.63 (m, 3H, H-4, H-6, CHH Bn), 4.30 – 4.24 (m, 2H, H-5, CHH Bn), 4.18 (d, J = 12.0 Hz, 1H, CHH Bn), 4.10 (dd, J = 10.2, 4.8 Hz, 1H, H-6'), 3.99 (t, J = 9.4 Hz, 1H, H-3'), 3.91 (dt, J = 9.5, 5.0 Hz, 1H, H-5'), 3.57 (t, J = 10.3 Hz, 1H, H-6'), 3.52 (t, J = 9.5 Hz, 1H, H-1')

4'), 3.49 (s, 3H CH₃ OMe), 3.37 (dd, J = 9.5, 3.9 Hz, 1H, H-2'); ¹³C NMR (126 MHz, CDCl₃) δ 166.1, 165.3, 165.2 (C=O), 138.7, 137.8, 137.4 (C_q), 133.5, 133.2, 133.2 (CH_{arom}), 130.1, 129.9, 129.9 (C_q), 129.9, 129.8, 129.8, 129.7, 129.0, 128.7, 128.7, 128.7, 128.6, 128.6, 128.6, 128.6, 128.5, 128.4, 128.4, 128.3, 128.3, 128.1, 127.7, 127.7, 127.6, 126.2 (CH_{arom}), 101.4 (CHPh), 99.1 (C-1'), 98.6 (C-1), 82.1 (C-4'), 78.7 (C-3'), 78.4 (C-2'), 75.4, 73.5 (CH₂ Bn), 72.4 (C-3), 72.1 (C-4), 70.6 (C-2), 69.5 (C-5'), 68.8 (C-6), 64.0 (C-5'), 63.4 (C-6), 55.5 (CH₃ OMe); diagnostic peaks for the βanomer: ¹H NMR (500 MHz, CDCl₃) δ 5.84 (dd, J = 9.8, 3.2 Hz, 1H, H-3), 5.59 (dd, J = 3.5, 1.8 Hz, 1H, H-2), 5.28 (s, 1H, CHPh), 5.15 (t, J = 9.8 Hz, 1H), 4.57 (d, J = 7.6 Hz, 1H), 4.40 (t, J = 9.7Hz, 1H), 3.75 (dd, J = 10.5, 4.9 Hz, 1H), 3.70 – 3.63 (m, 1H); ¹³C NMR (126 MHz, CDCl₃) δ 103.6 (C-1'), 101.0 (CHPh), 98.7 (C-1), 82.5, 81.3, 76.0, 75.1, 72.7, 71.1, 69.1, 68.3, 67.0, 65.9, 62.5.HRMS: [M+NH4]⁺ calcd for C₅₅H₅₂O₁₄NH₄ 954.36953, found 954.36920.

Disaccharide 16B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor 16. Yield: 86 mg, 98 μ mol, 98%, α : β = 10:1. Data for α-anomer: ¹H NMR (500 MHz, CDCl₃) δ 8.13 (dd, J = 8.3, 1.4 Hz, 2H, CH_{arom}), 8.01 -7.96 (m, 2H, CHarom), 7.97 - 7.91 (m, 2H, CHarom), 7.59 (dtt, J = 11.7, 7.4, 1.3 Hz, 2H, CHarom), 7.54 - 7.47 (m, 1H, CH_{arom}), 7.49 - 7.40 (m, 5H, CH_{arom}), 7.41 - 7.31 (m, 9H, CH_{arom}), 7.31 - 7.22 (m, 6H, CH_{arom}), 5.87 (dd, J = 9.6, 3.4 Hz, 1H, H-3), 5.63 (dd, J = 3.4, 1.9 Hz, 1H, H-2), 5.52 (s, 1H, CHPh), 5.25 (d, J = 4.1 Hz, 1H, H-1'), 4.92 (d, J = 1.9 Hz, 1H, H-1), 4.88 (d, J = 10.8 Hz, 1H, CHH Bn), 4.80 (dd, J = 12.1, 2.0 Hz, 1H, H-6), 4.70 (d, J = 10.8 Hz, 1H, CHH Bn), 4.65 (dd, J = 12.1, 3.7 Hz, 1H, H-6), 4.51 (t, J = 9.7 Hz, 1H, H-4), 4.27 (dd, J = 10.3, 4.9 Hz, 1H, H-6'), 4.22 (ddd, J = 9.8, 3.7, 2.0 Hz, 1H, H-5), 4.00 - 3.92 (m, 2H, H-3', H-5'), 3.65 - 3.59 (m, 2H, H-4', H-6'), 3.51 (s, 3H, CH₃ OMe), 3.25 (dd, J = 10.0, 4.1 Hz, 1H, H-2'); ¹³C NMR (126 MHz, CDCl₃) δ 166.2, 165.3 (C=O), 137.7, 137.2 (C_q), 135.4, 133.7, 133.5, 133.3, 133.2, 131.7, 131.6, 131.1 (CH_{arom}), 130.4, 130.0, 130.0 (C_q), 129.9, 129.9, 129.8, 129.8, 129.7, 129.6, 129.6, 129.1, 128.8, 128.7, 128.7, 128.7, 128.6, 128.6, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.0, 126.1, 124.6 (CH_{arom}), 101.4 (CHPh), 100.2 (C-1'), 98.6 (C-1), 82.5 (C-4'), 76.6 (C-3'), 75.2 (CH₂ Bn), 74.1 (C-4), 72.2 (C-3), 70.6 (C-2), 69.2 (C-5), 68.5 (C-6'), 64.0 (C-5'), 63.5 (C-6), 63.1 (C-2'), 55.6 (CH₃) OMe); diagnostic peaks for the β -anomer: ¹H NMR (500 MHz, CDCl₃) δ 5.68 (dd, J = 3.4, 1.8 Hz, 1H, H-2), 5.28 (s, 1H, CHPh), 4.42 (t, J = 9.7 Hz, 1H, H-4), 4.37 (d, J = 8.1 Hz, 1H, H-1'); ¹³C NMR (126 MHz, CDCl₃) δ 102.3 (C-1'), 101.2 (CHPh), 98.7 (C-1), 81.2, 79.6, 74.9, 74.8, 72.7, 71.1, 61.7. HRMS: [M+NH₄]⁺ calcd for C₄₆H₄₆O₁₃N₃NH₄: 866.33689, found 866.33809.




Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **A** and acceptor **18**. Yield: 83 mg, 87 µmol, 87% α : β > 20:1; ¹H NMR (400 MHz, CDCl₃) δ 7.99 – 7.92 (m, 2H, CH_{arom}), 7.50 (t, *J* = 7.5 Hz, 1H, CH_{arom}), 7.42 (td, *J* = 7.6, 2.8 Hz, 5H, CH_{arom}), 7.38 – 7.31 (m, 6H, CH_{arom}), 7.27 – 7.14 (m, 19H, CH_{arom}), 7.06 – 6.99 (m, 2H, CH_{arom}), 5.70 (t, *J* = 9.5 Hz, 1H, H-4), 5.48 (s, 1H, CHPh), 5.06 (d, *J* = 3.6 Hz, 1H, H-1'), 4.84 – 4.70 (m, 4H, H-1, 2x CHH Bn, CHH Bn), 4.60 (d, *J* = 11.2 Hz, 1H, CHH Bn), 4.52 (d, *J* = 11.9 Hz, 1H, CHH Bn), 4.47 (d, *J* = 11.9 Hz, 1H, CHH Bn), 4.38 – 4.26 (m, 2H, H-3, CHH Bn), 4.24 – 4.13 (m, 2H, H-6', CHH Bn), 4.06 – 3.95 (m, 3H, H-6, H-3',H-5'), 3.82 (t, *J* = 2.7 Hz, 1H, H-2), 3.75 – 3.59 (m, 3H, H-5, H-6, H-6'), 3.50 (t, *J* = 9.4 Hz, 1H, H-4'), 3.42 (s, 1H, CH₃ OMe), 3.37 (dd, *J* = 9.3, 3.6 Hz, 1H, H-2'). ¹³C NMR (101 MHz, CDCl₃) δ 165.4 (C=O), 138.8, 138.2, 138.1, 138.0, 137.6 (Cq), 133.1, 131.6, 131.1, 130.1, 130.0, 129.0, 128.6, 128.5, 128.4, 128.3, 128.2, 128.2, 127.9, 127.8, 127.7, 127.6, 127.5, 126.2 (CH_{arom}), 101.4 (CHPh), 99.2 (C-1'), 99.0 (C-1), 82.1 (C-4'), 78.6 (C-2'), 78.2 (C-3'), 77.1 (C-2), 76.2 (C-3), 75.2 (CH₂ Bn), 73.6 (CH₂ Bn), 73.1 (CH₂ Bn), 72.5 (CH₂ Bn), 70.7 (C-5), 70.2 (C-6), 70.0 (C-4), 69.1 (C-6'), 63.5 (C-5'), 55.2 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₅₅H₅₆O₁₂NH₄ 926.41100, found 926.40970.

Disaccharide 18B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor **18**. Yield: 74 mg, 87 µmol, 87%, $\alpha:\beta > 20: 1$. ¹H NMR (500 MHz, CDCl₃) δ 8.04 – 7.99 (m, 2H, CH_{arom}), 7.58 – 7.53 (m, 1H, CH_{arom}), 7.47 – 7.37 (m, 10H, CH_{arom}), 7.32 – 7.16 (m, 13H, CH_{arom}), 5.70 (t, *J* = 9.8 Hz, 1H, H-4), 5.52 (s, 1H, CHPh), 5.03 (d, *J* = 3.8 Hz, 1H, H-1'), 4.85 (dd, *J* = 6.4, 4.4 Hz, 2H, H-1, CHH Bn), 4.76 (d, *J* = 12.1 Hz, 1H, CHH Bn), 4.71 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.66 (d, *J* = 10.8 Hz, 1H, CHH Bn), 4.55 (d, *J* = 11.8 Hz, 1H, CHH Bn), 4.50 (d, *J* = 11.8 Hz, 1H, CHH Bn), 4.22 (dd, *J* = 9.5, 3.1 Hz, 1H, H-3), 4.17 (dd, *J* = 10.3, 4.8 Hz, 1H, H-6'), 4.04 – 3.90 (m, 3H, H-5, H-3', H-5'), 3.80 (dd, *J* = 3.2, 2.0 Hz, 1H, H-2), 3.74 – 3.63 (m, 3H, H-6 2x, H-6'), 3.60 (t, *J* = 9.4 Hz, 1H, H-4'), 3.43 (s, 3H, CH₃ OMe), 3.20 (dd, *J* = 9.9, 3.8 Hz, 1H, H-2'); ¹³C NMR (126 MHz, CDCl₃) δ 165.6 (C=O), 138.1, 137.9, 137.7, 137.4 (Cq), 133.1, 131.5, 130.1, 129.7, 129.1, 128.7, 128.6, 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 128.0, 127.9, 127.9, 127.7, 127.7, 127.5, 126.2 (CH_{arom}), 101.5 (CHPh), 100.3 (C-1'), 98.7 (C-1), 82.8 (C-4'), 77.4 (C-2), 77.4 (C-3), 76.3 (C-3'), 75.1 (CH₂ Bn), 73.7 (CH₂ Bn), 72.9 (CH₂ Bn), 70.7 (C-5), 70.2 (C-6), 69.7 (C-4), 68.9 (C-6'), 63.4 (C-5'), 63.1 (C-2'), 55.2 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₄₈H₄₉N₃O₁₁NH₄ 861.37053, found 861.36924.

Disaccharide 19A



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor A and acceptor 19. Yield: 79 mg, 82 μ mol, 82%, α ; β = 10:1. Data for α -anomer: ¹H NMR (500 MHz, CDCl₃) δ 8.12 – 7.14 (m, 30H, CH_{arom}), 5.42 (dd, *J* = 3.2, 2.0 Hz, 1H, H-2), 5.36 (s, 1H, CHPh), 5.17 (d, J = 11.0 Hz, 1H, CHH Bn), 5.03 (d, J = 3.7 Hz, 1H, H-1'), 4.90 (d, J = 2.0 Hz, 1H, H-1), 4.80 (d, J = 11.6 Hz, 1H, CHH Bn), 4.73 (d, J = 11.5 Hz, 1H, CHH Bn), 4.71 – 4.61 (m, 3H, 2x CHH Bn, CHH Bn), 4.57 (d, *I* = 11.1 Hz, 1H, CHH Bn), 4.52 (d, *J* = 12.0 Hz, 1H, CH*H* Bn), 4.24 (dd, *J* = 9.3, 3.1 Hz, 1H, H-3), 4.18 (t, *J* = 9.4 Hz, 1H, H-4), 4.03 – 3.95 (m, 2H, H-3', H-6'), 3.90 - 3.84 (m, 2H, H-5, H-6), 3.81 - 3.74 (m, 2H, H-6, H-5'), 3.53 -3.46 (m, 3H, H-2', H-4', H-6'), 3.41 (s, 3H, CH₃ OMe); ¹³C NMR (126 MHz, CDCl₃) δ 166.3 (C=O), 138.8, 138.8, 138.5, 138.2, 137.6, 135.4, 134.2, 133.3, 131.9, 131.4, 131.3, 130.3, 130.0, 129.9, 128.9, 128.7, 128.5, 128.5, 128.5, 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 128.0, 128.0, 127.9, 127.8, 127.7, 127.6, 127.6, 127.6, 127.6, 127.5, 127.5, 126.3, 126.1 (CH_{arom}), 101.3 (CHPh), 100.5 (C-1'), 98.1 (C-1), 82.1 (C-4'), 80.7 (C-3), 79.1 (C-2'), 78.2 (C-3'), 75.1 (CH₂ Bn), 73.8 (CH₂ Bn), 73.6 (C-4), 73.4 (CH₂ Bn), 72.4 (CH₂ Bn), 71.5 (C-2), 69.2 (C-5), 69.0 (C-6), 63.7 (C-6'), 55.3 (CH₃ OMe); Diagnostic peaks for β -anomer: ¹H NMR (500 MHz, CDCl₃) δ 5.50 (dd, J = 3.1, 2.1 Hz, 1H, H-2'), 5.49 (s, 1H, CHPh), 4.94 (d, J = 10.6 Hz, 1H, CHH Bn), 4.29 (dd, J = 10.5, 5.0 Hz, 1H, H-6'), 3.69 - 3.65 (m, 1H), 3.65 - 3.61 (m, 1H, H-6'), 3.40 (s, 3H, CH₃ OMe); ¹³C NMR (126 MHz, CDCl₃) δ 165.7 (C=O), 101.2 (CHPh), 100.6 (C-1'), 98.4 (C-1), 82.0 (C-4'), 81.7, 81.0, 75.5, 75.2 (CH₂ Bn), 74.6, 73.7 (CH₂ Bn), 72.1, 70.8, 69.5, 69.4 (CH₂ Bn), 69.1 (CH₂ Bn), 66.0, 55.2 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₅₅H₅₆O₁₂NH₄ 926.41100, found 926.40968.

Disaccharide 19B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor **19**. Yield: 78 mg, 93 µmol, 93%, $\alpha:\beta = 1:1$. Data reported for a 1:1 mixture of anomers: ¹H NMR (500 MHz, CDCl₃) δ 8.10 (ddd, J = 8.4, 6.8, 1.4 Hz, 4H), 7.60 - 7.53 (m, 2H), 7.50 - 7.45 (m, 2H), 7.42 - 7.20 (m, 42H), 5.55 (s, 1H, CHPhβ), 5.54 (dd, J = 3.4, 2.0 Hz, 1H, H-2 β), 5.46 (s, 1H, CHPh α), 5.40 (dd, J = 3.2, 1.9 Hz, 1H, H-2 α), 5.22 (d, J = 3.8 Hz, 1H, H-1'a), 5.03 (d, J = 10.4 Hz, 1H), 4.91 (d, J = 10.6 Hz, 1H), 4.89 - 4.85 (m, 3H), 4.83 (d, J = 11.0 Hz, 1H), 4.73 (dd, J = 11.5, 7.5 Hz, 3H), 4.65 (s, 1H), 4.59 - 4.51 (m, 6H), 4.47 (dd, J = 9.3, 3.3 Hz, 1H), 4.33 - 4.27 (m, 2H), 4.24 - 4.11 (m, 3H), 3.98 - 3.87 (m, 4H), 3.84 (ddt, J = 9.8, 3.9, 2.0 Hz, 2H), 3.78 (dt, J = 10.7, 1.9 Hz, 2H), 3.73 - 3.55 (m, 5H), 3.44 - 3.38 (m, 8H), 3.32 (dd, J = 9.4, 8.0 Hz, 1H, H-2' β); ¹³C NMR (126 MHz, CDCl₃) δ 166.1, 138.5, 138.5, 138.4, 138.3, 137.9, 137.9, 137.5, 137.2, 133.4, 133.3, 131.6, 131.1, 130.1, 130.0, 130.0, 129.9, 129.7, 129.2, 129.0, 128.6, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.3, 128.2, 128.2, 128.2, 128.1, 128.0, 128.0, 127.9, 127.8, 127.7, 127.7, 127.7, 126.3, 126.1, 101.5, 101.4 (CHPhaβ), 100.2 (C-1'a), 99.3 (C-1'β), 98.6, 98.3 (C-1αβ), 82.7, 81.8, 79.4, 77.9, 77.4, 77.2, 76.9, 76.6, 76.3, 75.1, 75.1, 75.0, 74.7, 73.6, 73.6, 73.5, 72.4, 71.7, 71.4, 69.0, 68.9, 68.8, 68.8, 68.7, 66.9, 66.3, 63.5, 63.4, 55.2, 55.2; HRMS: [M+NH₄]⁺ calcd for C₄₈H₄₉N₃O₁₁NH₄ 861.37053, found 861.36959.



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor A and acceptor 22. Yield: 77 mg, 76 μ mol, 76%, α : β = 17:1. Data for α-anomer: ¹H NMR (500 MHz, CDCl₃) δ 8.07 – 8.01 (m, 2H, CH_{arom}), 7.52 – 7.46 (m, 3H, CH_{arom}), 7.41 - 7.34 (m, 5H, CH_{arom}), 7.33 - 7.15 (m, 18H, CH_{arom}), 7.09 - 7.04 (m, 2H, CH_{arom}), 5.59 – 5.52 (m, 2H, H-3, CHPh), 4.91 (d, J = 3.7 Hz, 1H, H-1'), 4.86 – 4.82 (m, 2H, H-1, CHH Bn), 4.79 (d, J = 12.2 Hz, 1H, CHH Bn), 4.69 (d, J = 11.2 Hz, 1H, CHH Bn), 4.64 (d, J = 10.9 Hz, 1H, CHH Bn), 4.61 (s, 2H, CH₂ Bn), 4.58 (d, *J* = 12.2 Hz, 1H, CHH Bn), 4.52 (d, *J* = 10.9 Hz, 1H, CH*H* Bn), 4.31 (t, *J* = 9.5 Hz, 1H, H-4), 4.27 (dd, *J* = 10.2, 4.9 Hz, 1H, H-6[°]), 4.25 (dd, *J* = 3.1, 2.1 Hz, 1H, H-2), 4.12 (t, J = 9.3 Hz, 1H, H-3'), 4.06 (td, J = 10.0, 4.9 Hz, 1H, H-5'), 3.93 - 3.85 1H, H-4'), 3.49 (dd, J = 9.3, 3.7 Hz, 1H, H-2'), 3.41 (s, 3H, CH₃ OMe); ¹³C NMR (126 MHz, CDCl₃) & 166.0 (C=O), 138.8, 138.6, 138.5, 138.1, 137.5 (C_q), 133.2 (CH_{arom}), 130.1 (C_q), 129.9, 129.0, 128.5, 128.4, 128.4, 128.4, 128.3, 128.0, 127.8, 127.7, 127.6, 127.6, 127.5, 127.4, 126.2 (CHarom), 101.4 (CHPh), 99.8 (C-1), 99.5 (C-1'), 82.3 (C-4'), 78.9 (C-2'), 78.6 (C-3'), 76.1 (C-2), 75.3, 75.1 (CH₂ Bn), 74.5 (C-3), 73.7 (CH₂ Bn), 73.6 (C-4), 72.9 (CH₂ Bn), 72.0 (C-5), 69.2 (C-6), 69.0 (C-6'), 63.2 (C-5'), 55.1 (CH₃ OMe); Diagnostic peaks for β -anomer: ¹H NMR (500 MHz, CDCl₃) δ 5.39 (dd, *J* = 9.7, 3.5 Hz, 1H, H-3), 5.28 (s, 1H, CHPh), 5.04 (d, *J* = 10.4 Hz, 1H, CHH Bn), 4.41 (d, J = 7.7 Hz, 1H, H-1'); ¹³C NMR (126 MHz, CDCl₃) δ 104.2 (C-1'), 101.0 (CHPh), 99.4 (C-1), 81.5, 81.3, 80.8, 76.5, 74.1, 72.9, 72.4, 65.5, 55.0 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C55H56O12NH4 926.41100, found 926.40906.

Disaccharide 22B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor **22**. Yield: 44 mg, 51 µmol, 51%, $\alpha:\beta = 7:1$. Data for α -anomer: ¹H NMR (500 MHz, CDCl₃) δ 8.14 (dd, J = 8.2, 1.4 Hz, 2H, CH_{arom}), 7.62 – 7.54 (m, 1H, CH_{arom}), 7.53 – 7.43 (m, 5H, CH_{arom}), 7.40 – 7.25 (m, 15H, CH_{arom}), 7.22 – 7.14 (m, 3H), 7.13 – 7.07 (m, 2H, CH_{arom}), 5.62 – 5.53 (m, 2H, H-3, CHPh), 4.94 (d, J = 3.7 Hz, 1H, H-1'), 4.88 (d, J = 10.9 Hz, 1H, CHH Bn), 4.79 – 4.76 (m, 2H, H-1, CHH Bn), 4.71 (d, J = 10.8 Hz, 1H, CHH Bn), 4.63 (d, J = 11.0 Hz, 1H, CHH Bn), 4.58 (dd, J = 11.6, 2.8 Hz, 2H, 2x CHH Bn), 4.34 (t, J = 9.4 Hz, 1H, H-4), 4.27 (dd, J = 10.4, 4.9 Hz, 1H, H-6'), 4.20 (dd, J = 3.2, 2.0 Hz, 1H, H-2), 4.14 – 4.04 (m, 2H, H-3', H-5'), 3.92 – 3.86 (m, 2H, H-5, H-6), 3.79 – 3.67 (m, 3H, H-4', H-6, H-6'), 3.42 (s, 3H, CH₃ OMe), 3.26 (dd, J = 10.1, 3.7 Hz, 1H, H-2'); ¹³C NMR (126 MHz, CDCl₃) δ 166.0

(C=O), 138.6, 138.0, 138.0, 137.3 (C_q), 133.4 (CH_{arom}), 131.7 (C_q), 131.4, 129.9, 129.9, 129.2, 128.7, 128.6, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.2, 128.1, 128.1, 128.0, 128.0, 128.0, 127.8, 127.6, 127.6, 127.6, 126.2, 126.1 (CH_{arom}), 101.6 (CHPh), 100.7 (C-1'), 99.9 (C-1), 82.9 (C-4'), 77.5 (C-2), 75.6 (C-3'), 75.2 (CH₂ Bn x2), 74.2 (C-3), 73.6 (CH₂ Bn), 73.4 (C-4), 71.9 (C-5), 69.1 (C-6), 68.7 (C-6'), 63.3 (C-5'), 62.9 (C-2'), 55.2 (CH₃ OMe); Diagnostic peaks for the β-anomer: ¹H NMR (500 MHz, CDCl₃) δ 5.36 (dd, J = 9.5, 3.5 Hz, 1H, H-3), 5.30 (s, 1H, CHPh), 3.17 – 3.09 (m, 1H), 2.79 (t, J = 10.4 Hz, 1H); ¹³C NMR (126 MHz, CDCl₃) δ 102.4 (C-1'), 101.5 (CHPh), 99.2 (C-1); HRMS: [M+NH₄]⁺ calcd for C₄₈H₄₉N₃O₁₁NH₄ 861.37053, found 861.36930.





Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **A** and acceptor **23**. Yield: 73 mg, 77 µmol, 77%, $\alpha:\beta > 20:1.$ ¹H NMR (500 MHz, CDCl₃) δ 8.10 – 8.05 (m, 2H, CH_{arom}), 8.02 – 7.94 (m, 4H, CH_{arom}), 7.51 – 7.44 (m, 3H, CH_{arom}), 7.42 – 7.16 (m, 21H, CH_{arom}), 6.18 (t, *J* = 10.1 Hz, 1H, H-4), 5.73 (dd, *J* = 10.1, 3.1 Hz, 1H, H-3), 5.51 (s, 1H, CHPh), 4.96 (d, *J* = 3.7 Hz, 1H, H-1'), 4.93 (d, *J* = 1.9 Hz, 1H, H-1), 4.82 (d, *J* = 11.1 Hz, 1H, CHH Bn), 4.72 – 4.63 (m, 3H, H-6, CHH Bn, CHH Bn), 4.56 – 4.48 (m, 2H, H-6, CHH Bn), 4.39 (dd, *J* = 3.2, 1.9 Hz, 1H, H-2), 4.33 (ddd, *J* = 10.1, 4.7, 2.7 Hz, 1H, H-5), 4.25 (dd, *J* = 10.4 Hz, 1H, H-6'), 3.57 (t, *J* = 9.3 Hz, 1H, H-3'), 3.99 (td, *J* = 10.0, 4.9 Hz, 1H, H-5'), 3.66 (t, *J* = 10.4 Hz, 1H, H-6'), 3.57 (t, *J* = 9.5 Hz, 1H, H-4'), 3.51 (s, 3H, CH₃ OMe), 3.48 (dd, *J* = 9.4, 3.8 Hz, 1H, H-2'); ¹³C NMR (126 MHz, CDCl₃) δ 166.4, 166.1, 165.4 (C=O), 138.9, 138.3, 137.4 (Cq), 133.4, 133.3, 128.0, 128.0, 128.0, 127.8, 127.6, 127.6, 126.2 (CH_{arom}), 101.4 (CHPh), 100.1 (C-1), 99.7 (C-1'), 82.1 (C-4'), 78.5, 78.5 (C-2', C-3'), 75.5 (C-2), 75.4, 72.7 (CH₂ Bn), 72.3 (C-3), 69.0 (C-5), 68.9 (C-6'), 67.1 (C-4), 63.4 (C-5'), 63.3 (C-6), 55.5 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₅₅H₅₂O₁₄MH₄ 954.36953, found 954.36815.

Disaccharide 23B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor **23**. Yield: 42 mg, 51 μmol, 51%, α :β > 20:1. ¹H NMR (500 MHz, CDCl₃) δ 8.05 (dq, *J* = 7.0, 1.6 Hz, 4H, CH_{arom}), 8.00 – 7.93 (m, 2H, CH_{arom}), 7.54 – 7.45 (m, 4H, CH_{arom}), 7.40 – 7.27 (m, 15H, CH_{arom}), 6.04 (t, *J* = 10.1 Hz, 1H, H-4), 5.72 (dd, *J* = 10.1, 3.2 Hz, 1H, H-3), 5.56 (s, 1H, CHPh), 4.99 (d, *J* = 3.8 Hz, 1H, H-1'), 4.92 (d, *J* = 10.8 Hz, 1H, CHH Bn), 4.88 (d, *J* = 1.8 Hz, 1H, H-1), 4.71 (d, *J* = 10.8 Hz, 1H, CHH Bn), 4.65 (dd, *J* = 12.1,

2.9 Hz, 1H, H-6), 4.50 (dd, J = 12.1, 5.5 Hz, 1H, H-6), 4.37 – 4.30 (m, 2H, H-2, H-5), 4.27 (dd, J = 10.4, 4.9 Hz, 1H, H-6'), 4.13 (dd, J = 10.1, 9.1 Hz, 1H, H-3'), 4.02 (td, J = 10.0, 4.9 Hz, 1H, H-5'), 3.71 (dt, J = 11.5, 9.9 Hz, 2H, H-4', H-6'), 3.51 (s, 3H, CH₃ OMe), 3.34 (dd, J = 10.1, 3.8 Hz, 1H, H-2'); ¹³C NMR (126 MHz, CDCl₃) δ 166.3, 166.0, 165.4 (C=O), 138.0, 137.1, 133.5 (C_q), 133.4, 133.1, 131.7, 131.3, 130.0, 129.9, 129.9, 129.8, 129.3, 129.3, 129.2, 128.6, 128.6, 128.5, 128.4, 128.4, 128.4, 128.4, 128.2, 128.0, 126.2, 126.1 (CH_{arom}), 101.6 (CHPh), 100.7 (C-1'), 100.0 (C-1), 82.7 (C-4'), 76.7 (C-2), 76.2 (C-3'), 75.3 (CH₂ Bn), 71.7 (C-3), 68.8 (C-5), 68.7 (C-6'), 67.3 (C-4), 63.6 (C-6), 63.4 (C-5'), 63.1 (C-2'), 55.5 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₄₈H₄₅N₃O₁₃NH₄ 889.32906, found 889.32759

Disaccharide 25A



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **A** and acceptor **25**. 79 mg, 85 µmol, 85%, $\alpha:\beta > 20:1.$ ¹H NMR (400 MHz, CDCl₃) δ 7.99 – 7.14 (m, 30H, CH_{arom}), 5.53 (s, 1H, CHPh), 4.97 (d, *J* = 11.0 Hz, 1H, CHH Bn), 4.93 – 4.84 (m, 3H, H-1', 2x CHH Bn), 4.82 – 4.74 (m, 5H, CHH Bn, 4x CHH Bn), 4.66 (q, *J* = 3.9 Hz, 2H, H-1, H-6'), 4.59 (dd, *J* = 11.1, 6.4 Hz, 1H, H-6'), 4.27 (td, *J* = 10.0, 4.9 Hz, 1H, H-5), 4.05 – 3.94 (m, 4H, H-3, H-4, H-6, H-3'), 3.91 (dd, *J* = 10.3, 2.5 Hz, 1H, H-2), 3.82 (dd, *J* = 10.1, 4.9 Hz, 1H, H-5'), 3.66 – 3.54 (m, 2H, H-2', H-4'), 3.50 (t, *J* = 10.2 Hz, 1H, H-6), 3.36 (s, 3H, CH₃ OMe). ¹³C NMR (101 MHz, CDCl₃) δ 166.1 (C=O), 138.9, 138.4, 138.1, 137.9, 137.8, 133.2 (C_q), 129.9, 129.6, 128.8, 128.6, 128.5, 128.5, 128.4, 128.4, 128.2, 128.0, 127.9, 127.9, 127.8, 127.7, 127.6, 126.1 (CH_{arom}), 101.2 (CHPh), 101.0 (C-1'), 99.1 (C-1), 82.7 (C-4'), 79.3 (C-3'), 78.8 (C-2'), 78.0 (C-4), 77.5 (C-2), 75.3 (CH₂ Bn), 74.5 (CH₂ Bn), 74.1 (C-3), 73.6 (CH₂ Bn), 73.2 (CH₂ Bn), 69.0 (C-6), 68.5 (C-5'), 63.2 (C-5), 62.8 (C-6'), 55.4 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₅₅H₃₆O₁₂NH₄ 926.41100, found 926.40964.

Disaccharide 25B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor **25**. Yield: 84 mg, 100 μmol, 100%, $\alpha:\beta = 3:1$. Data for the α-anomer: ¹H NMR (400 MHz, CDCl₃) δ 8.01 (dd, J = 8.3, 1.5 Hz, 2H, CH_{arom}), 7.48 – 7.22 (m, 23H, CH_{arom}), 5.55 (s, 1H, CHPh), 4.97 (d, J = 10.7 Hz, 1H, CHH Bn), 4.93 (d, J = 3.7 Hz, 1H, H-1'), 4.90 – 4.75 (m, 4H, 2x CHH Bn, 2x CHH Bn), 4.72 (d, J = 2.8 Hz, 1H, H-1), 4.69 – 4.57 (m, 3H, 2x H-6, CHH Bn), 4.35 – 4.27 (m, 1H, H-5'), 4.07 (d, J = 2.2 Hz, 1H, H-4), 4.03 (t, J = 6.9 Hz, 1H, H-5), 4.01 – 3.92 (m, 3H, H-2, H-3, H-3'), 3.83 (dd, J = 10.2, 4.9 Hz, 1H, H-6'), 3.69 (t, J = 9.5 Hz, 1H, H-4'), 3.58 – 3.50 (m, 2H, H-2', H-6'), 3.38 (s, 3H, CH₃ OMe); ¹³C NMR (101

MHz, CDCl₃) δ 166.1 (C=O), 138.3, 138.1, 138.0, 137.6 (C_q), 133.4, 129.7, 129.6, 129.0, 128.6, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 128.2, 128.0, 128.0, 127.9, 127.9, 127.8, 127.7, 127.4, 126.1, 126.1 (CH_{arom}), 101.3 (CHPh), 99.7 (C-1[']), 98.9 (C-1), 82.9 (C-4[']), 77.2, 77.2, 77.2 (C-3, C-3['], C-4), 75.3 (CH₂ Bn), 74.5 (C-2), 73.5, 73.5 (CH₂ Bn), 68.8 (C-6[']), 68.5 (C-5), 64.1 (C-2[']), 63.3 (C-5[']), 62.8 (C-6), 55.5 (CH₃ OMe); diagnostic peaks for the β-anomer: ¹H NMR (400 MHz, CDCl₃) δ 5.49 (s, 1H, CHPh), 4.47 (dd, J = 11.4, 5.7 Hz, 1H, H-6), 3.35 (s, 3H, CH₃ OMe); 3.17 (td, J = 9.7, 5.0 Hz, 1H, H-5[']); ¹³C NMR (101 MHz, CDCl₃) δ 166.2 (C=O), 102.1 (C-1[']), 99.0 (C-1), 81.4, 78.9, 78.1, 74.9, 74.4, 74.0, 68.5, 67.6, 66.5, 66.0, 63.8; HRMS: [M+NH₄]⁺ calcd for C₄₈H₄₉N₃O₁₁NH₄ 861.37053, found 861.36949.

Disaccharide 26A



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor A and acceptor 26. Yield: 66 mg, 78 μ mol, 78%, α : β = 11:1. Data for the α-anomer: ¹H NMR (400 MHz, CDCl₃) δ 8.07 – 8.02 (m, 2H, CH_{arom}), 7.59 – 7.53 (m, 1H, CH_{arom}), 7.51 - 7.47 (m, 2H, CH_{arom}), 7.44 - 7.16 (m, 25H, CH_{arom}), 5.51 - 5.42 (m, 2H, H-3, CHPh), 4.94 (d, J = 11.2 Hz, 1H, CHH Bn), 4.86 – 4.76 (m, 4H, H-1, H-1', CHH Bn, CHH Bn), 4.73 (d, J = 10.6 Hz, 1H, CHH Bn), 4.68 (d, J = 12.3 Hz, 1H, CHH Bn), 4.62 (d, J = 11.8 Hz, 1H, CHH Bn), 4.38 – 4.31 (m, 2H, H-4, CHH Bn), 4.25 (d, J = 12.1 Hz, 1H, CHH Bn), 4.16 – 4.09 (m, 2H, H-2, H-5), 4.07 – 3.99 (m, 2H, H-3', H-5'), 3.86 (dd, J = 10.2, 6.5 Hz, 1H, H-6), 3.59 (dd, J = 10.3, 6.7 Hz, 1H, H-6'), 3.53 (t, J = 9.5 Hz, 1H, H-4'), 3.49 – 3.43 (m, 2H, H-2', H-6'), 3.42 (s, 3H, CH₃ OMe), 3.34 (t, J = 10.3 Hz, 1H, H-6'); 13C NMR (101 MHz, CDCl₃) δ 166.4 (C=O), 138.7, 138.2, 138.1, 137.8, 137.6, 133.2 (Cq), 129.9, 129.9, 128.9, 128.6, 128.5, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.2, 128.2, 128.1, 128.1, 128.1, 128.0, 128.0, 128.0, 127.9, 127.9, 127.8, 127.6, 127.6, 127.6, 127.5, 127.5, 127.4, 127.4, 126.0, 126.0 (CH_{arom}), 101.0 (CHPh), 100.2 (C-1'), 98.3 (C-1), 82.8 (C-4'), 79.5 (C-2'), 78.5 (C-3'), 77.2 (C-4), 75.1 (CH₂ Bn), 74.4 (CH₂ Bn), 73.5 (C-2), 73.1 (CH₂ Bn), 73.2 (CH₂ Bn), 72.6 (C-3), 69.2 (C-5), 68.7 (C-6'), 68.5 (C-6), 63.4 (C-5'), 55.4 (CH₃ OMe). Diagnostic peaks for the β -anomer: ¹H NMR (400 MHz, CDCl₃) δ 5.64 (dd, J = 10.4, 3.1 Hz, 1H, H-3), 5.10 (dd, J = 10.5, 2.9 Hz, 1H), 5.05 (d, J = 11.6 Hz, 1H, CHH Bn), 4.52 (d, J = 12.0 Hz, 1H), 4.47 – 4.43 (m, 2H, H-1'), 3.44 (s, 3H, CH₃ OMe). ¹³C NMR (101 MHz, CDCl₃) δ 165.8 (C=O), 103.4 (C-1'), 101.1 (CHPh), 98.4 (C-1), 82.7, 82.2, 81.5, 80.7, 76.3, 75.2 (CH₂ Bn), 75.0 (CH₂ Bn), 74.6 (CH₂ Bn), 74.1, 73.8, 73.3 (CH₂ Bn), 69.8, 68.9, 65.8, 63.3, 55.5 (CH₃ OMe); HRMS: [M+Na]⁺ calcd for C₅₅H₅₆O₁₂Na 931.36640, found 931.36295.

Disaccharide 26B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor **26**. Yield: 56 mg, 67 µmol, 67%, $\alpha:\beta = 3:1$. Data for the α-anomer: ¹H NMR (400 MHz, CDCl₃) δ 8.09 – 8.03 (m, 2H, CH_{arom}), 7.62 – 7.51 (m, 1H, CH_{aron}), 7.49 - 7.15 (m, 22H, CH_{aron}), 5.52 (dd, J = 10.9, 2.9 Hz, 1H, H-3), 5.43 (s, 1H, CHPh), 4.97 (d, J = 10.8 Hz, 1H, CHH Bn), 4.86 - 4.82 (m, 2H, H-1, H-1'), 4.78 (d, J = 10.7 Hz, 1H, CH*H* Bn), 4.72 (d, *J* = 8.9 Hz, 1H, C*H*H Bn), 4.68 (d, *J* = 12.2 Hz, 1H, CH*H* Bn), 4.61 (d, *J* = 11.9 Hz, 1H, CHH Bn), 4.47 (d, J = 11.9 Hz, 1H, CHH Bn), 4.43 (d, J = 2.9 Hz, 1H, H-4), 4.17 -4.09 (m, 2H, H-2, H-5), 4.07 – 4.00 (m, 1H, H-5'), 3.97 (dd, J = 9.9, 9.1 Hz, 1H, H-3'), 3.92 (t, J = 9.0 Hz, 1H, H-6), 3.61 - 3.54 (m, 2H, H-4', H-6), 3.42 (s, 3H, CH₃ OMe), 3.30 (t, J = 10.3 Hz, 1H, H-6'), 3.24 – 3.17 (m, 2H, H-2', H-6'); ¹³C NMR (101 MHz, CDCl₃) δ 166.2 (C=O), 138.0, 137.8, 137.6 (C_q), 137.5, 133.4, 130.0, 129.9, 129.0 (CH_{arom}), 128.8 (C_q), 128.7, 128.6, 128.6, 128.5, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.1, 128.0, 127.4, 126.1, 126.0 (CH_{arom}), 101.1 (CHPh), 98.6, 98.4 (C-1, C-1'), 82.9 (C-4'), 76.3 (C-3'), 75.2 (CH₂ Bn), 75.0 (C-4), 73.6 (CH₂ Bn), 73.3 (C-2), 73.1 (CH₂ Bn), 72.1 (C-2), 68.5 (C-5), 68.4 (C-6'), 67.0 (C-6), 63.4 (C-2'), 63.2 (C-5'), 55.6 (CH₃ OMe); diagnostic peaks for the β -anomer: ¹H NMR (400 MHz, CDCl₃) δ 5.60 (dd, J = 10.5, 3.0 Hz, 1H, H-3), 5.49 (s, 1H, CHPh), 4.36 (d, J = 8.0 Hz, 1H, H-1'), 4.34 (dd, J = 3.1, 1.2 Hz, 1H, H-4), 4.24 (dd, J = 10.5, 3.6 Hz, 1H, H-2), 3.43 (s, 3H, CH₃ OMe), 3.09 (td, J = 9.8, 5.0 Hz, 1H, H-5'); ¹³C NMR (101 MHz, CDCl₃) δ 165.9 (C=O), 102.4 (C-1'), 101.4 (CHPh), 98.6 (C-1), 81.5, 78.9, 75.4, 74.9, 74.2, 73.4, 72.4, 69.5, 68.7, 68.3, 66.4, 66.0, 55.6; HRMS: [M+Na]⁺ calcd for C48H49N3O11Na 866.32593, found 866.32307.



Ph-



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **A** and acceptor **27**. Yield: 70 mg, 70 μmol, 70%, α :β > 20:1. ¹H NMR (400 MHz, CDCl₃) δ 8.08 – 7.93 (m, 6H, CH_{arom}), 7.65 – 7.54 (m, 1H, CH_{arom}), 7.52 – 7.12 (m, 23H, CH_{arom}), 5.73 – 5.64 (m, 2H, H-2, H-3), 5.43 (s, 1H, CHPh), 5.25 (d, *J* = 2.9 Hz, 1H, H-1), 5.00 (d, *J* = 11.1 Hz, 1H, CHH Bn), 4.90 (d, *J* = 4.7 Hz, 1H, CHH Bn), 4.87 (d, *J* = 4.1 Hz, 1H, CHH Bn), 4.82 (d, *J* = 3.7 Hz, 1H, H-1'), 4.77 – 4.70 (m, 3H, CHH Bn, 2x H-6), 4.48 – 4.45 (m, 1H, H-4), 4.35 (t, *J* = 6.5 Hz, 1H, H-5), 4.22 (t, *J* = 9.4 Hz, 1H, H-3'), 4.15 (dt, *J* = 10.0, 5.0 Hz, 1H, H-5'), 3.60 (dd, *J* = 10.2, 4.7 Hz, 1H, H-6'). ¹³C NMR (101 MHz, CDCl₃) δ 166.4, 166.1, 166.0 (C=O), 138.8, 137.9, 137.6, 133.5, 133.3 (C_q), 129.9, 129.7, 129.5, 129.3, 128.9, 128.7, 128.6, 128.6, 128.5, 128.4, 128.2, 128.2, 127.9, 127.7, 126.2 (CH_{arom}), 101.3 (CHPh), 100.9 (C-1'), 97.5 (C-1), 82.7 (C-4'), 78.9 (C-2'), 78.7 (C-3'), 77.2 (C-4), 75.4 (CH₂ Bn), 74.6 (CH₂ Bn), 70.7 (C-2), 69.2 (C-3), 68.8 (C-6'), 68.4 (C-5), 63.7 (C-5'), 63.1 (C-6), 55.5 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₅₅H₅₂O₁₄NH₄ 954.36953, found 954.36827.



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor **27**. Yield: 87 mg, 100 µmol, 100%, α : β > 20:1. ¹H NMR (400 MHz, CDCl₃) δ 8.09 – 8.05 (m, 2H, CH_{arom}), 8.04 – 8.00 (m, 2H, CH_{arom}), 7.97 (dd, *J* = 7.1, 1.4 Hz, 2H, CH_{arom}), 7.61 – 7.27 (m, 19H, CH_{arom}), 5.76 (dd, *J* = 11.0, 2.8 Hz, 1H, H-2), 5.69 (dd, *J* = 11.0, 3.5 Hz, 1H, H-3), 5.43 (s, 1H, CHPh), 5.28 (d, *J* = 3.5 Hz, 1H, H-1), 5.01 (d, *J* = 10.7 Hz, 1H, CHH Bn), 4.98 (d, *J* = 3.8 Hz, 1H, H-1'), 4.87 (d, *J* = 10.8 Hz, 1H, CHH Bn), 4.82 – 4.70 (m, 2H, 2x H-6), 4.54 (d, *J* = 2.8 Hz, 1H, H-4), 4.42 (t, *J* = 7.0 Hz, 1H, H-6), 4.21 (t, *J* = 9.6 Hz, 1H, H-3'), 4.15 (dt, *J* = 10.0, 5.0 Hz, 1H, H-5'), 3.63 (t, *J* = 9.4 Hz, 1H, H-4'), 3.55 – 3.46 (m, 2H, H-2', H-6'), 3.45 (s, 3H, CH₃ OMe), 3.37 (t, *J* = 10.2 Hz, 1H, H-6'); ¹³C NMR (101 MHz, CDCl₃) δ 166.3, 166.1, 166.0 (C=O), 137.9, 137.3, 133.6, 133.4, 133.3 (C_q), 129.9, 129.8, 129.8, 129.8, 129.7, 129.6, 129.4, 129.0, 129.0, 128.8, 128.7, 128.6, 128.5, 128.5, 128.4, 128.3, 128.3, 128.2, 128.1, 127.9, 126.2 (CH_{arom}), 101.3 (CHPh), 99.5 (C-1'), 97.6 (C-1), 82.7 (C-4'), 76.6 (C-3'), 76.1 (C-4), 75.3 (CH₂ Bn), 70.4 (C-2), 68.9 (C-3), 68.4 (C-6'), 68.1 (C-5), 63.8 (C-5'), 63.6 (C-2'), 62.5 (C-6), 55.6 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₄₈H₄₅N₃O₁₃NH₄ 889.32906, found 889.32801.





Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **A** and acceptor **29**. Yield: 72 mg, 76 µmol, 76%, $\alpha:\beta = 16:1$. Data for α -anomer: ¹H NMR (500 MHz, CDCl₃) δ 7.97 – 7.90 (m, 2H, CH_{arom}), 7.54 – 7.49 (m, 1H, CH_{arom}), 7.42 – 7.31 (m, 10H, CH_{arom}), 7.28 – 7.12 (m, 17H, CH_{arom}), 5.83 (dd, *J* = 3.3, 1.2 Hz, 1H, H-4), 5.49 (s, 1H, CHPh), 5.27 (d, *J* = 3.6 Hz, 1H, H-1'), 4.84 – 4.80 (m, 2H, H-1, CHH Bn), 4.76 (d, *J* = 11.3 Hz, 1H, CHH Bn), 4.68 (d, *J* = 11.9 Hz, 1H, CHH Bn), 4.63 (d, *J* = 11.3 Hz, 1H, CHH Bn), 4.68 (d, *J* = 10.1, 4.9 Hz, 1H, CHH Bn), 4.63 (d, *J* = 11.3 Hz, 1H, CHH Bn), 4.03 (dd, *J* = 10.2, 3.2 Hz, 1H, H-3), 4.28 (dd, *J* = 10.1, 4.9 Hz, 1H, H-6'), 4.16 – 4.07 (m, 2H, H-5, H-5'), 4.03 (dd, *J* = 10.2, 3.6 Hz, 1H, H-2), 3.98 (t, *J* = 9.3 Hz, 1H, H-3'), 3.64 (t, *J* = 10.2 Hz, 1H, H-6'), 3.56 (t, *J* = 9.5 Hz, 1H, H-4'), 3.54 – 3.51 (m, 3H, H-2', 2x H-6), 3.43 (s, 3H, CH₃ OMe); ¹³C NMR (126 MHz, CDCl₃) δ 166.1 (C=O), 138.7, 138.3, 138.0, 137.9, 137.8 (Cq), 133.2, 130.0 (CH_{arom}), 129.9 (Cq), 128.9, 128.6, 128.5, 128.5, 128.5, 128.4, 128.4, 128.2, 128.2, 128.2, 128.1, 127.9, 127.8, 127.7, 127.5, 127.4, 126.3 (CH_{arom}), 101.4 (CHPh), 98.7 (C-1), 94.1 (C-1'), 82.2 (C-4'), 78.6 (C-3'), 78.3 (C-2'), 75.0 (CH₂ Bn), 74.3 (C-2), 73.7, 73.5, 72.7 (CH₂ Bn), 71.3 (C-3), 69.1, 69.0 (C-6, C-6'), 68.2 (C-5), 67.9 (C-4), 62.8 (C-5'), 55.5 (CH₃ OMe); diagnostic peaks for

the β-anomer: ¹H NMR (500 MHz, CDCl₃) δ 5.73 (dd, J = 3.6, 1.2 Hz, 1H, H-4), 5.53 (s, 1H, CHPh), 4.98 (d, J = 7.6 Hz, 1H, H-1'), 4.86 (d, J = 11.4 Hz, 1H, CHH Bn), 3.75 (t, J = 10.3 Hz, 1H), 3.41 (s, 3H), 3.30 (t, J = 7.9 Hz, 1H); ¹³C NMR (126 MHz, CDCl₃) δ 165.6, 103.1 (C-1'), 101.1 (CHPh), 98.6 (C-1), 82.5, 81.5, 80.8, 77.3, 75.4, 74.9, 74.9, 74.8, 73.8, 73.2, 72.4, 71.9, 68.3, 65.9, 55.7; HRMS: [M+NH₄]⁺ calcd for C₅₅H₅₆O₁₂NH₄ 926.41100, found 926.40952.

Disaccharide 29B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor **29**. Yield: 52 mg, 60 μ mol, 60%, α : β = 1.3:1. Data reported for a 1:1 mixture of anomers: ¹H NMR (500 MHz, CDCl₃) δ 8.11 - 8.06 (m, 2H), 8.05 - 8.02 (m, 2H), 7.61 - 7.55 (m, 2H), 7.49 - 7.40 (m, 8H), 7.39 - 7.31 (m, 12H), 7.29 - 7.19 (m, 20H), 5.84 (dd, J = 3.4, 1.3 Hz, 1H, H-4 α), 5.67 (dd, J = 3.6, 1.2 Hz, 1H, H-4 β), 5.54 (s, 1H, CHPha), 5.53 (s, 1H, CHPhb), 5.30 (d, *J* = 3.7 Hz, 1H, H-1'a), 4.90 - 4.82 (m, 4H), 4.81 - 4.77 (m, 2H, H-1'β, CHH Bn), 4.75 – 4.70 (m, 2H, H-1α, CHH Bn), 4.67 – 4.62 (m, 2H, H-1β, CHH Bn), 4.58 (d, J = 11.8 Hz, 1H), 4.52 - 4.46 (m, 2H), 4.44 - 4.38 (m, 2H), 4.38 - 4.27 (m, 3H), 4.19 - 4.584.10 (m, 3H), 4.08 (dd, J = 10.1, 3.6 Hz, 1H), 3.96 (dd, J = 9.5, 3.0 Hz, 1H), 3.95 - 3.91 (m, 1H), 3.76 (t, J = 10.3 Hz, 1H), 3.71 - 3.62 (m, 3H), 3.59 - 3.49 (m, 4H), 3.43 (s, 4H), 3.40 (s, 3H), 3.34 -3.26 (m, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 166.0, 165.9, 138.1, 138.0, 137.9, 137.8, 137.7, 137.6, 137.3, 133.3, 133.2, 130.0, 130.0, 129.9, 129.9, 129.8, 129.1, 129.0, 129.0, 128.7, 128.7, 128.6, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.2, 128.1, 128.1, 128.1, 127.9, 127.9, 127.8, 127.8, 127.8, 127.7, 126.3, 126.1, 125.1, 102.4 (C-1β), 101.5 (CHPha), 101.3 (CHPhβ), 98.7 (C-1a), 98.2 (C-1β), 94.0 (C-1'a), 82.8, 81.5, 78.9, 77.4, 77.2, 77.0, 76.9, 75.5, 75.0, 74.8, 74.6, 73.9, 73.7, 73.6, 73.5, 71.8, 70.9, 69.2, 68.8, 68.7, 68.6, 68.4, 67.8, 66.7, 66.5, 66.0, 62.8, 62.7, 55.6, 55.6; HRMS: [M+NH₄]⁺ calcd for C₄₈H₄₉N₃O₁₁NH₄ 861.37053, found 861.36925.

Disaccharide 30A



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **A** and acceptor **30**. Yield: 81 mg, 84 µmol, 84%, α : β >20:1. ¹H NMR (500 MHz, CDCl₃) δ 8.10 – 7.16 (m, 30H, CH_{arom}), 5.59 (dd, *J* = 10.5, 3.7, 0.8 Hz, 1H, H-2), 5.41 (s, 1H, CHPh), 5.05 (dd, *J* = 5.9, 3.7 Hz, 2H, H-1, H-1'), 4.99 (d, *J* = 11.6 Hz, 1H, CHH Bn), 4.86 (d, *J* = 11.5 Hz, 1H, CHH Bn), 4.77 (d, *J* = 11.4 Hz, 1H, CHH Bn), 4.66 (t, *J* = 11.2 Hz, 2H, CHH Bn, CHH Bn), 4.47 (dd, *J* = 11.7, 2.8 Hz, 2H, 2x CHH Bn), 4.37 (d, *J* = 11.8 Hz, 1H, CHH Bn), 4.22 (dd, *J* = 10.4, 2.8 Hz, 1H, H-3), 4.07 – 4.03 (m, 1H, H-4), 3.99 – 3.90 (m, 3H, H-5, H-3', H-5'), 3.82 (dd, *J* = 10.2, 4.9 Hz, 1H, H-6'), 3.60 – 3.45 (m, 4H, 2x H-6, H-2', H-4'), 3.42 – 3.36 (m, 1H, H-6'), 3.35 (s, 3H, CH₃ OMe); ¹³C NMR (126 MHz, CDCl₃) δ 166.19 (C=O), 138.8, 138.6, 138.2, 138.1, 137.6, 133.1, 130.0, 130.0, 128.9, 128.6, 128.5, 128.5, 128.4, 128.3, 128.3, 128.3,

128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.5, 126.3 (CH_{arom}), 101.3 (CHPh), 99.4 (C-1'), 97.7 (C-1), 82.5 (C-4'), 79.6 (C-2'), 78.5 (C-3'), 77.8 (C-3), 75.2 (C-4), 75.2 (CH₂ Bn), 75.0 (CH₂ Bn), 74.6 (CH₂ Bn), 73.6 (CH₂ Bn), 71.0 (C-2), 69.5 (C-5), 69.1 (C-6), 68.8 (C-6'), 63.3 (C-5'), 55.5 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₅₅H₅₆O₁₂NH₄ 926.41100, found 926.40731.

Disaccharide 30B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor **30**. Yield: 69 mg, 82 μ mol, 82%, α : β = 13:1. Data for α -anomer: ¹H NMR (500 MHz, CDCl₃) δ 8.09 – 7.18 (m, 25H, CH_{arom}), 5.62 (dd, J = 10.5, 3.7 Hz, 1H, H-2), 5.45 (s, 1H, CHPh), 5.10 (d, J = 3.6 Hz, 1H, H-1'), 5.04 (d, J = 3.8 Hz, 1H, H-1), 4.99 (d, J = 11.4 Hz, 1H, CHH Bn), 4.76 (d, J = 11.0 Hz, 1H, CHH Bn), 4.59 (dd, J = 11.2, 3.7 Hz, 2H, 2x CHH Bn), 4.51 (d, J = 11.8 Hz, 1H, CHH Bn), 4.44 (d, J = 11.7 Hz, 1H, CHH Bn), 4.31 (dd, J = 10.5, 2.9 Hz, 1H, H-3), 4.15 (dd, J = 2.9, 1.2 Hz, 1H, H-4), 4.09 - 3.95 (m, 3H, H-5, H-5', H-6'), 3.89 (dd, J = 9.9, 9.1 Hz, 1H, H-3'), 3.66 - 3.56 (m, 3H, 2x H-6, H-4'), 3.53 - 3.45 (m, 2H, H-2', H-6'), 3.35 (s, 3H, CH₃ OMe); ¹³C NMR (126 MHz, CDCl₃) δ 166.1 (C=O), 138.6, 138.0, 137.7, 137.4 (Cq), 133.1, 129.9, 129.9, 129.1, 129.0, 128.7, 128.6, 128.6, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.9, 127.9, 127.8, 127.8, 127.8, 126.2, 126.1 (CHarom), 101.4 (CHPh), 97.7 (C-1), 97.3 (C-1'), 82.8 (C-4'), 76.2 (C-3'), 75.7 (C-3), 75.2 (CH2 Bn), 75.0 (CH₂ Bn), 74.6 (C-4), 73.7 (2x CH₂ Bn), 70.7 (C-2), 69.3 (C-5), 68.8 (C-6'), 68.6 (C-6), 63.6 (C-2'), 63.3 (C-5), 55.6 (CH₃ OMe); Diagnostic peaks for β -anomer: ¹H NMR (500 MHz, CDCl₃) 5.57 (s, 1H, CHPh), 5.13 (d, J = 3.8 Hz, 1H, H-1), 4.65 (d, J = 8.0 Hz, 1H, H-1'); ¹³C NMR (126 MHz, CDCl₃) δ 104.3 (C-1'), 101.4 (CH Ph), 98.0 (C-1); HRMS: [M+NH₄]⁺ calcd for C₄₈H₄₀N₃O₁₁NH₄ 861.37053, found 861.36922.

Disaccharide 33A



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **A** and acceptor **33**. Yield: 85 mg, 89 µmol, 89%, $\alpha:\beta > 20:1$. ¹H NMR (500 MHz, CDCl₃) δ 8.06 – 7.99 (m, 2H, CH_{arom}), 7.41 – 7.14 (m, 28H, CH_{arom}), 5.63 (dd, J = 10.7, 3.1 Hz, 1H, H-3), 5.44 (s, 1H, CHPh), 4.98 (d, J = 3.5 Hz, 1H, H-1), 4.90 (d, J = 3.6 Hz, 1H, H-1'), 4.82 (d, J = 12.1 Hz, 1H, CHP h), 4.77 (d, J = 11.2 Hz, 1H, CHH Bn), 4.70 (d, J = 11.2 Hz, 1H, CHH Bn), 4.67 (d, J = 12.1 Hz, 1H, CHH Bn), 4.63 (d, J = 11.3 Hz, 1H, CHH Bn), 4.54 (d, J = 11.9 Hz, 1H, CHH Bn), 4.47 – 4.42 (m, 3H, H-2, 2x CHH Bn), 4.24 (d, J = 2.4 Hz, 1H, H-4), 4.15 (t, J = 6.5 Hz, 1H, H-5), 4.06 – 3.94 (m, 3H, H-3', H-5', H-6'), 3.63 – 3.48 (m, 6H, H-2', H-4', H-5, 2x H-6, H-6'), 3.43 (s, 3H, CH₃ OMe); ¹³C NMR (126 MHz, CDCl₃) δ 165.9 (C=O), 138.7, 138.4, 137.9, 137.9, 137.5, 133.1 (C_q), 129.7, 129.6, 128.8, 128.6, 128.5, 128.4, 128.3, 128.3, 128.1, 128.0, 128.0, 127.8, 127.5, 126.2 (CH_{arom}), 101.2 (CHPh), 97.2 (C-1), 96.6 (C-1'), 82.1 (C-

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4'), 78.8 (C-2'), 78.3 (C-3'), 75.4 (C-4), 75.3, 75.2, 73.5, 73.4 (CH₂ Bn), 72.3 (C-3), 71.6 (C-2), 68.9 (C-5), 68.8 (C-6), 68.7 (C-6'), 62.8 (C-5'), 55.4 (CH₃ OMe); HRMS: $[M+NH_4]^+$ calcd for $C_{55}H_{56}O_{12}NH_4$ 926.41100, found 926.40964.

Disaccharide 33B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor **33**. 44 mg, 51 μ mol, 51%, α : β = 3:1. Data for the α-anomer: ¹H NMR (500 MHz, CDCl₃) δ 8.06 – 8.01 (m, 2H, CH_{arom}), 7.49 – 7.17 (m, 23H, CH_{arom}), 5.63 (dd, J = 10.6, 3.1 Hz, 1H, H-3), 5.44 (s, 1H, CHPh), 5.01 (d, J = 3.5 Hz, 1H, H-1), 4.97 (d, J = 3.8 Hz, 1H, H-1'), 4.78 (d, J = 10.9 Hz, 1H, CHH Bn), 4.72 – 4.60 (m, 2H, CHH Bn, CHH Bn), 4.54 (d, J = 11.9 Hz, 1H, CHH Bn), 4.50 – 4.39 (m, 3H, H-2, 2x CHH Bn), 4.19 (d, J = 2.6 Hz, 1H, H-4), 4.16 (t, J = 6.5 Hz, 1H, H-5), 4.01 (dd, J = 10.1, 4.9 Hz, 1H, H-6'), 3.99 - 3.89 (m, 2H, H-3', H-5'), 3.61 - 3.52 (m, 5H, H-4', H-5, 2x H-6, H-6'), 3.48 (s, 3H, CH₃ OMe), 3.34 (dd, *J* = 10.1, 3.4 Hz, 1H, H-2'); ¹³C NMR (126 MHz, CDCl₃) δ 165.8 (C=O), 138.0, 137.9, 137.8, 137.3 (C_q), 133.3, 129.8, 129.7 (CH_{arom}), 129.6 (C_q), 129.0, 128.7, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 128.1, 127.9, 127.9, 127.9, 127.9, 127.8, 127.8, 126.2, 126.0 (CH_{arom}), 101.4 (CHPh), 97.4 (C-1), 97.2 (C-1'), 82.7 (C-4'), 75.8 (C-3'), 75.6 (C-4), 75.4, 75.1, 73.6 (CH₂ Bn), 72.8 (C-2), 72.0 (C-3), 68.9 (C-5), 68.7, 68.6 (C-6, C-6'), 63.2 (C-5'), 63.0 (C-2'), 55.7 (CH₃ OMe); diagnostic peaks for the β -anomer: ¹H NMR (500 MHz, CDCl₃) δ 5.59 (dd, J = 10.7, 3.2 Hz, 1H, H-3), 5.54 (s, 1H, CHPh), 4.29 (td, J = 10.5, 4.3 Hz, 2H, H-5'), 4.23 (d, J = 3.2 Hz, 1H, H-4), 3.75 (t, J = 10.3 Hz, 1H), 3.69 - 3.64 (m, 1H), 3.44 (s, 3H, CH₃ OMe); 13 C NMR (126 MHz, CDCl₃) δ 165.9 (C=O), 104.4 (C-1'), 101.3 (CHPh), 99.8 (C-1), 81.3, 79.2, 75.5, 74.8, 68.7, 68.6, 68.5, 66.2, 65.7, 55.6; HRMS: [M+NH₄]⁺ calcd for C₄₈H₄₀N₃O₁₁NH₄ 861.37053, found 861.36914.

Disaccharide 34A



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **A** and acceptor **34.** Yield: 89 mg, 88 µmol, 88%, α : β > 20:1. ¹H NMR (400 MHz, CDCl₃) δ 8.02 (ddd, *J* = 8.5, 2.6, 1.3 Hz, 4H, CH_{arom}), 7.83 – 7.73 (m, 2H, CH_{arom}), 7.66 – 7.59 (m, 1H, CH_{arom}), 7.57 – 7.52 (m, 1H, CH_{arom}), 7.50 – 7.12 (m, 22H, CH_{arom}), 5.99 (dd, *J* = 3.5, 1.3 Hz, 1H, H-4), 5.84 (dd, *J* = 10.6, 3.4 Hz, 1H, H-3), 5.36 (s, 1H, CHPh), 5.10 (d, *J* = 3.4 Hz, 1H, H-1), 4.92 – 4.85 (m, 2H, H-1', CHH Bn), 4.78 (d, *J* = 11.2 Hz, 1H, CHH Bn), 4.71 (d, *J* = 11.3 Hz, 1H, CHH Bn), 4.67 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.64 – 4.52 (m, 2H, H-5, H-6), 4.41 (dd, *J* = 10.6, 3.4 Hz, 1H, H-2), 4.34 (dd, *J* = 10.8, 5.2 Hz, 1H, H-6), 3.96 (t, *J* = 9.3 Hz, 1H, H-3'), 3.90 – 3.78 (m, 2H, H-5', H-6'), 3.54 – 3.42 (m, 6H, CH₃ OMe, H-2', H-4', H-6'). ¹³C NMR (101 MHz, CDCl₃) δ 166.1, 165.5, 165.5 (C=O), 138.7, 138.5, 137.4, 133.6, 133.3, 133.0 (C_q), 129.9, 129.8, 129.7, 129.6, 129.5, 129.4, 128.9, 128.7, 128.7, 128.5, 128.4, 128.4, 128.3, 128.1, 128.0, 128.0, 128.0, 127.6, 126.2 (CH_{arom}), 101.2 (CHPh), 97.6 (C-1), 97.3 (C-1'), 82.1 (C-4'), 78.9 (C-2'),

78.3 (C-3'), 75.2 (CH₂ Bn), 73.8 (CH₂ Bn), 72.1 (C-2), 69.5 (C-4), 69.3 (C-3), 68.7 (C-6'), 66.9 (C-5), 62.8 (C-5'), 62.7 (C-6), 55.7 (CH₃ OMe); HRMS: $[M+NH_4]^+$ calcd for C₅₅H₅₂O₁₄NH₄ 954.36953, found 954.36787.

Disaccharide 34B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor **34**. Yield: 76 mg, 87 μ mol, 87%, α : β = 6:1. Data for α-anomer: ¹H NMR (400 MHz, CDCl₃) δ 8.07 - 7.98 (m, 4H, CH_{arom}), 7.87 - 7.78 (m, 2H, CH_{arom}), 7.63 (ddt, J = 8.1, 7.0, 1.4 Hz, 1H, CH_{arom}), 7.55 (ddt, J = 8.1, 7.0, 1.3 Hz, 1H, CH_{arom}), 7.51 – 7.19 (m, 17H, CH_{arom}), 5.96 (dd, J = 3.6, 1.2 Hz, 1H, H-4), 5.83 (dd, J = 10.5, 3.5 Hz, 1H, H-3), 5.37 (s, 1H, CHPh), 5.15 (d, J = 3.5 Hz, 1H, H-1), 4.98 (d, J = 3.6 Hz, 1H, H-1'), 4.82 (d, J = 10.9 Hz, 1H, CHH Bn), 4.67 (d, J = 10.9 Hz, 1H, CHH Bn), 4.64 – 4.54 (m, 2H, H-5, H-6), 4.36 (m, 2H, H-2, H-6), 4.02 – 3.96 (t, J = 9.1 Hz, 1H, H-3'), 3.87 - 3.77 (m, 2H, H-5', H-6'), 3.56 (m, 4H, H-4', CH₃ OMe), 3.48 – 3.41 (m, 1H, H-6'), 3.33 (dd, J = 10.0, 3.6 Hz, 1H, H-2'). ¹³C NMR (101 MHz, CDCl₃) δ 166.1, 165.5, 165.4 (C=O), 137.8, 137.1, 133.6, 133.3, 133.2 (C_q), 129.9, 129.8, 129.6, 129.4, 129.3, 129.0, 128.7, 128.7, 128.5, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.3, 128.1, 128.1, 127.9, 126.1, 126.0 (CHarom), 101.3 (CHPh), 98.0 (C-1'), 97.8 (C-1), 82.6 (C-4'), 75.6 (C-3'), 75.1 (CH₂ Bn), 73.6 (C-2), 69.4 (C-4), 69.2 (C-3), 68.4 (C-6'), 66.8 (C-5), 63.3 (C-5'), 62.9 (C-2'), 62.6 (C-6), 55.9 (CH₃ OMe). Diagnostic peaks for β -anomer: ¹H NMR (400 MHz, CDCl₃) δ 5.99 (dd, *J* = 3.6, 1.2 Hz, 1H, H-4), 5.55 (s, 1H, CHPh), 5.12 (d, *J* = 3.6 Hz, 1H, H-1), 4.45 (d, *J* = 7.7 Hz, 1H, H-1'), 4.26 (dd, J = 10.5, 3.4 Hz, 1H, H-2), 3.52 (s, 3H, CH₃ OMe). ¹³C NMR (101 MHz, CDCl₃) δ 104.3 (C-1'), 101.5 (CHPh), 99.8 (C-1), 76.7 (C-2), 55.8 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₄₈H₄₅N₃O₁₃NH₄ 889.32906, found 889.32747.

Disaccharide 35A



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **A** and acceptor **35**. Yield: 75 mg, 83 mmol, 83%, $\alpha:\beta = 1.5:1$. Data reported for a 1:1 mixture: ¹H NMR (400 MHz, CDCl₃) δ 7.60 – 6.94 (m, 60H), 5.56 (s, 1H, CHPh β), 5.53 – 5.49 (m, 2H, H-1' α , CHPh α), 5.08 (d, *J* = 7.5 Hz, 1H, H-1' β), 4.94 – 4.71 (m, 9H), 4.67 (d, *J* = 2.4 Hz, 2H), 4.63 (d, *J* = 10.6 Hz, 1H), 4.60 – 4.52 (m, 3H), 4.50 – 4.38 (m, 6H), 4.35 – 4.30 (m, 1H), 4.21 – 4.07 (m, 3H), 3.99 (t, *J* = 9.3 Hz, 1H), 3.93 (d, *J* = 2.8 Hz, 1H, H-4 α), 3.90 (d, *J* = 2.8 Hz, 1H, H-4 β), 3.85 – 3.80 (m, 1H), 3.80 – 3.75 (m, 1H), 3.72 (dd, *J* = 9.2, 7.9 Hz, 1H), 3.66 – 3.53 (m, 10H), 3.50 (d, *J* = 8.5 Hz, 7H), 3.42 (ddd, *J* = 10.0, 8.9, 5.0 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 139.0, 138.7, 138.7, 138.2, 137.9, 137.9, 137.9, 137.5, 137.5, 129.0, 128.8, 128.6, 128.6, 128.6, 128.5, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 128.1, 128.1, 128.1, 128.1, 128.0, 128.0, 127.9, 127.9, 127.8, 127.7, 127.6, 127.5, 126.3, 126.1, 104.8 (C-1 α), 103.5 (C-

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1 β), 103.2 (C-1' β), 101.3 (CHPha), 101.2 (CHPh β), 96.8 (C-1' α), 82.8, 82.7, 82.3, 81.5, 81.3, 80.4, 79.1, 78.6, 77.2, 75.3, 75.0, 75.0, 74.7, 74.5, 73.7, 73.7, 73.5, 73.4, 73.3, 73.0, 73.0, 72.9, 72.8, 72.5, 69.1, 69.0, 68.8, 68.7, 66.0, 62.1, 56.7 (CH₃ OMea), 56.6 (CH₃ OMe β); HRMS: [M+NH₄]⁺ calcd for C₅₅H₅₈O₁₁NH₄ 912.43174, found 912.42989.

Disaccharide 35B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor 35. Yield: 80 mg, 96 μ mol, 96%, α ; β = 1:10. Data for the β-anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.49 – 7.20 (m, 25H), 5.54 (s, 1H, CHPh), 4.93 - 4.84 (m, 3H, H-1', 2x CHH Bn), 4.77 (d, J = 11.4 Hz, 1H, CHH Bn), 4.74 - 4.68 (m, 2H, CH₂ Bn), 4.55 (d, *J* = 11.7 Hz, 1H, CH*H* Bn), 4.45 (d, *J* = 11.9 Hz, 1H, C*H*H Bn), 4.40 (d, *J* = 11.7 Hz, 1H, CHH Bn), 4.33 – 4.27 (m, 2H, H-1, H-6'), 4.08 (dd, J = 9.6, 7.6 Hz, 1H, H-2), 3.93 (d, J = 2.8 Hz, 1H, H-4), 3.79 (t, J = 10.3 Hz, 1H, H-6'), 3.76 - 3.70 (m, 1H, H-4'), 3.63 (dd, J = 9.6, 2.8 Hz, 1H, H-3), 3.60 - 3.57 (m, 3H, H-3', 2x H-6), 3.55 - 3.46 (m, 5H, H-2', H-5, CH₃ OMe), 3.34 (td, J = 9.9, 4.9 Hz, 1H, H-5'); ¹³C NMR (101 MHz, CDCl₃) δ 138.6, 138.0, 137.9, 137.3 (C_q), 131.5, 129.1, 128.6, 128.6, 128.5, 128.5, 128.5, 128.4, 128.4, 128.3, 128.1, 128.1, 128.1, 128.0, 128.0, 127.9, 127.9, 127.6, 126.1 (CHarom), 102.6 (C-1), 102.2 (C-1'), 101.3 (CHPh), 83.0 (C-3), 81.6 (C-4'), 79.4 (C-2'), 77.2 (C-2), 74.9, 74.6, 73.6 (CH2 Bn), 73.3 (C-3'), 72.8 (C-4), 72.7 (CH2 Bn), 68.7, 68.7 (C-6, C-6'), 66.5, 66.2 (C-5, C-5'), 56.3 (CH₃ OMe); Diagnostic peaks for the α -anomer: ¹H NMR (400 MHz, CDCl₃) δ 5.53 (s, 1H, CHPh), 5.46 (d, *J* = 3.8 Hz, 1H, H-1'), 4.14 (dd, *J* = 10.2, 5.0 Hz, 1H), 4.01 (dd, J = 10.0, 7.7 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 104.9 (C-1), 101.4 (CHPh), 97.6 (C-1'), 82.9, 80.3, 76.0, 74.3, 73.4, 69.3, 63.2, 62.4, 58.0 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₄₈H₅₁N₃O₁₀NH₄ 847.39127, found 847.38959.

Disaccharide 36A



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **A** and acceptor **36**. Yield: 70 mg, 80 µmol, 89%, $\alpha:\beta = 1:2.4$. Data reported for a 1:2 mixture of anomers: ¹H NMR (500 MHz, CDCl₃) δ 7.68 – 7.01 (m, 75H), 5.77 (d, J = 4.1 Hz, 1H, H-1'a), 5.55 (s, 1H, CHPha), 5.48 (s, 2H, CHPhβ), 4.91 (d, J = 11.3 Hz, 3H), 4.84 (d, J = 2.8 Hz, 4H), 4.81 – 4.74 (m, 8H), 4.72 – 4.67 (m, 6H), 4.65 – 4.58 (m, 7H), 4.57 – 4.49 (m, 3H), 4.44 (d, J = 12.1 Hz, 1H), 4.29 (dd, J = 10.4, 4.9 Hz, 1H, H-6'a), 4.15 (dd, J = 10.5, 5.0 Hz, 2H, H-6' β), 4.04 – 3.94 (m, 3H), 3.90 (td, J = 9.7, 1.4 Hz, 2H, H-4 β), 3.80 – 3.72 (m, 8H), 3.71 – 3.65 (m, 2H), 3.61 (td, J = 9.4, 4.6 Hz, 3H), 3.56 – 3.49 (m, 3H), 3.43 (dd, J = 8.8, 7.7 Hz, 2H, H-4' β), 3.33 (s, 9H, CH₃ OMea β), 3.27 (td, J = 9.9, 5.0 Hz, 2H, H-5' β), 1.42 (d, J = 6.2 Hz, 3H, H-6a), 1.36 (d, J = 6.3 Hz, 6H, H-6 β); ¹³C NMR (126 MHz, CDCl₃) δ 139.4, 138.8, 138.6, 138.5, 138.4, 138.2, 138.0, 137.5, 137.5, 129.9, 129.6, 129.0, 128.0, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 128.1, 128.0, 128.0, 127.9, 127.9, 127.8, 127.7, 127.7, 127.7, 127.6, 127.6, 127.4, 127.3, 127.0, 126.7, 126.1, 103.9 (C-1' β), 10.2 (CHPha β), 99.5 (C-1 β), 98.8 (C-1a), 98.0

(C-1'a), 83.0 (C-4' β), 82.2 (C-4'a), 81.8, 81.5, 81.4, 80.7, 78.8, 78.7, 78.2, 77.4, 77.2, 76.9, 76.1, 75.7, 75.7, 75.4, 75.2, 73.9, 73.2, 73.0, 72.8, 72.6, 70.5, 69.0, 68.9, 67.9, 66.9, 65.9, 63.3, 54.9 (CH₃ OMe β), 54.8 (CH₃ OMe α), 19.3 (C-6 α), 18.2 (C-6 β); HRMS: [M+NH₄]⁺ calcd for C₄₈H₅₂O₁₀NH₄ 806.38987, found 806.38846.





Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor **36**. Yield: 54 mg, 75 µmol, 75%, α : β < 1:20. ¹H NMR (400 MHz, CDCl₃) δ 7.48 – 7.22 (m, 20H, CH_{arom}), 5.48 (s, 1H, CHPh), 4.91 (d, *J* = 11.1 Hz, 1H, CHH Bn), 4.77 (d, *J* = 11.2 Hz, 1H, CHH Bn), 4.72 (d, *J* = 12.4 Hz, 1H, CHH Bn), 4.69 – 4.63 (m, 3H, H-1, CHH Bn, CHH Bn), 4.60 – 4.54 (m, 2H, H-1', CHH Bn), 4.00 (dd, *J* = 10.5, 5.0 Hz, 1H, H-6'), 3.89 (t, *J* = 9.1 Hz, 1H, H-4), 3.80 – 3.69 (m, 3H, H-2, H-3, H-5), 3.66 – 3.55 (m, 2H, H-3', H-4'), 3.52 (t, *J* = 10.3 Hz, 1H, H-6'), 3.38 (dd, *J* = 9.0, 7.9 Hz, 1H, H-2'), 3.31 (s, 3H, CH₃ OMe), 3.19 (td, *J* = 9.4, 5.0 Hz, 1H, H-5'), 1.43 (d, *J* = 6.2 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 139.1, 138.4, 137.9, 137.3 (C_q), 131.5, 131.2, 129.1, 128.5, 128.5, 128.4, 128.4, 128.3, 128.0, 128.0, 127.7, 127.4, 126.8, 126.1 (CH_{arom}), 102.4 (C-1'), 101.3 (CHPh), 99.2 (C-1), 81.7 (C-4'), 81.4 (C-4), 79.5 (C-3'), 78.6 (C-3), 75.2 (C-2), 75.0, 73.1, 72.2 (CH₂ Bn), 68.6 (C-6'), 67.5, 67.4 (C-2', C-5), 66.1 (C-5'), 54.9 (CH₃ OMe), 18.1 (C-6); HRMS: [M+NH₄]⁺ calcd for C₄₁H₄₅N₃O₉NH₄ 741.34941, found 741.34849.

Disaccharide 37A



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **A** and acceptor **37**. Yield: 91 mg, 90 μ mol, 90%, α : β = 1.7:1. Data reported for a 2:1 mixture: ¹H NMR (400 MHz, CDCl₃) δ 7.76 – 7.06 (m, 75H), 5.61 (s, 1H, CHPhβ), 5.57 (s, 2H, ChPha), 5.14 – 5.06 (m, 3H, H-1'aβ), 5.02 – 4.97 (m, 3H), 4.93 (d, J = 11.6 Hz, 1H), 4.90 – 4.84 (m, 5H), 4.79 (d, J = 11.6 Hz, 2H), 4.76 – 4.64 (m, 8H), 4.60 (s, 4H), 4.51 (d, J = 10.9 Hz, 1H), 4.40 (d, J = 11.1 Hz, 1H), 4.38 – 4.31 (m, 2H), 4.12 (dd, J = 10.2, 4.9 Hz, 2H, H- $6'\alpha$), 4.07 (t, J = 9.3 Hz, 2H, H-4 α), 3.95 (t, J = 9.3 Hz, 1H, H-4 β), 3.86 – 3.81 (m, 6H), 3.81 – 3.73 (m, 3H), 3.73 - 3.60 (m, 6H), 3.45 (dd, J = 9.2, 6.9 Hz, 1H, H-2' β), 3.43 - 3.37 (m, 4H), 3.35 (s, 6H, CH₃ OMea), 1.42 (d, J = 5.9 Hz, 6H, H-6a), 1.39 (d, J = 6.2 Hz, 3H, H-6 β); ¹³C NMR (101 MHz, CDCl₃) δ 138.9, 138.4, 138.0, 138.0, 137.8, 131.7, 129.0, 128.9, 128.5, 128.5, 128.4, 128.4, 128.4, 128.3, 128.2, 128.2, 128.1, 128.1, 128.1, 128.0, 128.0, 127.9, 127.9, 127.9, 127.8, 127.8, 127.7, 127.6, 127.6, 127.5, 126.2, 126.1, 103.1 (C-1'β), 101.2 (CHPha), 101.2 (CHPhβ), 99.0 (C-1β, 99.0, 98.9 (C-1a, C-1'a), 82.8, 82.6, 81.9, 81.1, 80.5, 79.6, 79.1, 79.0, 77.9, 76.6, 75.3, 75.2, 75.1, 74.6, 74.4, 74.3, 72.9, 72.8, 72.2, 71.5, 69.1, 68.9, 68.0, 67.3, 65.7, 62.8, 54.9 (CH₃ OMeβ), 54.7 (CH₃ OMea), 18.3 (C-6α), 18.0 (C-6β); HRMS: [M+NH₄]⁺ calcd for C₄₈H₅₂O₁₀NH₄ 806.38987, found 806.38859.

Disaccharide 37B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor **37**. Yield: 72 mg, 99 μ mol, 99%, α : β = 1:10. Data for β-anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.76 – 7.64 (m, 2H, CH_{arom}), 7.47 (dd, J = 7.6, 2.2 Hz, 2H, CHarom), 7.43 - 7.25 (m, 16H, CHarom), 5.55 (s, 1H, CHPh), 4.94 - 4.86 (m, 2H, H-1', CHH Bn), 4.78 (d, J = 11.4 Hz, 1H, CHH Bn), 4.68 – 4.60 (m, 4H, H-1, CHH Bn, CH₂ Bn), 4.51 (d, J = 10.9 Hz, 1H, CHH Bn), 4.30 (dd, J = 10.5, 5.0 Hz, 1H, H-6'), 3.92 - 3.82 (m, 2H, H-3, H-4), 3.77 (dd, J = 3.0, 1.8 Hz, 1H, H-2), 3.72 (t, J = 10.3 Hz, 1H, H-6'), 3.68 – 3.62 (m, 2H, H-4', H-5), 3.47 (t, J = 9.2 Hz, 1H, H-3'), 3.39 (dd, J = 9.6, 7.9 Hz, 1H, H-2'), 3.36 - 3.29 (m, 4H, H-5', CH₃ OMe), 1.31 (d, J = 6.2 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 138.3, 138.2, 138.1, 137.3 (Cq), 131.6, 129.1, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.3, 128.2, 128.0, 127.9, 127.9, 127.8, 126.1 (CHarom), 102.1 (C-1'), 101.3 (CHPh), 98.9 (C-1), 81.9 (C-4'), 80.1 (C-3), 79.1 (C-3'), 77.4 (C-4), 74.9 (CH₂ Bn), 74.1 (C-2), 72.8, 72.0 (CH₂ Bn), 68.7 (C-6), 67.0 (C-5), 66.5 (C-2'), 65.8 (C-5'), 54.9 (CH₃ OMe), 17.9 (C-6); diagnostic peaks for the α-anomer: ¹H NMR (400 MHz, CDCl₃) δ 5.52 (s, 1H, CHPh), 5.06 (d, J = 3.8 Hz, 1H, H-1'), 4.03 (dd, J = 10.2, 4.9 Hz, 1H), 3.98 (t, J = 9.5 Hz, 1H), 1.41 (d, J = 6.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 101.3 (CHPh), 98.7 (C-1'), 82.9, 81.3, 80.8, 75.1, 74.3, 71.3, 68.0, 63.7, 62.8, 21.9 (C-6); HRMS: [M+NH₄]⁺ calcd for C₄₁H₄₅N₃O₉NH₄ 741.34941, found 741.34836.

Disaccharide 38A



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor A and acceptor 38. Yield: 79 mg, 100 μ mol, 100%, α : β = 7:1. Data for α-anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.45 - 7.12 (m, 25H, CH_{arom}), 5.53 (s, 1H, CHPh), 5.11 (d, J = 3.5 Hz, 1H, H-1'), 4.96 – 4.89 (m, 2H, 2x CHH Bn), 4.83 – 4.77 (m, 3H, 2x CHH Bn, CHH Bn), 4.74 (d, J = 11.8 Hz, 1H, CHH Bn), 4.61 – 4.54 (m, 3H, H-1, 2x CHH Bn), 4.19 - 4.10 (m, 3H, H-4, H-5', H-6'), 4.09 - 4.05 (m, 1H, H-3), 3.86 (dd, J = 2.9, 2.1 Hz, 1H, H-2), 3.70 - 3.58 (m, 5H, H-2', H-3', H-4', H-5, H-6'), 3.28 (s, 3H, CH₃ OMe), 1.33 (d, J = 5.4 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 138.7, 138.6, 138.2, 138.1, 137.7 (C_q), 131.6, 131.1, 128.9, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.2, 128.2, 128.2, 127.9, 127.9, 127.8, 127.8, 127.8, 127.7, 127.7, 127.6, 126.3 (CHarom), 101.3 (CHPh), 99.2 (C-1), 96.5 (C-1'), 82.6 (C-4'), 80.2, 79.2 (C-2', C-3'), 78.6 (C-4), 76.9 (C-3), 75.7 (CH₂ Bn), 75.3 (C-2), 75.2, 73.9, 73.3 (CH₂ Bn), 69.1 (C-6'), 68.2 (C-5), 63.0 (C-5'), 54.8 (CH₃ OMe), 18.1 (C-6); diagnostic peaks for the β -anomer: ¹H NMR (400 MHz, CDCl₃) δ 5.55 (s, 1H, CHPh), 5.00 (d, J = 11.3 Hz, 1H), 4.40 (d, J = 10.6 Hz, 1H), 4.31 (dd, J = 10.4, 5.0 Hz, 1H), 3.79 (dd, J = 3.3, 1.8 Hz, 1H, H-2); ¹³C NMR (101 MHz, CDCl₃) δ 103.9 (C-1'), 99.5 (C-1), 81.9, 81.4, 81.0, 79.6, 74.8, 73.6, 73.2, 67.8, 66.0; HRMS: [M+NH₄]⁺ calcd for 806.38987, found 806.38793.

Disaccharide 38B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor **38**. Yield: 49 mg, 68 μ mol, 68%, α : β = 1.4:1. Data reported for a 1:1 mixture of anomers: ¹H NMR (500 MHz, CDCl₃) δ 7.81 – 7.59 (m, 4H), 7.51 - 7.23 (m, 32H), 7.20 - 7.09 (m, 4H), 5.59 - 5.46 (m, 2H, CHPhaβ), 5.02 (d, J = 10.6 Hz, 1H), 4.96 - 4.91 (m, 3H), 4.85 (d, J = 10.6 Hz, 1H), 4.82 - 4.76 (m, 3H), 4.72 (d, J = 11.0 Hz, 4H), 4.65 $(d, J = 8.1 \text{ Hz}, 1\text{H}, 1^{2}\beta), 4.62 (d, J = 10.7 \text{ Hz}, 1\text{H}), 4.57 (d, J = 1.8 \text{ Hz}, 1\text{H}, 1^{2}\beta), 4.54 (d, J = 1.8 \text{ Hz}, 1^{2$ 10.6 Hz, 1H), 4.29 (dd, J = 10.5, 5.0 Hz, 1H, H-6' β), 4.22 (dd, J = 10.2, 4.9 Hz, 1H, H-6' α), 4.15 – 4.09 (m, 2H), 4.07 – 4.01 (m, 2H), 3.82 (dd, J = 3.2, 2.0 Hz, 1H, H-2a), 3.77 (dd, J = 3.3, 1.7 Hz, 1H, H-2β), 3.74 – 3.62 (m, 6H), 3.59 (t, J = 8.4 Hz, 1H), 3.46 (dd, J = 9.4, 8.1 Hz, 1H, H-2'β), 3.38 (dd, J = 10.0, 3.6 Hz, 1H, H-2'a), 3.33 (dt, J = 9.6, 4.9 Hz, 1H), 3.30 (s, 3H, CH₃ OMea), 3.29 (s, 3H, CH₃ OMeβ), 1.37 – 1.31 (m, 6H, H-6αβ); ¹³C NMR (126 MHz, CDCl₃) δ 138.7, 138.5, 137.9, 137.9, 137.8, 137.7, 137.5, 137.2, 135.4, 134.4, 131.8, 131.7, 131.5, 131.3, 131.2, 130.4, 130.3, 129.2, 129.0, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 128.0, 127.9, 127.8, 127.7, 126.3, 126.1, 103.0 (C-1'β), 101.4, 101.4 (CHPhaβ), 99.5 (C-1β), 98.3 (C-1a), 94.2 (C-1'a), 83.0, 81.8, 80.6, 79.9, 79.7, 79.5, 78.3, 76.1, 75.7, 75.2, 75.1, 75.0, 74.7, 73.6, 73.0, 72.6, 68.9, 68.0, 67.9, 66.9, 66.1, 62.9, 62.8, 54.8, 54.6, 18.1, 18.0; HRMS: [M+NH₄]⁺ calcd for C41H45N3O9NH4 741.34941, found 741.34778.

Disaccharide 39A



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **A** and acceptor **39**. Yield: 53 mg, 66 μ mol, 66%, α : β = 6:1. ¹H NMR (500 MHz, CDCl₃) δ 8.08 - 8.04 (m, 2H, CH_{arom}), 7.57 - 7.52 (m, 1H, CH_{arom}), 7.43 - 7.34 (m, 9H, CH_{aron}), 7.27 - 7.22 (m, 3H, CH_{aron}), 7.20 - 7.15 (m, 4H, CH_{aron}), 7.14 - 7.06 (m, 6H, CH_{arom}), 5.58 (dd, J = 3.2, 1.9 Hz, 1H, H-2), 5.51 (s, 1H, CHPh), 5.18 (d, J = 3.6 Hz, 1H, H-1'), 4.98 (d, *J* = 10.4 Hz, 1H, CHH Bn), 4.81 (d, *J* = 11.4 Hz, 1H, CHH Bn), 4.77 (d, *J* = 1.9 Hz, 1H, H-1), 4.68 (d, *J* = 11.4 Hz, 1H, CH*H* Bn), 4.64 (d, *J* = 10.4 Hz, 1H, CH*H* Bn), 4.53 (d, *J* = 12.1 Hz, 1H CHH Bn), 4.44 (d, J = 12.1 Hz, 1H, CHH Bn), 4.29 (dd, J = 9.5, 3.3 Hz, 1H, H-3), 4.23 (dd, J = 10.1, 4.9 Hz, 1H, H-6'), 4.10 – 4.01 (m, 2H, H-3', H-5'), 3.82 (dq, *J* = 9.4, 6.2 Hz, 1H, H-5), 3.71 – 3.67 (m, 1H, H-4), 3.67 – 3.63 (m, 1H, H-6'), 3.60 (t, J = 9.5 Hz, 1H, H-4'), 3.54 (dd, J = 9.3, 3.6 Hz, 1H, H-2'), 3.37 (s, 3H, CH₃ OMe), 1.40 (d, J = 6.2 Hz, 3H, H-6); ¹³C NMR (126 MHz, CDCl₃) δ 166.2 (C=O), 138.7, 138.1, 137.8, 137.7 (Cq), 133.4, 130.1 (CH_{arom}), 129.9 (Cq), 129.9, 128.9, 128.8, 128.6, 128.5, 128.5, 128.4, 128.3, 128.3, 128.2, 128.2, 128.1, 128.1, 128.0, 127.9, 127.8, 127.8, 127.6, 127.5, 126.4, 126.1 (CHarom), 101.3 (CHPh), 98.6 (C-1), 93.6 (C-1'), 82.3 (C-4'), 79.7 (C-4), 78.4, 78.3 (C-2', C-3'), 76.3, 75.1 (CH₂ Bn), 72.8 (C-3), 72.7 (CH₂ Bn), 69.1 (C-6'), 68.4 (C-2), 67.9 (C-5), 62.9 (C-5'), 55.1 (CH₃ OMe), 18.2 (C-6); diagnostic peaks for the β -anomer: ¹H NMR (500 MHz, CDCl₃) δ 5.47 (s, 1H, CHPh), 5.41 (dd, *J* = 3.5, 1.8 Hz, 1H, H-2), 4.36 (dd, *J* = 9.4, 3.5 Hz, 1H, H-3), 1.37 (d, J = 6.2 Hz, 3H, H-6); ¹³C NMR (126 MHz, CDCl₃) δ 165.9 (C=O), 103.7 (C-1'), 101.1 (CHPh), 98.5 (C-1), 81.6, 81.3, 80.8, 76.0, 74.9, 72.9, 68.8, 67.2, 66.0, 18.1 (C-6); HRMS: [M+NH₄]⁺ calcd for C₄₈H₅₀O₁₁NH₄ 820.36914, found 820.36629.

Disaccharide 39B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor **39**. Yield: 41 mg, 55 µmol, 55%, a: β = 1:1. Data reported for a 1:1 mixture of anomers: ¹H NMR (500 MHz, CDCl₃) δ 8.15 – 8.12 (m, 2H), 8.09 – 8.05 (m, 2H), 7.51 – 7.26 (m, 36H), 5.61 (dd, *J* = 3.3, 1.9 Hz, 1H, H-2a/ β), 5.57 (s, 1H, CHPh a/ β), 5.50 (s, 1H, CHPh a/ β), 5.34 (dd, *J* = 3.5, 1.8 Hz, 1H, H-2a/ β), 5.23 (d, *J* = 3.7 Hz, 1H, H-1'a), 5.04 (d, *J* = 10.5 Hz, 1H), 4.90 (d, *J* = 11.3 Hz, 1H), 4.87 – 4.83 (m, 2H), 4.77 – 4.70 (m, 5H), 4.69 (d, *J* = 11.1 Hz, 1H), 4.65 (d, *J* = 8.1 Hz, 1H, H-1' β), 4.59 (d, *J* = 10.4 Hz, 1H), 4.35 – 4.25 (m, 4H), 4.09 (td, *J* = 9.9, 4.8 Hz, 1H), 4.01 (dd, *J* = 10.0, 9.1 Hz, 1H), 3.86 – 3.75 (m, 3H), 3.74 – 3.59 (m, 6H), 3.54 (t, *J* = 9.3 Hz, 1H), 3.42 – 3.36 (m, 7H), 3.34 – 3.30 (m, 1H), 3.27 (dd, *J* = 10.0, 3.7 Hz, 1H), 1.42 – 1.37 (m, 6H); ¹³C NMR (126 MHz, CDCl₃) δ 166.0, 149.8, 137.2, 135.4, 134.5, 133.5, 133.3, 131.9, 131.7, 131.2, 130.4, 130.3, 130.0, 130.0, 129.1, 129.0, 128.7, 128.6, 128.6, 128.5, 128.4, 128.4, 128.4, 128.2, 128.2, 128.1, 128.0, 127.9, 126.3, 126.1, 125.1, 119.3, 102.4 (C-1' β), 101.4, 101.3 (CHPha β), 98.7, 98.3 (C-1a β), 93.9 (C-1'a), 82.8, 81.5, 80.7, 79.9, 79.2, 76.4, 75.3, 75.2, 74.9, 74.8, 72.9, 72.7, 68.8, 68.5, 67.7, 67.5, 67.3, 66.5, 66.1, 62.9, 62.5, 55.0, 55.0, 18.2, 18.1; HRMS: [M+NH₄]⁺ calcd for C₄₁H₄₃N₃O₁₀NH₄ 755.32667, found 755.32641

Disaccharide 40A



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **A** and acceptor **40**. Yield: 55 mg, 69 µmol, 69%, α :β >20:1. ¹H NMR (500 MHz, CDCl₃) δ 8.05 – 7.98 (m, 2H, CH_{arom}), 7.50 – 7.45 (m, 1H, CH_{arom}), 7.40 – 7.35 (m, 2H, CH_{arom}), 7.34 (d, *J* = 0.9 Hz, 4H, CH_{arom}), 7.31 – 7.25 (m, 10H, CH_{arom}), 7.25 – 7.19 (m, 5H, CH_{arom}), 5.50 (t, *J* = 9.6 Hz, 1H, H-4), 5.36 (s, 1H, CHPh), 4.87 – 4.84 (m, 2H, H-1', CHH Bn), 4.83 – 4.78 (m, 2H, 2x CHH Bn), 4.69 (d, *J* = 11.4 Hz, 1H, CHH Bn), 4.66 – 4.62 (m, 2H, 2x CHH Bn), 4.61 (d, *J* = 2.0 Hz, 1H, H-1), 4.09 (dd, *J* = 9.6, 3.0 Hz, 1H, H-3), 3.96 – 3.90 (m, 2H, H-2, H-3'), 3.87 – 3.76 (m, 3H, H-5, H-5', H-6'), 3.48 (dd, *J* = 9.4, 3.7 Hz, 1H, H-2'), 3.43 (t, *J* = 9.3 Hz, 1H, H-4'), 3.36 (s, 3H, CH₃ OMe), 3.30 – 3.21 (m, 1H, H-6'), 1.25 (d, *J* = 6.3 Hz, 3H, H-6); ¹³C NMR (126 MHz, CDCl₃) δ 165.7 (C=O), 138.7, 138.7, 138.3, 137.6 (C_q), 133.1 (CH_{arom}), 101.2 (CHPh), 100.3 (C-1), 100.2 (C-1'), 82.3 (C-4'), 79.7 (C-3), 79.5 (C-2'), 78.3 (C-3'), 76.2 (C-2), 75.1, 74.0, 73.8 (CH₂ Bn), 73.8 (C-4), 68.7 (C-6'), 66.9 (C-5), 63.4 (C-5'), 55.0 (CH₃ OMe), 17.8 (C-6); HRMS: [M+NH₄]⁺ calcd for C₄₈H₅₀O₁₁NH₄ 820.36914, found 820.36724.





Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor 40. Yield: 37 mg, 50 μ mol, 50%, α : β = 12:1. Data for the α -anomer: ¹H NMR (500 MHz, CDCl₃) δ 8.07 – 8.02 (m, 2H, CH_{arom}), 7.43 (dt, J = 7.4, 1.4 Hz, 3H, CHarom), 7.35 (qt, J = 5.2, 2.7 Hz, 8H, CHarom), 7.31 - 7.23 (m, 9H, CHarom), 5.51 (t, J = 9.7 Hz, 1H, H-4), 5.38 (s, 1H, CHPh), 4.91 (d, J = 3.6 Hz, 1H, H-1'), 4.83 (d, J = 12.2 Hz, 1H, CHH Bn), 4.78 (d, J = 11.0 Hz, 1H, CHH Bn), 4.73 (d, J = 12.2 Hz, 1H, CHH Bn), 4.71 (d, J = 1.9 Hz, 1H, H-1), 4.62 (d, J = 11.0 Hz, 1H, CHH Bn), 4.15 (dd, J = 9.7, 3.1 Hz, 1H, H-3), 4.00 (dd, J = 10.2, 4.9 Hz, 1H, H-6'), 3.92 (dd, J = 3.2, 2.0 Hz, 1H, H-2), 3.90 - 3.78 (m, 3H, H-3', H-5, H-5'), 3.50 (t, I = 9.4 Hz, 1H, H-4'), 3.40 (t, I = 10.3 Hz, 1H, H-6'), 3.37 (s, 3H, CH₃ OMe), 3.32 (dd, I = 10.3 Hz, 1H, H-6'), 3.37 (s, 3H, CH₃ O 10.0, 3.6 Hz, 1H, H-2'), 1.27 (d, J = 6.3 Hz, 3H, CH₃ OMe); ¹³C NMR (126 MHz, CDCl₃) δ 165.6 (C=O), 138.2, 137.8, 137.4 (C_q), 133.2 (CH_{arom}), 130.0 (C_q), 129.7, 129.7, 129.0, 128.6, 128.6, 128.5, 128.5, 128.5, 128.4, 128.2, 128.1, 128.1, 128.0, 127.9, 126.3 (CH_{arom}), 101.3 (CHPh), 99.3 (C-1), 97.8 (C-1'), 82.7 (C-4'), 77.0 (C-3), 75.9 (C-3'), 75.2 (C-2), 75.0, 73.4 (CH₂ Bn), 73.3 (C-4), 68.5 (C-6), 66.8 (C-5), 63.4, 63.3 (C-2', C-5'), 55.1 (CH₃ OMe), 17.7 (C-6); diagnostic peaks for the β anomer: ¹H NMR (500 MHz, CDCl₃) δ 4.95 (d, *J* = 11.0 Hz, 1H, CHH Bn), 4.39 (d, *J* = 7.9 Hz, 1H, H-1'), 4.30 (dd, J = 10.4, 5.0 Hz, 1H, H-6'), 3.73 (t, J = 8.9 Hz, 1H), 3.68 (t, J = 10.3 Hz, 1H), 3.62 $(t, J = 9.2 \text{ Hz}, 1\text{H}); {}^{13}\text{C} \text{ NMR}$ (126 MHz, CDCl₃) δ 104.0 (C-1'), 99.9 (C-1), 81.5, 81.1, 80.9, 79.6, 79.5, 75.2, 74.9, 73.6, 66.4, 66.1, 64.8, 55.0(CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₄₁H₄₃N₃O₁₀NH₄ 755.32867, found 755.32744.

Disaccharide 41A



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **A** and acceptor **42**. Yield: 68 mg, 83 µmol, 83%, $\alpha:\beta > 20:1.$ ¹H NMR (500 MHz, CDCl₃) δ 8.14 – 8.10 (m, 2H, CH_{arom}), 8.07 – 8.04 (m, 2H, CH_{arom}), 7.57 – 7.51 (m, 1H, CH_{arom}), 7.43 (t, *J* = 7.7 Hz, 2H, CH_{arom}), 7.40 – 7.36 (m, 1H, CH_{arom}), 7.34 – 7.28 (m, 5H, CH_{arom}), 7.21 – 7.09 (m, 13H, CH_{arom}), 5.59 (t, *J* = 9.8 Hz, 1H, H-4), 5.55 (dd, *J* = 3.5, 1.9 Hz, 1H, H-2), 5.29 (s, 1H, CHPh), 4.91 (d, *J* = 1.8 Hz, 1H, H-1), 4.88 (d, *J* = 3.6 Hz, 1H, H-1)', 4.55 (d, *J* = 11.3 Hz, 1H, CHH Bn), 4.49 – 4.40 (m, 3H, CHH Bn, CH₂ Bn), 4.33 (dd, *J* = 9.9, 3.4 Hz, 1H, H-3), 4.03 (dq, *J* = 9.7, 6.2 Hz, 1H, H-5), 3.82 (dd, *J* = 10.1, 4.8 Hz, 1H, H-6'), 3.72 (t, *J* = 9.4 Hz, 1H, H-3'), 3.67 (dt, *J* = 9.9, 5.0 Hz, 1H, H-5'), 3.46 (s, 3H, CH₃ OMe), 3.40 (t, *J* = 10.2 Hz, 1H, H-6'), 3.37 – 3.32 (m, 2H, H-2', H-4'), 1.33 (d, *J* = 6.2 Hz, 3H, H-6); ¹³C NMR (126 MHz, CDCl₃) δ 166.4, 165.8 (C=O), 138.7, 138.2, 137.6 (Cq), 133.4, 133.3, 130.2 (CH_{arom}), 129.8 (Cq), 129.8 (CH_{arom}), 129.6 (Cq), 128.8, 128.7, 128.6, 128.3, 128.2, 128.1, 128.0, 128.0, 128.0, 127.5, 127.5, 126.3

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(CH_{arom}), 101.1 (CHPh), 98.7 (C-1), 96.4 (C-1'), 81.9 (C-4'), 78.4 (C-3'), 78.0 (C-2'), 75.1 (CH₂ Bn), 73.0 (C-3), 72.9 (CH₂ Bn, 72.8 (C-4), 69.5 (C-2), 68.7 (C-6'), 66.7 (C-5), 63.2 (C-5'), 55.4 (CH₃ OMe), 17.8 (C-6); HRMS: $[M+NH_4]^+$ calcd for C₄₈H₄₈O₁₂NH₄ 834.34840, found 834.34724.





Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor **42**. Yield: 79 mg, 100 μ mol, 100%, α : β = 12:1. Data for the α-anomer: ¹H NMR (500 MHz, CDCl₃) δ 8.21 – 8.15 (m, 2H, CH_{arom}), 8.10 – 8.02 (m, 2H, CHarom), 7.74 - 7.63 (m, 3H, CHarom), 7.61 - 7.52 (m, 2H, CHarom), 7.52 - 7.44 (m, 3H, CHarom), 7.39 - 7.27 (m, 6H, CHarom), 7.21 (pd, J = 4.2, 2.0 Hz, 3H, CHarom), 7.18 - 7.15 (m, 1H, CH_{arom}), 7.14 – 7.08 (m, 2H, CH_{arom}), 5.62 (dd, J = 3.5, 1.9 Hz, 1H, H-2), 5.56 (t, J = 9.9 Hz, 1H, H-4), 5.32 (s, 1H, CHPh), 5.05 (d, J = 3.7 Hz, 1H, H-1'), 4.87 (d, J = 1.9 Hz, 1H, H-1), 4.64 (d, J = 10.9 Hz, 1H, CHH Bn), 4.46 (d, J = 10.9 Hz, 1H, CHH Bn), 4.38 (dd, J = 9.9, 3.4 Hz, 1H, H-3), 4.06 (dq, *J* = 9.7, 6.2 Hz, 1H, H-5), 3.98 (dd, *J* = 10.1, 4.8 Hz, 1H, H-6'), 3.71 (dd, *J* = 10.0, 9.1 Hz, 1H, H-3'), 3.66 (dt, J = 9.9, 5.0 Hz, 1H, H-5'), 3.51 (t, J = 10.2 Hz, 1H, H-6'), 3.48 - 3.43 (m, 4H, H-4', CH₃ OMe), 3.21 (dd, J = 10.0, 3.7 Hz, 1H, H-2'), 1.35 (d, J = 6.3 Hz, 3H, CH₃ OMe); ¹³C NMR (126 MHz, CDCl₃) δ 166.2, 165.6 (C=O), 137.8, 137.3 (C_q), 135.3, 134.5, 133.5, 133.4, 131.8, 131.6, 131.1, 130.3, 130.3, 130.1, 130.0, 129.7 (CHarom), 129.5, 129.4 (Cq), 128.9, 128.9, 128.7, 128.6, 128.6, 128.4, 128.3, 128.2, 128.0, 127.8, 126.2 (CH_{arom}), 101.2 (CHPh), 98.8 (C-1), 95.4 (C-1'), 82.3 (C-4'), 75.8 (C-3'), 74.9 (CH₂Bn), 72.5 (C-4), 72.2 (C-3), 68.5 (C-6'), 68.2 (C-2), 66.5 (C-5), 63.2 (C-5'), 62.7 (C-2'), 55.4 (CH₃ OMe), 17.8 (C-6); diagnostic peaks for the α-anomer: ¹H NMR (500 MHz, CDCl₃) & 5.70 (dd, *J* = 3.5, 1.8 Hz, 1H, H-2), 4.96 (dd, *J* = 9.8, 3.5 Hz, 1H, H-3), 4.33 - 4.27 (m, 1H); ¹³C NMR (126 MHz, CDCl₃) δ 165.7 (C=O), 103.1 (C-1'), 98.6 (CHPh), 98.3 (C-1), 81.2 (, 79.2, 71.8, 70.7, 66.8, 66.7, 17.8 (C-6); HRMS: [M+NH₄]⁺ calcd for C₄₁H₄₁N₃O₁₁NH₄ 769.30793, found 769.30679.

Disaccharide 42A



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **A** and acceptor **42**. Yield: 47 mg, 59 µmol, 59%, α : β >20:1. ¹H NMR (400 MHz, CDCl₃) δ 7.52 – 7.21 (m, 25H, CH_{arom}), 5.54 (s, 1H C*H*Ph), 4.97 – 4.88 (m, 3H, H-1', 2x C*H*H Bn), 4.86 – 4.80 (m, 2H, C*H*H Bn, C*H*H Bn), 4.74 (d, *J* = 11.9 Hz, 1H, C*H*H Bn), 4.70 – 4.66 (m, 2H, 2x CH*H* Bn), 4.65 – 4.60 (m, 2H, H-1, CH*H* Bn), 4.21 (td, *J* = 10.0, 4.9 Hz, 1H, H-5'), 4.12 (t, *J* = 9.3 Hz, 1H, H-3'), 4.02 – 3.95 (m, 2H, H-2, H-6'), 3.85 (dd, *J* = 9.2, 3.2 Hz, 1H, H-3), 3.70 – 3.57 (m, 4H, H-2', H-4', H-5, H-6'), 3.55 (t, *J* = 8.4 Hz, 1H, H-4), 3.31 (s, 3H,

CH₃ OMe), 1.33 (d, J = 6.2 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 139.0, 138.6, 138.6, 138.5, 137.7 (C_q), 135.4, 134.3, 131.9, 131.5, 131.2, 130.4, 129.0, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.3, 128.2, 128.0, 127.8, 127.7, 127.7, 127.6, 127.6, 126.2, 126.1 (CH_{arom}), 101.3 (CHPh), 98.5 (C-1), 97.9 (C-1'), 82.5 (C-4'), 80.1 (C-4), 79.5 (C-2'), 79.0 (C-3), 78.4 (C-3'), 75.3, 75.2 (CH₂ Bn), 75.0 (C-2), 73.0, 72.2 (CH₂ Bn), 69.1 (C-6'), 68.2 (C-5), 62.8 (C-5'), 54.8 (CH₃ OMe), 18.2 (C-6); HRMS: [M+NH₄]⁺ calcd for C₄₈H₅₂O₁₀NH₄ 806.38987, found 806.38837.

Disaccharide 42B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor 42. Yield: 56 mg, 77 μ mol, 77%, α : β = 3:1. Data for the α-anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.52 – 7.23 (m, 20H, CH_{arom}), 5.56 (s, 1H, CHPh), 5.02 (d, J = 10.9 Hz, 1H, CHH Bn), 4.97 – 4.89 (m, 2H, H-1', CHH Bn), 4.83 (d, J = 10.9 Hz, 1H, CHH Bn), 4.76 (d, J = 11.9 Hz, 1H, CHH Bn), 4.73 (d, J = 1.8 Hz, 1H, H-1), 4.68 - 4.62 (m, 2H, 2x CHH Bn), 4.31 (tt, J = 10.5, 5.1 Hz, 1H, H-5'), 4.19 (dd, J = 10.2, 9.0 Hz, 1H, H-3'), 4.07 (dd, *J* = 3.3, 1.8 Hz, 1H, H-2'), 3.97 (dd, *J* = 10.3, 4.9 Hz, 1H, H-6'), 3.87 (dd, *J* = 9.4, 3.1 Hz, 1H, H-3), 3.75 - 3.70 (m, 1H, H-4'), 3.68 - 3.60 (m, 2H, H-5, H-6'), 3.54 (t, J = 9.5 Hz, 1H, H-4), 3.35 (s, 3H, CH₃ OMe), 3.25 (dd, J = 10.1, 3.7 Hz, 1H, H-2'), 1.34 (d, J = 6.2 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 138.4, 138.2, 138.0, 137.4 (C_q), 135.3, 134.4, 131.7, 131.5, 131.1, 130.3, 130.2, 129.0, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.3, 128.2, 128.1, 128.1, 127.9, 127.7, 127.6, 127.5, 127.4, 126.1, 126.0 (CH_{arom}), 101.3 (CHPh), 98.1, 98.0 (C-1, C-1'), 83.0 (C-4'), 80.0(C-4), 78.5 (C-3), 75.3 (CH₂ Bn), 75.2 (C-3'), 75.0 (CH₂ Bn), 74.6 (C-2), 72.3 (CH₂ Bn), 68.8 (C-6'), 68.1 (C-5), 62.9, 62.7 (C-2', C-5'), 54.8 (CH₃ OMe), 17.8 (C-6); diagnostic peaks for the β-anomer: ¹H NMR (400 MHz, CDCl₃) δ 5.55 (s, 1H, CHPh), 4.59 (d, *J* = 7.8 Hz, 1H, H-1'), 3.32 (s, 3H, CH₃ OMe), 3.10 (qd, J = 7.4, 4.8 Hz, 1H), 1.31 (d, J = 5.8 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 81.4, 80.2, 74.9, 66.2; HRMS: [M+NH₄]⁺ calcd for C₄₁H₄₅N₃O₉NH₄ 741.34941, found 741.34786.

Disaccharide 43A



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **A** and acceptor **43**. Yield: 76 mg, 98 µmol, 98%, α : β > 20:1. ¹H NMR (400 MHz, CDCl₃) δ 7.55 – 7.10 (m, 25H, CH_{arom}), 5.52 (s, 1H, CHPh), 4.94 (d, *J* = 11.1 Hz, 1H, CHH Bn), 4.89 – 4.75 (m, 7H, H-1', 3x CHH Bn, 3x CHH Bn), 4.72 (d, *J* = 11.9 Hz, 1H, CHH Bn), 4.61 (d, *J* = 3.4 Hz, 1H, H-1), 4.30 (td, *J* = 10.0, 4.8 Hz, 1H, H-5'), 4.03 (t, *J* = 9.3 Hz, 1H, H-3'), 3.95 – 3.77 (m, 4H, H-2, H-3, H-5, H-6'), 3.74 (d, *J* = 2.4 Hz, 1H, H-4), 3.63 – 3.54 (m, 2H, H-2', H-4'), 3.50 (t, *J* = 10.2 Hz, 1H, H-6'), 3.36 (s, 3H, CH₃ OMe), 1.28 (d, *J* = 6.6 Hz, 3H, H-

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6); ¹³C NMR (101 MHz, CDCl₃) δ 139.1, 138.8, 138.4, 138.3, 137.9 (C_q), 128.9, 128.7, 128.6, 128.6, 128.5, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.9, 127.7, 127.7, 126.2 (CH_{arom}), 101.2 (CHPh), 101.0 (C-1'), 99.1 (C-1), 82.9 C-4'), 80.7 (C-4), 79.6 (C-2'), 79.1 (C-3'), 78.0 (C-2), 75.3 (CH₂ Bn), 74.4 (CH₂ Bn), 74.3 (C-3), 73.5 (CH₂ Bn), 73.1 (CH₂ Bn), 69.1 (C-6'), 66.6 (C-5), 63.2 (C-5'), 55.4 (CH₃ OMe), 16.4 (C-6); HRMS: [M+NH₄]⁺ calcd for C₄₈H₅₂O₁₀NH₄ 806.38987, found 806.38813.

Disaccharide 43B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor **43**. Yield: 73 mg, 100 μmol, 100%, α :β = 1.3:1. Data reported for a 1:1 mixture of anomers: ¹H NMR (400 MHz, CDCl₃) δ 7.57 – 7.19 (m, 40H), 5.60 – 5.48 (m, 2H, CHPhaβ), 5.01 – 4.88 (m, 4H), 4.88 – 4.74 (m, 8H), 4.72 – 4.62 (m, 3H), 4.57 (d, *J* = 3.7 Hz, 1H, H-1β), 4.38 (td, *J* = 10.0, 4.9 Hz, 1H, H-5'α), 4.25 (dd, *J* = 10.5, 4.9 Hz, 1H, H-6'β), 4.09 (dd, *J* = 9.3, 3.6 Hz, 1H, H-2β), 3.99 (t, *J* = 9.5 Hz, 1H), 3.94 – 3.80 (m, 8H), 3.76 – 3.62 (m, 3H), 3.54 (t, *J* = 10.3 Hz, 1H), 3.50 – 3.42 (m, 3H, CH₃ OMeα), 3.36 (s, 3H, CH₃ OMeβ), 3.35 (s, 3H), 3.23 (td, *J* = 9.7, 5.0 Hz, 1H,), 3.09 (t, *J* = 6.3 Hz, 1H), 1.33 (d, *J* = 6.6 Hz, 3H, H-6α), 1.16 (d, *J* = 6.4 Hz, 3H, H-6β); ¹³C NMR (101 MHz, CDCl₃) δ 139.0, 138.6, 138.6, 138.2, 138.0, 137.6, 137.2, 135.3, 134.4, 132.0, 131.5, 131.3, 130.3, 130.2, 129.1, 128.9, 128.5, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.2, 128.1, 127.9, 127.8, 127.7, 127.6, 127.5, 127.2, 126.1, 126.0, 125.3, 102.0 (C-1'β), 101.3 (CHPhβ), 101.2 (CHPha), 99.7 (C-1'α), 99.0 (C-1β), 98.7 (C-1a), 82.9, 81.6, 79.4, 79.0, 78.5, 77.3, 76.9, 76.7, 76.3, 75.2, 74.9, 74.6, 73.7, 73.6, 73.3, 73.2, 68.8, 68.6, 66.4, 66.3, 65.9, 65.4, 63.8, 62.9, 55.4, 55.3, 16.6; HRMS: [M+NH₄]⁺ calcd for C₄₁H₄₅N₃O₉NH₄ 741.34941, found 741.34811.

Disaccharide 44A



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **A** and acceptor **44**. Yield: 67 mg, 85 µmol, 85%, $\alpha:\beta = 14:1$. Data for α -anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.63 – 7.14 (m, 25H, CH_{arom}), 5.82 (d, *J* = 4.1 Hz, 1H, H-1'), 5.54 (s, 1H, CHPh), 4.96 – 4.64 (m, 8H, H-1, 3x CHH Bn, 2x CHH Bn), 4.56 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.48 (d, *J* = 12.3 Hz, 1H, CHH Bn), 4.36 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.24 (dd, *J* = 10.3, 5.0 Hz, 1H, H-6'), 4.14 – 3.93 (m, 6H, H-2, H-3, H-4, H-5, H-3', H-5'), 3.72 (t, *J* = 10.3 Hz, 1H, H-6'), 3.64 – 3.56 (t, *J* = 9.8 Hz, 1H, H-4'), 3.51 (dd, *J* = 9.5, 4.1 Hz, 1H, H-2'), 3.36 (s, 3H, CH₃ OMe), 1.31 (d, *J* = 6.6 Hz, 3H, H-6). ¹³C NMR (101 MHz, CDCl₃) δ 139.1, 138.8, 138.6, 138.5, 137.6 (C_q), 129.0, 128.6, 128.4, 128.4, 128.4, 128.3, 128.2, 128.2, 128.2, 128.1,

128.0, 128.0, 128.0, 127.9, 127.9, 127.7, 127.5, 127.4, 127.4, 126.1 (CH_{arom}), 101.2 (CHPh), 98.8 (C-1), 97.3 (C-1'), 82.1 (C-4'), 79.8 (C-2), 79.2 (C-2'), 78.2 (C-3'), 76.8 (C-3), 75.4 (CH₂ Bn), 74.7 (C-4), 74.2 (CH₂ Bn), 73.4 (CH₂ Bn), 72.2 (CH₂ Bn), 69.0 (C-6'), 66.2 (C-5), 63.0 (C-5'), 55.4 (CH₃ OMe), 17.8 (C-6). Diagnostic peaks for β-anomer: ¹H NMR (400 MHz, CDCl₃) δ 5.76 (s, 1H, CHPh), 3.40 (s, 1H, CH₃ OMe), 1.40 (d, *J* = 6.4 Hz, 3H, H-6). ¹³C NMR (101 MHz, CDCl₃) δ 105.38 (C-1'), 101.29 (CHPh), 97.54 (C-1), 82.94, 81.98, 81.38, 79.41, 79.06, 78.10, 75.43 (CH₂ Bn), 74.85 (CH₂ Bn), 74.09, 73.95 (CH₂ Bn), 72.09 (CH₂ Bn), 70.38, 68.94 (C-6'), 66.42, 55.37 (CH₃ OMe), 17.86 (C-6); HRMS: [M+NH₄]⁺ calcd for C₄₈H₅₂O₁₀NH₄ 806.38987, found 806.38843.

Disaccharide 44B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor **44**. Yield: 73 mg, 100 μ mol, 100%, α : β = 3:1. Data for the α -anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.50 – 7.26 (m, 20H, CH_{arom}), 5.70 (d, J = 4.0 Hz, 1H, H-1'), 5.57 (s, 1H, CHPh), 4.96 (d, J = 10.9 Hz, 1H, CHH Bn), 4.90 - 4.84 (m, 2H, CHH Bn, CHH Bn), 4.80 (d, J = 10.9 Hz, 1H, CHH Bn), 4.74 (d, J = 9.8 Hz, 1H, CHH Bn), 4.68 (d, J = 11.3 Hz, 1H, CHH Bn), 4.64 (d, J = 3.7 Hz, 1H, H-1), 4.27 – 4.14 (m, 2H, H-3, H-6'), 4.07 (t, J = 9.6 Hz, 1H, H-3'), 4.04 – 3.98 (m, 1H, H-5'), 3.97 – 3.91 (m, 3H, H-2, H-4, H-5), 3.77 – 3.65 (m, 2H, H-4', H-6'), 3.44 (dd, J = 10.1, 4.1 Hz, 1H, H-2'), 3.38 (s, 3H, CH₃ OMe), 1.26 (d, J = 6.3)Hz, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 138.7, 138.6, 138.1, 137.3 (C_a), 129.1, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.2, 128.2, 128.2, 128.1, 127.9, 127.9, 127.6, 127.4, 126.1, 126.1 (CH_{arom}), 101.4 (CHPh), 99.1 (C-1), 98.0 (C-1'), 82.7 (C-4'), 79.3 (C-2), 76.4 (C-3'), 75.8, 75.7 (C-3, C-4), 75.2, 73.8, 73.6 (CH₂ Bn), 68.8 (C-6'), 65.9 (C-5), 63.7 (C-2'), 63.1 (C-5'), 55.5 (CH₃ OMe), 17.5 (C-6); diagnostic peaks for the β-anomer: ¹H NMR (400 MHz, CDCl₃) δ 5.52 (s, 1H,CHPh), 4.49 (d, J = 7.5 Hz, 1H, H-1'), 1.35 (d, J = 6.7 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) & 102.8 (C-1'), 101.4 (CHPh), 98.8 (C-1), 81.4, 79.5, 78.0, 75.9, 74.9, 72.7, 68.6, 67.0, 66.5, 65.7, 16.8 (C-6); HRMS: [M+NH₄]⁺ calcd for C₄₁H₄₅N₃O₉NH₄ 741.34941, found 741.34831.

Disaccharide 45A



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **A** and acceptor **45**. Yield: 79 mg, 100 µmol, 100%, α : β = 3.2:1. Data for the α-anomer: ¹H NMR (500 MHz, CDCl₃) δ 7.51 – 7.14 (m, 25H, CH_{arom}), 5.61 (d, *J* = 3.7 Hz, 1H, H-1'), 5.56 (s, 1H, CHPh), 5.02 (d, *J* = 11.2 Hz, 1H, CHH Bn), 4.85 (d, *J* = 11.4 Hz, 1H, CHH Bn), 4.80 – 4.73 (m, 2H, CHH Bn, CHH Bn), 4.70 (dd, *J* = 11.6, 4.4 Hz, 2H, 2x CHH Bn), 4.61 (d, *J* = 12.2 Hz, 1H, CHH Bn), 4.57 – 4.52 (m, 2H, H-1, CHH Bn), 4.31 – 4.23 (m, 2H, H-3, H-6'), 4.11 (dd, *J* = 10.1, 3.6 Hz, 1H, H-2), 4.07 (t, *J* = 9.3 Hz, 1H, H-3'), 3.96 (td, *J* = 10.1)

10.4, 5.2 Hz, 1H, H-5'), 3.90 (qd, J = 6.3, 1.2 Hz, 1H, H-5), 3.75 (t, J = 10.4 Hz, 1H, H-6'), 3.65 (t, J = 9.4 Hz, 1H, H-4'), 3.63 – 3.60 (m, 2H, H-2', H-4), 3.30 (s, 3H, CH₃ OMe), 1.17 (d, J = 6.5 Hz, 3H, H-6); ¹³C NMR (126 MHz, CDCl₃) δ 138.6, 138.5, 138.5, 138.4, 137.5 (C_q), 128.7, 128.4, 128.4, 128.4, 128.3, 128.2, 128.2, 127.8, 127.8, 127.8, 127.6, 127.5, 127.5, 126.1 (CH_{arom}), 101.3 (CHPh), 98.4, 98.3 (C-1, C-1'), 82.2 (C-4'), 80.0 (C-4), 79.1 (C-2'), 77.9 (C-3'), 77.4 (C-2), 75.5, 75.1 (CH₂ Bn), 74.3 (C-3), 72.7, 72.5 (CH₂ Bn), 69.2 (C-6'), 66.3 (C-5), 63.6 (C-5'), 55.4 (CH₃ OMe), 16.7 (C-6); diagnostic peaks for the β -anomer: ¹H NMR (500 MHz, CDCl₃) δ 4.98 – 4.94 (m, 2H, 2x CHH Bn), 4.90 (d, J = 11.9 Hz, 1H, CH Bn), 3.56 – 3.51 (m, 2H), 3.47 – 3.40 (m, 1H, H-5'), 1.02 (d, J = 6.5 Hz, 3H, H-6); ¹³C NMR (126 MHz, CDCl₃) δ 101.8 (C-1'), 101.2 (CHPh), 98.8 (C-1), 83.0, 81.6, 78.0, 77.1, 75.0, 74.7, 73.7, 69.1, 66.0, 16.6 (C-6); HRMS: [M+NH₄]⁺ calcd for C₄₈H₅₂O₁₀NH₄ 806.38987, found 806.38824.

Disaccharide 45B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor 45. Yield: 64 mg, 88 μ mol, 88%, α : β = 1:2. Data reported for a 1:2 mixture of anomers: ¹H NMR (500 MHz, CDCl₃) δ 7.52 – 7.23 (m, 60H, CH_{arom}), 5.60 (s, 1H, CHPhα), 5.58 (s, 2H, CHPhβ), 5.51 (d, J = 3.7 Hz, 1H, H-1'a), 5.04 (d, J = 11.5 Hz, 2H), 4.97 (d, J = 11.1 Hz, 2H), 4.95 - 4.90 (m, 2H), 4.86 - 4.77 (m, 6H), 4.68 - 4.61 (m, 6H), 4.58 - 4.53 (m, 5H, H-1a, H-1 β , H-1 β), 4.30 - 4.20 (m, 3H), 4.18 (dd, J = 10.8, 2.8 Hz, 2H), 4.13 (dd, J = 10.2, 3.5 Hz, 1H), 4.05 (dd, J = 10.1, 9.0 Hz, 1H), 3.97 (dd, J = 10.1, 3.9 Hz, 3H), 3.90 - 3.83 (m, 3H), 3.80 - 3.72 (m, 8H), 3.68 (t, J = 9.2 Hz, 2H), 3.58 (dd, J = 2.8, 1.2 Hz, 1H), 3.50 $(dd, J = 9.3, 8.1 Hz, 2H, H-2'\beta), 3.39 - 3.33 (m, 2H), 3.31 (d, J = 10.4 Hz, 10H, H-2'a, CH₃)$ OMeaβ), 1.14 – 1.10 (m, 9H, H-6αβ); ¹³C NMR (126 MHz, CDCl₃) δ 138.8, 138.6, 138.3, 138.2, 137.8, 137.7, 137.3, 137.2, 135.3, 134.2, 132.0, 131.4, 131.3, 130.3, 129.2, 128.7, 128.5, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.0, 128.0, 128.0, 128.0, 127.9, 127.8, 127.7, 126.1, 126.0, 101.8 (C-1'β), 101.5 (CHPha), 101.3 (CHPhβ), 99.5 (C-1'a), 98.8 (C-1β), 98.2 (C-1a), 83.0, 81.8, 79.8, 79.8, 79.8, 78.2, 77.6, 75.5, 75.4, 75.2, 75.1, 75.0, 74.9, 73.7, 73.3, 69.0, 68.8, 67.1, 66.4, 66.2, 66.0, 63.6, 62.8, 55.4 (CH₃ OMeα), 55.4 (CH₃ OMeβ), 16.7 (C-6α), 16.6 (C-6β); HRMS: [M+NH₄]⁺ calcd for 741.34941, found 741.34841.

Disaccharide 46A



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **A** and acceptor **46**. Yield: 80 mg, 100 μ mol, 100%, α : β >20:1. ¹H NMR (500 MHz, CDCl₃) δ 8.11 – 8.03 (m, 2H, CH_{arom}), 7.61 – 7.56 (m, 1H, CH_{arom}), 7.46 – 7.40 (m, 4H, CH_{arom}), 7.38 – 7.33 (m, 3H, CH_{arom}), 7.32 – 7.28 (m, 5H, CH_{arom}), 7.25 – 7.16 (m,

13H, CH_{arom}), 5.50 (dd, J = 3.4, 1.2 Hz, 1H, H-4), 5.46 (s, 1H, CHPh), 5.28 (d, J = 3.8 Hz, 1H, H-1'), 4.74 – 4.70 (m, 2H, 2x CHH Bn), 4.69 – 4.63 (m, 3H, CHH Bn, 2x CHH Bn), 4.62 – 4.59 (m, 2H, H-1, CHH Bn), 4.33 – 4.26 (m, 2H, H-3, H-6'), 4.17 – 4.09 (m, 1H, H-5), 3.99 (dd, J = 10.1, 3.6 Hz, 1H, H-2), 3.91 (td, J = 9.9, 4.8 Hz, 1H, H-5'), 3.85 (t, J = 9.4 Hz, 1H, H-3'), 3.62 (t, J = 10.2 Hz, 1H, H-6'), 3.56 – 3.46 (m, 2H, H-2', H-4'), 3.40 (s, 3H, CH₃ OMe), 1.16 (d, J = 6.6 Hz, 3H, H-6); ¹³C NMR (126 MHz, CDCl₃) δ 166.4 (C=O), 138.8, 138.5, 138.4, 137.9 (C_q), 133.2 (CH_{arom}), 130.2 (C_q), 130.1, 128.9, 128.5, 128.5, 128.5, 128.3, 128.3, 128.2, 128.0, 127.9, 127.6, 127.5, 126.5 (CH_{arom}), 101.4 (CHPh), 99.9 (C-1'), 98.9 (C-1), 82.1 (C-4'), 78.9 (C-2'), 78.1 (C-3'), 75.4 (C-3), 75.2 (C-2), 75.1 (CH₂ Bn), 74.4 (C-4), 73.3, 72.6 (CH₂ Bn), 69.1 (C-6'), 65.1 (C-5), 63.4 (C-5'), 55.6 (CH₃ OMe), 16.4 (C-6); HRMS: [M+NH₄]⁺ calcd for C₄₈H₅₀O₁₁NH₄ 820.36914, found 820.36771.

Disaccharide 46B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **A** and acceptor **46**. Yield: 74 mg, 100 μ mol, 100%, α : β = 2:1. Data reported for a 2:1 mixture of anomers: ¹H NMR (400 MHz, CDCl₃) δ 8.13 – 8.09 (m, 4H), 8.08 - 8.04 (m, 2H), 7.65 - 7.19 (m, 54H), 5.62 (dd, J = 3.4, 1.3 Hz, 1H, H-4β), 5.55 (s, 1H, CHPh β), 5.53 (s, 2H, CHPh α), 5.51 (dd, J = 3.6, 1.3 Hz, 2H, H-4 α), 5.36 (d, J = 3.6 Hz, 2H, H-1'α), 4.90 – 4.82 (m, 4H), 4.78 (d, J = 11.2 Hz, 2H), 4.75 – 4.67 (m, 6H), 4.63 (d, J = 11.8 Hz, 2H), $4.57 (d, J = 7.9 Hz, 1H, H-1'\beta), 4.50 (d, J = 11.0 Hz, 2H), 4.38 - 4.26 (m, 5H), 4.18 - 4.07 (m, 5H), 4.18 - 4.0$ 4.05 (dd, J = 10.1, 3.5 Hz, 2H), 3.96 (dd, J = 10.2, 3.6 Hz, 1H), 3.84 (dd, J = 10.2, 9.0 Hz, 2H), 3.76 (t, J = 10.3 Hz, 1H), 3.69 (td, J = 9.8, 4.2 Hz, 3H), 3.61 (td, J = 9.2, 3.6 Hz, 3H), 3.44 - 3.35 (m, 10.13 Hz), 3.41 + 3.35 (m,10H), 3.32 (dd, J = 9.3, 8.0 Hz, 1H, H-2' β), 3.19 (dd, J = 10.2, 3.6 Hz, 2H, H-2' α), 1.21 – 1.16 (m, 9H, H-6αβ); ¹³C NMR (101 MHz, CDCl₃) δ 166.4, 166.3 (C=O), 138.4, 138.1, 138.0, 137.9, 137.7, 137.2, 135.4, 134.4, 133.3, 131.8, 131.7, 131.5, 131.3, 131.1, 130.3, 130.3, 130.1, 130.0, 129.9, 129.7, 129.1, 129.0, 128.6, 128.6, 128.5, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.2, 128.1, 128.1, 127.9, 127.8, 126.4, 126.1, 126.1, 101.6 (CHPha), 101.3 (CHPhb), 99.9 (C-1'a), 99.2 (C-1b), 98.5 (C-1'β), 98.4 (C-1α), 82.9, 76.9, 75.5, 75.0, 73.7, 73.3, 73.3, 68.9, 64.9, 64.8, 63.4, 62.9, 55.6, 16.3, 16.2; HRMS: [M+NH₄]⁺ calcd for C₄₁H₄₃N₃O₁₀ 755.32867, found 755.32722.

Disaccharide 47A



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **A** and acceptor **47**. Yield: 80 mg, 100 μ mol, 100%, α : β >20:1. ¹H NMR (500 MHz, CDCl₃) δ 8.00 – 7.96 (m, 2H, CH_{arom}), 7.73 – 7.63 (m, 3H, CH_{arom}), 7.59 – 7.51 (m, 2H, CH_{arom}), 7.46 (ddt, *J* = 7.0, 4.8, 2.2 Hz, 5H, CH_{arom}), 7.41 – 7.34 (m, 5H, CH_{arom}), 7.29

- 7.19 (m, 9H, CH_{arom}), 7.18 - 7.13 (m, 6H, CH_{arom}), 7.02 - 6.95 (m, 2H, CH_{arom}), 5.65 (dd, J = 10.4, 3.7 Hz, 1H, H-2), 5.55 (s, 1H, CHPh), 5.46 (d, J = 3.7 Hz, 1H, H-1'), 5.08 (d, J = 3.7 Hz, 1H, H-1), 5.03 (d, J = 11.3 Hz, 1H, CHH Bn 4.74 - 4.69 (m, 2H, CHH Bn, CHH Bn), 4.64 (d, J = 11.4 Hz, 1H, CHH Bn), 4.53 (dd, J = 10.4, 2.9 Hz, 1H, H-3), 4.35 - 4.26 (m, 3H, H-6', CH₂ Bn), 4.05 - 3.91 (m, 3H, H-3', H-5, H-5'), 3.76 (t, J = 10.4 Hz, 1H, H-6'), 3.72 (dd, J = 3.0, 1.2 Hz, 1H, H-4), 3.62 (t, J = 9.5 Hz, 1H, H-4'), 3.53 (dd, J = 9.3, 3.7 Hz, 1H, H-2'), 3.33 (s, 3H, CH₃ OMe), 1.25 (d, J = 6.5 Hz, 3H, H-6); ¹³C NMR (126 MHz, CDCl₃) δ 165.7 (C=O), 138.5, 138.3, 137.9, 137.4 (Cq), 135.3, 134.6, 133.2, 131.7, 131.6, 131.0, 130.4, 130.3 (CH_{arom}), 130.0 (Cq), 129.8, 129.0, 128.6, 128.6, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.2, 127.8, 127.6, 127.4, 127.3, 126.1, 124.9 (CH_{arom}), 101.4 (CHPh), 98.0 (C-1'), 97.4 (C-1), 81.9 (C-4'), 79.5 (C-4), 79.1 (C-2'), 77.6 (C-3'), 75.5 (CH₃ OMe), 16.7 (C-6); HRMS: [M+NH₄]⁺ calcd for C₄₈H₅₀O₁₁NH₄ 820.36914, found 820.36792.

Disaccharide 47B



Title compound was obtained as white foam via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor A and acceptor 47. Yield: 68 mg, 92 μ mol, 92%, α : β = 9:1. Data for the a-anomer: ¹H NMR (500 MHz, CDCl₃) δ 8.09 (dt, J = 8.4, 1.8 Hz, 2H, CH_{arom}), 7.73 – 7.69 (m, 2H, CH_{arom}), 7.68 - 7.63 (m, 1H, CH_{arom}), 7.61 - 7.52 (m, 2H, CH_{arom}), 7.48 - 7.41 (m, 7H, CHarom), 7.41 – 7.35 (m, 3H, CHarom), 7.33 – 7.19 (m, 9H, CHarom), 5.70 (dd, J = 10.5, 3.7 Hz, 1H, H-2), 5.57 (s, 1H, CHPh), 5.29 (d, J = 3.8 Hz, 1H, H-1'), 5.04 (d, J = 3.7 Hz, 1H, H-1), 4.95 (d, J = 11.8 Hz, 1H, CHH Bn), 4.82 (d, J = 11.1 Hz, 1H, CHH Bn), 4.74 (d, J = 11.6 Hz, 1H, CHH Bn), 4.65 (d, *J* = 11.1 Hz, 1H, CH*H* Bn), 4.40 (dd, *J* = 10.6, 2.8 Hz, 1H, H-3), 4.29 (dd, *J* = 10.4, 4.8 Hz, 1H, H-6'), 4.06 – 3.95 (m, 2H, H-5, H-5'), 3.90 (t, J = 9.6 Hz, 1H, H-3'), 3.77 (t, J = 10.4 Hz, 1H, H-6'), 3.70 (d, J = 2.8 Hz, 1H, H-4), 3.67 (t, J = 9.3 Hz, 1H, H-3'), 3.35 (s, 3H, CH₃ OMe), 3.20 $(dd, J = 10.0, 3.7 Hz, 1H, H-2'), 1.25 (d, J = 6.5 Hz, 3H, H-6); {}^{13}C NMR (126 MHz, CDCl_3) \delta 165.9$ (C=O), 138.1, 137.7, 137.2 (C_q), 135.3, 134.5, 133.2, 131.7, 131.6, 131.1, 130.3, 130.3 (CH_{arom}), 130.0 (C_q), 129.9, 129.7, 129.2, 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 127.9, 127.9, 126.1, 126.0 (CH_{arom}), 101.6 (CHPh), 100.1 (C-1'), 97.6 (C-1), 82.8 (C-4'), 80.2 (C-4), 75.7 (C-3), 75.5 (CH₂ Bn), 75.4 (C-3'), 74.9 (CH₂ Bn), 71.8 (C-2), 68.9 (C-6'), 66.6 (C-5'), 63.8 (C-5), 62.8 (C-2'), 55.5 (CH₃ OMe), 16.8 (C-6); diagnostic peaks for the β -anomer: ¹H NMR (500 MHz, CDCl₃) δ 5.42 (s, 1H, CHPh), 5.00 (d, J = 3.8 Hz, 1H, H-1), 4.69 (d, J = 11.6 Hz, 1H, CHH Bn), 3.58 (dd, J = 9.9, 4.5 Hz, 1H), 3.46 – 3.41 (m, 1H), 1.20 (d, J = 6.5 Hz, 3H, H-6); ¹³C NMR (126 MHz, CDCl₃) δ 102.6 (C-1'), 101.2 (CHPh), 97.8 (C-1), 81.5, 79.7, 79.6, 78.5, 75.4, 74.9, 70.2, 66.8, 66.3, 16.6 (C-6); HRMS: [M+NH₄]⁺ calcd for C₄₁H₄₃N₃O₁₀NH₄ 755.32867, found 755.32747.



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **A** and acceptor **48**. Yield: 82 mg, 100 µmol, 100%, $\alpha:\beta > 20:1$. ¹H NMR (400 MHz, CDCl₃) δ 8.21 – 8.16 (m, 2H, CH_{arom}), 8.10 – 8.03 (m, 2H, CH_{arom}), 7.77 – 7.65 (m, 2H, CH_{arom}), 7.60 – 7.53 (m, 2H, CH_{arom}), 7.52 – 7.42 (m, 4H, CH_{arom}), 7.40 – 7.32 (m, 8H, CH_{arom}), 7.21 – 7.11 (m, 8H, CH_{arom}), 6.99 – 6.94 (m, 2H, CH_{arom}), 5.64 – 5.58 (m, 2H, H-2, H-4), 5.40 (s, 1H, CHPh), 5.17 (d, *J* = 3.7 Hz, 1H, H-1), 5.07 (d, *J* = 3.6 Hz, 1H, H-1'), 4.57 – 4.47 (m, 2H, H-3, CHH Bn), 4.37 (d, *J* = 11.3 Hz, 1H, CHH Bn), 4.31 – 4.19 (m, 3H, H-5, CH₂ Bn), 4.12 (dd, *J* = 10.1, 4.8 Hz, 1H, H-6'), 3.86 (td, *J* = 9.9, 4.8 Hz, 1H, H-5'), 3.73 (t, *J* = 9.3 Hz, 1H, H-3'), 3.55 (t, *J* = 10.2 Hz, 1H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 166.6, 166.0 (C=O), 138.9, 138.3, 137.8 (Cq), 134.5, 133.4, 133.2, 131.6, 131.2, 130.2, 130.1, 130.0, 129.9, 128.9, 128.7, 128.5, 128.3, 128.2, 128.2, 128.0, 127.5, 126.4 (CH_{arom}), 101.5 (CHPh), 99.2 (C-1'), 97.8 (C-1), 81.9 (C-4'), 78.9 (C-2'), 78.2 (C-3'), 75.2 (CH₂ Bn), 73.5, 73.4 (C-3, C-4), 72.4 (CH₂ Bn), 71.4 (C-2), 69.0 (C-6), 65.2 (C-5), 63.6 (C-5'), 55.8 (CH₃ OMe), 16.5 (C-6); HRMS: [M+NH₄]⁺ calcd for C₄₈H₄₈O₁₂NH₄ 834.34840, found 834.34735.





Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor **48**. Yield: 75 mg, 100 µmol, 100%, $\alpha:\beta > 20:1$. ¹H NMR (400 MHz, CDCl₃) δ 8.22 – 8.17 (m, 2H, CH_{arom}), 8.14 – 8.08 (m, 2H, CH_{arom}), 7.74 – 7.65 (m, 3H, CH_{arom}), 7.62 – 7.53 (m, 3H, CH_{arom}), 7.50 – 7.44 (m, 6H, CH_{arom}), 7.41 – 7.35 (m, 5H, CH_{arom}), 7.20 – 7.11 (m, 5H, CH_{arom}), 5.65 (dd, *J* = 3.5, 1.3 Hz, 1H, H-4), 5.62 (dd, *J* = 10.5, 3.6 Hz, 1H, H-2), 5.46 (s, 1H, CHPh), 5.19 – 5.10 (m, 2H, H-1, H-1'), 4.65 (d, *J* = 10.9 Hz, 1H, CHH Bn), 4.49 (dd, *J* = 10.5, 3.5 Hz, 1H, H-3), 4.38 (d, *J* = 10.9 Hz, 1H, CHH Bn), 4.34 – 4.21 (m, 2H, H-5, H-6'), 3.93 (td, *J* = 9.9, 4.8 Hz, 1H, H-5'), 3.70 (dd, *J* = 10.1, 9.1 Hz, 1H, H-3'), 3.65 (t, *J* = 10.2 Hz, 1H, H-6'), 3.54 (t, *J* = 9.3 Hz, 1H, H-4'), 3.42 (s, 3H, CH₃ OMe), 3.15 (dd, *J* = 10.0, 3.7 Hz, 1H, H-2'), 1.26 (d, *J* = 6.5 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 166.6, 166.1 (C=O), 137.8, 137.6 (Cq), 135.4, 134.5, 133.5, 133.3, 131.7, 131.6, 131.1, 130.4, 130.3, 130.2, 129.9, 129.8, 129.6, 129.1 (CH_{arom}), 128.7 (Cq), 128.6 (CH_{arom}), 128.4 (Cq), 128.4, 128.3, 128.2, 128.2, 127.8, 126.4 (CH_{arom}), 101.6 (CHPh), 100.8 (C-1'), 97.7 (C-1), 82.6 (C-4'), 75.8 (C-3'), 75.0 (CH₂ Bn), 74.7 (C-3), 73.7 (C-4), 71.1 (C-2), 68.8 (C-6'), 65.2 (C-5), 63.6 (C-5'), 62.9 (C-2'), 55.7 (CH₃ OMe), 16.4 (C-6); HRMS: [M+NH₄]⁺ calcd for C₄₁H₄₁N₃O₁₁ 769.30793, found 769.30661





Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **A** and acceptor **49** Yield: 70 mg, 89 µmol, 89%, $\alpha:\beta = 1.3:1$. Data reported for a 1:1 mixture of anomers: ¹H NMR (400 MHz, CDCl₃) δ 7.67 (h, J = 7.0 Hz, 3H), 7.56 – 7.44 (m, 5H), 7.44 – 7.21 (m, 40H), 7.18 (dt, J = 4.7, 1.7 Hz, 2H), 5.55 (s, 1H, *CHP*ha), 5.52 (s, 1H, *CHP*h β), 5.05 – 4.98 (m, 5H), 4.97 – 4.85 (m, 5H), 4.82 (d, J = 3.6 Hz, 1H, H-1 α), 4.81 – 4.75 (m, 2H), 4.72 – 4.63 (m, 7H), 4.44 (dd, J = 10.1, 3.5 Hz, 1H, H-3 β), 4.22 – 4.16 (m, 2H), 4.15 – 4.09 (m, 2H), 4.05 (dt, J = 10.0, 5.0 Hz, 1H), 3.95 – 3.90 (m, 2H), 3.88 – 3.80 (m, 2H), 3.76 (t, J = 8.9 Hz, 1H), 3.73 – 3.56 (m, 6H), 3.55 – 3.48 (m, 2H, H-2' $\alpha\beta$), 3.37 (s, 4H), 3.27 (s, 3H), 1.14 (dd, J = 6.6, 4.0 Hz, 6H, H-6 $\alpha\beta$); ¹³C NMR (101 MHz, CDCl₃) δ 139.5, 139.4, 138.9, 138.7, 138.7, 138.6, 138.3, 137.6, 137.5, 135.4, 134.6, 131.8, 131.7, 131.2, 130.4, 130.3, 129.0, 128.6, 128.5, 128.4, 128.4, 128.3, 128.3, 128.3, 128.1, 128.0, 127.9, 127.8, 127.7, 127.7, 127.6, 127.4, 127.4, 127.3, 127.3, 126.2, 126.1, 124.9, 102.4 (C-1' β), 101.4 (CHPha), 101.1 (CHPh β), 100.8 (C-1' α), 99.8 (C-1 α), 97.9 (C-1 β), 82.4, 82.3, 81.6, 81.1, 79.3, 79.2, 78.5, 78.3, 78.2, 77.9, 77.6, 75.8, 75.2,

Disaccharide 49B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor **49**. Yield: 69 mg, 95 μ mol, 95%, α : β = 1:5.5. Data for the β-anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.50 – 7.25 (m, 20H, CH_{arom}), 5.53 (s, 1H, CHPh), 4.98 (d, J = 11.6 Hz, 1H, CHH Bn), 4.94 – 4.88 (m, 2H, 2x CHH Bn), 4.87 (d, J = 3.7 Hz, 1H, H-1), 4.79 (d, J = 11.3 Hz, 1H, CHH Bn), 4.68 (d, J = 11.9 Hz, 1H, CHH Bn), 4.63 (d, J = 11.5 Hz, 1H, CH*H* Bn), 4.47 (d, *J* = 7.9 Hz, 1H, H-1'), 4.35 (dd, *J* = 10.1, 3.6 Hz, 1H, H-2), 4.12 (dd, *J* = 10.6, 5.0 Hz, 1H, H-6'), 3.94 - 3.83 (m, 2H, H-3, H-5), 3.71 - 3.62 (m, 3H, H-4, H-4', H-6'), 3.58 (t, J = 9.2 Hz, 1H, H-3'), 3.49 (dd, J = 9.3, 7.8 Hz, 1H, H-2'), 3.42 (s, 3H, CH₃ OMe), 3.30 (td, J = 9.7, 5.0 Hz, 1H, H-5'), 1.14 (d, J = 6.4 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 139.2, 138.6, 137.9, 137.3 (C_q), 135.4, 134.3, 131.5, 129.1, 128.6, 128.5, 128.4, 128.3, 128.3, 128.3, 128.0, 127.8, 127.5, 127.3, 126.1 (CH_{arom}), 101.6 (C-1'), 101.3 (CHPh), 98.2 (C-1), 81.6 (C-4'), 79.4 (C-3'), 78.1 (C-4), 77.9 (C-3), 76.7 (C-2), 75.2, 75.0, 73.3 (CH₂ Bn), 68.6 (C-6'), 66.7 (C-2'), 66.4, 66.3 (C-5, C-5'), 55.5 (CH₃ OMe), 16.7 (C-6); diagnostic peaks for the α-anomer: ¹H NMR (400 MHz, CDCl₃) δ 5.58 (s, 1H, CHPh), 5.21 (d, J = 3.8 Hz, 1H, H-1'), 4.21 (dd, J = 10.4, 4.9 Hz, 1H, H-6'), 4.01 (td, J = 10.0, 4.9 Hz, 1H, H-5'), 3.40 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 101.5 (CHPh), 100.4 (C-1'), 99.6 (C-1), 82.9, 78.8, 75.1, 73.4, 70.0, 63.4, 61.9, 55.3; HRMS: [M+NH₄]⁺ calcd for C₄₁H₄₅N₃O₉ 741.34941, found 741.34828.

Disaccharide 50A



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **A** and acceptor **50**. Yield: 68 mg, 86 μ mol, 86%, α : β = 1:1.2. Data reported for a 1:1 mixture: ¹H NMR (500 MHz, CDCl₃) δ 7.39 - 7.23 (m, 50H), 5.53 (s, 1H, CHPha), 5.52 (d, *J* = 4.0 Hz, 1H, H-1'a), 5.50 (s, 1H, CHPhβ), 5.04 (d, *J* = 7.6 Hz, 1H, H-1'β), 4.96 (d, J = 11.7 Hz, 1H), 4.93 (d, J = 11.5 Hz, 1H), 4.91 (d, J = 7.8 Hz, 1H), 4.90 - 4.86 (m, 3H), 4.81 (d, J = 11.7 Hz, 1H), 4.79 - 4.75 (m, 3H), 4.72 - 4.58 (m, 5H), 4.51 (d, J = 12.1 Hz, 1H), 4.35 (d, J = 7.6 Hz, 1H), 4.34 - 4.29 (m, 1H), 4.29 - 4.23 (m, 1H), 4.18 - 4.16 (m, 2H), 4.12 (dd, J = 9.7, 7.6 Hz, 1H), 4.05 (t, J = 9.3 Hz, 1H), 3.78 (t, J = 8.9 Hz, 1H), 3.73 (dd, J = 9.8, 2.8 Hz, 1H), 3.68 - 3.59 (m, 4H), 3.58 – 3.53 (m, 5H), 3.51 – 3.42 (m, 4H), 3.41 (s, 3H), 3.35 (td, *J* = 9.7, 5.1 Hz, 1H), 1.22 $(d, J = 6.4 \text{ Hz}, 3H, H-6\alpha), 1.19 (d, J = 6.4 \text{ Hz}, 3H, H-6\beta); {}^{13}C \text{ NMR} (126 \text{ MHz}, CDCl_3) \delta 139.1,$ 138.9, 138.9, 138.7, 138.4, 138.3, 137.8, 137.6, 135.3, 134.2, 131.9, 131.4, 131.2, 130.3, 130.2, 128.9, 128.9, 128.5, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.3, 128.2, 128.2, 128.1, 128.1, 128.1, 128.0, 128.0, 127.8, 127.7, 127.6, 127.6, 127.6, 127.5, 127.5, 127.3, 126.5, 126.2, 126.1, 104.5 (C-1β), 102.8 (C-1α), 102.7 (C-1'β), 101.2 (CHPha), 101.1 (CHPhβ), 98.2 (C-1'α), 83.9, 83.0, 82.2, 81.8, 81.4, 81.2, 79.1, 78.7, 77.2, 76.6, 75.3, 75.1, 75.0, 74.9, 74.7, 74.6, 74.6, 73.1, 72.8, 71.5, 70.4, 70.2, 69.1, 65.7, 62.4, 56.9, 56.8, 17.1, 16.8; HRMS: [M+NH₄]⁺ calcd for C₄₈H₅₂O₁₀NH₄ 806.38987, found 806.38795.

Disaccharide 50B



Title compound was obtained as white solid via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor **51**. Yield: 68 mg, 93 μ mol, 93%, α : β <1:20. Data for the β-anomer: ¹H NMR (500 MHz, CDCl₃) δ 7.50 – 7.24 (m, 20H, CH_{arom}), 5.53 (s, 1H, CHPh), 4.97 (d, J = 11.7 Hz, 1H, CHPh), 4.92 - 4.87 (m, 3H, H-1', 2x CHH Bn), 4.79 (d, J = 11.3 Hz, 1H, CHH Bn), 4.69 – 4.64 (m, 2H, 2x CHH Bn), 4.33 – 4.26 (m, 2H, H-1, H-6'), 4.11 (dd, J = 9.7, 7.8 Hz, 1H, H-2), 3.67 - 3.62 (m, 2H, H-4', H-6'), 3.58 - 3.53 (m, 5H, H-3', H-4, CH₃ OMe), 3.50 - 3.45 (m, 2H, H-3, H-5), 3.41 (dd, J = 9.5, 8.1 Hz, 1H, H-2'), 3.36 (td, J = 9.7, 5.0 Hz, 1H, H-5'), 1.19 (d, J = 6.4 Hz, 3H, H-6); ¹³C NMR (126 MHz, CDCl₃) δ 139.1, 138.7, 138.1, 137.4 (C_q), 135.4, 134.4, 131.8, 131.6, 131.1, 130.3, 129.1, 128.6, 128.6, 128.5, 128.5, 128.4, 128.3, 128.3, 128.3, 128.2, 128.2, 127.9, 127.6, 127.5, 127.4, 126.1 (CH_{arom}), 104.3 (C-1), 102.1 (C-1'), 101.4 (CHPh), 81.9 (C-4'), 81.0 (C-3), 79.1 (C-3'), 78.4 (C-2), 76.9 (C-4), 75.0, 74.7, 73.4 (CH₂ Bn), 70.5 (C-5'), 68.8 (C-6'), 66.8 (C-2'), 66.0 (C-5'), 57.0 (CH₃ OMe), 16.8 (C-6); Diagnostic peaks for the α-anomer: ¹H NMR (500 MHz, CDCl₃) δ 5.56 (s, 1H, CHPh), 5.41 (d, *J* = 3.9 Hz, 1H, H-1'), 3.99 (dd, *J* = 9.8, 7.7 Hz, 1H); ¹³C NMR (126 MHz, CDCl₃) δ 102.5 (C-1), 101.5 (CHPh), 98.9 (C-1'), 84.1, 82.7, 75.0, 72.6, 63.2, 62.5, 56.8 (CH₃ OMe), 17.0 (C-6); HRMS: [M+NH₄]⁺ calcd for C₄₁H₄₅N₃O₉NH₄ 741.34941, found 741.34826.

Disaccharide 51A

Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor A and acceptor 51. Yield: 53 mg, 81 μ mol, 81%, α : β = 1:1.6. Data reported for a 1:1 mixture: ¹H NMR (500 MHz, CDCl₃) δ 7.41 – 7.22 (m, 27H), 5.56 (s, 2H, CHPhaβ), 5.12 - 5.07 (m, 2H, H-1'a, CHH Bn), 4.99 (d, J = 10.7 Hz, 1H), 4.97 - 4.91 (m, 2H), 4.89 (d, J = 10.9 Hz, 1H), 4.85 (d, J = 11.4 Hz, 1H), 4.82 - 4.78 (m, 2H), 4.74 (d, J = 12.1 Hz, 1H), 4.68 – 4.63 (m, 2H, H-1'β, CHH Bn), 4.62 – 4.58 (m, 2H), 4.29 (dd, J = 10.5, 5.0 Hz, 1H), 4.23 (dd, *J* = 10.3, 4.9 Hz, 1H), 4.12 (t, *J* = 9.3 Hz, 1H), 3.97 (tdd, *J* = 8.6, 7.2, 5.0 Hz, 2H), 3.88 (dddd, *J* = 20.8, 11.8, 4.9, 1.7 Hz, 2H), 3.80 - 3.68 (m, 4H), 3.64 (t, J = 9.4 Hz, 1H), 3.54 (dd, J = 9.4, 3.7 Hz, 1H, H-2'a), 3.47 (dd, J = 8.6, 7.6 Hz, 1H, H-2' β), 3.42 – 3.32 (m, 3H), 3.28 (ddt, J = 9.2, 6.5, 5.7Hz, 2H), 3.15 – 3.01 (m, 2H), 2.15 – 2.03 (m, 2H), 1.84 (tdd, J = 12.8, 11.3, 5.0 Hz, 1H), 1.68 (tdd, I = 12.8, 11.4, 5.9 Hz, 1H), 1.32 (d, I = 6.1 Hz, 3H), 1.25 (d, I = 6.1 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) & 138.9, 138.8, 138.7, 138.6, 138.3, 138.1, 137.5, 137.4, 135.4, 134.4, 131.9, 131.5, 131.2, 130.4, 130.3, 129.1, 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.2, 128.2, 128.1, 128.0, 127.9, 127.8, 127.8, 127.8, 127.7, 127.5, 126.1, 125.3, 101.3 (CHPha), 101.2 (CHPhβ), 100.9 (C-1'β), 100.0 (C-1'α), 83.4, 83.1, 82.5, 82.5, 82.5, 81.8, 81.2, 79.6, 79.1, 78.5, 76.2, 76.1, 75.6, 75.2, 75.1, 75.0, 73.7, 69.0, 69.0, 66.1, 65.3, 65.2, 63.1, 33.9, 31.4, 18.7, 18.6; HRMS: [M+NH₄]⁺ calcd for C₄₀H₄₄O₈NH₄ 670.33744, found 670.33579.

Disaccharide 51B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor **51**. Yield: 50 mg, 85 μ mol, 85%, α : β =1:13. Data for the β-anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.50 – 7.46 (m, 2H, CH_{arom}), 7.42 – 7.27 (m, 13H, CH_{arom}), 5.57 (s, 1H, CHPh), 4.96 (d, J = 10.7 Hz, 1H, CHH Bn), 4.92 (d, J = 11.3 Hz, 1H, CHH Bn), 4.80 (d, J = 11.3 Hz, 1H, CHH Bn), 4.61 (d, J = 10.7 Hz, 1H, CHH Bn), 4.51 (d, J = 7.9 Hz, 1H, H-1'), 4.27 (dd, J = 10.6, 5.0 Hz, 1H, H-6'), 3.99 – 3.88 (m, 2H, H-1_{eq}, H-3), 3.74 – 3.67 (m, 2H, H-4', H-6'), 3.54 (t, J = 9.3 Hz, 1H, H-3'), 3.43 (dd, J = 9.5, 7.9 Hz, 1H, H-2'), 3.41 - 3.32 (m, 2H, H-1_{ax}, H-5'), 3.27 (dq, J = 9.5, 6.1 Hz, 1H, H-5), 3.09 (t, J = 8.9 Hz, 1H, H-4), 2.12 (ddd, J = 13.2, 4.6, 2.2 Hz, 1H, H-2_{eq}), 1.77 (tdd, J = 12.8, 11.4, 4.9 Hz, 1H, H-2_{ax}), 1.31 (d, J = 6.1 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 138.7, 137.9, 137.1 (C_q), 129.1, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 127.9, 127.7, 126.0 (CH_{arom}), 101.3 (CHPh), 99.9 (C-1'), 82.9 (C-4), 81.7 (C-4'), 80.3 (C-3), 78.9 (C-3'), 76.0 (C-5), 75.1, 74.9 (CH₂ Bn), 68.6 (C-6'), 66.7 (C-2'), 66.2 (C-5'), 65.1 (C-1), 31.1 (C-2), 18.5 (C-6); diagnostic peaks for the α -anomer: ¹H NMR (400 MHz, CDCl₃) δ 5.59 (s, 1H, CHPh), 5.23 (d, J = 3.8 Hz, 1H, H-1'), 5.07 (d, J = 10.5 Hz, 1H, CHH Bn), 4.15 - 4.07 (m, 1H), 2.30 (tt, *J* = 8.7, 5.3 Hz, 2H, 2x H-2); ¹³C NMR (101 MHz, CDCl₃) δ 99.5 (C-1'), 87.0, 84.8, 70.7, 69.6, 63.2, 63.1, 29.7 (C-2); HRMS: [M+NH₄]⁺ calcd for C₃₃H₃₇N₃O₇NH₄ 605.29698, found 605.29618.

Disaccharide 52A Ph-20 BZO

Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor A and acceptor 52. Yield: 35 mg, 53 mmol, 53%, $\alpha;\beta = 5:1$. Data for the α -anomer: ¹H NMR (500 MHz, CDCl₃) δ 8.03 (dd, J = 8.3, 1.4 Hz, 2H, CH_{arom}), 7.54 - 7.50 (m, 1H, CHarom), 7.48 - 7.43 (m, 3H, CHarom), 7.42 - 7.30 (m, 7H, CHarom), 7.28 - 7.22 (m, 7H, CH_{arom}), 7.20 - 7.09 (m, 3H, CH_{arom}), 6.95 (dt, J = 6.6, 1.6 Hz, 2H, CH_{arom}), 5.50 (s, 1H, CHPh), 5.12 (t, J = 9.3 Hz, 1H, H-4), 4.97 (d, J = 3.7 Hz, 1H, H-1'), 4.80 (d, J = 11.1 Hz, 1H, CHH Bn), 4.67 (d, *J* = 11.1 Hz, 1H, CH*H* Bn), 4.31 (d, *J* = 12.4 Hz, 1H, C*H*H Bn), 4.23 (dd, *J* = 10.2, 4.9 Hz, 1H, H-6'), 4.15 (d, J = 12.3 Hz, 1H, CHH Bn), 4.04 – 3.98 (m, 2H, H-1eq, H-3'), 3.96 – 3.89 (m, 2H, H-3, H-5'), 3.67 (t, J = 10.3 Hz, 1H, H-6'), 3.55 – 3.46 (m, 3H, H-1ax, H-4', H-5), 3.34 (dd, J = 9.3, 3.7 Hz, 1H, H-2'), 2.14 – 1.96 (m, 2H, H-2_{ax}, H-2_{eq}), 1.24 (d, J = 6.2 Hz, 3H, H-6); ¹³C NMR (126 MHz, CDCl₃) δ 165.5 (C=O), 138.8, 138.1, 137.4 (C_q), 133.2, 129.8, 129.0, 128.6, 128.3, 128.2, 128.2, 127.7, 127.6, 127.5, 126.1 (CH_{arom}), 101.3 (CHPh), 99.4 (C-1), 82.2 (C-4'), 78.4 (C-1), 82.2 (C-4), 78.4 (C-1), 78.4 (C-1) 3'), 78.3 (C-2'), 77.8 (C-3), 76.8 (C-4), 75.4 (CH₂ Bn), 75.4 (C-5), 72.6 (CH₂ Bn), 69.0 (C-1), 65.5 (C-6'), 63.2 (C-5'), 33.5 (C-2), 18.2 (C-6); diagnostic peaks for the β-anomer: ¹H NMR (500 MHz, CDCl₃) δ 5.34 (s, 1H, CHPh), 4.86 – 4.83 (m, 2H, 2x CHH Bn), 4.77 – 4.71 (m, 2H, 2x CHH Bn), 4.52 (d, J = 7.6 Hz, 1H, H-1'); ¹³C NMR (126 MHz, CDCl₃) δ 165.8 (C=O), 102.9 (C-1'), 101.0 (CHPh), 81.4, 80.9, 79.1, 76.3, 75.6, 75.1, 75.0, 68.4, 66.0, 32.1 (C-2); HRMS: [M+NH₄]⁺ calcd for C40H42O9NH4 684.31671, found 684.31496.

Disaccharide 52B

Ph O O BZO DO BnO N₃

Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor 52. Yield: 36 mg, 60 μ mol, 60%, α : β = 1.4:1. Data reported for a 1:1 mixture: ¹H NMR (500 MHz, CDCl₃) δ 8.11 - 8.05 (m, 5H), 7.75 - 7.70 (m, 6H), 7.69 - 7.65 (m, 4H), 7.62 - 7.54 (m, 6H), 7.52 - 7.46 (m, 11H), 7.43 - 7.27 (m, 24H), 5.57 (s, 1H, CHPha), 5.36 (s, 1H, CHPhβ), 5.07 (t, J = 9.3 Hz, 1H, H-4a), 5.02 - 4.94 (m, 2H, H- $1'\alpha$, H-4 β), 4.90 (d, J = 10.8 Hz, 1H), 4.86 (d, J = 11.5 Hz, 1H) 4.75 (d, J = 11.5 Hz, 1H), 4.71 (d, J = 10.8 Hz, 1H), = 10.8 Hz, 1H), 4.38 (d, J = 7.9 Hz, 1H, h-1' β), 4.26 (dd, J = 10.3, 4.9 Hz, 1H), 4.06 - 3.92 (m, 6H), 3.88 (ddd, J = 11.3, 9.2, 5.3 Hz, 1H), 3.74 (t, J = 10.4 Hz, 1H), 3.65 (t, J = 9.3 Hz, 1H), 3.61 - 3.58 (m, 1H), 3.56 - 3.47 (m, 6H), 3.45 (t, J = 9.0 Hz, 1H), 3.36 (dd, J = 9.3, 8.0 Hz, 1H), 3.25 (dd, J = 9.3, 8.0 Hz, 1H), 3.26 (dd, J = 9.3, 8.0 Hz, 1H), 9.9, 3.8 Hz, 1H, H-2'a), 3.16 - 3.06 (m, 2H), 2.19 (ddt, J = 13.1, 5.3, 1.9 Hz, 1H), 2.13 - 2.07 (m, 1H), 2.05 – 1.93 (m, 2H), 1.38 – 0.98 (m, 6H); ¹³C NMR (126 MHz, CDCl₃) δ 165.8, 165.6, 149.6, 137.9, 137.9, 137.2, 137.1, 135.3, 134.5, 133.3, 133.1, 131.8, 131.7, 131.6, 131.1, 130.5, 130.3, 130.3, 130.2, 129.8, 129.6, 129.2, 129.1, 128.5, 128.5, 128.4, 128.4, 128.4, 128.3, 128.2, 128.2, 127.9, 126.1, 126.0, 125.1, 119.4, 102.2 (C-1'β), 101.5 (CHPha), 101.2 (CHPhβ), 100.2 (C-1'a), 82.8, 81.3, 80.3, 79.4, 78.9, 76.6, 76.5, 76.1, 75.3, 75.1, 75.1, 74.8, 68.8, 68.0, 66.5, 66.1, 65.5, 65.4, 63.2, 63.2, 33.6, 32.2, 18.2, 18.1; HRMS: [M+NH₄]⁺ calcd for C₃₃H₃₅N₃O₈NH₄ 619.27624, found 619.27524.

Disaccharide 53A

Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor A and acceptor 53. Yield: 63 mg, 97 μ mol, 97%, α : β =4:1. Data for the α-anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.42 – 7.20 (m, 20H, CH_{arom}), 5.57 (s, 1H, CHPh), 5.01 – 4.96 (m, 2H, H-1', CHH Bn), 4.93 – 4.86 (m, 2H, 2x CHH Bn), 4.81 (d, J = 11.5 Hz, 1H, CH*H* Bn), 4.70 (d, *J* = 11.9 Hz, 1H, CH*H* Bn), 4.62 (d, *J* = 11.6 Hz, 1H, CH*H* Bn), 4.24 (dd, *J* = 10.2, 4.8 Hz, 1H, H-6'), 4.09 (t, J = 9.3 Hz, 1H, H-3'), 4.03 – 3.94 (m, 2H, H-1, H-5'), 3.71 (t, J = 10.3 Hz, 1H, H-6'), 3.68 – 3.57 (m, 3H, H-2', H-3, H-4'), 3.47 (d, J = 2.7 Hz, 1H, H-4), 3.43 – 3.30 (m, 2H, H-1, H-5), 2.28 (qd, J = 12.2, 4.7 Hz, 1H, H-2), 1.74 – 1.67 (m, 1H, H-2), 1.11 (d, J = 6.3 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 138.9, 138.6, 138.4, 137.5 (C_q), 131.6, 129.0, 128.8, 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.2, 128.2, 128.2, 128.1, 128.1, 127.9, 127.9, 127.7, 127.5, 126.1, 126.1 (CH_{arom}), 101.3 (CHPh), 99.4 (C-1'), 82.4 (C-4'), 81.1 (C-3), 79.7 (C-2'), 78.4 (C-3'), 76.2 (C-4), 75.2 (CH₂ Bn), 75.0 (C-5), 74.6, 73.9 (CH₂ Bn), 69.0 (C-6'), 65.9 (C-1), 63.1 (C-5'), 28.8 (C-2), 17.7 (C-6); diagnostic peaks for the β -anomer: ¹H NMR (400 MHz, CDCl₃) δ 5.59 (s, 1H, CHPh), 4.66 (d, J = 7.7 Hz, 1H, H-1), 4.37 (dd, J = 10.4, 5.0 Hz, 1H, H-6'), 4.16 (ddd, J = 8.6, 6.5, 3.1 Hz, 1H), 3.90 (ddd, J = 11.9, 4.6, 2.7 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 102.5 (C-1), 101.2 (CHPh), 82.3, 81.6, 80.9, 79.0, 78.0, 75.5, 75.2, 74.8, 17.6; HRMS: [M+NH₄]⁺ calcd for C40H44O8NH4 670.33744, found 670.33601.

Disaccharide 53B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor **53**. Yield: 39 mg, 67 μmol, 67%, α:β =1:1.4. Data reported for a 1:1 mixture: ¹H NMR (400 MHz, CDCl₃) δ 7.79 – 7.60 (m, 7H, CH_{arom}), 7.56 – 7.23 (m, 28H, CH_{arom}), 5.59 (s, 2H, 2x CHPh), 5.06 (d, *J* = 3.6 Hz, 1H, H-1'a), 4.99 – 4.88 (m, 4H), 4.80 (d, *J* = 11.3 Hz, 1H), 4.75 (d, *J* = 11.1 Hz, 1H), 4.66 (t, *J* = 11.3 Hz, 2H), 4.51 (d, *J* = 7.9 Hz, 1H, H-1'β), 4.36 (dd, *J* = 10.5, 5.0 Hz, 1H), 4.25 (dd, *J* = 10.3, 4.9 Hz, 1H), 4.10 – 3.97 (m, 3H), 3.88 (ddd, *J* = 11.9, 4.6, 2.6 Hz, 1H), 3.84 – 3.68 (m, 5H), 3.59 – 3.52 (m, 3H), 3.51 – 3.35 (m, 7H), 2.42 – 2.17 (m, 2H), 1.82 – 1.68 (m, 2H), 1.22 – 0.90 (m, 6H, H-6αβ); ¹³C NMR (101 MHz, CDCl₃) δ 138.9, 137.9, 137.7, 137.3, 137.1, 135.4, 134.4, 131.9, 131.6, 131.5, 131.2, 130.3, 130.2, 129.2, 129.2, 128.7, 128.5, 128.4, 128.3, 128.3, 128.3, 128.2, 128.0, 128.0, 127.7, 127.6, 126.1, 126.1, 125.3, 101.5 (CHPhα), 101.4 (CHPhβ), 101.3 (C-1'β), 98.7 (C-1'α), 83.0, 81.6, 80.8, 79.8, 78.9, 77.9, 76.7, 76.1, 75.0, 75.0, 75.0, 75.0, 74.8, 68.8, 68.7, 66.6, 66.3, 65.9, 65.8, 63.4, 63.3, 28.5, 26.5, 17.7, 17.7; HRMS: [M+NH4]⁺ calcd for C₃₃H₃₇N₃O₇NH₄ 605.29698, found 605.29612.

Disaccharide 54A



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor A and acceptor 54. Yield: 67 mg, 100 μ mol, 100%, α : β = 8:1. Data for the α-anomer: ¹H NMR (400 MHz, CDCl₃) δ 8.13 – 8.07 (m, 2H, CH_{aron}), 7.77 – 7.59 (m, 3H, CHarom), 7.56 - 7.34 (m, 10H, CHarom), 7.28 - 7.09 (m, 12H, CHarom), 5.55 (d, J = 3.2 Hz, 1H, H-4), 5.53 (s, 1H, CHPh), 5.28 (d, J = 3.5 Hz, 1H, H-1'), 4.78 (d, J = 11.2 Hz, 1H, CHH Bn), 4.67 (d, J = 11.3 Hz, 1H, CHH Bn), 4.55 (d, J = 12.0 Hz, 1H, CHH Bn), 4.45 (d, J = 12.1 Hz, 1H, CHH Bn), 4.28 (dd, J = 9.6, 4.1 Hz, 1H, H-6'), 4.15 (ddd, J = 11.8, 4.9, 1.7 Hz, 1H, H-1eq), 4.00 - 3.92 (m, 2H, H-3, H-3'), 3.81 – 3.75 (m, 1H, H-5'), 3.71 (t, J = 9.9 Hz, 1H, H-6'), 3.67 – 3.62 (m, 1H, H-5), 3.61 – 3.54 (m, 2H, H-4', H-6'), 3.52 (dd, J = 9.3, 3.7 Hz, 1H, H-2'), 2.34 (qd, J = 12.6, 4.9 Hz, 1H, H-2_{ax}), 1.80 (ddt, J = 11.1, 5.0, 1.7 Hz, 1H, H-2_{eq}), 1.21 (d, J = 6.4 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 166.6 (C=O), 138.8, 138.1, 137.4 (C_q), 135.3, 134.4, 133.2, 131.9, 131.5 (CH_{arom}), 131.2 (C_q), 130.3, 130.2, 130.1, 129.9 (CH_{arom}), 129.9 (C_q), 129.0, 128.5, 128.3, 128.3, 128.3, 128.2, 128.2, 128.0, 128.0, 127.9, 127.8, 127.5, 127.5, 126.1, 126.0, 125.2 (CH_{arom}), 101.2 (CHPh), 94.0 (C-1'), 82.1 (C-4'), 78.6 (C-2'), 78.2 (C-3'), 75.3 (CH₂ Bn), 73.8 (C-5), 72.7 (CH₂ Bn), 71.8 (C-3), 69.0 (C-6'), 68.8 (C-4), 66.3 (C-1), 63.1 (C-5'), 28.2 (C-2), 17.5 (C-6); diagnostic peaks for the β -anomer: ¹H NMR (400 MHz, CDCl₃) δ 5.48 (d, J = 3.1 Hz, 1H, H-4), 4.85 (d, J = 11.5 Hz, 1H, CHH Bn), 4.73 (d, J = 11.5 Hz, 1H, CHH Bn), 4.62 (d, J = 9.1 Hz, 1H, H-1'), 4.34 (dd, J = 10.5, 5.0 Hz, 1H), 1.96 – 1.89 (m, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 166.0 (C=O), 101.1 (CHPh), 100.8 (C-1'), 82.0, 81.3, 80.8, 75.2, 75.0, 74.7, 74.1, 64.7, 26.9; HRMS: [M+NH₄]⁺ calcd for C40H42O9NH4 684.31671, found 684.31519.

Disaccharide 54B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor 54. Yield: 60 mg, 100 μ mol, 100%, α : β = 1.5:1. Data reported for a 1:1 mixture: ¹H NMR (400 MHz, CDCl₃) & 8.21 - 8.14 (m, 2H), 8.13 - 8.08 (m, 1H), 7.75 - 7.62 (m, 6H), 7.61 - 7.51 (m, 3H), 7.48 - 7.42 (m, 8H), 7.37 (ddd, J = 5.3, 3.3, 2.1 Hz, 4H), 7.34 – 7.20 (m, 12H), 5.56 (s, 1H, CHPha), 5.52 – 5.49 (m, 2H, H-4α, CHPhβ), 5.42 (d, J = 3.1 Hz, 1H, C-4 β), 5.26 (d, J = 3.7 Hz, 1H, H-1' α), 4.88 – 4.81 (m, 2H), 4.73 (d, J = 11.4 Hz, 1H), $4.65 (d, J = 10.9 Hz, 1H), 4.49 (d, J = 7.9 Hz, 1H, H-1'\beta), 4.36 - 4.25 (m, 2H), 4.14 (dtd, J = 11.7),$ 3.9, 1.7 Hz, 1H), 4.03 (dddd, J = 13.5, 12.0, 4.9, 3.2 Hz, 2H), 3.96 (dd, J = 9.9, 9.0 Hz, 1H), 3.84 (td, *J* = 9.8, 4.4 Hz, 1H), 3.75 (t, *J* = 10.1 Hz, 1H), 3.71 – 3.51 (m, 6H), 3.45 (t, *J* = 9.3 Hz, 1H), 3.39 – 3.29 (m, 2H), 2.33 – 2.16 (m, 2H), 1.93 (dd, J = 13.4, 4.4 Hz, 1H), 1.79 (ddt, J = 11.3, 5.2, 1.7 Hz, 1H), 1.22 (d, J = 6.4 Hz, 3H), 1.20 (d, J = 6.5 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 166.6, 166.4, 137.9, 137.9, 137.2, 137.2, 135.3, 134.6, 133.2, 133.0, 131.7, 131.7, 131.0, 130.4, 130.3, 130.3, 130.0, 130.0, 129.1, 129.1, 128.5, 128.4, 128.4, 128.4, 128.3, 128.2, 128.1, 128.1, 127.9, 126.1, 126.0, 124.9, 101.4 (CHPha), 101.3 (CHPhβ), 100.4 (C-1'β), 94.7 (C-1'α), 82.6, 81.3, 78.8, 76.2, 76.1, 75.0, 74.8, 74.0, 73.6, 72.2, 71.6, 68.9, 68.5, 68.2, 66.3, 66.1, 66.1, 65.8, 63.2, 62.8, 28.1, 27.1, 17.5, 17.4; HRMS: [M+NH4]+ calcd for C33H35N3O8NH4 619.27624, found 619.27510.

Disaccharide 55A

Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **A** and acceptor **55**. Yield: 64 mg, 98 µmol, 98%, α : β =1:1.6. Data reported for a 1:1 mixture: ¹H NMR (400 MHz, CDCl₃) δ 7.71 – 7.17 (m, 40H), 5.87 (d, *J* = 4.1 Hz, 1H, H-1' α), 5.54 (s, 1H, CHPh α), 5.53 (s, 1H, CHPh β), 4.94 – 4.88 (m, 2H), 4.84 (s, 2H), 4.81 (d, *J* = 11.4 Hz, 1H), 4.79 – 4.71 (m, 3H, H-1' β , 2x CHH Bn), 4.70 – 4.62 (m, 3H), 4.58 (d, *J* = 12.1 Hz, 1H), 4.40 (d, *J* = 11.8 Hz, 1H), 4.32 – 4.19 (m, 2H), 4.00 (t, *J* = 9.4 Hz, 1H), 3.96 – 3.87 (m, 2H), 3.84 – 3.74 (m, 2H), 3.72 – 3.66 (m, 1H), 3.65 – 3.58 (m, 2H), 3.53 (ddd, *J* = 11.7, 5.5, 2.6 Hz, 2H), 3.50 – 3.37 (m, 4H), 3.37 – 3.28 (m, 2H), 2.15 – 2.02 (m, 2H), 1.79 – 1.58 (m, 2H), 1.39 (d, *J* = 6.0 Hz, 3H), 1.34 (d, *J* = 6.0 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 139.2, 138.8, 138.6, 138.3, 138.1, 137.5, 137.4, 135.3, 134.4, 131.8, 131.6, 131.6, 131.1, 130.3, 130.2, 129.0, 129.0, 128.5, 128.4, 128.4, 128.3, 128.3, 128.3, 128.1, 128.1, 127.9, 127.8, 127.7, 127.6, 127.6, 127.5, 127.3, 127.0, 127.0, 126.1, 126.1, 103.7 (C-1' β), 101.2 (CHPh β), 101.1 (CHPh α), 97.8 (C-1' α), 84.2, 82.9, 82.1, 81.8, 81.7, 81.5, 79.2, 78.8, 78.7, 78.6, 76.2, 75.7, 75.4, 75.2, 75.1, 72.9, 71.9, 69.8, 68.9, 66.0, 65.4, 65.3, 63.2, 32.0, 31.3, 19.8, 18.7; HRMS: [M+NH₄]⁺ calcd for C₄₀H₄₄O₈NH₄ 670.33744, found 670.33617.

Disaccharide 55B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor 55. Yield: 57 mg, 97 μ mol, 97%, α : β =1:16. Data for the β-anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.49 – 7.26 (m, 15H, CH_{arom}), 5.52 (s, 1H, CHPh), 4.92 (d, J = 11.1 Hz, 1H, CHH Bn), 4.78 (d, J = 11.1 Hz, 1H, CHH Bn), 4.69 – 4.61 (m, 2H, CH₂ Bn), 4.60 (d, J = 8.1 Hz, 1H, H-1'), 4.13 (dd, J = 10.5, 4.9 Hz, 1H, H-6'), 3.95 - 3.85 (m, 1H, H-1_{eq}), 3.67 (t, *J* = 9.2 Hz, 1H, H-4'), 3.64 – 3.50 (m, 3H, H-3, H-3', H-6'), 3.45 – 3.30 (m, 4H, H-1_{ax}, H-2', H-4, H-5), 3.24 (td, J = 9.7, 5.0 Hz, 1H, H-5'), 2.06 (dd, J = 13.1, 5.0 Hz, 1H, H-2_{eq}), 1.76 - 1.60 (m, 1H, H-2_{ax}), 1.40 (d, J = 5.9 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 138.9, 137.8, 137.2 (C_q), 129.1, 128.5, 128.5, 128.4, 128.4, 128.3, 128.2, 128.0, 127.9, 127.6, 127.1, 126.0 (CHarom), 102.2 (C-1'), 101.3 (CHPh), 84.4 (C-4), 81.7 (C-4'), 79.4, 79.2 (C-3, C-3'), 75.7 (C-5), 75.0, 71.6 (CH₂ Bn), 68.6 (C-6'), 67.4 (C-2'), 66.1 (C-5'), 65.4 (C-1), 31.8 (C-2), 18.6 (C-6); Diagnostic peaks for the α -anomer: ¹H NMR (400 MHz, CDCl₃) δ 5.73 (d, J = 4.1 Hz, 1H, H-1²), 5.57 (s, 1H, CHPh), 4.24 (dd, J = 10.4, 4.9 Hz, 1H), 4.04 (t, J = 9.5 Hz, 1H), 2.16 (dd, J = 12.8, 5.1 Hz, 1H, H-2_{eq}); ¹³C NMR (101 MHz, CDCl₃) δ 101.9 (CHPh), 98.8 (C-1'), 84.3, 83.0, 82.6, 81.6, 80.9, 78.8, 75.9, 75.7, 72.2, 71.0, 70.8, 66.9, 63.2, 62.9, 62.4; HRMS: [M+NH₄]⁺ calcd for C₃₃H₃₇N₃O₇NH₄ 605.29698, found 605.29595.

Disaccharide 56A



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor A and acceptor 56. Yield: 65 mg, 100 μ mol, 100%, α : β =11:1. Data for the α-anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.56 - 7.43 (m, 5H, CH_{arom}), 7.42 - 7.25 (m, 15H, CH_{arom}), 5.50 (s, 1H, CHPh), 4.97 (d, J = 11.2 Hz, 1H, CHH Bn), 4.92 - 4.87 (m, 2H, C-1', CHH Bn), 4.84 (d, J = 11.2 Hz, 1H, CHH Bn), 4.76 (d, J = 12.0 Hz, 1H, CHH Bn), 4.61 – 4.56 (m, 2H, CH₂ Bn), 4.32 (td, J = 10.0, 4.9 Hz, 1H, H-5'), 4.21 (t, J = 9.3 Hz, 1H, H-3'), 4.04 (ddd, J = 11.6, 4.8, 2.0 Hz, 1H, H-1_{eq}), 3.90 (dd, J = 10.1, 5.0 Hz, 1H, H-6), 3.70 (dd, J = 2.6, 1.3 Hz, 1H, H-4), 3.62 - 3.56 (m, 2H, H-2', H-4'), 3.51 (t, J = 10.2 Hz, 1H, H-6), 3.47 - 3.34 (m, 3H, H-1ax, H-3, H-5), 2.14 - 2.01 (m, 1H, H-2), 1.77 - 1.65 (m, 1H, H-2), 1.34 (d, J = 6.4 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 139.0, 138.5, 138.3, 137.8 (C_q), 135.3, 134.6, 131.7, 131.6, 131.0, 130.4, 128.8, 128.6, 128.6, 128.5, 128.5, 128.4, 128.4, 128.4, 128.2, 128.0, 127.8, 127.8, 127.7, 127.7, 127.6, 127.6, 126.1 (CH_{arom}), 101.1 (CHPh), 100.5 (C-1'), 82.9 (C-4'), 79.6 (C-2'), 78.9 (C-3'), 78.2 (C-4), 77.6 (C-3), 75.2 (CH₂ Bn), 75.1 (C-5), 74.2 (CH₂ Bn), 70.2 (CH₂ Bn), 69.2 (C-6'), 66.0 (C-1), 62.8, 27.1 (C-2), 17.7 (C-6); diagnostic peaks for the β -anomer: ¹H NMR (400 MHz, CDCl₃) δ 5.56 (s, 1H, CHPh), 5.17 (d, J = 11.1 Hz, 1H, CHH Bn); ¹³C NMR (101 MHz, CDCl₃) δ 103.3 (C-1'), 101.1 (CHPh), 82.6, 81.6, 81.0; HRMS: [M+NH₄]⁺ calcd for C₄₀H₄₄O₈NH₄ 670.33744, found 670.33600.

Disaccharide 56B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor **56**. Yield: 55 mg, 93 μmol, 93%, $\alpha:\beta = 1.4:1$. Data reported for a 1:1 mixture of anomers: ¹H NMR (400 MHz, CDCl₃) δ 7.56 – 7.51 (m, 4H), 7.51 – 7.44 (m, 6H), 7.41 – 7.27 (m, 26H), 5.56 (s, 1H, CHPh β), 5.53 (s, 1H, CHPh α), 5.03 – 4.96 (m, 2H, H-1' α , CHH Bn), 4.94 – 4.88 (m, 1H), 4.84 – 4.77 (m, 3H, H-1' β , 2x CHH Bn), 4.71 (d, *J* = 12.3 Hz, 1H), 4.61 (d, *J* = 1.4 Hz, 2H), 4.53 (d, *J* = 12.2 Hz, 1H), 4.41 (td, *J* = 10.0, 5.0 Hz, 1H), 4.28 (dd, *J* = 10.5, 5.0 Hz, 1H), 4.19 (t, *J* = 9.6 Hz, 1H), 4.09 – 4.00 (m, 2H), 3.92 – 3.86 (m, 2H), 3.79 – 3.73 (m, 2H), 3.68 (dd, *J* = 10.3, 8.8 Hz, 2H), 3.59 – 3.35 (m, 10H), 3.33 – 3.25 (m, 1H), 2.22 (td, *J* = 12.4, 4.9 Hz, 1H), 2.04 (qd, *J* = 12.4, 4.9 Hz, 1H), 1.85 – 1.67 (m, 2H), 1.38 (d, *J* = 6.6 Hz, 3H, H-6α), 1.22 (d, *J* = 6.5 Hz, 3H, H-6 β); ¹³C NMR (101 MHz, CDCl₃) δ 138.3, 138.1, 137.6, 137.3, 135.4, 134.6, 131.7, 131.6, 131.0, 130.4, 130.3, 129.8, 129.1, 129.0, 128.6, 128.6, 128.5, 128.5, 128.4, 128.3, 128.3, 128.2, 128.2, 128.0, 127.9, 127.9, 127.8, 127.7, 127.3, 127.3, 126.1, 126.1, 124.8, 102.1 (C-1' β), 101.3 (CHPh β), 101.2 (CHPh α), 99.7 (C-1' α), 83.1, 81.7, 79.2, 78.0, 77.3, 77.2, 76.8, 75.5, 75.2, 75.0, 74.9, 74.5, 70.3, 70.0, 68.9, 68.7, 66.5, 66.1, 65.9, 63.9, 63.9, 62.8, 27.0, 26.4, 17.8; HRMS: [M+NH₄]⁺ calcd for C₃₃H₃₇N₃O₇NH₄ 605.29698, found 605.29626.

Disaccharide 57A

Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **A** and acceptor **57**, with the exceptions that 2,4,6-Tri-*tert*-butylpyridine was used instead of TTBP. Yield: 61 mg, 100 μ mol, 100%, α : β = 6:1. Data for the α -

anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.57 – 7.49 (m, 5H, CH_{arom}), 7.48 – 7.31 (m, 15H, CH_{arom}), 5.62 (s, 1H, CHPh), 5.47 (s, 1H, CHPh), 4.99 (d, *J* = 11.2 Hz, 1H, CHH Bn), 4.92 (d, *J* = 11.9 Hz, 1H, CHH Bn), 4.89 (d, *J* = 11.5 Hz, 1H, CHH Bn), 4.82 (d, *J* = 3.9 Hz, 1H, H-1), 4.69 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.44 – 4.36 (m, 2H, 2x CHH glycerol), 4.31 (dd, *J* = 10.2, 4.8 Hz, 1H, H-6), 4.05 (t, *J* = 9.3 Hz, 1H, H-3), 4.00 – 3.87 (m, 2H, H-5, CH Glycerol), 3.86 – 3.73 (m, 3H, H-6, 2x CHH glycerol), 3.68 (t, *J* = 9.4 Hz, 1H, H-4), 3.60 (dd, *J* = 9.4, 3.9 Hz, 1H, H-2); ¹³C NMR (101 MHz, CDCl₃) δ 138.7, 138.1, 137.5, 137.3 (C_q), 129.4, 129.1, 129.0, 128.7, 128.4, 128.4, 128.3, 128.2, 128.1, 128.0, 127.7, 126.1, 126.0, 124.8 (CH_{arom}), 101.3 (CHPh), 101.2 (CHPh), 98.2 (C-1), 82.0 (C-4), 79.2 (C-2), 78.4 (C-3), 75.4, 74.1 (CH₂ Bn), 70.6, 69.5 (CH₂ glycerol), 68.8 (C-6), 67.9 (CH glycerol), 63.0 (C-5); diagnostic peaks for the β-anomer: ¹H NMR (400 MHz, CDCl₃) δ 4.65 (d, *J* = 7.7 Hz, 1H, H-1), 4.49 (ddd, *J* = 10.8, 5.0, 2.1 Hz, 1H, CHH Glycerol); ¹³C NMR (101 MHz, CDCl₃) δ 103.9 (C-1), 81.9, 81.4, 80.9, 75.6, 75.2, 71.1, 69.6, 69.5, 68.7, 66.2; HRMS: [M+NH₄]⁺ calcd for C₃₇H₃₈O₈NH₄ 628.29049, found 628.28946.

Disaccharide 57B

Ph TO O BnO N₃ TO Ph

Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor B and acceptor 57, with the exceptions that 2,4,6-Tri-tertbutylpyridine was used instead of TTBP. Yield: 55 mg, 100 μ mol, 100%, α : β = 2.9:1. Data for the a-anomer: ¹H NMR (400 MHz, CDCl₃) & 7.52 - 7.44 (m, 3H, CH_{arom}), 7.42 - 7.29 (m, 12H, CH_{arom}), 5.59 (s, 1H, CHPh), 5.42 (s, 1H, CHPh), 5.00 (d, *J* = 3.7 Hz, 1H, H-1), 4.97 (d, *J* = 11.0 Hz, 1H, CHH Bn), 4.80 (d, J = 11.0 Hz, 1H, CHH Bn), 4.44 – 4.37 (m, 2H, 2x CHH glycerol), 4.28 (dd, J = 10.3, 4.8 Hz, 1H, H-6), 4.04 (dd, J = 9.9, 9.2 Hz, 1H, H-3), 4.01 - 3.94 (m, 1H, CH)glycerol), 3.90 (td, J = 9.9, 4.6 Hz, 1H, H-5), 3.80 - 3.70 (m, 4H, H-4, H-6, 2x CHH glycerol), 3.35 (dd, J = 10.0, 3.8 Hz, 1H, H-2); ¹³C NMR (101 MHz, CDCl₃) δ 137.8, 137.4, 137.1, 129.2 (C_q), 128.6, 128.4, 128.3, 128.1, 126.2, 126.1, 126.0 (CH_{arom}), 101.5, 101.4 (CHPh), 98.9 (C-1), 82.6 (C-1 4), 75.8 (C-3), 75.2 (CH₂ Bn), 70.5, 69.3 (CH₂ glycerol), 68.7 (C-6), 68.6 (CH glycerol), 63.4 (C-5), 62.8 (C-2); diagnostic peaks for the β -anomer: ¹H NMR (400 MHz, CDCl₃) δ 5.56 (s, 1H, CHPh), 5.41 (s, 1H, CHPh), 4.91 (d, J = 11.3 Hz, 1H, CHH Bn), 3.53 (t, J = 9.3 Hz, 1H), 3.40 (dd, J = 9.5, 8.0 Hz, 1H, H-2); ¹³C NMR (101 MHz, CDCl₃) δ 102.5 (C-1), 101.4 (CHPh), 101.3 (CHPh), 81.4, 78.8, 75.1, 70.9, 70.3, 69.7, 68.5, 66.4, 66.1, 65.0; HRMS: [M+NH₄]⁺ calcd for C₃₀H₃₁N₃O₇NH₄ 563.25003, found 563.24913.

Disaccharide 58A



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **A** and acceptor **58**, with the exceptions that 2,4,6-Tri-*tert*-butylpyridine was used instead of TTBP. Yield: 48 mg, 79 µmol, 79%, $\alpha:\beta = 1.6:1$. Data reported for a 2:1 mixture of anomers: ¹H NMR (400 MHz, CDCl₃) δ 7.55 – 7.46 (m, 20H), 7.41 – 7.24 (m, 40H), 5.58 (s, 1H, CHPh β), 5.57 (s, 2H, CHPh α), 5.57 (s, 1H, CHPh β), 5.56 (s, 2H, CHPh α), 5.16 (d, *J* = 10.6 Hz, 1H, CHH Bn β), 5.07 (d, *J* = 3.8 Hz, 2H, H-1 α), 4.92 (d, *J* = 11.3 Hz, 1H), 4.86 –

4.82 (m, 5H), 4.79 (d, *J* = 10.7 Hz, 1H, CH*H* Bnβ), 4.71 (d, *J* = 11.8 Hz, 2H), 4.38 (d, *J* = 12.1 Hz, 6H, 2x C*H*H glycerolaβ), 4.32 (dd, *J* = 10.5, 5.0 Hz, 1H), 4.26 – 4.12 (m, 7H), 4.11 – 4.01 (m, 6H), 3.82 – 3.68 (m, 7H), 3.67 – 3.58 (m, 5H), 3.53 (d, *J* = 1.6 Hz, 2H, CH glycerola), 3.39 (dt, *J* = 9.8, 4.9 Hz, 1H, H-5β); ¹³C NMR (101 MHz, CDCl₃) δ 139.0, 138.6, 138.4, 138.2, 137.6, 137.4, 135.4, 134.6, 131.6, 131.0, 130.4, 130.3, 129.1, 129.0, 129.0, 128.6, 128.5, 128.4, 128.4, 128.3, 128.3, 128.1, 128.0, 128.0, 127.8, 127.7, 127.6, 126.4, 126.3, 126.2, 126.1, 102.5 (C-1β), 101.6 (CHPha), 101.4 (CHPhβ), 101.4 (CHPhβ), 101.2 (CHPhβ), 96.8 (C-1a), 82.3, 81.8, 81.3, 80.9, 79.5, 78.5, 75.4, 75.4, 75.3, 73.0, 70.8, 70.1, 70.0, 69.6, 69.1, 68.8, 68.3, 68.1, 66.2, 62.9; HRMS: $[M+NH_4]^+$ calcd for $C_{37}H_{38}O_8NH_4$ 628.29049, found 628.28956.

Disaccharide 58B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor **58**, with the exceptions that 2,4,6-Tri-*tert*-butylpyridine was used instead of TTBP. Yield: 17 mg, 31 µmol, 31%, $\alpha:\beta = 1:3$. Data for the β -anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.52 – 7.44 (m, 5H, CH_{arom}), 7.43 – 7.29 (m, 10H, CH_{arom}), 5.57 (s, 1H, CHPh), 5.42 (s, 1H, CHPh), 4.91 (d, *J* = 11.3 Hz, 1H, CHH Bn), 4.79 (d, *J* = 11.3 Hz, 1H, CHH Bn), 4.45 (d, *J* = 8.0 Hz, 1H, C-1), 4.40 (dd, *J* = 11.3, 5.2 Hz, 2H, 2x CHH glycerol), 4.33 (dd, *J* = 10.5, 5.0 Hz, 1H, H-6), 4.05 – 3.99 (m, 1H, CH glycerol), 3.83 – 3.65 (m, 4H, H-4, H-6, 2x CHH glycerol), 3.54 (t, *J* = 9.3 Hz, 1H, H-3), 3.44 – 3.36 (m, 2H, H-2, H-5); ¹³C NMR (101 MHz, CDCl₃) δ 137.8, 137.5, 137.1 (C_q), 129.3, 128.5, 128.5, 128.4, 128.1, 126.2, 126.1 (CH_{arom}), 102.5 (C-1), 101.5, 101.4 (CHPh), 81.5 (C-4), 78.8 (C-3), 75.1 (CH₂ Bn), 72.0 (CH₂ glycerol), 69.5 (CH glycerol), 68.6 (C-6), 66.8, 66.1 (C-2, C-5); diagnostic peaks for the α-anomer: ¹H NMR (400 MHz, CDCl₃) δ 5.60 (s, 1H, CHPh), 5.43 (s, 1H, CHPh), 5.02 (d, *J* = 3.7 Hz, 1H, H-1), 4.97 (d, *J* = 11.0 Hz, 1H), 4.29 (dd, *J* = 10.3, 4.8 Hz, 1H), 3.90 (td, *J* = 9.9, 4.7 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 101.5 (CHPh), 99.0 (C-1), 82.7, 75.8, 75.2, 70.6, 69.4, 68.8, 68.7, 63.4, 62.8; HRMS: [M+NH₄]⁺ calcd for C₃₀H₃₁N₃O₇NH₄ 563.25003, found 563.24936.

Disaccharide 59A



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **A** and acceptor **59**, with the exceptions that 2,4,6-Tri-*tert*-butylpyridine was used instead of TTBP. Yield: 54 mg, 96 µmol, 96% α : β = 1:1. Data reported for a 1:1 mixture: ¹H NMR (400 MHz, CDCl₃) δ 7.61 – 7.48 (m, 8H), 7.47 – 7.30 (m, 28H), 5.60 – 5.59 (m, 2H, CHPha β), 5.01 – 4.93 (m, 3H), 4.88 (dd, *J* = 12.2, 7.6 Hz, 3H), 4.83 – 4.79 (m, 2H, H-1 α , CH*H* Bn), 4.68 (d, *J* = 12.0 Hz, 1H), 4.60 (d, *J* = 7.7 Hz, 1H, H-1 β), 4.35 (dd, *J* = 10.5, 5.0 Hz, 1H), 4.27 (dd, *J* = 10.2, 4.9 Hz, 1H), 4.12 – 4.04 (m, 2H), 4.03 – 3.93 (m, 3H), 3.92 – 3.83 (m, 6H), 3.82 – 3.69 (m, 5H), 3.65 (t, *J* = 9.4 Hz, 1H), 3.59 (dd, *J* = 9.4, 3.9 Hz, 1H, H-2 α), 3.55 – 3.50 (m, 1H),
3.43 (td, J = 9.9, 5.0 Hz, 1H), 1.51 (s, 3H), 1.49 (s, 3H), 1.46 (s, 3H), 1.44 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 138.8, 138.5, 138.3, 138.2, 137.4, 137.3, 135.3, 134.6, 131.8, 131.7, 131.6, 131.1, 131.0, 130.4, 130.3, 129.1, 129.0, 128.6, 128.5, 128.4, 128.3, 128.1, 128.0, 127.9, 127.7, 127.7, 126.1, 126.1, 103.4 (C-1 β), 101.3, 101.2 (CHPha, CHPh β) 98.3, 98.3 (C_q isopropylidene α , C_q isopropylidene β), 97.9 (C-1 α), 82.1, 81.9, 81.4, 80.9, 79.3, 78.5, 75.6, 75.4, 75.2, 73.9, 71.0, 69.5, 68.9, 68.8, 66.2, 63.9, 63.5, 62.9, 62.4, 62.1, 26.4, 24.3, 23.1, 21.0.; HRMS: [M+NH₄]⁺ calcd for C₃₃H₃₈O₈NH₄ 580.29049, found 580.29002

Disaccharide 59B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor 59, with the exceptions that 2,4,6-Tri-tertbutylpyridine was used instead of TTBP. Yield: 50 mg, 100 μ mol, 100% α : β = 1:10. Data for the β anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.75 - 7.66 (m, 3H, CH_{arom}), 7.55 - 7.52 (m, 1H, CH_{arom}), 7.47 (qd, J = 5.7, 4.9, 2.3 Hz, 3H, CH_{arom}), 7.42 – 7.26 (m, 10H, CH_{arom}), 5.56 (s, 1H, CHPh), 4.90 (d, J = 11.3 Hz, 1H, CHH Bn), 4.79 (d, J = 11.3 Hz, 1H, CHH Bn), 4.42 (d, J = 7.8 Hz, 1H, H-1), 4.30 (dd, J = 10.5, 5.0 Hz, 1H, H-6), 4.05 - 3.94 (m, 2H, 2x CHH Glycerol), 3.85 - 3.74 (m, 4H, H-6, CH glycerol, 2x CHH glycerol), 3.69 (t, J = 9.1 Hz, 1H, H-4), 3.53 (t, J = 9.2 Hz, 1H, H-3), 3.45 (dd, J = 9.5, 7.9 Hz, 1H, H-2), 3.37 (td, J = 9.8, 5.0 Hz, 1H, H-5), 1.46 (s, 3H, CH₃ isopropylidene), 1.40 (s, 3H, CH₃ isopropylidene); ¹³C NMR (101 MHz, CDCl₃) δ 137.8, 137.1 (C_q), 135.3, 134.6, 131.7, 131.6, 131.0, 130.4, 129.2, 128.5, 128.4, 128.4, 128.3, 128.0, 126.1 (CH_{arom}), 102.2 (C-1), 101.4 (CHPh), 98.4 (C_q isopropylidene), 81.4 (C-4), 78.9 (C-3), 75.0 (CH₂ Bn), 71.4 (CH glycerol), 68.6 (C-6), 66.3 (C-5), 66.1 (C-2), 63.7, 62.2 (CH₂ glycerol), 25.2, 22.0 (CH₃ isopropylidene); diagnostic peaks for the α -anomer: ¹H NMR (400 MHz, CDCl₃) δ 5.62 (s, 1H, CHPh), 5.03 – 4.98 (m, 2H, H-1, CHH Bn), 4.16 (dd, J = 10.0, 9.1 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 101.5 (CHPh), 98.4 (C-1), 84.5, 75.9, 69.9, 63.2, 62.8, 24.2, 23.3.; HRMS: [M+NH₄]⁺ calcd for C₂₆H₃₁N₃O₇NH₄ 515.25003, found 515.24996.

Disaccharide 60A



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **A** and acceptor **60**, with the exceptions that 2,4,6-Tri-*tert*-butylpyridine was used instead of TTBP and that the acceptor was added neat, rather than in solution. Yield: 53 mg, 97 µmol, 97%, α : β >20:1. ¹H NMR (400 MHz, CDCl₃) δ 7.49 (dd, *J* = 7.5, 2.1 Hz, 2H, CH_{arom}), 7.42 – 7.26 (m, 13H, CH_{arom}), 5.54 (s, 1H, CHPh), 4.91 (d, *J* = 11.2 Hz, 1H, CHH Bn), 4.86 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.84 – 4.79 (m, 2H, H-1, CHH Bn), 4.61 (d, *J* = 12.0

Hz, 1H, CH*H* Bn), 4.49 – 4.45 (m, 2H, 2x C*H*H glycerol), 4.41 (t, J = 2.8 Hz, 2H, 2x CH*H* glycerol), 4.23 (dd, J = 10.2, 4.8 Hz, 1H, H-6), 4.04 (t, J = 9.3 Hz, 1H, H-3), 3.95 (p, J = 2.8 Hz, 1H, CH glycerol), 3.85 (td, J = 10.0, 4.8 Hz, 1H, H-5), 3.69 (t, J = 10.3 Hz, 1H, H-6), 3.65 – 3.60 (m, 1H, H-4), 3.60 – 3.57 (m, 1H, H-2); ¹³C NMR (101 MHz, CDCl₃) δ 147.6 (C=O), 138.6, 138.3, 137.2 (C_q), 129.1, 128.7, 128.4, 128.3, 128.2, 128.1, 127.8, 126.1 (CH_{arom}), 101.4 (CHPh), 97.7 (C-1), 81.9 (C-4), 79.2 (C-2), 78.2 (C-3), 75.5, 74.1 (CH₂ Bn), 70.6, 69.1 (CH₂ glycerol), 68.8 (C-6), 66.2 (CH glycerol), 63.5 (C-5); HRMS: [M+NH₄]⁺ calcd for C₃₁H₃₂O₉NH₄ 566.23846, found 566.23774.

Disaccharide 60B



Title compound was obtained as colourless oil via the general procedure for Ph₂SO/Tf₂O mediated glycosylations with donor **B** and acceptor **60**, with the exceptions that 2,4,6-Tri-*tert*-butylpyridine was used instead of TTBP and that the acceptor was added neat, rather than in solution. Yield: 48 mg, 99 µmol, 99%, α : β >20:1. ¹H NMR (400 MHz, CDCl₃) δ 7.49 (dd, *J* = 7.3, 2.3 Hz, 2H, CH_{arom}), 7.43 – 7.28 (m, 8H, CH_{arom}), 5.57 (s, 1H, CHPh), 5.05 (d, *J* = 3.8 Hz, 1H, H-1), 4.96 (d, *J* = 10.9 Hz, 1H, CHH Bn), 4.79 (d, *J* = 10.9 Hz, 1H, CHH Bn), 4.51 (d, *J* = 2.4 Hz, 4H, 2x CH₂ glycerol), 4.27 (dd, *J* = 10.3, 4.9 Hz, 1H, H-6), 4.15 – 4.05 (m, 2H, H-3, CH glycerol), 3.94 (td, *J* = 9.9, 4.8 Hz, 1H, H-5), 3.78 – 3.69 (m, 2H, H-4, H-6), 3.42 (dd, *J* = 10.1, 3.8 Hz, 1H, H-2); ¹³C NMR (101 MHz, CDCl₃) δ 147.4 (C=O), 137.7, 137.0 (C_q), 129.3, 128.6, 128.4, 128.3, 128.1, 126.1 (CH_{arom}), 101.6 (CHPh), 98.5 (C-1), 82.5 (C-4), 75.8 (C-3), 75.3 (CH₂ Bn), 70.3, 69.9 (CH₂ glycerol), 68.6 (C-6), 67.2 (CH glycerol), 63.9 (C-5), 62.6 (C-2); HRMS: [M+NH₄]⁺ calcd for C₂₄H₂₅N₃O₈NH₄ 501.19799, found 501.19736.

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5

Chapter 5: Influence of N-protecting groups on the reactivity of glycosyl acceptors

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Results from this chapter are published in

Chemical Science, 2023, 14, 1532-1542

Introduction

2-Deoxy-2-aminosugars are important constituents of many biologically relevant carbohydrates and glycoconjugates, such as the glycosaminoglycans,^{1, 2} various cell surface carbohydrate antigens, such as the blood group determinants, bacterial oligosaccharides,^{3, 4} including pathogenic bacteria such as *Acinetobacter Baumannii*, an opportunistic pathogen with high rates of antibiotic resistance⁵ or *Vibrio vulnificus*, a bacterium that causes sepsis and necrotizing fasciitis, related to *Vibrio cholera*, the causative agent of cholera⁶ as well as in many secondary metabolites.⁷ (*Figure 1*). Many different aminosugars are found in nature, varying in the position on the carbohydrate ring (with a C-2-amino group occurring most often), the stereochemistry, as well as the nature of the substituent on the amine, which can be an *N*-alkyl, *N*-acyl/acetyl, *N*-sulfate, *N*-phosphate group. Non-substituted amines also commonly occur.



Figure 1: Representative structures of glycosaminoglycans (Heparin), carbohydrate antigens (sialyl Lewis X) and bacterial oligosaccharides (A. Baumannii and V. vulnificus) containing deoxy-amino sugars.

Because of their biological relevance, many 2-deoxy-2-aminosugar containing oligosaccharides have been synthesised to date.^{8, 9} To mask the amino group in the building blocks different types of protecting groups have been used. The *N*-protecting group in the donor glycoside is primarily selected based on the type of glycosidic linkage that has to be constructed. To install *cis*-glycosidic linkages, an azide on C-2 is by far the most commonly applied (and indeed almost solely used), while the construction of *trans*-linkages can be controlled by the use carbamate functionalities of amide groups. The previous chapter has shown that the nature of the functional groups on the carbohydrate ring also critically influence the nucleophilicity of the alcohol

function in the acceptor. A systematic series of 60 ether and ester protected acceptors was tested and showed that the reactivity of the acceptor is dependent on both the configuration and the protecting group pattern of the acceptor: equatorial alcohols in acceptors are more reactive than axial alcohols. Also, the configuration of the protected alcohols next to the OH-group are important, and acceptors in which the neighbouring protected alcohols take up an equatorial position, are more reactive than acceptors in which one of the flanking protected alcohols is axial. With regard to protecting group patterns, benzoyl protected acceptors are less reactive than benzyl protected acceptors. It is important to note that the configuration of the ester is also important, and substituting an axial ether for an ester has significantly less effect on the reactivity of the acceptor than substituting an equatorial ether for an ester.

It has long been recognized that the nature of the N-protecting group can have a significant effect on the reactivity of the aminosugar alcohol acceptor, although systematic investigations are relatively scarse.¹⁰ A prime example is presented by the Nacetyl glucosamine C-4-OH, which is a notoriously difficult acceptor to glycosylate.¹¹⁻¹⁶ Through a systematic survey Crich and Dudkin determined that intramolecular hydrogen bonding by the acetamide functionality was a prime factor in reducing the reactivity of the C-4-OH. Through the use of different N-protecting groups (a phthalimide or azide) the reactivity of the GlcN-C-4-OH could be effectively enhanced. This chapter describes the influence of three different N-protecting groups on the reactivity of glycosyl alcohol nucleophiles: an azide, a trifluoroacetyl (TFA) and trichloroacetyl (TCA) group, as these are amongst the most commonly employed Nprotecting groups.¹⁷⁻¹⁹ The influence of these protecting groups on the reactivity of the acceptor is investigated for both the C-3-OH and C-4-OH glucosamine acceptors. To investigate whether the orientation of the N-protecting groups is important for its effect on the reactivity of the acceptor, just like in the O-protecting groups in ether/ester protected acceptors, both glucosamine and mannosamine acceptors are probed.

The method used for measuring the reactivity of the acceptors is based on the stereoselectivity observed in glycosylation reactions with phenyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-1-thio- β -D-glucopyranoside (**Donor A**, *Figure 2A*) and phenyl 2-deoxy-2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-1-thio- β -D-glucopyranoside (**Donor B**). As described before, the stereoselectivity of glycosylation reactions of these is a measure for the reactivity of the acceptor.²⁰ More nucleophilic acceptors, provide β -selective glycosylations, while less nucleophilic acceptors lead to α -selectivity. The mechanism to explain the change in stereoselectivity is shown in *Figure 2*. Both thioglycoside donors form an α -triflate upon activation with Ph₂SO and Tf₂O. The more reactive acceptors react with the corresponding β -triflate or an oxocarbenium ion-like species to form the α -product.²¹ **Donor B** shows higher β -selectivity with the same acceptor than **Donor A**

because the electron-withdrawing azide on C-2 stabilises the anomeric triflate rendering the $S_N 2$ substitution of the α -triflate more predominant.²²



This work: structure-reactivity relations of azide and amide protected acceptors

Figure 2: A: Glycosylation mechanisms and the relation between stereoselectivity of **donor** A and **Donor** B and nucleophilicity of the acceptor, B: the reactivity trends found in chapter 4 and C: the structure-reactivity relations investigated in this work.

Results and discussion

In this study, 12 acceptors that can be divided in four groups based on the type of 2deoxy-2-aminosugar and the position of the hydroxyl function, were reacted with **Donor A** and **Donor B**: 1) glucosamine C-3-OH acceptors **1c-1e**; 2) glucosamine C-4-OH acceptors **2b-2d**; 3) mannosamine C-3-OH acceptors **3c-3e** and 4) mannosamine C-4-OH acceptors **2b-2d**. The results are summarized in *table 1*, in which also the results of the corresponding glucose and mannose acceptors **1a**, **1b**, **2a**, **3a**, **3b** and **4a** are provided a reference (see Chapter 4). When looking at the results of the glucosamine C-3-OH acceptors, it becomes apparent that the nature of the protecting group next to the alcohol has a significant influence its reactivity. An azide flanking the free hydroxy group decreases the reactivity of the acceptor **1a-1c**). The trichloroand trifluoroacetamides next to the alcohol decrease the reactivity of the acceptor even more, with the disarming effect of the trifluoroacetamide being stronger than that of the trichloroacetamide (acceptors 1d and 1e). Note how switching an O-benzyl group to a N-trifuoroacetyl group completely reverses the stereoselectivity of the acceptor, with acceptor 1a giving full β -selectivity with **Donor B**, while acceptor 1d gives nearly full α -selectivity with **Donor B**. On the other hand, the nature of the N-protecting group has an almost negligible effect on the reactivity of the C-4-OH glucose acceptors. All tested C-4-OH acceptors tested in this work provide high yielding glycosylations with very similar stereoselectivity with both Donor A and Donor B, regardless of the nature of the group on C-2 being an O-benzyl, an azide, a N-trifluoroacetamide or a Ntrichloroacetamide (acceptors 2a-2d). The results in the C-3-OH mannosamine series, show that, in line with the survey on O-protecting groups, not only the nature of the Nprotecting groups is important, but also the configuration of the N-functional group next to the acceptor alcohol is relevant for the reactivity of the acceptor. Similar to the differences in reactivity observed between glucose and mannose (acceptors 1a and 3a), where the alcohol next to an axial benzyl group is less reactive than the alcohol next to the equatorial one, the acceptor next to the equatorial azide (acceptor 1a) is more reactive than the acceptor next to the axial azide (acceptor 3a). Furthermore, in line with the reactivity of benzoylated glucose/galactose/mannose systems of the previous chapter, it turns out that the difference in reactivity between an axial benzyl group and an axial azide is less than the difference between an equatorial benzyl group and the corresponding azide (acceptor 1a vs 1c and acceptor 3a vs 3c). Similarly, there is little difference between the axial azide and the axial N-trifluoroacetyl or N-trichloroacetyl groups (acceptors 3c-3e) in contrast to the different effects when these groups are flanking the nucleophilic hydroxy group in an equatorial orientation (acceptor 1c-1e). It is noteworthy however, that in acceptors 3c-3e the N-trifluoroacetyl protected acceptor (3d) seems to be more reactive than N-trichloroacetyl protected acceptor 3e, which is more reactive than azide acceptor 3c. Finally, the nature of the protecting group has very little effect on the reactivity of the mannosamine C-4-OH acceptors. In line with the glucose/glucosamine series above, the mannose C-4-OH is not strongly effected by the nature of the function group at C-2. Whether it is an O-benzyl, an azide, *N*-trifluoroacetamide *N*-trichloroacetamide (acceptors or а 4a-4d) а the stereoselectivity with both Donor A and Donor B is all very similar, and all glycosylations are high yielding.

Position	Acceptor	Donor A		Donor B	
		Product (yield)	α:β	Product (yield)	α:β
3-OH glucose BnO HO HO XOMe	1a X = OBn	1aA (78%)	1:2.7	1aB (70%)	<1:20
	$\mathbf{1b} \mathbf{X} = \mathbf{OBz}$	1bA (99%)	1.8:1	1bB (93%)	1:4
	$1c X = N_3$	1cA (83%)	1.6:1	1cB (85%)	1:2.5
	1d X = NHTFA	1dA (96%)	>20:1	1dB (100%)	12:1
	1e X = NHTCA	1eA (65%)	11:1	1eB (63%)	3:1
4-OH glucose BnO O BnO X OMe	2a X = OBn	2aA (82%)	1:1	2aB (88%)	1:7
	2b $X = N_3$	2bA (94%)	1:1.1	2bB (100%)	1:3.3
	2c X = NHTFA	2cA (82%)	1.3:1	2cB (100%)	1:2.5
	2d X = NHTCA	2dA (81%)	1.1:1	2dB (100%)	1:3.5
3-OH mannose	3a X = OBn	3aA (82%)	8:1	3aB (70%)	1.1:1
	3b X = OBz	3bA (82%)	10:1	3bB (93%)	1:1
	$3c X = N_3$	3cA (100%)	7:1	3cB (75%)	1.8:1
	3d X = NHTFA	3dA (80%)	2.3:1	3dB (92%)	1:1.2
	3e X = NHTCA	3eA (57%)	5:1	3eB (80%)	1:1
4-OH mannose	4a X = OBn	4aA (76%)	1:2	4aB (72%)	<1:20
BnO X HO DO BnO	$\mathbf{4b} X = N_3$	4bA (100%)	1:2.5	4bB (100%)	1:14
	4c X = NHTFA	4cA (71%)	1:1.4	4cB (77%)	1:10
OMe	4d X = NHTCA	4dA (77%)	1:2.7	4dB (100%)	<1:20

Table 1: Results of glucosamine and mannosamine acceptors with different protecting groups. The results for glucose and mannose acceptors are given for reference

Conclusion

In conclusion, structure-reactivity relationships for a set of glycosyl acceptors with different *N*-protecting groups have been established, based on the stereoselectivity of these acceptors in glycosylations with two conformationally restricted glucosyl donors. Three different *N*-protecting groups were used in this study: an azide, a trifluoroacetamide and a trichloroacetamide group. These were surveyed on the 2-position of both glucosamine and mannosamine acceptors, to investigate the difference between equatorially and axially oriented *N*-functional groups, as it was found previously that the orientation of the flanking *O*-functional groups has a large influence on the reactivity of the acceptor alcohol. Both the C-3-OH and C-4-OH acceptors in the glucosamine and mannosamine series were investigated. The orientation of the *N*-protecting group proved to be important for its effect on the reactivity of the acceptor. It was found that, in line with the previsouly studied ether/ester protected acceptors, the influence of the protecting group on the reactivity is much larger when the group

next to the alcohol is equatorial then when it is placed axial. The nature of the protecting group is also important for the reactivity with the disarming effect of an azide being similar to that of an benzoyl ester and the trichloroacetamide and trifluoroacetamide group having an larger influence on the reactivity. The difference in reactivity between the mannosamine acceptor having either an axial azide or amide is smaller with the *N*-trifluoroacetamide mannosamine C-3-OH being the most reactive in the series. The different *N*-protecting groups do not significantly influence the reactivity of the glucosamine and mannosamine C-4-OH acceptors. Overall this study has shown that the reactivity of glycosamine acceptors can be tuned by the changing the nature of the *N*-protecting group, if this is suitable positioned. The effects observed in this study can likely be transposed to galactosamine and fucosamine systems and aid in the assembly of bacterial glycans.^{23, 24}

Experimental

General experimental procedures

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 (Tf₂O) was distilled over P₂O₅ and stored at -20°C under a nitrogen atmosphere. 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 F254, Merck) with UV detection by (254 nm) and by spraving with 20% sulfuric acid in ethanol or by spraying with a solution of (NH₄)₆Mo₇O₂₄·H₂O (25 g/L) and (NH₄)₄Ce(SO4)₄·2H₂O (10 g/L) in 10% aq. sulfuric acid followed by charring at ±250 °C. Highresolution 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. 1H and 13C NMR spectra were recorded on Bruker AV-400, Bruker DMX-400, and Bruker AV-500 NMR instruments. Chemical shifts (δ) are given in parts per million (ppm) relative to tetramethylsilane as an internal standard or the residual signal of the deuterated solvent. Coupling constants (1) are given in Hertz (Hz). All presented 13C-APT spectra are proton-decoupled. NMR peak assignments were made using COSY and HSQC. When necessary, additional NOESY, HMBC and HMBC-GATED 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 1H 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.

General procedure I: Ph₂SO/Tf₂O meditated glycosylations

Donor (0.1 mmol, 1 eq), Ph₂SO (0.13 mmol, 1.3 eq) and TTBP (0.25 mmol, 2.5 eq) were coevaporated twice with toluene, dissolved in 2 mL DCM and stirred for 30 min at RT with 3A molecular sieves. The solution was cooled to -80 °C and Tf₂O (22 μ L, 0.13 mmol, 2 eq) 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 eq) in DCM (0.4 mL, 0.5 M) was added. The reaction mixture was allowed to warm to -40 °C for and stirred between 4-24 hr at that temperature. The reaction was quenched with 1 mL sat aq NaHCO₃, 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 MgSO4, filtered, and concentrated in vacuo. Purification by silica gel flash column chromatography and/or sephadex LH-20 size-exclusion chromatography yielded the glycosylation product as a mixture of anomers.

General procedure II: azide reduction

The azide (1 eq) was dissolved in anhydrous THF, after which LiAlH₄ (1.5 eq, soln in Et₂O, THF or 2-MeTHF) was added dropwise while gaseous by-products were allowed to escape. After full conversion, the reaction mixture was cooled to 0 °C, and excess reagents were destroyed by careful and dropwise addition of water. The precipitated aluminium salts were filtered off and the solution was concentrated under reduced pressure. The residue was purified over silica or used directly in subsequent reactions.

General procedure III: TFA installation

The amine (1 eq) was dissolved in DCM, after which TEA (1.5 eq) and TFAA (1.5 eq) were added. After TLC indicates full conversion, the reaction mixture was diluted with DCM and washed with water. The organic phase was dried with $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica chromatography to yield the title compound.

General procedure IV: TCA installation

The amine (1 eq) was dissolved in DCM, after which TEA (1.5 eq) and trichloroacetyl chloride (1.5 eq) were added. After TLC indicates full conversion, the reaction mixture was diluted with DCM and washed with water. The organic phase was dried with MgSO₄ and concentrated under reduced pressure. The residue was purified by silica chromatography to yield the title compound.

General procedure V: DDQ mediated Nap deprotection

Nap protected acceptor (1 eq) was dissolved in 9:1 DCM/H₂O with DDQ (2 eq). After After TLC indicates full conversion, the reaction mixture was diluted with DCM and washed twice with sat. aq. NaHCO₃. The organic phase was dried with MgSO₄ and concentrated under reduced pressure. The residue was purified by silica chromatography to yield the title compound.

General procedure VI: reductive benzylidene opening

The benzylidene (1 eq) was dissolved in DCM and cooled to 0 °C, after which triethylsilane (10 eq) and TFA (10 eq) were added. After TLC indicates full conversion, the reaction mixture was quenched with sat. aq. NaHCO₃ and extracted twice with DCM. Combined organic phases were washed with sat .aq NaHCO₃. The organic phase was dried with MgSO₄ and concentrated under reduced pressure. The residue was purified by silica chromatography to yield the title compound.

Preparations of acceptors



Scheme S1: preparation of α -OMe glucosazide intermediates: reagents and conditions: a) i: amberlite-H⁺, methanol, reflux, ii: Ba(OH)₂, water, reflux, iii: Imidazole-1-sulfonyl azide-H₂SO₄, K₂CO₃, CuSO₄(H₂O)₅, methanol, iv: Ac₂O, pyridine, DMAP, 65% over 4 steps; b) i: Na, methanol, ii: PTSA, PhCH(OMe)₂, acetonitrile, 60 °C, 300 mbar, 71% over 2 steps; c) recrystallization from acetone/pentane; d) for **S4**: BnBr, NaH, DMF, 87%, e) for **S5**: NapBr, NaH, DMF, 88%; f) i: PTSA, methanol, 50 °C, ii: BnBr, NaH, DMF, 100% over 2 steps

Methyl 2-deoxy-2-azido-3,4,6-tri-O-acetyl-α,β-D-glucopyranoside (S2)

N-acetylglucosamine (S1, 30 g, 136 mmol) was dissolved in 700 mL methanol with 50 g amberlite-H⁺ and heated to a reflux overnight, after which the reaction mixture was filtered and concentrated under reduced pressure. The residue was dissolved in 1 L water with 50 g BaOH(H₂O)₈. After overnight reflux, the reaction mixture was cooled to RT and neutralised with dry ice (pH 7). Salts were removed by filtration and the solution was concentrated under reduced pressure. The residue was dissolved in methanol with K₂CO₃ (47 g, 340 mmol, 2.5 eq) and imidazole-1-sulfonyl azide hydrogen sulfate²⁵ (42,1 g, 163 mmol, 1.2 eq) and $CuSO_4(H_2O)_5$ (340 mg, 1.36 mmol, 0.01 eq). When TLC (EA/MeOH/H₂O 8:1:1, Rf = 0.6) shows a single spot, the reaction mixture was concentrated and dissolved in pyridine (274 mL, 3.4 mol, 25 eq). The solution was cooled to 0 °C and Ac₂O (103 mL, 1.08 mol, 8 eq) and DMAP (1.66 g, 13.6 mmol, 0.1 eq) were added. The reaction mixture was allowed to warm to RT overnight and concentrated. The residue was dissolved in ethyl acetate and washed with 1M HCl and sat. aq. NaHCO₃. The organic phase was dried with MgSO₄ and concentrated under reduced pressure, yielding the title compound as a red oil. Yield: 30.6 g, 89 mmol, 65%, α : β = 10:1. Data for the α anomer: ¹H NMR (400 MHz, CDCl₃) δ 5.48 (dd, *J* = 10.6, 9.2 Hz, 1H, H-3), 5.05 (dd, *J* = 10.2, 9.2 Hz, 1H, H-4), 4.88 (d, J = 3.5 Hz, 1H, H-1), 4.29 (dd, J = 12.4, 4.6 Hz, 1H, H-6), 4.10 (dd, J = 12.4, 2.3 Hz, 1H, H-6), 4.01 (ddd, J = 10.1, 4.6, 2.3 Hz, 1H, H-5), 3.47 (s, 3H, CH₃ OMe), 3.38 (dd, J = 10.6, 3.5 Hz, 1H, H-2), 2.10 (s, 3H, CH₃ Ac), 2.09 (s, 3H, CH₃ Ac), 2.04 (s, 3H, CH₃ Ac); ¹³C NMR (101 MHz, CDCl₃) δ 170.7, 170.1, 169.8 (C=O), 98.8 (C-1), 70.6 (C-3), 68.6 (C-4), 67.6 (C-5), 62.0 (C-6), 61.1 (C-2), 55.7 (CH₃ OMe), 20.8, 20.8, 20.7 (CH₃ Ac). Spectra in agreement with literature.²⁶

Methyl 2-deoxy-2-azido-4,6-O-benzylidene-a-D-glucopyranoside (S3)



Compound **S2** (30.7 g, 89.0 mmol) was dissolved in MeOH, and a catalytic amount of sodium was added. When TLC shows full deacetylation, the reaction mixture was acidified (pH = 5) using amberlite-H⁺, filtered, concentrated and coevaporated twice with toluene. The residue was dissolved in acetonitrile with PTSA-H₂O (1.69 g, 8.90 mmol, 0.1 eq) and benzaldehyde dimethyl acetal (18.8 mL, 125 mmol, 1.4 eq) and heated to 60 °C at 300 mbar. After full conversion, the reaction mixture was quenched with Et₃N (1.88 mL, 13.4 mL, 0.15 eq) and concentrated under reduced pressure. Silica chromatography (10%→20% acectone in pentane) yields the title compound as white solid. Yield: 19.5 g, 63.5 mmol, 71%, $\alpha:\beta$ = 10:1. Recrystallization from acetone/pentane yields 10 g of pure α -anomer as a white solid. ¹H NMR (400 MHz, CDCl₃) δ 7.52 – 7.47 (m, 2H, CH_{arom}), 7.41 – 7.35 (m, 3H, CH_{arom}), 5.52 (s, 1H, CHPh), 4.78 (d, *J* = 3.6 Hz, 1H, H-1), 4.27 (dd, *J* = 10.0, 4.6 Hz, 1H, H-6), 4.16 (ddd, *J* = 10.0, 9.1, 2.8 Hz, 1H, H-3), 3.82 (td, *J* = 9.7, 4.6 Hz, 1H, H-5), 3.73 (t, *J* = 10.2 Hz, 1H, H-6), 3.49 (t, *J* = 9.3 Hz, 1H, H-4), 3.43 (s, 3H, CH₃ OMe), 3.31 (dd, *J* = 10.0, 3.6 Hz, 1H, H-2), 2.93 (d, *J* = 2.9 Hz, 1H, 3-OH); ¹³C NMR (101 MHz, CDCl₃) δ 137.0 (C_q), 129.5, 128.5, 126.4 (CH_{arom}), 102.2 (CHPh), 99.5 (C-1), 81.9 (C-4), 69.2 (C-3), 68.9 (C-6), 63.3 (C-2), 62.3 (C-5), 55.6 (CH₃ OMe). Spectra in agreement with literature.²⁷

Methyl 2-deoxy-2-azido-3-O-benzyl-4,6-O-benzylidene-a-D-glucopyranoside (S4)



Compound **S3** (4.00 g, 13.0 mmol) was dissolved in DMF, after which BnBr (2.32 mL, 19.5 mmol, 1.5 eq) and NaH (60% dispersion in mineral oil, 781 mg, 19.5 mmol, 1.5 eq) were added. After TLC shows full conversion, the reaction mixture was quenched with 5x the volume in water. Precipitated solids were collected by filtration, dissolved in CHCl₃ and washed with water. The organic phase was dried with MgSO₄ and concentrated to yield the title compound as white powder. Yield: 4.52 g, 11.3 mmol, 87%. ¹H NMR (500 MHz, CDCl₃) δ 7.51 – 7.48 (m, 2H, CH_{arom}), 7.38 (ddt, *J* = 7.0, 5.8, 1.0 Hz, 5H, CH_{arom}), 7.34 – 7.27 (m, 3H, CH_{arom}), 5.58 (s, 1H, CHPh), 4.94 (d, *J* = 11.0 Hz, 1H, CHH Bn), 4.80 (d, *J* = 11.1 Hz, 1H, CHH Bn), 4.78 (d, *J* = 3.6 Hz, 1H, H-1), 4.29 (dd, *J* = 10.2, 4.8 Hz, 1H, H-6), 4.06 (dd, *J* = 9.9, 9.0 Hz, 1H, H-3), 3.87 (td, *J* = 9.9, 4.7 Hz, 1H, H-5), 3.76 (t, *J* = 10.3 Hz, 1H, H-6), 3.70 (t, *J* = 9.3 Hz, 1H, H-4), 3.46 – 3.42 (m, 4H, H-2, CH₃ OMe); ¹³C NMR (126 MHz, CDCl₃) δ 137.9, 137.3 (C_q), 129.2, 128.5, 128.4, 128.4, 128.0, 126.1 (CH_{arom}), 101.6 (CHPh), 99.5 (C-1), 82.9 (C-4), 76.5 (C-3), 75.2 (CH₂ Bn), 69.0 (C-6), 63.3 (C-2), 62.7 (C-5), 55.5 (CH₃ OMe). Spectra in agreement with literature.²⁸

Methyl 2-deoxy-2-azido-3-O-(2-naphtyl)methyl-4,6-O-benzylidene-α-D-glucopyranoside (S5)

The title compound was synthesised from **S3** as described for **S4** but 2-(Bromomethyl)naphthalene was used instead of benzyl bromide. Yield: 7.73 g, 17.3 mmol, 88%. ¹H NMR (500 MHz, CDCl₃) δ 7.80 (td, J = 6.0, 5.4, 3.5 Hz, 3H, CH_{arom}), 7.77 – 7.73 (m, 1H, CH_{arom}), 7.53 – 7.48 (m, 3H, CH_{arom}), 7.47 – 7.43 (m, 2H, CH_{arom}), 7.40 (dt, J = 4.6, 2.8 Hz, 3H, CH_{arom}), 5.60 (s, 1H, CHPh), 5.09 (d, J = 11.3 Hz, 1H, CHH Nap), 4.97 (d, J = 11.3 Hz, 1H, CHH Nap), 4.79 (d, J = 3.6 Hz, 1H, H-1), 4.30 (dd, J = 10.2, 4.7 Hz, 1H, H-6), 4.11 (dd, J = 9.9, 9.0 Hz, 1H, H-3), 3.88 (td, J = 9.9, 4.7 Hz, 1H, H-5), 3.80 – 3.71 (m, 2H, H-4, H-6), 3.47 (dd, J = 9.9, 3.6 Hz, 1H, H-2), 3.43 (s, 3H, CH₃ OMe); ¹³C NMR (126 MHz, CDCl₃) δ 137.3, 135.4, 133.4, 133.2 (C_q), 129.2, 128.5, 128.3, 128.1, 127.8, 127.2, 126.3, 126.2, 126.1, 126.0 (CH_{arom}), 101.7 (CHPh), 99.5 (C-1), 82.9 (C-4), 76.5 (C-3), 75.2 (CH₂ Nap), 69.1 (C-6), 63.4 (C-2), 62.7 (C-5), 55.6 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₂₅H₂₅N₃O₅NH₄ 465.21325, found 465.21285

Methyl 2-deoxy-2-azido-4,6-di-O-benzyl-3-O-(2-naphtyl)methyl-α-D-glucopyranoside (S6)



Compound S5 (7.70 g, 17.2 mmol) was dissolved in methanol with PTSA-H₂O (327 mg, 1.72 mmol, 0.1 eq) and heated to 50 °C. After removal of the benzylidene, Et₃N (0.48 mL, 3.44 mmol, 0.2 eq) was added and the reaction mixture was concentrated under reduced pressure. The residue was coevaporated with toluene and dissolved in DMF, after which benzyl bromide (6.13 mL, 51.6 mmol, 3 eq) and sodium hydride (60% dispersion in mineral oil, 2.07 g, 51.6 mmol, 3 eq) were added. After full conversion, the reaction was guenched with water and extracted with diethyl ether. The organic phase was dried with MgSO4 and concentrated. The residue was purified over silica (10% acetone in pentane) to yield the title compound as a colourless oil that slowly solidifies. Yield: 9.29 g, 17.4 mmol, 100%. ¹H NMR (400 MHz, CDCl₃) δ 7.83 - 7.74 (m, 4H, CHarom), 7.51 - 7.43 (m, 3H, CHarom), 7.35 - 7.30 (m, 4H, CHarom), 7.30 - 7.25 (m, 4H, CH_{arom}), 7.14 (dd, J = 6.7, 2.9 Hz, 2H, CH_{arom}), 5.04 (d, J = 10.9 Hz, 1H, CHH Bn/Nap), 4.99 (d, J = 10.9 Hz, 1H, CHH Bn/Nap), 4.87 - 4.78 (m, 2H, H-1, CHH Bn/Nap), 4.63 (d, J = 12.1 Hz, 1H, CHH Bn), 4.56 – 4.47 (m, 2H, 2x CHH Bn/Nap), 4.03 (dd, J = 10.2, 8.6 Hz, 1H, H-3), 3.84 – 3.71 (m, 3H, H-4, H-5, H-6), 3.68 (dd, *J* = 10.6, 1.9 Hz, 1H, H-6), 3.48 (dd, *J* = 10.2, 3.5 Hz, 1H, H-2), 3.42 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 138.1, 137.9, 135.5, 133.4, 133.2 (C_q), 128.5, 128.5, 128.3, 128.1, 128.0, 127.9, 127.8, 127.0, 126.1, 126.1, 126.0 (CH_{arom}), 98.8 (C-1), 80.7 (C-3), 78.3 (C-4), 75.6, 75.1, 73.7 (CH₂ Bn/Nap), 70.7 (C-5), 68.4 (C-6), 63.8 (C-2), 55.3 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₃₂H₃₃N₃O₅NH₄ 557.27585, found 557.25700



Scheme S2: preparation of 3-OH glucosamine acceptors: reagents and conditions: a) LiAlH₄, THF, 99%; b) for S8: TFAA, Et₃N, DCM, 77%; c) for S9: trichloroacetyl chloride, Et₃N, DCM, 98%; d) DDQ, 9:1 DCM/H₂O 88% for 1c, 93% for 1d, 70% for 1e

Methyl 2-deoxy-2-azido-4,6-di-O-benzyl-α-D-glucopyranoside (1c)



Title compound was synthesised from **S6** according to general procedure V as a colourless oil. Yield: 1.05 g, 2.64 mmol, 88%. $[\alpha]_D^{25} = 106.0^{\circ}$ (c = 0.91, CHCl₃); IR (thin film): 698, 737, 1047, 1105, 2106; ¹H NMR (400 MHz, CDCl₃) δ 7.39 – 7.17 (m, 10H, CH_{arom}), 4.80 (d, *J* = 3.6 Hz, 1H, H-1), 4.72 – 4.63 (m, 2H, 2x CHH Bn), 4.58 (d, *J* = 11.3 Hz, 1H, CHH Bn), 4.52 (d, *J* = 12.1 Hz, 1H, CHH Bn), 4.05 (ddd, *J* = 10.3, 8.7, 3.4 Hz, 1H, H-3), 3.79 – 3.71 (m, 2H, H-5, H-6), 3.71 – 3.66 (m, 1H, H-6), 3.57 (dd, *J* = 9.8, 8.7 Hz, 1H, H-4), 3.40 (s, 3H, CH₃ OMe), 3.28 (dd, *J* = 10.3, 8.6 Hz, 1H, H-2), 2.49 (d, *J* = 3.4 Hz, 1H, 3-OH); ¹³C NMR (101 MHz, CDCl₃) δ 138.1, 137.8 (C_q), 128.7, 128.5, 128.1, 128.1, 128.0, 127.9 (CH_{arom}), 98.8 (C-1), 78.3 (C-4), 74.9, 73.7 (CH₂ Bn), 72.3 (C-3), 70.2 (C-5), 68.4 (C-6), 63.3 (C-2), 55.4 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₂₁H₂₅N₃O₃NH₄ 417.21325, found 417.21254

Methyl 2-deoxy-2-amino-4,6-di-O-benzyl-3-O-(2-naphtyl)methyl-a-D-glucopyranoside (S7)



Title compound was synthesised form **S6** according to general procedure II as a colourless oil. Yield: 7.11 g, 13.8 mmol, 99%. ¹H NMR (400 MHz, CDCl₃) δ 7.83 – 7.72 (m, 4H, CH_{arom}), 7.48 – 7.42 (m, 3H, CH_{arom}), 7.37 – 7.24 (m, 8H, CH_{arom}), 7.19 – 7.14 (m, 2H, CH_{arom}), 5.09 (d, *J* = 11.7 Hz, 1H, CHH Bn/Nap), 4.86 (d, *J* = 11.6 Hz, 1H, CHH Bn/Nap), 4.81 (d, *J* = 10.9 Hz, 1H, CHH Bn/Nap), 4.75 (d, *J* = 3.6 Hz, 1H, H-1), 4.66 (d, *J* = 12.1 Hz, 1H, CHH Bn/Nap), 4.58 – 4.47 (m, 2H, 2x CHH Bn/Nap), 3.82 – 3.75 (m, 2H, H-5, H-6), 3.71 – 3.65 (m, 2H, H-4, H-6), 3.60 (t, *J* = 9.3 Hz, 1H, H-3), 3.35 (s, 3H, CH₃ OMe), 2.85 (dd, *J* = 9.7, 3.6 Hz, 1H, H-2); ¹³C NMR (101 MHz, CDCl₃) δ 138.2, 138.0, 136.1, 133.3, 133.0 (C_q), 128.4, 128.4, 128.3, 128.0, 127.9, 127.8, 127.7, 126.5, 126.2, 125.9, 125.8 (CH_{arom}), 100.7 (C-1), 84.0 (C-3), 78.9 (C-4), 75.6, 74.7, 73.6 (CH₂ Bn/Nap), 70.9 (C-5), 68.6 (C-6), 56.0 (C-2), 55.1 (CH₃ OMe); HRMS: [M+H]⁺ calcd for C₃₂H₃₅NO₅H 514.25880, found 514.25759

Methyl 2-deoxy-2-N-trifluoroacetyl-4,6-di-O-benzyl-3-O-(2-naphtyl)methyl-α-D-

glucopyranoside (S8)



The title compound was prepared from **S7** according to general procedure III as a white solid. Yield: 1.40 g, 2.23 mmol, 77%. ¹H NMR (400 MHz, CDCl₃) δ 7.84 – 7.74 (m, 3H, CH_{arom}), 7.65 (d, *J* = 1.6 Hz, 1H, CH_{arom}), 7.47 (dt, *J* = 6.9, 3.5 Hz, 2H, CH_{arom}), 7.40 – 7.27 (m, 9H, CH_{arom}), 7.19 (dt, *J* = 5.5, 2.2 Hz, 2H, CH_{arom}), 6.22 (d, *J* = 9.5 Hz, 1H, NH), 4.96 (d, *J* = 11.5 Hz, 1H, CHH Bn/Nap), 4.83 (d, *J* = 7.0 Hz, 1H, CHH Bn/Nap), 4.80 (d, *J* = 7.6 Hz, 1H, CHH Bn/Nap), 4.74 (d, *J* = 3.6 Hz, 1H, H-1), 4.65 (d, *J* = 12.1 Hz, 1H, CHH Bn/Nap), 4.55 (dd, *J* = 11.5, 9.9 Hz, 2H, 2X CHH Bn/Nap), 4.30 (td, *J* = 9.4, 3.4 Hz, 1H, H-2), 3.84 – 3.74 (m, 4H, H-3, H-4, H-5, H-6), 3.73 – 3.66 (m, 1H, H-6), 3.35 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 137.9, 135.2, 133.3, 133.2 (C_q), 128.6, 128.6, 128.1, 128.0, 128.0, 128.0, 127.9, 127.8, 127.1, 126.3, 126.2, 126.0 (CH_{arom}), 97.9 (C-1), 79.4, 78.6 (C-3, C-4), 75.3, 75.2, 73.7 (CH₂ Bn/Nap), 71.1 (C-5), 68.3 (C-6), 55.2 (CH₃ OMe), 53.3 (C-2); HRMS: [M+NH₄]⁺ calcd for C₃₄H₃₄F₃NO₆ 627.26765, found 627.26665



The title compound was prepared from **S7** according general procedure IV as a yellow oil that slowly solidifies. Yield: 1.93g, 2.93 mmol, 98%. ¹H NMR (400 MHz, CDCl₃) δ 7.82 – 7.74 (m, 3H, CH_{arom}), 7.71 – 7.68 (m, 1H, CH_{arom}), 7.47 – 7.43 (m, 2H, CH_{arom}), 7.41 (dd, *J* = 8.4, 1.7 Hz, 1H, CH_{arom}), 7.37 – 7.31 (m, 4H, CH_{arom}), 7.31 – 7.26 (m, 4H, CH_{arom}), 7.18 – 7.12 (m, 2H, CH_{arom}), 6.81 (d, *J* = 9.3 Hz, 1H, NH), 4.94 (d, *J* = 11.2 Hz, 1H, CHH Bn/Nap), 4.88 (d, *J* = 11.2 Hz, 1H, CHH Bn/Nap), 4.82 – 4.77 (m, 2H, H-1, CHH Bn/Nap), 4.65 (d, *J* = 12.1 Hz, 1H, CHH Bn), 4.57 – 4.50 (m, 2H, 2x CHH Bn), 4.29 (td, *J* = 9.6, 3.7 Hz, 1H, H-2), 3.89 – 3.75 (m, 4H, -3, H-4, H-5, H-6), 3.75 – 3.68 (m, 1H, H-6), 3.40 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 161.9 (C=O), 138.0, 137.9, 135.3, 133.1 (C_q), 128.6, 128.4, 128.1, 128.0, 128.0, 128.0, 127.9, 127.8, 126.8, 126.2, 126.0 (CH_{arom}), 98.1 (C-1), 80.3, 78.3 (C-3, C-4), 75.5, 75.1, 73.7 (CH₂ Bn/Nap), 71.0 (C-5), 68.4 (C-6), 55.4 (CH₃ OMe), 55.0 (C-2); HRMS: [M+NH₄]⁺ calcd for C₃₄H₃₄Cl₃NO₆NH₄ 675.17900, found 675.17786

Methyl 2-deoxy-2-N-trifluoroacetyl-4,6-di-O-benzyl-a-D-glucopyranoside (1d)



The title compound was prepared from **S8** according to general procedure V as colourless oil that slowly solidifies. Yield: 980 mg, 2.08 mmol, 93%. $[\alpha]_D^{25} = 46.3^\circ$ (c = 1.01, CHCl₃); IR (thin film): 698, 1051, 1152, 1717; ¹H NMR (400 MHz, CDCl₃) δ 7.38 – 7.27 (m, 8H, CH_{arom}), 7.23 – 7.18 (m, 2H, CH_{arom}), 6.54 (d, *J* = 9.0 Hz, 1H, NH), 4.78 (d, *J* = 3.7 Hz, 1H, H-1), 4.71 (d, *J* = 11.2 Hz, 1H,

CHH Bn), 4.66 (d, J = 12.1 Hz, 1H, CHH Bn), 4.58 (d, J = 11.2 Hz, 1H, CHH Bn), 4.54 (d, J = 12.1 Hz, 1H, CHH Bn), 4.15 (ddd, J = 10.4, 9.0, 3.7 Hz, 1H, H-2), 3.86 – 3.80 (m, 1H, H-3), 3.80 – 3.68 (m, 3H, H-5, 2x H-6), 3.64 – 3.56 (m, 1H, H-4), 3.37 (s, 3H, CH₃ OMe), 2.45 (d, J = 4.7 Hz, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 157.8 (q, J = 37.4 Hz, C=O), 138.0, 137.9 (C_q), 128.7, 128.6, 128.2, 128.1, 128.0, 127.9 (CH_{arom}), 115.9 (d, J = 287.9 Hz, CF₃) 97.6 (C-1), 78.3 (C-4), 75.0, 73.7 (CH₂ Bn), 73.1 (C-3), 70.6 (C-5), 68.4 (C-6), 55.3 (CH₃ OMe), 54.1 (C-2); HRMS: [M+NH₄]⁺ calcd for C₂₃H₂₆F₃NO₆ 487.20505, found 487.20455

Methyl 2-deoxy-2-*N*-trichloroacetyl-4,6-di-O-benzyl-α-D-glucopyranoside (1e)



The title compound was prepared from **S9** according to general procedure V as yellow oil. Yield: 1.04 g, 2.00 mmol, 70%. $[\alpha]_D^{25} = 56.5^{\circ}$ (c = 1.14, CHCl₃); IR (thin film): 698, 738, 820, 1053, 1118, 1515, 1713; ¹H NMR (400 MHz, CDCl₃) δ 7.39 – 7.27 (m, 8H, CH_{arom}), 7.22 (dd, *J* = 7.6, 1.9 Hz, 2H, CH_{arom}), 6.90 (d, *J* = 8.8 Hz, 1H, NH), 4.81 (d, *J* = 3.7 Hz, 1H, H-1), 4.75 (d, *J* = 11.2 Hz, 1H, CHH Bn), 4.66 (d, *J* = 12.1 Hz, 1H, CHH Bn), 4.58 (d, *J* = 11.2 Hz, 1H, CHH Bn), 4.54 (d, *J* = 12.1 Hz, 1H, CHH Bn), 4.58 (d, *J* = 11.2 Hz, 1H, CHH Bn), 4.54 (d, *J* = 12.1 Hz, 1H, CHH Bn), 4.58 (d, *J* = 10.4, 8.6, 4.3 Hz, 1H, H-3), 3.80 – 3.68 (m, 3H, H-5, 2x H-6), 3.62 (t, *J* = 9.0 Hz, 1H, H-4), 3.39 (s, 3H, CH₃ OMe), 2.47 (d, *J* = 4.8 Hz, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 162.7 (C=O), 138.1, 137.9 (C_q), 128.7, 128.5, 128.1, 128.0, 127.9 (CH_{arom}), 97.7 (C-1), 92.5 (CCl₃), 78.4 (C-4), 75.0, 73.7 (CH₂ Bn), 73.6 (C-3), 70.6 (C-5), 68.5 (C-6), 55.5, 55.4 (C-2, CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₂₃H₂₆Cl₃NO₆NH₄ 535.11640, found 535.11599



Scheme S3: preparation of 4-OH glucosamine acceptors: reagents and conditions: a) LiAlH₄, THF, 98%; b) for *S11*: TFAA, Et₃N, DCM, 77%; c) for *S12*: trichloroacetyl chloride, Et₃N, DCM, 77%; d) TES-H, TFA, DCM, 0 °C, 83% for *2b*, 78% for *2c*, 67% for *2d*

Methyl 2-deoxy-2-azido-3,6-di-O-benzyl-a-D-glucopyranoside (2b)



Title compound was prepared from **S4** according to general procedure VI as a colourless oil. Yield: 661 mg, 1.66 mmol, 83%. ¹H NMR (400 MHz, CDCl₃) δ 7.44 – 7.27 (m, 10H, CH_{arom}), 4.91 (d, *J* = 11.2 Hz, 1H, CHH Bn), 4.83 – 4.76 (m, 2H, H-1, CHH Bn), 4.61 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.54 (d, *J* = 12.0 Hz, 1H, CHH Bn), 3.80 (dd, *J* = 10.0, 8.1 Hz, 1H, H-3), 3.77 – 3.64 (m, 4H,

H-4, H-5, 2x H-6), 3.42 (s, 3H, CH₃ OMe), 3.37 (dd, J = 10.0, 3.6 Hz, 1H, H-2), 2.51 (d, J = 2.5 Hz, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 138.2, 137.8 (C_q), 128.8, 128.6, 128.3, 128.2, 128.0, 127.8 (CH_{arom}), 98.9 (C-1), 80.2 (C-3), 75.2, 73.8 (CH₂ Bn), 72.2 (C-4), 70.1 (C-5), 69.8 (C-6), 63.2 (C-2), 55.4 (CH₃ OBn). Spectra in agreement with literature.²⁸

Methyl 2-deoxy-2-amino-3-O-benzyl-4,6-O-benzylidene-α-D-glucopyranoside (S10)



Title compound was prepared from **S4** according to general procedure II as a white solid. 3.40 g, 9.15 mmol, 98%. ¹H NMR (400 MHz, CDCl₃) δ 7.53 – 7.47 (m, 2H, CH_{arom}), 7.41 – 7.26 (m, 8H, CH_{arom}), 5.58 (s, 1H, CHPh), 5.01 (d, *J* = 11.5 Hz, 1H, CHH Bn), 4.74 (d, *J* = 3.7 Hz, 1H, H-1), 4.68 (d, *J* = 11.4 Hz, 1H, CHH Bn), 4.29 (dd, *J* = 9.8, 4.4 Hz, 1H, H-6), 3.85 (ddd, *J* = 10.3, 8.5, 4.3 Hz, 1H, H-5), 3.80 – 3.74 (m, 1H, H-6), 3.70 – 3.58 (m, 2H, H-3, H-4), 3.39 (s, 3H, CH₃ OMe), 2.84 (dd, *J* = 9.3, 3.7 Hz, 1H, H-2), 1.49 (s, 2H, NH₂); ¹³C NMR (101 MHz, CDCl₃) δ 138.6, 137.6 (C_q), 129.0, 128.6, 128.4, 128.2, 127.9, 126.1 (CH_{arom}), 101.3, 101.2 (C-1, CHPh), 83.3, 80.1 (C-3, C-4), 75.0 (CH₂ Bn), 69.3 (C-6), 62.9 (C-5), 56.0 (C-2), 55.4 (CH₃ OMe). Spectra in agreement with literature.²⁹

<u>Methyl 2-deoxy-2-N-trifluoroacetyl-3-O-benzyl-4,6-O-benzylidene-α-D-glucopyranoside</u> (S11)



Title compound was prepared from **S10** according to general procedure III as white solid. Yield: 790 mg, 1.69 mmol, 77%.¹H NMR (400 MHz, CDCl₃) δ 7.53 – 7.49 (m, 2H, CH_{arom}), 7.44 – 7.37 (m, 3H, CH_{arom}), 7.35 – 7.28 (m, 3H, CH_{arom}), 7.27 – 7.23 (m, 2H, CH_{arom}), 6.24 (d, *J* = 9.3 Hz, 1H, NH), 5.61 (s, 1H, CHPh), 4.89 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.75 (d, *J* = 3.8 Hz, 1H, H-1), 4.66 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.33 – 4.22 (m, 2H, H-2, H-6), 3.85 – 3.72 (m, 4H, H-3, H-4, H-5, H-6), 3.37 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 137.9, 137.3 (C_q), 129.2, 128.6, 128.5, 128.2, 128.1, 126.1 (CH_{arom}), 101.5 (CHPh), 98.4 (C-1), 82.8 (C-3), 75.1 (C-4), 74.3 (CH₂ Bn), 68.9 (C-6), 62.8 (C-5), 55.5 (CH₃ OMe), 53.1 (C-2). Spectra in agreement with literature.³⁰

<u>Methyl 2-deoxy-2-N-trichloroacetyl-3-O-benzyl-4,6-O-benzylidene-α-D-glucopyranoside</u> (S12)



Title compound was prepared from **S10** according to general procedure IV as white solid. Yield: 870 mg, 1.68 mmol, 77%. ¹H NMR (400 MHz, CDCl₃) δ 7.56 – 7.47 (m, 2H, CH_{arom}), 7.47 – 7.36 (m, 3H, CH_{arom}), 7.34 – 7.27 (m, 5H, CH_{arom}), 6.76 (d, *J* = 9.1 Hz, 1H, NH), 5.61 (s, 1H, CHPh), 4.90 (d, *J* = 11.7 Hz, 1H, CHH Bn), 4.80 (d, *J* = 3.7 Hz, 1H, H-1), 4.71 (d, *J* = 11.8 Hz, 1H, CHH Bn), 4.34 – 4.28 (m, 1H, H-6), 4.23 (td, *J* = 9.3, 3.8 Hz, 1H, H-2), 3.87 – 3.80 (m, 4H, H-3, H-4, H-5, H-6), 3.41 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 161.9 (C=O), 138.0, 137.3 (C_q),

129.2, 128.6, 128.4, 128.1, 127.9, 126.1 (CH_{arom}), 101.5 (CHPh), 98.5 (C-1), 82.8 (C-3), 75.8 (C-4), 74.5 (CH₂ Bn), 69.0 (C-6), 62.8 (C-5), 55.6 (CH₃ OMe), 54.7 (C-2); HRMS: $[M+Na]^+$ calcd for C₂₃H₂₄Cl₃NO₆NH₄ 538.05614, found 538.05516

Methyl 2-deoxy-2-*N*-trifluoroacetyl-3,6-di-O-benzyl-α-D-glucopyranoside (2c)

The title compound was prepared from **S11** according to general procedure VI as a white solid. Yield: 600 mg, 1.28 mmol, 78%. ¹H NMR (400 MHz, CDCl₃) δ 7.41 – 7.27 (m, 10H, CH_{arom}), 6.28 (d, *J* = 9.3 Hz, 1H, NH), 4.76 (d, *J* = 11.6 Hz, 1H, CHH Bn), 4.75 – 4.67 (m, 2H, H-1, CHH Bn), 4.63 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.56 (d, *J* = 11.9 Hz, 1H, CHH Bn), 4.21 (td, *J* = 9.9, 3.6 Hz, 1H, H-2), 3.81 (td, *J* = 8.8, 2.7 Hz, 1H, H-4), 3.77 – 3.68 (m, 3H, H-5, 2x H-6), 3.60 (dd, *J* = 10.5, 8.5 Hz, 1H, H-3), 3.37 (s, 3H, CH₃ OMe), 2.71 (d, *J* = 2.7 Hz, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 138.0, 137.7 (C_q), 128.8, 128.7, 128.2, 128.1, 127.9 (CH_{arom}), 97.9 (C-1), 79.2 (C-3), 74.6, 73.9 (CH₂ Bn), 72.7 (C-4), 70.2 (C-6), 70.0 (C-5), 55.4 (CH₃ OMe), 52.7 (C-2). Spectra in agreement with literature.³⁰

Methyl 2-deoxy-2-N-trichloroacetyl-3,6-di-O-benzyl-a-D-glucopyranoside (2d)



The title compound was prepared from **S12** according to general procedure VI as colourless oil. Yield: 570 mg, 1.10 mmol, 67%. $[\alpha]_D^{25} = 52.8^{\circ}$ (c = 0.73, CHCl₃); IR (thin film): 698, 737, 820, 1029, 1055, 1515, 1713; ¹H NMR (400 MHz, CDCl₃) δ 7.38 – 7.26 (m, 10H, CH_{arom}), 6.83 (d, J = 9.3 Hz, 1H, NH), 4.81 – 4.76 (m, 2H, H-1, CHH Bn), 4.72 (d, J = 11.3 Hz, 1H, CHH Bn), 4.63 (d, J = 12.0 Hz, 1H, CHH Bn), 4.56 (d, J = 12.0 Hz, 1H, CHH Bn), 4.20 (ddd, J = 10.3, 9.2, 3.7 Hz, 1H, H-2), 3.82 – 3.70 (m, 4H, H-4, H-5, 2x H-6), 3.66 (dd, J = 10.4, 8.1 Hz, 1H, H-3), 3.41 (s, 3H, CH₃ OMe), 2.66 (d, J = 2.4 Hz, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 161.8 (C=O), 138.1, 137.8 (C_q), 128.7, 128.6, 128.1, 128.0, 127.9 (CH_{arom}), 98.2 (C-1), 92.6 (CCl₃), 80.0 (C-3), 74.7, 73.9 (CH₂ Bn), 72.1 (C-4), 70.2 (C-5), 70.0 (C-6), 55.5 (CH₃ OMe), 54.4 (C-2); HRMS: [M+NH₄]⁺ calcd for C₂₃H₂₆Cl₃NO₆NH₄ 535.11640, found 535.11593



Scheme S4: preparation of α -OMe mannosazide intermediates: reagents and conditions: *a*) i: Tf₂O, pyridine, DCM, -20 °C, ii: NaN₃, DMF, 70 °C, 51% over 2 steps; *b*) for **S15**: BnBr, NaH, DMF, 80%; *c*) for **S16**: NapBr, NaH, DMF 76%; *d*) i: PTSA, methanol, 50 °C, ii: BnBr, NaH, DMF, 79% over 2 steps

Methyl 2-deoxy-2-azido-4,6-O-benzylidene-α-D-mannopyranoside (S14)

S13 (28.2 g, 100 mmol) and pyridine (16.1 mL, 200 mmol, 2 eq) were dissolved in DCM and cooled to -20 °C, after which triflic anhydride (19.3 mL, 115 mmol, 1.15 eq) was added dropwise. The reaction mixture was allowed to warm to RT and subsequently quenched with water. Phases were separated and the organic phase was dried with MgSO₄ and concentrated. The residue was dissolved in DMF with NaN₃ (19.5 g, 300 mmol, 3 eq) and heated to 70 °C. After 18 hr, the reaction mixture was cooled to RT, diluted with water and extracted twice with diethyl ether. The organic phase was dried with MgSO₄ and concentrated. The residue was purified over silica (10%→20% acetone in pentane) to yield the title compound as yellow oil. Yield: 15.7 g, 51.2 mmol, 51%. ¹H NMR (400 MHz, CDCl₃) δ 7.50 – 7.46 (m, 2H, CH_{arom}), 7.38 (dd, *J* = 5.0, 2.0 Hz, 3H, CH_{arom}), 5.56 (s, 1H, CHPh), 4.67 (d, *J* = 1.4 Hz, 1H, H-1), 4.28 – 4.18 (m, 2H, H-3, H-6), 3.92 (dd, *J* = 4.0, 1.5 Hz, 1H, H-2), 3.88 (t, *J* = 9.4 Hz, 1H, H-4), 3.83 – 3.71 (m, 2H, H-5, H-6), 3.37 (s, 3H, CH₃ OMe), 2.77 (s, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 137.1 (C_q), 129.5, 128.5, 126.4 (CH_{arom}), 102.4 (CHPh), 100.2 (C-1), 79.1 (C-4), 69.0 (C-3), 68.8 (C-6), 63.7 (C-2), 63.4 (C-5), 55.3 (CH₃ OMe). Data in agreement with literature.³¹

Methyl 2-deoxy-2-azido-3-O-benzyl-4,6-O-benzylidene-a-D-mannopyranoside (S15)



S14 (6.15 g, 20 mmol) was dissolved in DMF and cooled to 0°C, after which benzyl bromide (3.56 mL, 30 mmol, 1.5 eq) and sodium hydride (60% dispersion in mineral oil, 1.20 g, 30 mmol, 1.5 eq) were added. After full conversion, the reaction was quenched with water and extracted with diethyl ether. The organic phase was dried with MgSO₄ and concentrated. The residue was purified over silica (5% acetone in pentane) to yield the title compound as yellow oil. Yield: 6.35 g, 16.0 mmol, 80%. ¹H NMR (400 MHz, CDCl₃) δ 7.52 – 7.46 (m, 2H, CH_{arom}), 7.41 – 7.27 (m, 8H, CH_{arom}), 5.62 (s, 1H, CHPh), 4.88 (d, *J* = 12.3 Hz, 1H, CHH bn), 4.73 (d, *J* = 12.1 Hz, 1H, CHH Bn), 4.65 (d, *J* = 1.5 Hz, 1H, H-1), 4.25 (dd, *J* = 9.7, 4.3 Hz, 1H, H-6), 4.15 – 4.06 (m, 2H, H-3, H-4), 4.00 – 3.97 (m, 1H, H-2), 3.88 – 3.79 (m, 1H, H-6), 3.80 – 3.73 (m, 1H, H-5), 3.34 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 138.1, 137.5 (C_q), 129.1, 128.5, 128.3, 127.8, 127.6, 126.2 (CH_{arom}), 101.7 (CHPh), 100.3 (C-1), 79.2, 75.7 (C-3, C-4), 73.3 (CH₂ Bn), 68.8 (C-6), 63.8 (C-5), 62.8 (C-2), 55.1 (CH₃ OMe). Spectra in agreement with literature.³²

<u>Methyl</u> 2-deoxy-2-azido-3-O-(2-naphtyl)methyl-4,6-O-benzylidene-α-D-mannopyranoside (S16)



The title compound was prepared from **S14** as described for **S15**, but 2-(Bromomethyl)naphthalene was used instead of benzyl bromide. Yield: 4.98 g, 11.1 mmol, 76%.

¹H NMR (400 MHz, CDCl₃) δ 7.85 – 7.78 (m, 3H, CH_{arom}), 7.74 – 7.68 (m, 1H, CH_{arom}), 7.53 – 7.43 (m, 5H, CH_{arom}), 7.41 – 7.36 (m, 3H, CH_{arom}), 5.64 (s, 1H, CHPh), 5.01 (d, *J* = 12.3 Hz, 1H, CHH Nap), 4.89 (d, *J* = 12.4 Hz, 1H, CHH Nap), 4.65 (d, *J* = 1.4 Hz, 1H, H-1), 4.25 (dd, *J* = 9.8, 4.4 Hz, 1H, H-6), 4.17 – 4.11 (m, 2H, H-3, H-4), 4.04 – 3.98 (m, 1H, H-2), 3.88 – 3.81 (m, 1H, H-6), 3.77 (ddd, *J* = 10.8, 5.5, 4.1 Hz, 1H, H-5), 3.32 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 137.5, 135.6, 133.4, 133.1 (C_q), 129.1, 128.4, 128.3, 128.1, 127.8, 126.3, 126.3, 126.2, 126.2, 126.0, 125.5 (CH_{arom}), 101.8 (CHPh), 100.2 (C-1), 79.1, 75.6 (C-3, C-4), 73.2 (CH₂ Nap), 68.8 (C-6), 63.7 (C-5), 62.7 (C-2), 55.1 (C-2); HRMS: [M+NH₄]⁺ calcd for C₂₅H₂₅N₃O₅NH₄ 465.21325, found 465.21276

Methyl 2-deoxy-2-azido-4,6-di-O-benzyl-3-O-(2-naphtyl)methyl-α-D-mannopyranoside (S17)



The title compound was prepared from **S16** as described for **S6**. Yield: 4.67 g, 8.65 mmol, 79%. ¹H NMR (500 MHz, CDCl₃) δ 7.84 – 7.79 (m, 3H, CH_{arom}), 7.78 – 7.73 (m, 1H, CH_{arom}), 7.51 – 7.44 (m, 3H, CH_{arom}), 7.38 – 7.29 (m, 4H, CH_{arom}), 7.30 – 7.23 (m, 4H, CH_{arom}), 7.16 – 7.09 (m, 2H, CH_{arom}), 4.92 – 4.82 (m, 3H, CHH Bn/Nap, CH₂ Bn/Nap), 4.71 (d, *J* = 1.8 Hz, 1H, H-1), 4.66 (d, *J* = 12.2 Hz, 1H, CHH Bn/Nap), 4.53 (d, *J* = 12.3 Hz, 1H, CHH Bn/Nap), 4.50 (d, *J* = 10.8 Hz, 1H, CHH Bn/Nap), 4.09 (dd, *J* = 9.2, 3.7 Hz, 1H, H-3), 3.95 (dd, *J* = 3.7, 1.8 Hz, 1H, H-2), 3.91 (t, *J* = 9.4 Hz, 1H, H-4), 3.78 – 3.62 (m, 3H, H-5, 2x H-6), 3.32 (s, 3H, CH₃ OMe); ¹³C NMR (126 MHz, CDCl₃) δ 138.3, 138.4, 133.4, 133.2 (C_q), 128.5, 128.4, 128.1, 128.0, 128.0, 127.8, 127.8, 127.7, 126.7, 126.2, 126.1, 125.9 (CH_{arom}), 99.2 (C-1), 79.9 (C-3), 75.4 (CH₂ Bn/Nap), 74.6 (C-4), 73.6, 72.7 (CH₂ Bn/Nap), 71.6 (C-5), 68.8 (C-6), 61.4 (C-2), 55.0 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₃₂N₃₃N₃O₅NH₄ 557.27585, found 557.27509



Scheme S5: preparation of 3-OH mannosamine acceptors: reagents and conditions: a) LiAlH₄, THF, 93%; b) for **S19**: TFAA, Et₃N, DCM, 80%; c) for **S20**: trichloroacetyl chloride, Et₃N, DCM, 97%; d) DDQ, 9:1 DCM/H₂O 65% for **3c**, 61% for **3d**, 61% for **3e**

Methyl 2-deoxy-2-azido-4,6-di-O-benzyl-a-D-mannopyranoside (3c)



The title compound was prepared from **S17** according to general procedure V. Yield: 391 mg, 0.98 mmol, 65%. ¹H NMR (400 MHz, CDCl₃) δ 7.40 – 7.28 (m, 8H, CH_{arom}), 7.22 (dd, *J* = 7.7, 1.9

Hz, 2H, CH_{arom}), 4.75 (d, J = 1.7 Hz, 1H, H-1), 4.73 – 4.65 (m, 2H, 2x CHH Bn), 4.60 – 4.51 (m, 2H, 2x CHH Bn), 4.10 (ddd, J = 9.1, 5.4, 3.9 Hz, 1H, H-3), 3.88 (dd, J = 4.0, 1.7 Hz, 1H, H-2), 3.79 – 3.73 (m, 2H, H-4, H-6), 3.71 – 3.65 (m, 2H, H-5, H-6), 3.36 (s, 3H, CH₃ OMe), 2.27 (d, J = 5.4 Hz, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 138.1 (C_q), 128.7, 128.5, 128.1, 128.1, 128.0, 127.8 (CH_{arom}), 99.2 (C-1), 76.1 (C-4), 75.0, 73.7 (CH₂ Bn), 71.6 (C-3), 71.3 (C-5), 68.8 (C-6), 63.8 (C-2), 55.2 (CH₃ OMe). Spectra in agreement with literature.³³

<u>Methyl 2-deoxy-2-amino-4,6-di-O-benzyl-3-O-(2-naphtyl)methyl-α-D-mannopyranoside</u> (S18)



The title compound was prepared from **S17** according to general procedure II. Yield: 3.34 g, 6.50 mmol, 93%. ¹H NMR (400 MHz, CDCl₃) δ 7.83 – 7.78 (m, 3H, CH_{arom}), 7.75 (dd, *J* = 6.1, 3.4 Hz, 1H, CH_{arom}), 7.49 – 7.42 (m, 3H, CH_{arom}), 7.37 – 7.31 (m, 4H, CH_{arom}), 7.31 – 7.25 (m, 4H, CH_{arom}), 7.19 – 7.14 (m, 2H, CH_{arom}), 4.87 (d, *J* = 10.9 Hz, 1H, CHH Bn/Nap), 4.82 (d, *J* = 11.7 Hz, 1H, CHH Bn/Nap), 4.77 (d, *J* = 11.8 Hz, 1H, CHH Bn/Nap), 4.73 (d, *J* = 1.6 Hz, 1H, H-1), 4.65 (d, *J* = 12.1 Hz, 1H, CHH Bn/Nap), 4.56 – 4.45 (m, 2H, 2x CHH Bn/Nap), 3.93 (dd, *J* = 9.0, 3.9 Hz, 1H, H-3), 3.84 (t, *J* = 9.2 Hz, 1H, H-4), 3.80 – 3.72 (m, 2H, H-5, H-6), 3.71 – 3.67 (m, 1H, H-6), 3.36 – 3.31 (m, 4H, H-2, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 138.5, 138.3, 135.9, 133.4, 133.1 (Cq), 128.5, 128.4, 128.3, 128.0, 128.0, 128.0, 127.9, 127.8, 127.7, 127.7, 126.5, 126.2, 126.0, 125.9 (CH_{arom}), 102.0 (C-1), 80.5 (C-3), 75.1 (CH₂ Bn/Nap), 74.1 (C-4), 73.6, 71.8 (CH₂ Bn/Nap), 71.1 (C-5), 69.0 (C-6), 55.0 (CH₃ OMe), 52.1 (C-2); HRMS: [M+H]⁺ calcd for C₃₂H₃₅NO₅H 514.25880, found 514.25811

<u>Methyl</u> 2-deoxy-2-*N*-trifluoroacetyl-4,6-di-O-benzyl-3-O-(2-naphtyl)methyl-α-Dmannopyranoside (S19)



The title product was prepared from **S18** according to general procedure III as colourless oil. Yield: 777 mg, 1.28 mmol, 80%. ¹H NMR (400 MHz, CDCl₃) δ 7.86 – 7.68 (m, 4H, CH_{arom}), 7.50 – 7.39 (m, 3H, CH_{arom}), 7.38 – 7.22 (m, 8H, CH_{arom}), 7.14 (dd, *J* = 6.6, 3.0 Hz, 2H, CH_{arom}), 6.97 (d, *J* = 9.2 Hz, 1H, NH), 4.91 (d, *J* = 11.2 Hz, 1H, CHH Bn/Nap), 4.86 (d, *J* = 10.8 Hz, 1H, CHH Bn/Nap), 4.78 (d, *J* = 1.7 Hz, 1H, H-1), 4.70 (ddd, *J* = 9.4, 4.5, 1.7 Hz, 1H, H-2), 4.66 – 4.58 (m, 2H, CHH Bn/Nap, CHH Bn/Nap), 4.49 – 4.40 (m, 2H, 2x CHH Bn/Nap), 4.14 (dd, *J* = 8.4, 4.4 Hz, 1H, H-3), 3.81 – 3.63 (m, 4H, H-4, H-5, 2x H-6), 3.36 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 138.2, 137.7, 135.2, 133.4, 133.2 (C_q), 128.6, 128.5, 128.3, 128.1, 128.1, 128.0, 128.0, 127.9, 127.8, 127.2, 126.3, 126.2, 126.1 (CH_{arom}), 99.4 (C-1), 77.4 (C-3), 75.3 (CH₂ Bn/Nap), 73.7 (C-4), 73.7, 71.8 (CH₂ Bn/Nap), 70.7 (C-5), 68.5 (C-6), 55.3 (CH₃ OMe), 50.0 (C-2); HRMS: [M+NH₄]⁺ calcd for C₃₄H₃₄F₃NO₆NH₄ 627.26765, found 627.26653







The title product was prepared from **S18** according to general procedure IV as colourless oil. Yield: 1.03 g, 1.56 mmol, 97%. ¹H NMR (400 MHz, CDCl₃) δ 7.82 – 7.70 (m, 4H, CH_{arom}), 7.49 – 7.41 (m, 3H, CH_{arom}), 7.33 – 7.23 (m, 8H, CH_{arom}), 7.16 (dd, *J* = 6.7, 3.0 Hz, 2H, CH_{arom}), 7.01 (d, *J* = 9.1 Hz, 1H, NH), 4.95 (d, *J* = 11.1 Hz, 1H, CHH Bn/Nap), 4.87 (d, *J* = 10.9 Hz, 1H, CHH Bn/Nap), 4.84 (d, *J* = 1.8 Hz, 1H, H-1), 4.67 – 4.57 (m, 3H, H-2, CHH Bn/Nap), 4.18 (q, *J* = 4.4 Hz, 1H, H-3), 3.81 – 3.74 (m, 3H, H-4, H-5, H-6), 3.70 (d, *J* = 9.7 Hz, 1H, H-6), 3.38 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 162.3 (C=O), 138.2, 138.0, 135.3, 133.4, 133.1 (C_q), 128.5, 128.5, 128.2, 128.1, 127.9, 127.8, 127.2, 126.4, 126.1, 126.0 (CH_{arom}), 99.3 (C-1), 77.7 (C-3), 75.3 (CH₂ Bn/Nap), 73.6 (C-4), 73.6, 71.5 (CH₂ Bn/Nap), 70.9 (C-5), 68.6 (C-6), 55.4 (CH₃ OMe), 51.1 (C-2); HRMS: [M+NH₄]⁺ calcd for C₃₄H₃₄Cl₃NO₆NH₄ 675.17900, found 675.17798

Methyl 2-deoxy-2-N-trifluoroacetyl-4,6-di-O-benzyl-a-D-mannopyranoside (3d)



The title product was prepared from **S19** according to general procedure V as colourless oil. Yield: 350 mg, 0.746 mmol, 61%. $[\alpha]_D^{25} = 56.6^\circ$ (c = 0.35, CHCl₃); IR (thin film): 689, 1065, 1133, 1160,1209, 1721; ¹H NMR (400 MHz, CDCl₃) δ 7.39 – 7.26 (m, 8H, CH_{arom}), 7.22 (dd, *J* = 7.7, 1.8 Hz, 2H, CH_{arom}), 7.03 (d, *J* = 8.6 Hz, 1H, NH), 4.78 – 4.71 (m, 2H, H-1, CHH Bn), 4.64 (d, *J* = 11.8 Hz, 1H, CHH Bn), 4.54 (d, *J* = 11.2 Hz, 1H, CHH Bn), 4.49 (d, *J* = 11.8 Hz, 1H, CHH Bn), 4.54 (d, *J* = 11.2 Hz, 1H, CHH Bn), 4.49 (d, *J* = 11.8 Hz, 1H, CHH Bn), 4.40 (ddd, *J* = 8.7, 4.6, 1.6 Hz, 1H, H-2), 4.23 (ddd, *J* = 9.2, 4.5, 3.2 Hz, 1H, H-3), 3.80 (dd, *J* = 10.3, 2.8 Hz, 1H, H-6), 3.76 – 3.67 (m, 2H, H-5, H-6), 3.62 (t, *J* = 9.3 Hz, 1H, H-4), 3.36 (s, 3H, CH₃ OMe), 2.34 (d, *J* = 3.3 Hz, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 138.1, 137.6 (C_q), 128.7, 128.6, 128.1, 128.1, 128.0 (CH_{arom}), 99.2 (C-1), 75.1 (C-4), 75.0, 73.8 (CH₂ Bn), 70.5 (C-5), 70.2 (C-3), 68.5 (C-6), 55.4 (CH₃ OMe), 53.7 (C-2); HRMS: [M+NH₄]⁺ calcd for C₂₃H₂₆F₃NO₆ 487.20505, found 487.20455

Methyl 2-deoxy-2-N-trichloroacetyl-4,6-di-O-benzyl-a-D-mannopyranoside (3e)



The title product was prepared from **S20** according to general procedure V as colourless oil. Yield: 482 mg, 0.929 mmol, 61%. $[\alpha]_D^{25} = 42.1^\circ$ (c = 0.35, CHCl₃); IR (thin film): 697, 821, 1069, 1515, 1720; ¹H NMR (400 MHz, CDCl₃) δ 7.36 – 7.22 (m, 10H, CH_{arom}), 6.95 (d, *J* = 8.3 Hz, 1H, NH), 4.78 (d, *J* = 1.8 Hz, 1H, H-1), 4.76 (d, *J* = 11.3 Hz, 1H, CHH Bn), 4.64 (d, *J* = 11.7 Hz, 1H, CHH Bn), 4.59 (d, *J* = 11.3 Hz, 1H, CHH Bn), 4.49 (d, *J* = 11.6 Hz, 1H, CHH Bn), 4.32 (ddd, *J* = 8.3, 4.3, 1.7 Hz, 1H, H-2), 4.27 (ddd, *J* = 8.9, 4.3, 3.1 Hz, 1H, H-3), 3.84 – 3.70 (m, 3H, H-5, 2x H-6), 3.68 (t, *J* = 9.2 Hz, 1H, H-4), 3.39 (s, 3H, CH₃ OMe), 2.26 (d, *J* = 3.3 Hz, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 162.9 (C=o), 138.1, 138.0 (C_q), 128.7, 128.5, 128.3, 128.2, 127.9, 127.8 (CH_{arom}), 99.1 (C-1), 74.9 (CH₂ Bn), 74.9 (C-4), 73.6 (CH₂ Bn), 70.8 (C-5), 70.5 (C-3), 68.6 (C-6), 55.4 (CH₃ OMe), 54.9 (C-2); HRMS: [M+NH₄]⁺ calcd for C₂₃H₂₆Cl₃NO₆NH₄ 535.11640, found 535.11565



Scheme S6: preparation of 4-OH mannosamine acceptors: reagents and conditions: a) LiAlH₄, THF, 85%; b) for **S22**: TFAA, Et₃N, DCM, 100%; c) for **S23**: trichloroacetyl chloride, Et₃N, DCM, 100%; d) TES-H, TFA, DCM, 0 °C, 70% for **4b**, 60% for **4c**, 73% for **4d**

Methyl 2-deoxy-2-azido-3,6-di-O-benzyl-a-D-mannopyranoside (4b)



The title product was prepared from **S15** according to general procedure VI as colourless oil. Yield: 705 mg, 1.77 mmol, 70%. $[\alpha]_D^{25} = 19.5^{\circ}$ (c = 0.28, CHCl₃); IR (thin film): 698, 970, 1070, 1138, 1365, 1454, 2105; ¹H NMR (500 MHz, CDCl₃) δ 7.43 – 7.26 (m, 10H, CH_{arom}), 4.75 (d, *J* = 11.6 Hz, 1H, CHH Bn), 4.69 (d, *J* = 1.7 Hz, 1H, H-1), 4.66 – 4.60 (m, 2H, CHH Bn, CHH Bn), 4.57 (d, *J* = 12.1 Hz, 1H, CHH Bn), 3.98 – 3.91 (m, 2H, H-2, H-4), 3.86 (dd, *J* = 9.2, 3.6 Hz, 1H, H-3), 3.76 – 3.67 (m, 3H, H-5, 2x H-6), 3.35 (s, 3H, CH₃ OMe), 2.58 (d, *J* = 2.4 Hz, 1H, OH); ¹³C NMR (126 MHz, CDCl₃) δ 138.1, 137.7 (C_q), 128.8, 128.5, 128.2, 128.1, 127.8, 127.8 (CH_{arom}), 99.4 (C-1), 79.4 (C-3), 73.7, 72.6 (CH₂ Bn), 71.1 (C-5), 70.2 (C-6), 68.0 (C-4), 60.4 (C-2), 55.1 (CH₃ OMe); HRMS: [M+NH₄]⁺ calcd for C₂₁H₂₅N₃O₅NH₄ 417.21325, found 417.21277

Methyl 2-deoxy-2-amino-3-O-benzyl-4,6-O-benzylidene-α-D-mannopyranoside (S21)



The title compound was prepared from **S15** according to general procedure II as colourless oil. Yield: 4.23 g, 11.4 mmol, 85%. ¹H NMR (400 MHz, CDCl₃) δ 7.53 – 7.47 (m, 2H, CH_{arom}), 7.41 – 7.27 (m, 8H, CH_{arom}), 5.62 (s, 1H, CHPh), 4.81 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.73 – 4.64 (m, 2H, H-1, CHH Bn), 4.29 – 4.24 (m, 1H, H-6), 4.07 – 4.00 (m, 1H, H-4), 3.92 (dd, *J* = 9.7, 4.2 Hz, 1H, H-3), 3.87 – 3.80 (m, 2H, H-5, H-6), 3.41 (dd, *J* = 4.3, 1.3 Hz, 1H, H-2), 3.36 (s, 3H, CH₃ OMe), 1.45 (s, 2H, NH₂); ¹³C NMR (101 MHz, CDCl₃) δ 138.6, 137.7 (C_q), 129.0, 128.5, 128.3, 127.8, 127.8, 126.2 (CH_{arom}), 103.1 (C-1), 101.8 (CHPh), 79.0 (C-4), 75.7 (C-3), 72.8 (CH₂ Bn), 69.1 (C-6), 63.6 (C-5), 55.1 (CH₃ OMe), 53.7 (C-2). Spectra in agreement with literature.³⁴

<u>Methyl 2-deoxy-2-N-trifluoroacetyl-3-O-benzyl-4,6-O-benzylidene-α-D-mannopyranoside</u> (S22)



The title compound was prepared from **S21** according to general procedure II as yellowish oil. Yield: 1.20 g, 2.57 mmol, 100 %. ¹H NMR (400 MHz, CDCl₃) δ 7.53 – 7.46 (m, 2H, CH_{arom}), 7.42 – 7.36 (m, 3H, CH_{arom}), 7.34 – 7.26 (m, 5H, CH_{arom}), 6.56 (d, *J* = 7.6 Hz, 1H, NH), 5.62 (s, 1H, CHPh), 4.85 (d, *J* = 1.3 Hz, 1H, H-1), 4.70 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.65 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.57 – 4.49 (m, 1H, H-2), 4.28 (dd, *J* = 9.4, 3.8 Hz, 1H, H-6), 4.13 (dd, *J* = 10.0, 4.9 Hz, 1H, H-3), 3.88 (ddd, *J* = 10.4, 9.0, 4.0 Hz, 1H, H-5), 3.85 – 3.78 (m, 1H, H-6), 3.76 – 3.70 (m, 1H, H-4), 3.38 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 137.5, 137.2 (C_q), 129.2, 128.6, 128.4, 128.1, 127.9, 126.2 (C_q), 102.0 (CHPh), 99.7 (C-1), 78.7 (C-4), 72.7 (C-3), 72.3 (CH₂ Bn), 68.8 (C-6), 63.0 (C-5), 55.4 (CH₃ OMe), 51.9 (C-2); HRMS: [M+NH₄]⁺ calcd for C₂₃H₂₄F₃NO₆NH₄ 485.18940, found 485.18902

<u>Methyl 2-deoxy-2-N-trichloroacetyl-3-O-benzyl-4,6-O-benzylidene-α-D-mannopyranoside</u> (S23)



The title compound was prepared from **S21** according to general procedure III as yellowish oil. Yield: 1.30 g, 2.52 mmol, 100%. ¹H NMR (400 MHz, CDCl₃) δ 7.53 – 7.48 (m, 2H, CH_{arom}), 7.42 – 7.26 (m, 8H, CH_{arom}), 7.02 (d, *J* = 7.3 Hz, 1H, NH), 5.63 (s, 1H, CHPh), 4.90 (d, *J* = 1.3 Hz, 1H, H-1), 4.71 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.64 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.48 (ddd, *J* = 7.4, 5.0, 1.4 Hz, 1H, H-2), 4.28 (dd, *J* = 9.7, 4.2 Hz, 1H, H-6), 4.15 (dd, *J* = 10.0, 4.9 Hz, 1H, H-3), 3.93 – 3.86 (m, 1H, H-5), 3.85 – 3.79 (m, 1H, H-6), 3.73 (t, *J* = 9.6 Hz, 1H, H-4), 3.39 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 162.5 (C=O), 137.6, 137.2 (C_q), 129.2, 128.5, 128.3, 127.9, 127.8, 126.2 (CH_{arom}), 101.9 (CHPh), 99.7 (C-1), 92.4 (CCl₃), 78.8 (C-4), 72.9 (C-3), 72.0 (CH₂ Bn), 68.9 (C-6), 62.9 (C-5), 55.4 (CH₃ OMe), 52.9 (C-2); HRMS: [M+NH₄]⁺ calcd for C₂₃H₂₄Cl₃NO₆NH₄ 533.10075, found 533.10041

Methyl 2-deoxy-2-N-trifluoroacetyl-3,6-di-O-benzyl-a-D-mannopyranoside (4c)



The title product was prepared from **S22** according to general procedure VI as colourless oil. Yield: 700 mg, 1.49 mmol, 60%. $[\alpha]_D^{25} = 20.2^{\circ}$ (c = 0.55, CHCl₃); IR (thin film): 698, 1072, 1135, 1162, 1453, 1724 ¹H NMR (400 MHz, CDCl₃) δ 7.37 – 7.27 (m, 10H, CH_{arom}), 6.95 (d, *J* = 9.1 Hz, 1H, NH), 4.81 – 4.74 (m, 2H, H-1, CHH Bn), 4.65 – 4.59 (m, 2H, H-2, CHH Bn), 4.56 (d, *J* = 11.9 Hz, 1H, CHH Bn), 4.41 (d, *J* = 10.9 Hz, 1H, CHH Bn), 3.92 – 3.84 (m, 1H, H-3), 3.83 – 3.68 (m, 4H, H-4, H-5, 2x H-6), 3.38 (s, 3H, CH₃ OMe), 2.55 (d, *J* = 1.5 Hz, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 137.8, 137.3 (C_q), 128.7, 128.6, 128.5, 128.3, 128.0, 127.8 (CH_{arom}), 99.6 (C-1), 77.0 (C- 3), 73.8, 71.8 (CH₂ Bn), 70.6 (C-4), 69.1 (C-6), 66.7 (C-6), 55.4 (CH₃ OMe), 49.6 (C-2); HRMS: [M+NH₄]⁺ calcd for C₂₃H₂₆F₃NO₆NH₄ 487.20505, found 487.20446

Methyl 2-deoxy-2-N-trichloroacetyl-3,6-di-O-benzyl-a-D-mannopyranoside (4d)



The title product was prepared from **\$23** according to general procedure VI as colourless oil. Yield: 950 mg, 1.83 mmol, 73%. $[\alpha]_D^{25} = -1.26^\circ$ (c = 1.35, CHCl₃); IR (thin film): 698, 819, 1073, 1133, 1203, 1281, 1367, 1454, 1515, 1720; ¹H NMR (400 MHz, CDCl₃) δ 7.37 – 7.27 (m, 10H, CH_{arom}), 6.95 (d, *J* = 8.8 Hz, 1H, NH), 4.85 (d, *J* = 1.7 Hz, 1H, H-1), 4.80 (d, *J* = 10.8 Hz, 1H, CHH Bn), 4.63 (d, *J* = 11.8 Hz, 1H, CHH Bn), 4.60 – 4.51 (m, 2H, H-2, CHH Bn), 4.42 (d, *J* = 10.8 Hz, 1H, CHH Bn), 3.92 (dd, *J* = 8.6, 4.2 Hz, 1H, H-3), 3.85 – 3.73 (m, 4H, H-4, H-5, 2x H-6), 3.41 (s, 3H, CH₃ OMe), 2.52 (d, *J* = 1.9 Hz, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 162.2 (C=O), 138.1, 137.4 (Cq), 128.7, 128.5, 128.5, 128.3, 127.8, 127.6 (CH_{arom}), 99.5 (C-1), 92.5 (CCl₃), 77.2 (C-3), 73.8, 71.6 (CH₂ Bn), 70.8 (C-4), 69.2 (CH₂ Bn), 66.8 (C-5), 55.5 (CH₃ OMe), 50.6 (C-2); HRMS: [M+NH₄]⁺ calcd for C₂₃H₂₆Cl₃NO₆NH₄ 535.11640, found 535.11757

Characterisation of glycosylation products



The title compound was synthesised from donor **A** and acceptor **1c** according to general procedure I as colourless oil. Yield: 69 mg, 83 µmol, 83%, $\alpha:\beta = 1.6:1$. Data reported for a 1:1 mixture of anomers: ¹H NMR (400 MHz, CDCl₃) δ 7.42 – 7.10 (m, 50H), 5.55 (s, 1H, CHPha), 5.51 (s, 1H, CHPh β), 5.44 (d, J = 3.8 Hz, 1H, H-1' α), 4.98 – 4.85 (m, 7H), 4.85 – 4.75 (m, 3H), 4.64 (d, J = 12.1 Hz, 1H), 4.61 – 4.54 (m, 2H), 4.52 (d, J = 12.0 Hz, 1H), 4.46 – 4.35 (m, 3H), 4.31 (d, J = 12.6 Hz, 1H), 4.28 – 4.12 (m, 5H), 3.84 – 3.69 (m, 5H), 3.69 – 3.50 (m, 6H), 3.47 (dd, J = 10.3, 3.6 Hz, 1H, H-2' β), 3.42 (d, J = 4.1 Hz, 7H), 3.33 (dd, J = 10.2, 3.5 Hz, 1H, H-2 β), 3.25 (dd, J = 10.3, 3.6 Hz, 1H, H-2a); ¹³C NMR (101 MHz, CDCl₃) δ 138.7, 138.6, 138.5, 138.4, 138.4, 138.0, 137.9, 137.8, 137.6, 137.4, 135.4, 138.1, 128.1, 128.1, 128.0, 127.9, 127.9, 127.8, 127.8, 127.8, 127.7, 127.7, 127.6, 127.4, 126.7, 126.2, 126.1, 125.3, 102.9 (C-1' β), 101.4 (CHPha), 101.2 (CHPh β), 99.5 (C-1' α), 99.3 (C-1 α), 98.9 (C-1 β , 82.8, 82.7, 81.8, 81.3, 78.9, 78.6, 78.5, 77.0, 76.8, 76.0, 75.6, 75.4, 75.3, 75.0, 74.2, 73.7, 73.7, 73.6, 70.2, 70.1, 69.5, 68.8, 68.3, 68.3, 65.9, 63.9, 63.5, 62.2, 55.3 (CH₃ OMe β), 55.2 (CH₃ OMe α); HRMS: [M+NH₄]⁺ calcd for C₄₈H₅₁N₃O₁₀ 847.39127, found 847.38982

Disaccharide 1cB



The title compound was synthesised from donor **B** and acceptor **1c** according to general procedure I as colourless oil. Yield: 65 mg, 85 µmol, 85%, α : β = 1:2.5. Data for the β -anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.42 – 7.25 (m, 20H, CH_{arom}), 5.52 (s, 1H, CHPh), 4.95 – 4.86 (m, 3H, H-1, CH₂ Bn), 4.84 – 4.76 (m, 2H, H-1', CHH Bn), 4.63 (d, *J* = 12.1 Hz, 1H, CHH Bn), 4.51 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.42 (d, *J* = 10.6 Hz, 1H, CHH Bn), 4.25 – 4.08 (m, 3H), 3.82 – 3.71 (m, 2H), 3.70 – 3.63 (m, 2H, H-4', H-6'), 3.60 (t, *J* = 9.1 Hz, 1H), 3.55 – 3.44 (m, 3H, H-2, H-2', H-6'), 3.42 (s, 3H, CH₃ OMe), 3.40 – 3.29 (m, 1H, H-5'); ¹³C NMR (101 MHz, CDCl₃) δ 138.3, 137.9, 137.9, 137.2 (C_q), 128.6, 128.5, 128.5, 128.5, 128.4, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 126.1 (CH_{arom}), 102.2 (C-1'), 101.4 (CHPh), 98.7 (C-1'), 81.7 (C-4'), 79.3, 78.7, 76.0, 75.2, 75.0, 73.7, 70.3, 68.6, 68.3, 66.7, 66.1, 64.1, 55.3 (CH₃ OMe); diagnostic peaks for the α-anomer: ¹H NMR (400 MHz, CDCl₃) δ 5.57 (s, 1H, CHPh), 5.45 (d, *J* = 3.9 Hz, 1H, H-1'), 4.68 (d, *J* = 12.1 Hz, 1H, CHH Bn), 3.17 (dd, *J* = 10.4, 3.6 Hz, 1H, H-2); ¹³C NMR (101 MHz, CDCl₃) δ 101.5 (CHPh), 99.3, 99.3 (C-1, C-1'), 82.9, 78.9, 76.3, 76.3, 74.1, 73.8, 69.4, 68.1, 63.5, 63.0, 61.7, 55.3; product contaminated with TTBP; HRMS: [M+NH₄]⁺ calcd for C₄₁H₄₄N₆O₉NH₄ 782.35080, found 782.34978

Disaccharide 1dA



The title compound was synthesised from donor A and acceptor 1d according to general procedure I as colourless oil. Yield: 86 mg, 96 μ mol, 96%, α : β > 20:1. ¹H NMR (400 MHz, CDCl₃) δ 7.72 - 7.61 (m, 3H, CH_{arom}), 7.57 - 7.52 (m, 1H, CH_{arom}), 7.50 - 7.43 (m, 3H, CH_{arom}), 7.41 -7.30 (m, 8H, CH_{arom}), 7.30 – 7.17 (m, 16H, CH_{arom}), 7.09 – 7.02 (m, 2H, CH_{arom}), 6.54 (d, J = 9.6 Hz, 1H, NH), 5.50 (s, 1H, CHPh), 5.07 (d, J = 3.6 Hz, 1H, H-1'), 5.00 (d, J = 11.1 Hz, 1H, CHH Bn), 4.86 (d, J = 11.2 Hz, 1H, CHH Bn), 4.78 – 4.70 (m, 3H, H-1, CHH Bn, CHH Bn), 4.62 – 4.54 (m, 2H, CHH Bn, CHH Bn), 4.48 (d, J = 12.0 Hz, 1H, CHH Bn), 4.38 – 4.25 (m, 3H, H-2, H-6', CHH Bn), 4.02 (t, J = 9.2 Hz, 1H, H-3'), 3.94 (ddt, J = 10.8, 5.2, 2.7 Hz, 1H, H-3), 3.88 (dt, J = 10.0, 5.0 Hz, 1H, H-5'), 3.78 - 3.75 (m, 2H, H-4, H-5), 3.74 - 3.69 (m, 1H, H-6), 3.66 - 3.55 (m, 3H, H-4', H-6, H-6'), 3.53 (dd, J = 9.3, 3.6 Hz, 1H, H-2'), 3.37 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 138.5, 138.4, 138.2, 137.9, 137.6 (C_q), 135.3, 134.5, 131.6, 131.6, 131.0, 130.3, 128.9, 128.5, 128.4, 128.3, 128.3, 128.2, 128.1, 128.1, 127.9, 127.8, 127.7, 127.6, 127.5, 127.5, 126.2 (CH_{arom}), 101.5 (CHPh), 99.8 (C-1'), 97.9 (C-1), 82.3 (C-4'), 79.8 (C-3), 79.2 (C-2'), 78.3 (C-3'), 77.6 (C-4), 75.2, 74.7, 73.8, 73.6 (CH₂ Bn), 70.5 (C-5), 68.8 (C-6'), 68.4 (C-6), 63.7 (C-5'), 55.3 (CH₃ OMe), 53.2 (C-2); HRMS: [M+NH₄]⁺ calcd for C₅₀H₅₂F₃NO₁₁NH₄ 917.38307, found 917.38163.

Disaccharide 1dB



The title compound was synthesised from donor **B** and acceptor **1d** according to general procedure I as colourless oil. Yield: 83 mg, 100 μ mol, 100%, α : β = 12:1. Data for the α -anomer: ¹H

NMR (400 MHz, CDCl₃) δ 7.41 – 7.24 (m, 20H, CH_{arom}), 6.52 (d, J = 9.7 Hz, 1H, NH), 5.50 (s, 1H, CHPh), 5.40 (d, J = 3.9 Hz, 1H, H-1'), 4.97 – 4.88 (m, 2H, 2x CHH Bn), 4.76 – 4.71 (m, 2H, H-1, CHH Bn), 4.67 (d, J = 12.1 Hz, 1H, CHH Bn), 4.58 – 4.50 (m, 2H, CHH Bn), 4.34 (td, J = 10.0, 3.7 Hz, 1H, H-2), 4.24 (dd, J = 10.3, 4.6 Hz, 1H, H-6), 4.04 – 3.94 (m, 2H, H-3, H-4), 3.86 (t, J = 9.2 Hz, 1H, H-3'), 3.83 – 3.73 (m, 3H, H-5, H-5', H-6), 3.71 (dd, J = 10.6, 1.8 Hz, 1H, H-6), 3.68 – 3.60 (m, 2H, H-4', H-6'), 3.42 – 3.34 (m, 4H, H-2', CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 157.4 (d, J = 37.3 Hz, C=O), 137.8, 137.7, 137.3 (C_q), 131.6, 131.0, 129.1, 128.6, 128.6, 128.5, 128.5, 128.4, 128.3, 128.0, 128.0, 127.9, 127.9, 127.5, 126.3 (CH_{arom}), 115.8 (d, J = 288.4 Hz, CF₃), 101.9 (CHPh), 98.9 (C-1'), 97.8 (C-1), 82.8 (C-4'), 78.6 (C-3'), 77.2 (C-4), 76.1 (C-3), 75.2, 74.3, 73.7 (CH₂ Bn), 70.7 (C-5), 68.6 (C-6'), 68.1 (C-6), 63.5 (C-5'), 63.0 (C-2'), 55.3 (CH₃ OMe), 52.7 (C-2); diagnostic peaks for the β-anomer: ¹H NMR (400 MHz, CDCl₃) δ 6.62 (d, J = 9.3 Hz, 1H, NH), 5.48 (s, 1H, CHPh); ¹³C NMR (101 MHz, CDCl₃) δ 103.2 (C-1'), 101.3 (CHPh), 81.6, 80.2, 79.6, 75.0, 66.4; HRMS: [M+NH₄]⁺ calcd for C₄₃H₄₅F₃N₄O₁₀NH₄ 852.34260, found 852.34131.

Disaccharide 1eA



The title compound was synthesised from donor A and acceptor le according to general procedure I as colourless oil. Yield: 62 mg, 65 μ mol, 65%, α : β = 11:1. Data for the α -anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.48 - 7.43 (m, 3H, CH_{arom}), 7.40 - 7.16 (m, 20H, CH_{arom}), 7.08 - 7.02 (m, 2H, CH_{arom}), 6.74 (d, J = 9.6 Hz, 1H, NH), 5.51 (s, 1H, CHPh), 5.20 (d, J = 3.7 Hz, 1H, H-1'), 4.94 (d, J = 11.2 Hz, 1H, CHH Bn), 4.86 (d, J = 11.3 Hz, 1H, CHH Bn), 4.81 (d, J = 12.0 Hz, 1H, CHH Bn), 4.75 – 4.71 (m, 2H, H-1, CHH Bn), 4.61 (d, J = 12.0 Hz, 1H, CHH Bn), 4.56 (d, J = 12.0 Hz, 1H, CHH Bn), 4.49 (d, J = 12.0 Hz, 1H, CHH Bn), 4.41 – 4.32 (m, 2H, H-6, CHH Bn), 4.23 (td, J = 9.9, 3.7 Hz, 1H, H-2), 4.06 (t, J = 9.3 Hz, 1H, H-3'), 4.04 - 3.93 (m, 2H, H-3, H-5'), 3.82 -3.76 (m, 2H, H-4, H-5), 3.72 (dd, J = 11.4, 2.1 Hz, 1H, H-6), 3.69 – 3.56 (m, 3H, H-4', H-6, H-6'), 3.53 (dd, J = 9.3, 3.7 Hz, 1H, H-2'), 3.39 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 161.9 (C=O), 138.6, 138.3, 138.3, 137.9, 137.6 (C_q), 128.9, 128.5, 128.4, 128.4, 128.4, 128.3, 128.2, 128.1, 128.1, 127.9, 127.8, 127.7, 127.7, 127.7, 127.5, 127.4, 126.2 (CHarom), 101.4 (CHPh), 99.1 (C-1'), 97.9 (C-1), 92.6 (CCl₃), 82.5 (C-4'), 79.3 (C-2'), 78.2, 78.1, 78.0 (C-3, C-3', C-4), 75.2, 74.3, 74.0, 73.6 (CH₂ Bn), 70.5 (C-5), 69.1 (C-6'), 68.4 (C-6), 63.4 (C-5'), 55.5 (CH₃ OMe), 54.6 (C-2); diagnostic peaks for the β -anomer: ¹H NMR (400 MHz, CDCl₃) δ 5.48 (s, 1H, CHPh); ¹³C NMR (101 MHz, CDCl₃) & 161.5 (C=O), 103.3 (C-1'), 101.2 (CHPh), 98.1 (C-1), 81.9, 81.6; HRMS: [M+NH₄]⁺ calcd for C₅₀H₅₂Cl₃NO₁₁NH₄ 965.29442, found 965.29281.

Disaccharide 1eB



The title compound was synthesised from donor **A** and acceptor **1e** according to general procedure I as colourless oil. Yield: 56 mg, 63 µmol, 63%, α : β = 3:1. Data for the α -anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.47 – 7.25 (m, 20H, CH_{arom}), 5.53 (d, *J* = 3.9 Hz, 1H, H-1'), 5.51 (s, 1H, CHPh), 4.96 – 4.86 (m, 2H, 2x CHH Bn), 4.80 – 4.73 (m, 2H, H-1, CHH Bn), 4.69 (d, *J* = 12.0
Hz, 1H, CHH Bn), 4.61 – 4.53 (m, 2H, 2x CHH Bn), 4.31 – 4.21 (m, 2H, H-2, H-6'), 4.10 – 4.01 (m, 2H, H-3, H-3'), 3.95 (td, J = 9.9, 4.9 Hz, 1H, H-5'), 3.89 (dd, J = 9.7, 8.6 Hz, 1H, H-4), 3.83 – 3.59 (m, 5H, H-4', H-5, 2x H-6, H-6'), 3.40 (s, 3H, CH₃ OMe), 3.34 (dd, J = 10.0, 3.9 Hz, 1H, H-2'); ¹³C NMR (101 MHz, CDCl₃) δ 162.3 (C=O), 137.8, 137.8, 137.7, 137.3 (C_q), 131.6, 131.0, 129.1, 128.6, 128.6, 128.5, 128.5, 128.4, 128.3, 128.0, 128.0, 127.9, 127.9, 127.9, 127.5, 126.2 (CH_{arom}), 101.6 (CHPh), 98.4 (C-1'), 97.9 (C-1), 92.4 (CCl₃), 82.9 (C-4'), 79.1 (C-4), 75.9, 75.8 (C-3, C-3'), 75.2, 74.1, 73.7 (CH₂ Bn), 70.7 (C-5), 68.8 (C-6'), 68.1 (C-6), 63.1 (C-5'), 63.0 (C-2'), 55.5 (CH₃ OMe), 54.4 (C-2); diagnostic peaks for the β-anomer: ¹H NMR (400 MHz, CDCl₃) δ 6.76 (d, J = 9.5 Hz, 1H, NH), 4.64 (d, J = 12.1 Hz, 1H, CHH Bn), 4.46 (d, J = 10.6 Hz, 1H, CHH Bn), 4.34 (ddd, J = 10.5, 9.5, 3.6 Hz, 1H, H-2), 4.15 (dd, J = 10.5, 5.0 Hz, 1H, H-6), 3.28 – 3.21 (m, 1H, H-5'); ¹³C NMR (101 MHz, CDCl₃) δ 161.6 (C=O), 102.7 (C-1'), 101.3 (CHPh), 98.0 (C-1), 81.6, 79.6, 79.0, 76.1, 74.9, 73.6, 68.5, 68.4, 66.5, 66.4, 55.4, 55.0; HRMS: [M+NH₄]⁺ calcd for C₄₃H₄₅Cl₃N₄₀₀NH₄ 900.25395, found 900.25272.

Disaccharide 2bA



The title compound was synthesised from donor **A** and acceptor **2b** according to general procedure I as colourless oil. Yield: 87 mg, 94 µmol, 94%, $\alpha:\beta = 1.1:1$. Data reported for a 1:1 mixture of anomers: ¹H NMR (400 MHz, CDCl₃) δ 7.53 – 7.23 (m, 50H), 5.56 (d, *J* = 3.5 Hz, 1H, H-1'a), 5.54 (s, 1H, CHPha), 5.48 (s, 1H, CHPh β), 4.99 (d, *J* = 10.3 Hz, 1H), 4.90 (d, *J* = 11.3 Hz, 2H), 4.87 – 4.53 (m, 14H), 4.39 (d, *J* = 7.9 Hz, 1H, H-1' β), 4.34 (d, *J* = 12.0 Hz, 1H), 4.21 – 4.10 (m, 3H), 4.09 – 3.96 (m, 3H), 3.94 – 3.79 (m, 6H), 3.70 – 3.54 (m, 7H), 3.53 – 3.33 (m, 11H), 3.10 (q, *J* = 7.8 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 138.5, 138.1, 138.0, 137.6, 137.5, 131.6, 131.1, 129.1, 129.0, 128.6, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.1, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 127.3, 126.1, 102.9 (C-1' β), 101.3, 101.2 (CHPha β), 98.7 (C-1a β), 97.8 (C-1'a), 82.7, 82.3, 81.8, 81.1, 80.6, 78.9, 78.8, 78.5, 76.9, 75.7, 75.4, 75.3, 75.1, 74.0, 73.5, 73.5, 73.5, 72.8, 70.5, 70.1, 69.0, 68.8, 68.7, 67.5, 65.9, 63.5, 63.0, 55.5, 55.4; HRMS: [M+NH₄]⁺ calcd for C₄₈H₅₁N₃O₁₀NH₄ 847.39127, found 847.39020.

Disaccharide 2bB



The title compound was synthesised from donor **B** and acceptor **2b** according to general procedure I as colourless oil. Yield: 76 mg, 100 µmol, 100%, $\alpha:\beta = 1:3.3$. Data for the β -anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.42 – 7.25 (m, 20H, CH_{arom}), 5.46 (s, 1H, CHPh), 4.96 – 4.87 (m, 2H, 2x CHH Bn), 4.79 – 4.70 (m, 4H, H-1, CHH Bn, 2x CHH Bn), 4.43 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.20 (d, *J* = 8.0 Hz, 1H, H-1'), 4.12 – 3.98 (m, 3H, H-4, H-6, H-6'), 3.88 (dd, *J* = 10.2, 8.9 Hz, 1H, H-3), 3.83 – 3.76 (m, 1H, H-5), 3.74 – 3.66 (m, 1H, H-6), 3.61 – 3.53 (m, 1H, H-4'), 3.49 – 3.41 (m, 4H, H-2, CH₃ OMe), 3.36 – 3.29 (m, 3H, H-2', H-3', H-6'), 3.00 (td, *J* = 9.8, 5.0 Hz, 1H, H-5'); ¹³C NMR (101 MHz, CDCl₃) δ 138.4, 137.8, 137.7, 137.2 (C_q), 135.3, 134.5, 131.7, 131.6,

131.0, 130.3, 129.2, 128.7, 128.6, 128.5, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.0, 127.9, 127.9, 127.7, 127.5, 126.1, 126.1 (CH_{arom}), 101.3 (CHPh), 101.2 (C-1'), 98.6 (C-1), 81.7 (C-4'), 79.1 (C-3'), 78.4 (C-3), 76.9 (C-3), 75.2, 74.8, 73.6 (CH₂ Bn), 70.3 (C-5), 68.4 (C-6'), 67.7 (C-6), 66.5 (C-2'), 65.9 (C-5'), 63.1 (C-2), 55.5 (CH₃ OMe); diagnostic peaks for the α -anomer: ¹H NMR (400 MHz, CDCl₃) δ 5.63 (d, *J* = 4.0 Hz, 1H, H-1'), 5.54 (s, 1H, *CHP*h), 4.85 (d, *J* = 3.5 Hz, 1H, H-1), 4.65 (d, *J* = 12.1 Hz, 1H, CHH Bn), 4.59 (d, *J* = 12.1 Hz, 1H, CHH Bn); HRMS: [M+NH₄]⁺ calcd for C₄₁H₄₄N₆O₉NH₄ 782.35080, found 782.34972.

Disaccharide 2cA



The title compound was synthesised from donor A and acceptor 2c according to general procedure I as colourless oil. Yield: 74 mg, 82 μ mol, 82%. α : β = 1.3:1. Data reported for a 1:1 mixture of anomers: ¹H NMR (400 MHz, CDCl₃) & 7.57 - 7.42 (m, 6H), 7.44 - 7.17 (m, 41H), 7.20 - 7.12 (m, 3H), 6.31 (d, J = 9.3 Hz, 1H, NHa), 6.19 (d, J = 9.2 Hz, 1H, NH β), 5.55 (s, 1H, CHPha), 5.48 (s, 1H, CHPhβ), 5.46 (d, J = 3.8 Hz, 1H, H-1'a), 4.94 – 4.89 (m, 2H), 4.89 – 4.82 (m, 2H), 4.81 – 4.71 (m, 7H), 4.68 (d, J = 7.9 Hz, 1H), 4.64 – 4.56 (m, 5H), 4.52 (d, J = 11.2 Hz, 1H), 4.43 (d, J = 7.8 Hz, 1H, H-1'β), 4.43 – 4.32 (m, 2H), 4.25 – 4.12 (m, 4H), 4.09 (dd, J = 9.9, 8.9 Hz, 1H), 3.99 (t, J = 9.3 Hz, 1H), 3.95 - 3.89 (m, 3H), 3.89 - 3.81 (m, 3H), 3.70 (dd, J = 10.9, 2.1 Hz, 1H), 3.68 - 3.52 (m, 5H), 3.56 - 3.48 (m, 2H), 3.43 (t, J = 10.3 Hz, 1H), 3.40 - 3.32 (m, 7H), 3.21 -3.05 (m, 1H); ¹³C NMR (101 MHz, CDCl₃) & 138.7, 138.5, 138.4, 138.4, 138.1, 137.9, 137.8, 137.6, 137.5, 137.5, 131.6, 131.0, 129.1, 129.0, 128.7, 128.7, 128.7, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.2, 128.2, 128.1, 128.1, 128.1, 128.0, 128.0, 128.0, 127.9, 127.9, 127.9, 127.8, 127.8, 127.8, 127.7, 127.7, 127.7, 126.1, 102.9 (C-1'β), 101.3 (CHPha), 101.2 (CHPhβ), 97.9 (C-1'a), 97.6 (C-1β), 97.6 (C-1a), 82.7, 82.2, 81.8, 81.1, 79.5, 78.9, 78.5, 77.1, 76.8, 75.7, 75.3, 75.1, 74.4, 73.8, 73.5, 73.4, 72.7, 72.6, 70.8, 70.6, 69.0, 68.8, 68.6, 67.4, 65.8, 63.6, 55.4, 55.3, 52.8, 52.3; HRMS: [M+NH₄]⁺ calcd for C₅₀H₅₂F₃NO₁₁NH₄ 917.38307, found 917.38154.



The title compound was synthesised from donor **A** and acceptor **2c** according to general procedure I as colourless oil. Yield: 84 mg, 100 µmol, 100%. α : β = 1:2.5. Data for the β -anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.56 – 7.51 (m, 2H, CH_{arom}), 7.47 – 7.30 (m, 18H, CH_{arom}), 6.26 (d, *J* = 9.2 Hz, 1H, NH), 5.52 (s, 1H, CHPh), 4.96 (d, *J* = 11.1 Hz, 1H, CHH Bn), 4.88 (d, *J* = 11.4 Hz, 1H, CHH Bn), 4.83 – 4.76 (m, 3H, H-1, CHH Bn, CHH Bn), 4.61 (d, *J* = 11.4 Hz, 1H, CHH Bn), 4.51 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.32 – 4.23 (m, 2H, H-1', H-2), 4.23 – 4.14 (m, 2H, H-4, H-6), 4.09 – 4.03 (m, 1H, H-2'), 3.84 – 3.72 (m, 2H, H-5, H-6), 3.69 (dd, *J* = 10.6, 8.9 Hz, 1H, H-3), 3.62 (t, *J* = 9.2 Hz, 1H, H-4'), 3.45 – 3.37 (m, 6H, H-2', H-3', H-6', CH₃ OMe), 3.08 (td, *J* = 9.8, 5.0 Hz, 1H, H-5'); ¹³C NMR (101 MHz, CDCl₃) δ 138.2, 137.8, 137.8, 137.2 (C_q), 129.2, 128.7, 128.5, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.5, 126.1,

126.1 (CH_{arom}), 101.3 (CHPh), 101.2 (C-1'), 97.7 (C-1), 81.8 (C-4'), 79.2 (C-3'), 77.1 (C-3), 76.8 (C-4), 74.9, 74.6, 73.6 (CH₂ Bn), 70.5 (C-5), 68.5 (C-6'), 67.7 (C-6), 66.6 (C-2'), 65.9 (C-5'), 55.4 (CH₃ OMe), 52.9 (C-2); diagnostic peaks for the α-anomer: ¹H NMR (400 MHz, CDCl₃) δ 6.57 (d, *J* = 9.7 Hz, 1H, NH), 5.64 (d, *J* = 4.0 Hz, 1H, H-1'), 5.60 (s, 1H, CHPh), 5.02 (d, *J* = 10.9 Hz, 1H, CH*H* Bn), 4.78 (d, *J* = 3.7 Hz, 1H, H-1); ¹³C NMR (101 MHz, CDCl₃) δ 97.9, 97.8 (C-1, C-1'), 82.6, 81.1, 76.3, 75.1, 74.5, 73.7, 72.3, 70.4, 68.7, 68.7, 63.6, 62.9, 53.3 (C-2); HRMS: [M+NH₄]⁺ calcd for C₄₃H₄₅F₃N₄O₁₀NH₄ 852.34260, found 852.34132.

Disaccharide 2dA



The title compound was synthesised from donor **A** and acceptor **2c** according to general procedure I as colourless oil. Yield: 77 mg, 82 µmol, 81%. α : β = 1.1:1. Data reported for a 1:1 mixture of anomers: ¹H NMR (500 MHz, CDCl₃) δ 7.54 – 7.42 (m, 6H), 7.40 – 7.17 (m, 44H), 6.83 (d, *J* = 9.4 Hz, 1H, NH α), 6.73 (d, *J* = 8.9 Hz, 1H, NH β), 5.54 (s, 1H, CHPha), 5.52 (d, *J* = 3.8 Hz, 1H, H-1' α), 5.45 (s, 1H, CHPh β), 4.93 – 4.87 (m, 3H), 4.85 – 4.74 (m, 7H), 4.69 – 4.55 (m, 7H), 4.44 (d, *J* = 7.8 Hz, 1H, H-1 β), 4.40 – 4.34 (m, 2H), 4.25 (dd, *J* = 9.7, 8.8 Hz, 1H), 4.21 – 4.07 (m, 4H), 4.01 – 3.96 (m, 2H), 3.95 – 3.83 (m, 4H), 3.73 – 3.64 (m, 2H), 3.63 – 3.52 (m, 6H), 3.48 (dd, *J* = 9.5, 3.8 Hz, 1H), 3.41 – 3.35 (m, 7H), 3.32 (t, *J* = 10.3 Hz, 1H), 3.14 – 3.08 (m, 1H); ¹³C NMR (126 MHz, CDCl₃) δ 161.7, 161.7 (C=O $\alpha\beta$), 138.7, 138.5, 138.5, 138.5, 138.1, 137.9, 137.9, 137.7, 137.6, 137.5, 135.3, 134.3, 131.9, 131.5, 131.2, 130.3, 129.0, 129.0, 128.6, 128.5, 128.4, 128.4, 128.4, 128.3, 128.1, 128.1, 128.0, 128.0, 127.9, 127.8, 127.8, 127.7, 127.6, 127.6, 127.6, 127.4, 126.1, 102.9 (C-1 β), 101.2, 101.1 (CHPh $\alpha\beta$), 97.8 (C-1 $\alpha\beta$), 97.6 (C-1' α), 92.6, 92.5 (CCl₃ $\alpha\beta$), 82.7, 82.2, 81.8, 81.1, 80.3, 78.8, 78.6, 77.9, 76.6, 75.6, 75.3, 75.0, 74.4, 73.6, 73.6, 73.5, 72.2, 71.9, 70.8, 70.4, 69.0, 68.7, 67.5, 65.8, 63.5, 55.6, 55.4, 54.3, 53.9; HRMS: [M+NH₄]⁺ calcd for C₅₀H₅₂Cl₃NO₁₁NH₄ 965.29442, found 965.29364.

Disaccharide 2dB



The title compound was synthesised from donor **A** and acceptor **2c** according to general procedure I as colourless oil. Yield: 88 mg, 100 µmol, 100%. α : β = 1:3.5. Data for the β -anomer: ¹H NMR (500 MHz, CDCl₃) δ 7.41 – 7.24 (m, 20H, CH_{arom}), 6.74 (d, *J* = 9.0 Hz, 1H, NH), 5.43 (s, 1H, CHPh), 4.90 (d, *J* = 11.1 Hz, 1H, CHH Bn), 4.85 (d, *J* = 11.1 Hz, 1H, CHH Bn), 4.82 (d, *J* = 3.7 Hz, 1H, H-1), 4.77 – 4.73 (m, 2H, CHH Bn, CHHBn), 4.61 (d, *J* = 11.0 Hz, 1H, CHH Bn), 4.46 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.25 (d, *J* = 7.7 Hz, 1H, H-1'), 4.20 (ddd, *J* = 10.5, 9.1, 3.7 Hz, 1H, H-2), 4.12 (dd, *J* = 10.0, 8.9 Hz, 1H, H-4), 4.06 (dd, *J* = 10.6, 5.0 Hz, 1H, H-6'), 4.02 (dd, *J* = 11.0, 2.9 Hz, 1H, H-6), 3.79 (dt, *J* = 9.9, 2.3 Hz, 1H, H-5), 3.76 – 3.68 (m, 2H, H-3, H-6), 3.53 (t, *J* = 9.2 Hz, 1H, H-4'), 3.41 (s, 3H, CH₃ OMe), 3.37 – 3.32 (m, 2H, H-2', H-3'), 3.25 (t, *J* = 10.3 Hz, 1H, H-6'), 3.00 (td, *J* = 9.7, 5.0 Hz, 1H, H-5'); ¹³C NMR (126 MHz, CDCl₃) δ 161.7 (C=O), 138.4, 137.8, 137.8, 137.2 (C_q), 131.9, 131.6, 129.1, 128.7, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3,

128.3, 128.2, 128.2, 128.0, 128.0, 127.9, 127.6, 127.6, 127.5, 126.1, 126.1 (CH_{arom}), 101.3 (CHPh), 101.1 (C-1'), 97.9 (C-1), 92.6 (CCl₃), 81.7 (C-4'), 79.1 (C-3'), 77.9 (C-3), 76.7 (C-4), 74.8, 74.7, 73.6 (CH₂ Bn), 70.5 (C-5), 68.4 (C-6'), 67.8 (C-6), 66.6 (C-2'), 65.8 (C-5'), 55.6 (CH₃ OMe) 54.4 (C-2); diagnostic peaks for the α -anomer: ¹H NMR (500 MHz, CDCl₃) δ 6.96 (d, *J* = 9.7 Hz, 1H, NH), 5.61 (d, *J* = 4.0 Hz, 1H, H-1'), 5.54 (s, 1H, CHPh), 4.96 (d, *J* = 11.0 Hz, 1H, CHH Bn), 4.36 (td, *J* = 9.9, 3.7 Hz, 1H, H-2); ¹³C NMR (126 MHz, CDCl₃) δ 161.6 (C=O), 101.3 (CHPh), 98.0 (C-1'), 82.6, 81.5, 76.3, 75.1, 74.4, 72.3, 70.2, 68.8, 68.7, 63.5, 62.8, 55.5 (CH₃ OMe), 55.0 (C-2); HRMS: [M+NH₄]⁺ calcd for C₄₃H₄₅Cl₃N₄O₁₀NH₄ 900.25395, found 900.25318.

Disaccharide 3cA



The title compound was synthesised from donor A and acceptor 3c according to general procedure I as colourless oil. Yield: 83 mg, 100 μ mol, 100%. $\alpha:\beta = 7:1$. Data for the α -anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.51 (dd, J = 7.8, 1.9 Hz, 2H, CH_{arom}), 7.41 – 7.16 (m, 21H, CH_{arom}), 7.10 - 7.05 (m, 2H, CH_{arom}), 5.55 (s, 1H, CHPh), 5.09 (d, J = 3.7 Hz, 1H, H-1'), 5.01 (d, J = 11.3 Hz, 1H, CHH Bn), 4.92 (d, J = 11.3 Hz, 1H, CHH Bn), 4.83 - 4.77 (m, 2H, H-1, CHH Bn), 4.73 (d, J = 12.2 Hz, 1H, CHH Bn), 4.65 – 4.58 (m, 2H, CHH Bn, CHH Bn), 4.49 (d, J = 12.2 Hz, 1H, CH*H* Bn), 4.42 (d, *J* = 11.3 Hz, 1H, CH*H* Bn), 4.32 (dd, *J* = 10.3, 4.9 Hz, 1H, H-6'), 4.19 – 4.07 (m, 3H, H-3, H-3', H-5'), 3.93 (dd, J = 3.8, 1.8 Hz, 1H, H-2), 3.89 (t, J = 9.5 Hz, 1H, H-4), 3.77 - 3.59 (m, 5H, H-4', H-5, 2x H-6, H-6'), 3.55 (dd, J = 9.4, 3.7 Hz, 1H, H-2'), 3.37 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 138.7, 138.6, 138.2, 138.1, 137.5 (C₄), 129.0, 128.5, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 128.0, 127.9, 127.9, 127.8, 127.7, 127.7, 127.6, 127.5, 126.2, 126.1 (C_q), 101.4 (CHPh), 100.3 (C-1'), 99.0 (C-1), 82.4 (C-4'), 79.7 (C-3), 78.9 (C-2'), 78.3 (C-3'), 75.3, 74.8 (CH₂ Bn), 74.0 (C-4), 73.6, 73.6 (CH₂ Bn), 71.7 (C-5), 69.2, 68.8 (C-6, C-6'), 63.9 (C-5'), 63.2 (C-2), 55.1 (CH₃ OMe); diagnostic peaks for the β -anomer: ¹H NMR (400 MHz, CDCl₃) δ 5.51 (s, 1H, CHPH); ¹³C NMR (101 MHz, CDCl₃) δ 101.9 (C-1'), 101.2 (CHPh), 99.1 (C-1), 81.9, 81.7, 81.4, 79.1, 77.9, 75.1, 75.0, 73.7, 71.6, 68.5, 66.1; HRMS: [M+NH₄]⁺ calcd for C48H51N3O10NH4 847.39127, found 847.39022.

Disaccharide 3cB



The title compound was synthesised from donor **B** and acceptor **3c** according to general procedure I as colourless oil. Yield: 57 mg, 75 µmol, 75%. α : β = 1.8:1. Data reported for a 2:1 mixture of anomers: ¹H NMR (400 MHz, CDCl₃) δ 7.57 – 7.14 (m, 60H), 5.58 (s, 2H, CHPha), 5.55 (s, 1H, CHPh β), 5.28 (d, *J* = 3.8 Hz, 2H, H-1'a), 4.95 (dd, *J* = 10.8, 5.3 Hz, 5H), 4.87 (d, *J* = 10.6 Hz, 1H), 4.83 – 4.77 (m, 4H), 4.74 – 4.64 (m, 6H), 4.59 – 4.45 (m, 6H), 4.43 – 4.38 (m, 2H, H-1' β , CH*H* Bn), 4.31 (dd, *J* = 10.4, 4.9 Hz, 2H), 4.24 (dd, *J* = 9.3, 3.7 Hz, 3H), 4.21 – 4.11 (m, 3H), 4.05 – 3.94 (m, 5H), 3.91 (dd, *J* = 3.8, 1.8 Hz, 2H), 3.87 (t, *J* = 9.2 Hz, 1H), 3.79 – 3.58 (m, 17H), 3.53 – 3.42 (m, 3H, H-2' $\alpha\beta$)), 3.35 (d, *J* = 1.6 Hz, 10H, H-5' β , CH₃ OMea β); ¹³C NMR (101 MHz, CDCl₃) δ 138.4, 138.1, 137.8, 137.2, 137.1, 129.2, 128.6, 128.5, 128.4, 128.4, 128.1,

128.1, 128.0, 127.9, 127.9, 127.8, 127.8, 127.8, 126.2, 126.1, 101.6 (CHPha), 101.5 (CHPhβ), 101.4 (C-1'β), 99.9 (C-1'α), 99.3 (C-1β), 99.0 (C-1α), 82.9, 81.7, 80.3, 79.8, 77.7, 76.2, 75.3, 75.0, 74.9, 74.8, 73.7, 73.6, 73.4, 71.7, 71.7, 68.9, 68.7, 68.6, 68.5, 66.5, 66.4, 63.9, 63.5, 63.2, 62.0, 55.1 (CH₃ OMeaβ); HRMS: $[M+NH_4]^+$ calcd for C₄₁N₄₄N₆O₉NH₄ 782.35080, found 782.34970.

Disaccharide 3dA



The title compound was synthesised from donor A and acceptor 3c according to general procedure I as colourless oil. Yield: 72 mg, 80 μ mol, 80%. α : β = 2.3:1. Data for the α -anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.38 – 7.17 (m, 25H), 5.50 (s, 1H, CHPh), 5.06 (d, I = 3.7 Hz, 1H, H-1'), 5.01 (d, J = 11.3 Hz, 1H, CHH Bn), 4.88 (d, J = 11.4 Hz, 1H, CHH Bn), 4.82 (d, J = 11.3 Hz, 1H, CHH Bn), 4.71 (d, J = 2.5 Hz, 1H, H-1), 4.62 – 4.55 (m, 2H, CHH Bn, CHH Bn), 4.54 – 4.47 (m, 2H, H-2, CHH Bn), 4.44 – 4.39 (m, 2H, 2x CHH Bn), 4.31 – 4.19 (m, 2H, H-3, H-6'), 4.02 (t, J = 9.4 Hz, 1H, H-3'), 3.87 (td, J = 9.9, 4.7 Hz, 1H, H-5'), 3.82 – 3.69 (m, 3H, H-4, H-5, H-6), 3.66 – 3.60 (m, 2H, H-6, H-6'), 3.57 (t, J = 9.5 Hz, 1H, H-4'), 3.52 (dd, J = 9.5, 3.7 Hz, 1H, H-2'), 3.37 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 138.7, 138.4, 138.1, 137.7 (C_q), 128.6, 128.6, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 128.1, 128.0, 128.0, 128.0, 127.8, 127.7, 127.6, 127.6, 127.5, 126.3, 126.1 (CHarom), 101.6 (CHPh), 100.3 (C-1'), 99.1 (C-1), 82.4 (C-4'), 78.8 (C-2'), 78.3 (C-3'), 77.6 (C-3), 75.2, 74.9 (CH₂ Bn), 73.9 (C-4), 73.8, 73.7 (CH₂ Bn), 70.9 (C-5), 69.0 (C-6'), 68.4 (C-6), 64.0 (C-5'), 55.4 (CH₃ OMe), 53.0 (C-2); diagnostic peaks for the β -anomer: ¹H NMR (400 MHz, CDCl₃) δ 5.39 (s, 1H, CHPh), 4.67 (d, *J* = 11.2 Hz, 1H, CHH Bn), 4.37 (d, *J* = 11.0 Hz, 1H, CHH Bn), 3.45 (t, J = 7.2 Hz, 1H, H-2'), 3.35 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 101.2 (CHPh), 99.7 (C-1'), 99.3 (C-1), 81.5, 81.2, 81.0, 74.8, 74.7, 74.4, 74.3, 73.7, 73.5, 70.7, 68.5, 65.9, 50.0; HRMS: [M+NH₄]⁺ calcd for C₅₀H₅₂F₃NO₁₁NH₄ 917.38307, found 917.38211.

Disaccharide 3dB



The title compound was synthesised from donor **B** and acceptor **3c** according to general procedure I as colourless oil. Yield: 77 mg, 92 µmol, 92%. α : β = 1:1.2. Data reported for a 1:1 mixture of anomers: ¹H NMR (400 MHz, CDCl₃) δ 7.49 (dtt, *J* = 14.2, 4.4, 2.1 Hz, 5H), 7.41 – 7.25 (m, 32H), 7.20 (ddd, *J* = 7.4, 5.9, 1.7 Hz, 3H), 5.56 (s, 1H, CHPh β), 5.54 (s, 1H, CHPh α), 5.28 (d, *J* = 3.7 Hz, 1H, H-1' α), 4.94 (d, *J* = 11.2 Hz, 1H), 4.90 (d, *J* = 11.2 Hz, 2H), 4.83 (d, *J* = 10.8 Hz, 1H), 4.80 – 4.75 (m, 2H), 4.73 (d, *J* = 11.1 Hz, 1H), 4.68 (d, *J* = 10.7 Hz, 1H, H-1 α), 4.66 (d, *J* = 8.0 Hz, 1H), 4.64 – 4.59 (m, 2H), 4.53 – 4.44 (m, 7H), 4.41 (d, *J* = 10.7 Hz, 1H), 4.36 – 4.26 (m, 3H), 4.11 (td, *J* = 9.9, 4.9 Hz, 1H), 4.03 (t, *J* = 9.6 Hz, 1H), 3.87 – 3.72 (m, 7H), 3.72 – 3.61 (m, 7H), 3.45 – 3.34 (m, 8H), 3.31 (dd, *J* = 10.1, 3.8 Hz, 1H, H-2' α); ¹³C NMR (101 MHz, CDCl₃) δ 138.1, 137.9, 137.8, 137.5, 137.5, 137.4, 137.1, 135.4, 134.3, 132.0, 131.5, 131.3, 130.3, 129.2, 129.1, 128.7, 128.6, 128.6, 128.5, 128.5, 128.4, 128.4, 128.4, 128.3, 128.2, 128.1, 128.1, 128.0, 128.0, 127.9, 127.8, 126.4, 126.1, 101.7, 101.4 (CHPha β), 99.9 (C-1' α), 99.4, 99.3 (C-1 $\alpha\beta$), 98.4 (C-1' β), 82.8, 81.8, 79.4, 75.6, 75.2, 75.1, 75.1, 75.0, 74.9, 74.9, 74.7, 73.8, 73.7, 72.8, 71.0, 70.5, 68.8, 68.6, 68.2,

68.2, 66.6, 66.3, 63.5, 63.0, 55.3, 53.1, 49.5; HRMS: $[M+NH_4]^+$ calcd for $C_{43}H_{45}F_3N_4O_{10}NH_4$ 852.34260, found 852.34134.

Disaccharide 3eA



The title compound was synthesised from donor A and acceptor 3c according to general procedure I as colourless oil. Yield: 54 mg, 57 μ mol, 57%. α : β = 5:1. Data for the α -anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.54 - 7.11 (m, 25H, CH_{arom}), 5.50 (s, 1H, CHPh), 5.07 (d, J = 3.8 Hz, 1H, H-1'), 5.04 (d, J = 11.4 Hz, 1H, CHH Bn), 4.88 (d, J = 11.3 Hz, 1H, CHH Bn), 4.79 - 4.69 (m, 3H, H-1, CHH Bn, CHH Bn), 4.61 (d, J = 12.1 Hz, 1H, CHH Bn), 4.56 (d, J = 11.7 Hz, 1H, CHH Bn), 4.50 – 4.36 (m, 3H, H-2, 2x CHH Bn), 4.35 – 4.26 (m, 2H, H-3, H-6'), 4.05 (t, J = 9.4 Hz, 1H, H-3'), 3.92 (td, J = 9.9, 4.8 Hz, 1H, H-5'), 3.85 – 3.75 (m, 2H, H-4, H-5), 3.72 (dd, J = 10.5, 2.9 Hz, 1H, H-6), 3.70 - 3.53 (m, 3H, H-4', H-6, H-6'), 3.52 (dd, I = 9.5, 3.8 Hz, 1H, H-2'), 3.39 (s, 3H, CH₃ OMe); ¹³C NMR (101 MHz, CDCl₃) δ 162.2 (C=O), 138.7, 138.4, 138.1, 138.0, 137.7 (C_q), 131.6, 131.1, 128.9, 128.6, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.1, 128.1, 128.0, 127.9, 127.9, 127.8, 127.8, 127.8, 127.7, 127.6, 127.6, 127.6, 127.5, 127.1, 126.4 (CH_{arom}), 101.4 (CHPh), 100.7 (C-1'), 98.9 (C-1), 92.5 (CCl₃), 82.4 (C-4'), 78.9 (C-2'), 78.3, 78.2 (C-3, C-3'), 75.1, 75.0 (CH₂ Bn), 73.7 (C-4), 73.7, 73.5 (CH₂ Bn), 71.1 (C-5), 69.0 (C-6'), 68.5 (C-6), 63.8 (C-5'), 55.4 (CH₃ OMe), 54.4 (C-2); ¹H NMR (400 MHz, CDCl₃) δ 5.32 (s, 1H, CHPh), 4.99 (d, J = 11.7 Hz, 1H, CHH Bn), 4.23 (dd, J = 10.2, 4.8 Hz, 1H, H-6'); ¹³C NMR (101 MHz, CDCl₃) δ 101.1 (CHPh), 99.7 (C-1[']), 99.1 (C-1), 81.4, 81.3, 81.0, 79.1, 76.4, 75.4, 74.7, 74.5, 74.3, 74.2, 73.2, 72.6, 71.4, 71.2, 54.5; HRMS: [M+NH₄]⁺ calcd for C₅₀H₅₂Cl₃NO₁₁NH₄ 965.29442, found 965.29366.

Disaccharide 3eB



The title compound was synthesised from donor **B** and acceptor **3c** according to general procedure I as colourless oil. Yield: 70 mg, 80 µmol, 80%. $\alpha:\beta = 1:1.1$. Data reported for a 1:1 mixture of anomers: ¹H NMR (400 MHz, CDCl₃) δ 7.41 – 7.20 (m, 40H), 7.08 – 6.98 (m, 2H, NH $\alpha\beta$), 5.56 (s, 1H, CHPh α), 5.54 (s, 1H, CHP $h\beta$), 5.24 (d, *J* = 3.7 Hz, 1H, H-1' α), 4.97 (d, *J* = 10.5 Hz, 1H), 4.94 – 4.89 (m, 2H), 4.85 (d, *J* = 10.8 Hz, 1H), 4.81 (d, *J* = 1.7 Hz, 1H, H-1 α/β), 4.78 (d, *J* = 11.0 Hz, 1H), 4.75 – 4.71 (m, 2H), 4.65 (d, *J* = 10.3 Hz, 1H), 4.62 (d, *J* = 10.1 Hz, 1H), 4.56 (d, *J* = 7.9 Hz, 1H, H-1' β), 4.54 – 4.43 (m, 5H), 4.40 (ddd, *J* = 8.9, 4.3, 1.8 Hz, 1H), 4.37 – 4.29 (m, 3H), 4.14 – 4.02 (m, 2H), 3.88 (t, *J* = 9.6 Hz, 1H), 3.84 – 3.64 (m, 12H), 3.46 – 3.35 (m, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 162.2, 162.1 (C=O), 138.1, 137.9, 137.9, 137.8, 137.8, 137.5, 137.1 (C_q), 135.4, 134.5, 131.7, 131.6, 131.0, 130.4, 130.3, 129.2, 129.0, 129.0, 128.6, 128.6, 128.5, 128.5, 128.4, 128.3, 128.3, 128.1, 128.0, 127.9, 127.9, 127.8, 126.4, 126.1 (CH_{arom}), 101.6, 101.4 (CHPh $\alpha\beta$), 100.2 (C-1' α), 99.1, 99.1 (C-1 $\alpha\beta$), 98.2 (C-1' β), 82.8, 81.8, 79.5, 75.9, 75.8, 75.2, 75.0, 75.0, 74.8, 73.6, 73.6, 72.9, 71.2, 70.8, 68.8, 68.7, 68.3, 66.6, 66.3, 63.5, 63.2, 55.4, 55.3, 54.5, 50.8; HRMS: [M+NH₄]⁺ calcd for C₄₃H₄₅Cl₃N₄O₁₀NH₄ 900.25395, found 900.25352.

Disaccharide 4bA



The title compound was synthesised from donor A and acceptor 4b according to general procedure I as colourless oil. Yield: 83 mg, 100 μ mol, 100%. $\alpha:\beta = 1:2.5$. Data for the β -anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.39 - 7.25 (m, 25H, CH_{arom}), 5.46 (s, 1H, CHPh), 4.92 - 4.84 (m, 2H, 2x CHH Bn), 4.79 (d, J = 11.4 Hz, 1H, CHH Bn), 4.74 (d, J = 11.0 Hz, 1H, CHH Bn), 4.69 -4.65 (m, 2H, H-1, CHH Bn), 4.61 – 4.56 (m, 2H, 2x CHH Bn), 4.43 (d, J = 7.7 Hz, 1H, H-1'), 4.36 (d, J = 12.1 Hz, 1H, CHH Bn), 4.21 - 4.09 (m, 2H, H-4, H-6'), 3.92 - 3.87 (m, 2H, H-2, H-3), 3.80 (dd, J = 10.8, 4.0 Hz, 1H, H-6), 3.62 - 3.54 (m, 4H, H-3', H-4', H-5, H-6), 3.45 - 3.38 (m, 1H, H-6'), 3.36 (s, 3H, CH₃ OMe), 3.34 - 3.30 (m, 1H, H-2'), 3.16 (td, J = 9.4, 5.0 Hz, 1H, H-5'); ¹³C NMR (101 MHz, CDCl₃) δ 138.8, 138.5, 138.4, 138.2, 137.5 (C_q), 135.3, 134.3, 131.9, 131.5, 131.2, 130.3, 129.0, 128.6, 128.5, 128.4, 128.3, 128.3, 128.3, 128.1, 128.0, 128.0, 127.9, 127.8, 127.7, 127.7, 127.7, 127.6, 127.4, 127.3, 127.1, 126.1 (CH_{arom}), 103.2 (C-1'), 101.1 (CHPh), 99.1 (C-1), 82.6 (C-1 2'), 81.7 (C-4'), 81.1 (C-3'), 77.3 (C-3), 75.5 (CH₂ Bn), 75.0 (C-4), 75.0, 73.4, 73.1 (CH₂ Bn), 71.5 (C-5), 68.8 (C-6'), 68.0 (C-6), 65.7 (C-5'), 62.2 (C-2), 55.2 (CH₃ OMe); diagnostic peaks for the aanomer: ¹H NMR (400 MHz, CDCl₃) δ 5.65 (d, J = 3.9 Hz, 1H, H-1'), 5.52 (s, 1H, CHPh), 4.54 (d, J = 11.9 Hz, 1H), 4.31 (d, J = 9.1 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 101.1 (CHPh), 99.0 (C-1), 97.8 (C-1'), 82.2, 80.5, 78.9, 78.6, 75.3, 71.7, 70.9, 70.1, 69.1, 68.9, 63.4, 60.5, 55.0; HRMS: [M+NH₄]⁺ calcd for C₄₈H₅₁N₃O₁₀NH₄ 847.39127, found 847.39012.

Disaccharide 4bB



The title compound was synthesised from donor **B** and acceptor **4b** according to general procedure I as colourless oil. Yield: 83 mg, 100 μ mol, 100%. α : β = 1:14. Data for the β -anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.78 – 7.60 (m, 3H, CH_{arom}), 7.46 (dq, J = 4.4, 2.4 Hz, 3H, CH_{arom}), 7.42 - 7.26 (m, 19H, CH_{arom}), 5.45 (s, 1H, CHPh), 4.89 (d, J = 11.2 Hz, 1H, CHH Bn), 4.80 (d, J = 11.8 Hz, 1H, CHH Bn), 4.78 – 4.72 (m, 2H, CHH Bn, CHH Bn), 4.70 (d, J = 1.6 Hz, 1H, H-1), 4.66 (d, *J* = 11.8 Hz, 1H, CH*H* Bn), 4.49 (d, *J* = 12.1 Hz, 1H, CH*H* Bn), 4.25 (d, *J* = 8.1 Hz, 1H, H-1'), 4.18 (t, J = 9.3 Hz, 1H, H-4'), 4.10 (dd, J = 10.6, 5.0 Hz, 1H, H-6'), 3.96 – 3.90 (m, 2H, C-3, C-6), 3.88 (dd, J = 3.8, 1.7 Hz, 1H, H-2'), 3.76 - 3.68 (m, 2H, H-5, H-6), 3.54 (t, J = 9.2 Hz, 1H, H-4'), 3.42 -3.37 (m, 2H, H-4', H-6'), 3.36 (s, 3H, CH₃ OMe), 3.28 (dd, J = 9.4, 8.1 Hz, 1H, H-2'), 3.07 (td, J = 9.7, 5.0 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 138.6, 138.1, 137.8, 137.3 (C_q), 135.4, 134.4, 131.8, 131.5, 131.2, 130.3, 130.3, 129.1, 128.6, 128.5, 128.4, 128.3, 128.3, 128.0, 127.9, 127.5, 127.0, 126.1 (CHarom), 101.6 (C-1'), 101.3 (CHPh), 99.2 (C-1), 81.7 (C-4'), 79.3 (C-3'), 77.5 (C-3), 75.0 (C-4), 74.9, 73.6, 73.1 (CH₂ Bn), 71.1 (C-5), 68.6 (C-6'), 68.2 (C-6), 66.7 (C-2'), 65.9 (C-5'), 62.1 (C-2), 55.1 (CH₃ OMe); diagnostic peaks for the α -anomer: ¹H NMR (400 MHz, CDCl₃) δ 5.63 (d, J = 4.0 Hz, 1H, H-1'), 5.54 (s, 1H, CHPh); HRMS: [M+NH₄]⁺ calcd for C₄₁H₄₄N₆O₉NH₄ 782.35080, found 782.34981.

Disaccharide 4cA Ph O O BnO BnO NHTFA BnO BnO BnO O OME

The title compound was synthesised from donor **A** and acceptor **4c** according to general procedure I as colourless oil. Yield: 64 mg, 71 µmol, 71%. α : β = 1:1.4. Data reported for a 1:1 mixture of anomers: ¹H NMR (400 MHz, CDCl₃) δ 7.43 – 7.18 (m, 50H), 7.04 (d, *J* = 9.1 Hz, 1H, NH α), 6.87 (d, *J* = 8.6 Hz, 1H, NH β) 5.70 (d, *J* = 3.9 Hz, 1H, H-1'a), 5.54 (s, 1H, CHPha), 5.51 (s, 1H, CHPh β), 4.93 – 4.88 (m, 2H), 4.85 – 4.72 (m, 7H), 4.70 – 4.64 (m, 4H), 4.61 (s, 2H), 4.58 – 4.49 (m, 3H), 4.39 (d, *J* = 7.7 Hz, 1H, H-1' β), 4.36 – 4.31 (m, 2H), 4.25 (dd, *J* = 9.0, 4.3 Hz, 1H), 4.21 – 4.07 (m, 3H), 4.00 – 3.88 (m, 5H), 3.83 (dd, *J* = 10.7, 3.2 Hz, 1H), 3.76 (ddd, *J* = 12.4, 8.5, 3.7 Hz, 1H), 3.73 – 3.69 (m, 1H), 3.67 – 3.57 (m, 6H), 3.57 – 3.52 (m, 1H), 3.51 – 3.46 (m, 2H), 3.41 – 3.33 (m, 7H), 3.18 (tt, *J* = 9.3, 4.8 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 138.8, 138.5, 138.4, 138.1, 137.9, 137.8, 137.7, 137.5, 137.5, 137.3, 135.4, 134.2, 132.0, 131.4, 131.3, 130.3, 130.2, 129.1, 129.0, 128.6, 128.5, 128.4, 128.4, 128.4, 128.3, 128.2, 128.1, 128.1, 128.0, 127.9, 127.8, 127.8, 127.7, 127.6, 127.5, 127.4, 126.1, 125.7, 103.4 (C-1' β), 101.2 (CHPha β), 99.1 (C-1 $\alpha\beta$), 97.4 (C-1' α), 82.5, 82.2, 81.7, 81.2, 78.9, 78.5, 78.2, 75.6, 75.4, 75.1, 75.0, 74.5, 73.6, 73.4, 73.3, 71.9, 71.0, 70.6, 70.0, 69.0, 68.9, 68.9, 68.0, 65.9, 63.6, 55.5, 55.4, 50.6, 49.5; HRMS: [M+NH₄]⁺ calcd for C₅₀H₅₂F₃NO₁₁NH₄ 917.38307, found 917.38203.

Disaccharide 4cB



The title compound was synthesised from donor B and acceptor 4c according to general procedure I as colourless oil. Yield: 64 mg, 77 μ mol, 77%. $\alpha:\beta = 1:10$. Data for the β -anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.76 - 7.60 (m, 3H, CH_{arom}), 7.49 - 7.45 (m, 3H, CH_{arom}), 7.42 - 7.26 (m, 19H, CH_{aron}), 6.94 (d, J = 8.8 Hz, 1H, NH), 5.49 (s, 1H, CHPh), 4.90 (d, J = 11.1 Hz, 1H, CHH Bn), 4.78 - 4.74 (m, 2H, H-1, CHH Bn), 4.72 - 4.66 (m, 2H, 2x CHH Bn), 4.60 - 4.49 (m, 3H, H-2, 2x CHH Bn), 4.24 (d, J = 8.1 Hz, 1H, H-1'), 4.05 (dd, J = 10.5, 5.0 Hz, 1H, H-6'), 4.01 - 3.92 (m, 3H, H-3, H-4, H-5), 3.79 (d, J = 8.8 Hz, 1H, H-5), 3.74 (dd, J = 10.6, 1.8 Hz, 1H, H-6), 3.60 (t, J = 9.2 Hz, 1H, H-4'), 3.53 (t, J = 10.3 Hz, 1H, H-6'), 3.44 (t, J = 9.3 Hz, 1H, H-3'), 3.38 (s, 3H, CH₃ OMe), 3.30 (dd, J = 9.4, 8.2 Hz, 1H, H-2'), 3.06 (td, J = 9.7, 5.0 Hz, 1H, H-5'); ¹³C NMR (101 MHz, CDCl₃) δ 138.0, 137.8, 137.6, 137.2 (C_q), 135.4, 134.4, 131.9, 131.5, 131.2, 130.3, 129.2, 128.7, 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 128.2, 128.2, 128.1, 127.7, 127.3, 126.1, 126.0 (CH_{arom}), 101.7 (C-1'), 101.4 (CHPh), 99.1 (C-1), 81.7 (C-4'), 79.3 (C-3'), 75.4 (C-3), 74.9 (CH₂ Bn), 74.6 (C-4), 73.7, 71.8 (CH₂ Bn), 70.2 (C-5), 68.6 (C-6'), 68.1 (C-6), 66.8 (C-2'), 66.0 (C-5'), 55.4 (CH₃ OMe), 50.3 (C-2); diagnostic peaks for the α-anomer: ¹H NMR (400 MHz, CDCl₃) δ 5.59 (d, J = 4.1 Hz, 1H, H-1'), 5.56 (s, 1H, CHPh); HRMS: $[M+NH_4]^+$ calcd for C43H45F3N4O10NH4 852.34260, found 875.34206.



The title compound was synthesised from donor A and acceptor 4d according to general procedure I as colourless oil. Yield: 73 mg, 77 μ mol, 77%. α : β = 1:2.7. Data for the β -anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.49 – 7.15 (m, 25H, CH_{arom}), 6.92 (d, *J* = 8.5 Hz, 1H, NH), 5.48 (s, 1H, CHPh), 4.89 (d, J = 11.3 Hz, 1H, CHH Bn), 4.85 – 4.80 (m, 2H, H-1, CHH Bn), 4.76 – 4.68 (m, 2H, CHH Bn, CHH Bn), 4.62 - 4.54 (m, 2H, 2x CHH Bn), 4.55 - 4.45 (m, 3H, H-1', H-2, CHH Bn), 4.35 (d, J = 11.7 Hz, 1H, CHH Bn), 4.07 (dd, J = 10.5, 5.1 Hz, 1H, H-6'), 4.02 - 3.94 (m, 2H, H-3, H-4), 3.84 (dd, J = 10.7, 3.3 Hz, 1H, H-6), 3.72 (td, J = 9.2, 2.3 Hz, 1H, H-5), 3.65 - 3.51 (m, 4H, H-2', H-3', H-6, H-6'), 3.40 – 3.33 (m, 4H, H-4', CH₃ OMe), 3.13 (td, *J* = 9.3, 4.9 Hz, 1H, H-5'); ¹³C NMR (101 MHz, CDCl₃) δ 162.1 (C=O), 138.5, 138.4, 138.3, 138.1, 137.4 (C_q), 129.1, 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.1, 128.0, 127.9, 127.8, 127.8, 127.8, 127.8, 127.7, 127.7, 127.5, 127.5, 127.3, 127.3, 126.1, 126.1 (CHarom), 103.3 (C-1'), 101.2 (CHPh), 99.0 (C-1'), 82.6 (C-4'), 81.7, 81.2 (C-2', C-3'), 75.5 (CH₂ Bn), 75.4 (C-3), 75.1 (CH₂ Bn), 74.5 (C-4), 73.3, 71.5 (CH₂ Bn), 70.8 (C-5), 68.8 (C-6'), 68.2 (C-6), 65.8 (C-5'), 55.5 (CH₃ OMe), 51.6 (C-2); ¹H NMR (400 MHz, CDCl₃) δ 5.73 (d, J = 4.0 Hz, 1H, H-1'), 5.51 (s, 1H, CHPh); ¹³C NMR (101 MHz, CDCl₃) δ 97.5 (C-1'), 82.2, 78.8, 78.5, 78.3, 77.5, 75.4, 75.4, 73.5, 73.2, 70.2, 69.1, 69.1, 68.9, 63.6, 55.5, 50.6; HRMS: [M+NH₄]⁺ calcd for C₅₀H₅₂Cl₃NO₁₁NH₄ 965.29442, found 965.29360.

Disaccharide 4dB



The title compound was synthesised from donor **B** and acceptor **4d** according to general procedure I as colourless oil. Yield: 88 mg, 100 µmol, 100%, $\alpha:\beta < 1:20$. ¹H NMR (400 MHz, CDCl₃) δ 7.47 – 7.41 (m, 2H, CH_{arom}), 7.42 – 7.26 (m, 18H, CH_{arom}), 6.96 (d, *J* = 8.8 Hz, 1H, NH), 5.47 (s, 1H, NH), 4.89 (d, *J* = 11.2 Hz, 1H, CHH Bn), 4.83 (d, *J* = 1.9 Hz, 1H, H-1), 4.77 (d, *J* = 9.7 Hz, 1H, CHH Bn), 4.83 (d, *J* = 1.1.7 Hz, 1H, CHH Bn), 4.77 (d, *J* = 9.7 Hz, 1H, CHH Bn), 4.74 (d, *J* = 9.7 Hz, 1H, CHH Bn), 4.67 (d, *J* = 11.7 Hz, 1H, CHH Bn), 4.58 – 4.46 (m, 3H, H-2, 2x CHH Bn), 4.33 (d, *J* = 8.1 Hz, 1H, H-1'), 4.06 – 3.93 (m, 4H, H-3, H-4, H6, H-6'), 3.83 – 3.80 (m, 1H, H-5), 3.77 (dd, *J* = 10.6, 1.9 Hz, 1H, H-6), 3.59 (t, *J* = 9.2 Hz, 1H, H-4'), 3.56 – 3.42 (m, 2H, H-3', H-6'), 3.40 (s, 3H, CH₃ OMe), 3.32 (dd, *J* = 9.4, 8.2 Hz, 1H, H-2'), 3.02 (td, *J* = 9.8, 5.0 Hz, 1H, H-5'); ¹³C NMR (101 MHz, CDCl₃) δ 162.1 (C=O), 138.1, 138.0, 137.8, 137.2 (C_q), 134.9, 133.4, 132.3, 131.9, 131.6, 131.5, 131.1, 129.2, 128.6, 128.5, 128.4, 128.3, 128.3, 128.1, 128.0, 127.9, 127.6, 127.2, 126.1 (CH_{arom}), 101.8 (C-1'), 101.3 (CHPh), 99.0 (C-1), 81.7 (C-4'), 79.3 (C-3'), 75.7 (C-3), 74.9 (CH₂ Bn), 74.7 (C-4), 73.6, 71.4 (CH₂ Bn), 70.3 (C-5), 68.5, 68.3 (C-6, C-6'), 66.9 (C-2'), 66.0 (C-5'), 55.5 (CH₃ OMe), 51.3 (C-2); HRMS: [M+NH₄]⁺ calcd for C₄₃H₄₅Cl₃N₄O₁₀NH₄ 900.25395, found 900.25314.

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6

Chapter 6: Mapping the reactivity of 2,3-di-N-acetyl glucuronic acid and 2,4-di-Nacetyl bacillosamine building blocks in the synthesis of a highly N-acetylated Acinetobacter Baumannii LUH5554 tetrasaccharide

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Introduction

The bacterial glycome presents an immensely diverse collection of polysaccharide structures and while the mammalian glycans are built up using a relatively small palette of monosaccharides with little structural variation, bacterial glycans are built up form hundreds of different monosaccharides having an enormous structural variety. Because of their unique structures, bacterial exopolysaccharides and capsular polysaccharides represent attractive targets for our immune system and these structures have been very successfully exploited in the development of vaccines to prevent bacterial infections.

Acinetobacter Baumannii is a Gram-negative bacterium and an opportunistic pathogen, primarily infecting people with a weakened immune system.¹ It is the "A" in the ESKAPE pathogens, six bacteria that have been identified by the World Health Organisation (WHO) as high risk pathogens because of their high rate of antibiotic resistance and (hospital-derived) infections.^{2,3} Because of the threat they present to global health, alternative strategies to combat the ESKAPE pathogens are direly needed and the development of active or passive immunisation strategies present attractive options. *A. baumannii* strains express a polysaccharide capsule, shielding the bacterial cell from its surrounding and environmental influences,⁴ and these carbohydrates may be attractive targets for vaccine development.^{5, 6} Synthetic fragments of these capsular polysaccharides can serve as well-defined antigens and be used for epitope mapping studies. They also allow for structural and interaction studies with binding partners, such as antibodies and immune cell receptors, at the atomic level.⁷⁻⁹

The capsular polysaccharide of *A. baumannii* LUH 5554 is built up of two rare monosaccharides, 2,4-di-*N*-acetyl- α -D-quinovose (2,4-di-*N*-acetyl bacillosamine, QuiNAc4NAc) and 2,3-di-*N*-acetyl- β -D-glucuronic acid (GlcNAc3NAcA) that form tetrasaccharide repeating units, with the structure [\rightarrow 4)- β -D-GlcpNAc3NAcA-(1 \rightarrow 3)- α -D-QuipNAc4NAc-(1 \rightarrow 3)- α -D-QuipNAc4NAc-(1 \rightarrow 4)- β -D-GlcpNAc3NAcA-(1 \rightarrow]

(*Figure 1*).¹⁰ Strikingly, the repeating unit does not contain a single alcohol functionality but only features deoxy centres, carboxylates and acetamide groups! This Chapter describes the assembly of the *A. baumannii* LUH 5554 tetrasaccharide repeating unit. It presents effective multi-Gram scale routes of synthesis towards the monosaccharide building blocks and maps their reactivity in model glycosylation reactions. These studies have allowed the stereoselective assembly of the tetrasaccharide and will be of benefit in synthesis campaigns directed at the assembly of other bacterial glycans. For example, the rare GlcNAc3NAcA and QuiNAc4NAc constituents can also be found in other bacteria such as *Fusobacterium nucleatum*, an anaerobic bacterium that lives in the human mouth where it causes periodontitis, furthermore the bacterium has been linked to colorectal cancer and pregnancy complications,¹¹ *Neisseria meningitidis*, which causes meningitis and other meningococcal diseases,¹² the halophilic bacterium *Haloferax denitrificans*,¹³ *Psychrobacter cryohalolentis*, a bacterium

that lives in cold briny environments,¹⁴ *Plesiomonas shigelloides*, which is responsible for severe cases of travellers' diarrhoea,¹⁵ and the marine bacterium *Pseudoalteromonas*.¹⁶



Figure 1: Representative structures of bacterial oligosaccharides containing 2,3-di-N-Acetyl glucuronic acid and/or 2,4-di-N-acylated bacillosamine.

Results and discussion

Retrosynthetic analysis

The retrosynthetic strategy towards the target *A. Baumannii* repeating tetrasaccharide is depicted in *Scheme 1*. It contains an *O*-allyl group on the reducing end which can be used for future conjugation or immobilisation purposes, but can also serve as a

temporary protecting group to create a donor synthon to generate longer oligosaccharide fragments.

The hydroxyl at the non-reducing end is protected with a levulinoyl (Lev) ester, that can be removed orthogonally to all other used protecting groups. The designed protecting group strategy should thus allow for the generation of a tetrasaccharide donor and tetrasaccharide acceptor building block that can be exploited in the [4n+4] assembly of larger oligomers.

The GlcNAc3NAcA units in the A. baumannii tetrasaccharide are liked in a 1,2-trans fashion, so a stereoselective glycosylation can be accomplished using neighbouring group participation. Previously, 2,3-di-N-troc protected GlcNAc3NAcA building blocks¹⁷ as well as a building block with a C-3-acetamide¹⁸ have been unsuccessful and therefore it was decided to use an N-trichloroacetyl protected building block (5). The bacillosamine units in the tetrasaccharide are linked in a 1,2-cis fashion and relatively little is known about the stereoselectivity of glycosylations of bacillosamine donors carrying non-participating groups.¹⁹ Approaches have been reported based on the use of 'in situ anomerisation' strategy,²⁰ and indirect methods, based on glycosylations with a galactose- or fucose donor followed by C-4 inversion have also been used.^{21, 22} Thus, here three building blocks were identified for the synthesis of the protected tetrasaccharide: a GlcNAc3NAcA acceptor for the reducing end with the anomeric allyl linker (2), a bacillosamine (QuiNAc4NAc) donor, which can be either a selenophenyl or N-phenyl trifluoroacetimidate (PTFAI) donor (3 or 4, respectively) and which has a C-2-azide as a non-participating masked amino functionality, and GlcNAc3NAcA donor 5 for the non-reducing end.



neigbouring group participation mediated β -selective 1,2-trans glycosylation \dot{f} acceptor reactivity mediated α -selective 1,2-cis glycosylation

GIcNAc3NAcA acceptor (2)

CO₂Me NPh

GlcNAc3NAcA donor (5)

QuiNAc4NAc donor X = SePh **(3)** or OC(=NPh)CF₃ **(4)**

Challenges: - 8 NHAc groups in 4 sugar rings

- 2 different 1,2-cis glycosidic bonds

Scheme 1: Synthetic targets and retrosynthetic analysis.

Synthesis of 2,4-di-*N*-acetyl bacillosamine and 2,3-di-*N*-acetyl glucuronic acid building blocks

The synthesis of the bacillosamine building block (*Scheme 2*) starts from D-fucose (**6**), which is transformed into 3,4-di-O-acetyl-D-fucal (7) in high yield over 3 steps. In the next step, the anomeric selenophenol and the C-2-azide were simultaneously installed.^{23, 24} After deacetylation under Zemplén conditions, a 2-naphthylmethyl (NAP) ether was regioselectively introduced *via* the intermediate dibutyltin ketal. The installation of the axial C-4-azide was first attempted using the C-4-triflate, but this proved unsuccessful because the triflate could not be isolated due to decomposition. The reaction between the C-4-mesylate and NaN₃ showed no conversion of the starting material but when the mesylate was treated with NaN₃ and TBABr at 70 °C,^{19,24} the desired di-azide was obtained in 71%. This synthesis could be performed on large scale and selenophenyl donor **3** was generated on a 26 mmol scale. Compound **3** can be used directly as donor or converted to PTFAI-donor **4** by NIS mediated hydrolysis followed by conversion into the imidate.



Scheme 2: Synthesis of the bacillosamine building blocks. Reagents and conditions: a) Ac_2O , pyridine; b) HBr/HOAc, DCM; c) Zn, NH₄Cl, EtOAc, 70 °C, 90% over 3 steps; d) Ph₂Se, BAIB, TMSN₃, DCM, -30 °C to -10 °C, 77%; e) NaOMe, MeOH, 82%; f) i: DBTO, toluene, 130 °C, ii: NapBr, TBAI, toluene, 100 °C, 81 %; g) MsCl, pyridine, 80%; h) NaN₃, TBABr, DMF, 70 °C, 71%; i) NIS, THF/H₂O, 99%; j) PTFAI-Cl, NaH, DCM, 64%.

The design of the α -O-allyl-2,3-diamino glucuronic acid building block was inspired by the work of Yin and Seeberger and coworkers, who reported the preparation of allyl 2deoxy-2-*N*-trichloroacetyl- α -D-glucopyranoside (**16a**, *Scheme 3A*) from glucosamine in 37% over 6 steps.¹⁸ Here, a more efficient route is presented, based on the work of Lin and Wang and coworkers.²⁵ First, glucosamine hydrochloride was selectively *O*silylated using HMDS in acetonitrile. Next, the trichloroacetyl protecting group was installed in excellent yield. In one pot, the silyl ethers were cleaved and the anomeric allyl group was installed through a Fischer glycosylation. This method yielded

compound 16a in 53% over 3 steps. In addition, 32% of β -anomer 16b was obtained (Scheme 3A). The anomers were separated and both converted to the two corresponding glucuronic acid building blocks. The synthesis of glucuronic acid building blocks from the α -anomer (*Scheme 3B*) starts with protection of the C-4- and C-6-alcohols with a benzylidene acetal. Subsequently the C-3 alcohol was inverted by oxidation with Dess-Martin periodinane followed by reduction with NaBH₄ to form allo-configured building block 19. The C-3-azide was installed by triflation of the axial alcohol, followed by substitution with NaN₃. The benzylidene was then removed using PTSA in methanol, yielding building block 22. The regioselective oxidation of the primary alcohol was effected with TEMPO/BAIB to give, after methylation, acceptor 24. The latter building block was assembled on 24 mmol scale and can be used as an acceptor, or turned into PTFAI-donor 5 by protection of the C-4-OH in a Steglich esterification with levulinic acid, deprotection of the anomeric allyl group using PdCl₂ and installation of the imidate. Acceptor 2 was synthesized in a similar fashion starting from β -anomer **16b** (*Scheme 3C*). The inversion of C-3-alcohol however, was achieved using a different strategy, because the oxidation-reduction sequence led to the formation of gluco-epimer alongside decomposition products. Thus, inversion of the C-3-alcohol in 27 was achieved by a Latrell-Dax epimerisation, through triflation of the alcohol followed by a substitution with NaNO2. Next triflation of the allose-configured compound 29 was attempted. This reaction was significantly slower than the reaction on the corresponding α -anomer and the generated triflate decomposed with extended reaction times. Therefore, a mesylate was installed instead, which was subsequently substituted using tetrabutylammonium azide at 70 °C.



Scheme 3: Synthesis of 2,3-di-N-acetyl glucuronic acid building blocks A: synthesis of 1-allyl-2trichloroacetamide glucosamine. Reagents and conditions: a) HMDS, ACN; b) TCACl, DCM/pyr 7:3, 0°C to RT, 99% over 2 steps; c) AcCl, allyl-OH, 0 to 80 °C, 53% of 16a and 32% of 16b; B: synthesis of α -O-allyl acceptor 24 and α -PTFAI donor 5. Reagents and conditions: a) PhCH(OMe)₂, PTSA, ACN, 60 °C, 300 mbar 86%; b) Dess-Martin periodinane, DCM; c) NaBH₄, MeOH, -10 °C to RT, 70% over 2 steps; d) Tf₂O, DMAP, DCM, 0 °C; e) NaN₃, DMF, 94% over 2 steps; f) PTSA, MeOH, reflux, 76%; g) TEMPO, BAIB, DCM/H₂O 2:1; h) MeI, NaHCO₃, DMF, 60% over 2 steps; i) LevOH, EDCI-HCl, DMAP, DCM, 100%; j) PdCl₂, MeOH/DCM, 3:2, 92% k) PTFAI-Cl, K₂CO₃, DCM/H₂O, 10:1, 70%; C: Synthesis of β -O-allyl acceptor 2. Reagents and conditions: a) PhCH(OMe)₂, PTSA, ACN, 60 °C, 300 mbar 94%; b) Tf₂O, pyridine, DCM, - 10 °C; c) NaNO₂, DMF, 54% over 2 steps; d) MsCl, pyridine; e: Bu₄NN₃, acetonitrile, 70 °C, 65% over 2 steps; f) PTSA, methanol, 60 °C, 97%; g) TEMPO, BAIB, DCM/H₂O 2:1; h) MeI, NaHCO₃, DMF, 52% over 2 steps.

Bacillosamine glycosylations

To study the glycosylating properties of the bacillosamine donors **3** and **4** their activation and the formation of reactive intermediates was studied by VT-NMR (*Figure 2*). When a mixture of donor **3** and Ph₂SO in CD₂Cl₂ was treated with Tf₂O at -80 °C, three new species were formed, which were identified as the α -triflate (**A**, H-1: 6.10 (d, *J* = 3.0 Hz)), the α -oxosulfonium triflate (**B**, H-1: 6.31 (d, *J* = 3.5 Hz)) and the β -oxosulfonium triflate (**C**, H-1: 5.61 (d, *J* = 8.3 Hz)). When the NMR probe was slowly warmed with 10 °C increments, the β -oxosulfoxonium triflate proved to be the least stable of the three intermediates and it almost fully disappeared at -40 °C, while decomposition of the other species started around -30 °C. When imidate donor **4** was treated with triflic acid at -80 °C, clean formation of the α -triflate was observed.



 $f_{1} = f_{1} = f_{1$

Next, the glycosylations of bacillosamine donor **3** were investigated in a series of Ph_2SO/Tf_2O mediated glycosylations (*Table 1*) with model acceptors of gradually varying nucleophilicity (EtOH-TFE).^{23, 26-28} These glycosylation showed that the stereochemical outcome of glycosylations with donor **3** is highly dependent on the nucleophilicity of the acceptor, with the glycosylation of ethanol giving nearly complete β -selectivity, while glycosylation of trifluoroethanol provided primarily the α -product. Next 2,3-di-*N*-acetyl glucuronic acid acceptor **24** and bacillosamine acceptor **34**, obtained by treatment of glycosylation product **3D** with DDQ, were glycosylated with **3**. Based on previous studies both the CO₂Me group²⁹ as well as the azide (*this thesis*, chapter 5) were expected to have a strong disarming effect on the neighbouring alcohol, lowering its nucleophilicity and thus rendering the glycosylations with the acceptor α -selective. Indeed, the glycosylations of **3** with acceptor **24** and acceptor **34** provided the desired α -product with good selectivity. The yield of the reaction with the diaminoglucuronic acid acceptor **24** was moderate.

н₃с∕он	FH ₂ C	`ОН F ₂ H(с^он	F₃С́ОН	MeO ₂ C HO N ₂	N ₃ HO-	L'of	
EtOH	MFE	. 1	DFE	TFE 24		Allyl	^N 30CF 34	
Donor		EtOH	MFE	DFE	TFE	24	34	
N	0	3A	3B	3C	3D	3E	3F	
NapO		1:8	1:2	2.9:1	22:1	12:1	6.6:1	
٢	[∿] 3ŚePh	(84%)	(75%)	(66%)	(94%)	(42%)	(75%)	

Table 1: Stereoselectivity of bacillosamine donor **3**, α : β ratios, yield in parentheses.

Conditions for pre-activation: 0.05 M donor in DCM, 1.3 eq Ph₂SO, 1.3 eq Tf₂O, 2.5 eq TTBP, 2 eq acceptor. Activation from -80 °C to -60 °C, glycosylation from -80 °C.

A potential mechanistic explanation for the stereochemical outcome of the glycosylations of donor **3** is given in *Figure 3*. Upon activation of donor **3** with Ph₂SO and Tf₂O, three reactive species are formed, the α -triflate, the α -oxosulfonium triflate and the β -oxosulfonium triflate, with the latter being the least stable. Strong nucleophiles can react with one of the (more stable) α -species in an S_N2-type reaction to form the β -product, while less reactive nucleophiles require a stronger electrophile, such as the more reactive β -oxosulfonium triflate to form the α -product. The least reactive nucleophiles react in an S_N1-like reaction to form the α -product.



Figure 3: Mechanistic rationale for the observed stereoselectivity of donor 3.

Synthesis of the tetrasaccharide

Next, the assembly of the target tetrasaccharide was undertaken, starting with optimization of the glycosylation between the bacillosamine donor and diaminoglucuronic acid acceptor (Table 2). Although the glycosylation of donor 3 and acceptor 24 under pre-activation conditions proceeded with high α -selectivity, the yield was relatively poor (Table 2, entries 1 and 2). When imidate donor 4 was reacted with the same acceptor using in-situ activation conditions, the desired product was obtained in high yield, but with no stereoselectivity (entry 3). When Ph₂SO was added to this activation procedure the α -selectivity was significantly improved, at the expense of a lower yield (entry 4). The increased stereoselectivity in the latter glycosylation suggests that the oxosulfonium triflates play an important role in determining the stereoselective outcome of the glycosylation reaction, with the most reactive covalent species C (Figure 2), providing the desired α -product. The yield of the pre-activation glycosylation could be further improved by decreasing the amount of Ph₂SO and Tf₂O and raising the temperature of the glycosylation reaction (entries 5-7). It has previously been shown that selenoglycosides can be completely activated using half an equivalent of Ph₂SO and Tf₂O.²³ The excess of diphenylsulfonium bistriflate, generated in the glycosylations described in entries 1 and 2, that is not used for the activation of the selenoglycoside may react with the acceptor alcohol, preventing it from being glycosylated.^{30, 31} Indeed, the use of a bit more than half an equivalent of the activator led to complete activation of the bacillosamine donor and the desired increase in yield. The glycosylation with β -O-allyl acceptor **2** proceeded best and delivered the target disaccharide with the highest vield (entry 7).

	N Naj		h		NPh N ₃ O CF ₃	N	
MeO ₂ C HO _{N3} TCAHN _{OAllyl} 24		Ĵ	MeO ₂ C HO N ₃) OAliyi NHTCA	HO N ₃ CO ₂ Me N ₃ O OAllyI N ₃ NHTCA		
Entry	Donor (eq)	Acceptor (eq)	Activator (eq)	Additive (eq)	Solvent Temp [°C]	Product (yield)	α:β
1	3 (1)	24 (2)	Ph ₂ SO/Tf ₂ O (1.3/1.3)	TTBP (2.5)	DCM -80 → -60	3E (42%)	12:1
2	3 (1.3)	24 (1)	Ph ₂ SO/Tf ₂ O (1.3/1.3)	TTBP (2.5)	DCM -80 → -60	3E (31%)	10:1
3	4 (1.3)	24 (1)	TMSOTf (0.2)	-	DCM -80 → 0	3E (83%)	1:1
4	4 (1.3)	24 (1)	TMSOTf (0.2)	Ph ₂ SO (1.5)	DCM -80 → 0	3E (38%)	9:1
5	3 (1.3)	24 (1)	Ph ₂ SO/Tf ₂ O (1.3/0.65)	TTBP (2.5)	DCM -80 → 0	3E (55%)	13:1
6	3 (1.3)	24 (1)	Ph ₂ SO/Tf ₂ O (0.65/0.65)	TTBP (2.5)	DCM -80 → 0	3E (65%)	13:1
7	3 (1.3)	2 (1)	Ph ₂ SO/Tf ₂ O (0.65/0.65)	TTBP (2.5)	DCM -80 → 0	35 (74%) ^a	10:1
8	3 (1.3)	36 (1)	Ph ₂ SO/Tf ₂ O (0.65/0.65)	TTBP (2.5)	DCM -80 → 0	37 (38%)	4.5:1
9	3 (1.3)	36 (1)	Ph ₂ SO/Tf ₂ O (0.65/0.65)	TTBP (2.5)	1:1 Et ₂ O/DCM -80 \rightarrow 0	37 (81%)	10:1

Table 2: Optimisation of the glycosylations of the bacillosamine donors.

Reactions with 3 A molecular sieves (rods, 3/16"). Entries 1-7 were performed with a donor concentration of 0.05 M. in entries 8 and 9, the concentration of the donor was 0.025 M due to lower solubility of acceptor **36.** *a*: yield based on 0.1 mmol scale. On 4 mmol scale, the yield was 81%

With disaccharide **35** the assembly of the target tetrasaccharide was continued (*scheme* **4**). Thus, product **35** was treated with DDQ to obtain disaccharide acceptor **36**. It was observed that this disaccharide had a relatively low solubility and therefore it was used in the ensuing glycosylation reaction at a lower concentration (0.025 M *vs* 0.05M used for the condensation before). This led to formation of the trisaccharide in moderate

yield and with moderate α -selectivity (table 2, entry 8). [§] Switching the solvent from DCM to a 1:1 mixture of DCM and diethyl ether increased both the α -selectivity and the yield (table 2, entry 9). Likely the decreased solvent polarity promotes the S_N2 reaction of the β -oxosulfonium triflate while leveraging its high reactivity. Unmasking the Nap ether with DDQ the delivered trisaccharide acceptor 38, which was reacted with donor 5 under in-situ activation conditions, to yield tetrasaccharide 39 in 59% yield on 670 µmol scale. Deprotection of the tetrasaccharide started with removal of the methyl and levulinoyl esters, When the tetrasaccharide was treated with sodium hydroxide for 2 hr at RT, the esters were selectively removed leaving the trichloroacetamides unscathed. Unfortunately, the subsequent Zn/AcOH reduction and subsequent acetylation to transform both the azides and trichloroactyl groups into the corresponding acetamides was unsuccessful. Investigations towards a full deprotection and acetylation sequence to successfully transform tetrasaccharide 39 into the target tetrasaccharide 1 are currently in progress.



Scheme 4: assembly of tetrasaccharide **39** Reagents and conditions: a) first donor **3**, Ph₂SO, TTBP, Tf₂O, DCM, -80 °C \rightarrow -60 °C \rightarrow -80 °C, then acceptor **2**, -80 °C \rightarrow 0 °C, 81%, $\alpha:\beta = 10:1$; b) DDQ, 9:1 DCM/H₂O, 89%; c) first donor **3**, Ph₂SO, TTBP, Tf₂O, 1:1 Et₂O/DCM, -80 °C \rightarrow -60 °C \rightarrow -80 °C, then acceptor **36**, -80 °C \rightarrow 0 °C, 81%, $\alpha:\beta = 10:1$; d) DDQ, 9:1 DCM/H₂O, 62%; e) first donor **5** and acceptor **38**, DCM, 0 °C, then TMSOTf, 59%, $\alpha:\beta < 1:20$; f) 1:1 THF/1M aq. NaOH, 2 hr at RT

⁹ An attempt was made to increase the α-selectivity by using *N*,*N*-methylphenylformamide as additive, but this yielded only a trace amount of trisaccharide, with 1,1'-linked donor and unreacted acceptor as the main products

Conclusions

The synthesis of a highly N-acetylated oligosaccharide from the capsule of Acinetobacter Baumannii, consisting of 2,4-di-N-acetyl bacillosamine and 2,3-di-Nacetyl glucuronic acid, was accomplished. To this end, scalable routes towards the rare monosaccharide building blocks were developed. Bacillosamine building block 3 was prepared on 26 mmol scale and 2,3-di-N-acetyl glucuronic acid building block 24 on a 23 mmol scale. Next, the glycosylating properties of the bacillosamine donors were investigated by low temperature NMR characterisation of reactive species that were formed upon activation and a series of glycosylation reactions with a set of model acceptors, of gradually decreasing nucleophilicity. Activation of the bacillosamine selenophenyl donor 3 with Ph₂SO and Tf₂O led to the formation of three reactive species upon reaction, the anomeric α -triflate, α -oxosulfonium triflate and the β oxosulfonium triflate. The latter β -oxosulfonium triflate proved to be the least stable of the three intermediates. PTFAI donor 4 generated only the α -triflate upon reaction with TfOH. It was found that the stereoselectivity of glycosylations of donor 3 under pre-activation conditions strongly depends on the nucleophilicity of the acceptor, as the stereoselectivity gradually changed from nearly completely β-selective for the most nucleophilic acceptor (ethanol) to completely α -selective for the weakest nucleophile (trifluoroethanol). The carbohydrate acceptors that were studied in the context of the assembly of the target A. baumannii tetrasaccharide provided α -selective glycosylations, which can be accounted for by the presence of the flanking de-activating groups in these acceptors (*i.e.* the neighboring methyl ester and azides). It was found that Ph_2SO played an important role in shaping the stereoselectivity of the glycosylations, pointing to the reactive β -oxosulfonium triflate as an important intermediate for the α -selective bacillosaminylation reactions. In these glycosylations, Ph₂SO thus functions as a nucleophilic additive to modulate the reactivity of the glycosylating species, similar to the formamide additives that have recently gained significant attention in the development of stereoselective glycosylation reactions. The developed protecting group scheme not only allowed to generate the target tetrasaccharide, it will also enable the generation of tetrasaccharide building blocks to assemble larger fragments of the A. baumannii polysaccharide in a [4n+4] glycosylation approach. These can be used to study the structural properties of these fascinating highly N-acetylated oligosaccharide structures and their interaction with components of the host immune system.

Experimental

General experimental procedures

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 (Tf₂O) was distilled over P₂O₅ and stored at -20°C under a nitrogen atmosphere. 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 F254, Merck) with UV detection by (254 nm) and by spraying with 20% sulfuric acid in ethanol or by spraying with a solution of (NH₄)₆Mo₇O₂₄·H₂O (25 g/L) and $(NH_4)_4Ce(SO4)_4\cdot 2H_2O$ (10 g/L) in 10% aq. sulfuric acid followed by charring at ±250 °C. Highresolution 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. 1H and 13C NMR spectra were recorded on Bruker AV-400, Bruker DMX-400, and Bruker AV-500 NMR instruments. Chemical shifts (δ) are given in parts per million (ppm) relative to tetramethylsilane as an internal standard or the residual signal of the deuterated solvent. Coupling constants (J) are given in Hertz (Hz). All presented 13C-APT spectra are proton-decoupled. NMR peak assignments were made using COSY and HSQC. When necessary, additional NOESY, HMBC and HMBC-GATED 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 1H 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.

3,4-di-O-acetyl-D-fucal (7)

D-fucose (**6**, 10 g, 60.9 mmol) was dissolved in pyridine (0.2 M), after which Ac_2O (29 mL, 305 mmol, 5 eq) was added. The reaction mixture was stirred overnight and concentrated. The residue was dissolved in ethyl acetate and washed with 1M HCl and sat. aq. NaHCO₃. The organic phase was dried with MgSO₄ and concentrated under reduced pressure to obtain the crude per-acetylated fucose, which was used without further purification. Per-acetylated fucose was dissolved in DCM (0.25 M) and cooled to 0 °C. HBr (33% in HOAc, 77 mL, 425 mmol, 7.5 eq) was added dropwise and the reaction was allowed to warm to RT. After 2 hr, the reaction

mixture was concentrated and azeotroped with toluene at 30 °C, yielding the anomeric bromide. The residue was dissolved in EtOAc (0.25 M) and washed with sat. aq. NaHCO₃. The organic phase was dried with MgSO₄, after which NH₄Cl (22.8 g, 425 mmol, 7.5 eq) and freshly activated zinc (27.8 g, 425 mmol, 7.5 eq) were added. The reaction mixture was heated to a reflux overnight, filtered and concentrated. The residue was purified over silica (5% Et₂O in pentane with 1% Et₃N) yielding the title compound as white solid. Yield: 10.9 g, 51 mmol, 90%. ¹H NMR (400 MHz, CDCl₃) δ 6.47 (dd, *J* = 6.3, 2.0 Hz, 1H, H-1), 5.58 (dtd, *J* = 4.9, 2.0, 1.1 Hz, 1H, H-3), 5.29 (dt, *J* = 4.9, 1.6 Hz, 1H, H-4), 4.64 (dt, *J* = 6.3, 1.9 Hz, 1H, H-2), 4.23 (qq, *J* = 6.5, 1.0 Hz, 1H, H-5), 2.16 (s, 3H, CH₃ Ac), 2.02 (s, 3H, CH₃ Ac), 1.28 (d, *J* = 6.6 Hz, 3H, H-6). ¹³C NMR (101 MHz, CDCl₃) δ 170.8, 170.5 (C=O), 146.2 (C-1), 98.4 (C-2), 71.6 (C-5), 66.3 (C-4), 65.1 (C-4), 20.9, 20.8 (CH₃ Ac), 16.6 (C-6). Spectra in agreement with literature.³²

Phenyl 2-deoxy-2-azido-3,4,-di-O-acetyl-1-seleno-a-D-fucopyranoside (8)



Compound 7 (19.38 g, 90.47 mmol) and diphenyl diselenide (28.24 g, 90.47 mmol, 1 eq) were dissolved in DCM (0.2M) and degassed with N₂ in an ultrasonic bath. After this, the solution was cooled to -30 °C and BIAB (29.14 g, 90.47 mmol, 1 eq) and TMSN₃ (23.69 mL, 180.9 mmol, 2 eq) were added. The reaction mixture was allowed to warm to -10 °C and kept at that temperature overnight. Excess reagents were quenched by the addition of 20 mL cyclohexene, after which the reaction mixture was allowed to warm to RT and concentrated under reduced pressure. Silica chromatography (2% acetone in pentane) yields the title compound as yellow oil. Yield: 28.70 g, 69.61 mmol, 77%. ¹H NMR (500 MHz, CDCl₃) δ 7.61 – 7.52 (m, 2H, CH_{arom}), 7.34 – 7.27 (m, 3H, CH_{arom}), 5.95 (d, *J* = 5.4 Hz, 1H, H-1), 5.32 (dd, *J* = 3.3, 1.2 Hz, 1H, H-4), 5.13 (dd, *J* = 10.8, 3.2 Hz, 1H, H-3), 4.50 (dd, *J* = 6.4 Hz, 1.2 Hz, 1H, H-5), 4.23 (dd, *J* = 10.8, 5.4 Hz, 1H, H-2), 2.17 (s, 3H, CH₃ Ac), 2.07 (s, 3H, CH₃ Ac), 1.09 (d, *J* = 6.5 Hz, 3H, H-6); ¹³C NMR (126 MHz, CDCl₃) δ 170.5, 169.9 (C=O), 134.9, 129.4 (CH_{arom}), 128.3 (Cq), 128.2 (CH_{arom}), 84.6 (C-1), 71.8 (C-3), 70.3 (C-4), 67.7 (C-5), 59.0 (C-2), 20.9, 20.8 (CH₃ Ac), 16.0 (C-6). Spectra in agreement with literature.

Phenyl 2-deoxy-2-azido-1-seleno-α-D-fucopyranoside (9)



Product 7 (28.70 g, 69.61 mmol) was dissolved in MeOH (0.5 M) and NaOMe (1.88 g, 34.80 mmol, 0.5 eq) was added. The mixture was stirred for 17 h after which the reaction was neutralized with Amberlite-H⁺, filtered and concentrated under reduced pressure. The product was recrystallized using EtOAc/pentane and concentrated mother liquor was purified via silica chromatography (15% acetone in pentane), yielding product 18 as a white solid. Total yield: 18.80 g, 57.28 mmol, 82%. ¹H NMR (300 MHz, CDCl₃) δ 7.65 – 7.52 (m, 2H, CH_{arom}), 7.37 – 7.22 (m, 3H, CH_{arom}), 5.91 (d, *J* = 5.3 Hz, 1H, H-1), 4.38 (q, *J* = 6.6 Hz, 1H, H-5), 4.06 (dd, *J* = 9.9, 5.3 Hz, 1H, H-2), 3.88 – 3.75 (m, 2H, H-3, H-4), 2.67 (s, 2H, 3-OH, 4-OH), 1.26 (d, *J* = 6.6 Hz, 3H,

H-6); ¹³C NMR (75 MHz, CDCl₃) 134.7, 129.4 (CH_{arom}), 128.7 (C_q), 128.1 (CH_{arom}), 85.2 (C-1), 71.7, 71.5 (C-3, C-4), 68.9 (C-5), 62.1 (C-2), 16.2 (C-6). Spectra in agreement with literature.³³

Phenyl 2-deoxy-2-azido-3-O-(2-naphthyl)methyl-1-seleno-a-D-fucopyranoside (10)



Compound 9 (18.8 g, 57.3 mmol) and Bu₂SnO (14.5 g, 58.4 mmol, 1.02 eq) were dissolved in toluene in a flask equipped with a Dean-Stark apparatus. The reaction mixture was heated to a vigorous reflux for under removal of water for 2 hr, after which NapBr (13.3 g, 60.1 mmol, 1.05 eq) and TBABr (19.4 g, 60.1 mmol, 1.05 eq) were added at 60 °C. The reaction mixture was then heated to a reflux for 1 hr, after which it was cooled to RT and guenched with 10% ag. KF solution. The phases were separated and the aqueous phase was extracted with ethyl acetate. Combined organic phases were washed with brine, dried with MgSO4 and concentrated. The residue was purified over silica (5% acetone in pentane) to yield the title compound as yellow solid. Yield: 21.7 g, 46.3 mmol, 81%. ¹H NMR (500 MHz, CDCl₃) δ 7.90 - 7.81 (m, 4H, CH_{arom}), 7.60 - 7.54 (m, 2H, CH_{arom}), 7.55 - 7.46 (m, 3H, CH_{arom}), 7.31 - 7.23 (m, 4H, CH_{arom}), 5.89 (d, J = 5.4 Hz, 1H, H-1), 4.91 (d, J = 11.2 Hz, 1H, CHH Nap), 4.85 (d, J = 11.5 Hz, 1H, CHH Nap), 4.28 (q, I = 6.6 Hz, 1H, H-5), 4.20 (dd, I = 10.2, 5.3 Hz, 1H, H-2), 3.89 (dt, I = 3.1, 1.5 Hz, 1H, H-4),3.74 (dd, J = 10.2, 3.1 Hz, 1H, H-3), 2.42 (t, J = 1.6 Hz, 1H, 4-OH), 1.24 (d, J = 6.6 Hz, 3H, H-6);¹³C NMR (126 MHz, CDCl₃) δ 134.6 (CH_{arom}), 133.4, 133.3 (C_q), 129.2, 128.8 (CH_{arom}), 128.6 (C_q), 128.1, 128.0, 127.9, 127.9, 127.1, 126.5, 126.4, 125.8 (CHarom), 85.3 (C-1), 79.4 (C-3), 72.4 (CH₂ Nap), 68.7, 68.7 (C-4, C-5), 60.4 (C-2), 16.2 (C-6). Spectra in agreement with literature.²⁴

Phenyl2-deoxy-2-azido-3-O-(2-naphthyl)methyl-4-O-methanesulfonyl-1-seleno-α-D-fucopyranoside (11)



Compound **10** (21.7g, 46.3 mmol) was dissolved in pyridine (0.5 M), after which methanesulfonyl chloride (5.4 mL, 69.4 mmol, 1.5 eq) was added dropwise. After full conversion as indicated by TLC, the reaction mixture was concentrated under reduced pressure. The residue was dissolved in DCM and washed with 1M HCl and sat. aq. NaHCO₃. The organic phase was dried with MgSO₄ and concentrated. Silica chromatography (15% acetone in pentane) yields the title compound as yellow oil. Yield: 20.3 g, 37.1 mmol, 80%). ¹H NMR (400 MHz, CDCl₃) δ 7.91 – 7.80 (m, 4H, CH_{arom}), 7.59 – 7.54 (m, 3H, CH_{arom}), 7.54 – 7.48 (m, 2H, CH_{arom}), 7.33 – 7.26 (m, 3H, CH_{arom}), 5.93 (d, *J* = 5.4 Hz, 1H, H-1), 5.11 (dd, *J* = 3.0, 1.1 Hz, 1H, H-4), 4.99 (d, *J* = 10.6 Hz, 1H, CHH Nap), 4.49 – 4.39 (m, 1H, H-5), 4.14 (dd, *J* = 10.4, 5.3 Hz, 1H, H-2), 3.85 (dd, *J* = 10.6 Hz, 1H, CH₄ map), 4.49 – 4.39 (m, 1H, H-5), 4.14 (dd, *J* = 10.4, 3.4 Hz, 1H, H-3), 2.99 (s, 3H, CH₃ Ms), 1.27 (d, *J* = 6.5 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 134.8 (CH_{arom}), 133.8, 133.4, 133.3 (C_q), 129.4, 128.7, 128.2, 128.2 (CH_{arom}), 127.9 (C_q), 127.9, 127.8, 126.5, 126.5, 126.2 (CH_{arom}), 84.6 (C-1), 79.0 (C-4), 77.5 (C-3), 73.2 (CH₂ Nap), 67.9 (C-5), 60.6 (C-2), 39.3 (CH₃ Ms), 16.6 (C-6). Spectra in agreement with literature.²⁴

Phenyl 2,4-dideoxy-2,4-diazido-3-O-(2-naphthyl)methyl-1-seleno- α -D-quinopyranoside (3)

Compound **9** (20.3 g, 37.1 mmol) was dissolved in DMF with NaN₃ (24.1 g, 371 mmol, 10 eq) and TBABr (35.8 g, 111 mmol, 3 eq), after which the reaction mixture was heated to 70 °C. When TLC showed full conversion of the starting material, the mixture was cooled to RT, diluted with water and extracted with diethyl ether. The organic phase was dried with MgSO₄ and concentrated under reduced pressure. The residue was purified over silica (1% acetone in pentane) yielding the title compound as a yellow oil. Yield: 13.0 g, 26.4 mmol, 71%. $[\alpha]_D^{25} = 176.3^{\circ}$ (c = 0.48, CHCl₃); IR (thin film): 741, 1084, 1269, 2105; ¹H NMR (400 MHz, CDCl₃) δ 7.92 – 7.79 (m, 4H, CH_{arom}), 7.61 – 7.53 (m, 3H, CH_{arom}), 7.51 – 7.44 (m, 2H, CH_{arom}), 7.33 – 7.25 (m, 3H, CH_{arom}), 5.81 (d, *J* = 5.3 Hz, 1H, H-1), 5.06 (d, *J* = 10.5 Hz, 1H, CHH Nap), 5.02 (d, *J* = 10.6 Hz, 1H, CHH Nap), 4.04 (dq, *J* = 10.1, 6.2 Hz, 1H, H-5), 3.87 (dd, *J* = 9.9, 5.3 Hz, 1H, H-2), 3.62 (t, *J* = 9.6 Hz, 1H, H-3), 3.20 (dd, *J* = 10.1, 9.3 Hz, 1H, H-4), 1.28 (d, *J* = 6.2 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 134.7 (CH_{arom}), 134.5, 133.4, 133.3 (C_q), 129.3, 128.4 (CH_{arom}), 128.3 (C_q), 128.2, 128.2, 127.8, 127.7, 126.4, 126.3, 126.3 (CH_{arom}), 84.7 (C-1), 81.0 (C-3), 76.0 (CH₂ Nap), 69.6 (C-5), 68.3 (C-4), 65.0 (C-2), 18.2 (C-6); HRMS: [M+H]⁺ calcd for C₂₃H₂₂N₆O₂SeH 495.10428 , found 495.10387.

2,4-dideoxy-2,4-diazido-3-O-(2-naphthyl)methyl-α,β-D-quinopyranose (12)

Compound 3 (1.80 g, 3.65 mmol) was dissolved in 0.25 M 1:1 and cooled to 0 °C. NIS (1.23 g, 5.47 mmol, 1.5 eq) was added and the reaction mixture was slowly allowed to warm to RT. After full conversion, excess NIS was quenched with sat. aq. Na₂S₂O₃. The reaction mixture was concentrated under reduced pressure, the residue was dissolved in DCM and washed with water. The organic phase was dried with MgSO4 and concentrated under reduced pressure. The residue was purified over silica ($10\% \rightarrow 20\%$ acetone) yielding the title compound as white solid. Yield: 1.28 g, 3.62 mmol, 99%, $\alpha:\beta = 1:1.1$; data reported for a 1:1 mixture of anomers: ¹H NMR (400 MHz, CDCl₃) δ 7.89 - 7.80 (m, 8H, CH_{arom}), 7.56 (td, J = 8.5, 1.7 Hz, 2H, CH_{arom}), 7.51 - 7.43 (m, 4H, CH_{arom}), 5.26 (t, J = 3.3 Hz, 1H, H-1α), 5.05 (d, J = 10.8 Hz, 3H, CHH Nap, CH₂ Nap), 4.97 $(d, J = 10.7 \text{ Hz}, 1\text{H}, \text{CH} \text{H} \text{ Nap}), 4.51 (dd, J = 7.9, 4.4 \text{ Hz}, 1\text{H}, \text{H}-1\beta), 3.94 - 3.83 (m, 2\text{H}, \text{H}-3\alpha, \text{H}-3\alpha)$ 5a), 3.62 (d, J = 4.6 Hz, 1H, 1-OH β), 3.44 (dd, J = 10.1, 2.8 Hz, 1H, H-2a), 3.37 (dd, J = 9.7, 7.8Hz, 1H, H-2 β), 3.29 (dd, J = 9.7, 8.8 Hz, 1H, H-3 β), 3.23 (dq, J = 9.6, 5.9 Hz, 1H, H-5 β), 3.16 (ddd, *J* = 10.2, 9.2, 2.2 Hz, 2H, H-4αβ), 3.04 (dd, *J* = 3.5, 1.3 Hz, 1H, 1-OHα), 1.34 (d, *J* = 5.9 Hz, 3H, H-6 β), 1.31 (d, J = 6.2 Hz, 3H, H-6 α); ¹³C NMR (101 MHz, CDCl₃) δ 134.7, 134.7, 133.4, 133.4, 133.3 (Cq), 128.5, 128.2, 128.2, 127.8, 127.8, 127.6, 127.6, 126.4, 126.3, 126.3, 126.3, 126.2 (CH_{aron}), 96.1 (C-1β), 92.1 (C-1α), 81.3 (C-3β), 78.5 (C-3α), 75.7, 75.7 (CH₂ Nap), 71.1 (C-5β), 68.7 (C-4β), 67.7 (C-2β, C-4α), 66.8 (C-5α), 64.2 (C-2α), 18.52 (C-6αβ); HRMS: [M+H-N₂]⁺ calcd for C17H18N4O3H 327.14517, found 327.14486

<u>N-phenyl-O-(2,4-dideoxy-2,4-diazido-3-O-(2-naphthyl)methyl-α,β-D-quinopyranosyl)</u> trifluoroacetimidate (4)



Compound 11 (1.28 g, 3.62 mmol) was dissolved in DCM, after which PTFAI-Cl (0.92 mL, 5.79 mmol, 1.6 eq) and NaH (60% dispersion in mineral oil, 220 mg, 5.43 mmol, 1.5 eq) were added. After 3 hr, an extra 0.5 eq of PTFAI-Cl and NaH were added. Upon full conversion, the reaction was quenched with water and extracted with DCM. The organic phase was dried with MgSO₄ and concentrated. The residue was purified over silica (98:1:1 pentane/Et₂O/Et₃N) to yield the title compound as a white solid. Yield: 1.21 g, 2.30 mmol, 64%, $\alpha:\beta = 1:3.5$. Data reported for a 0.3:1 mixture. ¹H NMR (500 MHz, CDCl₃, 323 K) δ 7.84 (ddd, *J* = 13.2, 6.5, 4.2 Hz, 5.2H, CH_{arom}), 7.59 - 7.51 (m, 1.3H, CH_{arom}), 7.47 (p, J = 5.1 Hz, 2.6H, CH_{arom}), 7.30 (t, J = 7.7 Hz, 2.6H, CH_{arom}), 7.11 (td, J = 7.5, 1.2 Hz, 1.3H, CH_{arom}), 6.88 - 6.80 (m, 2.6H, CH_{arom}), 6.34 (s, 0.3H, H-1a), 5.44 (s, 1H, H-1β), 5.07 – 5.03 (m, 1.6H, CHH Napβ, CH₂ Napα), 5.00 (d, J = 10.9 Hz, 1H, CHH Napβ), 3.84 $(t, J = 9.7 \text{ Hz}, 0.3\text{H}, \text{H}-3\alpha), 3.75 (dq, J = 12.2, 6.1 \text{ Hz}, 0\text{H}, \text{H}-5\alpha), 3.63 (t, J = 9.0 \text{ Hz}, 1.3\text{H}, \text{H}-2\alpha\beta),$ 3.40 - 3.27 (m, 1H, H-3β), 3.25 - 3.08 (m, 2.3H, H-4αβ, H-5β), 1.38 - 1.33 (m, 3.9H, H-6αβ); ¹³C NMR (126 MHz, CDCl₃, 323 K) δ 143.3, 134.8, 133.6, 133.5 (C_a), 129.0, 129.0, 128.5, 128.3, 128.2, 127.9, 127.9, 127.6, 127.5, 126.4, 126.3, 126.3, 126.3, 124.8, 119.6, 119.5, (CH_{arom}) 95.8 (C-1β), 93.9 (C-1α), 81.5 (C-3β), 78.8 (C-3α), 75.9 (CH₂ Napα), 75.8 (CH₂ Napβ), 72.1 (C-5β), 69.6 (C-5α), 68.3 (C-4α), 67.7 (C-4β), 65.9 (C-2β), 63.6 (C-2α), 18.5 (C-6α), 18.4 (C-6β); HRMS: [M+H-N₂]⁺, calcd for C25H22F3N5O3H 498.17475, found 498.17448

2-Deoxy-2-trichloroacetamido-1,3,4,6-tetra-O-trimethylsilyl-α-D-glucopyranose (15)



D-glucosamine hydrochloride (13, 43.1 g, 200 mmol) and HMDS (105 mL, 500 mmol, 2.5 eq) were dissolved in 500 mL acetonitrile and stirred for 3 hr at RT, after which the solids were filtered off and the reaction mixture was concentrated under reduced pressure, yielding 14. The residue was dissolved in 1L 7:3 DCM/pyridine and cooled to 0 °C. Trichloroacetyl chloride (24.7 mL) was added dropwise and the reaction mixture was allowed to warm to RT overnight after which solvents were removed under reduced pressure. The residue was dissolved in DCM and washed with water. The organic phase was dried with MgSO₄ and concentrated under reduced pressure, yielding the title compound as amber coloured oil, which was used without further purification. Yield: 121.7 g, 198 mmol, 99%. ¹H NMR (400 MHz, CDCl₃) δ 6.84 (d, *J* = 9.6 Hz, 1H, NH), 5.12 (d, *J* = 3.4 Hz, 1H, H-1), 3.94 (td, *J* = 9.6, 3.4 Hz, 1H, H-2), 3.79 (dd, *J* = 9.5, 7.7 Hz, 1H, H-3), 3.76 – 3.69 (m, 2H, 2x H-6), 3.68 – 3.60 (m, 2H, H-4, H-5), 0.19 (s, 9H, CH₃ TMS), 0.17 (s, 9H, CH₃ TMS), 0.16 (s, 9H, CH₃ TMS), 0.11 (s, 9H, CH₃ TMS); ¹³C NMR (101 MHz, CDCl₃) δ 161.8 (C=O), 91.9 (C-1), 73.5 (C-3), 73.1, 71.9 (C-4, C-5), 61.6 (C-6), 57.0 (C-2), 1.2 (CH₃ TMS), 0.9 (CH₃ TMS), 0.0 (CH₃ TMS), -0.2 (CH₃ TMS). Spectra in agreement with literature.²⁵

Allyl 2-deoxy-2-trichloroacetamido-α-D-glucopyranoside (16a)



Compound **15** (117 g, 191 mmol) was dissolved in 500 mL allyl alcohol and cooled to 0 °C, after which acetyl chloride (13.6 mL, 191 mmol, 1 eq) was added. When TLC shows full removal of the TMS groups, the temperature was raised to 80 °C. When TLC shows disappearance of the starting material, the temperature is lowered to 0 °C and the reaction in quenched with NaHCO₃ (32.1 g, 382 mmol, 2 eq). Solids were filtered off and the solvent was removed under vacuum. The residue is purified with silica chromatography (5% methanol in DCM), yielding the title compound as off-white solid. Yield: 37.1 g, 102 mmol, 53%. ¹H NMR (400 MHz, MeOD) δ 5.92 (dddd, *J* = 17.1, 10.5, 6.2, 5.1 Hz, 1H, CH₂-CH=CH₂), 5.32 (dq, *J* = 17.3, 1.7 Hz, 1H, CH₂-CH=CHH), 5.21 – 5.15 (m, 1H, CH₂-CH=CHH), 4.95 (d, *J* = 2.8 Hz, 1H, H-1), 4.23 (ddt, *J* = 13.2, 5.1, 1.5 Hz, 1H, CHH-CH=CH₂), 4.03 (ddt, *J* = 13.2, 6.2, 1.3 Hz, 1H, CHH-CH=CH₂), 3.88 – 3.80 (m, 3H, H-2, H-3, H-6), 3.71 (dd, *J* = 11.8, 5.6 Hz, 1H, H-6), 3.63 (ddd, *J* = 9.7, 5.6, 2.2 Hz, 1H, H-5), 3.42 – 3.36 (m, 1H, H-4); ¹³C NMR (101 MHz, MeOD) δ 164.2 (C=O), 135.2 (CH₂-CH=CH₂), 118.0 (CH₂-CH=CH₂), 96.9 (C-1), 74.1 (C-5), 72.2 (C-3, C-4), 69.3 (CH₂-CH=CH₂), 62.6 (C-6), 57.5 (C-2). Spectra in agreement with literature.³⁴ Further elution also yielded the β-anomer as orange solid. Yield: 22.0 g, 60.3 mmol, 32%, giving a total yield of 85%

Allyl 2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (16b)

¹H NMR (400 MHz, MeOD) δ 5.86 (ddt, *J* = 17.2, 10.7, 5.4 Hz, 1H, CH₂-CH=CH₂), 5.26 (dq, *J* = 17.3, 1.7 Hz, 1H, CH₂-CH=CHH), 5.10 (dq, *J* = 10.5, 1.5 Hz, 1H, CH₂-CH=CHH), 4.59 (d, *J* = 8.1 Hz, 1H, H-1), 4.33 (ddt, *J* = 13.2, 5.0, 1.6 Hz, 1H, CHH-CH=CH₂), 4.07 (ddt, *J* = 13.2, 5.7, 1.5 Hz, 1H, CHH-CH=CH₂), 3.88 (dd, *J* = 11.9, 2.1 Hz, 1H, H-6), 3.72 – 3.59 (m, 3H, H-2, , H-6), 3.35 – 3.24 (m, 2H); ¹³C NMR (101 MHz, MeOD) δ 164.5, 135.4, 117.2, 101.3, 78.0, 75.0, 72.3, 71.0, 62.7, 59.2. spectra in agreement with literature.³⁵

Allyl 2-deoxy-2-trichloroacetamido-4,6-O-benzylidene-α-D-glucopyranoside (17)



16a (37 g, 101 mmol), PTSA-H₂O (0.97 g, 5.1 mmol, 0.05 eq) and benzaldehyde dimethylacetal (16.8 mL, 112 mmol, 1.1 eq) were dissolved in 1L acetonitrile and heated to 60 °C at 300 mbar. After full conversion of the starting material, the reaction was quenched with 0.1 eq Et₃N and concentrated under reduced pressure. Crystallisation (DCM/pentane) yields the title compound as off-white solid. Yield: 39.7 g, 87 mmol, 86%. ¹H NMR (400 MHz, CDCl₃) δ 7.54 – 7.45 (m, 2H, CH_{arom}), 7.38 (qd, *J* = 3.7, 1.7 Hz, 3H, CH_{arom}), 6.96 (d, *J* = 8.7 Hz, 1H, NH), 5.88 (dddd, *J* = 16.9, 10.4, 6.4, 5.4 Hz, 1H, CH₂-CH=CH₂), 5.57 (s, 1H, CHPh), 5.31 (dq, *J* = 17.2, 1.5 Hz, 1H, CH₂-CH=CHH), 5.26 (dq, *J* = 10.4, 1.2 Hz, 1H, CH₂-CH=CHH), 4.99 (d, *J* = 3.8 Hz, 1H, H-1), 4.29 (dd, *J* = 10.1, 4.7 Hz, 1H, H-6), 4.26 – 4.15 (m, 2H, H-2, CHH-CH=CH₂), 4.08 – 4.00 (m, 2H, H-3, CHH-CH=CH₂), 3.89 (td, *J* = 9.8, 4.7 Hz, 1H, H-5), 3.78 (t, *J* = 10.3 Hz, 1H, H-6), 3.61 (t, *J* =

9.3 Hz, 1H, H-4), 2.63 (d, *J* = 3.2 Hz, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 162.5 (C=O), 137.0 (C_q), 133.0 (CH₂-CH=CH₂), 129.5, 128.5, 126.4 (CH_{arom}), 118.9 (CH₂-CH=CH₂), 102.1 (CHPh), 96.4 (C-1), 81.8 (C-4), 70.0 (C-3), 69.0, 68.8 (C-6, CH₂-CH=CH₂), 62.9 (C-5), 55.5 (C-2). Spectra in agreement with literature.¹⁸

Allyl 2-deoxy-2-trichloroacetamido-4,6-O-benzylidene-α-D-allopyranoside (19)



Compound 17 (39.1 g, 86 mmol) and Dess-Martin periodinane (47.6 g, 112 mmol, 1.3 eq) were dissolved in DCM and stirred until TLC showed full conversion. The reaction mixture was quenched with sat. aq. Na₂S₂O₃ and extracted with DCM. The combined organic phases were dried and concentrated to yield the crude ketone 18 which was used immediately in the next reaction. The ketone was dissolved in methanol and cooled to -10 °C, after which NaBH₄ (13.1 g, 345 mmol, 4 eq) was added in small portions. After the final addition, the reaction mixture was allowed to warm to RT. After full conversion of the starting material, the reaction mixture was concentrated under reduced pressure. The residue was dissolved in ethyl acetate and washed with water. The organic phase was dried with MgSO4 and concentrated. Silica chromatography (20% Et₂O in pentane) yields the title compound as colourless oil that slowly solidifies. Yield: 27.4 g, 60.6 mmol, 70% over 2 steps. ¹H NMR (400 MHz, CDCl₃) δ 7.49 (dd, J = 6.6, 3.1 Hz, 2H, CH_{arom}), 7.44 (d, J = 8.8 Hz, 1H, NH), 7.40 – 7.35 (m, 3H, CH_{arom}), 5.87 (dddd, J = 17.0, 10.4, 6.5, 5.2 Hz, 1H, CH₂-CH=CH₂), 5.62 (s, 1H, CHPh), 5.31 (dq, J = 17.2, 1.5 Hz, 1H, CH₂-CH=CHH), 5.24 (dq, *J* = 10.4, 1.2 Hz, 1H, CH₂-CH=CH*H*), 4.99 (d, *J* = 4.2 Hz, 1H, H-1), 4.37 (dd, *J* = 10.3, 5.1 Hz, 1H, H-6), 4.30 - 4.23 (m, 2H, H-3, CHH-CH=CH₂), 4.23 - 4.17 (m, 2H, H-2, H-5), 4.05 (ddt, J = 13.0, 6.5, 1.2 Hz, 1H, CHH-CH=CH₂), 3.79 (t, J = 10.3 Hz, 1H, H-6), 3.65 (dd, J = 9.7, 2.8 Hz, 1H, H-4), 2.75 (d, J = 5.9 Hz, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 161.8 (C=O), 137.0 (C_q), 133.0 (CH₂-CH=CH₂), 129.4, 128.5, 126.3 (CH_{arom}), 118.9 (CH₂-CH=CH₂), 102.0 (CHPh), 96.0 (C-1), 92.3 (CCl₃), 78.2 (C-4), 69.5 (CH₂-CH=CH₂), 69.1 (C-6), 67.3 (C-3), 57.7 (C-5), 51.2 (C-2). Spectra in agreement with literature.¹⁸

Allyl 2,3-dideoxy-2-trichloroacetamido-3-azido-4,6-O-benzylidene-a-D-glucopyranoside (21)



Compound **19** (27.4 g, 60.5 mmol) and DMAP (22.2 g, 182 mmol, 3 eq) were dissolved in DCM and cooled to -10 °C, after which triflic anhydride (20.3 mL, 121 mmol, 2 eq) was added dropwise, after which the reaction mixture was slowly allowed to warm to RT. After full of the starting material, the reaction mixture was acidified with 5 eq of acetic acid and washed with water. The organic phase was dried with MgSO₄ and concentrated at 25 °C, yielding triflate **20**. The crude triflate was dissolved in DMF with NaN₃ (19.7 g, 303 mmol, 5 eq) and stirred overnight, after which the reaction mixture was poured in 10x the volume of water under vigorous stirring. The precipitated solid was collected by filtration, washed with water, dissolved in DCM and washed with brine. Organic phase was dried with MgSO₄ and concentrated, yielding

the slightly impure title compound as a white solid. Yield: 24.7 g, 51.6 mmol, 85% over 2 steps. ¹H NMR (400 MHz, CDCl₃) δ 7.52 – 7.46 (m, 2H, CH_{arom}), 7.38 (dq, *J* = 8.5, 2.3 Hz, 3H, CH_{arom}), 6.90 (d, *J* = 9.5 Hz, 1H, NH), 5.87 (dddd, *J* = 17.0, 10.3, 6.5, 5.4 Hz, 1H, CH₂-CH=CH₂), 5.63 (s, 1H, CHPh), 5.35 – 5.25 (m, 2H, CH₂-CH=CH₂), 4.91 (d, *J* = 3.7 Hz, 1H, H-1), 4.32 (dd, *J* = 10.3, 4.8 Hz, 1H, H-6), 4.24 (ddt, *J* = 12.7, 5.4, 1.3 Hz, 1H, CHH-CH=CH₂), 4.13 (ddd, *J* = 10.8, 9.6, 3.7 Hz, 1H, H-2), 4.04 (ddt, *J* = 12.7, 6.6, 1.2 Hz, 1H, CHH-CH=CH₂), 3.98 – 3.89 (m, 2H, H-3, H-5), 3.80 (t, *J* = 10.3 Hz, 1H, H-6), 3.70 (t, *J* = 9.6 Hz, 1H, H-4); ¹³C NMR (101 MHz, CDCl₃) δ 162.0 (C=O), 136.7 (Cq), 132.7 (CH₂-CH=CH₂), 129.3, 128.5, 126.0 (CH_{arom}), 119.3 (CH₂-CH=CH₂), 101.6 (CHPh), 96.0 (C-1), 80.4 (C-4), 69.0 (CH₂-CH=CH₂), 68.8 (C-6), 63.3 (C-5), 61.3 (C-3), 53.6 (C-2). Spectra in agreement with literature.¹⁸

Allyl 2,3-dideoxy-2-trichloroacetamido-3-azido-α-D-glucopyranoside (22)



Compound **21** (24 g, 50.2 mmol) and PTSA-H₂O (0.96 g, 5.02 mmol, 0.1 eq) were dissolved in methanol (0.3 M) and heated to a gentle reflux. After full conversion, the reaction was cooled to RT, neutralised with 0.2 eq Et₃N and concentrated under reduced pressure. The residue was purified over silica (25% acetone in pentane) to yield the title compound as white solid. Yield: 14.9 g, 38.2 mmol, 76%. ¹H NMR (400 MHz, Acetone) δ 8.22 (d, *J* = 8.3 Hz, 1H, NH), 5.92 (dddd, *J* = 17.2, 10.7, 5.9, 5.0 Hz, 1H, CH₂-CH=CH₂), 5.35 (dq, *J* = 17.3, 1.7 Hz, 1H, CH₂-CH-CHH), 5.16 (dq, *J* = 10.5, 1.4 Hz, 1H, CH₂-CH=CHH), 5.08 (d, *J* = 5.7 Hz, 1H, 4-OH), 4.92 (d, *J* = 3.6 Hz, 1H, H-1), 4.24 (ddt, *J* = 13.4, 5.0, 1.6 Hz, 1H, CHH-CH=CH₂), 4.08 – 4.01 (m, 2H, H-3, CHH-CH=CH₂), 3.86 – 3.71 (m, 4H, 6-OH, H-2, 2x H-6), 3.70 – 3.59 (m, 2H, H-4, H-5); ¹³C NMR (101 MHz, Acetone) δ 162.6 (C=O), 134.9 (CH₂-CH=CH₂), 117.4 (CH₂-CH=CH₂), 96.0 (C-1), 73.6 (C-4), 71.1 (C-5), 68.7 (CH₂-CH=CH₂), 64.7 (C-3), 62.1 (C-6), 54.9 (C-2). Spectra in agreement with literature¹⁸

Methyl (Allyl 2,3-dideoxy-2-trichloroacetamido-3-azido-α-D-glucopyranosyl uronate) (24)



Compound **22** (14.8 g, 38.1 mmol) was dissolved in 300 mL 2:1 DCM/H₂O after which TEMPO (2.98 g, 19.1 mmol, 0.5 eq) and BAIB (30.7 g, 95 mmol, 2.5 eq) were added. After full conversion, the reaction mixture was concentrated under reduced pressure, yielding crude uronic acid **23**. The residue was coevaporated twice with toluene and dissolved in 200 mL DMF with NaHCO₃ (14.4 g, 171 mmol, 4.5 eq) and methyl iodide (17.8 mL, 286 mmol, 7.5 eq). After 18 hr, the reaction mixture was diluted with water and extracted twice with diethyl ether. Combined organic phases were dried with MgSO₄ and concentrated under reduced pressure. The residue was purified over silica (15% acetone in pentane) to yield the title compound as white solid. Yield: 9.5 g, 22.8 mmol, 60%. $[\alpha]_D^{25} = 70.5^{\circ}$ (c = 0.63, CHCl₃); IR (thin film): 821, 1057, 1518, 1717, 2111; ¹H NMR (400 MHz, CDCl₃) δ 6.82 (d, *J* = 9.4 Hz, 1H, NH), 5.88 (dddd, *J* = 17.0, 10.3, 6.6, 5.4 Hz, 1H, CH₂-CH-CH₂), 5.34 (dq, *J* = 17.2, 1.4 Hz, 1H, CH₂-CH=CHH), 5.29 (dq, *J* = 10.4, 1.1 Hz, 1H, CH₂-CH=CHH), 4.99 (d, *J* = 3.6 Hz, 1H, H-1), 4.29 (ddt, *J* = 12.5, 5.1, 1.2 Hz, 1H,

CHH-CH=CH₂), 4.24 (d, J = 9.7 Hz, 1H, H-5), 4.12 – 4.02 (m, 2, H-2, CHH-CH=CH₂), 3.92 (td, J = 9.6, 2.6 Hz, 1H, H-4), 3.87 (s, 3H, CH₃ CO₂Me), 3.77 (dd, J = 11.1, 9.3 Hz, 1H, H-3), 3.48 (d, J = 2.8 Hz, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 170.3 (C-6), 162.0 (C=O), 132.5 (CH₂-CH=CH₂), 119.6 (CH₂-CH=CH₂), 95.6 (C-1), 92.3 (CCl₃), 71.3 (C-4), 70.4 (C-5), 69.3 (CH₂-CH=CH₂), 63.5 (C-3), 53.2 (CH₃ CO₂Me), 52.7 (C-2); HRMS: [M+Na]⁺ calcd for C₁₂H₁₅Cl₃N₄O₆Na 438.99494, found 438.99469.

<u>Methyl</u> (Allyl 2,3-dideoxy-2-trichloroacetamido-3-azido-4-levulinoyl-α-D-glucopyranosyl uronate) (25)

MeO₂C LevO N₃TCAHNOAIIVI

24 (3.13 g, 7.50 mmol), levulinic acid (1.15 mL, 11.3 mmol, 1.5 eq) and DMAP (2.75 g, 22.5 mmol, 3 eq) were dissolved dichloromethane, after which EDC-HCl (2.16 g, 11.3 mmol, 1.5 eq) was added in portions. After full conversion of the starting material, the reaction mixture was diluted with DCM and washed with 1M aq. HCl and with sat. aq. NaHCO₃. The organic phase was dried with MgSO4 and concentrated under reduced pressure to yield the pure title compound as white solid. Yield: 3.87 g, 7.50 mmol, 100%. $[\alpha]_D^{25} = 89.8^\circ$ (c = 0.25, CHCl₃); IR (thin film): 756, 1057, 1152, 1251, 1518, 1717, 1759, 2111; ¹H NMR (400 MHz, CDCl₃) δ 6.83 (d, *J* = 9.4 Hz, 1H, NH), 5.86 (dddd, J = 17.1, 10.3, 6.7, 5.4 Hz, 1H, CH₂-CH=CH₂), 5.37 - 5.26 (m, 2H, CH₂-CH=CH₂), 5.12 (t, J = 9.8 Hz, 1H, H-4), 5.03 (d, J = 3.6 Hz, 1H, H-1), 4.33 (d, J = 9.9 Hz, 1H, H-5), 4.28 (ddt, J = 12.7, 5.4, 1.3 Hz, 1H, CHH-CH=CH₂), 4.18 (ddd, J = 11.0, 9.4, 3.7 Hz, 1H, H-2), 4.08 (ddt, J = 12.8, 6.7, 1.1 Hz, 1H, CHH-CH=CH₂), 3.89 (dd, J = 11.0, 9.7 Hz, 1H, H-3), 3.77 (s, 3H, CH₃ CO₂Me), 2.89 - 2.78 (m, 1H, CHH Lev), 2.77 - 2.71 (m, 1H, CHH Lev), 2.71 - 2.65 (m, 1H, CHH Lev), 2.64 – 2.54 (m, 1H, CHH Lev), 2.20 (s, 3H, CH₃ Lev); ¹³C NMR (101 MHz, CDCl₃) & 206.0 (C=O), 171.4, 167.8 (C-6, C=O), 161.9 (C=O), 132.3 (CH₂-CH=CH₂), 119.9 (CH₂-CH=CH₂), 95.3 (C-1), 70.4 (C-4), 69.5 (CH₂-CH=CH₂), 69.0 (C-5), 61.9 (C-3), 53.3 (CH₃ CO₂Me), 52.7 (C-2), 37.7 (CH₂ Lev), 29.9 (CH₃ Lev), 27.7 (CH₂ Lev); HRMS: [M+NH₄]⁺ calcd for C17H21Cl3N4O8NH4 532.07632, found 532.07594.

<u>Methyl (2,3-dideoxy-2-trichloroacetamido-3-azido-4-levulinoyl-α-D-glucopyranosyl uronate)</u> (26)



Compound **25** (5.93 g, 11.5 mmol) was dissolved in 100 mL 3:2 MeOH/DCM, and PdCl₂ (408 mg, 2.30 mmol, 0.2 eq) was added. After full conversion of the starting material the reaction mixture was filtered over celite and concentrated under reduced pressure. The residue was purified over silica (30% acetone in pentane) to yield the title compound as off-white foam. Yield: 5.01 g, 10.5 mmol, 92%. $[\alpha]_D^{25} = 131.3^{\circ}$ (c = 0.08, CHCl₃); IR (thin film): 1063, 1150, 1713, 1753, 2111; ¹H NMR (400 MHz, CDCl₃) δ 6.94 (d, J = 9.3 Hz, 1H, NH), 5.41 (s, 1H, H-1), 5.12 (t, J = 9.7 Hz, 1H, H-4), 4.55 (d, J = 9.9 Hz, 1H, H-5), 4.24 (s, 1H, OH), 4.17 (ddd, J = 10.9, 9.4, 3.5 Hz, 1H, H-2), 3.95 (dd, J = 10.8, 9.6 Hz, 1H, H-3), 3.76 (s, 3H, CH₃ CO₂Me), 2.90 – 2.80 (m, 1H, CHH Lev), 2.77 – 2.73 (m, 1H, CHH Lev), 2.71 – 2.67 (m, 1H, CHH Lev), 2.64 – 2.56 (m, 1H, CHH
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Lev), 2.21 (s, 3H, CH₃ Lev); 13 C NMR (101 MHz, CDCl₃) δ 171.5, 168.3 (C-6, C=O), 162.1 (C=O), 90.8 (C-1), 70.4 (C-4), 68.6 (C-5), 61.6 (C-3), 53.4 (CH₃ CO₂Me), 53.0 (C-2), 37.7 (CH₂ Lev), 30.0 (CH₃ Lev), 27.7 (CH₂ Lev); HRMS: [M+NH₄]⁺ calcd for C₁₄H₁₇Cl₃N₄O₈ 492.04502, found 492.04478

<u>N-Phenyl-O-(Methyl</u> (2,3-dideoxy-2-trichloroacetamido-3-azido-4-levulinoyl-α-Dglucopyranosyl uronate)) trifluoroacetimidate (5)



Compound 26 (4.99 g, 10.5 mmol) was dissolved in 100 mL DCM with 10 mL water, K₂CO₃ (4.35 g, 31.5 mmol, 3 eq) and PTFAI-Cl (5 mL, 31.5 mmol, 3 eq). The reaction mixture was stirred vigorously until TLC showed full conversion of the starting material, after which the reaction mixture was diluted with water and extracted twice with DCM. Combined organic phases were dried with MgSO4 and concentrated under reduced pressure. The residue was recrystallized from Et₂O to yield the title compound (pure α -anomer) as a white powder. The concentrated mother liquor was purified via silica chromatography ($20\% \rightarrow 30\%$ acetone in pentane with 1% Et₃N) to obtain extra product (enriched in α-anomer) as an orange solid. Total yield: 4.78 g, 7.39 g, 70%. $[\alpha]_{D}^{25} = 80.2^{\circ}$ (c = 0.27, CHCl₃); IR (thin film): 822, 1027, 1116, 1209, 1720, 1763, 2112; data for the α-anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.30 (t, J = 7.9 Hz, 2H, CH_{arom}), 7.14 (t, J = 7.5 Hz, 1H, CH_{arom}), 6.84 – 6.74 (m, 3H, NH, CH_{arom}), 6.55 (s, 1H, H-1), 5.25 (t, J = 9.6 Hz, 1H, H-4), 4.40 $(d, J = 9.7 \text{ Hz}, 1H, H-5), 4.37 - 4.30 \text{ (m, 1H, H-2)}, 4.10 - 3.99 \text{ (m, 1H, H-3)}, 3.79 \text{ (s, 3H, CH}_3)$ OMe), 2.90 – 2.59 (m, 4H, 2x CH₂ Lev), 2.21 (s, 3H, CH₃ Lev); ¹³C NMR (101 MHz, CDCl₃) δ 171.4, 166.9 (C-6, C=O), 129.0, 125.1, 119.3 (CHarom), 70.9 (C-5), 70.0 (C-4), 60.7 (C-3), 53.5 (CH₃ CO₂Me), 52.1 (C-2), 37.7 (CH₂ Lev), 29.9 (CH₃ Lev), 27.7 (CH₂ Lev); HRMS: [M+Na]⁺ calcd for $C_{22}H_{21}Cl_3F_3N_5O_8Na$ 668.0300, found 668.02966

Allyl 2-deoxy-2-trichloroacetamido-4,6-O-benzylidene-β-D-glucopyranoside (27)

16b (21.9 g, 60 mmol), PTSA-H₂O (571 mg, 3 mmol, 0.05 eq) and benzaldehyde dimethylacetal (9.95 mL, 66 mmol, 1.1 eq) were dissolved in 1L acetonitrile and heated to 60 °C. After full conversion of the starting material, 0.1 eq of triethylamine was added and the reaction mixture was concentrated under reduced pressure. The residue was recrystallized from DCM/pentane to yield the title compound as off-white solid. Yield: 25.4 g, 56.1 mmol, 94%. ¹H NMR (400 MHz, Acetone) δ 8.30 (d, *J* = 9.1 Hz, 1H, NH), 7.50 (dd, *J* = 6.6, 3.1 Hz, 2H, CH_{arom}), 7.42 – 7.31 (m, 3H, CH_{arom}), 5.88 (ddt, *J* = 17.2, 10.6, 5.3 Hz, 1H, CH₂-CH=CH₂), 5.65 (s, 1H, CHPh), 5.29 (dq, *J* = 17.3, 1.8 Hz, 1H, CH₂-CH=CHH), 5.11 (dq, *J* = 10.5, 1.5 Hz, 1H, CH₂-CH=CHH), 4.90 (d, *J* = 5.0 Hz, 1H, OH), 4.85 (d, *J* = 8.4 Hz, 1H, H-1), 4.35 – 4.21 (m, 2H, H-6, CHH-CH=CH₂), 4.16 – 4.05 (m, 2H, H-3, CHH-CH=CH₂), 3.88 (dt, *J* = 10.0, 9.1 Hz, 1H, H-2), 3.81 (t, *J* = 10.2 Hz, 1H, H-6), 3.59 (t, *J* = 9.2 Hz, 1H, H-4), 3.43 (td, *J* = 9.8, 5.0 Hz, 1H, H-5); ¹³C NMR (101 MHz, Acetone) δ 162.6 (C=O), 139.1 (Cq), 135.2 (CH₂-CH=CH₂), 129.6, 128.8, 127.3 (CH_{arom}), 116.9 (CH₂-CH=CH₂), 200 (CH₂-CH=CH₂), 200 (CH₂-CH=CH₂), 200 (CH₂-CH₂-CH₂), 200 (C

CH=CH₂), 102.1 (CHPh), 101.6 (C-1), 82.8 (C-4), 71.4 (C-3), 70.6 (CH₂-CH=CH₂), 69.1 (C-6), 67.3 (C-5), 59.5 (C-2). Spectra in agreement with literature.³⁵

Allyl 2-deoxy-2-trichloroacetamido-4,6-O-benzylidene-β-D-allopyranoside (29)

Compound 27 (20.5 g, 45.3 mmol) and pyridine (9.1 mL, 113 mmol, 2.5 eq) were dissolved in 250 mL DCM and cooled to -10 °C, after which triflic anhydride (11.4 mL, 67.9 mmol, 1.5 eq) was added dropwise. After full conversion, the reaction mixture was washed twice with 1M aq. CuSO₄. The organic phase was dried with MgSO₄ and concentrated at 30 °C, yielding the crude triflate 28 which was used without further purification. The triflate was dissolved in 50 mL DMF with NaNO₂ (31.2 g, 453 mmol, 10 eq) and stirred for 48 hr, after which the reaction mixture was diluted with water and extracted twice with diethyl ether. Organic phases were combined, dried with MgSO4 and concentrated under reduced pressure. Silica chromatography (20% acetone in pentane) yields the title compound as a white foam. Yield: 11.1 g, 24.4 mmol, 54%. $[\alpha]_D^{25} = -37.2^\circ$ $(c = 0.12, CHCl_3)$; IR (thin film): 757, 1089, 1513, 1717; ¹H NMR (400 MHz, CDCl_3) δ 7.48 (dd, J = 6.6, 3.2 Hz, 2H, CH_{arom}), 7.42 – 7.36 (m, 3H, CH_{arom}), 7.23 (d, J = 9.3 Hz, 1H, NH), 5.85 (dddd, J = 16.8, 10.7, 6.1, 4.9 Hz, 1H, CH₂-CH=CH₂), 5.62 (s, 1H, CHPh), 5.30 (dq, J = 17.2, 1.6 Hz, 1H, CH₂-CH=CHH), 5.19 (dq, J = 10.5, 1.3 Hz, 1H, CH₂-CH=CHH), 4.79 (d, J = 8.4 Hz, 1H, H-1), 4.43 - 4.34 (m, 2H, H-6, CHH-CH=CH₂), 4.32 (s, 1H, H-3), 4.15 (td, J = 8.4, 2.6 Hz, 1H), 4.08 (ddt, *J* = 13.1, 6.1, 1.4 Hz, 1H, CH*H*-CH=CH₂), 4.00 (td, *J* = 9.9, 5.0 Hz, 1H, H-2), 3.82 (t, *J* = 10.3 Hz, 1H, H-6), 3.68 (dd, J = 9.4, 2.5 Hz, 1H, H-4), 2.60 (s, 1H, OH); ¹³C NMR (101 MHz, CDCl₃) δ 161.6 (C=O), 136.9 (C_a), 133.5 (CH₂-CH=CH₂), 129.5, 128.6, 126.2 (CH_{arom}), 117.9 (CH₂-CH-CH₂), 101.9 (CHPh), 99.3 (C-1), 78.6 (C-4), 70.5 (CH₂-CH=CH₂), 69.1 (C-6), 68.4 (C-3), 63.5 (C-5), 53.8 (C-2); HRMS: [M+Na]⁺ calcd for C₁₈H₂₀Cl₃NO₆Na 474.02484, found 474.02447

<u>Allyl 2,3-dideoxy-2-trichloroacetamido-3-azido-4,6-O-benzylidene- β -D-glucopyranoside (31) Ph 0</u>



Compound **29** (10.5 g, 23.1 mmol) was dissolved in 25 mL pyridine, and mesyl chloride (3.59 mL, 46.4 mmol 2 eq) was added dropwise. After full conversion, the reaction mixture was diluted with ethyl acetate and washed twice with 1M aq. CuSO₄. The organic phase was dried with MgSO₄ and concentrated under reduced pressure, yielding the mesylate **30** as off-white foam, which was used directly without further purification. The crude mesylate was dissolved in 100 mL acetonitrile with freshly prepared tetrabutylammonium azide³⁶ (16.4 g, 57.5 mmol, 2.5 eq). The reaction mixture was heated to 70 °C until full conversion of the starting material. After which the reaction mixture was cooled to RT and poured in approx. 5 times the volume of water under vigorous stirring. The precipitate was collected by filtration, washed with water, dried and purified over silica (10%→20% acetone in pentane) yielding the impure title compound as white solid. Yield: 7.13 g, 14.9 mmol, 65%. $[\alpha]_D^{25} = -21.4^\circ$ (c = 0.21, CHCl₃); IR (thin film): 750, 1088, 1368, 1694, 2108; ¹H NMR (400 MHz, CDCl₃) δ 7.52 – 7.47 (m, 2H, CH_{arom}), 7.43 – 7.33 (m, 3H, CH_{arom}), 7.00 (d, *J* = 7.6 Hz, 1H, H-1), 5.85 (dddd, *J* = 16.9, 10.4, 6.4, 5.4 Hz, 1H, CH₂-CH-CH₂), 5.59 (s, 1H, CHPh), 5.29 (dq, *J* = 17.2, 1.5 Hz, 1H, CH₂-CH=CHH), 5.22 (dq, *J* = 10.3, 1.2 Hz, 1H,

CH₂-CH=CH*H*), 5.04 (d, J = 8.3 Hz, 1H, H-1), 4.46 – 4.30 (m, 3H, H-3, H-6, C*H*H-CH=CH₂), 4.10 (ddt, J = 12.7, 6.4, 1.3 Hz, 1H, CH*H*-CH=CH₂), 3.85 – 3.77 (m, 1H, H-6), 3.64 – 3.56 (m, 2H, H-4, H-6), 3.35 (dt, J = 10.9, 8.0 Hz, 1H, H-2); ¹³C NMR (101 MHz, CDCl₃) δ 162.3 (C=O), 136.7 (C_q), 133.1 (C_q), 129.3 (CH₂-CH=CH₂), 128.5, 126.2, 126.1 (CH_{arom}), 118.8 (CH₂-CH=CH₂), 101.6 (CHPh), 98.7 (C-1), 80.7 (C-4), 70.9 (CH₂-CH=CH₂), 68.7 (C-6), 67.2 (C-5), 60.7 (C-3), 58.1 (C-2); HRMS: [M+Na]⁺ calcd for C₁₈H₁₉Cl₃N₄O₃Na 499.03132 found 499.06137

Allyl 2,3-dideoxy-2-trichloroacetamido-3-azido-β-D-glucopyranoside (32)

Compound **31** (6.62 g, 13.8 mmol) and PTSA-H₂O (263 mg, 1.38 mmol, 0.1 eq) were dissolved in MeOH (0.25M) and heated to 60 °C. After full conversion, the reaction mixture was neutralised with triethylamine and concentrated under reduced pressure. The residue was precipitated using DCM/pentane, yielding the impure title compound as white solid. Yield: 5.20 g, 13.4 mmol, 97%. $[\alpha]_D^{25} = -164.8^{\circ}$ (c = 0.19, CHCl₃); IR (thin film): 668, 1047, 1075, 1527, 1697, 2106; ¹H NMR (400 MHz, Acetone) δ 8.44 (d, *J* = 9.1 Hz, 1H, NH), 5.86 (dddd, *J* = 17.2, 10.6, 5.6, 5.0 Hz, 1H, CH₂-CH=CH₂), 5.26 (dq, *J* = 17.3, 1.8 Hz, 1H, CH₂-CH=CHH), 5.12 – 5.05 (m, 2H, OH, CH₂-CH=CHH), 4.76 (d, *J* = 8.3 Hz, 1H, H-1), 4.29 (ddt, *J* = 13.4, 4.9, 1.6 Hz, 1H, CHH-CH=CH₂), 4.08 (ddt, *J* = 13.4, 5.7, 1.6 Hz, 1H, CHH-CH=CH₂), 3.91 – 3.82 (m, 2H, H-3, H-6), 3.75 – 3.67 (m, 2H, H-2, H-6), 3.57 (td, *J* = 9.4, 5.8 Hz, 1H, H-4), 3.38 (ddd, *J* = 9.7, 5.2, 2.2 Hz, 1H, H-5); ¹³C NMR (101 MHz, Acetone) δ 162.6 (C=O), 135.2 (CH₂-CH=CH₂), 116.9 (CH₂-CH=CH₂), 100.7 (C-1), 78.3 (C-5), 70.9 (C-4), 70.2 (CH₂-CH=CH₂), 67.8 (C-6), 62.3 (C-5), 56.7 (C-2); HRMS: [M+Na]⁺ calcd for C₁₁H₁₅Cl₃N₄O₅Na 411.00002, found 411.00021.

Methyl (Allyl 2,3-dideoxy-2-trichloroacetamido-3-azido-β-D-glucopyranosyl uronate) (2)

Compound **32** (5.20 g, 13.4 mmol) was suspended in 90 mL 2:1 DCM/H₂O and TEMPO (1.04 g, 6.67 mmol, 0.5 eq) and BAIB (10.8 g, 33.4 mmol, 2.5 eq) were added under vigorous stirring. After full conversion, the reaction mixture was concentrated under reduced pressure, yielding crude acid **33**. The residue was coevaporated 3x with toluene and dissolved in DMF. K₂CO₃ (5.05 g, 60.1 mmol, 4.5 eq) and methyl iodide (6.23 mL, 100 mmol, 7.5 eq) were added and the reaction mixture was stirred for 18 hr, after which it was diluted with water and extracted twice with diethyl ether. Organic phases were combined, dried with MgSO₄ and concentrated under reduced pressure. Silica chromatography (20% acetone in pentane) yields the title compound as a white solid. Yield: 2.87 g, 6.87 mmol, 52%. $[\alpha]_D^{25} = -18.1^\circ$ (c = 0.28, CHCl₃); IR (thin film): 823, 1040, 1087, 1258, 1530, 1697, 1734, 2108; ¹H NMR (400 MHz, CDCl₃) δ 7.01 (d, *J* = 7.4 Hz, 1H, NH), 5.85 (dddd, *J* = 17.0, 10.4, 6.4, 5.3 Hz, 1H, CH₂-CH=CH₂), 5.29 (dq, *J* = 17.2, 1.4 Hz, 1H, CH₂-CH=CHH), 5.22 (dq, *J* = 10.4, 1.4 Hz, 1H, CH₂-CH=CHH), 5.07 (d, *J* = 8.2 Hz, 1H, H-1), 4.38 (ddt, *J* = 12.7, 5.3, 1.3 Hz, 1H, CHH-CH=CH₂), 4.25 (dd, *J* = 11.1, 9.2 Hz, 1H, H-3), 4.12 (ddt, *J* = 12.7, 6.5, 1.3 Hz, 1H, CHH-CH=CH₂), 3.99 (d, *J* = 9.7 Hz, 1H, H-5), 3.86 (s, 4H, H-4, CH₃) CO₂Me), 3.42 (s, 1H, OH), 3.26 (dt, *J* = 11.1, 7.8 Hz, 1H, H-2); ¹³C NMR (101 MHz, CDCl₃) δ

169.6 (C-6), 162.3 (C=O), 133.0 (CH₂-CH=CH₂), 118.9 (CH₂-CH=CH₂), 98.3 (C-1), 74.5 (C-5), 72.0 (C-4), 70.9 (CH₂-CH=CH₂), 62.9 (C-3), 57.3 (C-2), 53.2 (CH₃ CO₂Me); HRMS: [M+Na]⁺ calcd for C₁₂H₁₅Cl₃N₄O₆ 438.99494, found 438.994455.

Procedure for VT-NMR experiments of bacillosamine donors

Donor 4 (30 µmol) or a mixture of donor 3 (30 µmol) and Ph₂SO (39 µmol) was coevaporated with toluene, dissolved in 0.6 mL of CD_2Cl_2 under nitrogen atmosphere and transferred to an oven-dried NMR tube flushed with nitrogen gas and sealed with an NMR tube septum. The magnet was cooled to -80 °C, locked, and shimmed and the sample was measured prior to activation. In a separate cold bath (-80 °C) the sample was treated with Tf₂O (donor 3, 39 µmol) or TfOH (donor 4, 39 µmol) and shaken and recooled 3x. Thecold 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 of equilibration time for every temperature.

General procedure for model glycosylations

Donor (0.1 mmol, 1 eq), Ph₂SO (0.13 mmol, 1.3 eq) and TTBP (0.25 mmol, 2.5 eq) were coevaporated twice with toluene, dissolved in 2 mL DCM and stirred for 30 min at RT with 3 Å molecular sieves. The solution was cooled to -80 °C and Tf₂O (22 μ L, 0.13 mmol, 2 eq) 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 eq) in DCM (0.4 mL, 0.5 M) 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 eq) in DCM (0.4 mL, 0.5 M) was added. The reaction mixture was allowed to warm to -60 °C for and stirred for 2 hr at that temperature. The reaction was quenched with 2 mL sat aq NaHCO₃, 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 MgSO4, filtered, and concentrated in vacuo. Purification by silica gel flash column chromatography and/or sephadex LH-20 size-exclusion chromatography yielded the glycosylation product as a mixture of anomers.

Ethyl 2,4-dideoxy-2,4-diazido-3-O-(2-naphthyl)methyl-α,β-D-quinopyranoside (3A)



The title comound was synthesised from donor **3** and ethanol according to the genereral procedure for model glycosylations as colourless oil. Yield: 32 mg, 84 µmol, 84%, α : β = 1:8. Data for the β -anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.88 – 7.80 (m, 4H, CH_{arom}), 7.55 (dd, *J* = 8.6, 1.6 Hz, 1H, CH_{arom}), 7.50 – 7.44 (m, 2H, CH_{arom}), 5.06 (d, *J* = 10.8 Hz, 1H, CHH Nap), 4.96 (d, *J* = 10.8 Hz, 1H, CHH Nap), 4.25 (d, *J* = 8.0 Hz, 1H, H-1), 3.95 (dq, *J* = 9.4, 7.1 Hz, 1H, CHH Et), 3.62 (dq, *J* = 9.4, 7.1 Hz, 1H, CHH Et), 3.43 (dd, *J* = 9.7, 8.1 Hz, 1H, H-2), 3.28 (t, *J* = 9.3 Hz, 1H, H-3), 3.23 – 3.11 (m, 2H, H-4, H-5), 1.35 (d, *J* = 5.8 Hz, 3H, H-6), 1.28 (t, *J* = 7.1 Hz, 3H, CH₃ Et); ¹³C NMR (101 MHz, CDCl₃) δ 134.9, 133.4, 133.3 (C_q), 128.4, 128.2, 128.2, 127.8, 127.5, 127.5, 126.3, 126.3, 126.2, 126.2, 126.2, (CH_{arom}), 101.8 (C-1), 81.3 (C-3), 75.5 (CH₂ Nap), 70.8 (C-5), 67.8 (C-4), 66.3 (C-2), 66.0 (CH₂ Et), 18.5 (C-6), 15.2 (CH₂ Et); diagnostic peaks for the α -anomer: ¹H NMR (400 MHz, CDCl₃) δ 4.88 (d, *J* = 3.5 Hz, 1H, H-1), 3.89 (dd, *J* = 10.1, 9.2 Hz, 1H), 3.74 (dq, *J* = 9.8, 7.1 Hz, 1H, CHH Et), 3.34 (dd, *J* = 10.1, 3.5 Hz, 1H, H-2); ¹³C NMR

(101 MHz, CDCl₃) δ 97.5 (C-1), 78.7, 68.8, 66.5, 64.0, 63.6, 18.5, 15.1; HRMS: [M+NH₄]⁺ calcd for C₁₉H₂₂N₆O₃NH₄ 400.20916, found 400.20904.

2-Fluoroethyl 2,4-dideoxy-2,4-diazido-3-O-(2-naphthyl)methyl-α,β-D-quinopyranoside (3B)

The title comound was synthesised from donor 3 and 2-fluoroethanol according to the genereral procedure for model glycosylations as colourless oil. Yield: 30 mg, 75 μ mol, 75%, α : β = 1:2. Data reported for a 1:2 mixture of anomers: ¹H NMR (400 MHz, CDCl₃) δ 7.86 (dddt, J = 9.6, 7.7, 5.3, 2.4 Hz, 12H, CH_{arom}), 7.56 (ddd, J = 8.6, 7.1, 1.7 Hz, 3H, CH_{arom}), 7.51 - 7.43 (m, 6H, CH_{arom}), 5.08 – 5.02 (m, 4H, CHH Napαβ, CHH Napα), 4.96 (d, J = 10.8 Hz, 2H, CHH Napβ), 4.92 (d, J = 3.5 Hz, 1H, H-1α), 4.72 - 4.62 (m, 3H, CH₂-CHHFaβ), 4.60 - 4.49 (m, 3H, CH₂-CHHFaβ), 4.31 $(d, J = 8.1 Hz, 2H, H-1\beta), 4.13 - 3.98 (m, 2H, CHH-CH_2F\beta), 3.96 - 3.74 (m, 5H, H-5a, CHH-CH_2F\beta)$ CH₂Fα, CH*H*-CH₂Fαβ), 3.74 – 3.66 (m, 1H, H-5α), 3.46 (dd, *J* = 9.7, 8.1 Hz, 2H, H-2β), 3.38 (dd, J = 10.1, 3.5 Hz, 1H, H-2a), 3.29 (t, J = 9.3 Hz, 2H, H-3 β), 3.25 – 3.12 (m, 5H, H-4 $\alpha\beta$, H-5 β), 1.36 $(d, J = 5.7 \text{ Hz}, 6H, H-6\beta), 1.32 (d, J = 6.2 \text{ Hz}, 3H, H-6\alpha); {}^{13}\text{C} \text{ NMR} (101 \text{ MHz}, \text{CDCl}_3) \delta 134.7,$ 133.3, 133.3, 133.2 (C_q), 128.3, 128.1, 128.1, 127.7, 127.7, 127.4, 127.4, 126.3, 126.2, 126.2, 126.1, 126.1 (C_q), 102.1 (C-1 β), 98.0 (C-1 α) 82.7 (d, J = 170.1 Hz, CH₂-CH₂F β), 82.4 (d, J = 170.4 Hz, CH₂-CH₂Fα), 81.1 (C-3β), 78.4 (C-3α), 75.5, 75.5 (CH₂ Napαβ), 70.8 (C-5β), 68.9 (d, *J* = 20.2 Hz, CH_2 - $CH_2F\beta$) 68.6 (C-4 α), 67.6 (C-4 β), 67.3 (d, J = 20.1 Hz, CH_2 - $CH_2F\alpha$), 66.7 (C-5 α), 66.3 (C-2 β), 63.5 (C-2 α), 18.4 (C-6 β), 18.4 (C-6 α); HRMS: [M+NH₄]⁺ calcd for C₁₉H₂₁FN₆O₃NH₄ 418.19974, found 418.19933.

2,2-Difluoroethyl 2,4-dideoxy-2,4-diazido-3-O-(2-naphthyl)methyl-α,β-D-quinopyranoside (<u>3C</u>)

The title comound was synthesised from donor **3** and 2,2-difluoroethanol according to the genereal procedure for model glycosylations as colourless oil. Yield: 28 mg, 66 µmol, 66%, α : β = 2.9:1. Data for the α -anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.89 – 7.80 (m, 4H, CH_{arom}), 7.56 (dd, J = 8.4, 1.7 Hz, 1H, CH_{arom}), 7.50 – 7.44 (m, 2H, CH_{arom}), 6.11 – 5.75 (m, 1H, CH₂-CHF₂), 5.03 (d, J = 1.8 Hz, 2H, CH₂ Nap), 4.90 (d, J = 3.5 Hz, 1H, H-1), 3.88 – 3.73 (m, 3H, H-3, CH₂-CHF₂), 3.69 – 3.61 (m, 1H, H-5), 3.39 (dd, J = 10.2, 3.5 Hz, 1H, H-2), 3.17 (dd, J = 10.2, 9.3 Hz, 1H, H-4), 1.33 (d, J = 6.2 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 134.7, 133.4, 133.3 (C_q), 128.4, 128.2, 127.8, 127.5, 126.3, 126.3, 126.2 (CH_{arom}), 113.8 (t, J = 241.0 Hz, CH₂-CHF₂), 98.5 (C-1), 78.3 (C-3), 75.7 (CH₂ Nap), 68.5 (C-4), 67.3 (t, J = 28.7 Hz, CH₂-CHF₂), 67.2 (C-5), 63.5 (C-2), 18.4 (C-6); diagnostic peaks for the β -anomer: ¹H NMR (400 MHz, CDCl₃) δ 5.05 (d, J = 10.7 Hz, 1H, CHH Nap), 4.29 (d, J = 8.0 Hz, 1H, H-1), 3.98 (dtd, J = 17.6, 12.0, 3.3 Hz, 1H, CHH-CHF₂), 3.45 (dd, J = 9.7, 8.0 Hz, 1H, H-2), 3.28 (t, J = 9.3 Hz, 1H, H-3), 1.36 (d, J = 5.8 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 102.3 (C-1), 81.1, 71.1, 67.6, 66.3, 18.4; HRMS: [M+NH₄]⁺ calcd for C₁₉H₂₀F₂N₆O₃NH₄ 436.19032, found 436.19015

2,2,2-Trifluoroethyl

2,4-dideoxy-2,4-diazido-3-O-(2-naphthyl)methyl-α,β-D-

The title comound was synthesised from donor **3** and 2,2,2-trifluoroethanol according to the genereral procedure for model glycosylations as colourless oil. Yield: 41 mg, 94 μmol, 94%, α :β = 22:1. Data for the α-anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.91 – 7.80 (m, 4H, CH_{arom}), 7.56 (dd, J = 8.4, 1.7 Hz, 1H, CH_{arom}), 7.51 – 7.43 (m, 2H, CH_{arom}), 5.05 (d, J = 10.5 Hz, 1H, CHH Bn), 5.01 (d, J = 10.6 Hz, 1H, CHH Bn), 4.93 (d, J = 3.6 Hz, 1H, H-1), 3.95 (qd, J = 8.5, 1.7 Hz, 2H, CH₂-CF₃), 3.86 (dd, J = 10.2, 9.3 Hz, 1H, H-3), 3.64 (dq, J = 10.1, 6.2 Hz, 1H, H-5), 3.40 (dd, J = 10.1, 3.6 Hz, 1H, H-2), 3.17 (dd, J = 10.2, 9.3 Hz, 1H, H-4), 1.33 (d, J = 6.2 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 134.6, 133.4, 133.3 (Cq), 128.5, 128.2, 127.8, 127.5, 126.3, 126.3, 126.2 (CH_{arom}), 123.5 (q, J = 278.5 Hz, CH₂-CF₃), 98.6 (C-1), 78.2 (C-3), 75.7 (CH₂ Nap), 68.4 (C-4), 67.5 (C-5), 65.1 (q, J = 35.3 Hz, CH₂-CF₃), 63.3 (C-2), 18.4 (C-6); diagnostic peaks for the β-anomer: ¹H NMR (400 MHz, CDCl₃) δ 4.33 (d, J = 8.0 Hz, 1H, H-1), 4.14 (dq, J = 12.6, 8.7 Hz, 1H), 4.10 (s, 1H), 3.46 (dd, J = 9.7, 8.0 Hz, 1H, H-2), 3.28 (t, J = 9.3 Hz, 1H), 1.35 (d, J = 5.7 Hz, 3H, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 101.8 (C-1), 81.0, 71.2, 66.3; HRMS: [M+NH₄]⁺ calcd for C₁₉H₁₉F₃N₆O₃NH₄ 454.18090, found 454.18074

2,2,2-Trifluoroethyl 2,4-dideoxy-2,4-diazido-α-D-quinopyranoside (34)



3D (166 mg, 0.38 mmol) and DDQ (129 mg, 0.57 mmol, 1.5 eq) were dissolved in 9:1 DCM/H₂O (0.3M) after full conversion, the reaction mixture was diluted with DCM and washed twice with sat. aq. NaHCO₃. The organic phase was dried with MgSO₄ and concentrated under reduced pressure. The residue was purified over silica (15% Et₂O in pentane) to yield the title product as colourless oil. Yield: 71 mg, 0.24 mmol, 63%. ¹H NMR (300 MHz, CDCl₃) δ 4.96 (d, *J* = 3.6 Hz, 1H, H-1), 4.06 – 3.89 (m, 3H, H-3, CH₂-CF₃), 3.66 (dqd, *J* = 10.1, 6.3, 0.7 Hz, 1H, H-5), 3.30 (dd, *J* = 10.2, 3.6 Hz, 1H, H-2), 3.11 (dd, *J* = 10.1, 9.3 Hz, 1H, H-4), 2.92 (d, *J* = 4.1 Hz, 1H, OH), 1.34 (d, *J* = 6.3 Hz, 3H, H-6); ¹³C NMR (75 MHz, CDCl₃) δ 98.4 (C-1), 70.6 (C-3), 68.6 (C-4), 67.4 (C-5), 65.2 (q, *J* = 35.4 Hz, CH₂-CF₃) 63.1 (C-2), 18.3 (C-6)

Disaccharide 3E



The title comound was synthesised from donor **3** and acceptor **34** according to the genereral procedure for model glycosylations as colourless oil. Yield: 48 mg, 75 µmol, 75%, α : β = 6.6:1. Data for the α-anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.91 – 7.82 (m, 4H, CH_{arom}), 7.58 (dd, *J* = 8.4, 1.7 Hz, 1H, CH_{arom}), 7.51 – 7.45 (m, 2H, CH_{arom}), 5.31 (d, *J* = 3.7 Hz, 1H, H-1'), 5.04 (s, 2H, CH₂ Nap), 5.00 (d, *J* = 3.7 Hz, 1H, H-1), 4.03 – 3.92 (m, 3H, H-5/H-5', CH₂-CF₃), 3.87 – 3.77 (m, 2H, H-3, H-3'), 3.73 (dq, *J* = 10.0, 6.2 Hz, 1H, H-5/H-5'), 3.48 (dd, *J* = 10.2, 3.7 Hz, 1H, H-2'),

3.24 – 3.13 (m, 2H, H-4, H-4'), 3.04 (dd, J = 10.4, 3.6 Hz, 1H, H-2), 1.40 – 1.36 (m, 6H, H-6, H-6'); ¹³C NMR (101 MHz, CDCl₃) δ 134.7, 133.4, 133.3 (C_q), 128.5, 128.2, 127.8, 127.6, 126.3, 126.3, 126.2 (CH_{arom}), 99.3, 99.2 (C-1, C-1'), 78.5 (C-3'), 75.7 (C-3), 75.5 (CH₂ Nap), 69.6, 68.8 (C-4, C-4'), 67.8, 67.8 (C-5, C-5'), 65.1 (q, J = 35.6 Hz, CH₂-CF₃) 63.9 (C-2'), 61.2 (C-2), 18.8, 18.2 (C-6, C-6'); diagnostic peaks for the β-anomer: ¹H NMR (400 MHz, CDCl₃) δ 4.65 (d, J = 7.9 Hz, 1H, H-1'), 4.09 (dd, J = 10.2, 9.2 Hz, 1H), 3.59 (dq, J = 10.2, 6.1 Hz, 1H), 3.41 (dd, J = 10.2, 3.6 Hz, 1H, H-2), 3.34 (t, J = 9.5 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 101.4 (C-1'), 98.4 (C-1), 81.3, 75.9, 75.7, 71.0, 67.7, 67.0, 66.6, 66.3, 63.3, 18.4, 18.4

Disaccharide 3F



Pre-activation: Donor 3 (100-130 μ mol, 1-1.3 eq), Ph₂SO (0.65-1.3 eq) and TTBP (2.5 eq) were coevaporated twice with toluene and dissolved in DCM (0.05 M donor). 3Å molecular sieves were added and the reaction mixture was stirred for 30-60 min at RT, before being cooled to -80 °C. Tf₂O (0.65-1.3 eq) was added and the reaction was allowed to warm to -60 °C and kept at that temperature for 1 min. before being recooled to -80 °C. Acceptor 24 (1-2 eq) was added dropwise over 30 s as a freshly prepared 0.5M solution in DCM. The reaction mixture was then allowed to warm to the specified temperature and guenched with 2 mL sat. aq. NaHCO₃ after 2 hr (-50 °C or - 60 °C) or 30 s (0 °C). 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 MgSO4, filtered, and concentrated in vacuo. Purification by silica gel flash column chromatography and/or sephadex LH-20 size-exclusion chromatography yielded the glycosylation product as a mixture of anomers. In situ activation: donor 4 (130 µmol, 1.3 eq), acceptor 24 (1 eq) and Ph₂SO (0 or 1.5 eq) twice with toluene and dissolved in DCM (0.05 M donor). 3Å molecular sieves were added and the reaction mixture was stirred for 30-60 min at RT, before being cooled to -80 °C. TMSOTf (0.2 eq) was added and the reaction mixture was slowly allowed to warm to 0 °C and guenched with 2 mL sat. aq. NaHCO3. 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 MgSO4, filtered, and concentrated in vacuo. Purification by silica gel flash column chromatography and/or sephadex LH-20 size-exclusion chromatography yielded the glycosylation product as a mixture of anomers. Data for the α-anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.92 – 7.81 (m, 4H, CH_{arom}), 7.56 (dd, J = 8.4, 1.7 Hz, 1H, CH_{arom}), 7.51 - 7.43 (m, 3H, CH_{arom}), 6.83 (d, J = 9.7 Hz, 1H, NH), 5.88 (dddd, J = 17.1, 10.3, 6.8, 5.4 Hz, 1H, CH₂-CH-CH₂), 5.38 - 5.28 (m, 3H, H-1', CH₂-CH=CH₂), 5.03 (d, J = 10.5 Hz, 1H, CHH Nap), 5.00 (d, J = 10.5 Hz, 1H, CHH Nap), 4.94 (d, J = 3.6 Hz, 1H, H-1), 4.32 -4.16 (m, 3H, H-2, H-5, CHH-CH=CH₂), 4.07 (ddt, J = 12.8, 6.8, 1.1 Hz, 1H, CHH-CH=CH₂), 3.92 (t, J = 9.5 Hz, 1H, H-4), 3.85 - 3.78 (m, 4H, H-3, CH₃ CO₂Me), 3.77 - 3.69 (m, 1H, H-3'), 3.54 – 3.36 (m, 2H, H-2', H-5'), 3.12 (dd, J = 10.1, 9.4 Hz, 1H, H-4'), 1.28 (d, J = 6.2 Hz, 3H, H-6'); ¹³C NMR (101 MHz, CDCl₃) & 168.4 (C-6), 162.1 (C=O), 134.6, 133.4, 133.3 (C_q), 132.3 (CH₂-CH=CH₂), 128.4, 128.2, 127.8, 127.6, 126.3, 126.3, 120.0 (CH_{arom}), 98.6 (C-1'), 95.4 (C-1), 78.5 (C- 3'), 76.3 (C-4), 75.7 (CH₂ Nap), 70.9 (C-5), 69.3 (CH₂-CH=CH₂), 68.4 (C-4'), 67.7 (C-5'), 64.6 (C-3), 64.0 (C-2'), 53.4 (C-2), 53.0 (CH₃ CO₂Me), 18.3 (C-6); Diagnostic peaks for the β -anomer: ¹H NMR (500 MHz, CDCl₃) δ 4.96 (d, *J* = 3.4 Hz, 1H, H-1), 4.39 (d, *J* = 8.0 Hz, 1H, H-1'), 3.37 (dd, *J* = 9.6, 8.0 Hz, 1H, H-2'), 1.39 (d, *J* = 6.0 Hz, 3H, H-6'); ¹³C NMR (126 MHz, CDCl₃) δ 101.6 (C-1'); HRMS: [M+NH₄]⁺ calcd for C₂₉H₃₁Cl₃N₁₀O₈NH₄ 770.17302, found 770.17275

Disaccharide 35



Donor 3 (2.61 g, 5.29 mmol, 1.3 eq), Ph₂SO (535 mg, 2.65 mmol, 0.65 eq) and TTBP (2.53 g, 10.2 mmol, 2.5 eq) were coevaporated twice with toluene and dissolved in 100 mL anhydrous DCM. 3Å molecular sieves were added and the reaction mixture was stirred for 30-60 min at RT, before being cooled to -80 °C. Tf₂O (0.44 mL, 2.65 mmol, 0.65 eq) was added and the reaction was allowed to warm to -60 °C and kept at that temperature for 1 min. before being recooled to -80 °C. Acceptor 35 (1.70 g, 4.07 mmol, 1 eq.) was added dropwise over 30 s as a freshly prepared 0.5M solution in DCM. The reaction mixture was then slowly allowed to warm to 0 °C and quenched with 200 mL sat. aq. NaHCO₃. 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 MgSO4, filtered, and concentrated in vacuo. Purification by silica gel flash column chromatography (15% acetone in pentane) yields the title compound as white foam. Yield: 2.48 g, 3.29 mmol, 81%, α : β = 10:1. $[\alpha]_{D}^{25} = 61.0^{\circ}$ (c = 0.50, CHCl₃); IR (thin film): 757, 1033, 1073, 1563, 1696, 1753, 2109; ¹H NMR (500 MHz, CDCl₃) δ 7.91 – 7.80 (m, 4H, CH_{arom}), 7.57 (dd, J = 8.4, 1.6 Hz, 1H, CH_{arom}), 7.50 - 7.45 (m, 2H, CH_{arom}), 7.10 (d, J = 7.3 Hz, 1H, NH), 5.83 (dddd, J = 17.0, 10.4, 6.4, 5.3 Hz, 1H, CH₂-CH=CH₂), 5.28 (dq, J = 17.1, 1.5 Hz, 1H, CH₂-CH=CHH), 5.25 (d, J = 3.6 Hz, 1H, H-1'), 5.22 (dq, J = 10.4, 1.3 Hz, 1H, CH₂-CH=CHH), 5.07 (d, J = 8.0 Hz, 1H, H-1), 5.02 (d, J = 3.5 Hz, 2H, CH₂ Nap), 4.39 (dd, J = 10.8, 9.0 Hz, 1H, H-3), 4.34 (ddt, J = 12.8, 5.2, 1.4 Hz, 1H, CHH-CH=CH₂), 4.07 (ddt, *J* = 12.6, 6.4, 1.2 Hz, 1H, CHH-CH=CH₂), 4.03 (d, *J* = 9.4 Hz, 1H, H-5), 3.88 (t, J = 9.2 Hz, 1H, H-4), 3.79 (s, 3H, CH₃ CO₂ Me), 3.73 (t, J = 9.8 Hz, 1H, H-3'), 3.50 (dd, J = 1.00 Hz, 1H, H-3') 10.2, 3.6 Hz, 1H, H-2'), 3.45 (dg, J = 10.2, 6.2 Hz, 1H, H-5'), 3.35 (dt, J = 10.8, 7.7 Hz, 1H, H-2), 3.12 (t, J = 9.9 Hz, 1H, H-4'), 1.28 (d, J = 6.2 Hz, 3H, H-6'); ¹³C NMR (126 MHz, CDCl₃) δ 167.8 (C-6), 162.5 (C=O), 134.6, 133.4, 133.3 (Cq), 133.0 (CH₂-CH=CH₂), 128.4, 128.2, 127.8, 127.7, 126.4, 126.2 (CH_{arom}), 118.9 (CH₂-CH=CH₂), 98.6 (C-1[']), 97.9 (C-1), 92.1 (CCl₃) 78.7 (C-3[']), 77.4 (C-4), 75.8 (CH₂ Nap), 75.4 (C-5), 70.8 (CH₂-CH=CH₂), 68.4 (C-4'), 67.8 (C-5'), 64.1 (C-2'), 63.3 (C-3), 58.1 (C-2), 53.0 (CH₃ CO₂ Me), 18.3 (C-6); HRMS: [M+X]⁺ calcd for C₂₉H₃₁Cl₃N₁₀O₈NH₄ 770.17302, found 770.17284. The β -anomer was removed by silica chromatography in the next step.

Disaccharide 36



Disaccharide 35 (2.45 g, 3.25 mmol) and DDQ (1.48 g, 6.50 mmol, 2 eq) were dissolved in 100 mL 9:1 DCM/H₂O and stirred at room temperature until TLC indicated full conversion of the starting material. After which the reaction mixture was transferred to a separatory funnel and washed twice with sat. aq. NaHCO3. The organic phase was dried with MgSO4 and concentrated under reduced pressure. The residue was purified over silica (20% acetone) to provide the title compound as white solid. Yield: 1.77 g, 2.88 mmol, 89%. $[\alpha]_D^{25} = 57.2^\circ$ (c = 1.28, CHCl₃); IR (thin film): 1036, 1070, 1530, 1694, 1750, 2109; ¹H NMR (500 MHz, CDCl₃) δ 7.21 (d, *J* = 7.6 Hz, 1H, NH), 5.82 (dddd, J = 17.0, 10.4, 6.4, 5.3 Hz, 1H, CH₂-CH=CH₂), 5.30 – 5.25 (m, 2H, H-1', CH₂-CH=CHH), 5.21 (dd, J = 10.4, 1.4 Hz, 1H, CH₂-CH=CHH), 5.01 (d, J = 8.0 Hz, 1H, H-1), 4.38 -4.30 (m, 2H, H-3, CHH-CH=CH₂), 4.12 - 4.00 (m, 2H, H-5, CHH-CH=CH₂), 3.91 - 3.84 (m, 2H, H-3', H-4), 3.81 (s, 3H, CH₃ CO₂Me), 3.48 - 3.37 (m, 3H, H-2, H-2', H-5'), 3.12 (d, J = 4.2 Hz, 1H, OH), 3.06 (t, J = 9.8 Hz, 1H, H-4'), 1.28 (d, J = 6.2 Hz, 3H, H-6'); ¹³C NMR (126 MHz, CDCl₃) & 168.1 (C-6), 162.6 (C=O), 133.0 (CH₂-CH=CH₂), 118.9 (CH₂-CH=CH₂), 98.4 (C-1'), 98.1 (C-1), 77.0 (C-4), 75.3 (C-5), 71.3 (C-3'), 70.8 (CH2-CH=CH2), 68.5 (C-4), 67.5 (C-5'), 63.9 (C-2'), 63.6 (C-3), 58.0 (C-2), 53.1 (CH₃ CO₂ Me), 18.2 (C-6'); HRMS: [M+NH₄]⁺ calcd for C16H23Cl3N10O8NH4 630.11042, found 630.11019

Trisaccharide 37



Donor **3** (64 mg, 0.13 mmol, 1.3 eq), Ph₂SO (13 mg, 0.065 mmol, 0.65 eq) and TTBP (62 mg, 0.25 mmol, 2.5 eq) were coevaporated twice with toluene and dissolved in 2.6 mL 1:1 Et₂O/DCM. 3Å molecular sieves were added and the reaction mixture was stirred for 60 min at RT, before being cooled to -80 °C. Tf₂O (130 µL of a freshly prepared 0.5M sln. in 1:1 Et₂O/DCM, 0.065 mmol, 0.65 eq) was added and the reaction was allowed to warm to -60 °C and kept at that temperature for 1 min. before being recooled to -80 °C. Acceptor **36** (1.70 g, 4.07 mmol, 1 eq.) was added dropwise over 30 s as a freshly prepared 0.05M solution in 1:1 DCM/Et₂O. The reaction mixture was then slowly allowed to warm to 0 °C and quenched with 2 mL sat. aq. NaHCO₃. 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 MgSO4, filtered, and concentrated in vacuo. Purification by silica gel flash column chromatography (15% acetone in pentane) yields the title compound as white foam. Yield: 77 mg, 81 µmol, 81%, $\alpha:\beta = 10:1. [\alpha]_D^{25} = 103.0^\circ$ (c = 0.52, CHCl₃); IR (thin film): 756, 821, 1070, 1527, 1696, 1753, 2109; ¹H NMR (400 MHz, CDCl₃) δ 7.93 – 7.81 (m, 4H, CH_{arom}), 7.58 (dd, *J* = 8.5, 1.7 Hz, 1H, CH_{arom}), 7.51 – 7.43 (m, 2H, CH_{arom}), 7.10 (d, *J* = 7.4 Hz, 1H, NH),

5.82 (dddd, *J* = 17.0, 10.4, 6.5, 5.3 Hz, 1H, CH₂-C*H*=CH₂), 5.40 (d, *J* = 3.7 Hz, 1H, H-1'), 5.37 (d, *J* = 3.7 Hz, 1H, H-1"), 5.27 (dq, *J* = 17.3, 1.5 Hz, 1H, CH₂-CH=CHH), 5.22 (dq, *J* = 10.3, 1.3 Hz, 1H, CH₂-CH=CHH), 5.04 (s, 2H, CH₂ Nap), 5.03 (d, *J* = 8.1 Hz, 1H, H-1), 4.39 (dd, *J* = 10.8, 9.1 Hz, 1H, H-3), 4.33 (ddt, *J* = 12.7, 5.3, 1.4 Hz, 1H, CHH-CH=CH₂), 4.10 – 4.05 (m, 1H, CHH-CH=CH₂), 4.03 (d, *J* = 9.4 Hz, 1H, H-5), 3.96 – 3.86 (m, 2H, H-4, H-5'), 3.85 – 3.77 (m, 4H, H-3", CH₃ CO₂Me), 3.70 (dd, *J* = 10.4, 9.3 Hz, 1H, H-3'), 3.52 – 3.46 (m, 2H, H-2", H-5"), 3.42 (dt, *J* = 10.9, 7.8 Hz, 1H, H-2), 3.22 – 3.11 (m, 3H, H-2', H-4', H-4"), 1.37 (d, *J* = 6.2 Hz, 3H, H-6'), 1.33 (d, *J* = 6.2 Hz, 3H, H-6"); ¹³C NMR (101 MHz, CDCl₃) δ 167.9 (C-6), 162.5 (C=O), 134.7, 133.4, 133.3 (C_q), 132.9 (CH₂-CH=CH₂), 129.3, 128.4, 128.2, 127.8, 127.6, 126.3, 126.2 (CH_{arom}), 119.0 (CH₂-CH=CH₂), 98.8, 98.8 (C-1', C-1"), 97.9 (C-1), 92.0 (CCl₃), 78.5 (C-3"), 76.7 (C-4), 75.7 (CH₂ Nap), 75.2, 75.1 (C-3', C-5), 70.8 (CH₂-CH=CH₂), 69.3, 68.8 (C-4', C-4"), 67.9, 67.8 (C-5', C-5"), 63.9 (C-2"), 63.4 (C-3), 62.4 (C-2'), 58.2 (C-2), 53.0 (CH₃ CO₂Me), 18.7 (C-6'), 18.0 (C-6"); HRMS: [M+NH₄]⁺ calcd for C₃₅H₃₉Cl₃N₁₆O₁₀NH₄ 966.24389, found 966.24377. The β-anomer was removed by silica chromatography in the next step.

Trisaccharide 38



Trisaccharide 37 (1.90 g, 2.00 mmol) and DDQ (0.91 g, 4.00 mmol, 2 eq) were dissolved in 50 mL 9:1 DCM/H₂O and stirred at room temperature until TLC indicated full conversion of the starting material. After which the reaction mixture was transferred to a separatory funnel and washed twice with sat. aq. NaHCO3. The organic phase was dried with MgSO4 and concentrated under reduced pressure. The residue was purified over silica (20% acetone) to provide the title compound as white solid. Yield: 996 mg, 1.23 mmol, 62%. $[\alpha]_D^{25} = 102.1^\circ$ (c = 0.32, CHCl₃); IR (thin film): 757, 1069, 1257, 1527, 1696, 1751, 2109; ¹H NMR (500 MHz, CDCl₃) δ 7.08 (d, J = 7.4 Hz, 1H, NH), 5.82 (dddd, J = 17.0, 10.4, 6.5, 5.3 Hz, 1H, CH₂-CH=CH₂), 5.39 (d, J = 3.8 Hz, 1H, H-1'), 5.36 (d, J = 3.7 Hz, 1H, H-1"), 5.28 (dq, J = 17.2, 1.5 Hz, 1H, CH₂-CH=CHH), 5.22 (dq, J = 10.3, 1.3 Hz, 1H, CH₂-CH=CHH), 5.04 (d, J = 8.0 Hz, 1H, H-1), 4.40 (dd, J = 10.8, 9.1 Hz, 1H, H-3), 4.33 (ddt, J = 12.7, 5.3, 1.4 Hz, 1H, CHH-CH=CH₂), 4.07 (ddt, J = 12.7, 6.4, 1.3 Hz, 1H, CHH-CH=CH₂), 4.03 (d, J = 9.4 Hz, 1H, H-5), 4.00 – 3.88 (m, 3H, H-3", H-4, H-5"), 3.82 (s, 3H, CH₃ CO₂Me), 3.71 – 3.66 (m, 1H, H-3'), 3.50 (dq, *J* = 12.4, 6.2 Hz, 1H, H-5'), 3.41 (dt, *J* = 10.2, 7.4 Hz, 1H, H-2), 3.37 (dd, *J* = 10.3, 3.8 Hz, 1H, H-2''), 3.18 (dd, *J* = 10.4, 3.7 Hz, 1H, H-2'), 3.15 - 3.07 (m, 2H, H-4', H-4''), 2.86 (d, J = 3.7 Hz, 1H, OH), 1.37 (d, J = 6.2 Hz, 3H, H-6''), 1.33 (d, J = 6.2 Hz, 3H, H-6'); ¹³C NMR (126 MHz, CDCl₃) δ 167.9 (C-6), 162.5 (C=O), 132.9 (CH₂-CH=CH₂), 119.0 (CH₂-CH=CH₂), 98.8, 98.7 (C-1', C-1"), 97.9 (C-1), 92.0 (CCl₃) 76.7 (C-4), 75.2, 75.2 (C-3', C-5), 70.9 (C-3"), 70.8 (CH₂-CH=CH₂), 69.4, 69.0 (C-4', C-4"), 67.9 (C-5"), 67.6 (C-5"), 63.7 (C-2"), 63.4 (C-3), 62.3 (C-2'), 58.2 (C-2), 53.1 (CH₃ CO₂Me), 18.6 (C-6"), 18.0 (C-6'); HRMS: [M+NH₄]⁺ calcd for C₂₄H₃₁Cl₃N₁₆O₁₀NH₄ 826.18129, found 826.18079

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Donor 5 (960 mg, 1.49 mmol, 1.3 eq) and acceptor 38 (925 mg, 1.14 mmol, 1 eq) were coevaporated twice with toluene and dissolved in 30 mL DCM. 3Å molecular sieves were added and the reaction mixture was stirred for 30 min at RT, before being cooled to 0 °C. TMSOTf (2,28 mL of a freshly prepared 0.1 M solution in DCM, 0.228 mmol, 0.2 eq) was added. After TLC shows complete disappearance of acceptor 39, the reaction mixture was quenched with 0.2 mL triethylamine, filtered over a small plug of celite and concentrated under reduced pressure. The residue was purified over silica ($20\% \rightarrow 40\%$ acetone in pentane) to yield the title compound as pinkish foam. Yield: 855 mg, 0.67 mmol, 59%. $[\alpha]_D^{25} = 32.0^\circ$ (c = 0.70, CHCl₃); IR (thin film): 757, 821, 1039, 1259, 1527, 1700, 1717, 1754, 2106; ¹H NMR (500 MHz, CDCl₃) δ 7.26 (d, J = 7.4 Hz, 1H, NH), 7.15 (d, *J* = 7.4 Hz, 1H, NH), 5.82 (dddd, *J* = 17.0, 10.4, 6.4, 5.3 Hz, 1H, CH₂-CH-CH₂), 5.38 (d, J = 3.8 Hz, 1H, H-1'), 5.37 - 5.34 (m, 2H, H-1", H-1"), 5.27 (dq, J = 17.2, 1.5 Hz, 1H, CH₂-CH=CHH), 5.21 (dq, J = 10.4, 1.3 Hz, 1H, CH₂-CH=CHH), 5.10 (t, J = 9.7 Hz, 1H, H-4""), 5.03 (d, *J* = 8.0 Hz, 1H, H-1), 4.49 (dd, *J* = 11.0, 9.7 Hz, 1H, H-3³³), 4.39 (dd, *J* = 10.8, 9.1 Hz, 1H, H-3), 4.33 (ddt, J = 12.8, 5.3, 1.4 Hz, 1H, CHH-CH=CH₂), 4.14 (d, J = 9.9 Hz, 1H, H-5"), 4.07 $(ddt, J = 12.8, 6.5, 1.2 Hz, 1H, CHH-CH=CH_2), 4.03 (d, J = 9.4 Hz, 1H, H-5), 3.98 (dd, J = 10.2),$ 9.3 Hz, 1H, H-3"), 3.93 - 3.85 (m, 2H, H-4, H-5"), 3.81 (s, 3H, CH₃ CO₂Me), 3.74 (s, 3H, CH₃ CO_2Me , 3.69 – 3.61 (m, 1H, H-3'), 3.53 – 3.36 (m, 4H, H-2, H-2", H-2", H-5'), 3.17 (dd, J =10.4, 3.8 Hz, 1H, H-2'), 3.13 - 3.06 (m, 2H, H-4', H-4"), 2.85 - 2.71 (m, 2H, CH₂ Lev), 2.71 - 2.57 (m, 2H, CH₂ Lev), 2.20 (s, 3H, CH₃ Lev), 1.35 (d, J = 6.2 Hz, 3H, H-6"), 1.32 (d, J = 6.2 Hz, 3H, H-6'); ¹³C NMR (126 MHz, CDCl₃) δ 206.1, 171.5 (C=O), 167.9, 167.0 (C-6, C-6'''), 162.6, 162.5 (C=O), 132.9 (CH₂-CH=CH₂), 118.9 (CH₂-CH=CH₂), 98.8, 98.7, 98.5 (C-1', C-1", C-1"), 98.0 (C-1), 77.6 (C-3"), 76.9 (C-4), 75.6 (C-3"), 75.2 (C-5), 73.3 (C-5""), 71.1 (C-4""), 70.8 (CH₂-CH=CH₂), 69.0 (C-4'), 67.8 (C-5'), 67.6 (C-5"), 67.1 (C-4"), 63.3 (C-3), 63.1 (C-2"), 62.4 (C-2'), 61.1 (C-3"), 58.1, 57.6 (CH₃ CO₂Me), 53.2, 53.0 (C-2, C-2"), 37.8 (CH₂ Lev), 29.9 (CH₃ Lev), 27.8 (CH₂ Lev), 18.6 (C-6"), 18.0 (C-6'); HRMS: [M+NH₄]⁺ calcd for C₃₈H₄₆Cl₆N₂₀O₁₇NH₄ 1284.17955, found 1248.1789

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Chapter 7: summary and future prospects

Chapter 7

Summary

One of the key challenges in synthetic carbohydrate chemistry is the formation of a glycosidic bond between two carbohydrate building blocks. The main reason that synthesis of carbohydrate oligomers is more challenging than other biomolecules, such as peptides and oligonucleotides, is that with glycosylation a new stereocenter is introduced. And where *1,2-trans* glycosidic bonds can usually be synthesised by means of neighbouring group participation, for the stereoselective and high yielding formation of *1,2-cis* glycosidic bonds no universally applicable technique exists.

In a typical glycosylation reaction, a donor is activated to form a (variety of) electrophilic species which can react with a nucleophilic acceptor, following a reaction mechanism having both S_N1 and S_N2 character. On the S_N1 -side of the spectrum oxocarbenium ions partake in the mechanism while covalent intermediates act as the product forming intermediates on the S_N2 -side. The result of a glycosylation reaction is influenced by the properties of both donor and acceptor and can be affected by external factors as well. Because the challenges in carbohydrate synthesis are typically solved for a specific synthetic problem, a general understanding of what effect changing a single variable has on the mechanistic pathway, and thus the (stereochemical) outcome is not available. This in turn means that synthesis of glycosidic bonds typically requires a considerable amount of optimisation at the expense of a significant amount of time and resources. The goal of this thesis is to systematically investigate how changes in stereochemistry and protecting group patterns on the donor and acceptor affect the mechanism and outcome of glycosylation reactions, to enable a more rational design of synthesis routes.

Chapter 1 presents the challenges associated with the chemical synthesis of carbohydrates and shows some solutions that have been developed for stereoselective glycosylation. Here, the $S_N 1/S_N 2$ mechanism continuum is described, as well as methods for investigating both ends of the spectrum together with some key results. Finally, the role of the reactivity of the acceptor in the outcome of the glycosylation reaction is discussed.



Figure 1: Donors and acceptors used in chapters **2** and **3**. 1: the D-isomer is shown for ease of comparison, but the L-isomer was used in the experiments.

Chapter 2 describes an investigation to the influence of the stereochemistry of the donor on the S_N mechanistic pathway of the glycosylation reaction via a combination of computational chemistry and glycosylation experiments. First, all eight diastereomeric per-O-benzyl pyranosyl donors, as well as their 6-deoxy analogues (1-8 and 9-16 respectively, Figure 1) were synthesised. Next, conformation energy landscape (CEL)-maps for all the corresponding oxocarbenium ions were generated to theoretically determine the conformational preference of the oxocarbenium ions, thereby predicting the expected stereochemical outcome of a glycosylation reaction which follows a S_N1 pathway. Finally, all donors were reacted with two nucleophiles which typically react following an S_N1 -type mechanism, namely TES-D and allyl-TMS. The stability of the conformers found in CEL maps can be explained by considering the "preferences" of the substituents to stabilize (or minimize destabilization of) the oxocarbenium ions. Oxocarbenium ions where the C-3 and C-4 alkoxy groups are placed in a pseudo-axial fashion are more stable compared to their pseudo-equatorial equivalents. For C-2 and C-5 a pseudo-equatorial orientation is preferred. When all 4 substituents can be placed in the preferred orientations, as is the case for gulose/6deoxy gulose, the ion has a strong preference for that conformation (${}^{4}H_{3}$ half chair). Also, with 3 out of 4 substituents optimally orientated, the ions show a strong preference for that conformation. When only 2 substituents can be placed in the preferred orientation, the energy differences between conformations are a lot smaller. One further observation is that the preferences for 6-deoxy oxocarbenium ions are very similar to those of their 6-OBn analogues in most cases, although the absolute energy differences are different. This is also apparent in the outcome of the glycosylation reactions.

For the reactions with TES-D, the orientation of the C-2 substituent is the most important in determining the stereochemical outcome, as all of these reactions are highly *1,2-cis* selective. This in agreement with the CEL maps in most cases, except for talose and 6-deoxy glucose, where a ~1:1 mixture is predicted and for idose, where α -selectivity was predicted, but complete β -selectivity was observed.

Reactions with Allyl-TMS gave different results. When the C-2 group is equatorial, the reaction proceeds with full α -selectivity like with TES-D. When the C-2 group is placed in an axial manner however, the reaction shifts from β -selectivity for the TES-D reactions to α -selectivity with allyl-TMS. A possible explanation are the steric interactions between the substituents and the nucleophile that disfavour attack on the *cis*-side. Following a Curtin-Hammett kinetic scenario, attack can then take place on a higher energy oxocarbenium ion conformer *via* a lower energy transition state leading to the *trans*-product. Understanding the possible Curtin-Hammett scenarios occurring during the nucleophilic addition of allyl-TMS to an oxocarbenium ion is currently a topic of active research.¹

Chapter 3 focuses on the mechanistic pathways which involve a covalent intermediate. Variable temperature (VT) NMR was used to characterise the covalent species formed upon activation of donors **1-8** (see *Figure 1*). The observed species were either a mixture of α -triflate and α -oxosulfonium triflate, a mixture of α -triflate and α , β -oxosulfonium triflates. β -Triflates were not observed for any of the donors.

Next, the donors were coupled with five alcohol acceptors of varying nucleophilicity (EtOH-HFIP, see *Figure 1*) to probe the influence of the nucleophilicity on the reaction path and the stereochemical outcome of the glycosylations. In the reactions with the EtOH-MFE-DFE-TFE series, the configuration of C-3 appeared to be a key determining factor in the relation between nucleophilicity and stereoselectivity. When the C-3 substituent is equatorial, a clear trend is observed where more nucleophilic acceptors give higher β -selectivity and less nucleophilic acceptors provide higher α -selectivity. When the C-3 groups are axial, α : β mixtures are obtained with no clear relation between nucleophilicity and stereoselectivity. A possible mechanistic explanation for these observations is that for the donors having an equatorially oriented

C-3 group, the most reactive acceptors can substitute the more stable covalent α -species, yielding the β -products, while less reactive acceptors can only react with the more reactive β -species to yield the α -product. When the substituent at C-3 is axial, the reactivity difference between the covalent α - and β -species is smaller because of destabilizing 1,3-diaxial interactions between the triflate and the C-3 group. The S_N2 substitution of the β -species, is also hindered by the group on C-3. These steric interactions counteract one another leading to overall poor selectivity.

The glycosylations with HFIP were all completely α -selective, regardless of the stereochemistry of C-2 or C-3. This stands in contrast to the outcome of related reactions with TES-D, the nucleophile used to benchmark S_N1 reaction pathways, where reactions are always highly *1,2-cis* selective, suggesting that the glycosylations with weak *O*-nucleophiles occurs via a different mechanism than nucleophilic addition to an oxocarbenium ion.

In **Chapter 4** a system based on the use of two conformationally restricted glucosyl donors is described to unravel the structure-reactivity relations of a set of 60 acceptors. The stereochemical outcome of the glycosylation reactions of these two donors is highly dependent on the nucleophilicity of the acceptor, as determined by glycosylations with the EtOH-HFIP model acceptors. The most nucleophilic acceptors react with full β -selectivity, while decreasing the nucleophilicity of the acceptor gradually leads to full α -selectivity.

This property was used to measure the reactivity of a large set of carbohydrate acceptors. By systematically varying the protecting group pattern on D-glucose, D-mannose, D-galactose, L-rhamnose and L-fucose acceptors and "measuring" their reactivity, it was possible to determine which structural features determine the reactivity of the acceptor. Two kinds of model acceptors were also introduced. The first kind consist of carbohydrate-like acceptors stripped to only their "essential" substituents, based on 1,2,6-trideoxy glucose and galactose with varying protecting group patterns. The second kind of model acceptors are C-2-OH glycerol acceptors with a cyclic protecting group on C-1 and C-3. These acceptors resemble carbohydrates acceptors in the sense that they are secondary alcohols next to two protected oxygen atoms. Unlike carbohydrate acceptors however, they are not chiral, so the stereochemical outcome of the glycosylation reactions is not determined by diastereomeric interactions.

Analysis of the results from the glycosylation reactions reveals that both the configuration as well as the protecting group pattern of the acceptor play a key role in determining the reactivity of the acceptor (*Figure 2*). With regard to the configuration of the acceptor, equatorial alcohols are more reactive than axial alcohols (light blue circles and blue squares vs black triangles). The orientation of the functional group next to the nucleophilic alcohol is also important, and alcohols having only equatorial

neighbours are more reactive than alcohols which are next to an axial neighbour (light blue circles vs blue squares). With regard to the protecting group pattern, benzoyl protected acceptors are less reactive than their benzyl protected counterparts. The magnitude of this effect depends on which benzyl group is replaced with a benzoyl group, since the effect is much larger when an equatorial benzyl group next to the alcohol is changed for a benzoyl group than when the same is done with an axial benzyl group next to the alcohol (blue squares, red diamonds and yellow triangles).



Figure 2: Relations between the structure and the reactivity (measured as percentage β -product) of glycosyl acceptors found in chapter 4.

Chapter 5 builds on chapter 4, by using the same methodology that was applied on benzyl/benzoyl protected acceptors to determine the influence of common *N*-protecting groups (*i.e* azide, tricholoroacetamide (TCA) and trifluoroacetamide (TFA)) on the reactivity of glycosyl acceptors. The acceptors used in this study were C-4-OH glucosamine acceptors, since the C-4-OH *N*-acetylglucosamine acceptors are notorious for their poor nucleophilicity and C-3-OH glucosamine acceptors, to investigate the effect of different protecting groups next to the nucleophilic alcohol. The C-4-OH and C-3-OH mannosamine acceptors were added in order to determine the influence of the configuration of the protected amine on the reactivity of the acceptor.

Like with benzyl/benzoyl protected acceptors, both the configuration and the nature of the protecting group are important for the reactivity of the acceptor. For both the C-4-OH glucosamine and mannosamine acceptors, the nature of the protecting group has little influence on the reactivity of the acceptors, since all glycosylations within the same acceptor series proceeded with similar stereoselectivity and high yield. With the C-3-

OH glucosamine and mannosamine acceptors, similar trends were observed as in the acceptor series in chapter 4. The first observation is that an azide has a disarming effect that is comparable to that of a *O*-benzoyl group and that acetamides have a larger disarming effect, with the trifluoroacetamides being more disarming than the trichloroacetamides. The configuration of the protected amine next to the alcohol was also found to be important for the reactivity of the acceptor. As observed for the ether protected acceptors, the C-3-OH glucosazide acceptor is more reactive than the C-3-OH mannosazide acceptor. Also, in line to the results of chapter 4, the disarming effect of the N-protecting groups on equatorial amines next to the alcohol is much more significant than the disarming effect of the N-protecting groups of the neighboring axial amines.

In **Chapter 6**, the obtained knowledge described in Chapters 2-5 is used to synthesize the repeating unit of a capsular polysaccharide found on Acinetobacter baumannii LUH 5554, a Gram-negative bacterium that has been designated by the World Health Organization as a high risk pathogen due to its high level of antibiotic resistance. This polysaccharide is built up from repeating tetramers with the structure $[\rightarrow 4)$ - β -D-GlcpNAc3NAcA-(1 \rightarrow 3)- α -D-QuipNAc4NAc-(1 \rightarrow 3)- α -D-QuipNAc4NAc-(1 \rightarrow 4)- β -D-GlcpNAc3NAcA-(1 \rightarrow] (*Figure 3*) which encompass the two rare sugars 2,4-di-*N*-acetyl- α -D-quinovose (2,4-di-*N*-acetyl bacillosamine, QuiNAc4NAc) and 2,3-di-*N*-acetyl- β -Dglucuronic acid (GlcNAc3NAcA). What makes this structure special, is that it contains *N*-acetyl groups, carboxylates and deoxy centers, but not a single hydroxyl group!



Figure 3: Structure of the oligosaccharide from A. Baumannii LUH 5554.

Synthetic routes for producing multi-gram quantities of the bacillosamine and 2,3-di-*N*-acetyl glucuronic acid building blocks were developed starting from D-fucose and Dglucosamine-HCl. The reactivity of the bacillosamine donors was then studied to develop methods for the construction of the 1,2-*cis* linkages. Model glycosylations with fluorinated ethanol acceptors showed that the stereoselectivity of the studied selenophenol bacillosamine donor strongly depends on the nucleophilicity of the acceptor under pre-activation conditions, with ethanol providing complete β -selectivity and 2,2,2-trifluoroethanol nearly complete α -selectivity. The azides and methyl esters on the carbohydrate acceptors should have a disarming effect on the nucleophilic alcohol based on previous studies and, as expected, glycosylation with both the 2,3-diN-acetyl glucuronic acid acceptors and the bacillosamine acceptors proceed with high α -selectivity.

In order to investigate the mechanism underlying this selectivity, VT-NMR was used to study the reactive intermediates formed from the bacillosamine donors. When the selenophenol donor was activated with Ph₂SO and Tf₂O, a mixture of the α -triflate, α -oxosulfonium triflate and β -oxosulfonium triflate was formed. The β -oxosulfonium triflate appeared to be the most reactive, as judged by the lowest decomposition temperature. On the other hand, activation of the corresponding PTFAI donor with TfOH, led to the formation of only the α -triflate. Based on observations in glycosylations between the selenophenol donor or imidate donor with the 2,3-di-*N*-acetyl glucuronic acid acceptors (see below) it is expected that the oxosulfonium triflates play a role in determining the selectivity of the selenophenol donor.

With this knowledge in hand, the tetrasaccharide could be assembled. Eventually 855 mg (670 μ mol) of protected tetrasaccharide building block was obtained, which can be deprotected, or used for the synthesis of larger oligomers (see below).

Future prospects

The goal of this thesis has been to systematically map structure-reactivity relationships for both donor and acceptor building blocks and shine light on the different mechanisms of the glycosylation reaction to enable the rational design of synthetic routes towards complex oligosaccharides. The following section describes some suggestions for follow-up studies to further increase the understanding of the glycosylation reaction.

Influence of oxosulfonium species on the outcome of the glycosylation reaction

Chapter 6 shows the use of VT-NMR to characterise the reactive species that are formed when either a selenophenol or an imidate donor are activated with Ph_2SO/Tf_2O or TfOH, respectively (*Figure 4*). The selenophenol donor provided a mixture of α -triflate, α -oxosulfonium triflate and β -oxosulfonium triflate, while the imidate only delivered the α -triflate. The glycosylations with the 2,3-di-*N*-acetyl glucuronic acid acceptor suggest a prominent role for the oxosulfonium triflates in determining the stereoselectivity of the reaction. When this acceptor was reacted with the selenophenol donor under pre-activation conditions, high α -selectivity was obtained. While the reaction with the imidate donor led to a mixture of α - and β -products. The α -selectivity could be restored in the reaction with the imidate donor by adding Ph₂SO, suggesting an important role for the intermediate oxosulfonium species.

$N_{apO}^{N_3} \xrightarrow{1/2} N_{apO}^{N_3} \xrightarrow{N_3} \xrightarrow{N_3} N_{apO}^{N_3} \xrightarrow{N_3} \xrightarrow{N_3} N_{apO}^{N_3} \xrightarrow{N_3} $	-O_⊕ S-Ph Ph
$N_{apO} \xrightarrow{N_{apO}} (CF_{3}) \xrightarrow{NPh} (CF_{3}) \xrightarrow{TfOH} (N_{apO} \xrightarrow{N_{3}} (CF_{3}) (CF_{3}) \xrightarrow{N_{3}} (CF_{3}) (CF$	
$N_{apo} \longrightarrow N_{apo} N_{apo} \longrightarrow N_{a$	
Entry LG Activation α:β	
1 α-SePh Ph ₂ SO/Tf ₂ O 10-13:1	
2 α,β -OC(=NPh)CF ₃ TMSOTf 1:1	
3 α,β -OC(=NPh)CF ₃ TMSOTf+Ph ₂ SO 9:1	

Figure 4: Selected observations from chapter 6

Figure 5 shows an example from literature where the difference in reactivity between triflates and oxosulfonium triflates was used. When Crich and Li reacted sialic acid donor I with a stoichiometric amount of Ph₂SO, triflate II was formed, followed by immediate elimination to give glycal III. However, when an excess of Ph₂SO was used under otherwise similar conditions, a mixture of oxosulfonium triflates IV and V was formed. These species enabled the formation of the glycosylation products with a variety of acceptors.²



Figure 5: A literature example which illustrates the reactivity difference between triflates and oxosulfonium triflates. When sialic acid donor I gets activated with Tf_2O and an stoichiometric amount of Ph₂SO, triflate II is formed, followed by immediate elimination to glycal III. When an excess of Ph₂SO was used, oxosulfonium triflates IV and V are formed, which can successfully react with different acceptors.²

When thiophenol donors 1-8 (*Figure 1*) were activated with Ph_2SO and Tf_2O , oxosulfonium species were generated as determined by the VT-NMR measurements. Based on the observations described above, it is not unreasonable to expect that these

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oxosulfonium species play a role in shaping the stereochemical outcome of the glycosylation reactions, as reported in chapter 3. An interesting follow-up study would be to transform these thiophenol donors into the corresponding (PTFAI) imidates and use transform these into the corresponding triflates and perform glycosylations with the EtOH-HFIP acceptors to systematically investigate the role that the oxosulfonium species play in glycosylation reactions.

Relative reactivity values of acceptors with donors that react via an $S_N 1$ or an $S_N 2$ mechanism

In chapter 4 and chapter 5 structure-reactivity relationships for glycosyl acceptors are established based on the stereoselectivity of these acceptors in reactions with two glycosyl donors. A quantitative expression of the nucleophilicity of acceptors remains challenging nonetheless. Although multiple attempts, both computational and experimental, have been undertaken,³ an acceptor equivalent to the widely used relative reactivity values (RRVs) used to describe the reactivity of glycosyl donors⁴⁻⁶ does not yet exist. In a recent paper by Wong, Wang and coworkers the "AKa" value was proposed as a measurement of acceptor reactivity. This value can be determined by measuring the relative reaction rate between an acceptor hydroxyl group and dihydropyran under acidic conditions in a flow system.⁷

A problem in competition experiments in which two acceptors are made to compete for one donor in a "real" glycosylation reaction, is the potential occurrence of four different products, that are formed via different pathways. The relative reactivity of an acceptor may depend on the mechanistic pathway, complicating the interpretation of the obtained values. To establish how relative acceptor reactivity depends on the mechanistic pathway, acceptor competition experiments can be probed using two different kinds of donors that react via different mechanisms on opposite ends of the S_N1/S_N2 mechanism continuum (*Figure 6*). Glycosylation of donor **D1**, a tetra-benzoyl PTFAI galactosyl donor, proceed via a displacement of a dioxolenium ion in an S_N2 type mechanism (*Figure 6A*).⁸⁻¹⁰ While glycosylations of donor **D2**, a DTBS protected galactopyranose PTFAI donor, follow an S_N1 -type mechanism to form the α -product.¹¹ *Figure 6C* shows a selection of acceptors, described in chapter 4 and 5, for a set of competition experiments (A1-A11, *Figure 6C*).



Figure 6: A) reaction mechanism of donor D1; B) reaction mechanism of donor D2; C) acceptors tested in this work.

For the competition experiments, a limiting amount of donor was reacted under *in situ* activation conditions with 2 equivalents of acceptor to ensure that an excess of each acceptor was always present. Due to the stereoselective nature of the reactions, only two products are formed in each reaction: product I and product II according to equation (1). The ratio between the two formed products can be used as a measure for the relative reactivity of two acceptors in a given mechanistic pathway.

$Donor (1 eq) + Acceptor I (2 eq) + Acceptor II (2 eq) \rightarrow product I + product II (1)$

The results of the competition experiments are summarised in *Table 1*. These results show that with S_N2 -donor D1, the relative reactivity of the acceptors parallels the structure-reactivity relations found in chapter 4 and chapter 5. Benzyl protected acceptors are more reactive than benzoyl protected acceptors (A1>A2; A3>A4 and A6>A7), alcohols next to equatorial ethers are more reactive than alcohols next to axial ethers (A5>A6 and A9>A8) and TFA groups are more disarming than azides (A10>A11).

With S_N1 -donor D2 on the other hand, benzoyl protected acceptors A2 and A4 appear to be more reactive than their benzylated counterparts A1 and A3. Alcohols next to equatorial ethers appear to be (slightly) more reactive than alcohols next to axial ethers (A5>A6).

These results indicate that the relative nucleophilicity of the acceptors in glycosylation reactions proceeding with different mechanisms are governed by different factors. While the trend for the S_N2 -substitutions seems to be correlated to the electron density on the acceptor alcohol oxygen, which decreases with increasing electron withdrawing capacity of the protecting/functional groups, the relative reactivity of the acceptors in the S_N1 -substitutions correlate to the relative acidity of the alcohols, with the more acidic alcohols being more reactive in the substitution reactions. More acceptors need to be screened to shed further light on the relative acceptor reactivity under these conditions.

Entry	Donor	Acceptor I	Acceptor II	Product I:II	yield
1	D1	A1	A2	>20:1	80%
2	D1	A3	A4	3.5:1	89%
3	D1	A5	A6	11:1	92%
4	D1	A6	A7	9:1	90%
5	D1	A8	A9	1:2	85%
6	D1	A10	A11	16:1	79%
7	D2	A1	A2	1:3.5	100%
8	D2	A3	A4	1:3.9	100%
9	D2	A5	A6	1.5:1	100%

Table 1: results of the competition experiments

Conditions: 0.05*M Donor in DCM* 1 *eq donor,* 2 *eq acceptor I,* 2 *eq acceptor II,* 0.1 *eq TMSOTf* **D1***:* 0°C, **D2***:* -40 °C to 0 °C.

Synthesis of oligomers of the A. Baumannii LUH 5554 tetrasaccharide

Chapter 6 describes the synthesis of the tetrasaccharide repeating unit of the A. Baumannii LUH 5554 capsular polysaccharide. Since a relatively large amount of protected tetrasaccharide building block was obtained, the synthesis of oligomers is an attractive perspective. A strategy for this oligomer synthesis is depicted in *Figure 7*. The tetrasaccharide building block is orthogonally protected at the reducing and the non-reducing end. This property can be used to generate tetramer donor and acceptor building blocks. For the synthesis of the acceptor, the levulinoyl ester can be removed selectively with H_2NNH_2 -HOAc,¹² while the allyl group at the reducing end can be removed with catalytic PdCl₂ and turned into the imidate with conditions similar to those described in chapter 6 to generate a donor synthon. After glycosylation, the

obtained octas acceptor, which can react with the tetrameric donor. This process can be repeated multiple times to get the octa-, dodeca-, hexadeca- and icosas acceptor.



Figure 7: Retrosynthetic analysis towards oligomers of the A. Baumannii LUH 5554 tetrasaccharide.

With the obtained oligosaccharides the structure of the oligomers can be investigated by an approach combining NMR spectroscopy and computational chemistry. It will be of interest to see how the "lack of oxygen" substituents and the presence of all the acetamides affects the secondary structure of the saccharides. These structural studies can be followed by the immunological evaluation to investigate whether antibodies can be elicited by protein conjugates of the oligomers (the generation of which can be done exploiting the allyl group as a conjugation handle) that recognize the capsular polysaccharide, and if so, what the minimal epitope is.¹³

Chapter 7

Experimental

General procedure I: Glycosylation with D1 or D2

Donor **D1** or **D2** (1 eq) and the acceptor (1-2 eq) were coevaporated twice with toluene and dissolved in DCM (0.05 M donor). 3A molecular sieves were added and the mixture was stirred for 30 min at RT, after which it was cooled to 0 °C and 0.1-0.2 eq of TMSOTf was added. After full conversion after the starting material, the reaction was quenched with sat. aq. NaHCO₃ and extracted with DCM. The organic phase was dried with MgSO₄ and concentrated under reduced pressure. The disaccharides were isolated by size-exclusion chromatography (Sephadex LH-20 1:1 DCM/MeOH)

Competition experiments with D1

Donor **D1** (1 eq), acceptor I (2 eq) and acceptor II were coevaporated twice with toluene and dissolved in DCM (0.05 M donor). 3A molecular sieves were added and the mixture was stirred for 30 min at RT, after which it was cooled to 0 °C and 0.1 eq of TMSOTf was added. After full conversion after the starting material, the reaction was quenched with sat. aq. NaHCO₃ and extracted with DCM. The organic phase was dried with MgSO₄ and concentrated under reduced pressure. The mixture of disaccharide products was isolated by size-exclusion chromatography (Sephadex LH-20 1:1 DCM/MeOH). Selection of diagnostic peaks for determining the ratio of product I to product II was done by comparing the 1H-NMR spectrum of the mixture to the 1H-NMR spectra of both reference compounds.

Competition experiments with D2

Competition experiments with **D2** were done in a procedure similar to those for **D1**. The only difference is that TMSOTf was added at -40 °C, after which the reaction mixture was allowed to warm to 0 °C.

Disaccharide D1A1



According to the general procedure I from D1 and A1. Yield: 88 mg, 84 µmol, 84% a: β <1:20. ¹H NMR (500 MHz, CDCl₃) δ 8.05 – 8.00 (m, 2H), 7.94 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.87 – 7.83 (m, 2H), 7.79 – 7.74 (m, 2H), 7.58 – 7.52 (m, 2H), 7.52 – 7.45 (m, 5H), 7.44 – 7.34 (m, 9H), 7.33 – 7.20 (m, 9H), 7.19 – 7.14 (m, 1H), 5.86 (dd, *J* = 3.5, 1.1 Hz, 1H), 5.70 (dd, *J* = 10.4, 8.1 Hz, 1H), 5.30 (dd, *J* = 10.4, 3.5 Hz, 1H), 5.18 (d, *J* = 11.1 Hz, 1H), 4.91 (d, *J* = 11.1 Hz, 1H), 4.84 – 4.74 (m, 3H), 4.65 (d, *J* = 12.3 Hz, 1H), 4.58 (d, *J* = 3.7 Hz, 1H), 4.40 (dd, *J* = 11.2, 6.2 Hz, 1H), 4.32 (d, *J* = 12.2 Hz, 1H), 4.19 (dd, *J* = 11.2, 7.6 Hz, 1H), 3.53 (ddd, *J* = 13.2, 10.8, 3.0 Hz, 2H), 3.44 (dd, *J* = 10.8, 1.9 Hz, 1H), 3.30 (s, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 165.9, 165.5, 165.5, 165.0, 139.5, 138.4, 137.9, 133.5, 133.4, 133.3, 129.9, 129.9, 129.8, 129.8, 129.7, 129.6, 129.2, 129.1, 128.9, 128.7, 128.5, 128.4, 128.4, 128.2, 128.2, 127.9, 127.3, 127.3, 100.5, 98.6, 79.9, 78.7, 76.8, 75.3, 73.7, 73.7,

71.9, 71.0, 70.4, 69.6, 67.9, 67.6, 61.5, 55.5; HRMS: $[M+NH_4]^+$ calcd for $C_{62}H_{58}O_{15}NH_4$ 1060.41140, found 1060.41099

Disaccharide D1A2



According to the general procedure **I** from D1 and A2. Yield: 75 mg, 70 µmol, 70%, $\alpha:\beta < 1:20.$ ¹H NMR (500 MHz, CDCl₃) δ 8.06 – 8.03 (m, 2H), 8.01 – 7.96 (m, 8H), 7.90 – 7.87 (m, 2H), 7.76 – 7.71 (m, 2H), 7.62 (ddt, *J* = 8.8, 7.3, 1.3 Hz, 1H), 7.60 – 7.55 (m, 2H), 7.50 – 7.27 (m, 13H), 7.24 – 7.16 (m, 5H), 6.09 (dd, *J* = 10.3, 9.0 Hz, 1H), 5.78 – 5.71 (m, 2H), 5.40 (dd, *J* = 10.3, 3.4 Hz, 1H), 5.24 (dd, *J* = 10.3, 3.7 Hz, 1H), 5.13 (d, *J* = 3.8 Hz, 1H), 4.92 (d, *J* = 7.9 Hz, 1H), 4.59 (dd, *J* = 12.1, 2.0 Hz, 1H), 4.53 (dd, *J* = 12.1, 4.2 Hz, 1H), 4.22 (dd, *J* = 10.1, 9.0 Hz, 1H), 4.13 (ddd, *J* = 10.1, 4.2, 1.9 Hz, 1H), 3.94 – 3.89 (m, 1H), 3.84 (dd, *J* = 11.2, 6.3 Hz, 1H), 3.76 (dd, *J* = 11.3, 7.1 Hz, 1H), 3.38 (s, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 166.1, 166.0, 165.7, 165.6, 165.4, 165.4, 164.9, 133.6, 133.6, 133.5, 133.4, 133.3, 133.2, 130.1, 130.1, 130.0, 129.9, 129.9, 129.9, 129.8, 129.8, 129.7, 129.7, 129.7, 129.7, 129.2, 128.9, 128.8, 128.7, 128.7, 128.6, 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 101.2, 97.0, 76.4, 72.0, 72.0, 71.4, 70.5, 70.0, 68.4, 67.6, 62.5, 61.2, 55.6; HRMS: [M+NH₄]⁺ calcd for C₆₂H₅₂O₁₈NH₄ 1102.34919, found 1102.34951.

Disaccharide D1A3

BzO -0 BnO-

According to the general procedure I from D1 and A3. Yield: 80 mg, 99 µmol, 99%, $\alpha:\beta < 1:20.$ ¹H NMR (400 MHz, CDCl₃) δ 8.05 – 7.94 (m, 6H), 7.83 – 7.77 (m, 2H), 7.63 – 7.48 (m, 5H), 7.47 – 7.35 (m, 7H), 7.34 – 7.28 (m, 2H), 7.28 – 7.21 (m, 4H), 6.01 (dd, *J* = 3.4, 1.1 Hz, 1H), 5.83 (dd, *J* = 10.4, 7.8 Hz, 1H), 5.63 (dd, *J* = 10.4, 3.4 Hz, 1H), 5.19 (d, *J* = 10.6 Hz, 1H), 5.02 (d, *J* = 7.9 Hz, 1H), 4.73 – 4.59 (m, 2H), 4.39 (dd, *J* = 11.0, 7.4 Hz, 1H), 4.31 (ddd, *J* = 7.2, 5.9, 1.2 Hz, 1H), 4.05 (ddd, *J* = 11.4, 8.5, 5.2 Hz, 1H), 3.80 (ddd, *J* = 12.8, 11.4, 4.9 Hz, 1H), 1.27 (d, *J* = 6.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 166.1, 165.7, 165.6, 165.3, 138.9, 133.6, 133.5, 133.4, 130.0, 129.9, 129.9, 129.7, 129.5, 129.2, 128.9, 128.8, 128.6, 128.5, 128.4, 128.4, 128.3, 127.7, 98.7, 82.5, 79.9, 76.0, 75.2, 71.9, 71.3, 70.4, 68.1, 64.9, 61.8, 31.1, 18.6; HRMS: [M+NH₄]⁺ calcd for C₄₇H₄₄O₁₂NH₄ 818.31710, found 818.31713.

Disaccharide D1A4

BzO Q BzO BzC

According to the general procedure I from D1 and A4. Yield: 81 mg, 100 μ mol, 100%, α : β = 1:10. Data for the β -anomer: ¹H NMR (400 MHz, CDCl₃) δ 8.15 – 8.10 (m, 2H), 8.02 – 7.97 (m, 2H),

7.97 – 7.90 (m, 2H), 7.87 – 7.81 (m, 2H), 7.80 – 7.73 (m, 2H), 7.61 – 7.33 (m, 15H), 7.28 – 7.14 (m, 5H), 5.85 (dd, J = 3.4, 1.1 Hz, 1H), 5.62 (dd, J = 10.4, 7.7 Hz, 1H), 5.51 (dd, J = 10.4, 3.4 Hz, 1H), 4.96 (t, J = 9.2 Hz, 1H), 4.92 (d, J = 7.9 Hz, 1H), 4.18 (dd, J = 10.9, 6.0 Hz, 1H), 4.06 (dddd, J = 20.4, 9.1, 6.0, 2.5 Hz, 2H), 3.94 (dd, J = 10.9, 7.4 Hz, 1H), 3.89 (ddd, J = 11.9, 5.3, 2.0 Hz, 1H), 3.49 – 3.44 (m, 1H), 3.39 (td, J = 12.3, 2.2 Hz, 1H), 2.03 – 1.90 (m, 1H), 1.78 – 1.65 (m, 2H), 1.25 (d, J = 6.2 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 165.8, 165.6, 165.4, 164.9, 133.5, 133.4, 133.3, 133.2, 133.1, 130.3, 129.9, 129.8, 129.7, 129.7, 129.6, 129.4, 128.9, 128.8, 128.6, 128.6, 128.6, 128.5, 128.4, 128.4, 128.3, 128.2, 128.2, 128.0, 100.3, 78.8, 75.7, 75.1, 71.8, 71.0, 70.1, 67.7, 65.2, 61.3, 31.7, 18.2; diagnostic peaks for the α-anomer: ¹H NMR (400 MHz, CDCl₃) δ 6.03 (dd, J = 3.4, 1.3 Hz, 1H), 5.89 (dd, J = 10.9, 3.4 Hz, 1H), 4.76 (t, J = 6.4 Hz, 1H), 4.43 (dd, J = 11.4, 4.7 Hz, 1H), 2.19 (dd, J = 12.8, 5.3 Hz, 1H), 1.13 (d, J = 6.2 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 98.3, 77.4, 76.8, 68.2, 63.0, 32.6; HRMS: [M+NH₄]⁺ calcd for C₄₇H₄₂O₁₃NH₄ 832.29637, found 832.29592.

Disaccharide D1A5



According to the general procedure **I** from D1 and A5. Yield: 104 mg, 100 µmol, 100%, $\alpha:\beta < 1:20$. ¹H NMR (400 MHz, CDCl₃) δ 8.01 (td, J = 8.6, 1.4 Hz, 4H), 7.90 (dd, J = 8.3, 1.4 Hz, 2H), 7.81 – 7.76 (m, 2H), 7.55 – 7.46 (m, 3H), 7.43 – 7.30 (m, 10H), 7.29 – 7.19 (m, 11H), 7.10 – 7.04 (m, 2H), 6.01 (dd, J = 3.5, 1.1 Hz, 1H), 5.88 (dd, J = 10.5, 8.0 Hz, 1H), 5.69 (dd, J = 10.5, 3.5 Hz, 1H), 5.51 (d, J = 8.0 Hz, 1H), 5.29 (d, J = 10.5 Hz, 1H), 4.67 – 4.53 (m, 4H), 4.49 – 4.43 (m, 2H), 4.41 – 4.28 (m, 3H), 4.18 (d, J = 12.3 Hz, 1H), 3.73 – 3.55 (m, 4H), 3.37 (dd, J = 9.6, 3.5 Hz, 1H), 3.26 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 166.0, 165.7, 165.5, 165.4, 138.7, 138.0, 138.0, 133.4, 133.4, 133.3, 133.2, 130.0, 129.9, 129.8, 129.5, 129.1, 128.9, 128.6, 128.6, 128.5, 128.4, 128.3, 128.3, 128.1, 128.1, 127.9, 127.8, 127.7, 101.1, 97.9, 80.9, 78.7, 75.4, 75.0, 73.9, 73.6, 71.8, 71.0, 70.7, 69.7, 68.5, 68.2, 61.6, 55.1; HRMS: [M+NH₄]⁺ calcd for C₆₂H₅₈O₁₅NH₄ 1060.41140, found 1060.41118.

Disaccharide D1A6



According to the general procedure **I** from D1 and A6. Yield: 96 mg, 92 µmol, 92%, $\alpha:\beta < 1:20$. ¹H NMR (400 MHz, CDCl₃) δ 8.00 (ddd, J = 8.5, 3.6, 1.4 Hz, 4H), 7.92 – 7.87 (m, 2H), 7.80 – 7.74 (m, 2H), 7.60 – 7.50 (m, 2H), 7.48 – 7.13 (m, 23H), 7.03 (dd, J = 6.8, 2.7 Hz, 2H), 5.97 (dd, J = 3.5, 1.1 Hz, 1H), 5.90 (dd, J = 10.5, 7.9 Hz, 1H), 5.60 (dd, J = 10.4, 3.4 Hz, 1H), 5.12 (d, J = 10.9 Hz, 1H), 4.99 (d, J = 7.9 Hz, 1H), 4.67 (d, J = 2.1 Hz, 1H), 4.62 (d, J = 12.1 Hz, 1H), 4.56 – 4.47 (m, 3H), 4.42 – 4.28 (m, 4H), 4.25 – 4.18 (m, 1H), 4.01 – 3.91 (m, 1H), 3.77 – 3.70 (m, 4H), 3.26 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 166.0, 165.7, 165.6, 165.2, 138.9, 138.5, 138.1, 133.6, 133.4, 133.3, 130.0, 129.9, 129.9, 129.8, 129.5, 129.3, 129.1, 128.8, 128.7, 128.5, 128.4, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.5, 99.5, 98.8, 79.1, 75.6, 74.7, 73.7, 73.4, 72.9, 72.0, 71.9, 71.4, 12.5, 128.5, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.5, 127.5, 99.5, 98.8, 79.1, 75.6, 74.7, 73.7, 73.4, 72.9, 72.0, 71.9, 71.4, 12.5, 128.

70.4, 69.4, 68.1, 61.7, 54.8; HRMS: $[M+NH_4]^+$ calcd for $C_{62}H_{58}O_{15}NH_4$ 1060.41140, found 1060.41145.

Disaccharide D1A7



According to the general procedure I from D1 and A7. Yield: 86 mg, 79 µmol, 79%, $\alpha;\beta = 1:1$. Data reported for a 1:1 mixture of anomers: ¹H NMR (400 MHz, CDCl₃) δ 8.24 – 8.21 (m, 2H), 8.19 – 8.13 (m, 3H), 8.11 – 7.97 (m, 12H), 7.75 – 7.71 (m, 2H), 7.70 – 7.67 (m, 2H), 7.66 – 7.60 (m, 6H), 7.59 – 7.50 (m, 9H), 7.48 – 7.40 (m, 12H), 7.38 – 7.29 (m, 13H), 7.22 – 7.05 (m, 13H), 6.02 (dd, *J* = 3.4, 1.4 Hz, 1H), 5.92 – 5.84 (m, 3H), 5.79 (dd, *J* = 10.1, 3.3 Hz, 1H), 5.72 (dd, *J* = 3.3, 1.8 Hz, 1H), 5.64 – 5.59 (m, 3H), 5.47 (dd, *J* = 10.3, 3.3 Hz, 1H), 5.37 (dd, *J* = 3.5, 1.9 Hz, 1H), 5.02 – 4.96 (m, 2H), 4.93 (dd, *J* = 6.9, 1.8 Hz, 2H), 4.69 – 4.61 (m, 4H), 4.60 – 4.53 (m, 2H), 4.45 (dd, *J* = 12.1, 4.7 Hz, 1H), 4.41 – 4.31 (m, 3H), 4.29 – 4.22 (m, 2H), 4.17 (ddd, *J* = 10.1, 5.2, 3.0 Hz, 1H), 3.97 (dd, *J* = 10.9, 6.9 Hz, 1H), 3.46 (s, 3H), 3.32 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 166.3, 166.2, 166.1, 166.0, 165.6, 165.5, 165.4, 165.1, 164.9, 164.5, 133.6, 133.6, 133.4, 133.4, 133.3, 133.2, 133.1, 133.0, 132.8, 130.3, 130.0, 130.0, 129.9, 129.9, 129.8, 129.8, 129.7, 129.6, 129.5, 129.4, 129.2, 128.8, 128.7, 128.7, 128.6, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 99.6, 98.6, 98.5, 98.3, 74.4, 74.0, 72.0, 71.8, 71.1, 70.0, 69.4, 69.4, 69.0, 68.9, 68.9, 68.4, 68.1, 68.0, 67.7, 67.5, 63.3, 63.1, 61.6, 55.6, 55.3; HRMS: [M+NH₄]⁺ calcd for C₆₂H₅₂O₁₈NH₄ 1102.34919, found 1102.34904.

Disaccharide D1A8



According to the general procedure I from D1 and A8. Yield: 90 mg, 86 µmol, 86%, $\alpha:\beta < 1:20.$ ¹H NMR (400 MHz, CDCl₃) δ 8.14 – 8.09 (m, 2H), 8.02 – 7.97 (m, 2H), 7.87 – 7.82 (m, 2H), 7.81 – 7.74 (m, 2H), 7.64 – 7.57 (m, 1H), 7.54 – 7.45 (m, 3H), 7.43 – 7.35 (m, 4H), 7.34 – 7.15 (m, 21H), 7.08 – 7.03 (m, 2H), 6.04 – 5.95 (m, 2H), 5.59 (dd, *J* = 10.3, 3.5 Hz, 1H), 5.13 (d, *J* = 8.0 Hz, 1H), 5.07 (d, *J* = 3.6 Hz, 1H), 4.84 (d, *J* = 11.5 Hz, 1H), 4.61 (dd, *J* = 11.3, 6.7 Hz, 1H), 4.46 (dt, *J* = 11.6, 5.7 Hz, 4H), 4.41 – 4.32 (m, 3H), 4.28 (dd, *J* = 10.2, 3.6 Hz, 1H), 3.91 – 3.82 (m, 2H), 3.76 (dd, *J* = 3.1, 1.3 Hz, 1H), 3.51 (dd, *J* = 6.4, 1.9 Hz, 2H), 3.39 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 166.1, 165.7, 165.7, 165.3, 138.7, 138.1, 133.7, 133.4, 133.3, 133.1, 130.2, 129.9, 129.8, 129.4, 129.4, 129.1, 128.8, 128.7, 128.6, 128.6, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 127.8, 127.7, 127.3, 127.2, 103.3, 99.8, 80.0, 77.2, 76.0, 74.9, 73.5, 73.3, 72.2, 71.6, 69.9, 69.2, 69.1, 68.3, 62.4, 55.6; HRMS: [M+NH₄]⁺ calcd for C₆₂H₅₈O₁₅NH₄ 1060.41140, found 1060.41120.

Disaccharide D1A9



According to the general procedure **I** from D1 and A9. Yield: 94 mg, 90 µmol, 90%, $\alpha:\beta < 1:20.$ ¹H NMR (400 MHz, CDCl₃) δ 8.15 – 8.08 (m, 2H), 8.03 – 7.98 (m, 2H), 7.89 – 7.84 (m, 2H), 7.84 – 7.78 (m, 2H), 7.65 – 7.58 (m, 1H), 7.57 – 7.45 (m, 3H), 7.44 – 7.36 (m, 4H), 7.34 – 7.15 (m, 19H), 7.07 (ddd, *J* = 5.7, 2.7, 1.5 Hz, 2H), 6.03 (dd, *J* = 3.5, 1.1 Hz, 1H), 5.89 (dd, *J* = 10.4, 8.1 Hz, 1H), 5.55 (dd, *J* = 10.4, 3.4 Hz, 1H), 5.34 (d, *J* = 8.1 Hz, 1H), 4.72 (dd, *J* = 10.9, 5.9 Hz, 1H), 4.55 – 4.45 (m, 3H), 4.44 – 4.31 (m, 6H), 4.24 (d, *J* = 12.0 Hz, 1H), 4.07 (ddd, *J* = 9.7, 7.6 Hz, 1H), 3.59 (d, *J* = 2.8 Hz, 1H), 3.53 (s, 4H), 3.49 – 3.40 (m, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 166.2, 165.7, 165.5, 138.6, 138.3, 137.9, 133.6, 133.4, 133.3, 133.0, 130.2, 129.9, 129.9, 129.8, 129.7, 129.5, 129.2, 129.0, 128.7, 128.6, 128.5, 128.4, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.6, 127.5, 104.0, 102.2, 80.7, 80.3, 73.9, 73.5, 73.4, 73.2, 72.3, 71.7, 70.9, 68.9, 68.3, 62.2, 57.3; HRMS: [M+NH₄]⁺ calcd for C₆₂H₃₈O₁₅NH₄ 1060.41140, found 1060.41110.

Disaccharide D1A10



According to the general procedure **I** from D1 and A10. Yield: Yield: 88 mg, 90 µmol, 90%, a: β <1:20. ¹H NMR (400 MHz, CDCl₃) δ 8.07 – 7.97 (m, 4H), 7.95 – 7.90 (m, 2H), 7.82 – 7.75 (m, 2H), 7.57 – 7.48 (m, 4H), 7.41 (dt, *J* = 10.1, 7.6 Hz, 6H), 7.35 – 7.27 (m, 9H), 7.26 – 7.18 (m, 6H), 5.99 (d, *J* = 3.4 Hz, 1H), 5.84 (dd, *J* = 10.4, 7.9 Hz, 1H), 5.65 (dd, *J* = 10.4, 3.4 Hz, 1H), 5.28 (d, *J* = 7.9 Hz, 1H), 5.23 (d, *J* = 10.7 Hz, 1H), 4.79 (d, *J* = 3.5 Hz, 1H), 4.60 – 4.51 (m, 3H), 4.48 (d, *J* = 10.2, 3.5 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 166.0, 165.6, 165.6, 165.5, 138.5, 137.9, 133.5, 133.4, 133.3, 129.9, 129.9, 129.9, 129.5, 129.4, 129.1, 128.9, 128.7, 128.5, 128.5, 128.4, 128.0, 127.9, 127.7, 101.1, 98.5, 78.1, 75.6, 75.1, 73.6, 71.8, 71.3, 70.4, 70.3, 68.4, 68.1, 63.6, 61.5, 55.3; HRMS: [M+NH₄]⁺ calcd for C₃₅H₅₁N₃O₁₄NH₄ 995.37093, found 995.37058.

Disaccharide D1A11



According to the general procedure **I** from D1 and A10. Yield: 80 mg, 76 µmol, 76%, $\alpha:\beta < 1:20$. ¹H NMR (400 MHz, CDCl₃) δ 8.02 (dt, *J* = 8.4, 1.6 Hz, 2H), 7.95 – 7.87 (m, 4H), 7.77 – 7.71 (m, 2H), 7.61 – 7.25 (m, 19H), 7.23 – 7.15 (m, 5H), 6.59 – 6.48 (m, 1H), 5.98 (dd, *J* = 3.5, 1.0 Hz, 1H), 5.80 (dd, *J* = 10.4, 7.8 Hz, 1H), 5.52 (dd, *J* = 10.4, 3.4 Hz, 1H), 5.20 (d, *J* = 10.9 Hz, 1H), 5.03 (d, *J* = 7.9 Hz, 1H), 4.66 – 4.56 (m, 4H), 4.50 (d, *J* = 12.1 Hz, 1H), 4.36 – 4.22 (m, 4H), 3.78 – 3.70 (m, 3H), 3.68 – 3.63 (m, 1H), 3.32 (s, 3H); 13 C NMR (101 MHz, CDCl₃) δ 166.1, 165.8, 165.6, 165.6, 138.4, 138.0, 133.6, 133.5, 133.4, 133.4, 130.0, 130.0, 129.9, 129.9, 129.8, 129.5, 129.1, 129.0, 128.7, 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 127.9, 127.9, 127.8, 127.8, 100.8, 97.8, 77.3, 75.7, 75.0, 73.6, 71.8, 71.3, 70.8, 70.3, 68.5, 67.9, 61.4, 55.2, 53.3; HRMS: [M+NH₄]⁺ calcd for C₅₇H₅₂F₃NO₁₅NH₄ 1065.36273, found 1065.36259.

Disaccharide D2A1



According to the general procedure I from D2 and A1. Yield: 95 mg, 100 μmol, 100%, α:β >20:1. ¹H NMR (400 MHz, CDCl₃) δ 7.50 – 7.15 (m, 25H), 5.75 (d, *J* = 3.9 Hz, 1H), 5.04 (d, *J* = 11.2 Hz, 1H), 4.78 (dd, *J* = 11.7, 7.9 Hz, 3H), 4.73 – 4.67 (m, 2H), 4.66 – 4.57 (m, 3H), 4.52 (d, *J* = 12.1 Hz, 1H), 4.44 (d, *J* = 12.2 Hz, 1H), 4.37 – 4.32 (m, 1H), 4.10 (dd, *J* = 9.5, 8.5 Hz, 1H), 4.04 – 3.95 (m, 2H), 3.94 – 3.87 (m, 2H), 3.78 (dd, *J* = 12.4, 2.0 Hz, 1H), 3.75 – 3.66 (m, 2H), 3.59 (ddd, *J* = 12.8, 10.1, 2.8 Hz, 2H), 3.50 (d, *J* = 5.2 Hz, 1H), 3.46 – 3.37 (m, 4H), 1.08 (s, 9H), 1.01 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 139.0, 138.7, 138.3, 138.1, 138.0, 128.5, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.1, 127.8, 127.8, 127.7, 127.6, 127.6, 127.3, 127.2, 97.9, 96.8, 82.2, 80.4, 77.8, 74.5, 74.0, 73.6, 73.6, 73.6, 71.1, 71.0, 70.9, 69.4, 69.2, 67.7, 66.9, 55.2, 27.7, 27.4, 23.4, 20.8; HRMS: [M+NH₄]⁺ calcd for C₃₆H₇₀O₁₁SiNH₄ 964.50256, found 964.50209.

Disaccharide D2A2



According to the general procedure I from D2 and A2. Yield: 99 mg, 100 μmol, 100%, α:β >20:1. ¹H NMR (400 MHz, CDCl₃) δ 8.10 – 8.05 (m, 2H), 8.00 (dt, J = 8.4, 1.2 Hz, 4H), 7.63 – 7.57 (m, 1H), 7.53 – 7.44 (m, 5H), 7.43 – 7.26 (m, 10H), 7.11 (s, 5H), 6.19 (dd, J = 10.0, 8.5 Hz, 1H), 5.22 – 5.09 (m, 3H), 4.70 – 4.58 (m, 3H), 4.51 (dd, J = 12.0, 3.9 Hz, 1H), 4.44 – 4.36 (m, 2H), 4.33 – 4.23 (m, 2H), 4.21 (d, J = 11.9 Hz, 1H), 3.92 (d, J = 1.8 Hz, 2H), 3.83 – 3.71 (m, 2H), 3.57 (q, J = 1.5 Hz, 1H), 3.41 (s, 3H), 0.97 (s, 9H), 0.78 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 166.4, 166.2, 165.6, 139.0, 138.1, 133.5, 133.4, 133.1, 130.1, 130.0, 130.0, 130.0, 129.9, 129.8, 129.7, 129.7, 129.2, 128.7, 128.6, 128.5, 128.5, 128.4, 128.3, 127.7, 127.5, 98.5, 96.9, 77.6, 73.2, 72.9, 72.8, 72.6, 72.5, 71.2, 71.1, 68.5, 68.4, 67.0, 63.5, 55.4, 27.7, 27.2, 23.4, 20.6; HRMS: [M+NH₄]⁺ calcd for C₅₆H₆₄O₁₄SiNH₄ 1006.44036, found 1006.44041.

Disaccharide D2A3



According to the general procedure I from D2 and A3. Yield: 71 mg, 100 μmol, 100%, α:β >20:1. ¹H NMR (400 MHz, CDCl₃) δ 7.46 – 7.39 (m, 2H), 7.34 – 7.28 (m, 2H), 7.27 – 7.22 (m, 8H), 7.21 – 7.17 (m, 3H), 5.13 (d, *J* = 11.4 Hz, 1H), 5.07 (d, *J* = 3.6 Hz, 1H), 4.79 (dd, *J* = 12.0, 5.5 Hz, 2H), 4.69 (dd, *J* = 14.4, 12.0 Hz, 2H), 4.61 – 4.54 (m, 2H), 4.23 (dd, *J* = 10.2, 2.9 Hz, 1H), 3.82 (ddd, *J* = 12.4, 1.7 Hz, 1H), 3.99 (dd, *J* = 10.2, 3.6 Hz, 1H), 3.88 (dd, *J* = 10.2, 2.9 Hz, 1H), 3.82 (ddd, *J* = 11.8, 4.9, 1.6 Hz, 1H), 3.78 – 3.68 (m, 2H), 3.34 (td, *J* = 12.2, 2.0 Hz, 1H), 3.26 (dq, *J* = 9.2, 6.1 Hz, 1H), 3.03 (t, *J* = 8.9 Hz, 1H), 2.01 (ddt, *J* = 12.9, 5.3, 1.5 Hz, 1H), 1.74 – 1.62 (m, 1H), 1.22 (d, *J* = 6.1 Hz, 3H), 1.06 (s, 9H), 0.97 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 139.0, 138.5, 128.4, 128.4, 128.3, 128.0, 127.6, 127.6, 127.4, 100.3, 83.5, 82.0, 77.6, 76.2, 74.9, 74.0, 73.8, 71.1, 70.7, 67.8, 67.2, 65.3, 33.8, 27.8, 27.4, 23.6, 20.8, 18.7; HRMS: [M+NH₄]⁺ calcd for C₄₁H₅₆O₈SiNH₄ 722.40827, found 722.40806.

Disaccharide D2A4



According to the general procedure I from D2 and A4. Yield: 72 mg, 100 μmol, 100%, α:β >20:1. ¹H NMR (400 MHz, CDCl₃) δ 8.08 – 7.99 (m, 2H), 7.55 – 7.47 (m, 1H), 7.40 – 7.27 (m, 8H), 7.17 – 7.11 (m, 3H), 7.01 – 6.94 (m, 2H), 5.02 (t, J = 9.3 Hz, 1H), 4.88 (t, J = 1.5 Hz, 1H), 4.57 (d, J = 12.0 Hz, 1H), 4.53 (d, J = 11.9 Hz, 1H), 4.43 (t, J = 1.3 Hz, 1H), 4.31 (d, J = 12.2 Hz, 1H), 4.23 – 4.15 (m, 2H), 4.05 (dd, J = 12.4, 1.7 Hz, 1H), 3.99 – 3.93 (m, 1H), 3.89 (ddd, J = 11.3, 9.1, 5.2 Hz, 1H), 3.75 (t, J = 1.4 Hz, 2H), 3.70 (q, J = 1.6 Hz, 1H), 3.54 – 3.39 (m, 2H), 2.03 (ddt, J = 13.0, 4.1, 1.9 Hz, 1H), 1.86 (ddt, J = 12.8, 11.3, 6.3 Hz, 1H), 1.23 (d, J = 6.2 Hz, 3H), 1.02 (s, 9H), 0.89 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 165.7, 139.2, 138.6, 133.0, 130.4, 129.9, 128.4, 128.3, 128.1, 128.1, 127.7, 127.4, 127.3, 99.7, 78.2, 77.8, 76.6, 75.3, 73.3, 72.8, 71.4, 71.1, 68.0, 67.2, 65.5, 33.3, 27.8, 27.3, 23.5, 20.7, 18.2; HRMS: $[M+NH_4]^+$ calcd for C₄₁H₅₄O₉SiNH₄ 736.38754, found 736.38728. Disaccharide D2A5



According to the general procedure **II** from D2 and A5. Yield: 93 mg, 98 µmol, 98%, $\alpha:\beta > 20:1$. ¹H NMR (400 MHz, CDCl₃) δ 7.46 – 7.42 (m, 2H), 7.36 – 7.19 (m, 17H), 7.18 – 7.08 (m, 5H), 7.04 – 6.98 (m, 2H), 5.46 (d, *J* = 3.6 Hz, 1H), 4.93 (d, *J* = 11.6 Hz, 1H), 4.81 (d, *J* = 11.6 Hz, 1H), 4.76 – 4.71 (m, 2H), 4.65 (dd, *J* = 11.7, 4.4 Hz, 2H), 4.58 (d, *J* = 12.0 Hz, 1H), 4.52 (d, *J* = 10.8 Hz, 1H), 4.42 (d, *J* = 12.0 Hz, 1H), 4.38 (dd, *J* = 11.2, 4.2 Hz, 2H), 4.26 (dd, *J* = 9.8, 8.7 Hz, 1H), 4.22 (dd, *J* = 3.0, 1.1 Hz, 1H), 3.99 – 3.94 (m, 2H), 3.91 (dd, *J* = 12.6, 1.6 Hz, 1H), 3.86 (dd, *J* = 10.1, 2.9 Hz, 1H), 3.78 (dd, *J* = 10.0, 8.7 Hz, 1H), 3.72 – 3.68 (m, 1H), 3.65 (dd, *J* = 10.6, 3.3 Hz, 1H), 3.61 – 3.50 (m, 3H), 3.34 (s, 3H), 1.00 (s, 9H), 0.93 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 139.1, 138.4, 138.3, 138.0, 137.9, 128.6, 128.5, 128.5, 128.3, 128.2, 128.1, 128.0, 127.8, 127.6, 127.5, 127.4, 127.1, 97.9, 97.5, 79.1, 79.0, 78.1, 74.5, 74.1, 73.7, 73.6, 73.5, 73.1, 70.8, 70.6, 69.9, 68.5, 67.1, 6.9, 55.1, 27.8, 27.4, 23.5, 20.7; HRMS: [M+NH₄]⁺ calcd for C₅₆H₇₀O₁₁SiNH₄ 964.50256, found 964.50252.

Disaccharide D2A6



According to the general procedure **II** from D2 and A6. Yield: 87 mg, 92 µmol, 92%, $\alpha:\beta > 20:1.^{1}H$ NMR (400 MHz, CDCl₃) δ 7.52 – 6.86 (m, 25H), 5.09 (d, *J* = 11.4 Hz, 1H), 5.05 (d, *J* = 3.5 Hz, 1H), 4.84 (d, *J* = 1.9 Hz, 1H), 4.78 – 4.68 (m, 4H), 4.66 – 4.56 (m, 2H), 4.50 (d, *J* = 12.1 Hz, 1H), 4.40 (dd, *J* = 11.9, 10.2 Hz, 2H), 4.30 (d, *J* = 2.9 Hz, 1H), 4.06 (dd, *J* = 9.2, 3.2 Hz, 1H), 3.97 – 3.89 (m, 3H), 3.88 – 3.80 (m, 2H), 3.75 (ddd, *J* = 12.9, 5.2, 2.9 Hz, 1H), 3.72 – 3.65 (m, 3H), 3.42 (s, 1H), 3.36 (s, 3H), 1.02 (s, 9H), 0.93 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 139.1, 139.1, 138.6, 138.5, 138.4, 128.4, 128.4, 128.3, 128.2, 127.7, 127.6, 127.6, 127.5, 127.5, 127.4, 127.3, 100.4, 97.7, 79.5, 77.4, 77.4, 74.6, 74.6, 74.0, 73.5, 73.4, 71.9, 71.3, 71.0, 70.7, 69.5, 67.7, 67.2, 55.0, 27.8, 27.4, 23.5, 20.7; HRMS: [M+NH₄]⁺ calcd for C₅₆H₇₀O₁₁SiNH₄ 964.50256, found 964.50245.
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Samenvatting in het Nederlands

De synthese van koolhydraten, ook wel suikers genoemd, is moeilijker dan de synthese van andere biomoleculen zoals peptiden of oligonucleotiden. Wanneer twee suikers aan elkaar gekoppeld worden, wordt er een nieuw stereocentrum geïntroduceerd. Terwijl 1,2-*trans* glycosidische bindingen betrouwbaar gesynthetiseerd kunnen worden met behulp van sturing door een ester of amide groep op de naburige koolstof in de ring, is er voor de selectieve vorming van *1,2-cis* glycosidische bindingen nog geen universeel toepasbare techniek.

Bij een typische glycosyleringsreactie wordt een donor geactiveerd om zo een (verscheidenheid aan) elektrofiele intermedairen te vormen, die kunnen reageren met een nucleofiele acceptor volgens een reactiemechanisme met zowel S_N1 - als S_N2 -karakter. Aan de S_N1 -kant van het spectrum nemen oxocarbeniumionen deel aan het mechanisme, terwijl covalente intermedairen fungeren als glycosylerend agens aan de S_N2 -kant. De uitkomst van een glycosyleringsreactie wordt beïnvloed door de eigenschappen van zowel de donor als de acceptor, en kan ook worden beïnvloed door externe factoren.

Het doel van dit proefschrift is om systematisch te onderzoeken hoe veranderingen in stereochemie en beschermende groepen op de donor en acceptor het mechanisme en de uitkomst van glycosyleringsreacties beïnvloeden. Dit onderzoek zal een meer rationeel ontwerp van oligosaccharide syntheseroutes mogelijk maken.

Hoofdstuk 1 introduceert de uitdagingen in de chemische synthese van koolhydraten en presenteert enkele oplossingen die gevonden zijn voor stereoselective glycosyleringsreacties. Het SN1/SN2-continuüm van de glycosyleringsreactiemechanisme wordt beschreven, evenals methoden om beide uiteinden van het spectrum te onderzoeken. Tenslotte wordt de rol van de reactiviteit van de acceptor in de uitkomst van de glycosyleringsreactie besproken.

In **Hoofdstuk 2** wordt de invloed van de configuratie van de donor op de stereochemische uitkomst van S_N 1 reacties onderzocht door middel van een combinatie van computationele en experimentele chemie. Hiervoor zijn eerst alle acht diastereomere pyranosyl donoren, beschermd met enkel benzyl groepen gesynthetiseerd, tezamen met hun 6-deoxy analogen. Vervolgens werd de conformationele voorkeur van de oxocarbenium ionen – en daarmee de verwachte uitkomst van de S_N 1 reacties – berekend door de generatie van *conformational energy landscape* (CEL) platen. Tenslotte werden de reacties van de donoren met twee

nucleofielen die reageren via een S_N1 mechanisme, namelijk TES-D en allyl-TMS, bestudeerd.

De stabiliteit van de conformeren die in de CEL-platen gevonden werd, kan verklaard worden door de "voorkeuren" van de substituenten om het oxocarbenium ion het meest te stabiliseren, danwel het minst te destabiliseren. Wanneer de C-3 of C-4 alkoxy groepen op een pseudo-axiale manier geplaatst zijn, dan is het oxocarbenium ion stabieler dan wanneer deze groepen pseudo-equatoriaal geplaatst zijn. Voor C-2 en C-5 heeft een pseudo-equatoriale oriëntatie de voorkeur. Wanneer alle vier de substituenten in de voorkeursoriëntaties kunnen worden geplaatst, zoals het geval is voor gulose/6deoxygulose, heeft het ion een sterke voorkeur voor een enkele goed gedefiniëerde conformatie (⁴H₃ half-stoel). Met drie van de vier substituenten optimaal georiënteerd, vertonen de ionen ook een sterke voorkeur voor die conformatie. Wanneer slechts twee substituenten in de voorkeursoriëntatie kunnen worden geplaatst, zijn de energieverschillen tussen de verschillende conformeren een stuk kleiner en kan het oxocarbenium ion meerdere conformaties aannemen. Een andere observatie is dat de voorkeuren voor 6-deoxy oxocarbeniumionen in de meeste gevallen sterk lijken op die van hun 6-O-benzyl-evenkniën, alhoewel de absolute energieverschillen verschillen. Dit blijkt ook uit de uitkomst van de glycosyleringsreacties.

In de reacties met TES-D, is de oriëntatie van de substituent van C-2 in de donor moleculen de belangrijkste factor voor de stereochemische uitkomst van de glycosyleringsreactie gebleken. Alle reacties waren zeer *1,2-cis* selectief. Dit is in overeenstemming met de voorspelde waarden van de CEL-platen, behalve voor talose en 6-deoxyglucose, waar een 1:1 mengsel wordt voorspeld en voor idose, waar α selectiviteit werd voorspeld, maar volledige β -selectiviteit werd waargenomen.

Reacties met allyl-TMS gaven andere resultaten. Wanneer de C-2-groep van de donorglycosiden equatoriaal is, verloopt de reactie met volledige α -selectiviteit zoals bij TES-D. Wanneer de C-2-groep echter axiaal is geplaatst, verschuift selectiviteit van de reactie om meer van het 1,2-*trans* product te geven. Een mogelijke verklaring voor deze observatie zijn de sterische interacties tussen de substituenten en het inkomende nucleofiel, die aanval op de *cis*-zijde ongunstig maken. Volgens een Curtin-Hammett kinetisch scenario kan dan een aanval plaatsvinden op een oxocarbenium ion conformeer met hogere energie omdat dit een overgangstoestand met lagere energie oplevert.

In **Hoofdstuk 3** staan de mechanismes die verlopen via een covalent tussenproduct centraal. Variabele temperatuur (VT) NMR is gebruikt om de reactieve deeltjes te karakteriseren, die gevormd worden door activatie van de donoren. De waargenomen deeltjes waren ofwel een mengsel van α -triflaat en α -oxosulfoniumtriflaat, een mengsel van α -triflaat en α , β -oxosulfoniumtriflaten of een mengsel van α , β oxosulfoniumtriflaten. β -Triflaten werden bij geen van de donoren waargenomen. Vervolgens werden de geactiveerde donoren gekoppeld met vijf alcohol acceptoren, die door een toenemend aantal fluor-atomen (EtOH: 0, MFE: 1, DFE: 2, TFE: 3 en HFIP: 6), steeds minder nucleofiel zijn, om de relatie tussen de nucleofiliciteit van de acceptor en het mechanisme van de reactie te onderzoeken. In de reacties met EtOH, MFE, DFE en TFE blijkt vooral de configuratie van C-3 belangrijk te zijn voor de relatie tussen de reactiviteit van de acceptor en de stereochemische uitkomst van de glycosylering. Wanneer de substituent op C-3 equatoriaal is, wordt een duidelijke trend waargenomen waarbij meer nucleofiele acceptoren een hogere β-selectiviteit geven en minder nucleofiele acceptoren een hogere α -selectiviteit. Wanneer de C-3-groepen axiaal zijn, worden α : β -mengsels verkregen zonder duidelijke relatie tussen nucleofiliciteit en stereoselectiviteit. Een mogelijke mechanistische verklaring voor deze waarnemingen is dat voor de donoren met een equatoriaal georiënteerde C-3-groep, de meest reactieve acceptoren reageren met de stabielere covalente α -deeltjes, wat de β -producten oplevert, terwijl minder reactieve acceptoren alleen kunnen reageren met de meer reactieve β -deeltjes, wat leidt tot het α -product. Wanneer de substituent op C-3 axiaal is, is het reactiviteitsverschil tussen de covalente α - en β -deeltjes kleiner vanwege destabiliserende 1,3-diaxiale interacties tussen het axiale α-triflaat- en de C-3-groep. De S_N 2-substitutie van het β -deeltje wordt ook belemmerd door de groep op C-3. Deze sterische interacties werken elkaar tegen, wat leidt tot een algehele slechte selectiviteit. De glycosyleringen met HFIP waren allemaal volledig a-selectief, ongeacht de stereochemie van C-2 of C-3. Dit staat in contrast met de uitkomst van gerelateerde

reacties met TES-D, een nucleofiel dat veel gebruikt is om S_N 1-reactieroutes te karakteriseren, waarin hoge *1,2-cis* selectiviteit wordt gezien. Dit suggereert dat de glycosyleringen met zwakke O-nucleofielen via een ander mechanisme plaatsvinden dan nucleofiele additie aan een oxocarbenium ion.

In **Hoofdstuk 4** wordt een systeem beschreven om de structuur-reactiviteits relaties van een set van 60 acceptoren te bepalen, dat gebaseerd is op het gebruik van twee conformationeel vastgelegde glycosyl donoren. De stereochemische uitkomst van de glycosyleringsreacties met deze twee donoren is sterk afhankelijk van de nucleofiliciteit van de acceptor, zoals bepaald door middel van glycosyleringen met de EtOH, MFE, DFE, TFE en HFIP-modelacceptoren. De meest nucleofiele acceptoren reageren met volledige β -selectiviteit, terwijl het verminderen van de nucleofiliciteit van de acceptor geleidelijk leidt tot volledige α -selectiviteit. Deze reactiviteit-stereoselectiviteit relatie werd gebruikt om de reactiviteit van een groot aantal suikeracceptoren te bepalen. Door systematisch het beschermengroep patroon op D-glucose-, D-mannose-, D-galactose-, L-rhamnose- en L-fucose-acceptoren te variëren en hun reactiviteit te "meten", was het mogelijk om te bepalen welke structurele kenmerken de reactiviteit van de acceptor bepalen. Er werden ook twee soorten modelacceptoren geïntroduceerd. De eerste soort bestaat uit suikerachtige acceptoren, gebaseerd op 1,2,6-trideoxyglucose en 1,2,6trideoxygalactose, die alleen de "essentiële" substituenten bevatten, met verschillende patronen van beschermgroepen. De tweede soort modelacceptoren zijn C-2-OHglycerolacceptoren met een cyclische beschermende groep op C-1 en C-3. Deze acceptoren lijken op suikeracceptoren omdat het secundaire alcoholen zijn, die geflankeerd worden door twee beschermde hydroxyl groepen. In tegenstelling tot suikeracceptoren zijn deze alcoholen niet chiraal, dus de stereochemische uitkomst van de glycosyleringsreacties wordt niet beïnvloed door diastereomere interacties. De resultaten van de glycosyleringsreacties laten zien dat zowel de configuratie van de acceptor als het patroon van de beschermgroepen op de acceptor een sleutelrol spelen bij het bepalen van de reactiviteit van de acceptor. Met betrekking tot de configuratie van de acceptor zijn equatoriale alcoholen reactiever dan axiale alcoholen. De oriëntatie van de functionele groep naast de nucleofiele alcohol is ook belangrijk, en alcoholen met alleen equatoriale buren zijn reactiever dan alcoholen die zich naast een axiale buur bevinden. Met betrekking tot het patroon van beschermgroepen zijn benzoylbeschermde acceptoren minder reactief dan hun benzyl-beschermde tegenhangers. De grootte van dit effect hangt af van welke benzylgroep wordt vervangen door een benzoylgroep, aangezien het effect veel groter is wanneer een equatoriale benzylgroep naast de alcohol wordt vervangen door een benzoylgroep dan wanneer hetzelfde wordt gedaan met een naburige axiale benzylgroep.

Hoofdstuk 5 bouwt voort op hoofdstuk 4, door gebruik te maken van dezelfde methodologie die werd toegepast op benzyl/benzoyl-beschermde acceptoren om de invloed van de meest gebruikte N-beschermengroepen (azide, trichlooracetamide (TCA) en trifluoracetamide (TFA)) op de reactiviteit van acceptor te bepalen. De acceptoren die in deze studie werden gebruikt, waren C-4-OH glucosamine-acceptoren, aangezien de C-4-OH N-acetylglucosamine-acceptoren berucht zijn vanwege hun slechte nucleofiliciteit en C-3-OH glucosamine-acceptoren, om het effect van verschillende beschermgroepen naast de nucleofiele alcohol te onderzoeken. De C-4-OH en C-3-OH mannosamine-acceptoren werden toegevoegd om de invloed van de configuratie van het beschermde amine op de reactiviteit van de acceptor te bepalen. Net als bij de benzyl/benzoyl-beschermde acceptoren, zijn zowel de configuratie als de aard van de beschermende groepen belangrijk voor de reactiviteit van de acceptor. Voor zowel de glucosamine C-4-OH als de mannosamine acceptoren heeft de aard van de N-beschermende groep weinig invloed op de reactiviteit van de acceptoren, aangezien alle glycosyleringen binnen dezelfde acceptorreeks verliepen met vergelijkbare stereoselectiviteit en hoge opbrengst. Bij de glucosamine en mannosamine C-3-OH acceptoren werden vergelijkbare trends waargenomen als bij de acceptorreeks in hoofdstuk 4. De eerste observatie is dat een azide een deactiverend effect heeft dat vergelijkbaar is met dat van een O-benzoylgroep en dat gehalogeneerde acetamides een groter deactiverend effect hebben dan de azides, waarbij de trifluoracetamides meer

deactiverend zijn dan de trichlooracetamides. De configuratie van het beschermde amine naast de alcohol bleek ook belangrijk te zijn voor de reactiviteit van de acceptor. Zoals waargenomen voor de alcohol beschermde acceptoren, is de C-3-OHglucosazide-acceptor reactiever dan de C-3-OH-mannosazide-acceptor. In lijn met de resultaten van hoofdstuk 4, is het deactiverende effect van de *N*-beschermgroepen op equatoriale amines naast de nucleofiele alcohol veel groter dan het deactiverende effect van de *N*-beschermgroepen van de naburige axiale amines.

In **Hoofdstuk 6** wordt de kennis die in de hoofdstukken 2-5 is opgedaan toegepast op de synthese van de repeterende eenheid van een *Acinetobacter Baumannii* capsulair polysaccharide . *A. Baumannii* is een Gram-negatieve bacterie die door de Wereldgezondheidsorganisatie is aangemerkt als een pathogeen met een hoog risico vanwege de hoge mate van antibioticaresistentie. Het polysacharide bestaat uit repeterende eenheden van vier suikers met de structuur $[\rightarrow 4)$ - β -D-GlcpNAc3NAcA- $(1\rightarrow 3)$ - α -D-QuipNAc4NAc- $(1\rightarrow 3)$ - α -D-QuipNAc4NAc- $(1\rightarrow 4)$ - β -D-GlcpNAc3NAcA-

 $(1\rightarrow)$ met de twee zeldzame suikers 2,4-di-*N*-acetyl- α -D-quinovose (2,4-di-*N*-acetyl bacillosamine, QuiNAc4NAc) en 2,3-di-*N*-acetyl- β -D-glucuronzuur (GlcNAc3NAcA). Wat de structuur van deze polysacharide bijzonder maakt, is dat deze geen enkele vrije alcohol groep bezit!

Uitgaande van D-fucose en D-glucosamine-HCl werden synthetische routes ontwikkeld om meerdere grammen van de vereiste bacillosamine en 2,3-diaminoglucuronzuur bouwstenen te produceren. De reactiviteit van de bacillosaminedonoren werd vervolgens bestudeerd om methoden te ontwikkelen voor de constructie van de 1,2-cis bindingen. Modelglycosyleringen met gefluoreerde ethanolacceptoren toonden aan dat de stereoselectiviteit van de bestudeerde selenofenol bacillosamine donor onder preactiveringscondities sterk afhangt van de nucleofiliteit van de acceptor, waarbij ethanol zorgt volledige β -selectiviteit laat zien en 2,2,2-trifluorethanol bijna alleen maar α product levert. De aziden en methylesters op de koolhydraatacceptoren zouden een deactiverend effect moeten hebben op de nucleofiliciteit van het vrije alcohol moeten hebben, op basis van de eerdere studies. Inderdaad, verloopt de glycosylering met zowel de 2,3-di-*N*-acetylglucuronzuuracceptoren als de bacillosamine-acceptoren met hoge α -selectiviteit.

Om het onderliggende mechanisme van deze selectiviteit te onderzoeken werd VT-NMR gebruikt om de reactieve intermediairen gevormd uit de bacillosaminedonoren te bestuderen. Wanneer de selenofenoldonor werd geactiveerd met Ph₂SO en Tf₂O, werd een mengsel van het α -triflaat, α -oxosulfoniumtriflaat en β -oxosulfoniumtriflaat gevormd. Het β -oxosulfoniumtriflaat bleek het meest reactief te zijn, op basis van de laagste ontledingstemperatuur. De activering van de overeenkomstige PTFAI-donor met TfOH leidde tot de selectieve vorming van het α -triflaat. Op basis van de glycosyleringen van de selenofenoldonor en imidaatdonor met de 2,3-di-N- acetylglucuronzuuracceptoren wordt verwacht dat de oxosulfoniumtriflaten een rol spelen bij het bepalen van de selectiviteit van de selenofenoldonor. Met deze kennis in de hand kon het tetrasaccharide worden samengesteld. Uiteindelijk werd 855 mg (670 μ mol) van een beschermd tetrasaccharide-bouwsteen verkregen, welke ontschermd kan worden of kan worden gebruikt voor de synthese van grotere oligomeren.

List of Publications

Mapping the reactivity of 2,3-di-N-acetyl glucuronic acid and 2,4-di-*N*-acetyl bacillosamine building blocks in the synthesis of a highly *N*-acetylated Acinetobacter Baumannii LUH5554 tetrasaccharide

<u>van Hengst JMA</u>, Verhoeks V, de Bra D, Vlaming JCG, Schoenmakers J, Overkleeft HS, van der Marel GA, Codée JDC *Manuscript in preparation*

Selective peroxygenase-catalysed oxidation of toluene derivates to benzaldehydes

Wang Y, Teetz N, Holtmann D, Alcalde M, <u>van Hengst JMA</u>, Liu X, Wang M, Qi W, Zhang W, Hollmann F. *ChemCatChem 2023*, *15*, *e202300645*

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means equal contribution

Academic CV



Jacob van Hengst was born on 28 July 1993 in Rotterdam, the Netherlands. From 2005 to 2011 he attended the Johan de Witt Gymnasium in Dordrecht, where he obtained his secondary education degree (VWO) cum laude with a specialisation in science and technology (NG/NT). He competed in the National Chemistry Olympiad in 2010 and 2011, were he reached the top 20 and the 1st place respectively. In 2011 Jacob started with his bachelor Molecular Science and Technology at Leiden University and Delft University of Technology. As part of his bachelor, he worked on the PEGylation of Gdloaded zeolite nanoparticles for MRI purposes under supervision of Wuyuan Zhang and Kristina Djanashvili at the TU Delft. In 2014 he obtained his BSc Degree cum laude. In that same year, he started with his master's degree in chemistry at Leiden University with a specialisation in chemical biology. During his master's Jacob worked a year in the molecular physiology group under supervision of Anthe Janssen and Mario van der Stelt. He worked on the synthesis and in vitro evaluation of covalent inhibitors for serine hydrolase DAGLa. A large part of this internship was the optimisation of the synthesis of a key intermediate over 10 steps. His master's degree was obtained in 2017. In the same year Jacob started with his PhD in the group of Jeroen Codée and Gijs van der Marel at Leiden University. His work focussed on mechanistic research and method development within carbohydrate chemistry. Key findings are the way that substituents on the donor influence the S_N1 and S_N2 side of the reaction, how the nucleophilicity of the acceptor influences the glycosylation mechanism, how the reactivity of the acceptor is dependent on configuration and protecting group pattern and how this acquired knowledge can be applied in the total synthesis of complex oligosaccharide. Parts of his work are published in Angewandte Chemie, Chemical Science and Nature communications and presented at the CHAINS 2021 conference. Since September 2022 Jacob works as a postdoc in the group of Frank Hollmann at the TU Delft on enzymatic oxidations using environmentally benign oxidants like oxygen or hydrogen peroxide.

Acknowledgments

Completing this PhD thesis has been a remarkable and challenging endeavour, and I am deeply grateful for the collaborative spirit and invaluable contributions of those who have stood by me throughout this process. Their belief in my abilities and their willingness to lend a helping hand have made all the difference.

First of all, I would like to take the opportunity to thank my supervisors Jeroen and Gijs for giving me the opportunity to work on this project, for their excellent training and their invaluable support throughout the entirety of my doctoral journey.

Next, I would like to thank all of my colleagues. Biosyn is a rather large research group, so it is impossible for me to acknowledge everyone personally, but please know that your support, whether big or small, is deeply appreciated. Your contributions have played a significant role in shaping my academic journey, and I am grateful for your presence and assistance.

With that out of the way Stefan, thank you for training me in carbohydrate chemistry when I started my PhD as someone with a medicinal chemistry background. Also, a special thanks to Koen V, Thomas and Wouter, with whom I collaborated most closely. Together we could shine some light on the still challenging problems regarding stereoselective glycosylation. Thanks to all other people from the EE4 lab: Alex, Andy, Coralie, Dennis, Florian, Jerre, Jurriaan, Koen R, Mark, Tim and all the students. I really enjoyed working together with you on the lab, and without you my PhD wouldn't be the same!

Some other colleagues I would like to acknowledge are Joey and Vincent V, for continuing the work on the beautiful *Acinetobacter Baumannii* oligosaccharide. Hessel, for all our great discussions about our (potential) projects. Hugo, whose shared appreciation for memes and fine German musical art greatly enriched my experience throughout this research endeavour and Ward for introducing me to the wonderful chemistry of the 2-deoxy-2-amino sugars.

I would also like to thank my students: Annabel, for her help with the development of the synthetic routes of the rare carbohydrate donors used in chapter 2 and 3. Daan and Joeri for their work on the total synthesis of the *Acinetobacter Baumannii* tetrasaccharide described in chapter 6 and Rik for his contributions towards the acceptor reactivity study in chapter 4.

I would also like to express my gratitude towards the technicians of Biosyn: Hans, Nico and Rian for supporting the research of the group. A special thanks to Hans for measuring so many HRMS samples in a short timespan at the end of my PhD.

Measuring NMR was a crucial part of my PhD, so I would like to thank the people from the NMR-department, Fons and Karthick. Thank you for keeping the NMR running smoothly, for your help with my VT-NMR experiments and finally for keeping so many of my samples safe and organised for so long when I forgot to pick them up again.

I also want to thank the all the TOAs, whose hard work made teaching practical courses a pleasant experience. A special thanks goes to Trudie for her extraordinary support and her willingness to always help out with everything, to Marco for teaching me how to maintain and repair a rotavap and to Arjan for helping me with the IR measurements.

Last but not least, I would like to thank all my friends and family. And especially my girlfriend Maaike for all the love she gives me. Thanks to my parents and my siblings Lara and Marijn, without whose unconditional support I would never have made it this far. Finally I would like to thank my aunt Desiree, to whom I have dedicated this thesis. Unfortunately you cannot be physically present anymore, but know that you are always in my heart.