Reactivity and selectivity in glycosylation reactions

Vorm, S. van der

Chapter 9

Summary and future prospects

Summary

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

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

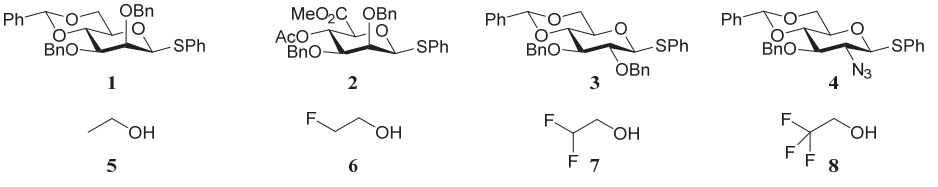


Figure 1. Donors **1**-**4** and model acceptors **5**-**8** used in Chapters **3** and **4**.

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

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

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

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

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

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

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

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

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

Future prospects

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

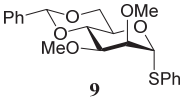
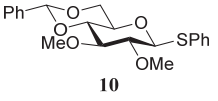
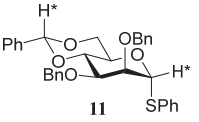
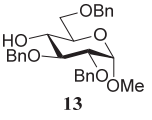
Kinetic Isotope Effects

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

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

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

Table 1. Kinetic isotope effects measured for glycosylation reactions.

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

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

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

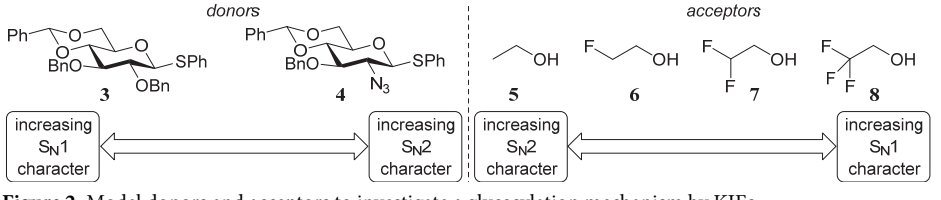


Figure 2. Model donors and acceptors to investigate a glycosylation mechanism by KIEs.

Cation-clock kinetics

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

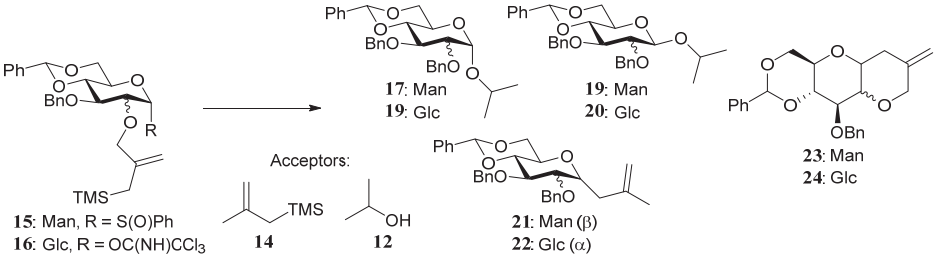


Figure 3. Cation-clock substitution products from external and internal nucleophiles.

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

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

Preactivation-based competition experiments

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

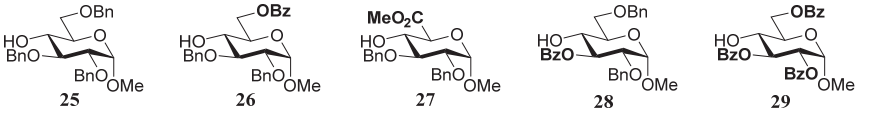
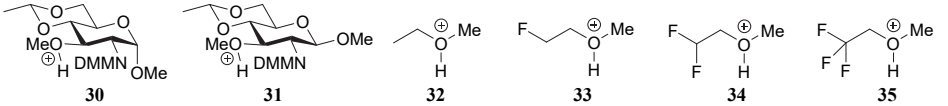


Figure 4. Selection of carbohydrate acceptors bearing functional groups influencing the reactivity of the acceptor.

Computational evaluation of the reactivity of the acceptor

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



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

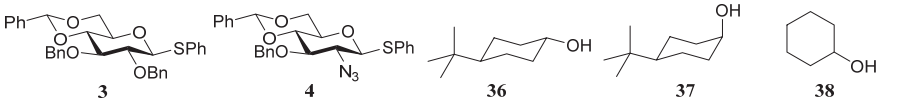
ΔE = -107.6 kcal·mol^{-1} ΔE = -99.7 kcal·mol^{-1}

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

Assessing steric and conformational effects in acceptor reactivity

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

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



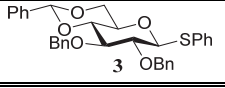
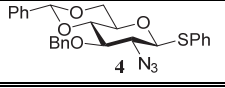
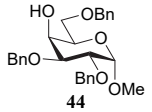
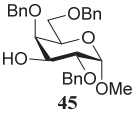
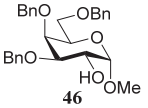
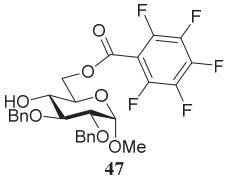
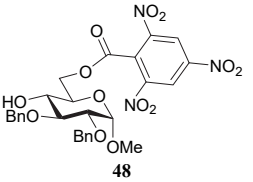
3 **4** **36** **37** **38**

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

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

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

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

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

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

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

Experimental and computational evaluation of 5-deoxy furanosyl oxocarbenium ions

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

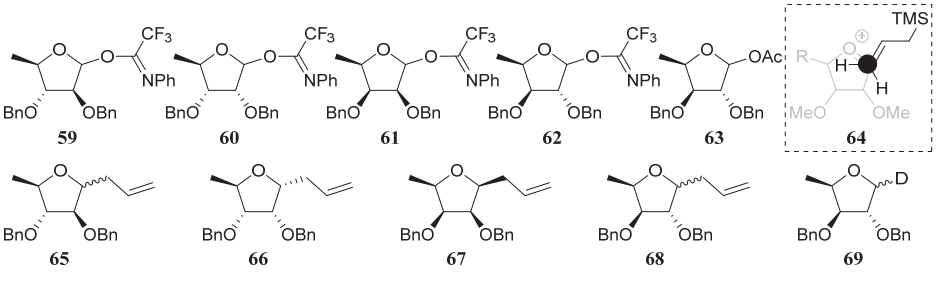
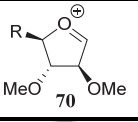
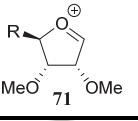
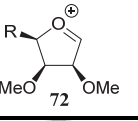
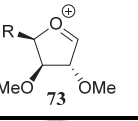
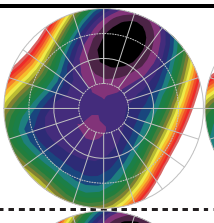
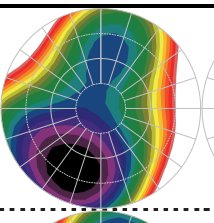
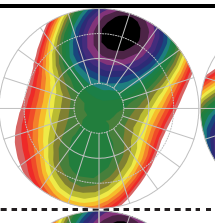
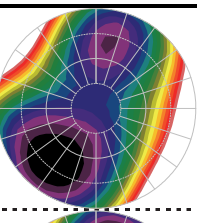
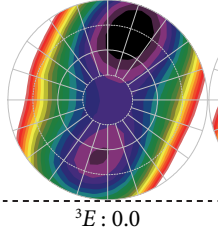
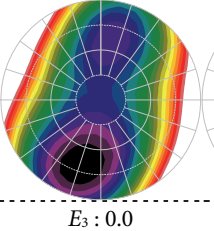
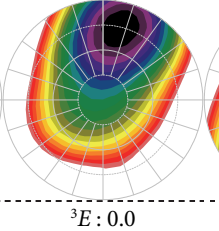
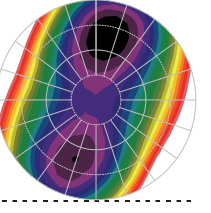
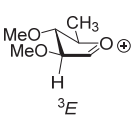
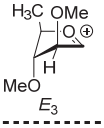
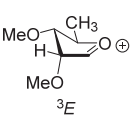
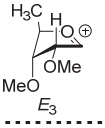
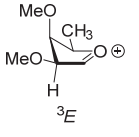
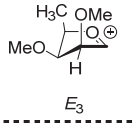
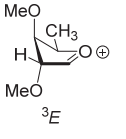
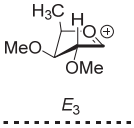


Figure 6. Imidate donors **59**-**62**, acetyl donor **63** and glycosylation products **65**-**69** of 5-deoxy furanosides. Inset: top view of the protruding C–H bonds on the acceptor.

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

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

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

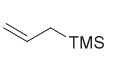
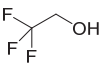
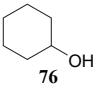
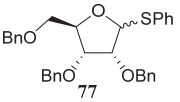
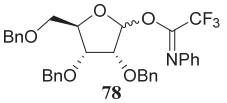
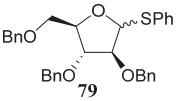
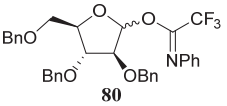
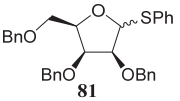
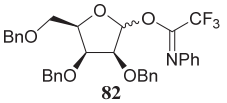
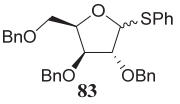
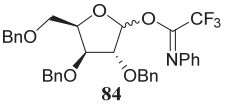
[a]Allyl-TMS was the acceptor. [b]TES-D was the acceptor, acetyl donor **63**, see experimental section. *Reagents and conditions:* donor (0.1 mmol), acceptor (0.4 mmol), TfOH (0.01 mmol), DCM (1 mL), 3Å M.S., -75°C

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

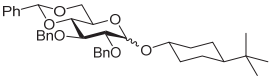
Furanoside *O*-glycosylations

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

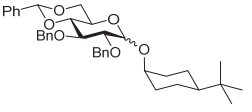
Table 7. Glycosylations of furanosides with model acceptors.

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

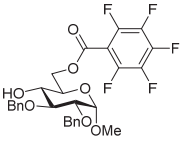
Experimental section



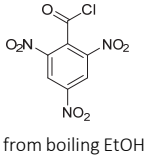
Trans-4-*tert*-butylcyclohexyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranoside (39). Donor **3** and acceptor **36** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 yielding product **39** (38 mg, 65 µmol, 65%, α:β = 1 : 2.5) as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



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

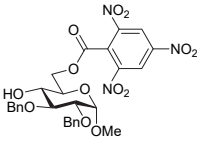


Methyl 2,3-di-*O*-benzyl-6-O-(2,3,4,5,6-pentafluorobenzoyl)-α-D-glucopyranoside (47). Methyl 2,3-di-*O*-benzyl-α-D-glucopyranoside[22] (374 mg, 1.0 mmol, 1 eq.) was converted to the title compound **47** following general procedure **C** of Chapter 6 (pentafluorobenzoyl chloride; 145 µL, 1.05 mmol, 1.05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

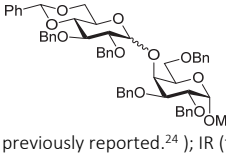


2,4,6-Trinitrobenzoyl chloride (S1). Toluene (2.1 mL, 20 mmol) was dissolved in 17 mL H_2SO_4 and cooled to 0°C. To this mixture a solution of HNO_3 (99%, 4.2 mL) in 15 mL H_2SO_4 was slowly added (15 min, temperature remains below 40°C). When addition was complete, the reaction mixture was slowly heated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

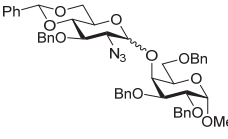
10.8 mmol) was added in small portions, mainting a temperature below 35°C (ice-bath). After stirring overnight at room temperature, the reaction mixture was poured on ice and the precipitate collected, washed with cold H_2O, dried and crystallized from boiling H_2O to yield 2,4,5-trinitrobenzoic acid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



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

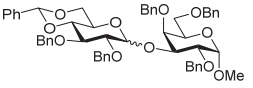


Methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranosyl)-2,3,6-tri-*O*-benzyl-α-D-galactopyranoside (49). Donor **3** and acceptor **44** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 yielding product **49** (60 mg, 72 µmol,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

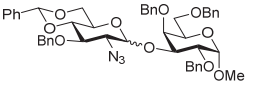


Methyl 4-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranosyl)-2,3,6-tri-*O*-benzyl-α-D-galactopyranoside (50). Donor **4** and acceptor **44** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 yielding product **50** (70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

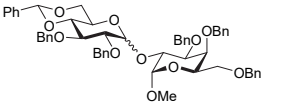
J = 9.8, 5.0 Hz, H-5'); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 139.0, 138.6, 138.3, 138.0, 137.2 (C_q), 102.1 (C-1'), 101.4 (CHPh), 98.9 (C-1), 81.6, 79.0, 78.4, 76.4, 75.0, 73.9, 73.8, 73.4, 69.6, 69.0, 68.6, 66.5 (C-2'), 66.0 (C-5'), 55.5 (OMe); HRMS: $[M+Na]^+$ calcd for $C_{48}H_{51}N_3O_{10}Na$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



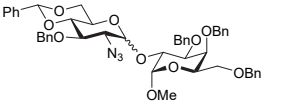
Methyl 3-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranosyl)-2,4,6-tri-*O*-benzyl-α-D-galactopyranoside (51). Donor **3** and acceptor **45** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 yielding product **51** (76 mg, 85 µmol, 85%, α:β = 6 : 1) as a colorless oil. R_f: 0.25 and 0.51 (4/1 pentane/EtOAc); IR (thin film): 696, 735, 1028, 1049, 1074, 1088, 1350, 1368, 154, 2864, 2914; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.48 – 7.45 (m, 2H, CH_{arom}), 7.40 – 7.14 (m, 28H, CH_{arom}), 5.54 (s, 1H, C*H*Ph), 5.06 (d, 1H, *J* = 3.6 Hz, H-1'), 5.00 (d, 1H, *J* = 11.3 Hz, C*H*H Bn), 4.91 (d, 1H, *J* = 11.5 Hz, C*H*H Bn), 4.84 (d, 1H, *J* = 11.4 Hz, C*H*H Bn), 4.80 – 4.75 (m, 2H, CH*H* Bn, C*H*H Bn), 4.68 (d, 1H, *J* = 11.5 Hz, CH*H* Bn), 4.62 (d, 1H, *J* = 3.5 Hz, H-1), 4.56 (d, 1H, *J* = 11.9 Hz, CH*H* Bn), 4.47 (d, 1H, *J* = 11.8 Hz, C*H*H Bn), 4.37 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.36 (d, 1H, *J* = 11.4 Hz, CH*H* Bn), 4.23 (td, 1H, *J* = 10.0, 4.9 Hz, H-5'), 4.16 (dd, 1H, *J* = 10.1, 4.9 Hz, H-6'), 4.10 (t, 1H, *J* = 9.3 Hz, H-3'), 4.04 (dd, 1H, *J* = 10.2, 2.8 Hz, H-3), 3.96 (dd, 1H, *J* = 10.2, 3.6 Hz, H-2), 3.91 (dd, 1H, *J* = 2.8, 1.1 Hz, H-4), 3.83 (t, 1H, *J* = 6.9 Hz, H-6), 3.64 (t, 1H, *J* = 9.5 Hz, H-4'), 3.63 (t, 1H, *J* = 10.2 Hz, H-6'), 3.62 (dd, 1H, *J* = 9.4, 3.5 Hz, H-2'), 3.48 – 3.46 (m, 2H, H-5, H-6), 3.31 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 139.1, 138.7, 138.3, 138.1, 138.1, 137.8 (C_q), 128.5, 128.5, 128.5, 128.4, 128.2, 128.2, 128.2, 128.2, 128.1, 127.9, 127.9, 127.8, 127.7, 127.4, 126.3 (CH_{arom}), 101.3 (CHPh), 98.5 (C-1'), 98.5 (C-1), 82.7 (C-4'), 79.8 (C-2'), 78.7 (C-3'), 78.2 (C-3), 75.8 (C-2), 75.5 (C-4), 75.1, 75.0, 74.6, 73.6, 73.4 (CH_2 Bn), 69.3 (C-5), 69.2 (C-6), 69.0 (C-6'), 63.1 (C-5'), 55.3 (OMe); Diagnostic peaks β-anomer: ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.52 – 7.48 (m, 2H, CH_{arom}), 7.42 – 7.16 (m, 28H, CH_{arom}), 5.57 (s, 1H, C*H*Ph), 5.04 (d, 1H, *J* = 7.7 Hz, H-1'), 5.00 (d, 1H, *J* = 11.5 Hz, C*H*H Bn), 4.98 (d, 1H, *J* = 11.4 Hz, C*H*H Bn), 4.94 (d, 1H, *J* = 11.3 Hz, C*H*H Bn), 4.84 (d, 1H, *J* = 11.5 Hz, CH*H* Bn), 4.82 (d, 1H, *J* = 11.3 Hz, CH*H* Bn), 4.65 (d, 1H, *J* = 11.5 Hz, CH*H* Bn), 4.63 (d, 1H, *J* = 11.8 Hz, C*H*H Bn), 4.55 (d, 1H, *J* = 3.7 Hz, H-1), 4.48 (d, 1H, *J* = 11.6 Hz, C*H*H Bn), 4.40 (d, 1H, *J* = 11.6 Hz, CH*H* Bn), 4.32 (dd, 1H, *J* = 10.5, 5.1 Hz, H-6'), 4.32 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.24 (dd, 1H, *J* = 10.1, 3.1 Hz, H-3), 3.99 (dd, 1H, *J* = 10.1, 3.7 Hz, H-2), 3.97 – 3.93 (m, 2H, H-4, H-6), 3.79 – 3.74 (m, 2H, H-3', H-6'), 3.69 (t, 1H, *J* = 9.3 Hz, H-4), 3.54 – 3.52 (m, 2H, H-5, H-6), 3.46 (dd, 1H, *J* = 8.7, 7.8 Hz, H-2'), 3.40 (td, 1H, *J* = 9.9, 5.1 Hz, H-5'), 3.31 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 103.9 (C-1'), 101.2 (CHPh), 98.5 (C-1), 82.9 (C-2'), 81.9 (C-4'), 81.1(C-3'), 77.9, 75.3, 75.3, 75.2, 73.7, 73.6, 69.1, 69.1, 68.9, 65.8 (C-5'), 55.4 (OMe); HRMS: $[M+Na]^+$ calcd for $C_{55}H_{58}O_{11}Na$ 917.3877, found 917.3885.



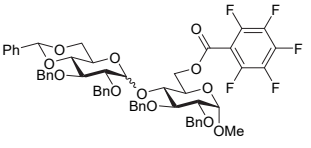
Methyl 3-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranosyl)-2,4,6-tri-*O*-benzyl-α-D-galactopyranoside (52). Donor **4** and acceptor **45** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 yielding product **52** (73 mg, 88 µmol, 88%, α:β = 1 : 1.3) as a colorless oil. R_f: 0.43 and 0.66 (4/1 pentane/EtOAc); IR (thin film): 696, 735, 995, 1028, 1047, 1092, 1350, 1369, 1454, 2108, 2866, 2910; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.48 – 7.21 (m, 57.5H, CH_{arom}), 5.57 (s, 1.3H, C*H*Phβ), 5.55 (s, 1H, C*H*Phα), 5.13 (d, 1H, *J* = 3.6 Hz, H-1'α), 5.01 (d, 1H, *J* = 11.2 Hz, C*H*H Bnα), 4.94 – 4.84 (m, 6.2H, 4xC*H*H Bn, H-1'β), 4.80 (d, 1.3H, *J* = 11.2 Hz, CH*H* Bnβ), 4.76 (d, 1H, *J* = 11.9 Hz, C*H*H Bnα), 4.75 (d, 1H, *J* = 11.0 Hz, CH*H* Bnα), 4.65 (d, 1H, *J* = 3.6 Hz, H-1α), 4.60 – 4.53 (m, 5.9H, 4xCH*H* Bn, H-1β), 4.48 (d, 1H, *J* = 11.7 Hz, C*H*H Bnα), 4.48 (d, 1.3H, *J* = 11.8 Hz, C*H*H Bnβ), 4.40 (d, 1H, *J* = 11.7 Hz, CH*H* Bnα), 4.40 (d, 1.3H, *J* = 11.7 Hz, CH*H* Bnβ), 4.31 (dd, 1.3H, *J* = 10.4, 5.1 Hz, H-6'β), 4.27 – 4.22 (m, 2H, H-5'α, H-6'α), 4.19 (dd, 1.3H, *J* = 10.1, 3.2 Hz, H-3β), 4.12 (dd, 1H, *J* = 10.3, 2.9 Hz, H-3α), 4.10 – 4.04 (m, 2.3H, H-2β, H-3'α), 4.02 – 3.97 (m, 2H, H-2α, H-4α), 3.95 – 3.87 (m, 3.6H, H-4β, H-5α, H-5β), 3.78 – 3.64 (m, 4.6H, H-4'α, H-4'β, H-6'α, H-6'β), 3.56 – 3.49 (m, 6.9H, H-2'α, H-3'β, H-6α, H-6α, H-6β, H-6β), 3.42 (dd, 1.3H, *J* = 9.5, 8.0 Hz, H-2'β), 3.36 (td, 1.3H, *J* = 9.9, 5.1 Hz, H-5'β), 3.33 (s, 3H, CH_3 OMeα), 3.31 (s, 3.9H, CH_3 OMeβ); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 138.7, 138.7, 138.3, 138.2, 138.1, 138.0, 137.9, 137.8, 137.6, 137.2 (C_q), 129.1, 129.0, 128.6, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.2, 128.1, 128.1, 128.0, 128.0, 127.9, 127.9, 127.9, 127.9, 127.8, 127.7, 126.3, 126.1 (CH_{arom}), 102.9 (C-1'β), 101.5 (CHPhα), 101.4 (CHPhβ), 98.5 (C-1α), 98.3 (C-1β), 96.1 (C-1'α), 83.0 (C-4'α), 81.8 (C-4'β), 79.1 (C-3'β), 77.4, 77.3 (C-2β, C-4β), 76.8 (C-3β), 76.2 (C-3'α), 75.8 (C-3α), 75.3 (C-2α), 75.2, 75.1, 75.0, 75.0 (CH_2 Bn), 74.1 (C-4α), 73.7, 73.6, 73.6, 73.6 (CH_2 Bn), 69.1, 69.0 (C-5α, C-5β), 69.0, 68.9, 68.8, 68.7 (C-6α, C-6β, C-6'α, C-6'β), 66.9 (C-2'β), 66.0 (C-5'β), 63.6 (C-2'α), 62.9 (C-5'α), 55.4, 55.4 (OMe); HRMS: $[M+Na]^+$ calcd for $C_{48}H_{51}N_3O_{10}Na$ 852.3472, found 852.3482.



Methyl 2-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-galactopyranoside (53). Donor **3** and acceptor **46** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 yielding product **53** (78 mg, 87 µmol, 87%, α:β = 10 : 1) as a colorless oil. R_f: 0.60 (4/1 pentane/EtOAc); IR (thin film): 696, 734, 1028, 1053, 1076, 1085, 1366, 1454, 2864, 2914; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.44 – 7.12 (m, 30H, CH_{arom}), 5.51 (s, 1H, C*H*Ph), 4.92 – 4.86 (m, 4H, 2xC*H*H Bn, H-1, H-1'), 4.86 – 4.80 (m, 3H, 2xC*H*H Bn, CH*H* Bn), 4.71 (d, 1H, *J* = 12.3 Hz, CH*H* Bn), 4.67 (d, 1H, *J* = 11.5 Hz, CH*H* Bn), 4.52 (d, 1H, *J* = 11.3 Hz, CH*H* Bn), 4.51 (d, 1H, *J* = 11.8 Hz, C*H*H Bn), 4.43 (d, 1H, *J* = 11.7 Hz, CH*H* Bn), 4.33 (dd, 1H, *J* = 10.3, 3.5 Hz, H-2), 4.25 (td, 1H, *J* = 10.0, 5.0 Hz, H-5'), 4.15 (dd, 1H, *J* = 10.1, 5.0 Hz, H-6'), 4.13 (t, 1H, *J* = 9.2 Hz, H-3'), 4.02 (dd, 1H, *J* = 10.3, 2.8 Hz, H-3), 3.95 (dd, 1H, *J* = 2.9, 1.2 Hz, H-4), 3.94 – 3.91 (m, 1H, H-6), 3.62 (t, 1H, *J* = 10.2 Hz, H-6'), 3.61 – 3.53 (m, 4H, H-2', H-4', H-5, H-6), 3.42 (s, 3H); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 138.9, 138.7, 138.6, 138.2, 138.0, 137.8 (C_q), 128.8, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.1, 128.1, 128.1, 127.9, 127.9, 127.9, 127.9, 127.7, 127.6, 127.6, 126.3 (CH_{arom}), 101.3 (CHPh), 97.0 (C-1), 95.5 (C-1'), 82.3 (C-4'), 78.9 (C-2'), 78.6 (C-3'), 77.6 (C-3), 75.2 (CH_2 Bn), 75.1 (C-4), 75.0, 73.7, 73.4, 73.4 (CH_2 Bn), 72.0 (C-2), 69.5 (C-5), 69.2 (C-6), 69.0 (C-6'), 62.4 (C-5'), 55.2 (OMe); Diagnostic peaks β-anomer: ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 5.54 (s, 1H, C*H*Ph), 5.00 (d, 1H, *J* = 11.2 Hz, C*H*H Bn), 3.76 (t, 1H, *J* = 10.3 Hz), 3.77 – 3.66 (m, 2H), 3.41 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 105.0 (C-1'), 101.2 (CHPh), 100.0 (C-1), 82.1, 81.4, 81.0, 78.4, 75.1, 75.0, 73.6, 73.0, 69.3, 69.1, 68.8, 66.0, 62.4, 55.2; HRMS: $[M+Na]^+$ calcd for $C_{55}H_{58}O_{11}Na$ 917.3877, found 917.3874.

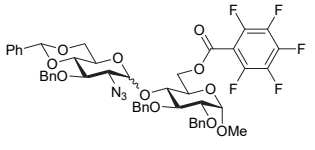


Methyl 2-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-galactopyranoside (54). Donor **4** and acceptor **46** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 yielding product **54** (60 mg, 73 µmol, 73%, α:β = 1 : 1.3) as a colorless oil. R_f: 0.74 (4/1 pentane/EtOAc); IR (thin film): 696, 735, 997, 1028, 1051, 1090, 1356, 1368, 1454, 2108, 2866, 2912; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.49 – 7.22 (m, 57.5H, CH_{arom}), 5.55 (s, 1.3H, C*H*Phβ), 5.54 (s, 1H, C*H*Phα), 4.98 (d, 1H, *J* = 3.7 Hz, H-1'α), 4.94 – 4.86 (m, 6.9H, 5xC*H*H Bn, H-1α), 4.85 (d, 1.3H, *J* = 3.7 Hz, H-1β), 4.79 (d, 1.3H, *J* = 11.3 Hz, CH*H* Bn), 4.75 (d, 1H, *J* = 11.0 Hz, CH*H* Bn), 4.74 (d, 1H, *J* = 11.6 Hz, C*H*H Bn), 4.69 (d, 1.3H, *J* = 11.5 Hz, CH*H* Bn), 4.65 (d, 1H, *J* = 11.5 Hz, CH*H* Bn), 4.58 (d, 1H, *J* = 8.0 Hz, H-1'β), 4.54 – 4.50 (m, 3.3H, C*H*H Bn, 2xCH*H* Bn), 4.47 (d, 1.3H, *J* = 11.8 Hz, C*H*H Bn), 4.43 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.39 (d, 1.3H, *J* = 11.8 Hz, CH*H* Bn), 4.31 – 4.23 (m, 3.3H, H-2α, H-5', H-6'β), 4.17 (dd, 1H, *J* = 10.2, 5.0 Hz, H-6'α), 4.16 (dd, 1.3H, *J* = 9.7, 3.7 Hz, H-2β), 4.08 (dd, 1H, *J* = 9.8, 9.2 Hz, H-3'α), 3.97 – 3.89 (m, 6.9H, H-3α, H-3β, H-4α, H-4β, H-5α, H-5β), 3.74 (t, 1.3H, *J* = 10.3 Hz, H-6'β), 3.73 – 3.65 (m, 3.3H, H-4'α, H-4'β, H-6'α), 3.62 – 3.55 (m, 3.9H, H-2'β, H-3'β, H-6β), 3.52 (dd, 2H, *J* = 6.4, 3.2 Hz, H-6α), 3.43 (s, 3H, CH_3 OMeα), 3.43 (dd, 1H, *J* = 9.9, 3.7 Hz, H-2'α), 3.39 (s, 3.9H, CH_3 OMeβ), 3.36 (td, 1.3H, *J* = 10.0, 5.0 Hz, H-5'β); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 138.7, 138.6, 138.6, 138.1, 138.1, 138.0, 137.9, 137.9, 137.6, 137.2 (C_q), 129.1, 129.0, 128.6, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.0, 127.9, 127.9, 127.8, 127.8, 127.8, 127.8, 127.7, 126.3, 126.1 (CH_{arom}), 103.6 (C-1'β), 101.5, 101.4 (CHPh), 100.0 (C-1β), 97.1 (C-1α), 95.6 (C-1'α), 82.9 (C-4'α), 81.6 (C-4'β), 79.6 (C-3'β), 78.1, 77.9, 77.5 (C-2β, C-3α, C-3β), 76.2 (C-3'α), 75.2, 74.9 (C-4α, C-4β), 75.1, 75.1, 75.0, 75.0 (CH_2 Bn), 73.7, 73.6, 73.3, 73.3 (CH_2 Bn), 72.5 (C-2α), 69.4, 69.2 (C-5α, C-5β), 69.1, 69.0 (C-6α, C-6β), 68.9 (C-6'α), 68.6 (C-6'β), 66.1 (C-5'β), 65.9 (C-2'β), 63.0 (C-2'α), 62.7 (C-5'α); HRMS: $[M+Na]^+$ calcd for $C_{48}H_{51}N_3O_{10}Na$ 852.3472, found 852.3488.

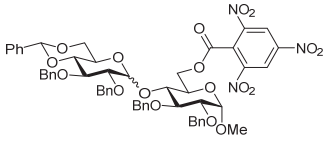


Methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranosyl)-2,3-di-*O*-benzyl-6-*O*-(2,3,4,5,6-pentafluorobenzoyl)-α-D-glucopyranoside (55). Donor **3** and acceptor **47** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 yielding product **55** (71 mg, 71 µmol, 71%, α:β = 1.4 : 1) as a colorless oil. R_f: 0.82 (4/1 pentane/EtOAc); IR (thin film): 696, 735, 1007, 1028, 1047, 1076, 1088, 1227, 1325, 1454, 1496, 1524, 1740, 2870, 2926; Data reported as a 1 : 0.7 mixture of anomers: ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC, HMBC): δ 7.51 – 7.18 (m, 42.5H), 5.56 (d, 1H, *J* = 3.9 Hz, H-1'α), 5.52 (s, 0.7H, C*H*Phβ), 5.49 (s, 1H, C*H*Phα), 4.97 (d, 1H, *J* = 11.5 Hz, C*H*H Bnα), 4.95 – 4.90 (m, 3.1H, C*H*H Bnα, 3xC*H*H Bnβ), 4.83 (d, 0.7H, *J* = 10.7 Hz, CH*H* Bnβ), 4.81 – 4.74 (m, 5.1H, 2xCH*H* Bnα, 2xCH*H* Bnβ, C*H*H Bnβ, H-6α), 4.73 – 4.67 (m, 2H, 2xC*H*H Bnα), 4.63 (dd, 0.7H, *J* = 12.0, 2.0 Hz, H-6β), 4.62 (d, 0.7H, *J* = 12.1 Hz, CH*H* Bnβ), 4.59 – 4.51 (m, 5.4H, 2xCH*H* Bnα, H-1α, H-1β, H-1'β, H-6α), 4.49 (dd, 0.7H, *J* = 12.0, 4.2 Hz, H-6β), 4.20 (dd, 0.7H, *J* = 10.5, 5.0 Hz, H-6'β), 4.12 (dd, 1H, *J* = 10.3, 4.7 Hz, H-6'α), 4.08 (dd, 1H, *J* = 9.4, 8.7 Hz, H-3α), 4.05 – 4.00 (m, 2H, H-3'α, H-5α), 3.91 – 3.84 (m, 1.7H, H-3β, H-4α), 3.82 – 3.73 (m, 2.4H, H-

3'$_\beta$, H-4$_\beta$, H-5'$_\alpha$), 3.70 (ddd, 0.7H, *J* = 9.8, 4.1, 1.9 Hz, H-5$_\beta$), 3.67 – 3.58 (m, 2.7H, H-4'$_\alpha$, H-4'$_\beta$, H-6'$_\alpha$), 3.56 – 3.50 (m, 2.7H, H-2$_\alpha$, H-2'$_\alpha$, H-6'$_\beta$), 3.48 – 3.44 (m, 1.4H, H-2$_\beta$, H-2'$_\beta$), 3.39 (s, 3H, CH_3 OMe$_\alpha$), 3.38 (s, 2.1H, CH_3 OMe$_\beta$), 3.29 (td, 0.7H, *J* = 9.9, 5.0 Hz, H-5'$_\beta$); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC, HMBC): δ 158.7, 158.5 (C=O), 146.8, 144.8 (CF-*ortho*), 144.5, 142.4 (CF-*para*), 139.1, 139.0 (C_q), 138.8 (CF-meta), 138.6, 138.5, 138.3, 138.1, 137.9, 137.4, 137.3 (C_q), 136.8 (CF-*meta*), 129.1, 129.0, 128.6, 128.6, 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.1, 128.1, 128.0, 128.0, 127.8, 127.8, 127.7, 127.7, 127.6, 127.3, 126.9, 126.1, 126.0 (CH_{arom}), 107.8 ($C_{q\text{-}ipso}$), 103.4 (C-1'$_\beta$), 101.3 (CHPh$_\alpha$), 101.2 (CHPh$_\beta$), 98.4 (C-1'$_\alpha$), 98.3 (C-1$_\beta$), 97.9 (C-1$_\alpha$), 82.8 (C-2'$_\beta$), 82.3 (C-4'$_\alpha$), 81.8 (C-4'$_\beta$), 81.6 (C-3'$_\beta$), 81.2 (C-3$_\alpha$), 80.3 (C-2$_\alpha$), 79.9 (C-3$_\beta$), 79.2 (C-2$_\beta$), 78.8 (C-2'$_\alpha$), 78.6 (C-3'$_\alpha$), 78.1 (C-4$_\beta$), 75.9, 75.7, 75.3, 75.2, 74.7 (CH_2 Bn), 74.6 (C-4$_\alpha$), 74.1, 73.8, 73.5 (CH_2 Bn), 69.0 (C-6'$_\alpha$), 68.8 (C-6'$_\beta$), 68.4 (C-5$_\beta$), 67.9 (C-5$_\alpha$), 66.2 (C-5'$_\beta$), 65.4 (C-6$_\alpha$), 64.5 (C-6$_\beta$), 63.7 (C-5'$_\alpha$), 55.6 (OMe$_\beta$), 55.5 (OMe$_\alpha$); ^{19}F NMR ($CDCl_3$, 471 MHz): δ -137.33 (dp, 2F, *J* = 16.6, 5.4 Hz, *ortho*F$_5$Bz$_\alpha$), -137.83 (dp, 1.4F, *J* = 16.5, 5.4 Hz, *ortho*F$_5$Bz$_\beta$), -147.86 – -148.26 (m, 1.7F, *para*F$_5$Bz$_{\alpha,\beta}$), -160.23 (tt, 1.4F, *J* = 21.1, 5.8 Hz, *meta*F$_5$Bz$_\beta$), -160.41 (tt, 2F, *J* = 21.1, 5.8 Hz, *meta*F$_5$Bz$_\alpha$); HRMS: $[M+Na]^+$ calcd for $C_{55}H_{51}F_5O_{12}Na$ 1021.3198, found 1021.3237.



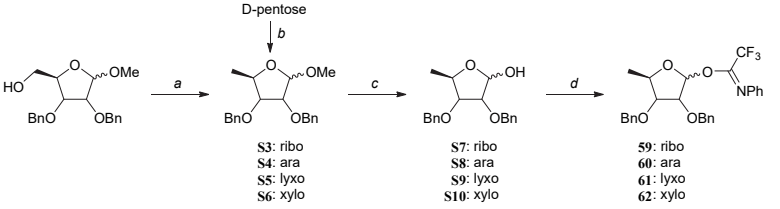
Methyl 4-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α/β-D-glucopyranosyl)-2,3-di-*O*-benzyl-6-*O*-(2,3,4,5,6-pentafluorobenzoyl)-α-D-glucopyranoside (56). Donor **4** and acceptor **47** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 yielding product **56** (75 mg, 80 µmol, 80%, α:β = 1 : 1.7) as a colorless oil. R_f: 0.69 and 0.82 (4/1 pentane/EtOAc); IR (thin film): 696, 735, 997, 1003, 1028, 1047, 1092, 1227, 1325, 1454, 1498, 1524, 1653, 1740, 2110, 2872, 2914; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.46 – 7.42 (m, 5.4H, CH_{arom}), 7.40 – 7.25 (m, 48.6H, CH_{arom}), 5.58 (d, 1H, *J* = 4.1 Hz, H-1'$_\alpha$), 5.53 (s, 1H, C*H*Ph$_\alpha$), 5.49 (s, 1.7H, C*H*Ph$_\beta$), 5.12 (d, 1H, *J* = 10.6 Hz, C*H*H Bn$_\alpha$), 4.97 (d, 1H, *J* = 10.9 Hz, C*H*H Bn$_\alpha$), 4.94 – 4.88 (m, 6.1H, 3xCHH Bn$_\beta$, CHH Bn$_\alpha$), 4.84 (dd, 1.7H, *J* = 12.1, 2.1 Hz, H-6$_\beta$), 4.79 – 4.73 (m, 5.4H, 2xCHH Bn$_\alpha$, 2xCHH Bn$_\beta$), 4.68 (dd, 1H, *J* = 11.9, 2.4 Hz$_\alpha$), 4.65 (dd, 1.7H, *J* = 12.2, 4.0 Hz, H-6$_\beta$), 4.63 – 4.57 (m, 5.4H, CH*H* Bn$_\alpha$, CH*H* Bn$_\beta$, H-1$_\alpha$, H-1$_\beta$), 4.50 (dd, 1H, *J* = 11.9, 4.4 Hz, H-6$_\alpha$), 4.41 (d, 1.7H, *J* = 8.1 Hz, H-1'), 4.16 (dd, 1H, *J* = 10.3, 4.9 Hz, H-6'$_\alpha$), 4.10 (dd, 1H, *J* = 9.4, 8.8 Hz, H-3$_\alpha$), 4.05 – 4.00 (m, 2.7H, H-3'$_\alpha$, H-6'$_\beta$), 3.99 – 3.90 (m, 4.4H, H-3$_\beta$, H-5$_\alpha$, H-5$_\beta$), 3.84 – 3.76 (m, 3.7H, H-4$_\alpha$, H-4$_\beta$, H-5'$_\alpha$), 3.70 – 3.60 (m, 5.4H, H-3'$_\beta$, H-4$_\alpha$, H-4'$_\beta$, H-6'$_\alpha$), 3.54 (dd, 1H, *J* = 9.6, 3.5 Hz, H-2$_\alpha$), 3.49 (dd, 1.7H, *J* = 9.6, 3.6 Hz, H-2$_\beta$), 3.47 (t, 1.7H, *J* = 10.3 Hz, H-6'$_\beta$), 3.43 (dd, 1.7H, *J* = 9.2, 8.2 Hz, H-2'$_\beta$), 3.40 (s, 5.1H, CH_3 OMe$_\beta$), 3.39 (s, 3H, CH_3 OMe$_\alpha$), 3.35 (dd, 1H, *J* = 10.1, 4.1 Hz, H-2'$_\alpha$), 3.20 (ddd, 1.7H, *J* = 9.9, 9.0, 5.0 Hz, H-5'$_\beta$); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 158.8, 158.7 (m, C=O), 146.7, 144.7, 144.4, 142.5 (m, CF_{arom}), 139.2 (C_q), 138.8 (m, CF_{arom}), 138.7, 138.1, 137.8, 137.8, 137.7, 137.1 (C_q), 136.8 (m, CF_{arom}), 129.2, 129.1, 128.7, 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.3, 128.2, 128.2, 128.0, 128.0, 127.6, 127.6, 127.6, 127.3, 126.1, 126.0 (CH_{arom}), 107.8 (m, $C_{q(ipso\text{-}F5Bz)}$), 102.2 (C-1'$_\beta$), 101.3, 101.3 (CHPh), 99.1 (C-1'$_\alpha$), 98.2 (C-1$_\beta$), 97.8 (C-1$_\alpha$), 82.6 (C-4$_\alpha$), 81.7 (C-4'$_\beta$), 81.2 (C-3$_\alpha$), 80.6 (C-2$_\alpha$), 79.9 (C-3$_\beta$), 79.8 (C-3'$_\beta$), 79.4 (C-2$_\beta$), 78.3 (C-4$_\beta$), 76.2 (C-3'$_\alpha$), 75.6 (C-4$_\alpha$), 75.5, 75.2, 75.1, 75.0, 73.7, 73.4 (CH_2 Bn), 68.6 (C-6'$_\alpha$), 68.5 (C-6'$_\beta$), 68.1, 67.7 (C-5$_\alpha$, C-5$_\beta$), 66.8 (C-2'$_\beta$), 66.3 (C-5'$_\beta$), 65.4 (C-6$_\alpha$), 64.8 (C-6$_\beta$), 63.7 (C-5'$_\alpha$), 62.9 (C-2'$_\alpha$), 55.7 (OMe$_\alpha$), 55.6 (OMe$_\beta$); ^{19}F NMR ($CDCl_3$, 471 MHz): δ -137.42 (dp, *J* = 16.7, 5.5 Hz), -137.96 (dp, *J* = 16.5, 5.5 Hz), -147.83 – -148.02 (m), -160.08 (tt, *J* = 21.1, 5.8 Hz), -160.31 (tt, *J* = 21.1, 5.9 Hz); HRMS: $[M+Na]^+$ calcd for $C_{48}H_{44}F_5N_3O_{11}Na$ 956.2794, found 956.2816.



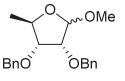
Methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-glucopyranosyl)-2,3-di-*O*-benzyl-6-*O*-(2,4,6-trinitrobenzoyl)-α-D-glucopyranoside (57). Donor **3** and acceptor **48** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 yielding product **57** (78 mg, 75 µmol, 75%, α:β = 2.1 : 1) as a colorless oil. R_f: 0.43 (4/1 pentane/EtOAc); IR (thin film): 698, 735, 1028, 1047, 1074, 1088, 1269, 1342, 1454, 1545, 1557, 1755, 2872, 2928; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC, HMBC): δ 8.97 (s, 2H, CH_{arom} NO_2Bz), 7.38 – 7.14 (m, 25H, CH_{arom}), 5.53 (d, 1H, *J* = 3.9 Hz, H-1'), 5.38 (s, 1H, C*H*Ph), 5.06 (dd, 1H, *J* = 11.7, 2.2 Hz, H-6), 4.97 – 4.86 (m, 3H, 2xC*H*H Bn, H-6), 4.80 – 4.64 (m, 6H, 2xC*H*H Bn, 2xCH*H* Bn, H-1, H-6), 4.57 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.54 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.11 – 4.04 (m, 2H, H-3, H-5), 4.01 (t, 1H, *J* = 9.3 Hz, H-3'), 3.87 – 3.83 (m, 2H, H-5', H-6'), 3.80 (dd, 1H, *J* = 9.8, 8.6 Hz, H-4), 3.57 – 3.49 (m, 4H, H-2, H-2', H-4', H-6'), 3.41 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC, HMBC): δ 160.6 (C=O), 147.8, 147.1 (C_q NO_2), 138.9, 138.6, 138.1, 137.9, 137.3, 129.6 (C_q), 129.0, 128.6, 128.5, 128.4, 128.3, 128.3, 128.3, 128.1, 128.1, 128.1, 128.1, 127.8, 127.8, 127.7, 127.3, 127.0, 126.1, 125.9, 124.5 (CH_{arom}), 101.0 (CHPh), 98.0 (C-1'), 97.8 (C-1), 82.1 (C-4'), 81.1 (C-3), 80.3 (C-2), 78.9 (C-2'), 78.5 (C-3'), 75.3, 74.6 (CH_2 Bn), 74.3 (C-4), 73.9, 73.4 (CH_2 Bn), 68.9 (C-6'), 68.3 (C-5), 66.9 (C-6), 63.3 (C-5'), 55.7 (OMe); Diagnostic peaks for the β-anomer: ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 9.13 (s, 2H, CH_{arom} NO_2Bz), 5.49 (s, 1H, C*H*Ph), 4.49 (dd, 1H, *J* = 12.0, 2.8 Hz, H-6), 4.17 (dd, 1H, *J* = 10.4, 4.9 Hz, H-6'), 3.63

(t, 1H, *J* = 9.3 Hz, H-4'), 3.45 (dd, 1H, *J* = 8.8, 7.7 Hz, H-2'), 3.42 (dd, 1H, *J* = 10.0, 4.0 Hz, H-2), 3.39 (s, 3H, CH_3 OMe); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 160.5 (C=O), 147.8, 147.2 (C_q NO_2), 139.1, 138.5, 138.3, 137.4, 129.7 (C_q), 129.0 - 124.6 (CH_{arom}), 103.0 (C-1'), 101.2 (CHPh), 98.2 (C-1), 83.1 (C-2'), 81.9 (C-4'), 81.5 (C-3'), 79.8 (C-3), 78.9 (C-2), 77.9 (C-4), 75.8 , 75.7, 73.5 (CH_2 Bn), 68.8 (C-6'), 68.2 (C-5), 66.6 (C-5'), 66.0 (C-6), 55.7 (OMe); HRMS: $[M+Na]^+$ calcd for $C_{55}H_{53}N_3O_{18}Na$ 1066.3222, found 1066.3257.

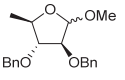
Preparation of 5-deoxy furanosyl imidates.



Reagents and conditions: (a) *i*. TsCl, pyridine, DCM; *ii*. $LiAlH_4$, Et_2O, **S5**: 75%, **S6**: 80%; (b) *i*. AcCl, MeOH; *ii*. Ph_3P, I_2, imidazole, THF, *iii*. $Pd(OH)_2$/C, H_2, DiPEA; *iv*. BnBr, NaH, DMF, **S3**: 40%, **S4**: 52%; (c) $HCOOH/H_2O$ (4/1 v/v, 0.05 M), 50°C, **S7**: 86%, **S8**: 72%, **S9**: 92%, **S10**: 92%; (d) 2,2,2-trifluoro-*N*-phenylacetimidoyl chloride (0.95 eq.), DBU (1 eq.) in DCM (0.25 M), 0°C, **77**: 48%, **79**: 56%, **81**: 44%, **83**: 66%.

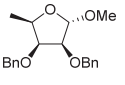


Methyl 2,3-di-*O*-benzyl-5-deoxy-α/β-D-ribofuranoside (S3). To a 0°C solution of D-ribose (3 g, 20 mmol) in MeOH (70 mL) was added AcCl (0.6 mL, 9 mmol, 0.45 eq.) and the reaction was stirred overnight at room temperature. The reaction was quenched by the addition of solid K_2CO_3 (5 g), stirred for 10 min, then filtered and concentrated under reduced pressure. The crude methyl glycoside was dissolved in THF (80 mL) and Ph_3P (7.9 g, 30 mmol, 1.5 eq.) and imidazole (2.7 g, 40 mmol, 2 eq.) were added and the reaction mixture brought to reflux. To the boiling reaction mixture was slowly added a solution of I_2 (7.6 g, 30 mmol, 1.5 eq.) in THF (30 mL). After 3 h the reaction was cooled to room temperature, MeOH (10 mL) was added and the reaction mixture was concentrated under reduced pressure. The residue was filtered over silica gel (5% MeOH in DCM) and the filtrate was concentrated under reduced pressure. The crude iodide was dissolved in MeOH (60 mL) and DiPEA (5 mL, 29 mmol). $Pd(OH)_2$ (20% on C, 0.85 g) was added and the reaction flask was purged with N_2. The flask was subsequently purged with H_2 for 5 min and then kept under a H_2 atmosphere (balloon) for 3 h. The reaction mixture was purged with N_2, filtered over Celite and evaporated. The residue was dissolved in 5% MeOH in DCM and filtered over silica gel, the filtrate concentrated under reduced pressure and coevaporated once with toluene. The crude material was dissolved in DMF (50 mL), cooled to 0°C, and treated with BnBr (4.2 mL, 35 mmol) and NaH (60% dispersion in mineral oil, 1.2 g, 30 mmol) and stirred overnight. The reaction mixture was quenched by the addition of H_2O, and then extracted three times with Et_2O. The combined organic layers were washed with 0.1 M aq. HCl, H_2O, and brine. The organic layer was dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography 0% to 10% EtOAc in pentane) to give the title compound as a colourless oil (1.93 g, 5.9 mmol, 30%, β anomer. The α anomer (10%) was impure and discarded). Data for the β-anomer: R*f*: 0.50 (9/1 pentane/EtOAc). $[\alpha]_D^{20}$ = +35.9° (*c* = 0.66, $CHCl_3$); IR (thin film): 698, 737, 935, 1028, 1038, 1111, 1454, 2911, 2926, 2972; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HH-NOESY, HSQC): δ 7.40 – 7.25 (m, 10H, CH_{arom}), 4.87 (s, 1H, H-1), 4.68 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.60 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.58 (d, 1H, *J* = 11.9 Hz, C*H*H Bn), 4.45 (d, 1H, *J* = 11.9 Hz, CH*H* Bn), 4.24 (dq, 1H, *J* = 7.3, 6.3 Hz, H-4), 3.84 (dd, 1H, *J* = 4.6, 1.0 Hz, H-2), 3.74 (dd, 1H, *J* = 7.3, 4.6 Hz, H-3), 3.33 (s, 3H, CH_3 OMe), 1.30 (d, 3H, *J* = 6.3 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.0, 137.9 (C_q), 128.5, 128.5, 128.1, 127.9, 127.9 (CH_{arom}), 106.3 (C-1), 83.2 (C-3), 80.0 (C-2), 77.3 (C-4), 72.5, 72.4 (CH_2 Bn), 55.0 (CH_3 OMe), 20.6 (C-5); HRMS: $[M+Na]^+$ calcd for $C_{20}H_{24}O_4Na$ 351.1572, found 351.1582.

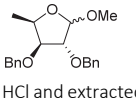


Methyl 2,3-di-*O*-benzyl-5-deoxy-α/β-D-arabinofuranoside (S4). To a 0°C solution of D-arabinose (3 g, 20 mmol) in MeOH (70 mL) was added AcCl (0.8 mL, 12 mmol, 0.6 eq.) and the reaction was stirred overnight at room temperature. The reaction was quenched by the addition of solid K_2CO_3 (5 g), stirred for 10 min, then filtered and concentrated under reduced pressure. The crude methyl glycoside was dissolved in THF (80 mL) and Ph_3P (7.9 g, 30 mmol, 1.5 eq.) and imidazole (2.7 g, 40 mmol, 2 eq.) were added and the reaction mixture brought to reflux. To the boiling reaction mixture was slowly added a solution of I_2 (7.6 g, 30 mmol, 1.5 eq.) in THF (30 mL). After 2 h the reaction was cooled to room temperature, MeOH (10 mL) was added and the reaction mixture was concentrated under reduced pressure. The residue was filtered over silica gel (5% MeOH in DCM) and the filtrate was concentrated under reduced pressure to give nearly pure methyl 5-iodo arabinoside (4.12 g, 15 mmol, 75%). The crude iodide (1.37 g, 5 mmol) was dissolved in MeOH (25 mL) and DiPEA (2.6 mL, 15 mmol, 3 eq.). $Pd(OH)_2$

(20% on C, 0.4 g) was added and the reaction flask was purged with N_2. The flask was subsequently purged with H_2 for 5 min and then kept under a H_2 atmosphere (balloon) for 3 h. The reaction mixture was purged with N_2, filtered over Celite and evaporated. The residue was dissolved in 5% MeOH in DCM and filtered over silica gel, the filtrate concentrated under reduced pressure and coevaporated once with toluene to give 4.15 mmol (83%) of reduced compound. The crude material (4 mmol) was dissolved in DMF (20 mL), cooled to 0°C, and treated with BnBr (1.43 mL, 12 mmol, 3 eq.) and NaH (60% dispersion in mineral oil, 480 mg, 12 mmol, 3 eq.) and stirred overnight. The reaction mixture was quenched by the addition of H_2O, and then extracted three times with Et_2O. The combined organic layers were washed with sat. aq. NH_4Cl, H_2O, and brine. The organic layer was dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (2% to 12% EtOAc in pentane) to give the title compound as a colourless oil (1.1 g, 3.5 mmol, 84%) in 52% over four steps, α:β = 2:1 anomeric mixture. IR (thin film): 698, 748, 1049, 1109, 1452, 2926; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.47 – 7.18 (m, 10H, CH_{arom}), 4.87 (s, 1H, H-1), 4.59 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.57 (d, 1H, *J* = 11.8 Hz, C*H*H Bn), 4.54 – 4.46 (m, 2H, 2xCH*H* Bn), 4.09 (p, 1H, *J* = 6.3 Hz, H-4), 3.97 (dd, 1H, *J* = 3.5, 1.0 Hz, H-2), 3.59 (dd, 1H, *J* = 7.1, 3.5 Hz, H-3), 3.37 (s, 3H, CH_3 OMe), 1.32 (d, 3H, *J* = 6.3 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.0, 137.7 (C_q), 128.6, 128.5, 128.1, 128.0, 127.9, 127.9 (CH_{arom}), 107.1 (C-1), 89.1 (C-2), 88.8 (C-3), 76.8 (C-4), 72.4, 72.2 (CH_2 Bn), 54.9 (OMe), 18.8 (C-5); Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.43 – 7.24 (m, 10H, CH_{arom}), 4.74 – 4.67 (m, 2H, C*H*H Bn, H-1), 4.66 – 4.57 (m, 3H, CH_2 Bn, CH*H* Bn), 4.06 – 3.95 (m, 3H, H-2, H-3, H-4), 3.37 (s, 3H, CH_3 OMe), 1.33 (d, 3H, *J* = 6.2 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.3, 137.8 (C_q), 128.5, 128.3, 128.0, 127.9, 127.8 (CH_{arom}), 101.5 (C-1), 87.1 (C-3/4), 84.5 (C-2), 77.6 (C-3/4), 72.6, 72.6 (CH_2 Bn), 54.9 (OMe), 22.3 (C-5); HRMS: $[M+NH_4]^+$ calcd for $C_{20}H_{28}NO_4$ 346.20128, found 346.20131.

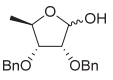


Methyl 2,3-di-*O*-benzyl-5-deoxy-α-D-lyxofuranoside (S5). To a solution of methyl 2,3-di-*O*-benzyl-α-D-lyxofuranoside[25] (1.03 g, 3.0 mmol, 1 eq.) and pyridine (1.4 mL, 18 mmol, 6 eq.) in DCM (15 mL) was added TsCl (2.3 g, 12 mmol, 4 eq.) and the reaction mixture was stirred for two days. The reaction mixture was poured into 1 M aq. HCl and extracted twice with Et_2O. The combined organic layers were washed with H_2O, sat. aq. $NaHCO_3$, and brine, then dried with $MgSO_4$, filtered and concentrated under reduced pressure. After coevaporation with dry toluene, the crude tosylate was dissolved in Et_2O (30 mL) and $LiAlH_4$ (4 M in Et_2O, 2.5 mL, 10 mmol, 5 eq.) was slowly added. The solution was refluxed for 3 h and then cooled to 0°C and quenched with EtOAc and H_2O. The reaction mixture was poured in 0.1 M HCl and extracted twice with Et_2O. The combined organic layers were washed with H_2O, sat. aq. $NaHCO_3$, and brine, then dried ($MgSO_4$), filtered and concentrated under reduced pressure. Purification by flash column chromatography (1/0 to 85/15 pentane/EtOAc) gave the title compound as a colourless oil, which crystalized on standing. Yield: 740 mg, 2.25 mmol, 75%. m.p. 34-36 °C. $[\alpha]_D^{20}$ = +16.0° (*c* = 1.0, $CHCl_3$); IR (neat): 692, 729, 955, 1015, 1028, 1051, 1098, 1132, 1159, 1366, 1450, 2899, 1933, 2976; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HH-NOESY, HSQC): δ 7.38 – 7.23 (m, 10H, CH_{arom}), 5.00 (d, 1H, *J* = 2.8 Hz, H-1), 4.73 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.66 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.62 – 4.53 (m, 2H, 2xCH*H* Bn), 4.23 (qd, 1H, *J* = 6.4, 4.6 Hz, H-4), 3.96 (t, 1H, *J* = 4.6 Hz, H-3), 3.92 (dd, 1H, *J* = 4.7, 2.8 Hz, H-2), 3.36 (s, 3H, CH_3 OMe), 1.32 (d, 3H, *J* = 6.5 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 138.4, 138.1 (C_q), 128.4, 128.3, 127.8, 127.7, 127.6 (CH_{arom}), 106.7 (C-1), 84.0 (C-2), 78.9 (C-3), 75.7 (C-4), 73.2, 72.6 (CH_2 Bn), 55.5 (OMe), 15.7 (C-5); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): $^2J_{C1,H2}$ = -2.5 Hz, $^2J_{C2,H1}$ = -1.2 Hz; HRMS: $[M+Na]^+$ calcd for $C_{20}H_{24}O_4Na$ 351.1572, found 351.1580.

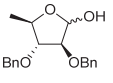


Methyl 2,3-di-*O*-benzyl-5-deoxy-α/β-D-xylofuranoside (S6). To a solution of methyl 2,3-di-*O*-benzyl-α-D-xylofuranoside[26] (2.2 g, 6.39 mmol, 1 eq.) in pyridine (15 mL) was added TsCl (2.4 g, 12.8 mmol, 2 eq.) and the reaction mixture was stirred overnight. The reaction mixture was poured into 1 M aq. HCl and extracted twice with Et_2O. The combined organic layers were washed with 1 M HCl, H_2O, sat. aq. $NaHCO_3$, and brine, then dried with $MgSO_4$, filtered and concentrated under reduced pressure. After coevaporation with dry toluene, the crude tosylate was dissolved in Et_2O (60 mL) and $LiAlH_4$ (4 M in Et_2O, 5 mL, 20 mmol, 3.1 eq.) was slowly added. The solution was refluxed for 8 h and then cooled to 0°C and quenched with EtOAc and H_2O. The reaction mixture was poured in 0.1 M HCl and extracted twice with Et_2O. The combined organic layers were washed with H_2O, sat. aq. $NaHCO_3$, and brine, then dried ($MgSO_4$), filtered and concentrated under reduced pressure. Purification by flash column chromatography (1/0 to 85/15 pentane/EtOAc) gave the title compound as a colourless oil. Yield: 1.68 g, 5.1 mmol, 80% as an α:β = 1:1.2 anomeric mixture. R*f*: 0.55 and 0.38 (9/1 pentane/EtOAc). IR (neat): 696, 735, 1026, 1063, 1107, 1454, 2870, 2909, 2930; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.39 – 7.26 (m, 22H, CH_{arom}), 4.86 (d, 1.2H, *J* = 1.9 Hz, H-1β), 4.77 (d, 1H, *J* = 4.3 Hz, H-1α), 4.65 (d, 1H, *J* = 12.0 Hz, C*H*H Bnα), 4.62 – 4.48 (m, 7.8H, CH*H* Bnα, CH_2 Bnα, 2xCH_2 Bnβ), 4.40 – 4.31 (m, 2.2H, H-4α, H-4β), 4.15 (dd, 1H, *J* = 6.7, 5.4 Hz, H-3α), 4.02 (dd, 1.2H, *J* = 3.2, 1.9 Hz, H-2β), 3.98 (dd, 1H, *J* = 5.4, 4.3 Hz, H-2α), 3.91 (dd, 1.2H, *J* = 5.8, 3.2 Hz, H-3β), 3.40 (s, 3.6H, CH_3 OMeβ), 3.39

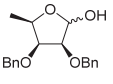
(s, 3H, CH_3 OMeα), 1.32 (d, 3.6H, *J* = 6.6 Hz, H-5β), 1.25 (d, 3H, *J* = 6.6 Hz, H-5α); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 138.3, 138.1, 137.8, 137.7 (C_q), 128.4, 128.4, 128.4, 128.1, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 127.5 (CH_{arom}), 108.1 (C-1β), 100.3 (C-1α), 87.4 (C-2β), 84.4 (C-2α), 82.5 (C-3β), 82.3 (C-3α), 76.9 (C-4β), 73.4 (C-4α), 72.6, 72.2, 72.0, 71.9 (CH_2 Bn), 55.5 (OMeβ), 55.0 (OMeα), 16.2 (C-5β), 15.6 (C-5α); HRMS: $[M+Na]^+$ calcd for $C_{20}H_{24}O_4Na$ 351.1572, found 351.1585.



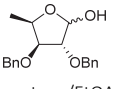
2,3-di-*O*-benzyl-5-deoxy-α/β-D-ribofuranose (S7). The title compound was generated from **S3** (1.1 g, 3.35 mmol) by the general procedure for methyl furanoside hydrolysis, conditions A (50°C, 2 h) as described in Chapter 7. Yield: 86% α:β = 1:2.5 (909 mg, 2.9 mmol) as a colourless oil. R*f*: 0.16 (8/2 pentane/EtOAc). Spectroscopic data were in accord with those previously reported.[27] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.42 – 7.26 (m, 15.5H, CH_{arom}), 5.34 (d, 0.55H, *J* = 2.9 Hz, H-1β), 5.30 (dd, 1H, *J* = 11.2, 4.2 Hz, H-1α), 4.74 – 4.67 (m, 3.1H, 2x C*H*H Bnα, 2x C*H*H Bnβ), 4.65 – 4.58 (m, 2.55H, C*H*H Bnβ, 2xCH*H* Bnα), 4.46 (d, 0.55H, *J* = 11.9 Hz, CH*H* Bnβ), 4.33 (qd, 1H, *J* = 6.5, 3.4 Hz, H-4α), 4.26 (d, 1H, *J* = 11.3 Hz, 1-OHα), 4.29 – 4.17 (m, 0.55H, H-4β), 3.93 (t, 1H, *J* = 4.5 Hz, H-2α), 3.85 (dd, 0.55H, *J* = 4.6, 0.9 Hz, H-2β), 3.79 (dd, 0.55H, *J* = 7.4, 4.6 Hz, H-3β), 3.62 (dd, 1H, *J* = 4.9, 3.4 Hz, H-3α), 3.16 (d, 0.55H, *J* = 3.4 Hz, 1-OHβ), 1.33 (d, 1.65H, *J* = 6.3 Hz, H-5β), 1.17 (d, 3H, *J* = 6.6 Hz, H-5α); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 137.9, 137.9, 137.6, 137.4 (C_q), 128.6, 128.6, 128.5, 128.5, 128.2, 128.1, 128.0, 127.9 (CH_{arom}), 100.1 (C-1β), 95.9 (C-1α), 82.8 (C-3β), 81.8 (C-3α), 80.4 (C-2β), 77.3, 77.3, 77.2 (C-2α, C-4α, C-4β), 72.9, 72.8, 72.6, 72.3 (CH_2 Bn), 20.6 (C-5β), 19.8 (C-5α); HRMS: $[M+Na]^+$ calcd for $C_{19}H_{22}O_4Na$ 337.1410, found 337.1425.



2,3-di-*O*-benzyl-5-deoxy-α/β-D-arabinofuranose (S8). The title compound was generated from **S4** (600 mg, 1.87 mmol) by the general procedure for methyl furanoside hydrolysis, conditions A (50°C, 2 h) as described in Chapter 7. Yield: 72% α:β = 1:2.5 (413 mg, 1.31 mmol) as a colourless oil. R*f*: 0.54 (7/3 pentane/EtOAc). IR (neat): 694, 733, 995, 1055, 1207, 1454, 1497, 2872, 2905, 2928, 2972, 3030, 3395; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.39 – 7.26 (m, 14H, CH_{arom}), 5.38 (d, 1H, *J* = 6.8 Hz, H-1α), 5.31 (dd, 0.4H, *J* = 8.6, 4.3 Hz, H-1β), 4.67 – 4.49 (m, 5.6H, 2xCH_2 Bnα, 2xCH_2 Bnβ), 4.35 (qd, 1H, *J* = 6.4, 4.8 Hz, H-4α), 3.98 (dd, 1H, *J* = 2.5, 0.9 Hz, H-2α), 4.00 – 3.89 (m, 0.8H, H-2β, H-4β), 3.78 (d, 0.4H, *J* = 8.6 Hz, 1-OHβ), 3.75 (dd, 0.4H, *J* = 5.1, 4.3 Hz, H-3β), 3.66 (ddd, 1H, *J* = 4.7, 2.5, 0.7 Hz, H-3α), 3.37 (d, 1H, *J* = 6.8 Hz, 1-OHα), 1.35 (d, 1.2H, *J* = 6.4 Hz, H-5β), 1.31 (d, 3H, *J* = 6.5 Hz, H-5α); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 137.8, 137.6, 137.5, 137.1 (C_q), 128.7, 128.6, 128.6, 128.3, 128.2, 128.1, 128.0, 128.0, 127.9, 127.9, 127.8 (CH_{arom}), 100.9 (C-1α), 96.0 (C-1β), 87.6 (C-2α), 87.4 (C-3α), 86.7 (C-3β), 83.2 (C-2β), 78.6 (C-4α), 76.5 (C-4β), 72.7, 72.3, 72.3, 72.0 (CH_2 Bn), 20.9 (C-5β), 19.4 (C-5α); HRMS: $[M+Na]^+$ calcd for $C_{19}H_{22}O_4Na$ 337.1410, found 337.1426.

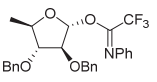


2,3-di-*O*-benzyl-5-deoxy-α/β-D-lyxofuranose (S9). The title compound was generated from **S5** (370 mg, 1.13 mmol) by the general procedure for methyl furanoside hydrolysis, conditions A (50°C, 1.5 h) as described in Chapter 7. Yield: 92% α:β = 1:4 (327 mg, 1.04 mmol) as a colourless oil. R*f*: 0.35 (7/3 pentane/EtOAc). IR (thin film): 698, 735, 1058, 1159, 1454, 2926, 3408; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.43 – 7.27 (m, 12.5H), 5.49 (t, 0.25H, *J* = 3.1 Hz, H-1α), 5.24 (dd, 1H, *J* = 12.2, 3.9 Hz, H-1β), 4.89 (d, 1H, *J* = 11.6 Hz, C*H*H Bnβ), 4.81 – 4.73 (m, 1.25H, CHH Bnα, CHH Bnβ), 4.70 (d, 0.25H, *J* = 12.1 Hz, C*H*H Bnα), 4.67 – 4.57 (m, 2.5H, 2xCH*H* Bnα, 2xCH*H* Bnβ), 4.37 (qd, 0.25H, *J* = 6.5, 4.7 Hz, H-4α), 4.25 (d, 1H, *J* = 12.2 Hz, 1-OHβ), 4.09 – 4.01 (m, 1.25H, H-3α, H-4β), 3.96 – 3.89 (m, 2.25H, H-2α, H-2β, H-3β), 3.04 (d, 0.25H, *J* = 3.5 Hz, 1-OHα), 1.35 (d, 3H, *J* = 6.5 Hz, H-5β), 1.31 (d, 1H, *J* = 6.5 Hz, H-5α); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.4, 138.1, 137.9, 137.7 (C_q), 128.6, 128.5, 128.5, 128.4, 128.0, 128.0, 127.9, 127.8, 127.8 (CH_{arom}), 100.2 (C-1α), 95.6 (C-1β), 84.7 (C-2α), 79.9 (C-3β), 78.8 (C-3α), 78.5 (C-2β), 76.0 (C-4α), 75.6 (C-4β), 74.2, 73.3, 72.6, 72.0 (CH_2 Bn), 16.6 (C-5β), 15.9 (C-5α); HRMS: $[M+Na]^+$ calcd for $C_{19}H_{22}O_4Na$ 337.1410, found 337.1428.

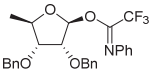


2,3-di-*O*-benzyl-5-deoxy-α/β-D-xylofuranose (S10). The title compound was generated from **S6** (887 mg, 2.7 mmol) by the general procedure for methyl furanoside hydrolysis, conditions A (50°C, 2 h) as described in Chapter 7. Yield: 92% α:β = 1.1:1 (778 mg, 2.47 mmol) as a colourless oil. R*f*: 0.37 (8/2 pentane/EtOAc). IR (neat): 694, 733, 1026, 1057, 1207, 1454, 1497, 2870, 2932, 3030, 3400; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.39 – 7.26 (m, 19H, CH_{arom}), 5.44 (dd, 0.9H, *J* = 9.0, 4.4 Hz, H-1α), 5.23 (d, 1H, *J* = 11.0 Hz, H-1β), 4.64 – 4.50 (m, 5.7H, CH_2 Bnα, CH_2 Bnβ, C*H*H Bnα, C*H*H Bnβ), 4.48 (d, 1H, *J* = 11.9 Hz, CH*H* Bnβ), 4.44 (d, 0.9H, *J* = 12.2 Hz, CH*H* Bnα), 4.39 – 4.30 (m, 1.9H, H-4α, H-4β), 3.98 (d, 1H, *J* = 1.2 Hz, H-2β), 3.95 (dd, 0.9H, *J* = 4.4, 2.1 Hz, H-2α), 3.91 (d, 0.9H, *J* = 9.0 Hz, 1-OHα), 3.81 (dd, 0.9H, *J* = 4.2, 2.1 Hz, H-3α), 3.77 (ddd, 1H, *J* = 3.9, 1.3, 0.7 Hz, H-3β), 3.35 (d, 1H, *J* = 11.0 Hz, 1-OHβ), 1.37 (d, 3H, *J* = 6.6 Hz, H-5β), 1.26 (d, 2.7H, *J* = 6.5 Hz, H-5α); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 138.0, 137.6, 137.3, 137.0 (C_q), 128.8, 128.7, 128.6, 128.6, 128.4, 128.2, 128.1, 128.1, 128.0, 127.9, 127.8, 127.7

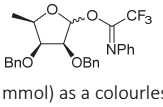
(CH_{arom}), 101.1 (C-1β), 95.7 (C-1α), 85.3 (C-2β), 82.5 (C-3α), 82.3 (C-2α), 81.5 (C-3β), 78.0 (C-4β), 74.7 (C-4α), 73.3, 72.5, 72.1, 72.0 (CH_2 Bn), 15.5 (C-5β), 14.6 (C-5α); HRMS: $[M+Na]^+$ calcd for $C_{19}H_{22}O_4Na$ 337.1410, found 337.1429.



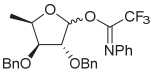
2,3-di-*O*-benzyl-5-deoxy-1-*O*-(*N*-[phenyl]trifluoroacetimidoyl)-α-D-arabinofuranoside (59). The title compound was generated from **61** (330 mg, 1.05 mmol) by the general procedure for imidate donor synthesis, conditions B as described in Chapter 7. Yield: 56% α only (286 mg, 0.59 mmol) as a colourless oil. R*f*: 0.55 (9/1 pentane/Et_2O). $[\alpha]_D^{20}$ = -1.1° (*c* = 0.75, $CHCl_3$); IR (thin film): 696, 905, 1103, 1120, 1161, 1207, 1330, 1454, 1707, 2932; ^{1}H NMR ($CDCl_3$, *T* = 323 K, 500 MHz, HH-COSY, HSQC): δ 7.36 – 7.24 (m, 12H, CH_{arom}), 7.11 – 7.02 (m, 1H, NPh), 6.81 (d, 2H, *J* = 7.7 Hz, NPh), 6.19 (bs, 1H, H-1), 4.65 – 4.50 (m, 4H, 2xCH_2 Bn), 4.32 (p, 1H, *J* = 6.2 Hz, H-4), 4.21 (d, 1H, *J* = 2.7 Hz, H-2), 3.69 (dd, 1H, *J* = 6.3, 2.8 Hz, H-3), 1.35 (d, 3H, *J* = 6.3 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, *T* = 323 K, 126 MHz, HSQC): δ 144.2 (C_q NPh), 138.0, 137.5 (C_q Bn), 128.8, 128.8, 128.6, 128.6, 128.2, 128.1, 128.0, 127.8, 124.4, 119.9 (CH_{arom}), 116.3 (q, *J* = 286.3 Hz, CF_3), 104.0 (C-1), 88.9 (C-3), 88.0 (C-2), 80.1 (C-4), 72.6, 72.6 (CH_2 Bn), 18.9 (C-5); HRMS: only mass of hydrolysis found $[M+Na]^+$ calcd for $C_{19}H_{22}O_4Na$ 337.1416, found 337.1416.



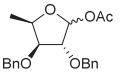
2,3-di-*O*-benzyl-5-deoxy-1-*O*-(*N*-[phenyl]trifluoroacetimidoyl)-β-D-ribofuranoside (60). The title compound was generated from **62** (355 mg, 1.13 mmol) by the general procedure for imidate donor synthesis, conditions B as described in Chapter 7. Yield: 48% β only (264 mg, 0.54 mmol) as a colourless oil. R*f*: 0.75 (8/2 pentane/Et_2O). $[\alpha]_D^{20}$ = +82.8° (*c* = 1.09, $CHCl_3$); IR (thin film): 696, 1092, 1151, 1207, 1454, 1712, 2872, 2930; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.35 – 7.24 (m, 12H, CH_{arom}), 7.08 (t, 1H, *J* = 7.5 Hz, NPh), 6.81 (d, 2H, *J* = 7.7 Hz, NPh), 6.19 (bs, 1H, H-1), 4.68 (d, 1H, *J* = 11.9 Hz, C*H*H Bn), 4.60 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.56 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.48 (d, 1H, *J* = 11.7 Hz, CH*H* Bn), 4.36 (p, 1H, *J* = 6.4 Hz, H-4), 4.05 (d, 1H, *J* = 4.3 Hz, H-2), 3.79 (dd, 1H, *J* = 7.6, 4.5 Hz, H-3), 1.35 (d, 3H, *J* = 6.3 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 144.1 (C_q NPh), 143.55 (q, *J* = 37.1 Hz, CF_3-*C*=NPh), 137.8, 137.7, 137.7, 128.9, 128.6, 128.2, 128.1, 128.1, 127.9, 124.4, 119.8 (CH_{arom}), 116.17 (q, *J* = 285.7 Hz, CF_3), 102.9 (C-1), 82.9 (C-3), 79.4 (C-2), 79.2 (C-4), 72.9, 72.5 (CH_2 Bn), 20.1 (C-5); HRMS: only mass of hydrolysis found $[M+Na]^+$ calcd for $C_{19}H_{22}O_4Na$ 337.1416, found 337.1420.



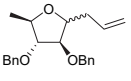
2,3-di-*O*-benzyl-5-deoxy-1-*O*-(*N*-[phenyl]trifluoroacetimidoyl)-α-D-lyxofuranoside (61). The title compound was generated from **63** (195 mg, 0.62 mmol) by the general procedure for imidate donor synthesis, conditions B as described in Chapter 7. Yield: 44% α:β = 1:4 (132 mg, 0.27 mmol) as a colourless oil. IR (thin film): 696, 1091, 1207, 1454, 1716, 2868; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, *T* = 328 K, 500 MHz, HH-COSY, HSQC): δ 7.34 – 7.24 (m, 12H, CH_{arom}), 7.09 – 7.05 (m, 1H, NPh), 6.82 (dd, 2H, *J* = 8.4, 1.0 Hz, NPh), 6.26 (bs, 1H, H-1), 4.69 (d, 1H, *J* = 11.8 Hz, C*H*H Bn), 4.68 – 4.60 (m, 2H, CH_2 Bn), 4.55 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.39 (p, 1H, *J* = 6.3 Hz, H-4), 4.15 (dd, 1H, *J* = 4.7, 1.9 Hz, H-2), 4.08 (t, 1H, *J* = 5.1 Hz, H-3), 1.34 (d, 3H, *J* = 6.5 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, *T* = 328 K, 126 MHz, HSQC): δ 144.2 (C_q NPh), 143.8 (q, *J* = 35.4 Hz, *C*=NPh), 138.3, 137.8 (C_q Bn), 128.8, 128.6, 128.5, 128.0, 127.9, 127.9, 127.8, 124.4, 119.9 (CH_{arom}), 116.38 (q, *J* = 286.0 Hz, CF_3) 103.5 (C-1), 82.8 (C-2), 78.3 (C-3), 78.1 (C-4), 73.4, 73.0 (CH_2 Bn), 15.8 (C-5); Diagnostic peaks β-anomer: ^{1}H NMR ($CDCl_3$, *T* = 328 K, 500 MHz, HH-COSY, HSQC): δ 7.40 – 7.18 (m, 12H, CH_{arom}), 7.04 – 6.99 (m, 1H, NPh), 6.75 (d, 2H, *J* = 7.9 Hz, NPh), 6.35 (bs, 1H, H-1), 4.90 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.74 – 4.60 (m, 3H, CH*H* Bn, CH_2 Bn), 4.23 (qd, 1H, *J* = 6.5, 4.7 Hz, H-4), 4.05 – 4.01 (m, 1H, H-2), 3.95 (t, 1H, *J* = 4.9 Hz, H-3), 1.37 (d, 3H, *J* = 6.6 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, *T* = 328 K, 126 MHz, HSQC): δ 144.6 (C_q NPh), 139.0, 137.9 (C_q Bn), 128.7, 128.6, 128.3, 128.0, 127.6, 127.5, 127.4, 124.0, 120.0 (CH_{arom}), 97.2 (C-1), 81.0 (C-2), 78.8 (C-4), 76.4 (C-3), 73.5, 73.3 (CH_2 Bn), 16.1 (C-5); HRMS: only mass of hydrolysis found $[M+Na]^+$ calcd for $C_{19}H_{22}O_4Na$ 337.1416, found 337.1422.



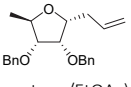
2,3-di-*O*-benzyl-5-deoxy-1-*O*-(*N*-[phenyl]trifluoroacetimidoyl)-α/β-D-xylofuranoside (62). The title compound was generated from **64** (285 mg, 0.91 mmol) by the general procedure for imidate donor synthesis, conditions B as described in Chapter 7. Yield: 66% α:β = 1:3 (290 mg, 0.59 mmol) as a colourless oil. R*f*: 0.41 (9/1 pentane/Et_2O). IR (thin film): 696, 1085, 1154, 1207, 1454, 1708, 2864; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.35 – 7.21 (m, 16H, CH_{arom}), 7.09 – 7.02 (m, 1.33H, NPh), 6.82 – 6.77 (m, 1H, NPh), 6.74 (d, 0.33H, *J* = 7.5 Hz, NPh), 6.32 (bs, 0.33H, H-1α), 6.18 (bs, 1H, H-1β), 4.67 – 4.47 (m, 6.67H, 2xCH_2 Bnα, 2xCH_2 Bnβ, H-4α, H-4β), 4.27 (d, 1H, *J* = 2.3 Hz, H-2β), 4.18 – 4.14 (m, 0.67H, H-2α, H-3α), 3.97 (dd, 1H, *J* = 5.7, 2.6 Hz, H-3β), 1.37 (d, 3H, *J* = 6.7 Hz, H-5β), 1.27 (d, 1H, *J* = 6.6 Hz, H-5α); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 144.3, 144.2 (C_q NPh), 138.2, 138.1, 137.8, 137.6 (C_q Bn), 129.5, 128.8, 128.6, 128.5, 128.1, 128.1, 128.0, 127.9, 127.8, 127.6, 127.6, 126.5, 124.2, 120.7, 119.8 (CH_{arom}), 116.23 (q, *J* = 286.4 Hz, CF_3), 103.8 (C-1β), 97.8 (C-1α), 86.1 (C-2β), 84.3 (C-2α), 82.6 (C-3β), 81.7 (C-3α), 80.1 (C-4β), 76.4 (C-4α), 73.4, 72.6, 72.5, 72.4 (CH_2 Bn), 15.8 (C-5β), 15.4 (C-5α); HRMS: only mass of hydrolysis found $[M+Na]^+$ calcd for $C_{19}H_{22}O_4Na$ 337.1416, found 337.1417.



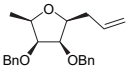
Acetyl 2,3-di-*O*-benzyl-5-deoxy-α/β-D-xylofuranoside (63). The title compound was generated from **S10** (220 mg, 0.7 mmol) by the general procedure for acetyl donor synthesis as described in Chapter 7. Yield: 95% α:β = 1:2.5 (236 mg, 0.66 mmol) as a colourless oil. IR (thin film): 604, 696, 735, 1007, 1090, 1231, 1373, 1454, 1741, 2934, 3030; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.39 – 7.23 (m, 14H, CH_{arom}), 6.28 (d, 0.4H, *J* = 4.1 Hz, H-1α), 6.12 (s, 1H, H-1β), 4.64 (d, 1H, *J* = 12.0 Hz, C*H*H Bnβ), 4.62 – 4.42 (m, 6H, CH*H* Bnβ, CH_2 Bnβ, 2xCH_2 Bnα, H-4α, H-4β), 4.15 – 4.08 (m, 1.8H, H-2α, H-2β, H-3α), 3.89 (dd, 1H, *J* = 5.2, 2.3 Hz, H-3β), 2.06 (s, 1.2H, CH_3 OAcα), 2.04 (s, 3H, CH_3 OAcβ), 1.34 (d, 3H, *J* = 6.6 Hz, H-5β), 1.27 (d, 1.2H, *J* = 6.5 Hz, H-5α); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 170.3, 170.2 (C=O), 138.0, 137.8, 137.4, 137.4 (C_q), 128.5, 128.4, 128.0, 128.0, 128.0, 127.8, 127.7, 127.5, 127.5 (CH_{arom}), 100.5 (C-1β), 94.2 (C-1α), 85.8 (C-2β), 83.6 (C-2α), 81.9 (C-3β), 81.5 (C-3α), 79.1 (C-4β), 75.7 (C-4α), 73.2, 72.2, 72.1, 71.8 (CH_2 Bn), 21.4 (CH_3 OAcβ), 21.2 (CH_3 OAcα), 15.5 (C-5β), 15.4 (C-5α); HRMS: $[M+Na]^+$ calcd for $C_{21}H_{24}O_5Na$ 379.1521, found 379.1525.



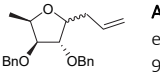
Allyl 2,3-di-*O*-benzyl-1,5-dideoxy-α/β-D-arabinofuranoside (65). Donor **59** and allyltrimethylsilane (4 eq.) were condensed using the general procedure for furanosyl imidate glycosylations at -78°C for 90 h with TfOH as the promotor. Yield = 28 mg, 83 µmol, 83% as a colourless oil (α:β = 40:60). R_f: 0.55 (85/15 pentane/EtOAc). IR (thin film): 698, 737, 1028, 1069, 1098, 1454, 2866, 2900, 2974; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HH-NOESY, HSQC): δ 7.39 – 7.27 (m, 10H, CH_{arom}), 5.89 – 5.77 (m, 1H, CH allyl), 5.17 – 5.03 (m, 2H, CH_2 allyl), 4.59 (d, 0.6H, *J* = 12.0 Hz, C*H*H Bnβ), 4.56 – 4.44 (m, 3.4H, CH*H* Bnβ, CH_2 Bnβ, 2xCH_2 Bnα), 4.14 (qd, 0.4H, *J* = 6.5, 4.4 Hz, H-4α), 4.08 (td, 0.4H, *J* = 6.7, 4.1 Hz, H-1α), 3.96 (td, 0.6H, *J* = 7.0, 3.7 Hz, H-1β), 3.92 (qd, 0.6H, *J* = 6.5, 3.8 Hz, H-4β), 3.84 (dd, 0.4H, *J* = 4.0, 2.8 Hz, H-2α), 3.82 (dd, 0.6H, *J* = 3.7, 0.9 Hz, H-2β), 3.75 (dd, 0.4H, *J* = 4.3, 2.8 Hz, H-3α), 3.65 (dd, 0.6H, *J* = 3.8, 1.0 Hz, H-3β), 2.51 (tq, 1.2H, *J* = 6.9, 1.3 Hz, CH_2 allylicβ), 2.44 – 2.34 (m, 0.4H, CH_2 allylicα), 1.34 (d, 1.8H, *J* = 6.5 Hz, H-5β), 1.31 (d, 1.2H, *J* = 6.5 Hz, H-5α); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.2, 138.1, 138.0, 138.0 (C_q), 135.1 (CH allylβ), 134.5 (CH allylα), 128.6, 128.6, 128.6, 128.5, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7 (CH_{arom}), 117.6 (CH_2 allylα), 117.0 (CH_2 allylβ), 89.7 (C-3α), 88.7 (C-3β), 87.6 (C-2α), 83.6 (C-2β), 81.4 (C-1α), 80.9 (C-1β), 79.9 (C-4β), 78.1 (C-4α), 72.1, 72.0, 71.8, 71.6 (CH_2 Bn), 38.0 (CH_2 allylicα), 33.5 (CH_2 allylicβ), 20.1 (C-5β), 19.5 (C-5α); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): α-anomer: $^2J_{C1,H2}$ = -0.7 Hz, $^2J_{C2,H1}$ = -4.2 Hz, $^3J_{Callyl,H2}$ = +3.7 Hz, β-anomer: $^2J_{C1,H2}$ = +2.2 Hz, $^2J_{C2,H1}$ = +3.4 Hz, $^3J_{Callyl,H2}$ = +0.3 Hz; HRMS: $[M+Na]^+$ calcd for $C_{22}H_{26}O_3Na$ 361.1780, found 361.1780.



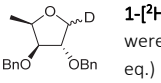
Allyl 2,3-di-*O*-benzyl-1,5-dideoxy-α-D-ribofuranoside (66). Donor **60** and allyltrimethylsilane (4 eq.) were condensed using the general procedure for furanosyl imidate glycosylations at -78°C for 90 h with TfOH as the promotor. Yield = 30 mg, 89 µmol, 89% as a colourless oil. R_f: 0.61 (85/15 pentane/EtOAc). $[\alpha]_D^{20}$ = +50.9° (*c* = 1.0, $CHCl_3$); IR (thin film): 696, 737, 914, 1026, 1094, 1273, 1454, 2926, 2970, 3032; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HH-NOESY, HSQC): δ 7.42 – 7.25 (m, 10H, CH_{arom}), 5.80 (ddt, 1H, *J* = 17.1, 10.2, 6.9 Hz, CH allyl), 5.10 (dq, 1H, *J* = 17.2, 1.6 Hz, C*H*H allyl), 5.04 (ddt, 1H, *J* = 10.2, 2.1, 1.1 Hz, CH*H* allyl), 4.81 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.67 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.59 (d, 1H, *J* = 11.7 Hz, CH*H* Bn), 4.54 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.17 (dq, 1H, *J* = 7.5, 6.2 Hz, H-4), 4.05 (td, 1H, *J* = 7.0, 4.0 Hz, H-1), 3.97 (t, 1H, *J* = 4.1 Hz, H-2), 3.61 (dd, 1H, *J* = 7.5, 4.2 Hz, H-3), 2.54 – 2.41 (m, 2H, CH_2 allylic), 1.24 (d, 3H, *J* = 6.2 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.6, 138.1 (C_q), 135.2 (CH allyl), 128.6, 128.4, 127.9, 127.8, 127.8, 127.7 (CH_{arom}), 117.0 (CH_2 allyl), 85.7 (C-3), 79.4 (C-1), 77.8 (C-2), 75.5 (C-4), 73.5, 72.8 (CH_2 Bn), 34.6 (CH_2 allylic), 19.6 (C-5); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): α-anomer: $^2J_{C1,H2}$ = +0.9 Hz, $^2J_{C2,H1}$ = +1.6 Hz, $^3J_{Callyl,H2}$ = +1.5 Hz; HRMS: $[M+Na]^+$ calcd for $C_{22}H_{26}O_3Na$ 361.1780, found 361.1779.



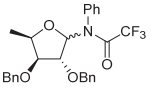
Allyl 2,3-di-*O*-benzyl-1,5-dideoxy-β-D-lyxofuranoside (67). Donor **61** and allyltrimethylsilane (4 eq.) were condensed using the general procedure for furanosyl imidate glycosylations at -78°C for 90 h with TfOH as the promotor. Yield = 19 mg, 56 µmol, 56% as a colourless oil. R_f: 0.25 (85/15 pentane/EtOAc). $[\alpha]_D^{20}$ = -7.1° (*c* = 0.63, $CHCl_3$); IR (thin film): 696, 735, 912, 1028, 1065, 1086, 1159, 1454, 2866, 2926, 3030, 3064; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.39 – 7.26 (m, 10H, CH_{arom}), 5.84 (ddt, 1H, *J* = 17.2, 10.2, 6.9 Hz, CH allyl), 5.10 (ddt, 1H, *J* = 17.2, 2.1, 1.5 Hz, C*H*H allyl), 5.03 (ddt, 1H, *J* = 10.2, 2.2, 1.2 Hz, CH*H* allyl), 4.79 (d, 1H, *J* = 11.8 Hz, C*H*H Bn), 4.70 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.61 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.57 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.16 – 4.08 (m, 1H, H-4), 4.04 – 3.98 (m, 2H, H-2, H-3), 3.94 – 3.88 (m, 1H, H-1), 2.53 – 2.46 (m, 2H, CH_2 allylic), 1.33 (d, 3H, *J* = 6.4 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.7, 138.6 (C_q), 135.7 (CH allyl), 128.5, 128.4, 127.7, 127.6, 127.6, 127.5 (CH_{arom}), 116.7 (CH_2 allyl), 80.4 (C-3), 79.4 (C-2), 78.8 (C-1), 75.1 (C-4), 73.4, 73.1 (CH_2 Bn), 35.4 (CH_2 allylic), 16.9 (C-5); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): $^2J_{C1,H2}$ = +1.5 Hz, $^2J_{C2,H1}$ = +1.5 Hz, $^3J_{Callyl,H2}$ = +0.5 Hz; HRMS: $[M+Na]^+$ calcd for $C_{22}H_{26}O_3Na$ 361.1780, found 361.1779.



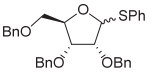
Allyl 2,3-di-*O*-benzyl-1,5-dideoxy-α/β-D-xylofuranoside (68). Donor **62** and allyltrimethylsilane (4 eq.) were condensed using the general procedure for furanosyl imidate glycosylations at -78°C for 90 h with TfOH as the promotor. Isolated yield = 28 mg, calculated product yield = 20 mg, 60 µmol, 60% (α:β = 60:40), intermixed with amide **74** (16%). R_f: 0.58 (80/20 pentane/EtOAc). IR (thin film): 696, 734, 914, 1028, 1067, 1086, 1205, 1454, 2866, 2930, 3032; ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.39 – 7.19 (m, 17H, CH_{arom}), 5.87 – 5.76 (m, 1.7H, CH allyl), 5.14 – 5.02 (m, 3.4H, CH_2 allyl), 4.59 – 4.52 (m, 2.7H, 3xC*H*H Bn), 4.50 – 4.44 (m, 4.4H, 3xCH*H* Bn, CH_2 Bn), 4.29 (qd, 1H, *J* = 6.5, 4.0 Hz, H-4α), 4.17 (td, 1H, *J* = 7.1, 4.0 Hz, H-1α), 4.08 (qd, 0.7H, *J* = 6.4, 3.7 Hz, H-4β), 3.88 (dd, 1H, *J* = 4.0, 1.4 Hz, H-2α), 3.83 (td, 0.7H, *J* = 6.7, 3.9 Hz, H-1β), 3.80 (dd, 1H, *J* = 4.0, 1.4 Hz, H-3α), 3.77 – 3.73 (m, 1.4H, H-2β, H-3β), 2.49 – 2.34 (m, 3.4H, CH_2 allylic), 1.33 (d, 2.1H, *J* = 6.4 Hz, H-5β), 1.26 (d, 3H, *J* = 6.5 Hz, H-5α); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 138.3, 138.3, 138.1, 138.0 (C_q), 135.4 (CH allylα), 134.7 (CH allylβ), 129.2, 128.6, 128.6, 128.5, 128.4, 128.2, 127.9, 127.9, 127.9, 127.8, 127.8, 127.8, 127.7, 127.7, 127.6 (CH_{arom}), 117.3 (CH_2 allylβ), 116.8 (CH_2 allylα), 86.9 (C-2β), 84.2 (C-3β), 82.9 (C-1β), 82.8 (C-3α), 82.5 (C-2α), 79.4 (C-1α), 77.1 (C-4β), 75.8 (C-4α), 72.3, 72.2 (CH_2 Bnα), 71.8, 71.6 (CH_2 Bnβ), 38.6 (CH_2 allylicβ), 33.9 (CH_2 allylicα), 14.8 (C-5α), 14.3 (C-5β); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): α-anomer: $^2J_{C1,H2}$ = +2.0 Hz, $^2J_{C2,H1}$ = +2.0 Hz, $^3J_{Callyl,H2}$ = +0.4 Hz; β-anomer:$^2J_{C2,H1}$ = -4.4 Hz, $^3J_{Callyl,H2}$ = +3.7 Hz; HRMS: $[M+Na]^+$ calcd for $C_{22}H_{26}O_3Na$ 361.1780, found 361.1779.



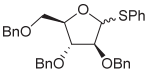
1-[^{2}H]-1,4-anhydro-2,3-di-*O*-benzyl-5-deoxy-α/β-D-xylitol (69). Donor **60** and triethylsilane-*d* (4 eq.) were condensed using the procedure published by van Rijssel *et al.*[20] -78°C for 90 h with TMSOTf (1.3 eq.) as the promotor. Yield = 23 mg, 77 µmol, 77% as a colourless oil (α:β = 40:60). R_f: 0.42 (9/1 pentane/EtOAc). IR (thin film): 709, 1026, 1096, 1109, 1267, 1452, 2933; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.38 – 7.27 (m, 10H, CH_{arom}), 4.61 (d, 1H, *J* = 12.2 Hz, C*H*H Bn), 4.50 (d, 1H, *J* = 12.2 Hz, CH*H* Bn), 4.49 (s, 2H, CH_2 Bn), 4.14 (t, 0.6H, *J* = 5.5 Hz, H-1β), 4.15 – 4.06 (m, 2H, H-2, H-4), 3.80 (dd, 1H, *J* = 3.8, 1.2 Hz, H-3), 3.71 (dt, 0.4H, *J* = 2.7, 1.3 Hz, H-1α), 1.30 (d, 3H, *J* = 6.4 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.2, 137.9 (C_q), 128.6, 128.6, 128.0, 127.9, 127.7 (CH_{arom}), 83.3 (C-3), 82.9 (C-2), 76.8 (C-4), 71.9, 71.7 (CH_2 Bn), 71.1 (t, *J* = 22.4 Hz, C-1), 71.1 (t, *J* = 22.4 Hz, C-1), 14.1 (C-5); ^{2}H NMR ($CHCl_3$, 77 MHz): δ 4.18 (s, 0.4D, D-1α), 3.74 (s, 0.6D, D-1β); ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): α-anomer: $^2J_{C2,H1}$ = +1.2 Hz; β-anomer:$^2J_{C2,H1}$ = -4.5 Hz.



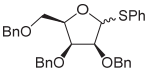
2,3-di-*O*-benzyl-1,5-dideoxy-1-*N*-[phenyl]trifluoroacetyl-α/β-D-xylofuranoside (74). Intermixed with **68**. The anomeric amide was formed in an α:β = 96:4 ratio. Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 500 MHz, HH-COSY, HSQC): δ 7.40 – 7.20 (m, 15H, CH_{arom}), 6.31 (d, 1H, *J* = 5.6 Hz, H-1), 4.69 (d, 1H, *J* = 11.1 Hz, C*H*H Bn), 4.54 (d, 1H, *J* = 11.2 Hz, CH*H* Bn), 4.50 – 4.46 (m, 1H, C*H*H Bn), 4.42 (dd, 1H, *J* = 5.7, 3.3 Hz, H-4), 4.34 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 3.52 – 3.47 (m, 2H, H-2, H-3), 1.03 (d, 3H, *J* = 6.1 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 126 MHz, HSQC): δ 156.5 (C=O), 137.8, 137.4 (C_q Bn), 134.6 (C_q Ph), 132.1 - 127.6 (CH_{arom}), 116.1 (q, *J* = 289 Hz, CF_3, 87.8 (C-1), 83.1 (C-2), 81.6 (C-3), 76.6 (C-4), 74.1, 72.0 (CH_2 Bn), 15.1 (C-5); ^{19}F NMR ($CDCl_3$, 471 MHz): δ -68.08 ; ^{13}C HSQC-HECADE NMR ($CDCl_3$, 126 MHz): $^2J_{C1,H2}$ = +1.2 Hz, $^2J_{C2,H1}$ = +2.0 Hz;



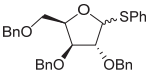
Phenyl 2,3,5-tri-*O*-benzyl-1-thio-α/β-D-ribofuranoside (77). A solution of 1,2,3,5-tetra-O-acetyl-α/β-D-ribofuranose[20] (1.59 g, 3.43 mmol, 1 eq.), thiophenol (0,40 mL, 3.77 mmol, 1.1 eq.) and $BF_3{\cdot}OEt_2$ (0.51 mL, 4.12 mmol, 1.2 eq.) at 0°C was stirred for 2 h. The reaction was quenched with sat. aq. $NaHCO_3$ and the mixture was extracted with EtOAc and washed with brine. The organic layer was dried ($MgSO_4$), filtered and concentrated *in vacuo*. Flash column chromatography of the residue (1/0 to 19/1 pentane/EtOAc) afforded the title compound as a colourless oil (Yield = 1.237 g, 2.41 mmol, 70%, α:β = 1:2.7). Spectroscopic data was previously reported[28] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.81 – 7.36 (m, 55.5H, CH_{arom}), 5.97 (d, 1H, *J* = 5.3 Hz, H-1α), 5.73 (d, 2.7H, *J* = 3.7 Hz, H-1β), 4.99 (d, 1H, *J* = 11.7 Hz, C*H*H Bnα), 4.92 (d, 1H, *J* = 12.1 Hz, C*H*H Bnα), 4.84 (d, 1H, *J* = 11.7 Hz, CH*H* Bnα), 4.80 (d, 2.7H, *J* = 11.9 Hz, C*H*H Bnβ), 4.75 – 4.63 (m, 16.5H, 2xC*H*H Bnβ, 3xCH*H* Bnβ, C*H*H Bnα, CH*H* Bnα, H-4α), 4.61 (d, 1H, *J* = 12.1 Hz, CH*H* Bnα), 4.58 – 4.54 (m, 2.7H, H-4β), 4.38 (t, 1H, *J* = 5.5 Hz, H-2α), 4.20 (t, 1H, *J* = 5.4 Hz, H-3α), 4.18 – 4.14 (m, 5.4H, H-2β, H-3β), 3.80 (dd, 1H, *J* = 10.9, 3.3 Hz, H-5α), 3.74 (d, 5.4H, *J* = 4.5 Hz, H-5β, H-5β), 3.71 (dd, 1H, *J* = 10.8, 3.5 Hz, H-5α); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 137.9, 137.9, 137.8, 137.5, 137.4, 137.2, 136.4, 133.3 (C_q), 131.9, 130.4, 128.6, 128.5, 128.1, 128.1, 128.0, 127.8, 127.7, 127.6, 127.5, 127.5, 127.4, 127.3, 127.3, 127.3, 127.3, 127.2, 126.2 (CH_{arom}), 90.4 (C-1α), 88.4 (C-1β), 81.7 (C-4β), 80.6 (C-4α), 80.2 (C-2β), 78.3 (C-2α), 77.2 (C-3β), 76.9 (C-3α), 73.0, 72.9, 72.9, 72.2, 71.8 (CH_2 Bn), 70.0 (C-5β), 69.0 (C-5α); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): α-anomer: $^2J_{C1,H2}$ = +2.0 Hz; β-anomer: $^2J_{C2,H1}$ = -2.9 Hz; HRMS: $[M+Na]^+$ calcd for $C_{32}H_{32}O_4SNa$ 535.19135, found 535.19064.



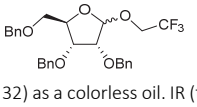
Phenyl 2,3,5-tri-*O*-benzyl-1-thio-α/β-D-arabinofuranoside (79). A solution of 1,2,3,5-tetra-O-acetyl-α/β-D-arabinofuranose[20] (889 mg, 1.92 mmol, 1 eq.), thiophenol (0.22 mL, 2.11 mmol, 1.1 eq.) and $BF_3{\cdot}OEt_2$ (0.30 mL, 2.31 mmol, 1.2 eq.) at 0°C was stirred for 2 h. The reaction was quenched with sat. aq. $NaHCO_3$ and the mixture was extracted with EtOAc and washed with brine. The organic layer was dried ($MgSO_4$), filtered and concentrated *in vacuo*. Flash column chromatography of the residue (1/0 to 19/1 pentane/EtOAc) afforded the title compound as a colourless oil (Yield = 291 mg, 0.57 mmol, 30%, α:β = 4:1). Spectroscopic data for the β-anomer was reported previously.[29] Data for the α-anomer: IR (thin film): 693, 734, 1026, 1068, 1270, 1361, 1453, 1722, 2864; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.54 – 7.46 (m, 2H, CH_{arom}), 7.38 – 7.18 (m, 18H, CH_{arom}), 5.62 (d, 1H, *J* = 2.8 Hz, H-1), 4.66 – 4.45 (m, 6H, 3xCH_2 Bn), 4.40 (dt, 1H, *J* = 6.7, 4.4 Hz, H-4), 4.13 (t, 1H, *J* = 3.1 Hz, H-2), 4.05 (dd, 1H, *J* = 6.7, 3.3 Hz, H-3), 3.68 (dd, 1H, *J* = 10.9, 3.9 Hz, H-5), 3.63 (dd, 1H, *J* = 10.9, 4.8 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.1, 137.7, 137.3, 134.9 (C_q), 131.2, 128.9, 128.5, 128.4, 128.4, 128.0, 128.0, 127.8, 127.8, 127.7, 127.6, 127.1 (CH_{arom}), 90.3 (C-1), 88.5 (C-2), 83.4 (C-3), 80.5 (C-4), 73.3, 72.3, 72.1 (CH_2 Bn), 69.0 (C-5); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): α-anomer: $^2J_{C1,H2}$ = +0.6 Hz, $^2J_{C2,H1}$ = -4.0 Hz; HRMS: $[M+Na]^+$ calcd for $C_{32}H_{32}O_4SNa$ 535.19135, found 535.19024.



Phenyl 2,3,5-tri-*O*-benzyl-1-thio-α/β-D-lyxofuranoside (81). A solution of 1,2,3,5-tetra-O-acetyl-α/β-D-lyxofuranose[20] (1.86 g, 4.02 mmol, 1 eq.), thiophenol (0.50 mL, 4.43 mmol, 1.1 eq.) and $BF_3{\cdot}OEt_2$ (0.60 mL, 4.83 mmol, 1.2 eq.) at 0°C was stirred for 2 h. The reaction was quenched with sat. aq. $NaHCO_3$ and the mixture was extracted with EtOAc and washed with brine. The organic layer was dried ($MgSO_4$), filtered and concentrated *in vacuo*. Flash column chromatography of the residue (1/0 to 19/1 pentane/EtOAc) afforded the title compound as a colourless oil (Yield = 1.11 g, 2.17 mmol, 54%, α:β = 97:3). Data for the α-anomer: IR (thin film): 693, 733, 1025, 1072, 1453, 2859; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.49 – 7.43 (m, 2H, CH_{arom}), 7.31 – 7.16 (m, 17H, CH_{arom}), 5.54 (d, 1H, *J* = 6.0 Hz, H-1), 4.70 (d, 1H, *J* = 11.7 Hz, C*H*H Bn), 4.60 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.55 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.53 (d, 1H, *J* = 11.7 Hz, CH*H* Bn), 4.51 (d, 1H, *J* = 11.9 Hz, C*H*H Bn), 4.44 (d, 1H, *J* = 11.9 Hz, CH*H* Bn), 4.27 (td, 1H, *J* = 6.2, 3.8 Hz, H-4), 3.99 (t, 1H, *J* = 4.1 Hz, H-3), 3.94 (dd, 1H, *J* = 5.9, 4.4 Hz, H-2), 3.80 (dd, 1H, *J* = 9.9, 6.3 Hz, H-5), 3.70 (dd, 1H, *J* = 9.9, 6.2 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.0, 138.0, 137.4, 134.0 (C_q), 131.7, 128.8, 128.4, 128.3, 128.2, 127.8, 127.8, 127.8, 127.7, 127.6, 127.6, 127.2 (CH_{arom}), 88.4 (C-1), 83.2 (C-2), 79.0 (C-4), 76.8 (C-3), 73.5, 73.3, 72.6 (CH_2 Bn), 68.2 (C-5); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): $^2J_{C1,H2}$ = -2.2 Hz, $^2J_{C2,H1}$ = -4.5 Hz; HRMS: $[M+Na]^+$ calcd for $C_{32}H_{32}O_4SNa$ 535.19135, found 535.19018.

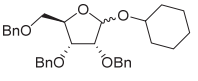


Phenyl 2,3,5-tri-*O*-benzyl-1-thio-α/β-D-xylofuranoside (81). A solution of 1,2,3,5-tetra-O-acetyl-α/β-D-xylofuranose[20] (3.55 g, 7.68 mmol, 1 eq.), thiophenol (0.90 mL, 8.45 mmol, 1.1 eq.) and $BF_3{\cdot}OEt_2$ (1.15 mL, 9.22 mmol, 1.2 eq.) at 0°C was stirred for 2 h. The reaction was quenched with sat. aq. $NaHCO_3$ and the mixture was extracted with EtOAc and washed with brine. The organic layer was dried ($MgSO_4$), filtered and concentrated *in vacuo*. Flash column chromatography of the residue (1/0 to 19/1 pentane/EtOAc) afforded the title compound as a colourless oil (Yield = 2.07 g, 4.04 mmol, 53%, α:β = 1:0.8). Spectroscopic data for the α-anomer was reported previously.[29] ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.55 – 7.47 (m, 4H, CH_{arom}), 7.40 – 7.14 (m, 32H, CH_{arom}), 5.80 (d, 1H, *J* = 5.0 Hz, H-1α), 5.37 (d, 0.8H, *J* = 2.9 Hz, H-1β), 4.69 – 4.37 (m, 12.6H, 3xCH_2 Bnα,β, H-4α), 4.21 (dd, 1H, *J* = 5.0, 2.3 Hz, H-2α), 4.15 – 4.11 (m, 0.8H, H-2β), 4.09 (dd, 1H, *J* = 4.5, 2.3 Hz, H-3α), 4.03 (dd, 0.8H, *J* = 4.7, 1.8 Hz, H-3β), 3.87 – 3.76 (m, 2.6H, H-5α, H-5β,β), 3.71 (dd, 1H, *J* = 10.1, 5.8 Hz, H-5α); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.1, 137.7, 137.6, 137.3, 135.6, 135.3 (C_q), 130.9, 128.8, 128.7, 128.4, 128.3, 128.2, 127.9, 127.8, 127.7, 127.6, 127.6, 127.6, 127.5, 126.9, 126.5 (CH_{arom}), 90.0 (C-1α), 89.9 (C-1β), 86.6 (C-2β), 83.7 (C-2α), 81.6 (C-3α), 81.5 (C-3β), 81.2 (C-4β), 78.1 (C-4α), 73.3, 73.2, 72.8, 72.1, 71.8, 71.7 (CH_2 Bn), 68.6 (C-5β), 67.7 (C-5α); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): α-anomer: $^2J_{C1,H2}$ = +2.5 Hz, $^2J_{C2,H1}$ = +0.7 Hz; β-anomer: $^2J_{C1,H2}$ = 0 Hz, $^2J_{C2,H1}$ = -4.5 Hz; HRMS: $[M+Na]^+$ calcd for $C_{32}H_{32}O_4SNa$ 535.19135, found 535.19046.

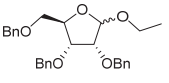


2,2,2-Trifluoroethyl 2,3,5-tri-*O*-benzyl-α/β-D-ribofuranoside (86). Donor **77** and acceptor **8** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 (2h at -60°C) yielding product **86** (42.7 mg, 85 µmol, 85%, α:β = 68 : 32) as a colorless oil. IR (thin film): 697, 735, 1028, 1046, 1114, 1153, 1279, 1454, 2861, 2930; Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.39 – 7.26 (m, 13H, CH_{arom}), 7.20 (dd, 2H, *J* = 7.7, 1.8 Hz, CH_{arom}), 5.13 (t, 1H, *J* = 2.1 Hz, H-1), 4.72 (d, 1H, *J* = 12.5 Hz, C*H*H Bn), 4.68 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.62 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.53 (d, 1H, *J* = 12.5 Hz, CH*H* Bn), 4.48 (d, 1H, *J* = 12.2 Hz, C*H*H Bn), 4.41 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.28 – 4.22 (m, 1H, H-4), 4.04 (q, 2H, *J* = 8.9 Hz, CH_2 TFE), 3.89 – 3.84 (m, 2H, H-2, H-3), 3.45 (dd, 1H, *J* = 10.5, 3.6 Hz, H-5), 3.36

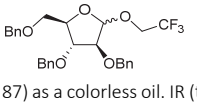
(dd, 1H, *J* = 10.6, 4.1 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.3, 137.9, 137.8 (C_q), 128.5, 128.4, 128.2, 128.0, 127.9, 127.8, 127.8, (CH_{arom}), 124.3 (d, *J* = 279.5 Hz), 101.5 (C-1), 82.6 (C-4), 77.9 (C-3), 75.3 (C-2), 73.6, 72.8, 72.6 (CH_2 Bn), 69.9 (C-5), 64.2 (q, *J* = 34.4 Hz, *CH*$_2$-CF_3); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): $^2J_{C1,H2}$ = +3.5 Hz, $^2J_{C2,H1}$ = +4.4 Hz; Data for the β-anomer:: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.36 – 7.24 (m, 15H, CH_{arom}), 5.06 (s, 1H, H-1), 4.69 – 4.42 (m, 6H, 3xCH_2 Bn), 4.36 (ddd, 1H, *J* = 7.4, 5.5, 3.3 Hz, H-4), 4.08 (dd, 1H, *J* = 7.4, 4.6 Hz, H-3), 3.95 (d, 1H, *J* = 4.6 Hz, H-2), 3.90 – 3.70 (m, 1H, CH_2 TFE), 3.63 (dd, 1H, *J* = 10.6, 3.3 Hz, H-5), 3.46 (dd, 1H, *J* = 10.6, 5.5 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.1, 137.6 (C_q), 128.6, 128.5, 128.1, 128.1, 128.0, 128.0, 128.0, 127.9, 127.8 (CH_{arom}), 124.0 (q, *J* = 278.3 Hz, CF_3), 105.1 (C-1), 81.2 (C-4), 79.5 (C-2), 78.0 (C-3), 73.3, 72.7, 72.7 (CH_2 Bn), 70.6 (C-5), 63.9 (q, *J* = 34.5 Hz, *CH*$_2$-CF_3); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): $^2J_{C2,H1}$ = -1.0 Hz; HRMS: $[M+Na]^+$ calcd for $C_{28}H_{29}F_3O_5Na$ 525.18593, found 525.18488.



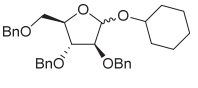
Cyclohexyl 2,3,5-tri-*O*-benzyl-α/β-D-ribofuranoside (87). Donor **77** and acceptor **76** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 (2h at -60°C) yielding product **87** (26.2 mg, 52 µmol, 52%, α:β = 64 : 36) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.42 – 7.19 (m, 22.5H, CH_{arom}), 5.19 – 5.15 (m, 1.5H, H-1α,β), 4.74 – 4.41 (m, 9H, 3xCH_2 Bnα,β), 4.32 (td, 0.5H, *J* = 6.3, 4.1 Hz, H-4β), 4.24 (q, 1H, *J* = 4.1 Hz, H-4α), 4.00 (dd, 0.5H, *J* = 6.8, 4.8 Hz, H-3β), 3.86 – 3.80 (m, 1.5H, H-2β, H-3α), 3.76 (dd, 1H, *J* = 6.9, 4.2 Hz, H-2α), 3.65 – 3.49 (m, 2.5H, H-5β,β, CH Cγα,β), 3.46 (dd, 1H, *J* = 10.6, 3.7 Hz, H-5α), 3.37 (dd, 1H, *J* = 10.6, 4.2 Hz, H-5α), 2.01 – 1.11 (m, 15H, CH_2 Cγα,β); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.7, 138.4, 138.3, 138.2, 138.1 (C_q), 128.5, 128.4, 128.4, 128.4, 128.3, 128.1, 128.1, 128.1, 127.9, 127.9, 127.8, 127.8, 127.7, 127.6 (CH_{arom}), 103.3 (C-1β), 99.7 (C-1α), 81.0 (C-4α), 80.3 (C-2β, C-4β), 78.9 (C-3β), 77.4 (C-2α), 76.3 (CH Cγα), 75.6 (C-3α), 75.3 (CH Cγβ), 73.5, 73.3, 72.4, 72.3 (CH_2 Bn), 71.9 (C-5β), 70.1 (C-5α), 33.9, 33.7, 32.1, 31.6, 25.8, 25.8, 24.7, 24.6, 24.3, 24.1 (CH_2 Cγ); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): α-anomer:: $^2J_{C1,H2}$ = +1.2 Hz; β-anomer:: $^2J_{C1,H2}$ = -0.5 Hz; HRMS: $[M+Na]^+$ calcd for $C_{32}H_{38}O_5Na$ 525.26115, found 525.26028.



Ethyl 2,3,5-tri-*O*-benzyl-α/β-D-ribofuranoside (88). Donor **77** and acceptor **5** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 (2h at -60°C) yielding product **88** (32.4 mg, 72 µmol, 72%, α:β = 81 : 19) as a colorless oil. IR (thin film): 694, 739, 1044, 1090, 1444, 2879, 2930, 3065; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.38 – 7.26 (m, 18H, CH_{arom}), 5.02 (d, 1.2H, *J* = 4.2 Hz, H-1α,β), 4.73 – 4.40 (m, 7.2H, 3xCH_2 Bnα,β), 4.37 – 4.30 (m, 0.2H, H-4β), 4.25 (q, 1H, *J* = 3.9 Hz, H-4α), 4.04 (dd, 0.2H, *J* = 7.0, 4.7 Hz, H-3β), 3.88 – 3.80 (m, 2.2H, H-2β, H-3α, C*H* Etα), 3.79 – 3.69 (m, 1.2H, H-2α, C*H* Etβ), 3.65 – 3.57 (m, 1.2H, H-5β, CH*H* Etα), 3.52 (dd, 0.2H, *J* = 10.6, 5.9 Hz, H-5β), 3.47 – 3.38 (m, 1.2H, H-5α, CH*H* Etβ), 3.35 (dd, 1H, *J* = 10.5, 4.2 Hz, H-5α), 1.28 (t, 3H, *J* = 7.1 Hz, CH_3 Etα), 1.11 (t, 0.6H, *J* = 7.1 Hz, CH_3 Etβ); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.4, 138.0, 138.0 (C_q), 131.2, 129.4, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.1, 128.0, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 124.9 (CH_{arom})105.1 (C-1β), 101.1 (C-1α), 81.6 (C-4α), 80.4 (C-4β), 79.9 (C-2β), 78.7 (C-3β), 77.6 (C-2α), 75.3 (C-3α), 73.5, 73.2, 72.5, 72.5, 72.4, 72.3 (CH_2 Bn), 71.6 (C-5β), 70.1 (C-5α), 63.8 (CH_2 Etα), 63.3 (CH_2 Etβ), 15.4 (CH_3 Etα), 15.1 (CH_3 Etβ); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): α-anomer: $^2J_{C1,H2}$ = +1.4 Hz, $^2J_{C2,H1}$ = +2.2 Hz HRMS: $[M+Na]^+$ calcd for $C_{28}H_{32}O_5Na$ 471.21420, found 471.21324.

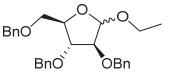


2,2,2-Trifluoroethyl 2,3,5-tri-*O*-benzyl-α/β-D-arabinofuranoside (90). Donor **79** and acceptor **8** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 (2h at -60°C) yielding product **90** (40 mg, 80 µmol, 80%, α:β = 13 : 87) as a colorless oil. IR (thin film): 697, 736, 1072, 1116, 1161, 1279, 1454, 2879, 2930; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.43 – 7.31 (m, 18H, CH_{arom}), 5.19 (s, 0.2H, H-1α), 5.01 (d, 1H, *J* = 3.8 Hz, H-1β), 4.77 – 4.49 (m, 7.2H, CH_2 Bnα,β), 4.29 – 4.25 (m, 0.2H, H-4α), 4.21 – 4.13 (m, 3.2H, H-2α, H-2β, H-3β, H-4β), 3.99 (dd, 0.2H, *J* = 6.9, 3.2 Hz, H-3α), 3.89 – 3.79 (m, 2.4H, CH_2 TFEα,β), 3.69 (dd, 0.2H, *J* = 10.8, 3.5 Hz, H-5α), 3.63 (dd, 0.2H, *J* = 10.8, 5.4 Hz, H-5α), 3.59 – 3.50 (m, 2H, H-5β, H-5β); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.1, 137.9, 137.7, 137.5 (C_q), 128.9, 128.6, 128.5, 128.5, 128.4, 128.2, 128.1, 128.0, 127.9, 127.9, 127.9, 127.8 (CH_{arom}), 124.1 (q, *J* = 278.8 Hz, CF_3), 106.4 (C-1α), 100.6 (C-1β), 87.9 (C-2α), 84.3 (C-2β), 83.4 (C-3α), 82.4 (C-3β), 81.3 (C-4α), 80.8 (C-4β), 73.5, 73.4, 72.7, 72.6, 72.3, 72.3 (CH_2 Bn), 71.8 (C-5β), 69.5 (C-5α), 64.0 (q, *J* = 34.6 Hz, *CH*$_2$-CF_3 α), 63.8 (q, *J* = 34.4 Hz, *CH*$_2$-CF_3 β); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): α-anomer: $^2J_{C1,H2}$ = -2.1 Hz, $^2J_{C2,H1}$ = -1.8 Hz; β-anomer: $^2J_{C1,H2}$ = +2.1 Hz, $^2J_{C2,H1}$ = +1.8 Hz; HRMS: $[M+Na]^+$ calcd for $C_{28}H_{29}F_3O_5Na$ 525.18593, found 525.18480.

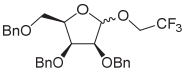


Cyclohexyl 2,3,5-tri-*O*-benzyl-α/β-D-arabinofuranoside (91). Donor **79** and acceptor **76** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as

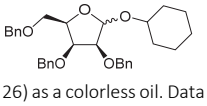
described in Chapter 3 (2h at -60°C) yielding product **91** (39mg, 78 µmol, 78%, α:β = 44 : 56) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.46 – 7.20 (m, 27H, CH_{arom}), 5.27 (d, 0.8H, *J* = 1.2 Hz, H-1α), 5.15 (d, 1H, *J* = 4.3 Hz, H-1β), 4.76 – 4.50 (m, 10.8H, 3xCH_2 Bnα,β), 4.26 (ddd, 0.8H, *J* = 7.3, 5.2, 3.4 Hz, H-4α), 4.17 – 4.08 (m, 3.8H, H-2β, H-3β, H-4β), 4.07 (dd, 0.8H, *J* = 3.6, 1.6 Hz, H-2α), 3.97 (dd, 0.8H, *J* = 7.2, 3.6 Hz, H-3α), 3.72 – 3.55 (m, 5.4H, H-5α,β, H-5α,β, CH Cyα,β), 2.00 – 1.12 (m, 18H, CH_2 Cyα,β); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.4, 138.3, 138.2, 138.1, 137.9, 137.8 (C_q), 128.5, 128.5, 128.4, 128.4, 128.2, 128.0, 128.0, 127.9, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7 (CH_{arom}), 104.1 (C-1α), 98.8 (C-1β), 88.9 (C-2α), 84.1, 83.8 (C-2β, C-3β), 83.6 (C-3α), 80.1, 80.1 (C-4α,β), 76.0, 75.0 (CH Cyα,β), 73.5 (CH_2 Bn), 73.4 (C-5β), 73.1, 72.4, 72.3, 72.2, 72.0 (CH_2 Bn), 69.8 (C-5α), 33.8, 33.8, 31.9, 31.8, 29.8, 25.8, 25.7, 24.6, 24.4, 24.4, 24.2 (CH_2 Cyα,β); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): α-anomer: $^{2}J_{C1,H2}$ = -2.2 Hz, $^{2}J_{C2,H1}$ = -1.5 Hz; β-anomer: $^{2}J_{C1,H2}$ = +1.2 Hz, $^{2}J_{C2,H1}$ = +4.0 Hz; HRMS: $[M+Na]^+$ calcd for $C_{32}H_{38}O_5Na$ 525.26115, found 525.25999.



Ethyl 2,3,5-tri-*O*-benzyl-α/β-D-arabinofuranoside (92). Donor **79** and acceptor **5** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 (2h at -60°C) yielding product **92** (22.7 mg, 51 µmol, 51%, α:β = 30 : 70) as a colorless oil. IR (thin film): 696, 735, 1099, 1453, 2862, 2902; ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.37 – 7.22 (m, 15H, CH_{arom}), 5.06 (d, 0.7H, *J* = 1.3 Hz, H-1α), 4.85 (d, 0.3H, *J* = 4.2 Hz, H-1β), 4.69 – 4.45 (m, 6H, 3xCH_2 Bnα,β), 4.21 (ddd, 0.7H, *J* = 6.9, 5.3, 3.6 Hz, H-4α), 4.14 – 4.03 (m, 0.9H, H-2β, H-3β, H-4β), 4.02 (dd, 0.7H, *J* = 3.3, 1.4 Hz, H-2α), 3.91 (dd, 0.7H, *J* = 6.9, 3.2 Hz, H-3α), 3.79 (dq, 0.7H, *J* = 9.8, 7.1 Hz, C*H*H Etα), 3.74 – 3.35 (m, 3.3H, H-5β,β, H-5α,α, C*H*H Etα, CH_2 Etβ), 1.22 (t, 2.1H, *J* = 7.1 Hz, CH_3 Etα), 1.17 (t, 0.9H, *J* = 7.1 Hz, CH_3 Etβ); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.3, 138.2, 138.2, 138.0, 137.9, 137.8 (C_q), 128.5, 128.5, 128.5, 128.5, 128.3, 128.0, 127.9, 127.9, 127.8, 127.8, 127.8, 127.7, 127.7 (CH_{arom}), 106.0 (C-1α), 100.4 (C-1β), 88.6 (C-2α), 84.3 (C-2β), 83.6 (C-3α,β), 80.6 (C-4α), 80.3 (C-4β), 73.5, 73.4, 72.8, 72.6, 72.4, 72.2, 72.1, 69.9 (CH_2 Bn, C-5α,β), 63.3 (CH_2 Etβ), 63.2 (CH_2 Etα), 15.3 (CH_3 Etα), 15.2 (CH_3 Etβ); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): α-anomer: $^{2}J_{C1,H2}$ = -2.0 Hz, $^{2}J_{C2,H1}$ = -1.1 Hz; β-anomer: $^{2}J_{C1,H2}$ = +0.3 Hz, $^{2}J_{C2,H1}$ = +1.8 Hz; HRMS: $[M+Na]^+$ calcd for $C_{28}H_{32}O_5Na$ 471.21420, found 471.21298.

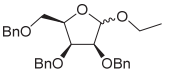


2,2,2-Trifluoroethyl 2,3,5-tri-*O*-benzyl-α/β-D-lyxofuranoside (94). Donor **81** and acceptor **8** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 (2h at -60°C) yielding product **94** (49 mg, 98 µmol, 98%, α:β = 48 : 52) as a colorless oil. Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.35 – 7.25 (m, 15H, CH_{arom}), 5.19 (d, 1H, *J* = 2.1 Hz, H-1), 4.68 (d, 1H, *J* = 11.8 Hz, C*H*H Bn), 4.66 (d, 1H, *J* = 12.1 Hz, C*H*H Bn), 4.61 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.60 (d, 1H, *J* = 12.1 Hz, CH*H* Bn), 4.52 (d, 1H, *J* = 11.8 Hz, CH*H* Bn), 4.50 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.37 (q, 1H, *J* = 5.7 Hz, H-4), 4.21 (t, 1H, *J* = 5.1 Hz, H-3), 4.06 – 3.94 (m, 2H, H-2, C*H*H-CF_3), 3.84 (dq, 1H, *J* = 12.4, 8.6 Hz, CH*H*-CF_3), 3.78 – 3.74 (m, 2H, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.2, 138.0, 137.7 (C_q), 128.6, 128.5, 128.0, 128.0, 127.9, 127.9, 127.8 (CH_{arom}), 124.0 (q, *J* = 278.3 Hz, CF_3), 105.7 (C-1), 82.3 (C-2), 79.1 (C-4), 77.9 (C-3), 73.6, 73.5, 72.8 (CH_2 Bn), 69.6 (C-5), 64.7 (q, *J* = 34.6 Hz, CH_2-CF_3); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): $^{2}J_{C1,H2}$ = -1.9 Hz, $^{2}J_{C2,H1}$ = -1.1 Hz; Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.39 – 7.22 (m, 15H, CH_{arom}), 5.12 (d, 1H, *J* = 4.6 Hz, H-1), 4.86 (d, 1H, *J* = 12.2 Hz, C*H*H Bn), 4.71 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.58 (d, 2H, *J* = 12.0 Hz, 2xCH*H* Bn), 4.54 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.51 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.19 (dt, 1H, *J* = 7.2, 5.1 Hz, H-4), 4.07 (t, 1H, *J* = 5.3 Hz, H-3), 4.00 (dd, 1H, *J* = 9.0, 1.2 Hz, C*H*H-CF_3), 3.96 (dd, 1H, *J* = 8.9, 0.9 Hz, CH*H*-CF_3), 3.89 (t, 1H, *J* = 5.2 Hz, H-2), 3.74 (dd, 1H, *J* = 10.2, 5.1 Hz, H-5), 3.68 (dd, 1H, *J* = 10.1, 7.2 Hz, H-5); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.5, 138.1, 137.7 (C_q), 128.6, 128.5, 128.3, 128.0, 128.0, 127.9, 127.8, 127.8, 127.6 (CH_{arom}), 124.3 (q, *J* = 279.1 Hz, CF_3), 100.1 (C-1), 79.7 (C-2), 79.5 (C-4), 75.1 (C-3), 73.6, 73.6, 72.6 (CH_2 Bn), 69.7 (C-5), 64.0 (q, *J* = 34.4 Hz, CH_2-CF_3); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): $^{2}J_{C1,H2}$ = +2.0 Hz, $^{2}J_{C2,H1}$ = +2.3 Hz; HRMS: $[M+Na]^+$ calcd for $C_{28}H_{29}F_3O_5Na$ 525.18593, found 525.18468.

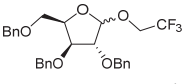


Cyclohexyl 2,3,5-tri-*O*-benzyl-α/β-D-lyxofuranoside (95). Donor **81** and acceptor **76** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 (2h at -60°C) yielding product **95** (36 mg, 72 µmol, 72%, α:β = 73 : 26) as a colorless oil. Data for the α-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.36 – 7.23 (m, 15H, CH_{arom}), 5.27 (d, 1H, *J* = 2.7 Hz, H-1), 4.69 (d, 1H, *J* = 12.0 Hz, C*H*H Bn), 4.65 – 4.59 (m, 3H, 2x*CH*H Bn, CH*H* Bn), 4.54 (d, 1H, *J* = 11.9 Hz, CH*H* Bn), 4.50 (d, 1H, *J* = 12.0 Hz, CH*H* Bn), 4.36 (dt, 1H, *J* = 6.9, 5.2 Hz, H-4), 4.20 (t, 1H, *J* = 4.9 Hz, H-3), 3.90 (dd, 1H, *J* = 4.6, 2.7 Hz, H-2), 3.78 (dd, 1H, *J* = 10.1, 5.1 Hz, H-5), 3.72 (dd, 1H, *J* = 10.1, 7.0 Hz, H-5), 3.58 (tt, 1H, *J* = 9.2, 4.1 Hz, CH Cy), 1.92 – 1.84 (m, 2H, CH_2 Cy), 1.69 (d, 2H, *J* = 5.8 Hz, CH_2 Cy), 1.55 – 1.47 (m, 1H, CH_2 Cy), 1.34 – 1.15 (m, 5H, CH_2 Cy); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.4, 138.4, 138.2 (C_q), 128.5, 128.4, 128.4, 128.0, 127.8, 127.8, 127.8, 127.7, 127.7 (CH_{arom}), 103.3 (C-1), 83.0 (C-2), 78.2, 78.0 (C-3, C-4), 75.7 (CH Cy), 73.5, 73.4, 72.6 (CH_2

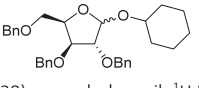
Bn), 69.8 (C-5), 33.8, 31.9, 25.8, 24.4, 24.2 (CH_2 Cy); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): $^2J_{C1,H2}$ = -2.2 Hz, $^2J_{C2,H1}$ = -1.5 Hz; Data for the β-anomer: ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.38 – 7.26 (m, 15H, CH_{arom}), 5.14 (d, 1H, *J* = 4.6 Hz, H-1), 4.85 (d, 1H, *J* = 12.4 Hz, C*H*H Bn), 4.74 (d, 1H, *J* = 12.2 Hz, C*H*H Bn), 4.58 (d, 1H, *J* = 12.4 Hz, CH*H* Bn), 4.57 (d, 1H, *J* = 12.2 Hz, CH*H* Bn), 4.56 (d, 1H, *J* = 11.9 Hz, C*H*H Bn), 4.51 (d, 1H, *J* = 11.9 Hz, CH*H* Bn), 4.19 (dt, 1H, *J* = 6.9, 5.3 Hz, H-4), 4.06 (t, 1H, *J* = 5.7 Hz, H-3), 3.82 – 3.71 (m, 3H, H-2, H-5, H-5), 3.62 (ddd, 1H, *J* = 13.6, 9.6, 3.8 Hz, CH Cy), 1.91 (d, 2H, *J* = 10.0 Hz, CH_2 Cy), 1.81 – 1.71 (m, 2H, CH_2 Cy), 1.57 – 1.48 (m, 1H, CH Cy), 1.40 – 1.18 (m, 5H, CH_2 Cy); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 139.0, 138.5, 138.3 (C_q), 128.5, 128.4, 128.2, 128.0, 127.9, 127.8, 127.7, 127.6, 127.4 (CH_{arom}), 98.6 (C-1), 79.0 (C-2), 78.9 (C-4), 76.1 (CH Cy), 75.8 (C-3), 73.6, 73.3, 72.3 (CH_2 Bn), 70.8 (C-5), 33.8, 32.0, 25.9, 24.6, 24.4 (CH_2 Cy); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): $^2J_{C1,H2}$ = +1.8 Hz, $^2J_{C2,H1}$ = +2.2 Hz; HRMS: $[M+Na]^+$ calcd for $C_{32}H_{38}O_5Na$ 525.26115, found 525.26001.



Ethyl 2,3,5-tri-*O*-benzyl-α/β-D-lyxofuranoside (96). Donor **81** and acceptor **5** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 (2h at -60°C) yielding product **96** (34 mg, 76 µmol, 76%, α:β = 78 : 22) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.36 – 7.25 (m, 19.5H), 5.13 (d, 1H, *J* = 2.6 Hz, H-1α), 4.97 (d, 0.3H, *J* = 4.6 Hz, H-1β), 4.83 (d, 0.3H, *J* = 12.5 Hz, C*H*H Bnβ), 4.70 – 4.48 (m, 7.5H, 3xCH_2 Bnα, 2xCH_2 Bnβ, CH*H* Bnβ), 4.36 (dt, 1H, *J* = 7.0, 5.2 Hz, H-4α), 4.20 (t, 1H, *J* = 5.0 Hz, H-3α), 4.18 (dt, 0.3H, *J* = 6.8, 5.5 Hz, H-4β), 4.05 (t, 0.3H, *J* = 5.6 Hz, H-3β), 3.91 (dd, 1H, *J* = 4.6, 2.6 Hz, H-2α), 3.82 – 3.68 (m, 4.2H, H-2β, H-5α,α, H-5β,β, C*H*H Etα,β), 3.60 (dq, 0.3H, *J* = 10.1, 7.0 Hz, CH*H* Etβ), 3.47 (dq, 1H, *J* = 9.7, 7.0 Hz, CH*H* Etα), 1.24 (t, 0.9H, *J* = 7.1 Hz, CH_3 Etβ), 1.18 (t, 3H, *J* = 7.1 Hz, CH_3 Etα); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.7, 138.4, 138.3, 138.1 (C_q), 128.5, 128.5, 128.4, 128.4, 128.3, 128.0, 128.0, 127.9, 127.9, 127.8, 127.8, 127.8, 127.7, 127.5 (CH_{arom}), 105.2 (C-1α), 99.9 (C-1β), 82.8 (C-2α), 79.1 (C-2β), 79.1 (C-4β), 78.2 (C4α), 78.1 (C-3α), 75.2 (C-3β), 73.5, 73.4, 72.6, 72.4 (CH_2 Bn), 70.5 (C-5β), 69.8 (C-5α), 63.9 (CH_2 Etα), 63.8 (CH_2 Etβ), 15.4 (CH_2 Etβ), 15.3 (CH_2 Etα); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): α-anomer: $^2J_{C1,H2}$ = -2.2 Hz, $^2J_{C2,H1}$ = -1.7 Hz; β-anomer: $^2J_{C1,H2}$ = +0.8 Hz, $^2J_{C2,H1}$ = +2.0 Hz; HRMS: $[M+Na]^+$ calcd for $C_{28}H_{32}O_5Na$ 471.21420, found 471.21299.



2,2,2-Trifluoroethyl 2,3,5-tri-*O*-benzyl-α/β-D-xylofuranoside (98). Donor **83** and acceptor **8** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 (2h at -60°C) yielding product **98** (42.7 mg, 85 µmol, 85%, α:β = 84 : 16) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.44 – 7.27 (m, 18H, CH_{arom}), 5.17 (s, 0.2H, H-1β), 5.11 (d, 1H, *J* = 4.2 Hz, H-1α), 4.72 – 4.44 (m, 8.4H, 3xCH_2 Bnα,β ,H-4α,β), 4.38 (dd, 1H, *J* = 7.2, 6.0 Hz, H-3α), 4.16 – 3.85 (m, 2.2H, H-2α,β, H-3β), 3.82 – 3.71 (m, 1.4H, H-5α,β,β), 3.65 (dd, 1H, *J* = 10.7, 6.8 Hz, H-5α); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.2, 138.1, 137.7, 137.5, 137.3 (C_q), 129.8, 128.6, 128.6, 128.5, 128.5, 128.4, 128.2, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7, (CH_{arom}), 124.1 (q, *J* = 278.8 Hz, CF_3), 106.9 (C-1β), 99.8 (C-1α), 86.5 (C-2β), 84.0 (C-2α), 81.8 (C-3β), 81.3 (C-3α), 81.0 (C-4β), 76.8 (C-4α), 73.6, 73.5, 72.8, 72.7, 72.3 (CH_2 Bn), 69.6 (C-5β), 69.3 (C-5α), 64.4 (q, *J* = 34.5 Hz, CH_2CF_3 β), 64.2 (q, *J* = 34.5 Hz CH_2CF_3 α); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): α-anomer: $^2J_{C1,H2}$ = +2.0 Hz, $^2J_{C2,H1}$ = +2.1 Hz; β-anomer: $^2J_{C1,H2}$ = -1.7 Hz, $^2J_{C2,H1}$ = -1.2 Hz; HRMS: $[M+Na]^+$ calcd for $C_{28}H_{29}F_3O_5Na$ 525.18593, found 525.18492.



Cyclohexyl 2,3,5-tri-*O*-benzyl-α/β-D-xylofuranoside (99). Donor **83** and acceptor **76** were condensed using the general procedure for Tf_2O/Ph_2SO mediated glycosylations as described in Chapter 3 (2h at -60°C) yielding product **99** (39.7 mg, 79 µmol, 79%, α:β = 62 : 38) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.40 – 7.22 (m, 24H, CH_{arom}), 5.17 – 5.14 (m, 2H, H-1α,β), 4.69 – 4.35 (m, 11.2H, 3xCH_2 Bnα,β, H-4α,β), 4.33 (dd, 0.6H, *J* = 7.1, 5.9 Hz, H-3α), 4.08 (dd, 1H, *J* = 6.2, 3.5 Hz, H-3β), 4.03 – 3.95 (m, 1.6H, H-2α,β), 3.78 (dd, 1H, *J* = 10.3, 4.7 Hz, H-5β), 3.78 – 3.67 (m, 1.6H, H-5α,β), 3.68 – 3.54 (m, 2.2H, H-5α, CH Cyα,β), 1.95 – 1.86 (m, 3.2H, CH_2 Cyα,β), 1.80 – 1.66 (m, 3.2H, CH_2 Cyα,β), 1.52 (d, 1.6H, *J* = 5.9 Hz, CH_2 Cyα,β), 1.45 – 1.15 (m, 8H, CH_2 Cyα,β); ^{13}C-APT NMR ($CDCl_3$, 101 MHz, HSQC): δ 138.5, 138.4, 138.1, 137.9, 137.9 (C_q), 128.5, 128.5, 128.4, 128.2, 128.0, 127.9, 127.9, 127.7, 127.7, 127.6, 127.6, 127.6 (CH_{arom}), 105.0 (C-1β), 97.8 (C-1α), 87.6 (C-2β), 84.2 (C-2α), 82.2 (C-3β), 82.0 (C-3α), 79.4 (C-4β), 75.9, 75.8, 75.7 (C-4α, CH_{Cy} α,β), 73.6, 73.5, 72.6, 72.3, 72.0 (CH_2 Bn), 70.1 (C-5β), 69.6 (C-5α), 33.9, 33.6, 32.1, 31.8, 25.8, 25.8, 24.6, 24.5, 24.3, 24.2 (CH_2 Cyα,β); ^{13}C-HSQC-HECADE NMR (101 MHz, $CDCl_3$): α-anomer: $^2J_{C1,H2}$ = +1.4 Hz, $^2J_{C2,H1}$ = +2.0 Hz; β-anomer: $^2J_{C1,H2}$ = -2.5 Hz, $^2J_{C2,H1}$ = -1.5 Hz; HRMS: $[M+Na]^+$ calcd for $C_{32}H_{38}O_5Na$ 525.26115, found 525.26005.

Footnotes and references

(1) Singleton, D. A.; Thomas, A. A. *J. Am. Chem. Soc.* **1995**, *117* (36), 9357–9358.

(2) Singleton, D. A.; Szymanski, M. J. *J. Am. Chem. Soc.* **1999**, *121* (40), 9455–9456.

(3) Crich, D.; Chandrasekera, N. S. *Angew. Chem. Int. Ed.* **2004**, *43* (40), 5386–5389.

(4) Huang, M.; Garrett, G. E.; Birlirakis, N.; Bohé, L.; Pratt, D. A.; Crich, D. *Nat. Chem.* **2012**, *4* (8), 663–667.

(5) Chan, J.; Tang, A.; Bennet, A. J. *J. Am. Chem. Soc.* **2012**, *134* (2), 1212–1220.

(6) El-Badri, M. H.; Willenbring, D.; Tantillo, D. J.; Gervay-Hague, J. *J. Org. Chem.* **2007**, *72* (13), 4663–4672.

(7) Bennet, A. J.; Sinnott, M. L. *J. Am. Chem. Soc.* **1986**, *108* (23), 7287–7294.

(8) Zhang, Y.; Bommuswamy, J.; Sinnott, M. L. *J. Am. Chem. Soc.* **1994**, *116* (17), 7557–7563.

(9) Indurugalla, D.; Bennet, A. J. *J. Am. Chem. Soc.* **2001**, *123* (44), 10889–10898.

(10) Lee, J. K.; Bain, A. D.; Berti, P. J. *J. Am. Chem. Soc.* **2004**, *126* (12), 3769–3776.

(11) Sinnott, M. L.; Jencks, W. P. *J. Am. Chem. Soc.* **1980**, *102* (6), 2026–2032.

(12) Kwan, E. E.; Park, Y.; Besser, H. A.; Anderson, T. L.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2017**, *139* (1), 43–46.

(13) Huang, M.; Retailleau, P.; Bohé, L.; Crich, D. *J. Am. Chem. Soc.* **2012**, *134* (36), 14746–14749.

(14) Adero, P. O.; Furukawa, T.; Huang, M.; Mukherjee, D.; Retailleau, P.; Bohé, L.; Crich, D. *J. Am. Chem. Soc.* **2015**, *137* (32), 10336–10345.

(15) Huang, M.; Furukawa, T.; Retailleau, P.; Crich, D.; Bohé, L. *Carbohydr. Res.* **2016**, *427*, 21–28.

(16) I. Colombo, M.; A. Rúveda, E.; A. Stortz, C. *Org. Biomol. Chem.* **2011**, *9* (8), 3020–3025.

(17) Zhang, Q.; van Rijssel, E. R.; Walvoort, M. T. C.; Overkleeft, H. S.; van der Marel, G. A.; Codée, J. D. C. *Angew. Chem. Int. Ed.* **2015**, *54* (26), 7670–7673.

(18) Cid, M. B.; Alfonso, F.; Martín-Lomas, M. *Chem. – Eur. J.* **2005**, *11* (3), 928–938.

(19) The cause of this drop in stereoselectivity remains speculative, but it can be due to the increased electron density around the aromatic ring causing a coordination or hydrogen-bond formation inadvertably increasing the acceptor's nucleophilicity. Another explanation is consistent with the observarion that trinitrotoluene and its analogues react (via several possible mechanism) on the ipso and ortho position with nucleophiles, instead of reacting on the carbonyl. (see Terrier, F. *Chem. Rev.* **1982**, *82* (2), 77–152; Meyer, V. *Berichte Dtsch. Chem. Ges.* **1894**, *27* (3), 3160–3161 and Cohen, J. B.; Armes, H. P. *J. Chem. Soc. Trans.* **1906**, *89* (0), 454–462). Its increased electron withdrawing capabilities has rendered the carbonyl in effect a less electron withdrawing group, as it has to give electron density back to the carbonyl carbon whereas it is normaly heavily polarized (C→O).

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

(21) Frihed, T. G.; Bols, M.; Pedersen, C. M. *Chem. Rev.* **2015**, *115* (11), 4963–5013.

(22) van der Vorm, S.; Hansen, T.; Overkleeft, H. S.; van der Marel, G. A.; Codee, J. D. C. *Chem. Sci.* **2017**, *8* (3), 1867–1875.

(23) Lyčka, A.; Macháček, V.; Jirman, J. *Collect. Czechoslov. Chem. Commun.* **1987**, *52* (12), 2946–2952.

(24) Liotta, L. J.; Capotosto, R. D.; Garbitt, R. A.; Horan, B. M.; Kelly, P. J.; Koleros, A. P.; Brouillette, L. M.; Kuhn, A. M.; Targontsidis, S. *Carbohydr. Res.* **2001**, *331* (3), 247–253.

(25) Veeneman, G. H.; Gomes, L. J. F.; van Boom, J. H. *Tetrahedron* **1989**, *45* (23), 7433–7448.

(26) Li, K.-Y.; Jiang, J.; Witte, M. D.; Kallemeijn, W. W.; van den Elst, H.; Wong, C.-S.; Chander, S. D.; Hoogendoorn, S.; Beenakker, T. J. M.; Codée, J. D. C.; et al. *Eur. J. Org. Chem.* **2014**, *2014* (27), 6030–6043.

(27) Rodríguez, M. A.; Boutureira, O.; Matheu, M. I.; Díaz, Y.; Castillón, S. *Eur. J. Org. Chem.* **2007**, *2007* (15), 2470–2476.

(28) Kametani, T.; Kawamura, K.; Honda, T. *J. Am. Chem. Soc.* **1987**, *109* (10), 3010–3017.

(29) Hiranuma, S.; Kajimoto, T.; Wong, C.-H. *Tetrahedron Lett.* **1994**, *35* (29), 5257–5260.