α-Selective Xylofuranosylation Using a 2,3-*O*-Xylylene Protected Donor

by

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Abstract

Furanose-containing molecules are widespread in nature and have been identified as important constituents of glycoconjugates from numerous pathogenic microorganisms. Although significant advances in the synthesis of 1,2-*cis*-glycofuranosides have been made, there are still some challenges. In particular, almost no studies investigating the synthesis of 1,2-*cis*-xylofuranosides have been carried out. Previous studies by our group have demonstrated that the utility 2,3-*O*-xylylene protected arabinofuranosyl donors in the synthesis of 1,2-*cis*-(β)-arabinofuranosides. Therefore, we wanted to expand this methodology to the synthesis of 1,2-*cis*-(α)-xylofuranosides. Several 2,3-*O*-xylylene protected xylofuranosyl donors were synthesized, glycosylations employing them have been optimized and the substrate scope of the reaction has been explored. Finally, to demonstrate the utility of the methodology, a 5-deoxy-5-methylthio-α-xylofuranose-(MTX) containing pentasaccharide fragment of mycobacterial LAM was synthesized.

Preface

This thesis is submitted for the degree of Master of Science at the University of Alberta. The research described herein was conducted under the supervision of Professor Todd L. Lowary in the Department of Chemistry, University of Alberta, between September 2013 and July 2016.

This thesis is original, unpublished, independent work by the author, Li Zhang.

At the end, may this thesis be useful for all the readers and for future related research.

July 2016

Li Zhang

Acknowledgments

First and foremost, it is with great pleasure and privilege that I express my sincere gratitude, appreciations and respect to my supervisor, Professor Todd L. Lowary, for constant support, guidance and sustained encouragement throughout the past three years. I feel very fortunate to have had the opportunity to work with him and learn from him over the years. All of these invaluable advices and experience is something to cherish for a lifetime.

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Finally, I would like to thank all my friends and family for their unconditional love and support.

Table of Contents

List of Schemes

List of Tables

List of Figures

List of Abbreveations

$[\alpha]_D$	Specific rotation (sodium D line)
Å	Angstrom
Ac	Acetyl
Ac_2O	Acetic anhydride
AG	Arabinogalactan
AgOTf	Silver trifluoromethanesulfonate
app	Apparent
Ar	Aromatic
Ara*f*	Arabinofuranose
BCB	2-(Benzyloxycarbonyl)-benzyl
Bn	Benzyl
br s	Broad singlet (NMR spectra)
BSP	1-Benzenesulfinyl piperidine
BTF	Benzotrifluoride
Bu	Butyl
Bz	Benzoyl
COSY	Correlation spectroscopy
CPS	Capsular polysaccharide
CSA	Camphorsulfonic acid
DCC	*N*,*N*′-Dicyclohexylcarbodiimide

DCE	1,2-Dichloroethane
DDQ	2,3-Dichloro-5,6-dicyano-*p*-benzoquinone
DIAD	Diisopropyl azodicarboxylate
DMAP	4-Dimethylaminopyridine
DMF	*N,N*-Dimethylformamide
DMTST	Dimethylthiomethyl sulfonium trifluoromethanesulfonate
DTBMP	2,6-Di-*tert*-butyl-4-methylpyridine
DTBS	3,5-*O*-Di-*tert*-butylsilane
Et	Ethyl
Fru*f*	Fructofuranose
Fuc*f*	Fucofuranose
Gal	Galactose
Gal*f*	Galactofuranose
Glc*f*	Glucofuranose
HAD	Hydrogen-bond-mediated aglycone delivery
HMBC	Heteronuclear Multiple Bond Correlation
HMQC	Heteronuclear Multiple Quantum Coherence
HSQC	Heteronuclear Single Quantum Coherence
IAD	Intramolecular aglycone delivery
IDCP	Iodonium dicollidine perchlorate
IDCT	Iodonium collidine triflate
LAM	Lipoarabinomannan

LM	Lipomannan
Man	Mannose
ManLAM	Mannosylated lipoarabinomannan
Manp	Mannopyranose
Me	Methyl
MTX	5-Deoxy-5-methylthio-xylofuranose
NAP	2-Naphthylmethyl
NIS	*N*-Iodosuccinimide
Ph	Phenyl
PI	Phosphatidylinositol
PMB	*para*-Methoxybenzyl
PPh_3	Triphenylphosphine
ppm	parts per million
Py	Pyridine
q	Quartet (NMR spectra)
Quin	5-*O*-(2-Quinolinecarbonyl)
R_f	Retention factor
s	Singlet (NMR spectra)
t	Triplet (NMR spectra)
TB	Tuberculosis
TBAF	Tetrabutylammonium fluoride
TBDPS	*tert*-Butyldiphenylsilyl

TBDPSCl	*tert*-Butyl(chloro)diphenylsilane
Tf_2O	Trifluoromethanesulfonic anhydride
TFA	Trifluoroacetic acid
TfOH	Trifluoromethanesulfonic acid
THF	Tetrahydrofuran
TIPDS	3,5-*O*-Tetraisopropyldisiloxanylidene
TLC	Thin layer chromatography
Tol	*p*-Tolyl
triflic	Trifluoromethanesulfonic
TTBP	2,4,6-Tri-*tert*-butylpyrimidine
WHO	World Health Organization

Chapter 1： Introduction

1.1. 1,2-*cis* Glycofuranosides in Nature

Furanose-containing glycoconjugates are widespread in nature and have been identified as important constituents of glycoconjugates from numerous pathogenic microorganisms, including various bacteria,[1–2] plants,[3] fungi,[4] protozoa[5] and archaebacteria.[6] Because they are present in many microorganisms, especially pathogenic ones, and absent in mammals, furanose-containing glycoconjugates and their derivatives become promising candidates for many new drugs.[7] Recently, the structures of many of these furanose-containing glycoconjugates have been identified.

Among glycofuranosidic bonds, glycofuranosides are of major interest because of their relatively high abundance in nature. There are two types of *O*-glycofuranosides: 1,2-*cis* and 1,2-*trans*. Of these, 1,2-*cis*-furanosides are relevant to this thesis and the discussion below will focus on them. There are two major types of 1,2-*cis*-glycofuranosides, which are, depending on number of carbon atoms in the monosaccharide, 1,2-*cis*-hexofuranosides/hexulofuranosides and 1,2-*cis*-pentofuranosides. Representative examples of common 1,2-*cis*-glycofuranosides are shown in Fig. 1.

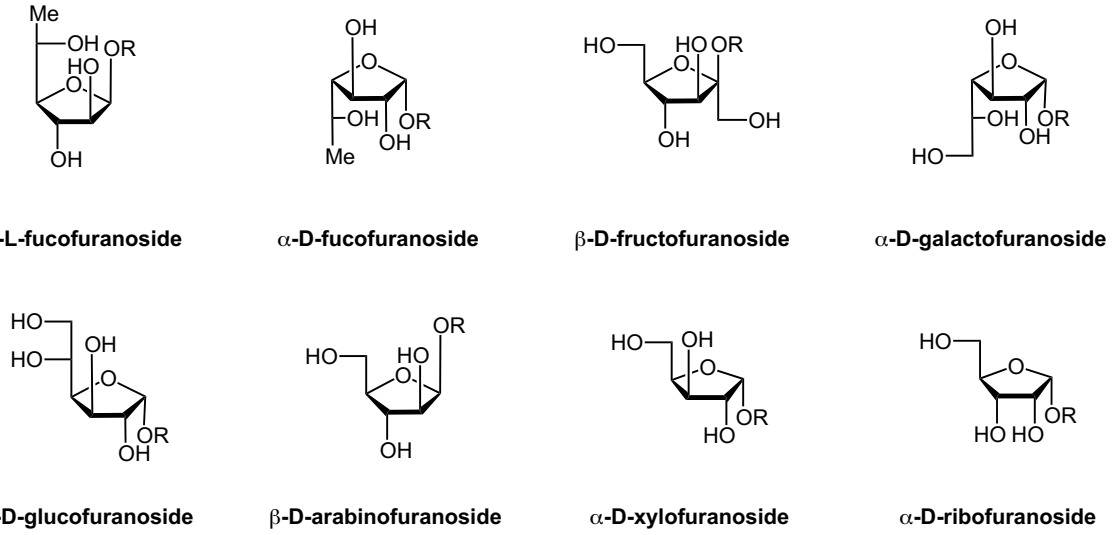
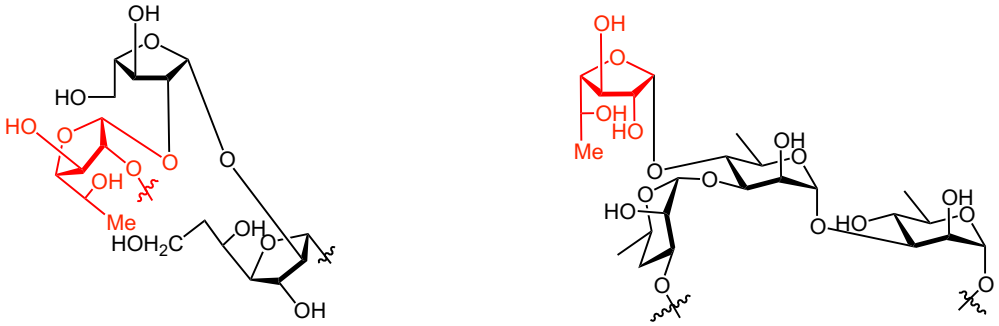


Figure 1 Representative examples of common 1,2-*cis*-glycofuranosides

1.1.1. 1,2-*cis*-Hexofuranosides/Hexulofuranosides in Nature

Although several 1,2-*cis*-hexofuranosides have been identified as constituents of glycoconjugates, those that contain glycosides of fucofuranose (Fuc*f*), fructofuranose (Fru*f*), galactofuranose (Gal*f*) or glucofuranose (Glc*f*)[13–17] are the most common. The 1,2-*cis* configuration of fucofuranosides is found in both L- and D-series. D-Fucofuranose-containing glycoconjugates have been found in several bacteria and all examples identified to date are in the 1,2-*cis* configuration.[8–12] For instance, the repeating unit of a capsular polysaccharide from *Campylobacter jejuni* 176.83, which causes enteritis in human,[8] is a trisaccharide containing α-D-fucofuranose, β-L-arabinose and 6-deoxy-β-D-*altro*-heptose (Figure 1.2). Also, α-D-fucofuranose is also found to be a major constituent of the outer membrane polysaccharide of the phytopathogenic

bacteria *Xanthomonas campestris* and *Pseudomonas syringae*.[9–10] The repeating unit of this polysaccharide is shown in Figure 2.



Trisaccharide repeating unit from *C. jejuni*

Tetrasaccharide repeating unit from *Xanthomonas campestris*

Figure 2 Natural α-D-Fuc*f*-containing glycoconjugates

L-Fuc*f* is the most abundant form of fucofuranose. For example, hygromycin A (Figure 3), an antibiotic isolated from *Streptomyces hygroscopicus* NRRL 2388 that has a broad spectrum of activity against both gram-negative and gram-positive bacteria, contains a 5-dehydro-α-L-fucofuranose residue (Figure 1.3).[18] Another antibiotic, which is produced by *Streptomyces gilvotanareus* and by *Streptomyces collinus* ssp. *Albescens*, is *C*-L-fucofuranosyl compound, named gilvocarcin V or toromycin, depending on the producing species.[19–23]

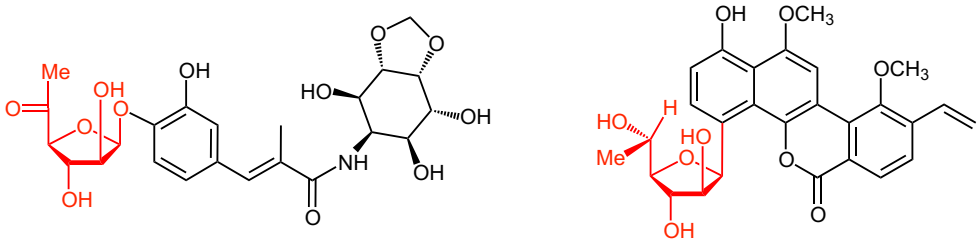


Figure 3 Natural α-L-Fuc*f*-containing glycoconjugates

Among the hexulofuranosides, fructofuranose (Fru*f*) is the most common. Fru*f* residues are found in some bacterial polysaccharides. Only D-fructose has been reported in nature and this monosaccharide usually occurs in the 1,2-*cis* (β)-furanoside forms. For example, Fru*f*-containing glycans (Figure 4) are important constituents in the capsular polysaccharides (CPS) of some strains of *Campylobacter jejuni*, a leading cause of human enteritis.[24] The CPS of the *Campylobacter jejuni* genome sequenced strain NCTC 11168 has a repeating unit that contains fructofuranose branches.[25–26] Additionally, polyfructofuranosides produced by bacteria and plants and can be divided into two types: levan-type and inulin-type species (Figure 4). Levan-type species are composed of β-(2→6) linked Fru*f* residues and inulin-type species are composed of β-(2→1) linked Fru*f* residues.[27]

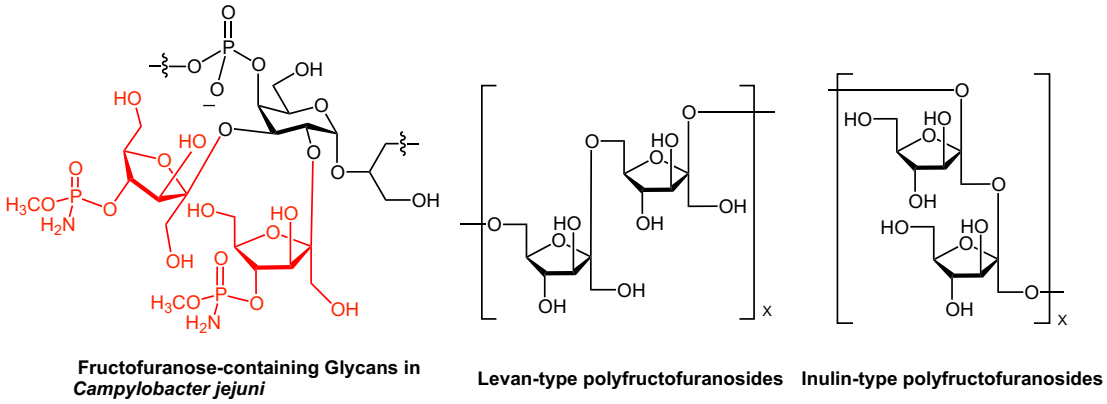
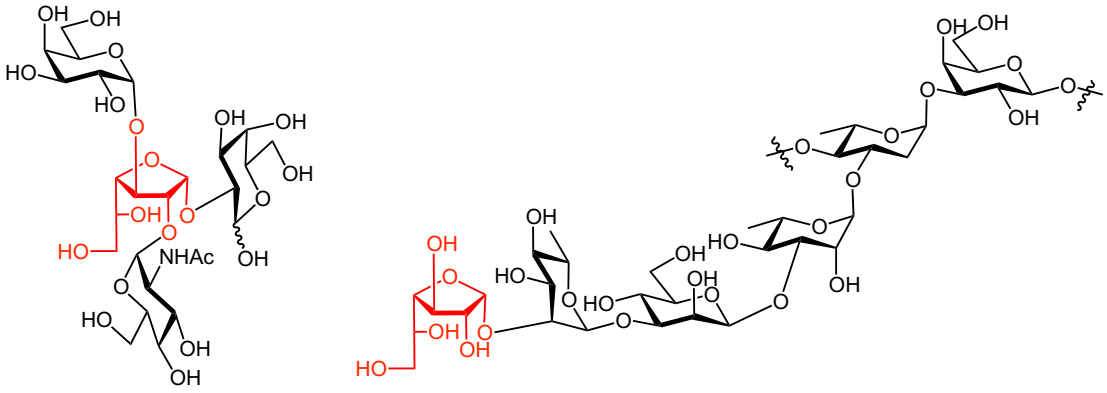


Figure 4 β-D-Fru*f*-containing glycans in nature

Glycoconjugates containing α-D-galactofuranose (Gal*f*) residues are produced by lower organisms. For instance, a cellulose-containing protein complex known as the cellulosome has been isolated from the bacteria *Clostridium thermocellum.*[28] Structural analysis of the cellulosome also revealed a tetrasaccharide unit containing α-D-Gal*f*. In addition, α-D-Gal*f* residues are important constituents of polysaccharides from *Azospirillum irakense* KBC1,[29–30] which is a Gram-negative plant-growth-promoting rhizobacteria. The chemical structure of the polysaccharide chain is composed of the branched hexasaccharide repeating unit (Figure 5).



D-Gal*f* containing fragment of the cellulosome from *Clostridium thermocellum*

Branched hexasaccharide repeating unit from *Azospirillum*

Figure 5 Gal*f*-containing glycans in nature

1.1.2. 1,2-*cis*-Pentofuranosides in Nature

Arabinose exists in all possible ring and absolute configurations in nature: D-arabinopyranose, L-arabinopyranose, D-arabinofuranose and L-arabinofuranose. For the L-form, L-arabinofuranose (Ara*f*) is more common than the pyranose forms. L-Ara*f* usually exists as the 1,2-*trans* (α)-isomers in glycoconjugates from the plant kingdom, where it is an important component of pectins, hydroxyproline-rich glycoproteins and arabinoxylans.[31–33]

For the D-form of this monosaccharide, D-Ara*f* is the most widespread in nature. D-Ara*f* is found in 1,2-*cis* (β) and 1,2-*trans* (α) forms in carbohydrates present in the cell wall of the Actinomycetes family, such as *Rhodococus, Nocardia* and *Mycobacteria*. Among these organisms are two important human pathogens, *Mycobacterium leprae*

and *Mycobacterium tuberculosis,* which cause human leprosy and tuberculosis, respectively. The mycobacterial cell wall consists of lipids and polysaccharides, including two major components: arabinogalactan (AG) and lipoarabinomannan (LAM). A schematic drawing of the AG is presented in Figure 6.[34−36] The arabinan includes about 70 D-Ara*f* residues. The major linear arabinan chain is attached via α-(1→5)-linkages and the arabinan also contains α-(1→3)-linked and β-(1→2)-linked residues. A key motif in the AG is hexasaccharide **1**, which contains two 1,2-*cis* (β)-D-Ara*f* residues. This motif is often esterified with mycolic acids.

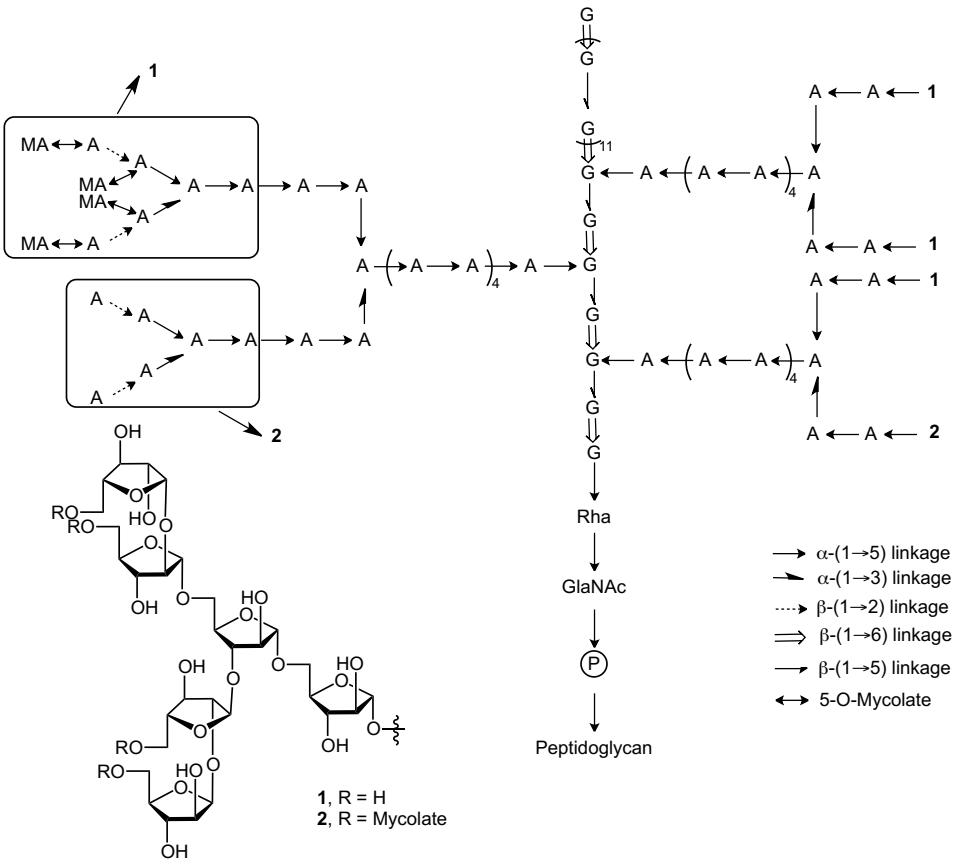


Figure 6 Schematic representation of mycobacterial arabinogalactan (AG)

The arabinan domain of LAM is similar to that of the AG and it also contains hexasaccharide **1** at the nonreducing termini. In addition, LAM also contains an unusual thiosugar, 5-deoxy-5-methylthio-xylofuranose (MTX), which is attached to a mannose reside in LAM via an α-(1→4) linkage (Figure 7). This is another example of a 1,2-*cis*-furanoside linkage.

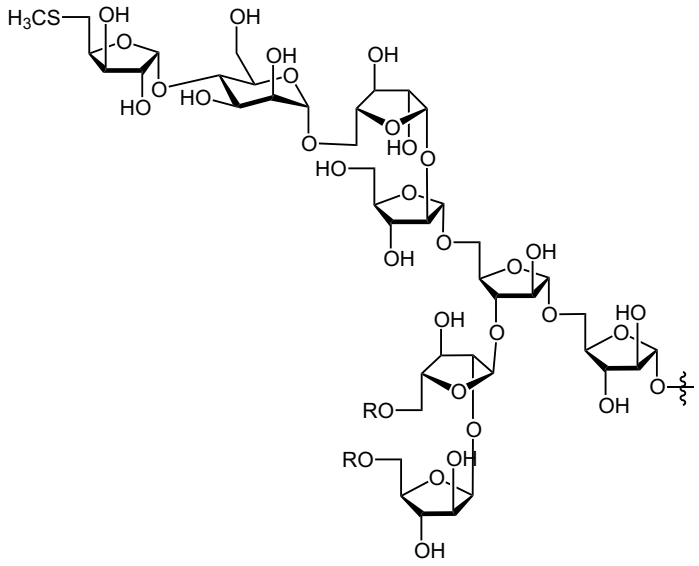


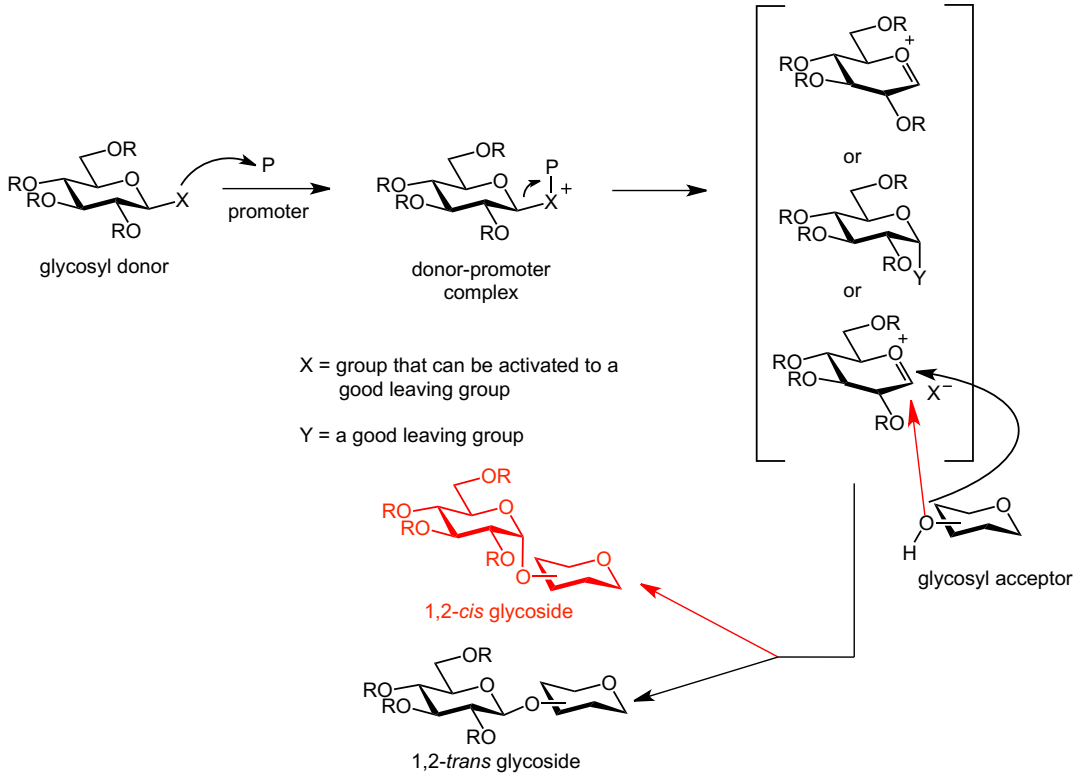
Figure 7 MTX-containing fragment of LAM

1.2. The difficulties and methodologies for stereoselective 1,2-*cis*-furanosylation

1.2.1. The difficulties of stereoselective 1,2-*cis*-glycofuranosylation

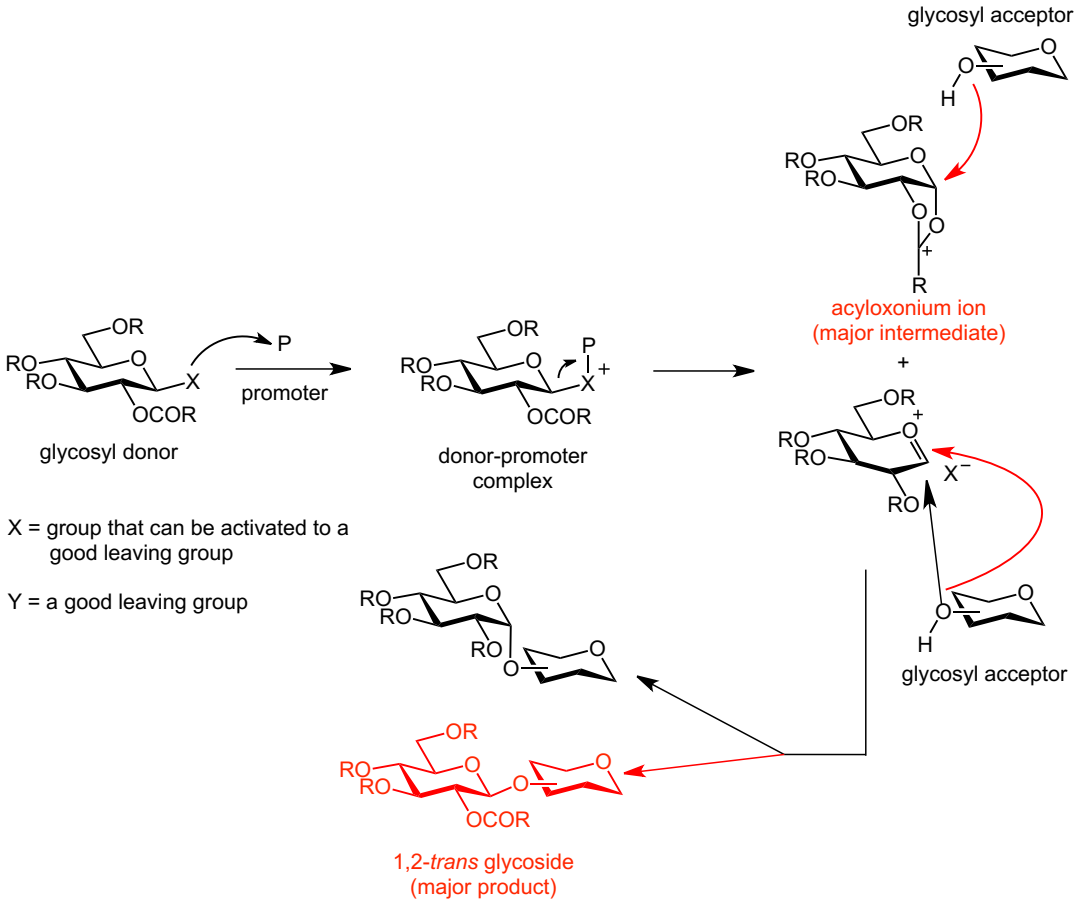
Glycosylation is the most important reaction in the carbohydrate chemistry. The reaction involves the coupling of a glycosyl acceptor and a glycosyl donor in the presence of a promoter or activator, to generate a glycosidic bond. The general

mechanistic pathway for a glycosylation is shown in Scheme 1. Upon activation, the donor forms an electrophilic intermediate, which is often depicted as an oxacarbenium ion. The nature of the electrophilic intermediate is still debatable and the subject of current study, but it is almost certainly a species that exists as an ion-pair or, in some cases, a covalent species.[36–38] The glycosyl acceptor can then attack either from the bottom or top face of the ring, to give rise to 1,2-*cis*- or 1,2-*trans*-glycosides. The stereoselectivity of a glycosylation is influenced by several factors, such as the anomeric effect, the protecting group on O-2 of the glycosyl donor, the solvent, the structure of both donor and the acceptor and the glycosylation protocol.[39]



Scheme 1 General glycosylation mechanism

1,2-*trans*-Glycosides can be formed relatively straightforwardly via the neighboring group participation effect, to form a dioxalenium ion intermediate, by using donors with an acyl substituent on O-2 (Scheme 2). The glycosyl acceptor can only attack from the top face because the bottom face is blocked by the dioxalenium ion. This leads to the formation of 1,2-*trans*-linkages with high stereoselectivity.



Scheme 2 General glycosylation mechanism with a participating group at C-2

The formation of 1,2-*cis*-glycosides is typically much more difficult, especially for the 1,2-*cis*-furanosides. It is necessary to synthesize 1,2-*cis*-glycosides using a

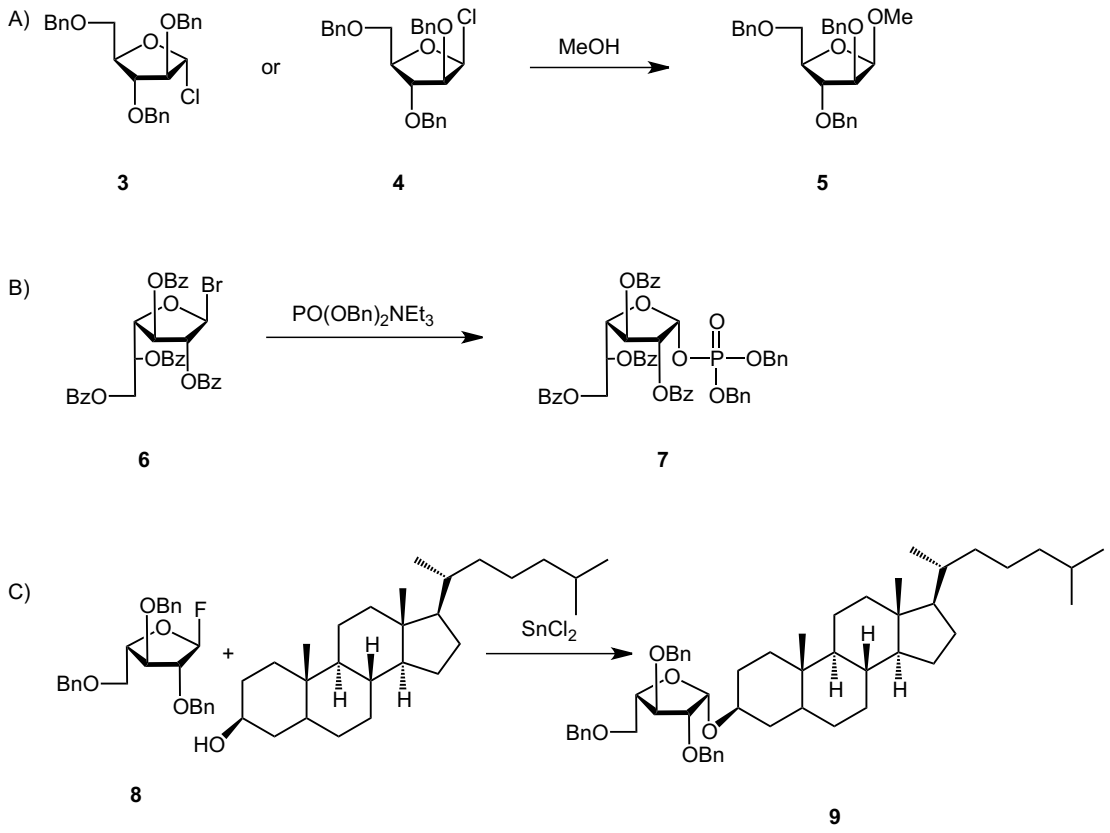
non-participating group in the donor, but often non-participating groups do not provide access to the 1,2-*cis*-glycosides with good stereoselectivity. Also, in comparison to the synthesis of 1,2-*cis*-pyranosides, the formation of 1,2-*cis*-furanosides is more challenging due to the conformational flexibility of the five-membered ring and the lack of anomeric effect.

1.2.2. Methods for the stereoselective synthesis of 1,2-*cis*-furanosides

1.2.2.1 Glycosyl halide donors

In early reports by Fletcher and Glaudemans,[44] the preparation of 1,2-*cis*-furanosides was achieved using glycosyl halide donors with non-participating groups (e.g., benzyl). For example, methanolysis of 2,3,5-tri-*O*-benzyl-*α*-D-arabinofuranosyl chloride (**3**) or 2,3,5-tri-*O*-benzyl-*β*-D-arabinofuranosyl chloride (**4**) generated methyl 2,3,5-tri-*O*-benzyl-*β*-D-arabinofuranoside (**5**) with high β-selectivity (Scheme 3A). The authors proposed that the reaction proceeds via an S_N1 ion-pair mechanism. This approach can also be used in the nucleophilic substitution of furanosyl halide donors with phosphates.[45] Treatment 2,3,5,6-tetra-*O*-benzoyl-β-D-galactofuranosyl bromide (**6**) with triethylammonium dibenzyl phosphate affords dibenzyl 2,3,5,6-tetra-*O*-benzoyl-α-D-galactofuranosyl phosphate (**7**) (Scheme 3B). On the other hand, Mukaiyama and co-workers proposed this reaction proceeded via an S_N2 mechanism by using furanosyl fluorides as donors.[46] The β-linked L-arabinofuranoside (**9**) was generated as the major product when 2,3,5-tri-*O*-benzyl-α-L-arabinofuranosyl

fluoride (**8**) was treated with 3β-cholestanol in the presence of stannous chloride (Scheme 3C). However, this method only proceeded smoothly with simple primary alcohols or phosphates. When this approach was extended to synthesize disaccharides, only the hydrolyzed donor was formed.[47]

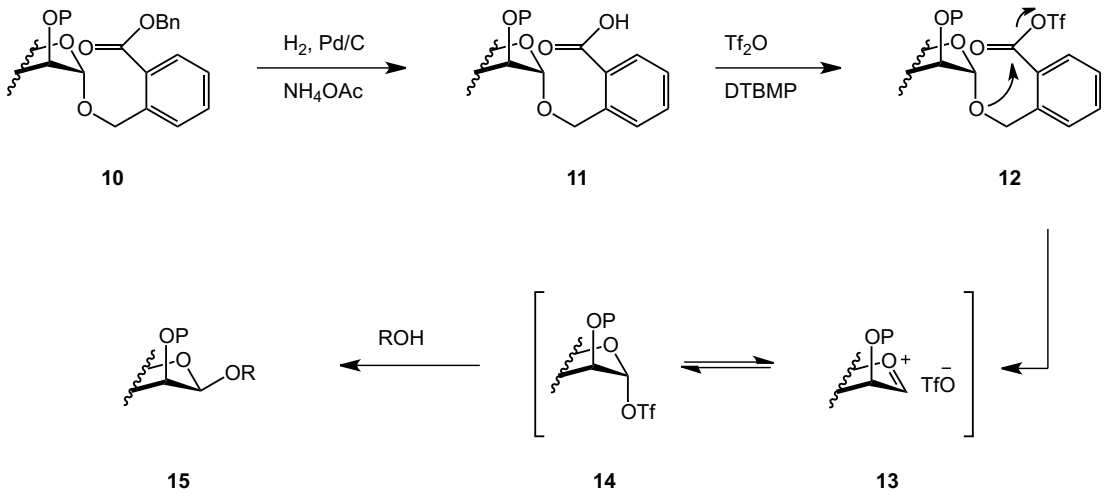


Scheme 3 Synthesis of 1,2-*cis*-glycofuranosides from glycosyl halides[44–46]

1.2.2.2. Use of 2-(benzyloxycarbonyl)-benzyl (BCB) glycoside donors

Kim and co-workers have developed a latent–active glycosylation methodology using 2-(benzyloxycarbonyl)-benzyl (BCB) glycosides for the highly efficient

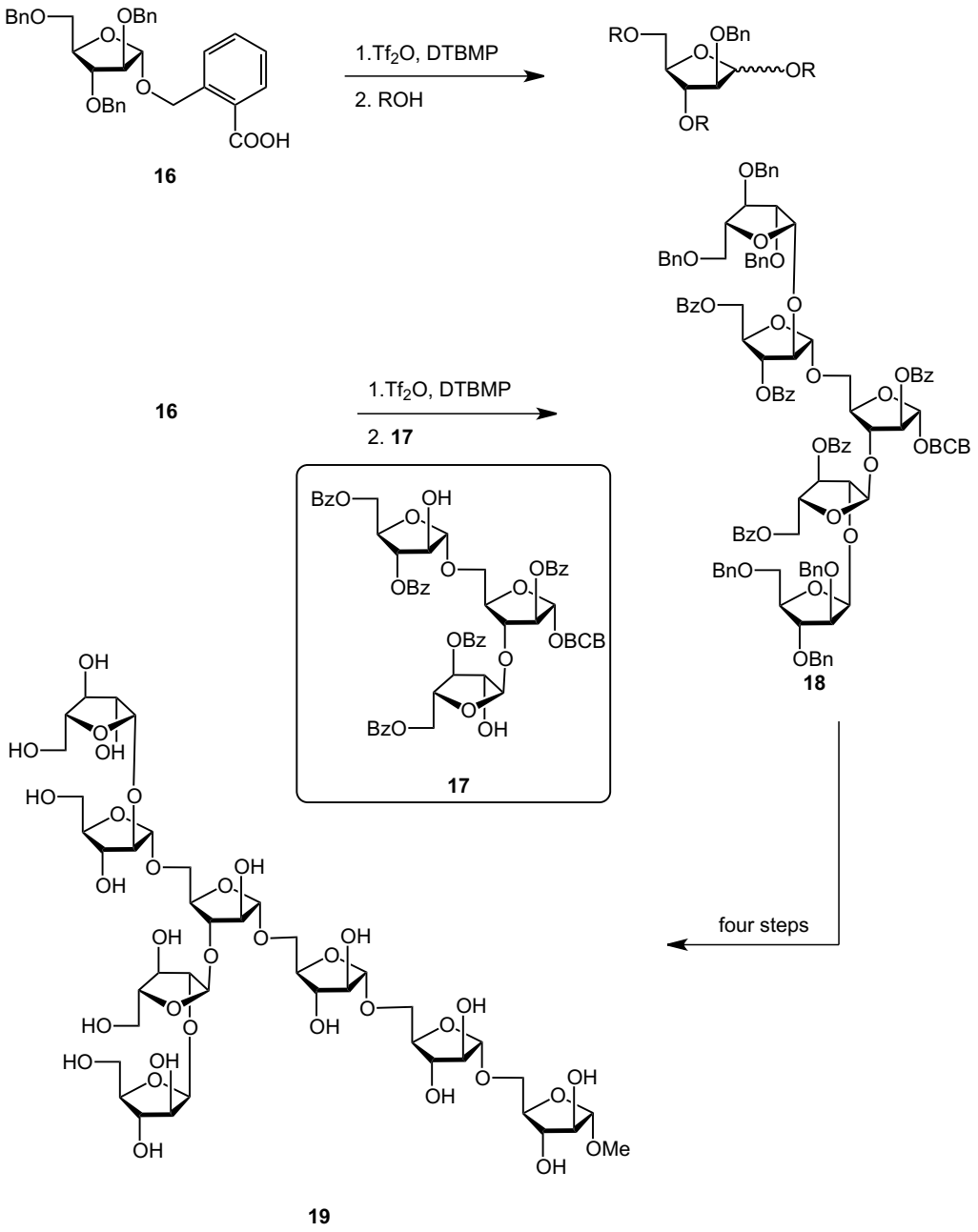
stereoselective synthesis of β-mannopyranosides and 2-deoxy glycosides[48] (Scheme 4). A 2-carboxybenzyl glycosyl donor (e.g., **11**) was obtained from 2-(benzyloxycarbonyl)-benzyl (BCB) glycosides **10** upon treatment with hydrogen, palladium on carbon and ammonium acetate by chemoselective hydrogenolyisis of the benzyl ester. Treatment of **11** with triflic anhydride and 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP) leads to the formation of triflate ester **12**. Then, spontaneous lactonization of **12** affords oxacarbenium ion **13** and glycosyl triflate **14**, which reacts with glycosyl acceptors to generate the glycoside **15**.



Scheme 4 Synthesis of β-mannopyranosides via 2-(hydroxycarbonyl)-benzyl donors[48]

Kim's group extended this methodology to synthesize β-arabinofuranosides.[49] Reaction of arabinofuranosyl donor **16** (Scheme 5) with various acceptors following their protocol led to the highly selective formation of β-arabinofuranosides. The synthesis of an octaarabinofuranoside (**19**), a fragment of mycobacterial LAM, was

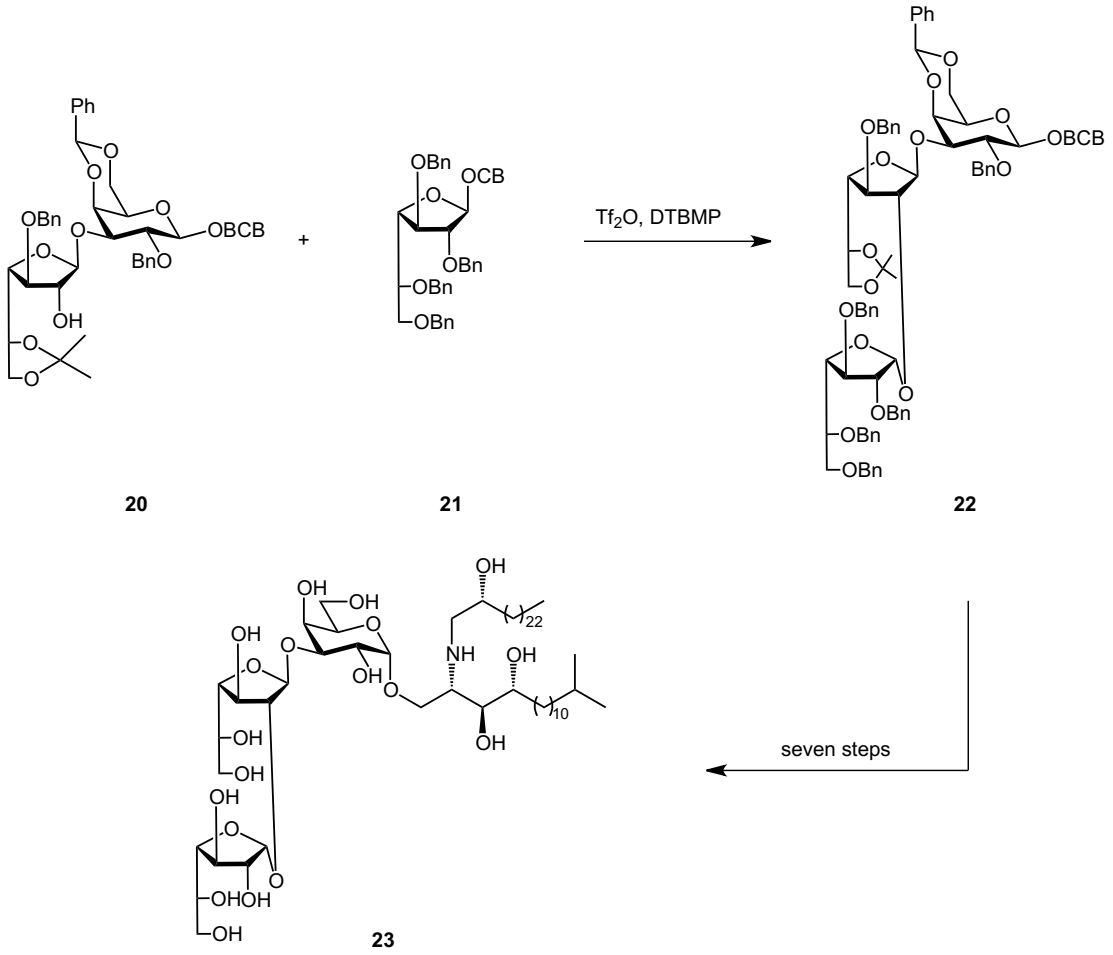
achieved using this latent–active glycosylation method. The key step in the synthesis of **19** was the reaction of trisaccharide acceptor **17** with **16**, which proceeded smoothly to yield the pentasaccharide **18** with complete β-selectivity. The desired octaarabinofuranoside **19** was generated from **18** in four steps.



Scheme 5 2-CB glycoside-mediated direct β-D-arabinofuranosylation and the synthesis of an octaarabinofuranoside motif (**19**) from mycobacterial LAM[49]

In addition, The CB glycoside method was extended to α-stereoselective galactofuranosylation to synthesize agelagalastatin (**23**, Scheme 6), an antineoplastic

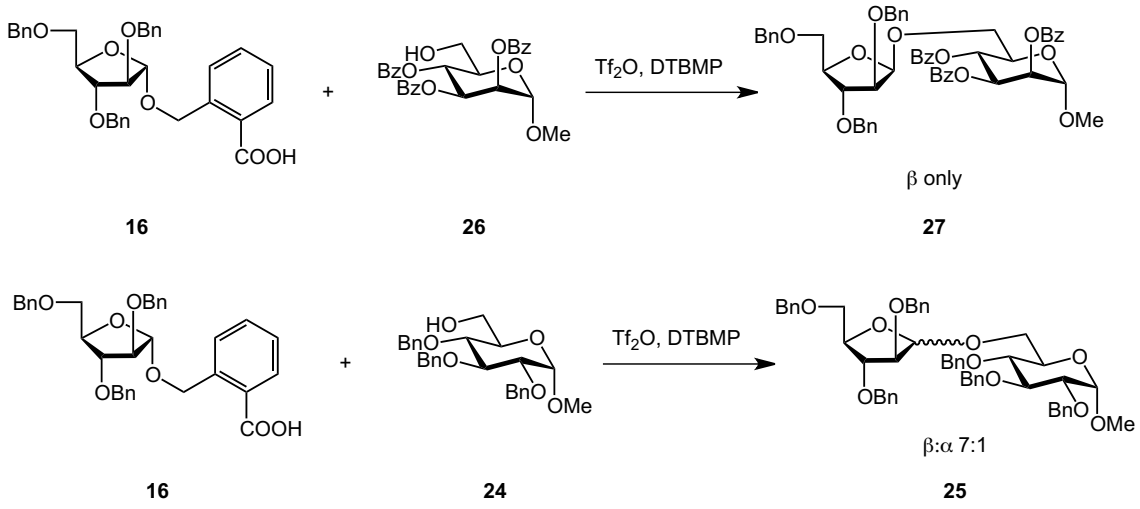
glycosphingolipid.[50] Glycosylation of disaccharide **20** with galactofuranosyl donor **21** was carried out by treatment with Tf_2O and DTBMP to give only the α-trisaccharide **22** in 91% yield. Agelagalastatin was achieved in seven steps from **22** in 45% overall yield.



Scheme 6 2-CB glycoside-mediated direct α-D-galactofuranosylation used in the synthesis of agelagalastatin[50]

However, a limitation of this method is that the stereoselectivity is acceptor-dependent. Higher β-selectivity was observed with glycosyl acceptors having

electron-withdrawing benzoyl protecting groups (e.g., **24**, Scheme 7) than those carrying benzyl protecting groups (e.g., **26**).



Scheme 7 Acceptor-dependent stereoselective arabinofuranosylation using 2-CB glycoside donors[48]

1.2.2.3. Intramolecular aglycone delivery (IAD) method

Often the use of specific protecting groups can control the stereoselectivity of a glycosylation reaction. For example, when an ester group is on O-2 of a glycosyl donor, 1,2-*trans*-glycosides are formed due to neighboring group participation during the reaction (see above). In contrast, 1,2-*cis*-glycosides can be generated by a two-step tethering–glycosylation process, which is called intramolecular aglycon delivery (IAD)[51] (Figure 8). A temporary tether is introduced in the first step between the glycosyl acceptor and glycosyl donor. Then, intramolecular glycosylation is initiated,

which is proposed to proceed via a five-member ring transition state to yield the 1,2-*cis*-glycoside.

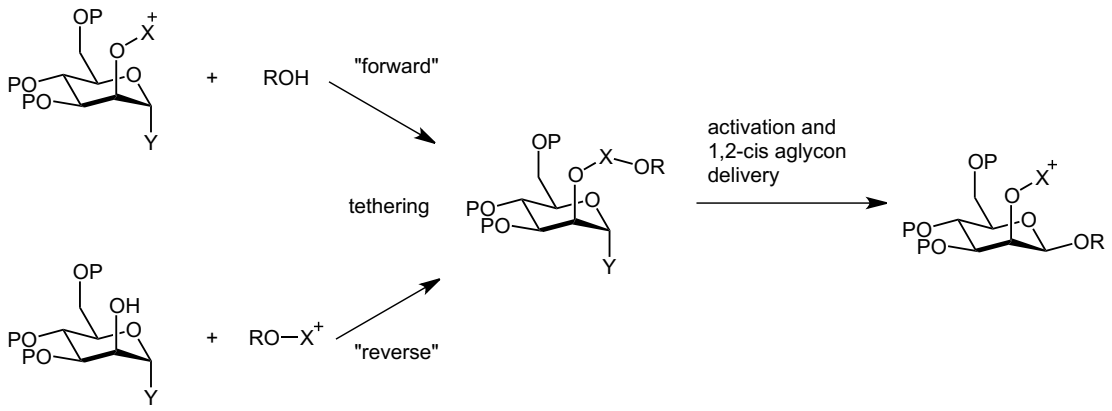
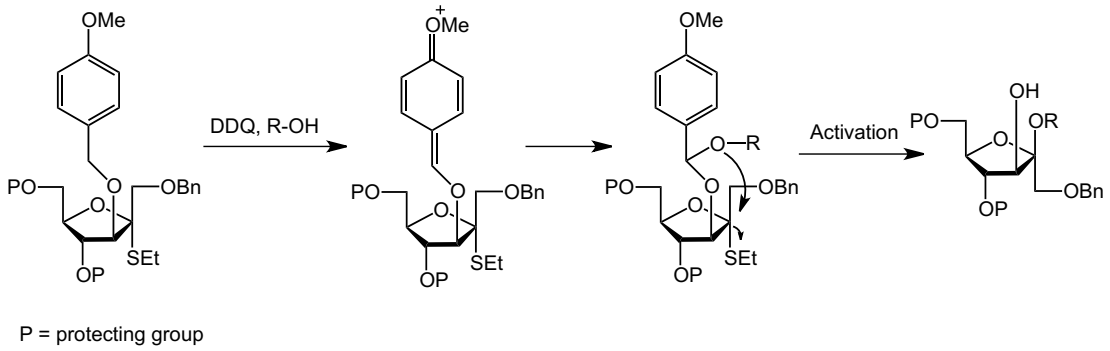


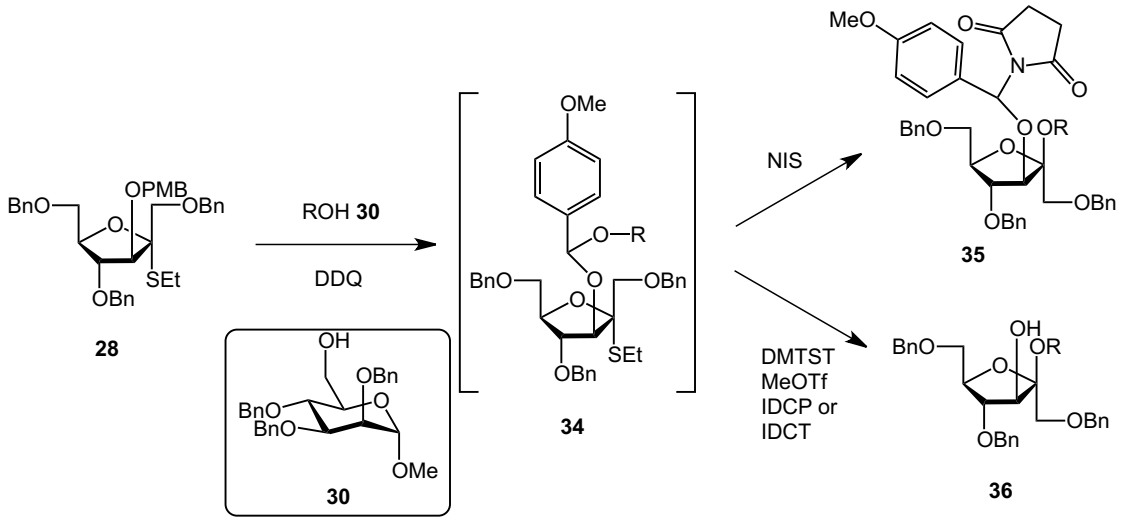
Figure 8 1,2-*cis* Glycosylation using intramolecular aglycon delivery[51]

The most common IAD method uses *para*-methoxybenzyl (PMB) acetals as the tether (PMB-IAD).[78] In 1996, Krog-Jensen and Oscarson reported the first application of this approach to the synthesis of β-fructofuranosides[52–53] (Scheme 8). The PMB ether precursor was oxidized to the corresponding oxacarbenium ion upon treatment with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ). The oxacarbenium ion then reacted with the glycosyl acceptor to generate the acetal. Treatment of this crude mixture with a glycosylation activator gave the 1,2-*cis* glycoside.



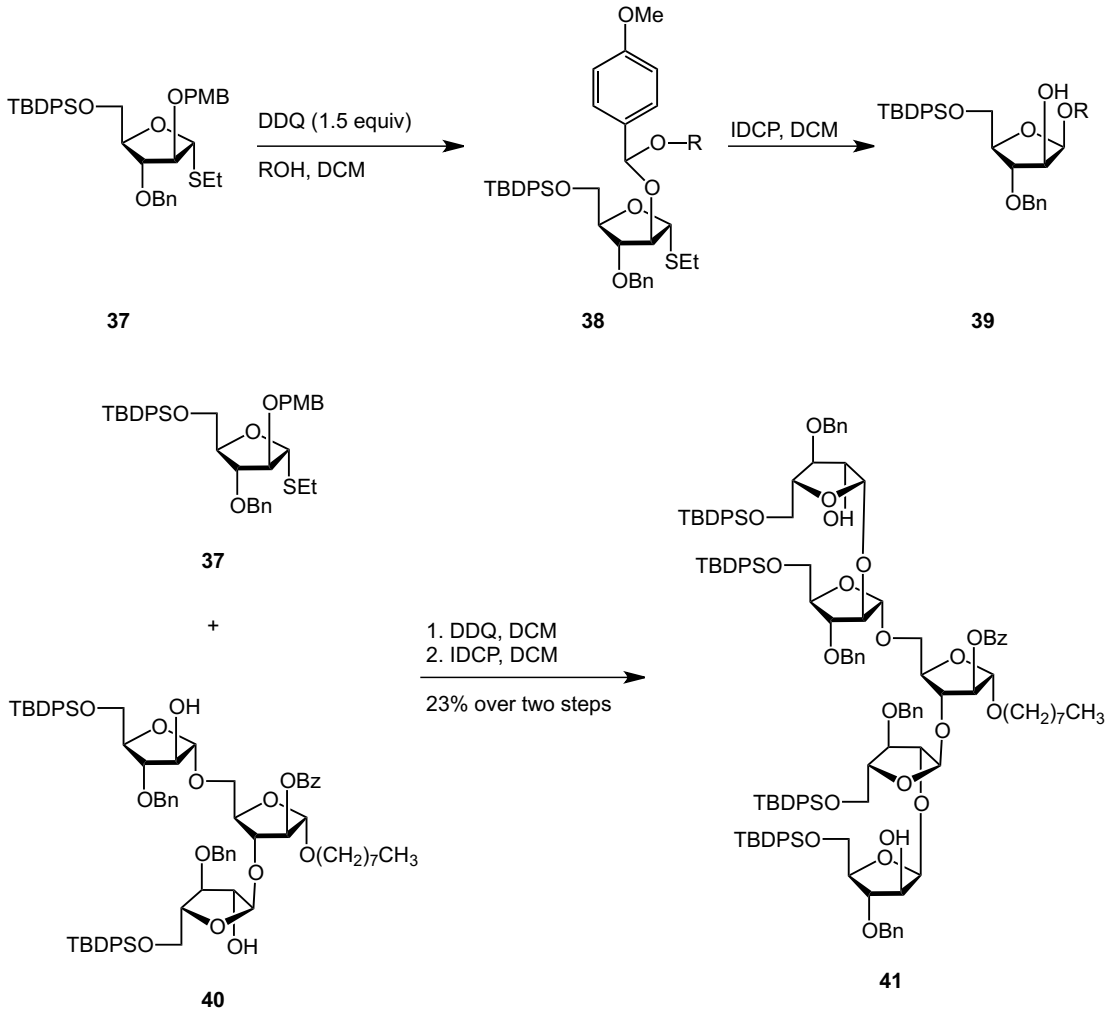
Scheme 8 General approach to synthesize β-fructofuranosides by PMB-IAD[52]

In Oscarson's paper (Scheme 9),[53] it was reported that oxidation of the PMB group in **28** forms an oxacabenium ion, which is captured by a glycosyl acceptor (**30** or **31**) to generate the acetal **34**. The formation of the β-fructofuranoside can be achieved via an intramolecular glycosylation, upon treatment with thiophilic promoters. If dimethylthiomethyl sulfonium trifluoromethanesulfonate (DMTST), iodonium collidine triflate (IDCT) or iodonium dicollidine perchlorate (IDCP) were used, the β-linked fructofuranosides **36** were produced in different yields. However, the reaction conditions were very sensitive both during the formation of acetal **34** and its activation. The optimization of the glycosylation conditions, especially the promoter, had to be performed independently for different acceptors. If *N*-iodosuccinimide (NIS) was used as the promoter, the NIS adduct **35** was formed; this compound was stable and could not be hydrolyzed.



Scheme 9 Synthesis of β-D-fructofuranosides using PMB-IAD[53]

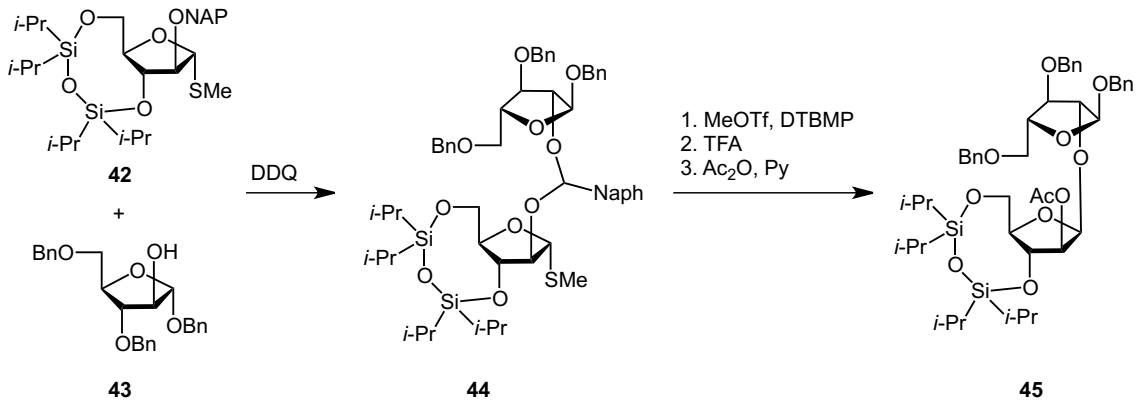
Later, Prandi and co-workers used the PMB-IAD methodology for the construction of β-arabinofuranoside linkages.[54–57] Tethering of the 2-*O*-PMB protected arabinose donor **37** (Scheme 10) to different glycosyl acceptors upon treatment with DDQ gave the acetal **38**, which could be purified by chromatography. Activation of **38** with IDCP resulted in the formation of only β-arabinofuranosides in moderate yield.



Scheme 10 β-Arabinofuranosylation with PMB-IAD and its application to a pentasaccharide[54]

Prandi's group has applied this methodology to the synthesis of a pentasaccharide fragment from mycobacterial AG and LAM. Bis-β-arabinosylation of the 2-*O*-PMB protected arabinose donor **37** and trisaccharide acceptor **40** led to the formation of pentasaccharide **41**. Although only the desired bis-β-arabinosylated pentasaccharide **41** was formed, the glycosylation yield was disappointing, only 23%.

Recently, Ito and co-workers have developed IAD methodology using a napthylmethyl ether at O-2 (NAP-IAD) to synthesize β-arabinofuranosides (Scheme 11).[58–59] Formation of **44** from 2-*O*-NAP protected thioarabinofuranosyl donor **42** and acceptor **43** proceeded smoothly. Subsequent IAD, acidic workup and acetylation lead to the formation of the β-arabinofuranoside **45** in good yield. They also demonstrated the utility of NAP-IAD as the key step in the synthesis of a docosasaccharide (22-residue) arabinan motif of mycobacterial AG.[58]



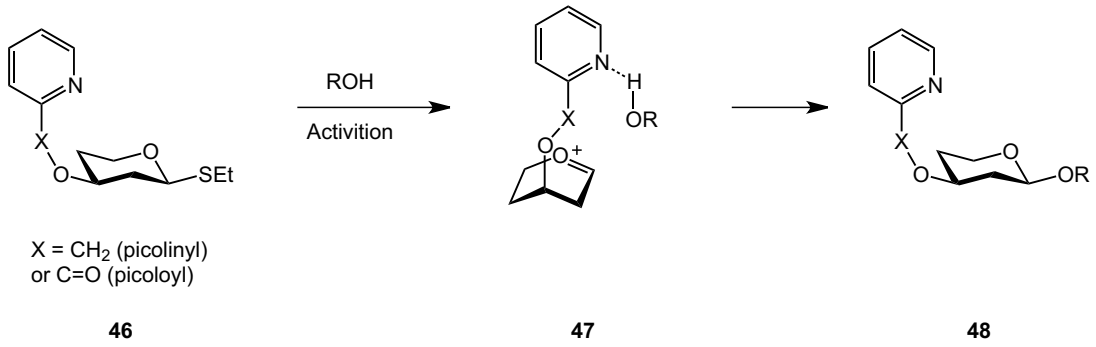
42 + **43** → **44** → **45**

Scheme 11 β-Arabinofuranosylation using NAP-IAD[58]

1.2.2.4. Hydrogen-bond-mediated aglycone delivery (HAD)

Demchenko and Yasomanee have developed the hydrogen-bond-mediated aglycone delivery (HAD) method for the synthesis both 1,2-*cis*- and 1,2-*trans*-linkages[60] (Scheme 12). The basic concept of this strategy depends on the fact that glycosyl donors and acceptors can form intermolecular hydrogen bonds that can influence the access of the acceptor to the donor. This can lead to high or complete

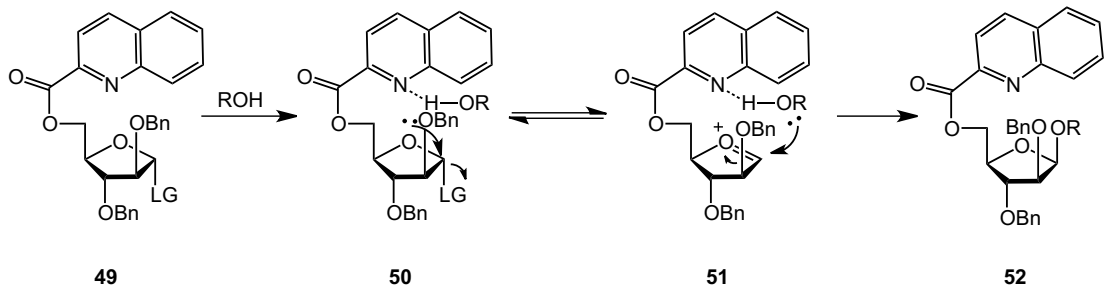
facial selectivity in glycoside synthesis. The approach has been applied to β-galactopyranosides, α- and β-glucopyranosides, β-rhamnopyranosides and β-mannopyranosides.[60] Usually, a 3-, 4- or 6-*O*-picolinyl or picoloyl group is installed (e.g., **46**) into the donor. During the reaction, the nitrogen can hydrogen bond with the acceptor (**47**), directing it to attack from the *syn* position with respect to protecting group. The result is a high yielding and highly stereoselective glycosylation (**48**).



Scheme 12 Hydrogen-bond-mediated aglycone delivery (HAD) method developed by Demchenko[60]

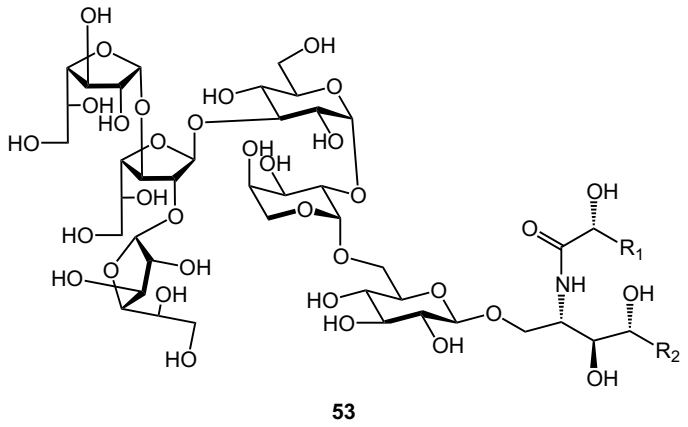
Later, Yang and co-workers applied the HAD methodology to the construction of β-arabinofuranosides[61] (Scheme 13). The acceptor can be tethered via a hydrogen-bond to the 5-*O*-(2-quinolinecarbonyl) (Quin) substituted arabinofuranosyl donor (**49**) to form intermediate **50**. Upon subsequent activation of the thioglycoside, the acceptor will attack from the β-side of the oxacarbenium ion (**51**), which leads to the

formation of β-arabinofuranoside **52**. The use of **49** provides the desired products with excellent β-selectivity in high yields, for a wide range of acceptor substrates.



Scheme 13 β-Arabinofuranosylation using the 5-*O*-(2-quinolinecarbonyl) substituted arabinofuranosyl donor **49**[61]

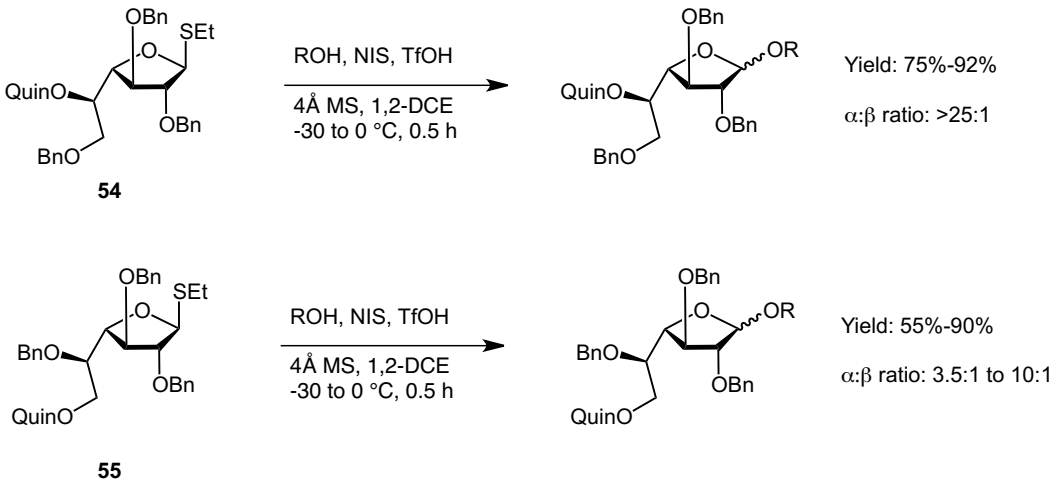
Yang and co-workers have also established a highly stereoselective methodology for the synthesis 1,2-*cis*-(α)-D-galactofuranosides using 5-*O*-Quin-carrying thioglycoside donors.[62] In this regard, Yang *et al.* achieved in 2016 the first total synthesis of the marine glycolipid vesparioside B (**53**, Figure 9), a novel hexaglycosylated glycosphingolipid from the Caribbean sponge *Spheciospongia vesparia*.[63]



53

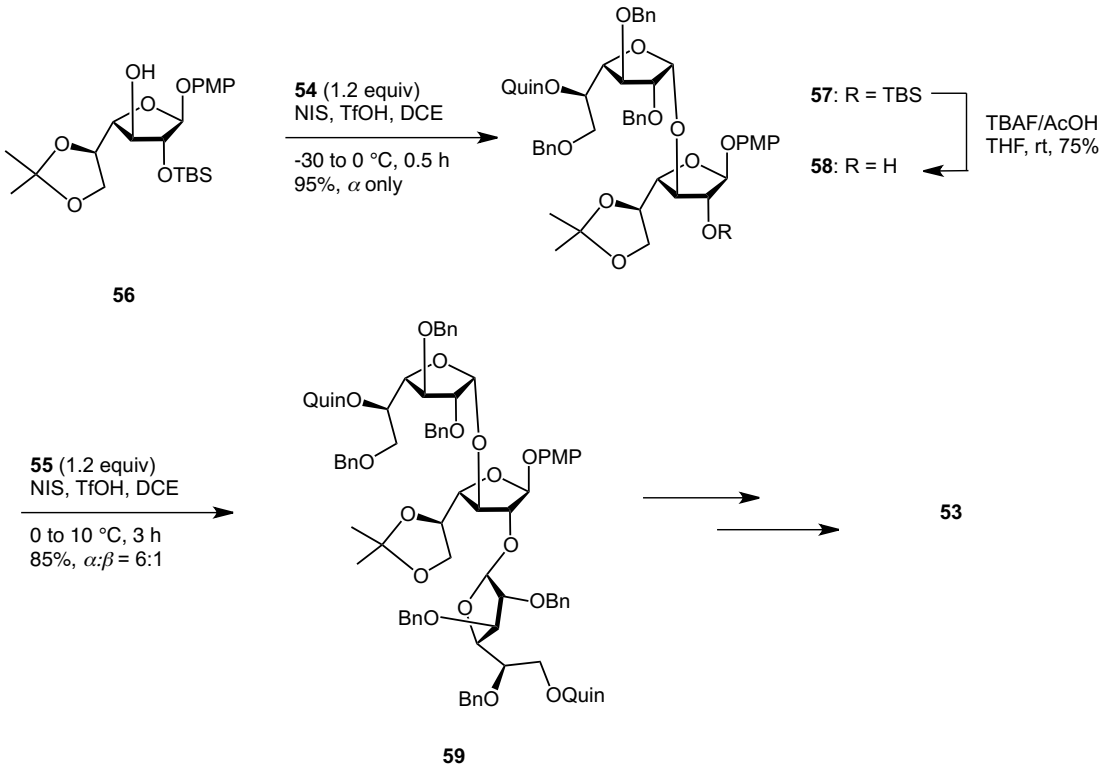
Figure 9 Structure of the marine glycolipid vesparioside B[63]

In the course of developing a synthesis of **53**, both the 5- and 6-*O*-Quin-substituted Gal*f* thioglycoside donors (**54** and **55**, Scheme 14) were prepared and their glycosylation steroselectivity was evaluated with diverse acceptors. The reaction was promoted by NIS and TfOH in 1,2-dichloroethane (DCE) (Scheme 14). The glycosylation of both donors showed 1,2-*cis*-stereoselectivity, but the 5-*O*-Quin-substituted donor (**54**) was superior to 6-*O*-Quin-substituted donor (**55**). Both higher yields and α-selectivity were observed.



Scheme 14 Glycosylation of Quin-substituted Gal*f* thioglycoside donors[63]

Next, this method was used a key step in the synthesis of **53** (Scheme 15). Galactofuranose derivative **56** was reacted with 5-*O*-Quin-substituted Gal*f* thioglycoside donor **54** to afford disaccharide **57** in excellent yield and with high α-selectivity. Subsequent removal of the *tert*-butyldimethylsilyl (TBS) group by treatment with tetra-*n*-butylammonium fluoride (TBAF) gave the disaccharide acceptor **58**, which was coupled with the 6-*O*-Quin-equipped building block **55** to afford trisaccharide **59**. Complete deprotection of **59** provided **53**.

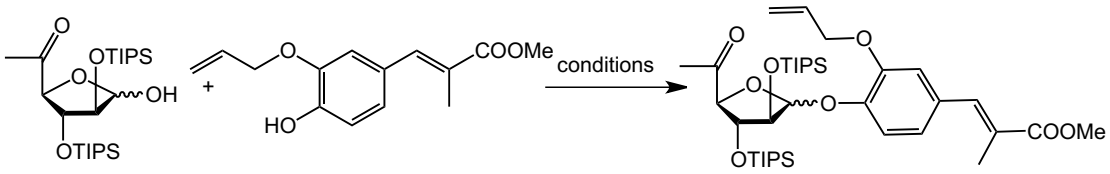


Scheme 15 Total synthesis of vesparioside B[63]

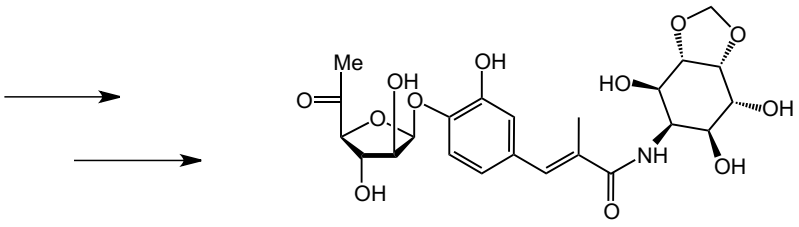
1.2.2.5. Mitsunobu glycosylation

Reducing sugars (1-hydroxy sugars) can be successfully employed to form the 1,2-*cis*-furanosides under Mitsunobu conditions. For example, Donohoe *et al.* have reported a method for synthesizing hygromycin A (**29**) by using the Mitsunobu glycosylation between furanose reducing sugar (**60**) and phenol (**61**) (Table 1).[64] The optimization showed that the α/β ratio varied significantly depending on the reaction solvent. Toluene was the best choice and the desired β-isomer was obtained in 83% yield with high stereoselectivity when the reaction was performed at 60 ˚C with slow addition of diisopropyl azodicarboxylate (DIAD).

Table 1 Optimization of Mitsunobu glycosylation in the synthesis of hygromycin A[64]



60 **61** **62**



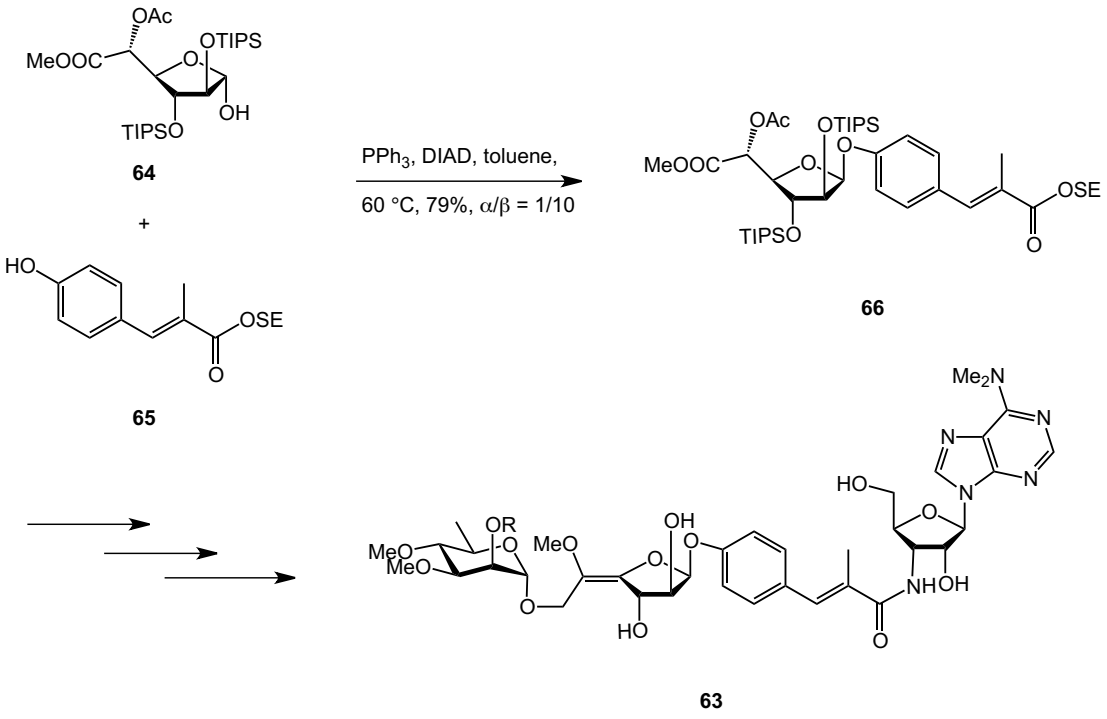
29

Entry	Conditions	**60** (α/β ratio)	Yield of **62** (α/β)
1	DIAD, PPh_3, THF, RT	83:17	47% (40/60)
2	DIAD, PPh_3, CH_2Cl_2, RT	86:14	68% (29:71)
3	DIAD, PPh_3, toluene, RT	86:14	80% (25:75)
4	DIAD, PPh_3, toluene, 60 ˚C	86:14	75% (17:83)
5	DIAD, PPh_3, toluene, 60 ˚C	86:14	83% (10:90) [a]
6	ADDP, PBu_3, toluene, RT	86:14	69% (100:0)

[a]. slow addition of DIAD

In similar work, Yu and co-workers completed the total synthesis of the nucleoside antibiotic A201A (**63**) by using Mitsunobu glycosylation to realize the 1,2-*cis*-furanosidic linkage.[65] The desired 1,2-*cis*-glycoside **66** was generated in 79%

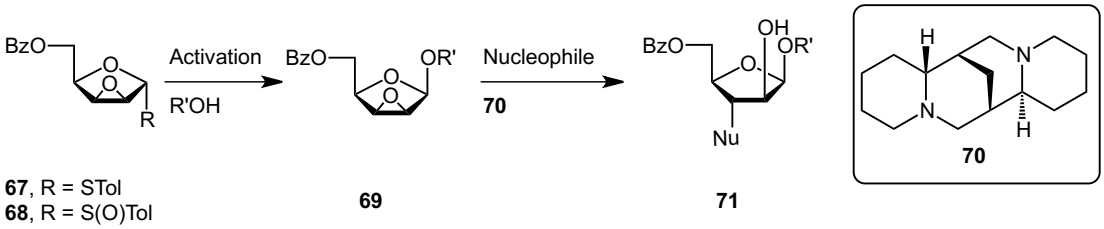
yield with excellent β-selectivity under optimized Mitsunobu glycosylation conditions. Finally, **63** was obtained from **66** in several steps.



Scheme 16 Total synthesis of A201A

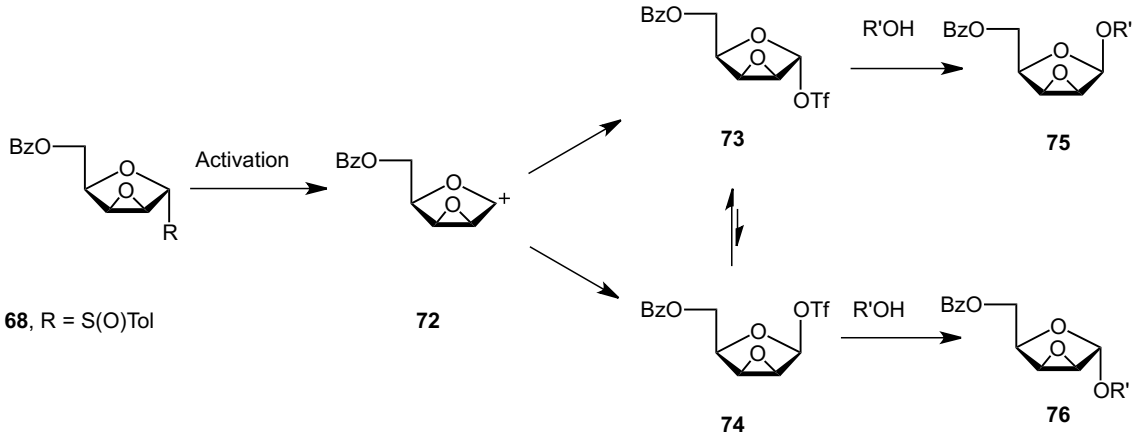
1.2.2.6. 2,3-Anhydrosugars

Lowary and co-workers have reported a methodology for synthesizing 2,3-anhydro-β-lyxofuranosyl glycosides and β-arabinofuranosides using epoxy thioglycoside **67** (Scheme 17) and glycosyl sulfoxides **68** as glycosylating agents.[66−67] Glycosylation of a range of alcohols and subsequent opening of the epoxide ring, afforded β-arabinofuranosides **71** in excellent yields. Regioselective opening of the epoxide by nucleophiles required lithium alkoxides and the use of (−)-sparteine (**70**).



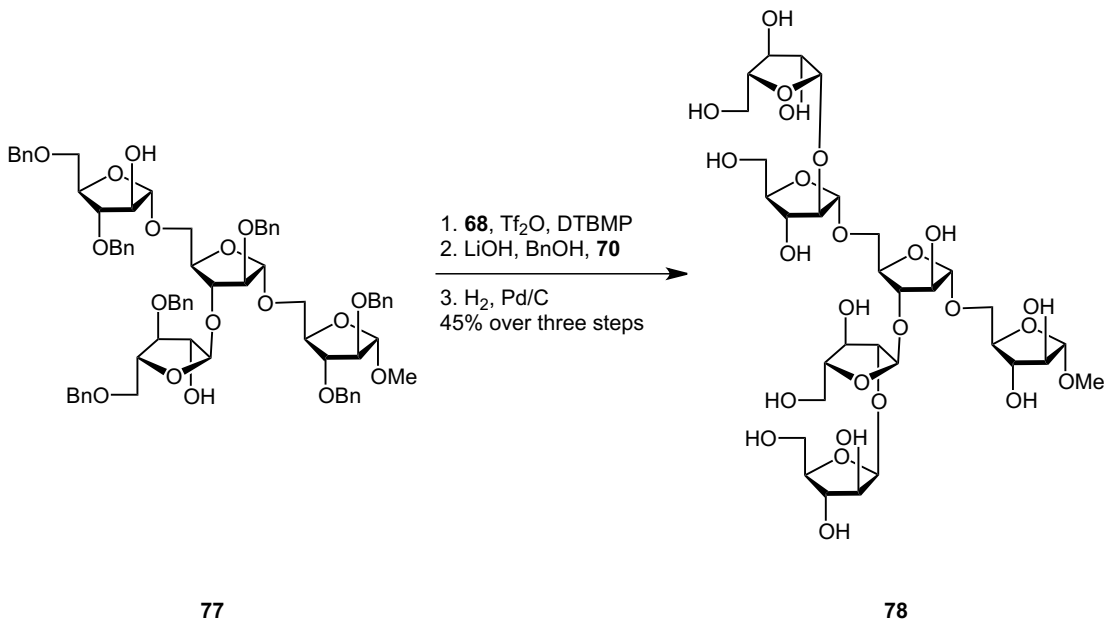
Scheme 17 Synthesis of 1,2-*cis* arabinofuranosides via 2,3-anhydrosugars[66]

Studies were carried out to understand the selectivity of the glycosylation with the glycosyl sulfoxide donor **68**. It was demonstrated that treatment of **68** (Scheme 18) with triflic anhydride led to the stereoselective formation of an α-glycosyl triflate intermediate **73**, which predominated over the β-glycosyl triflate intermediate **74**. Formation of the β-glycoside **75** resulted from an S_N2-like displacement of **73** by the acceptor alcohol.[66]



Scheme 18 Proposed mechanism for glycosylation of 2,3-anhydrosugar sulfoxide **68**[66]

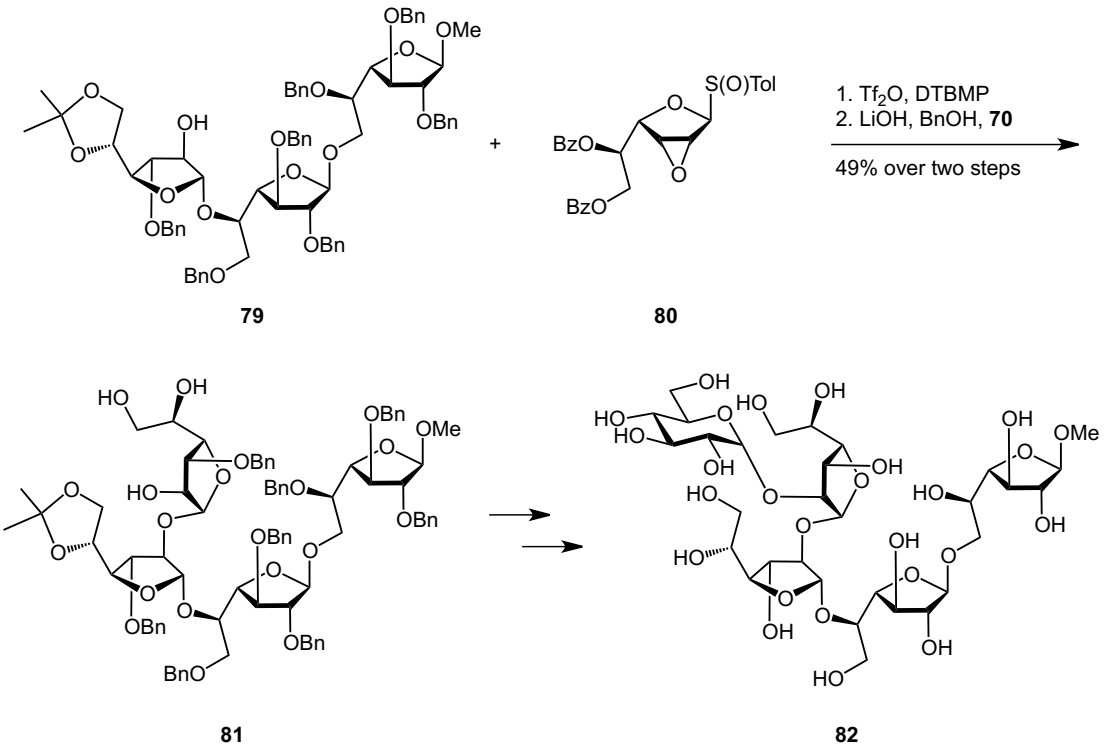
To demonstrate the utility of this methodology, the method was applied successfully to arabinofuranosyl hexasaccharide **78** (Scheme 19).[67]



77 **78**

Scheme 19 Synthesis of the hexasaccharide **78** via 2,3-anhydrosugar sulfoxide 68[67]

Furthermore, α-galactofuranosides can also be synthesized by using 2,3-anhydrosugar donors.[68–69] For example, the synthesis of a pentasaccharide fragment of varianose (**82**) was reported by Lowary and co-workers in 2006 (Scheme 20). The introduction of the α-galactofuranoside was achieved via 2,3-anhydrosugar sulfoxide **80**. The desired tetrasaccharide **81** was achieved in two steps: glycosylation and subsequent opening of the epoxide ring, in 49% yield with excellent stereoselectivity. Then, **81** was converted to the desired pentasaccharide **82** was in several steps.

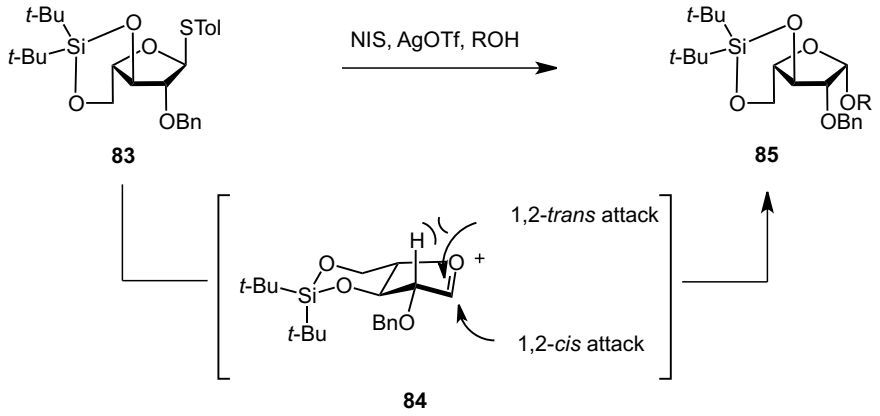


Scheme 20 Synthesis of the pentasaccharide **82** via 2,3-anhydrosugar donor 80[68–69]

1.2.2.7. Use of 3,5-*O*-di-*tert*-butylsilane (DTBS) protected donors

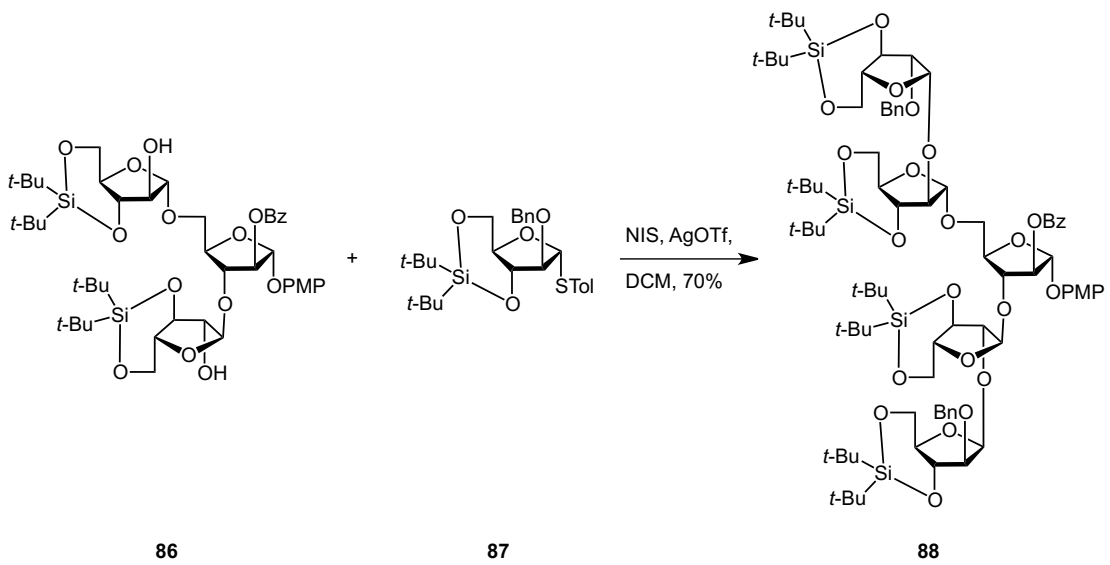
The Boons group has demonstrated the utility of conformationally-restricted donors, which employ a 3,5-*O*-di-*tert*-butylsilane protecting group, in the stereoselective synthesis of β-arabinofuranosides.[70] As illustrated in Scheme 21, the arabinofuranosyl oxacarbenium ion **84** (generated from an L-arabinose derivative) is locked in an E_3 conformer, in which O-3 and C-5 are in the pseudoequatorial position. This conformation was also supported by the computational investigations. Subsequent nucleophilic attack from the β face is more favorable because α-face attack is unfavourable due to the eclipsing interactions between the H-2 hydrogen and the

incoming nucleophile. Glycosylation of a range of glycosyl acceptors with the DTBS-protected donor **83** gave the deseired β-arabinofuranosides with excellent stereoselcetivity and in in good yield.



Scheme 21 Synthesis of β-arabinofuranosides via DTBS protected donors[70]

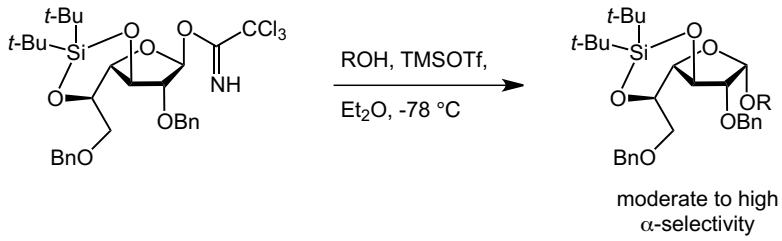
This methodology has been applied to the preparation of a 22-residue arabinan fragment of mycobacterial AG (Scheme 22).[71]



86 **87** **88**

Scheme 22 Synthesis of the key building block of arabinan fragment of mycobacterial AG[71]

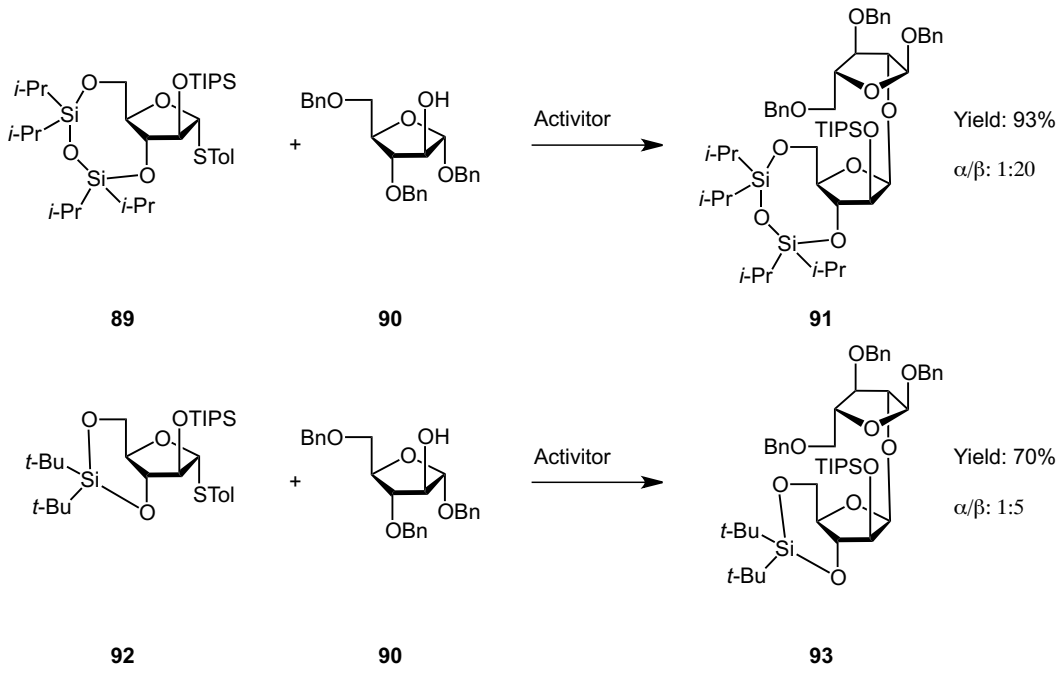
Later, Gallo-Rodriguez and coworkers have reported that 1,2-*cis* α-D-galactofurnosides can be synthesized from conformationally constrained 3,5-*O*-DTBS-D-galactofuranosyl trichloroacetimidate donors.[79] Galactofurnosylation proceeds smoothly and with moderate to high α-selectivity with several glycosyl acceptors using diethyl ether as the solvent at –78 °C. They also found that the stereoselectivity strongly depend on the acceptor.



Scheme 23 1,2-*cis*-Galactofurnosylation via 3,5-*O*-DTBS-D-galactofuranosyl trichloroacetimidate donors[79]

1.2.2.8. Use of 3,5-*O*-tetraisopropyldisiloxanylidene (TIPDS) protected donors

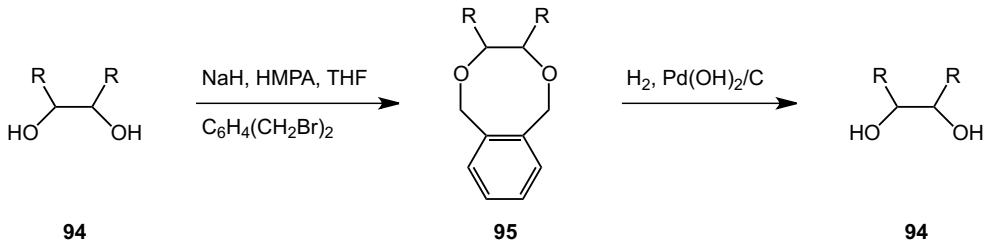
Ito and co-workers have developed the conformationally constrained 3,5-*O*-tetraisopropyldisiloxanylidene (TIPDS)-protected thioglycoside **89** for the stereoselective synthesis of β-arabinofuranosides.[72] They found that **89** (α/β = 1:20) afforded higher β-stereoselectivity than the DTBS-protected thioglycoside donor **92** (α/β = 1:5). A heptaarabinofuranoside fragment of mycobacterial AG was synthesized to demonstrate the utility of this methodology.



Scheme 24 Comparison of different conformationally-restricted donors by Ito and coworkers[72]

1.3. The *o*-xylylene protecting group in carbohydrate chemistry

Poss and Smyth first published the use of the di-*O*-*o*-xylylene bis-ether for the protection of 1,2- or 1,3-diols.[73] The *o*-xylylene protecting group can be introduced by the treatment of a diol with α,α′-dibromo-*o*-xylene under basic conditions; it can be removed by hydrogenolysis (Scheme 25). This group has been used in carbohydrate chemistry as a conformationally restricting group.



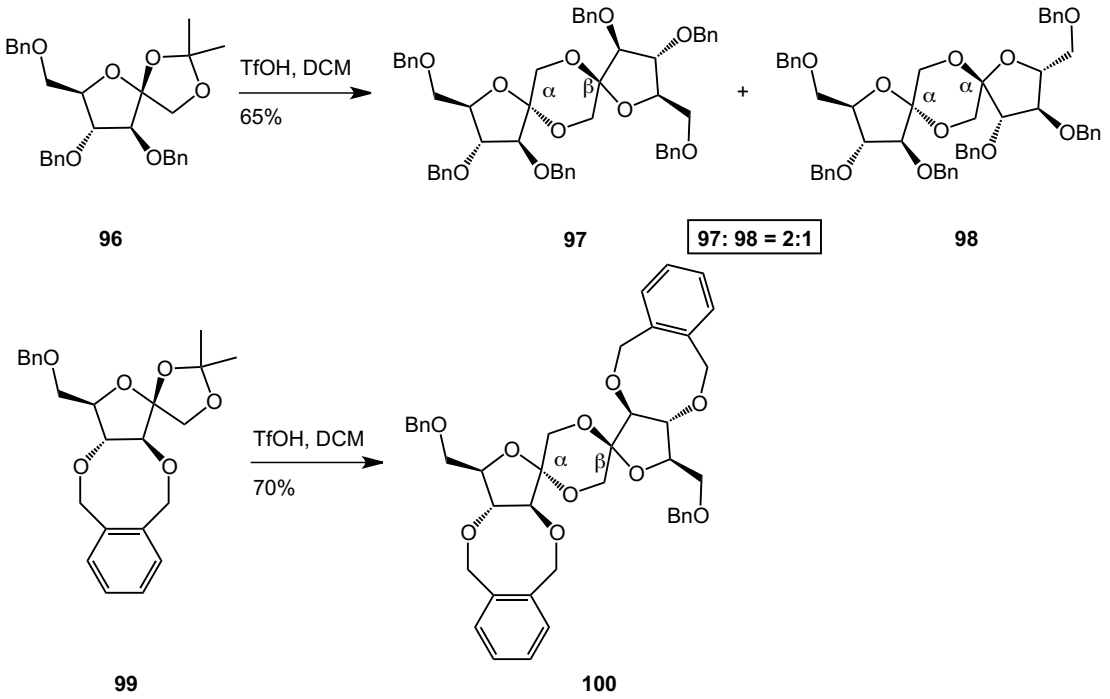
94 **95** **94**

Scheme 25 Protection and deprotection of *o*-xylylene bis-ether

1.3.1. Stereoselective synthesis of tricyclic spirodisaccharides

Fernandez and co-workers have introduced the use of the *o*-xylylene protecting group in the stereoselective synthesis of di-D-fructose dianhydrides (tricyclic spirodisaccharides),[74] which are prebiotic food products isolated from higher plants or microorganisms.[75]

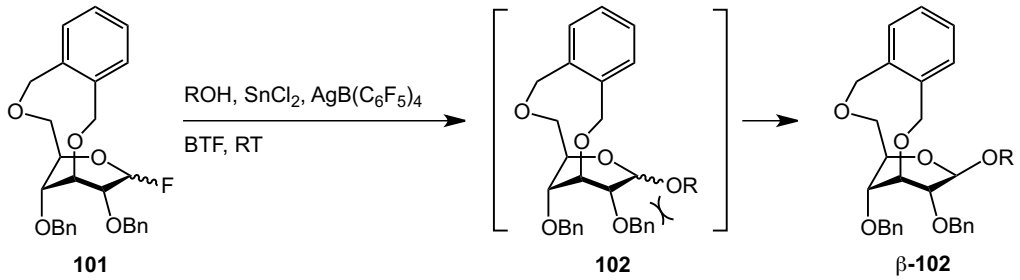
As illustrated in Scheme 26, these compounds could be synthesized from the tri-*O*-benzylated 1,2-*O*-isopropylidene-β-D-fructofuranose derivative **96**. Activation by trifluoromethanesulfonic (triflic) acid led to the formation of a two-compound mixtures of the α,β (**97**) and β,β (**98**) bis-spiroketal disaccharide in a 2:1 ratio in 65% yield. In contrast, triflic acid-promoted activation of the 3,4-*O*-xylylene protected 1,2-*O*-isopropylidene-β-D-fructofuranose derivative **99** afforded only the thermodynamically favored α,β-bis-spiroketal disaccharide **100** in 70% yield. No β,β-bis-spiroketal disaccharide was detected. Thus, the *o*-xylylene protecting group has a stereodirecting effect in the synthesis of bis-spirodisaccharides.



Scheme 26 Synthesis of di-D-fructose dianhydrides.[74]

1.3.2. β-Selective glucopyranosylation

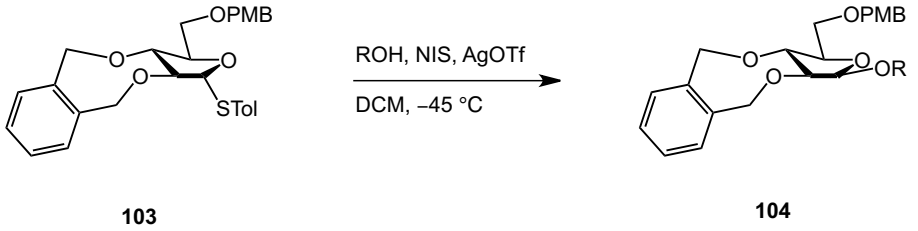
Yamada and co-workers have reported a completely β-stereoselective glycosylation using 3,6-*O*-xylylene-protected axial-rich glucosyl fluorides.[76] In their investigations, the 3,6-*O*-xylylene-protected glucosyl fluoride **101** was shown to react with a range of glycosyl acceptors promoted by $SnCl_2$−$AgB(C_6F_5)_4$ in benzotrifluoride (BTF), leading to the formation β-glucopyranosides in good to excellent yield. In the early stages of the glycosylation, both α- and β-glucopyranosides were detected; however, the α-glucopyranosides isomerize to the β-glucopyranosides catalyzed by $HB(C_6F_5)_4$ (Scheme 27).



Scheme 27 β-Stereoselective glycosylation using a 3,6-*O*-xylylene-protected glucopyranosyl fluoride[76]

1.3.3. β-Selective arabinofuranosylation

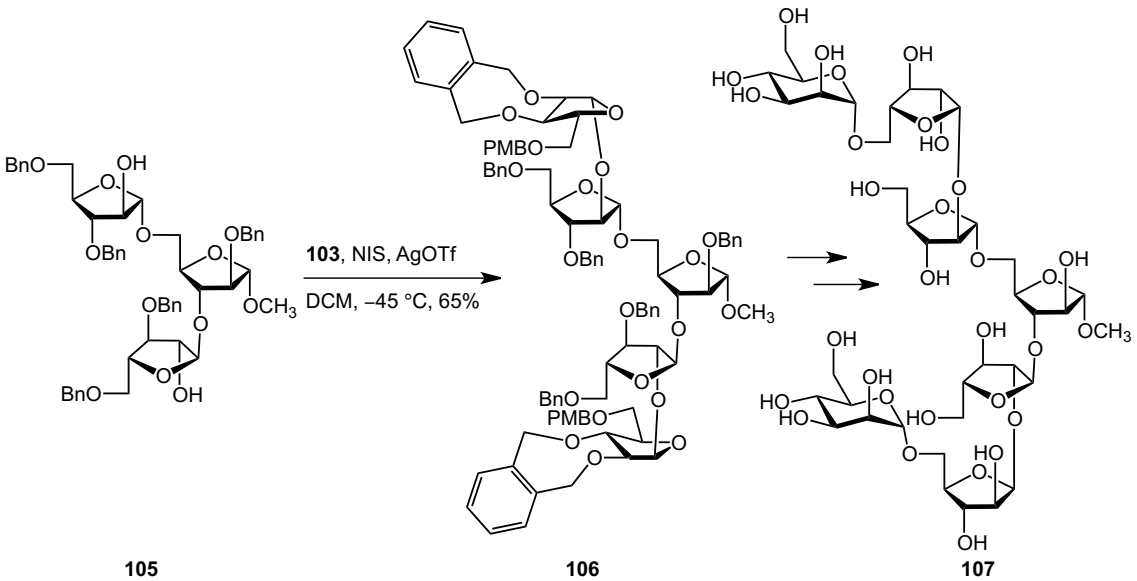
Stereoselective β-arabinofuranosylation using 2,3-*O*-xylylene protected donors was reported by Imamura and Lowary in 2010 (Scheme 28).[77] Optimization of the glycosylation showed that the stereoselectivity was affected by reaction conditions and a 5-*O*-PMB protecting group was necessary to achieve the highest stereoselectivity. For example, when thioglycoside (**103**) was treated with various acceptors under NIS–AgOTf activation in dichloromethane at −45 ˚C, the β-arabinofuranosides were formed as the predominant product.



103 **104**

Scheme 28 Stereoselective β-arabinofuranosylation using 2,3-*O*-xylylene protected donors[77]

The methodology was applied to the synthesis of a heptasaccharide fragment **107** of mycobacterial LAM (Scheme 29). Glycosylation of **105** with **103** proceeded smoothly to give pentasaccharide **106** in 65% yield with excellent stereoselectivity. The heptasaccharide target **107** was generated from **106** in several more steps.



105 **106** **107**

Scheme 29 Synthesis of a heptasaccharide fragment in mycobacterial LAM using xylylene-protected thioglycoside **103**[77]

1.4. Overview of thesis research

As discussed above, although huge advances in the synthesis of 1,2-*cis*-glycofuranosides have been achieved in the past decades, there are still some challenges. In particular, almost no studies investigating the synthesis of 1,2-*cis*-xylofuranosides have been carried out. As outlined in the section above, previous studies by our group[77] have demonstrated that the utility 2,3-*O*-xylylene protected arabinofuranosyl donors in the synthesis of 1,2-*cis* (β)-arabinofuranosides. Therefore, we wanted to expand this methodology to the synthesis of 1,2-*cis* (α)-xylofuranosides.

In Chapter 2, several 2,3-*O*-xylylene protected xylofuranosyl donors have been synthesized. Also, glycosylation optimization has been performed and the substrate scope of the reaction has been explored. Finally, to demonstrate the utility of this methodology, a 5-deoxy-5-methylthio-xylofuranose (MTX) containing pentasaccharide fragment of mycobacterial LAM was synthesized.

Chapter 2: α-Selective xylofuranosylation using a 2,3-*O*-xylylene protected donor

2.1. Introduction

Tuberculosis (TB), which is caused by *Mycobacterium tuberculosis* (Mtb), remains a major cause of death, resulting in two million deaths each year.[91] One of the reasons TB is difficult to treat is that there are unusual molecules in the Mtb cell wall, which provide a natural barrier to antibiotics and which act to neutralize the host response.[80] Lipoarabinomannan (LAM), a phosphatidylinositol-anchored glycolipid, is a major polysaccharide component of the Mtb cell wall, and has been identified as an important factor to neutralize cytotoxic oxygen free radicals and inhibit the production of cytokines.[81–82] The structure of LAM is well understood. At its core is a phosphatidylinositol (PI) linker, to which us bound a mannan consisting of α-(1→6) and α-(1→2)-linked D-mannopyranose residues. An arabinan, containing α-(1→5), α-(1→2) and α-(1→3)-linked arabinofuranose residues, is attached at the termini of the mannan chain. In particularly virulent strains, such as *Mycobacterium tuberculosis*, *Mycobacterium avium* and *Mycobacterium bovis*, the arabinan is capped with short mannopyranosyl oligosaccharides, and the molecule is termed mannosylated lipoarabinomannan (ManLAM).[83]

An unusual methylthiopentosyl residue has been found linked to mannosyl caps of ManLAM in both clinical isolates (CSU2025 and MT10326) and laboratory strains (H37Rv25 and H37Ra25) of Mtb.[84] In 2004, Homans and coworkers demonstrated that this motif is a 5-deoxy-5-methylthio-xylofuranose (MTX) residue.[85] In 2006, Lowary

and coworkers established that MTX is of the D-configuration and is linked α-(1→4) to mannosyl caps of ManLAM.[86] The MTX residue has been suggested to have important biological functions, such as inhibiting cytokine response.[87] Although other biological functions or the biosynthetic pathway of the MTX residue has not been established, its distribution across several mycobacterial strains suggests this motif plays an important biological role. The synthesis of MTX-containing fragments (Figure 10) of LAM is essential to provide materials for investigating its biological role or understanding its biosynthetic pathway. A challenge in the synthesis of this compound is stereoselectively introducing the α-xylofuranoside linkage.

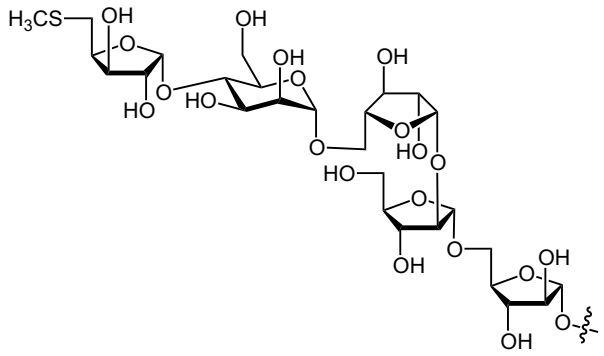


Figure 10 MTX-containing fragments of LAM

As outlined in the previous chapter, several methods for the synthesis of 1,2-*cis* furanosides, especially 1,2-*cis*-arabinofuranosides, have been reported. These include using conformationally-flexible donors and conformationally-restricted donors.[44–78] Among the conformationally-flexible donors, the IAD,[51–53] HAD[60–63] and 2-(benzyloxycarbonyl)-benzyl (BCB) glycoside methodology have been demonstrated

to be effective for the synthesis of 1,2-*cis*-arabinofuranosides. The use conformationally-restricted donors such as 3,5-DTBS-[70–71] or 3,5-TIPDS-protected donors[72] has also shown promise.

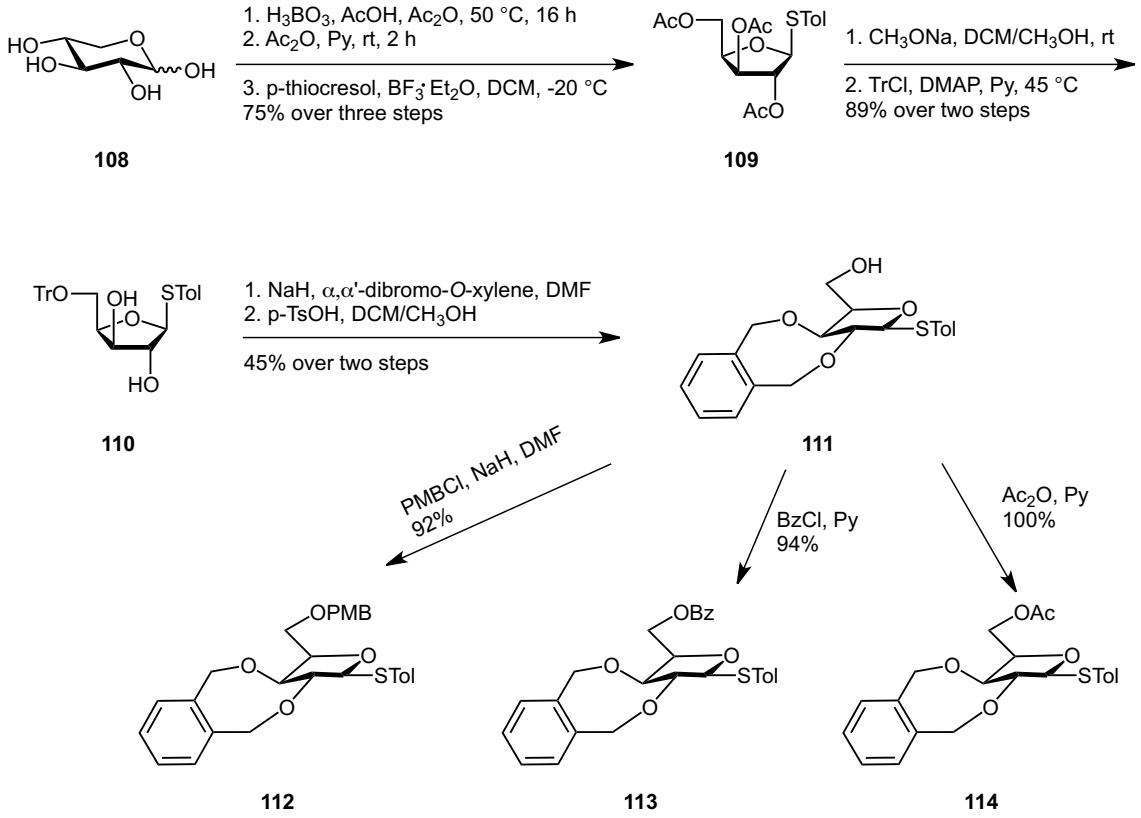
Recently, Lowary and co-workers have developed methodology for the stereoselective synthesis of β-arabinofuranosides using 2,3-*O*-xylylene protected donors.[77] This methodology is based on the fact that the conformation of arabinofuranose is locked by the 2,3-*O*-xylylene group, which leads to preferential formation of the 1,2-*cis*-glycosides. Based on this success in making β-arabinofuranosides, we wanted to apply the same approach to the synthesis of α-xylofuranosides. In this thesis, I describe the development of a new α-selective xylofuranosylation methodology that uses 2,3-*O*-xylylene-protected xylosfuranose thioglycosides as donors. Moreover, to demonstrate the utility of the methodology, the synthesis of an MTX-containing fragment of LAM was carried out.

2.2. α-Selective xylofuranosylation using a 2,3-*O*-xylylene protected donor

2.2.1. Preparation of 2,3-*O*-xylylene-protected xylofuranoside donors

A set of xylofuranoside donors **112–114**, all carrying 2,3-*O*-xylylene group, were designed and prepared as detailed in Scheme 30. The known *p*-thiocresyl thioglycosides **109** was prepared from D-xylose. First, 1,2,3,5-tetra-*O*-acetyl-xylofuranose was obtained from D-xylose using a boric acid-mediated process, which

was developed by Furneaux *et al*.[88] Then, the *p*-thiocresyl thioglycoside **109** was produced upon reaction of the tetraacetate with *p*-thiocresol and boron trifluoride diethyl etherate. Thioglycoside **109** was obtained in 75% yield from D-xylose with a β/α ratio of >20:1. Deacetylation of **109** with sodium methoxide afforded a thioglycoside triol, which was not purified, but was instead directly tritylated providing **110** in 89% yield over two steps. Then, **111** was obtained in 45% yield from **110** via the incorporation of the xylylene group upon treatment with of α,α′-dibromo-*o*-xylene and NaH in DMF, and subsequent removal of the trityl group. Xylofuranoside donors **112–114** were generated from **111** under standard conditions. A PMB group was introduced on O-5 to obtain building block **112** in 92% yield. Benzoylation of **111** with benzoyl chloride and pyridine afforded **113** in 94% yield. Acetylation of **111** with acetic anhydride and pyridine gave **114** in 100% yield.

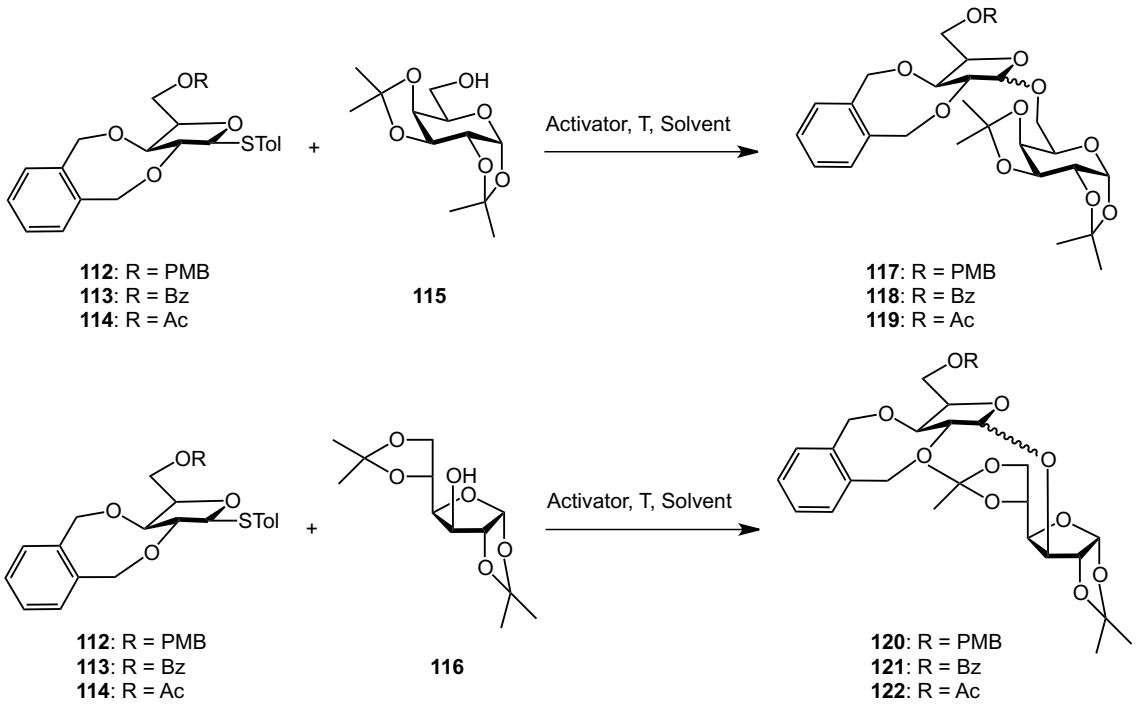


Scheme 30 Preparation of 2,3-*O*-xylylene-protected xylofuranoside donors

2.2.2. Optimization of the glycosylation conditions

With the xylofuranoside donors **112–114** in hand, I first explored their reactions with 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose **115** and 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose **116** (Table 2). Most of the glycosylations employed 1.3 equiv of donor and 1.0 equiv of acceptor. The product stereochemistry was identified by the coupling constant between H-1 and H-2 ($^3J_{1,2}$) in the ^{1}H NMR spectrum of the product. For the 1,2-*cis* (α) isomer, $^3J_{1,2}$ is about 5.0 Hz. In contrast, for the 1,2-*trans* (β) isomer, $^3J_{1,2}$ is about 2.5 Hz.[92]

Table 2 Optimization of glycosylation conditions



Entry	Donor	ROH	Conc. (mM)	*t* (°C)	Activator	Solvent	Yield[a] (α:β)[b]
1	**112α**	**115**	0.03	−78 to −40	NIS–AgOTf	CH_2Cl_2	83% (1:2.9)
2	**112β**	**115**	0.03	−78 to −40	NIS–AgOTf	CH_2Cl_2	86% (1:3.2)
3	**112**	**115**	0.03	−78 to −40	NIS–AgOTf	CH_2Cl_2–CH_3CN (1:3)	86% (1:1.3)
4	**112**	**115**	0.03	−78 to −40	NIS–AgOTf	CH_3CH_2CN	81% (1:2.3)
5	**112**	**115**	0.03	0 to r.t.	NIS–AgOTf	Toluene–Dioxane (1:3)	82% (1.8:1)
6	**112**	**115**	0.03	−78 to −40	NIS–AgOTf	Diethyl Ether	88% (2.3:1)
7	**112**	**116**	0.03	−10 to 0	NIS–AgOTf	Toluene–Dioxane (1:3)	53% (2.3:1)
8	**112**	**116**	0.03	−60 to r.t.	$(Ph)_2SO$–Tf_2O–TTBP	CH_2Cl_2	–

9	**113**	**115**	0.03	−78 to −40	NIS–AgOTf	CH_2Cl_2	88% (1:1.4)
10	**113**	**115**	0.03	−25 to −10	NIS–AgOTf	CH_3CH_2CN	59% (1:1.2)
11	**113**	**115**	0.3	r.t.	NIS–AgOTf	Dioxane	96% (1.5:1)
12	**113**	**115**	0.03	r.t.	NIS–AgOTf	Dioxane	75% (1.9:1)
13	**113**	**115**	0.03	−78 to −40	NIS–AgOTf	Diethyl Ether	90% (1.1:1)
14	**113**	**115**	0.03	−60 to r.t.	$(Ph)_2SO$–Tf_2O–TTBP	CH_2Cl_2	68% (1.7:1)
15	**114**	**115**	0.03	−60 to r.t.	$(Ph)_2SO$–Tf_2O–TTBP	CH_2Cl_2	–
16	**114**	**115**	0.1	r.t.	NIS–AgOTf	Diethyl Ether	69% (9.3:1)
17	**114**	**115**	0.015	r.t.	NIS–AgOTf	Diethyl Ether	66% (9.5:1)
18	**114 (1.7 equiv)**	**115**	0.015	r.t.	NIS–AgOTf	Diethyl Ether	78% (9.5:1)
19	**114 (2.5 equiv)**	**115**	0.015	r.t.	NIS–AgOTf	Diethyl Ether	73% (9.5:1)
20	**114**	**115**	0.015	−50 to −40	NIS–AgOTf	CH_2Cl_2-CH_3CN (1:3)	(~ 1:4)
21	**114**	**116**	0.015	r.t.	NIS–AgOTf	Diethyl Ether	79% (7.7:1)

a. Combined yield of α- and β-isomers. *b*. Determined from the ratio of H-1 resonances in the ^{1}H NMR spectrum of the corresponding isomer mixture.

The effect of the configuration of donor on the glycosylation was explored first (Table 2). The glycosylation was run using **112α** (Entry 1) or **112β** (Entry 2) as the donor and **115** as the acceptor under the same conditions. Both reactions afforded disaccharide **117** in excellent yield with similar slight β-stereoselectivity. These

reactions showed that the configuration of donor does not affect the stereoselectivity of this glycosylation.

Then the effect of the reaction solvent on the stereoselectivity of the glycosylation reaction was studied. As shown in Table 2.1 (Entries 2–6), when donor **112** reacted with acceptor **115** in the presence of *N*-iodosuccinimdie (NIS) and silver triflate (AgOTf) as the promoter in different solvents, disaccharide **117** was obtained in different stereoselectivity. The use of diethyl ether (Entry 6) or a 1:3 mixture of toluene and dioxane (Entry 5) provided the best α-selectivity. These results are consistent with previous reports[89–90] indicating that that ethereal solvents (e.g., diethyl ether, tetrahydrofuran or dioxane) tend to increase α-stereoselectivity in glycosylations.

In addition, the effect of acceptor concentration on the stereoselectivity of the glycosylation was explored. Both xylofuranosylation at comparatively high concentration (0.3 mM, Entry 11) and low concentration (0.03 mM, Entry 12) provided the desired disaccharide **118** in excellent yield with similar α/β ratio. Thus, the concentration of acceptor does not affect the stereoselectivity of this glycosylation.

I also studied the effect using the 1-benzenesulfinyl piperidine, triflic anhydride and 2,4,6-tri-tert-butylpyrimidine (BSP–Tf_2O–TTBP) promotor system to effect this xylofuranosylation. Coupling between **113** and **115** (Entry 14) proceeded to give higher α-stereoselectivity than the use of the standard NIS–AgOTf system. However, the yield

decreased markedly. Moreover, no desired disaccaride was generated when I attemped to couple **112** and **116** (Entry 8) and **114** and **115** (Entry 15) using the BSP–Tf_2O–TTBP system. Given these conclusions, all future work focused on the use of NIS–AgOTf as the promotor.

The effects of remote O-5 protecting group in the donor were next explored. As depicted in Table 2.1 Entry 6, when 2,3-*O*-xylylene-protected xylofuranoside donor bearing electron-rich *p*-methoxybenzyl at O-5 **112** reacted with glycosyl acceptor **115**, the desired disaccharide **117** was generated in good yield and with moderate α-selectivity (α/β = 2.3:1). On the other hand, when glycosyl donor **113** bearing electron-withdrawing benzoyl group at O-5 **113** was used, the glycosylation showed no stereoselectivity (α/β = 1.1:1, Entry 13). In contrast, and surprisingly, when glycosyl donor **114** reacted with glycosyl acceptor **115**, the desired disaccharide **119** was obtained in good yield and with excellent α-selectivity (α/β = 9.5:1, Entry 17). Thus, further work focused on donors with an O-5 acetyl group.

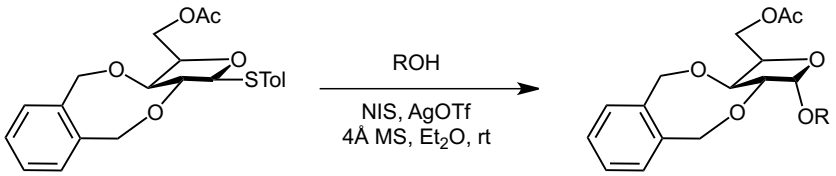
Finally, glycosylations at room temperature in diethyl ether with different equivalents of glycosyl donor **114** were examined (Entries 17–19) in the coupling with **115**. When 1.7 equiv. of glycosyl donor was used, the desired disaccharide **119** was formed in the best yield (78%) compared to the other two reactions. The α-selectivity (α/β = 9.5:1) was the same in all cases. In conclusion, after this work we identified optimized conditions for these glycosylations: reaction of of 1.7 equiv. of donor **114**

and 1.0 equiv. of a glycosyl acceptor in the presence of 2.5 equiv. of NIS and 0.25 equiv. of AgOTf in diethyl ether at room temperature. Under these these conditions, the desired glycoside can be formed in high yield and with excellent α-selectivity.

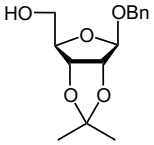
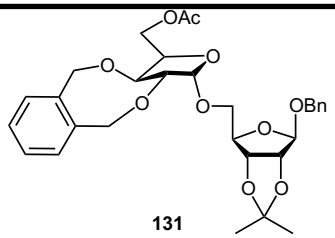
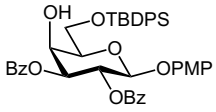
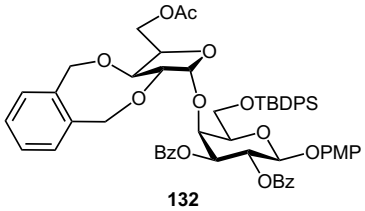
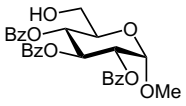
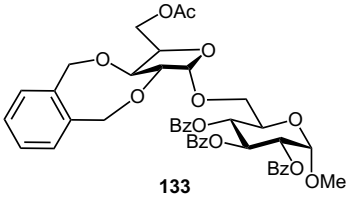
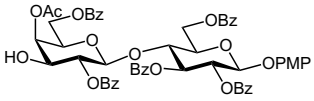
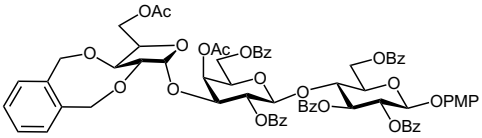
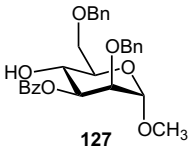
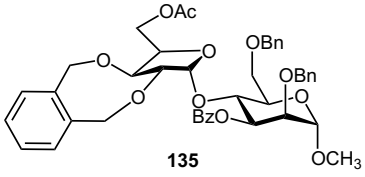
2.2.3. Substrate scope of the xylofuranosylation

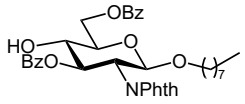
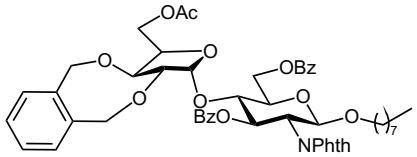
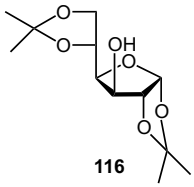
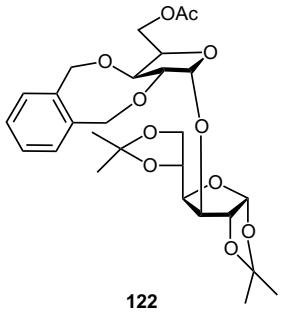
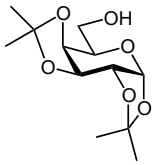
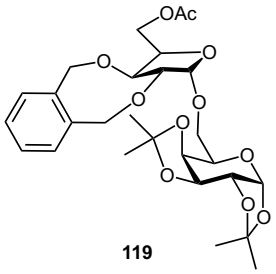
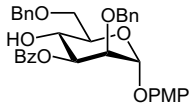
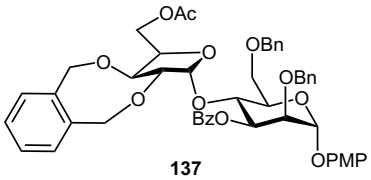
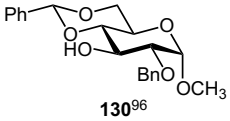
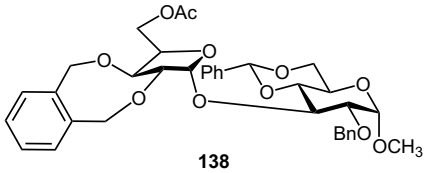
With the optimized glycosylation in hand, investigation of its use with a range of glycosyl acceptors was undertaken. Glycosylations with a broad range of carbohydrates including ribofuranosyl, galactopyranosyl, glucopyranosyl, mannopyranosyl and glucofuranosyl acceptors proceeded smoothly, providing the corresponding disaccharide or trisaccharide products **119**, **122**, **131–137** (Table 3, Entries 1–9) in good to excellent yield (67–96%) with excellent α-stereoselectivity (α/β 7:1 to >20:1). Interestingly, glycosylation of **114** and **130** (Entry 10), an acceptor that has a conformationally constrained 4,6-*O*-benzylidene protecting group, showed no stereoselectivity (α/β 1.2:1). The reasons for the poor selectivity with this acceptor is not known.

Table 3 Xylofuranosylation of glycosyl donor **114** with various acceptors



114

Entry	Acceptor	Product	Yield (%) [b]	α:β [c]
1	 **123**[95]	 **131**	96	7.4:1
2	 **124**	 **132**	67	>20:1
3	 **125**[96]	 **133**	92	7.8:1
4	 **126**	 **134**	94	13.3:1
5	 **127**	 **135**	93	17.7:1

6	 **128**	 **136**	86	>20:1
7	 **116**	 **122**	79	7.7:1
8	 **115**	 **119**	73	9.3:1
9	 **129**	 **137**	92	>20:1
10	 **130**[96]	 **138**	71	1.2:1

[a] Reaction conditions: 1.7 equiv. of donor, 1 equiv. of acceptor, 2.5 equiv. of NIS and 0.25 equiv. of AgOTf. [b] Combined yield of α and β-isomers. [c] Determined by the ratio of H-1 peak from the ^{1}H NMR spectrum of the corresponding isomer mixture.

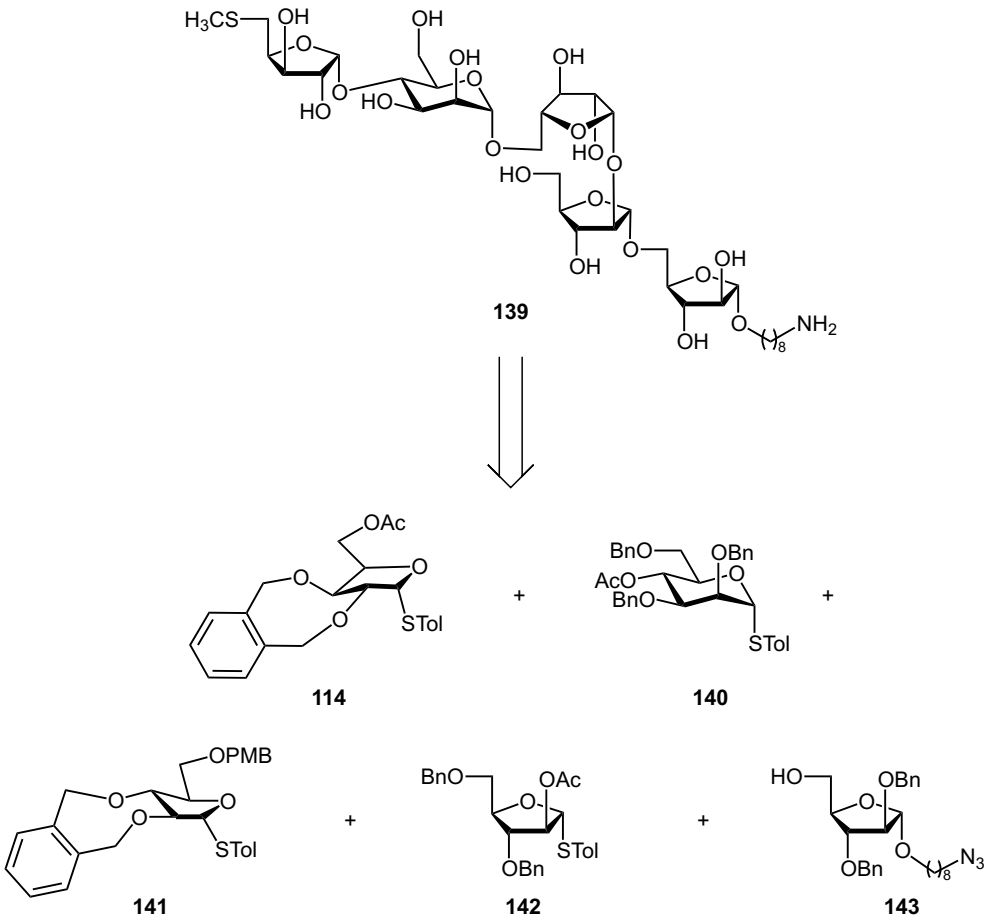
Significantly, glycosylation of mannopyranosyl acceptors **127** and **129**, which contain a free C-4 hydroxyl group, afforded biologically relevant α-D-Xyl*f*-(1→4)-α-D-Man*p* disaccharides **135** and **137** in excellent yield with excellent α-stereoselectivity (α/β >20:1). This motif is related to the nonreducing terminal motif of MTX-capped mycobacterial ManLAM.

2.3. Synthesis of an MTX-containing pentasaccharide fragment of ManLAM

With the successful implementation of using a 2,3-*O*-xylylene-protected xylofuranoside donor for the stereoselective synthesis of α-xylofuranosides and the optimized formation of the α-D-Xyl*f*-(1→4)-α-D-Man*p* disaccharide motif, I turned my attention to a more complex target. The method was applied to the synthesis of an MTX-containing pentasaccharide fragment of ManLAM (**139**), which can be conjugated to microarray and identified the biomarkers differentiating TB and non-TB samples.

2.3.1. Retrosynthetic analysis

Retrosynthetically, pentasaccharide **139** can be accessed via a linear approach, from five building blocks: **114**, **140**, **141**, **142** and **143** (Scheme 31). Building block **141** was chosen as it would allow the easy formation of the 1,2-*cis*-arabinofuranoside linkage.



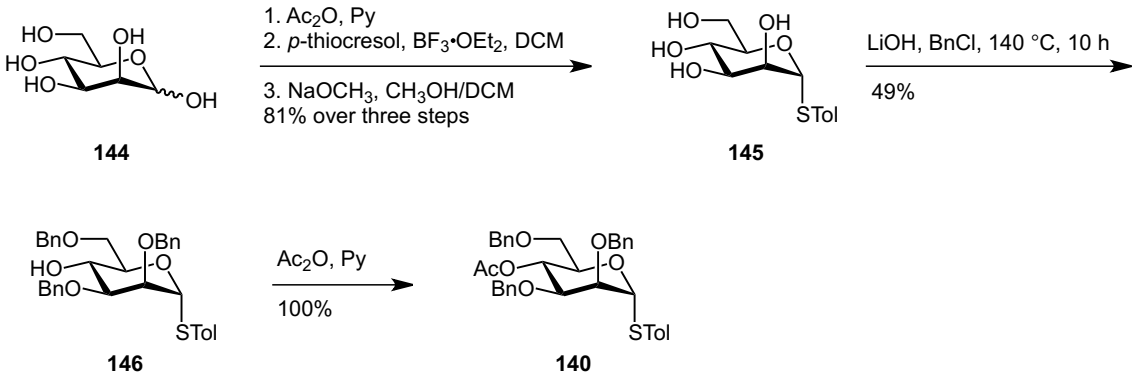
Scheme 31 Retrosynthetic analysis of the MTX-containing pentasaccharide **139**.

2.3.2. Synthesis of MTX-containing pentasaccharide fragment in ManLAM

2.3.2.1. Synthesis of *p*-tolyl 4-*O*-acetyl-2,3,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (140).

To prepare building block **140**, commercially available D-mannose (**144**) was first peracetylated. This product was then treated with *p*-thiocresol and boron trifluoride diethyl etherate and the resulting product was subsequently deacetylated with sodium methoxide. After these three steps, thioglycoside tetraol **145** was obtained in 81%

yield. Regioselective benzylation was then achieved by treatment with lithium hydroxide and benzyl chloride at 140 °C for 10 h, affording the 2,3,6-tri-*O*-benzylated thiomannoside **146** in 49% yield. Acetylation of **146** in acetic anhydride and pyridine provided building block **140** in quantitative yield.

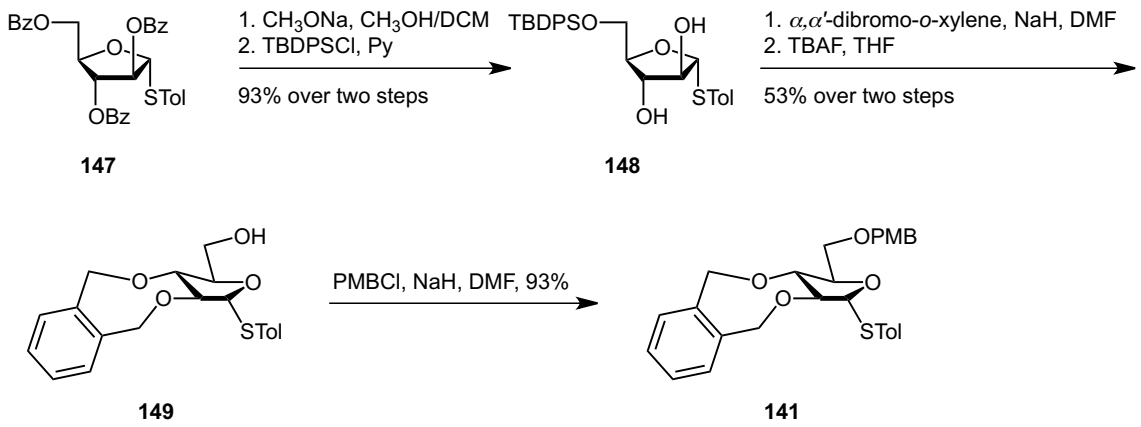


Scheme 32 Synthesis of building block **140**

2.3.2.2. Synthesis of *p*-tolyl 5-*O*-*p*-methoxybenzyl-1-thio-2,3-*O*-xylylene-α-D-arabinofuranoside (141)

The 2,3-*O*-xylylene-protected arabinofuranosyl donor **141** was prepared as depicted in Scheme 33. Deacetylation of *p*-thiocresyl thioglycoside **147**[93] with sodium methoxide afforded crude thioglycoside triol, onto which was introduced a *tert*-butyldiphenylsilyl (TBDPS) group on O-5 by reaction with pyridine and TBDPS chloride. This sequence provided **148** in 93% yield in two steps from **147**. Next **149** was obtained in 53% yield from **148** via the incorporation of the xylylene group upon reaction with α,α′-dibromo-*o*-xylene and NaH in DMF and subsequent removal of the

TBDPS group in tetra-*n*-butylammonium fluoride (TBAF) and THF. Finally, a PMB group was introduced on O-5 to obtain building block **141** in 93% yield.

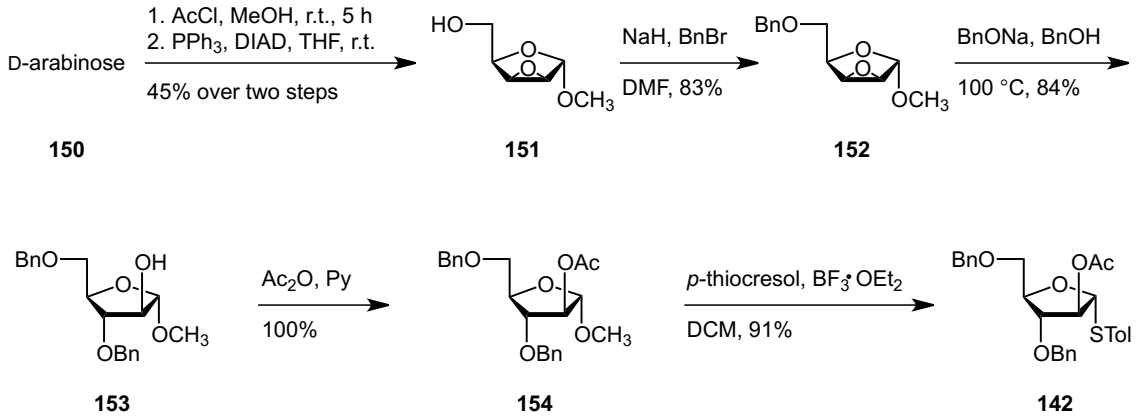


Scheme 33 Synthesis of building block **141**

2.3.2.3. Synthesis of *p*-tolyl 2-*O*-acetyl-3,5-di-*O*-benzyl-1-thio-α-D-arabino furanoside (142).

Illustrated in Scheme 34 is the synthesis of building block **142** from D-arabinose **150**. Reaction of D-arabinose **150** with acetyl chloride and methanol provided methyl α-D-arabinofuranoside. Epoxide **151** was then formed via Mitsunobu reaction upon treatment with triphenylphosphine and diisopropyl azodicarboxylate (DIAD). Compound **151** was obtained in 45% yield over two steps. Epoxide **151** was then treated with benzyl bromide and sodium hydride in DMF to give the 5-*O*-benzyl-protected epoxide **152** in 83% yield. Regioselective ring opening of 5-*O*-benzyl-protected epoxide **152** with sodium benzylate in benzyl alcohol at 100 °C afforded compound **153** in 84% yield. The compound was was acylated to form **154**

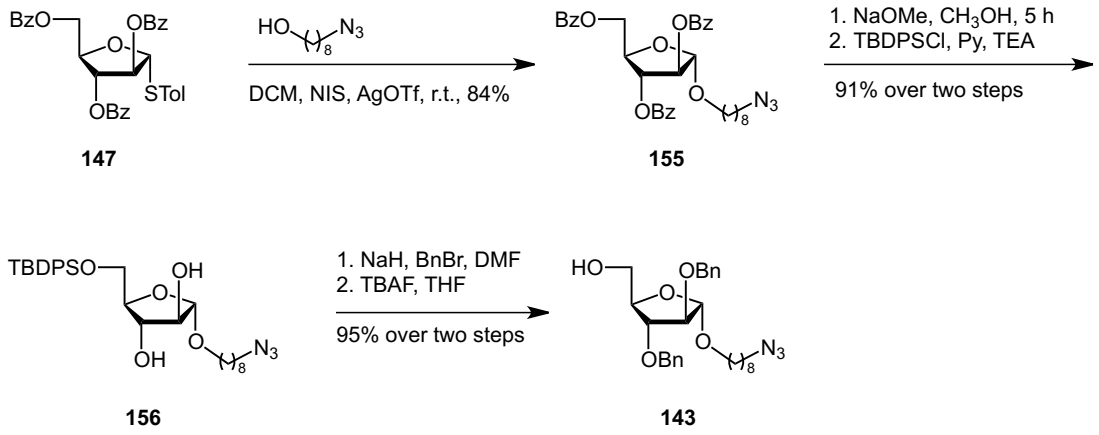
in quantitative yield. Finally, thioglycoside **142** was obtained in 91% yield upon reaction of **154** with *p*-thiocresol and boron trifluoride diethyl etherate.



Scheme 34 Synthesis of building block **142**

2.3.2.4. Synthesis of 8-azidooctyl 2,3-di-*O*-benzyl-α-D-arabinofuranoside (143)

Building block **143** was derived from *p*-thiocresyl thioglycoside **147** in five steps (Scheme 35). First 8-azidooctyl arabinofuranoside **155** was produced in 84% yield upon glycosylation of 8-azido-1-octanol with thioglycoside **147** promoted by NIS and AgOTf. The acyl groups in 8-azidooctyl arabinofuranoside **155** were then cleaved and a TBDPS group was incorporated into O-5 to afford **156** in 91% yield. Finally, **143** was generated via benzylation of **156** and subsequent removal of the TBDPS group with TBAF in THF in excellent yield.



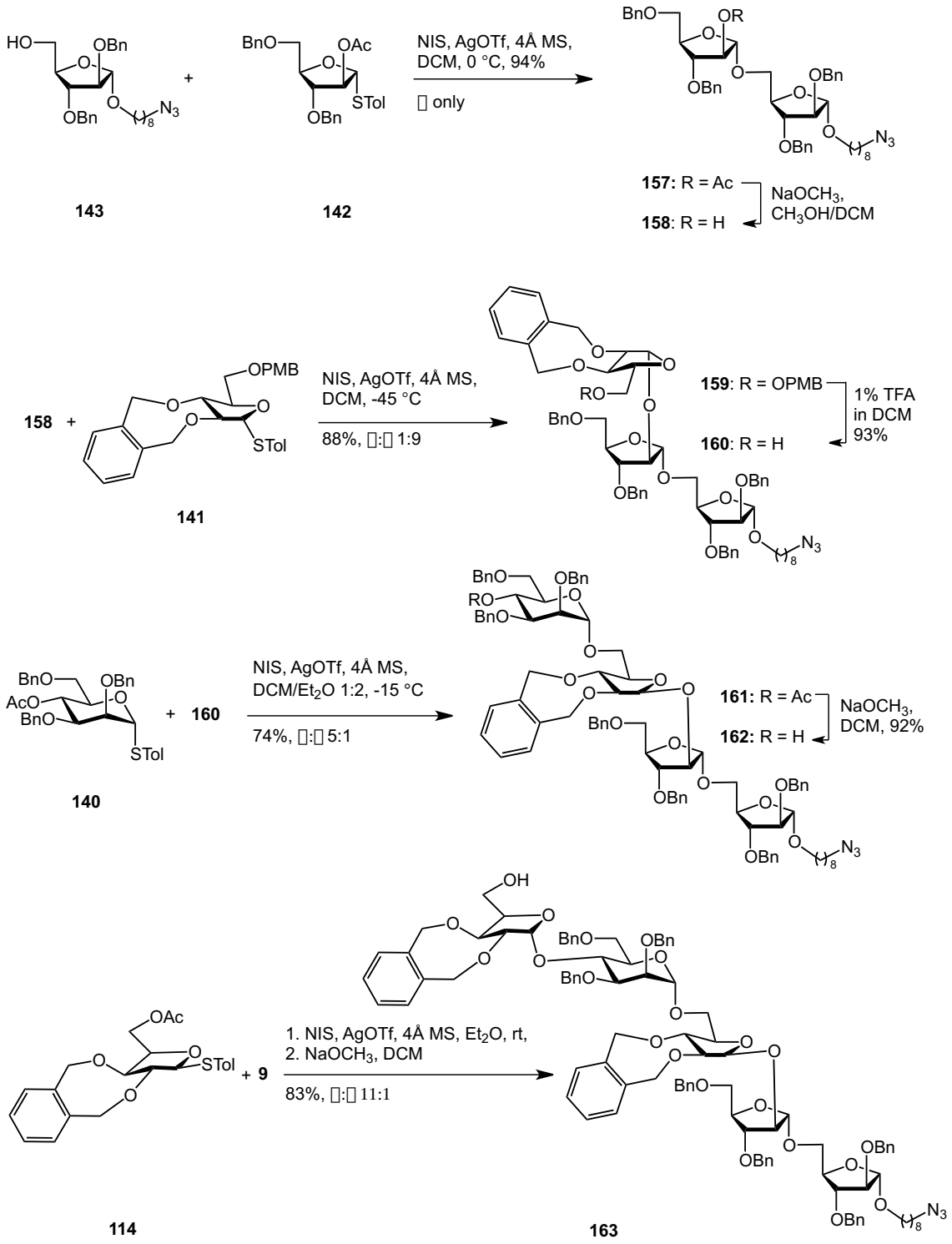
Scheme 35 Synthesis of building block **144**

2.3.2.5. Synthesis of MTX-containing pentasaccharide fragment

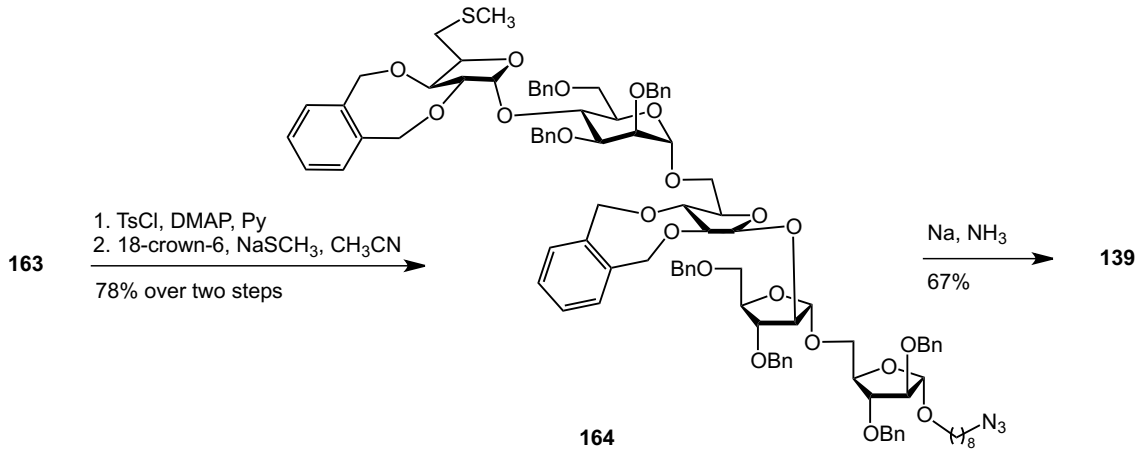
With all the building blocks in hand, pentasaccharide **139** was synthesized using a linear strategy (Scheme 36). All glycosylation reactions were promoted by NIS–AgOTf. First, disaccharide **157** was synthesized by coupling of arabinofuranosyl acceptor **143** with arabinofuranosyl donor **142**. The product, **157**, was obtained in 94% yield as only the α-isomer. Subsequent removal of acetyl group afforded disaccharide acceptor **158** in 100% yield. The resulting disaccharide acceptor **158** was then glycosylated with 2,3-*O*-xylylene-protected arabinofuranosyl donor **141** to form trisaccharide **159** in 88% yield with excellent β-selectivity. Next, the PMB group was removed with 1% trifluoroacetic acid (TFA) in CH_2Cl_2 to give trisaccharide acceptor **160** in 93% yield. Coupling the mannopyranosyl donor **140** with trisaccharide acceptor **160** afforded tetrasaccharide α-isomer **161** in 74% yield with α:β 5.5:1. These compounds could be separated and the desired α-glycoside was deacetylated with

sodium methoxide to generate, in 92% yield, the tetrasaccharide acceptor **162**. The final glycosylation was the key one: coupling of tetrasaccharide acceptor **162** with xylofuranosyl donor **114**. This reaction gave an 11:1 α:β mixture of products, which were inseparable. Subsequent deacetylation provided pentasaccharide **163**, in which the α:β mixture could be seperated, in 83% yield over two steps.

Having assembled the pentasaccharide core, the final steps were introduction of the thiomethyl group and deprotection (Scheme 37). Tosylation of **163** and subsequent thiolate substitution yielded desired product **164** in 78% yield over the two steps. With the methylthio group in place, deprotection of the benzyl ether protecting groups and xylylene bisethers was achieved by Birch reduction. Thus, treatment of pentasaccharide **164** in THF at −78 °C with liquid ammonia and sodium produced **139** in 67% yield.



Scheme 36 Synthesis of MTX-containing pentasaccharide fragment **163**



Scheme 37 The thiolate displacement and deprotection of **163**

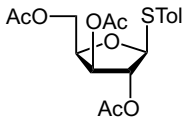
2.4. Summary

In conclusion, a novel stereoselective α-xylofuranosylation employing conformationally constrained 2,3-*O*-xylylene-protected xylofuranosyl donor has been developed and optimization of glycosylation conditions showed that treatment of 1.7 equiv. of *p*-tolyl 5-*O*-acetyl-1-thio-2,3-*O*-xylylene-α-D-xylofuranoside (**114**) with 1.0 equiv. of various acceptor, the reaction proceeds smoothly in the presence of 2.5 equiv. of NIS and 0.25 equiv. of AgOTf in diethyl ether at room temperature with high yield and high α-selectivity. It was also successfully applied to the synthesis of MTX-containing pentasaccharide fragment in LAM.

2.5. Experimental section

General Methods: All reagents used were purchased from commercial sources and were used without further purification unless noted. Solvents used in reactions were

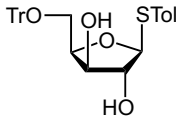
purified by successive passage through columns of alumina and copper under nitrogen. Unless stated otherwise, all reactions were carried out under a positive pressure of argon. Reactions were monitored by TLC on Silica Gel 60-F_{254} (0.25 mm) and spots were visualized under UV light (254 nm) and/or stained by charring with acidified anisaldehyde solution in ethanol. Column chromatography was performed on Silica Gel 60 (40–60 μm) or C_{18} silica gel (35–70 μm, Toronto Research Chemicals). ^{1}H NMR spectra were recorded at 500 MHz, and chemical shifts are referenced to $CHCl_3$ (7.26, $CDCl_3$) or CH_3OD (3.35, CD_3OD). ^{13}C NMR spectra were recorded at 125 MHz, and ^{13}C chemical shifts are referenced to $CDCl_3$ (77.06, $CDCl_3$) or CD_3OD (49.0, CD_3OD). Assignments of NMR spectra were made on the basis of two-dimensional experiments (^{1}H–^{1}H COSY, HSQC and HMBC). ESI-MS spectra were recorded on samples suspended in THF or CH_3OH with added NaCl. Optical rotations were measured at 22 ± 2 °C at the sodium D-line (589 nm) and are in units of deg·mL(dm·g)$^{-1}$. Acceptors **115–116** (commercial available), **123–130**[95–96] were prepared as described previously.



***p*-Tolyl 2,3,5-tri-*O*-acetyl-1-thio-β-D-xylofuranoside (109)**[94]**:** D-xylose (1.90 g, 12.60 mmol), boric acid (1.71 g, 27.72 mmol) and acetic acid (10 mL) were stirred at 50 °C for 1 h before acetic anhydride (10 mL) was added. The mixture was heated at 50 °C for

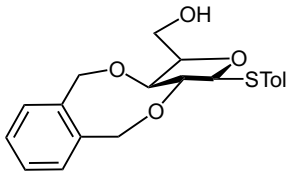
14 h. The boric acid was removed as trimethyl borate by the addition of methanol (10 mL). The resulting mixture was concentrated to 10 mL and then methanol (5 mL) was added. The mixture was concentrated to 5 mL. Acetic anhydride (10 mL) and pyridine (10 mL) were added and the solution was stirred at rt for 2 h. Following the addition of ice (10 g), the solution was stirred for 1 h and then extracted with CH_2Cl_2. The combined CH_2Cl_2 extracts were washed with 7% aq. $CuSO_4$ solution and water. The organic layer was dried with anhydrous Na_2SO_4, filtered and concentrated. The crude product was purified by flash chromatography (7:3, hexane–EtOAc) to give crude 1,2,3,5-tetra-*O*-acetyl-D-xylofuranose (4.0 g, 12.56 mmol) as a yellowish oil. This material was then dissolved in dry CH_2Cl_2 (40 mL) and cooled to −20 °C before *p*-thiocresol (1.84 g, 15.08 mmol) was added. The mixture was stirred for 10 min and $BF_3{\cdot}OEt_2$ (8.0 g, 31.4 mmol) was added dropwise over 10 min. After 2 h, the mixture was neutralized by the addition of Et_3N (8.0 mL), diluted with CH_2Cl_2 and then washed with saturated aq. solution of sodium bicarbonate, water and brine. The organic layer was dried with anhydrous Na_2SO_4, filtered and concentrated. The crude product was purified by chromatography (5:1, hexane–EtOAc) to give **109** (3.45 g, 76%) as colorless oil. R_f 0.51 (2:1, hexane–EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 7.41 (app dd, 2H, J = 7.9, 2.2 Hz, ArH), 7.11 (app dd, 2H, J = 8.0, 0.5 Hz, ArH), 5.28 (dd, 1H, $J_{2,3}$ = 2.2 Hz, $J_{3,4}$ = 5.0 Hz, H-3), 5.24 (dd, 1H, $J_{1,2}$ = 3.3 Hz, $J_{2,3}$ = 2.2 Hz, H-2), 5.17 (d, 1H, $J_{1,2}$ = 3.3 Hz, H-1), 4.43 (ddd, 1H, $J_{3,4}$ = 5.0 Hz, $J_{4,5a}$ = 10.2 Hz, $J_{4,5b}$ = 6.4 Hz, H-4), 4.29 (dd,

1H, $J_{4,5a}$ = 5.2 Hz, $J_{5a,5b}$ = 11.7 Hz, H-5a), 4.23 (dd, 1H, $J_{4,5b}$ = 6.4 Hz, $J_{5a,5b}$ = 11.7 Hz, H-5b), 2.31 (s, 3H, ArCH_3), 2.07 (s, 3H, C(O)CH_3), 2.05 (s, 3H, C(O)CH_3), 2.03 (s, 3H, C(O)CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 170.5 (C=O), 169.5 (C=O), 169.1 (C=O), 138.2 (Ar), 133.2 (2C, Ar), 129.7 (2C, Ar), 129.3 (Ar), 90.1 (C-1), 80.3 (C-4), 78.3 (C-2), 75.2 (C-3), 62.0 (C-5), 21.0 (ArCH$_3$), 20.7 (C(O)CH$_3$), 20.7 (C(O)CH$_3$), 20.5 (C(O)CH$_3$); HRMS-ESI *m/z* $[M + Na]^+$ calcd for $C_{18}H_{22}NaO_7S$: 405.0979, found: 405.0980.



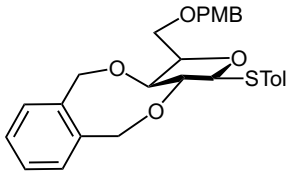
***p*-Tolyl 1-thio-5-*O*-trityl-β-D-xylofuranoside (110)[94]:** To a solution of **109** (3.0 g, 7.85 mmol) in CH_2Cl_2–methanol (2:1, 15 mL) was added sodium methoxide (70.6 mg, 0.78 mmol). The mixture was stirred at rt for 4 h and then neutralized by the addition of Amberlite IR-120 H^+ resin. Then, the mixture was filtered and concentrated to furnish a syrup, that was dissolved in pyridine (15 mL) at rt before DMAP (0.383 g, 3.14 mmol) and trityl chloride (3.71 g, 13.3 mmol) were added. The reaction mixture was stirred at 45 °C for 12 h and then poured into ice water (40 mL) and extracted with CH_2Cl_2 (2 × 40 mL). The combined CH_2Cl_2 extracts were washed with 7% aq. $CuSO_4$ solution (3 × 30 mL) and water (2 × 40 mL). The organic layer was dried with anhydrous Na_2SO_4, filtered and concentrated. The crude product was purified by column chromatography

(4:1, hexane–EtOAc) to give **110** (3.48 g, 89%) as colorless oil. R_f 0.6 (1:1, hexanes–EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.51–7.45 (m, 8H, ArH), 7.32–7.28 (m, 6H, ArH), 7.26–7.22 (m, 3H, ArH), 7.15–7.10 (m, 2H, ArH), 5.23 (d, 1H, $J_{1,2}$ = 3.7 Hz, H-1), 4.35–4.28 (m, 2 H, H-2, H-3), 4.21–4.17 (m, 1H, H-4), 3.61 (dd, 1H, $J_{4,5a}$ = 4.6 Hz, $J_{5a,5b}$ = 10.4 Hz, H-5a), 3.29 (dd, 1H, $J_{4,5b}$ = 6.4 Hz, $J_{5a,5b}$ = 10.4 Hz, H-5b), 3.26 (br s, 1H, OH), 2.33 (s, 3H, ArCH_3), 2.26 (br s, 1H, OH); ^{13}C NMR (125 MHz, $CDCl_3$,) δ_C 143.4 (3C, Ar), 137.7 (Ar), 132.3 (3C, Ar), 130.6 (Ar), 129.8 (3C, Ar), 128.6 (4C, Ar), 128.0 (4C, Ar), 127.2 (3C, Ar), 91.4 (C-1), 87.6 (C(Ph)$_3$), 82.0 (C-4), 80.2 (C-2), 78.1 (C-3), 62.9 (C-5), 21.1 (ArCH$_3$); HRMS-ESI *m/z* [M + Na]$^+$ calcd for $C_{31}H_{30}NaO_4S$: 521.1757, found 521.1758.



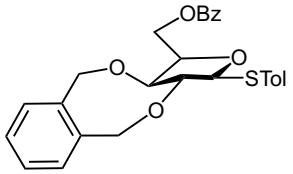
***p*-Tolyl 1-thio-2,3-*O*-xylylene-β-D-xylofuranoside (111):** To a solution of **110** (2.26 g, 4.56 mmol) in DMF (40 mL) were added NaH (400 mg, 10.0 mmol) and α,α'-dibromo-*o*-xylene (1.32 g, 5.02 mmol) slowly at 0 °C. After stirring for 2 h at rt, the reaction was quenched by the addition of satd aq. NH_4Cl. Dilution of the mixture with CH_2Cl_2 provided a solution that was then washed with brine. The organic layer was dried with anhydrous Na_2SO_4, filtered and concentrated. The crude product was purified by flash column chromatography (20:1 hexane–EtOAc) to give the crude

product. The obtained crude product was dissolved in CH_2Cl_2–methanol (7:3, 20 mL) and then *p*-TsOH (80 mg) was added. The mixture was stirred for 14 h and then neutralized by the addition of Et_3N. Then the mixture was concentrated to syrup, which was purified by column chromatography (6:1 hexane–EtOAc) to give **111** (990 mg, 41% over two steps) as a colorless oil. R_f 0.3 (3:1, hexanes–EtOAc); $[\alpha]_D = -78.3$ (c = 0.9, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.43−7.32 (m, 6H, ArH), 7.10−7.06 (m, 2H, ArH), 5.07 (d, 1H, $J_{1,2}$ = 7.3 Hz, H-1), 4.93 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.92 (d, 1H, J_{gem} = 12.5 Hz, ArCH_2), 4.82 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.75 (d, 1H, J_{gem} = 12.6 Hz, ArCH_2), 4.26 (dd, 1H, $J_{2,3}$ = 5.4 Hz, $J_{3,4}$ = 7.9 Hz, H-3), 4.16 (ddd, 1H, $J_{3,4}$ = 7.9 Hz, $J_{4,5a}$ = 5.1 Hz, $J_{4,5b}$ = 5.1 Hz, H-4), 4.04 (dd, 1H, $J_{1,2}$ = 7.3 Hz, $J_{2,3}$ = 5.4 Hz, H-2), 3.76–3.73 (m, 2H, H-5), 2.34 (app t, 1H, J = 7.1 Hz , OH), 2.31 (s, 3H ArCH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 137.8 (Ar), 136.3 (Ar), 135.2 (Ar), 132.4 (2C, Ar), 131.7 (Ar), 131.4 (Ar), 129.9 (Ar), 129.7 (Ar), 129.7 (2C, Ar), 129.6 (Ar), 89.0 (C-1), 85.3 (C-2), 81.4 (C-3), 80.6 (C-4), 69.8 (ArCH$_2$), 68.90 (ArCH$_2$), 61.8 (C-5), 21.1 (ArCH$_3$); HRMS-ESI m/z $[M + Na]^+$ calcd for $C_{20}H_{22}NaO_4S$: 381.1131. Found: 381.1128.



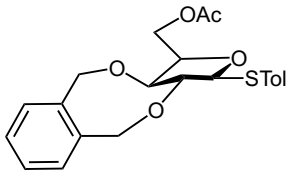
***p*-Tolyl 5-*O*-*p*-methoxybenzyl-1-thio-2,3-*O*-xylylene-β-D-xylofuranoside (112):** To a solution of **111** (358 mg, 1.00 mmol) in DMF (6.0 mL) at 0 °C were added NaH (60 mg,

1.50 mmol) and PMBCl (173 μL, 1.50 mmol). The solution was stirred for 2 h at rt and the reaction was then quenched by the addition of satd aq. NH_4Cl. Dilution of the mixture with CH_2Cl_2 provided a solution that was then washed with brine. The organic layer was subsequently dried with anhydrous Na_2SO_4, filtered, concentrated and the residue was purified by silica gel column chromatography (5:1, hexanes–EtOAc) to give **112** (439 mg, 92%) as a white solid. R_f 0.5 (3:1, hexanes–EtOAc); $[\alpha]_D = -56.8$ (*c* = 0.8, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.43−6.86 (m, 12H, ArH), 5.21 (d, 1H, $J_{1,2}$ = 5.1 Hz, H-1), 4.81 (d, 1H, J_{gem} = 11.6 Hz, ArC*H*$_2$), 4.69 (d, 1H, J_{gem} = 11.5 Hz, ArC*H*$_2$), 4.61 (d, 1H, J_{gem} = 11.5 Hz, ArC*H*$_2$), 4.56 (d, 1H, J_{gem} = 11.6 Hz, ArC*H*$_2$), 4.51 (d, 1H, J_{gem} = 11.6 Hz, ArC*H*$_2$), 4.43 (d, 1H, J_{gem} = 11.6 Hz, ArC*H*$_2$), 4.41 (q, 1H, *J* = 5.8 Hz, H-4), 4.12 (dd, 1H, $J_{2,3}$ = 3.6 Hz, $J_{3,4}$ = 5.8 Hz, H-3), 4.08 (dd, 1H, $J_{1,2}$ = 5.1 Hz, $J_{2,3}$ = 3.6 Hz, H-2), 3.81−3.78 (m, 4H, H-5a, OCH_3), 3.74 (dd, 1H, $J_{5a,5b}$ = 10.3 Hz, $J_{4,5a}$ = 6.2 Hz, H-5b), 2.28 (s, 3H, ArC*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 159.3 (Ar), 137.6 (Ar), 135.6 (Ar), 132.3 (2C, Ar), 130.5 (Ar), 130.4 (Ar), 129.7 (2C, Ar), 129.5 (Ar), 129.5 (2C, Ar), 129.2 (Ar), 128.8 (Ar), 128.4 (Ar), 128.1 (Ar), 113.8 (2C, Ar), 89.6 (C-1), 87.8 (C-2), 80.1 (C-3), 77.3 (C-4), 73.2 (Ar*C*H$_2$), 70.7 (Ar*C*H$_2$), 70.0 (Ar*C*H$_2$), 68.5 (C-5), 55.5 (OCH_3), 21.2 (Ar*C*H$_3$); HRMS-ESI *m/z* $[M + Na]^+$ calcd for $C_{28}H_{30}NaO_5S$: 501.1706. Found: 501.1699.



***p*-Tolyl 5-*O*-benzoyl-1-thio-2,3-*O*-xylylene-β-D-xylofuranoside (113):** To a solution of **110** (358 mg, 1.00 mmol) in pyridine (5.0 mL) at 0 °C was added BzCl (179 μL, 1.50 mmol). The reaction mixture was stirred for 1 h at rt. The reaction was quenched by the addition of CH_3OH, followed by co-evaporation with toluene to remove the pyridine. The crude residue was diluted with CH_2Cl_2 and washed with 2M HCl, H_2O, satd aq. $NaHCO_3$, and brine. The organic layer was subsequently dried with anhydrous Na_2SO_4, filtered, concentrated and the residue was purified by silica gel column chromatography (6:1, hexanes–EtOAc) to give **113** (434 mg, 94%) as a colorless oil. R_f 0.60 (3:1, hexanes–EtOAc); $[\alpha]_D$ = −34.2 (*c* = 0.7, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.00−7.28 (m, 11H, ArH), 7.04−7.00 (m, 2H, ArH), 5.06 (d, 1H, $J_{1,2}$ = 7.4 Hz, H-1), 4.98 (d, 1H, J_{gem} = 12.8 Hz, ArCH_2), 4.86 (d, 1H, J_{gem} = 12.6 Hz, ArCH_2), 4.82 (d, 1H, J_{gem} = 12.8 Hz, ArCH_2), 4.74 (d, 1H, J_{gem} = 12.6 Hz, ArCH_2), 4.59 (dd, 1H, $J_{4,5a}$ = 2.9 Hz, $J_{5a,5b}$ = 11.9 Hz, H-5a), 4.47 (ddd, $J_{3,4}$ = 7.9 Hz, $J_{4,5a}$ = 2.9 Hz, $J_{4,5b}$ = 7.2 Hz, H-4), 4.41 (dd, 1H, $J_{4,5b}$ = 7.2 Hz, $J_{5a,5b}$ = 11.9 Hz, H-5b), 4.30 (dd, 1H, $J_{2,3}$ = 5.5 Hz, $J_{3,4}$ = 7.9 Hz, H-3), 4.03 (dd, 1H, $J_{1,2}$ = 7.5 Hz, $J_{2,3}$ = 5.5 Hz, H-2), 2.29 (s, 3H, ArCH_3); ^{13}C NMR (175 MHz, $CDCl_3$) δ_C 179.0 (C=O), 166.4 (Ar), 137.9 (Ar), 136.0 (Ar), 135.6 (Ar), 133.1 (2C, Ar), 132.8 (Ar), 131.7 (Ar), 131.3 (Ar), 130.3 (Ar), 129.7 (2C, Ar),

129.6 (Ar), 129.5 (2C, Ar), 129.3 (Ar), 128.2 (2C, Ar), 88.8 (C-1), 84.7 (C-2), 80.9 (C-3), 78.6 (C-4), 69.8 (Ar*C*H_2), 68.9 (Ar*C*H_2), 64.0 (C-5), 21.1 (Ar*C*H_3); HRMS-ESI *m/z* $[M + Na]^+$ calcd for $C_{27}H_{26}NaO_5S$: 485.1393, found: 485.1387.



***p*-Tolyl 5-*O*-acetyl-1-thio-2,3-*O*-xylylene-β-D-xylofuranoside (114):** To a solution of **111** (358 mg, 1.0 mmol) in pyridine (5.0 mL) was added acetic anhydride (5.0 mL) at rt. The solution was stirred for 2 h at rt and then the reaction was quenched by the addition of CH_3OH, followed by co-evaporation with toluene to remove the pyridine. The residue was purified by silica gel column chromatography (6:1, hexanes–EtOAc) to afford **114** (381 mg, 95%) as an colorless oil. R_f 0.3 (4:1, hexanes–EtOAc); $[\alpha]_D$ = −132.2 (*c* = 1.2, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.42−7.29 (m, 6H, ArH), 7.09−7.04 (m, 2H, ArH), 5.01 (d, 1H, $J_{1,2}$ = 7.5 Hz, H-1), 4.96 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.85 (d, 1H, J_{gem} = 12.6 Hz, ArCH_2), 4.81 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.72 (d, 1H, J_{gem} = 12.6 Hz, ArCH_2), 4.34−4.28 (m, 2H, H-4, H-5b), 4.22 (dd, 1H, $J_{2,3}$ = 5.4 Hz, $J_{3,4}$ = 7.7 Hz, H-3), 4.15 (dd, 1H, $J_{4,5a}$ = 7.9 Hz, $J_{5a,5b}$ = 12.8 Hz, H-5a), 3.92 (dd, 1H, $J_{1,2}$ = 7.5 Hz, $J_{2,3}$ = 5.4 Hz, H-2), 2.31 (s, 3H, ArCH_3), 2.02 (s, 3H, C(O)CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 170.9 (C=O), 137.9 (Ar), 136.2 (Ar), 135.6 (Ar), 132.9 (Ar), 131.7 (Ar), 131.4 (Ar), 129.8 (Ar), 129.7 (Ar), 129.7 (Ar), 129.6 (Ar), 129.5 (Ar),

88.9 (C-1), 84.9 (C-2), 80.7 (C-3), 78.5 (C-4), 69.9 (Ar*C*H_2), 68.8 (Ar*C*H_2), 63.6 (C-5), 21.2 (Ar*C*H_3), 21.1 (C(O)*C*H_3); HRMS-ESI *m/z* $[M + Na]^+$ calcd for $C_{22}H_{24}NaO_5S$: 423.1242. Found: 423.1248.

General Procedure for Glycosylation Reactions

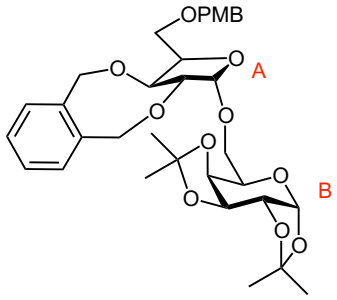
Method A: NIS–AgOTf as the promoter

To a mixture of donor (0.314 mmol) and acceptor (0.210 mmol) in CH_2Cl_2 (15 mL) at rt was added 4 Å molecular sieves (300 mg). After stirring for 1 h, the mixture was cooled to –78 °C, before NIS (0.473 mmol) and AgOTf (0.0473 mmol) were added. The reaction temperature was slowly increased to –40 °C as the dry ice sublimed. When the reaction was complete as determined by TLC (usually after 1 h), the reaction was quenched by the addition of Et_3N. The solution was diluted with CH_2Cl_2 and filtered through Celite. The filtrate was then washed with satd aq. $Na_2S_2O_3$ and brine. The organic layer was subsequently dried with anhydrous Na_2SO_4, filtered, concentrated and the residue was purified by silica gel column chromatography to give the product as a colorless oil.

Method B: BSP–Tf_2O–Tf_2O as the promoter

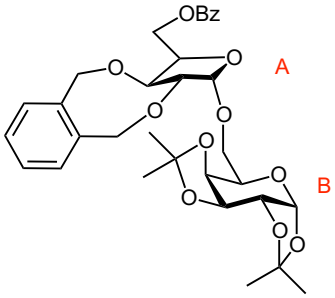
To a mixture of donor (0.192 mmol), 1-benzenesulfinyl piperidine (BSP) (0.128 mmol), 2,4,6-tri-*tert*-butylpyrimidine (TTBP) (0.384 mmol) and 4 Å molecular sieves (250 mg)

in CH_2Cl_2 (10 mL) at –60 °C was added triflic anhydride (Tf_2O). After 5 min, a solution of acceptor (0.128 mmol) in CH_2Cl_2 (1 mL) was added to the solution. The mixture was stirred for 5 min at –60 °C and then warmed to rt by removing from the cooling bath. After 1 h, the solution was diluted with CH_2Cl_2 and filtered through Celite. The filtrate was then washed with satd aq. $NaHCO_3$ and brine. The organic layer was subsequently dried with anhydrous Na_2SO_4, filtered, concentrated and the residue was purified by silica gel column chromatography.



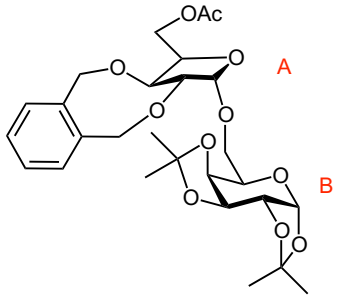
5-*O*-*p*-Methoxybenzyl-2,3-*O*-xylylene-α-D-xylofuranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (117): R_f 0.40 (2:1, hexanes–EtOAc); $[\alpha]_D$ = +48.9 (*c* = 0.9, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.41−7.37 (m, 2H, ArH), 7.36−7.31 (m, 2H, ArH), 7.28−7.23 (m, 2H, ArH), 6.88−6.83 (m, 2H, ArH), 5.52 (d, 1H, $J_{1,2}$ = 5.0 Hz, H-1A), 4.94 (d, 1H, $J_{1,2}$ = 2.5 Hz, H-1B), 4.88 (d, 1H, J_{gem} = 12.5 Hz, ArCH_2), 4.85 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.74 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.71 (d, 1H, J_{gem} = 12.5 Hz, ArCH_2), 4.53 (dd, 1H, $J_{2,3}$ = 2.4 Hz, $J_{3,4}$ = 7.9 Hz, H-3A), 4.51 (d, 1H, J_{gem} = 11.6 Hz, ArCH_2), 4.43 (d, 1H, J_{gem} = 11.6 Hz, ArCH_2), 4.37 (ddd, $J_{4,5}$ = 5.0 Hz, $J_{5,6a}$ = 7.2 Hz, $J_{5,6b}$ = 7.2 Hz, H-5B), 4.28 (dd, 1H, $J_{1,2}$ = 5.0 Hz, $J_{2,3}$ = 2.8 Hz,

H-2A), 4.18−4.12 (m, 2H, H-2B, H-4B), 4.09 (ddd, $J_{4,5a}$ =1.6 Hz, $J_{3,4}$ = $J_{4,5b}$ = 7.2 Hz, H-4A), 3.95−3.88 (m, 2H, H-3B, H-5aA), 3.79 (s, 3H, OCH_3), 3.69−3.64 (m, 2H, H-6aB, H-6bB), 3.61 (dd, 1H, $J_{4,5b}$ = 4.6 Hz, $J_{5a,5b}$ = 9.3 Hz, H-5bA), 1.54 (s, 3H, CH_3), 1.39 (s, 3H, CH_3), 1.33 (s, 3H, CH_3), 1.28 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 159.1 (Ar), 136.5 (Ar), 135.6 (Ar), 131.6 (Ar), 131.5 (Ar), 130.8 (Ar), 129.6 (Ar), 129.6 (Ar), 129.2 (Ar), 113.7 (Ar), 109.2 (Ar), 108.5 (Ar), 108.2 (C-1B), 96.3 (C-1A), 87.2 (C-2B), 81.6 (C-4B), 80.1 (C-5B), 72.8 (Ar*C*H_2), 71.1 (C-4A), 70.6 (C-2A), 70.6 (C-3A), 70.1 (C-6B), 69.3 (Ar*C*H_2), 69.1 (Ar*C*H_2), 67.0 (C-3B), 66.9 (C-5A), 55.2 (OCH_3), 26.1 (CH_3), 26.0 (CH_3), 25.0 (CH_3), 24.4 (CH_3); HRMS-ESI *m/z* $[M + Na]^+$ calcd for $C_{33}H_{42}NaO_{11}$: 637.2625, found: 637.2633.



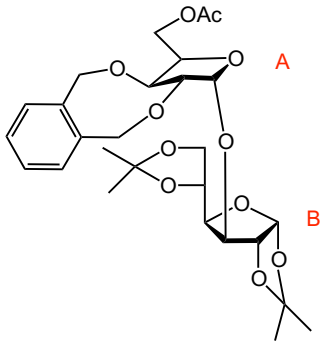
5-*O*-Benzoyl-2,3-*O*-xylylene-α-D-xylofuranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (118): R_f 0.40 (3:2, hexanes–EtOAc); $[\alpha]_D$ = +54.3 (*c* = 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.11−8.02 (m, 2H, ArH), 7.57−7.50 (m, 1H, ArH), 7.45−7.30 (m, 6H, ArH), 5.49 (d, 1H, $J_{1,2}$ = 5.0 Hz, H-1A), 5.01 (d, 1H, $J_{1,2}$ = 2.0

Hz, H-1B), 4.88 (d, 1H, J_{gem} = 10.1 Hz, ArCH_2), 4.85 (d, 1H, J_{gem} = 12.6 Hz, ArCH_2), 4.74 (d, 1H, J_{gem} = 12.6 Hz, ArCH_2), 4.72 (d, 1H, J_{gem} = 10.1 Hz, ArCH_2), 4.58−4.51 (m, 2H, H-4B, H-6aB), 4.53 (dd, 1H, $J_{2,3}$ = 2.4 Hz, $J_{3,4}$ = 7.9 Hz, H-3A), 4.50−4.44 (m, 1H, H-6bB), 4.28−4.21 (m, 3H, H-2A, H-2B, H-5B), 3.96−3.85 (m, 3H, H-4A, H-3B, H-5aA), 3.59−3.51 (m, 1H, H-5bA), 1.52 (s, 3H, CH_3), 1.30 (s, 3H, CH_3), 1.29 (s, 3H, CH_3), 1.19 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 166.3 (C=O), 136.3 (Ar), 135.4 (Ar), 132.81 (Ar), 131.7 (Ar), 131.5 (Ar), 130.4 (Ar), 129.7 (2C, Ar), 129.7 (Ar), 129.7 (Ar), 128.3 (2C Ar), 108.5 (C-1B), 96.3 (C-1A), 87.2 (C-2B), 81.6 (C-2A), 79.1 (C-4B), 71.0 (C-3B), 70.5 (C-3A), 70.5 (C-5B), 69.3 (Ar*C*H_2), 69.1 (Ar*C*H_2), 66.9 (C-5A), 66.8 (C-4A), 65.2 (C-6B), 26.0 (CH_3), 25.8 (CH_3), 24.9 (CH_3), 24.2 (CH_3); HRMS-ESI *m/z* $[M + Na]^+$ calcd for $C_{32}H_{38}NaO_{11}$: 621.2312, found: 621.2309.



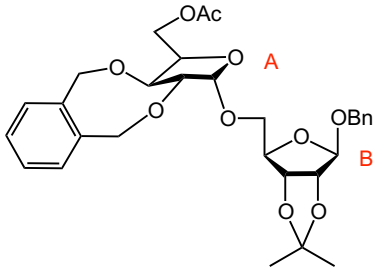
5-*O*-Acetyl-2,3-*O*-xylylene-α-D-xylofuranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (119): R_f 0.40 (1:1, hexanes–EtOAc); $[\alpha]_D$ = +23.5 (*c* = 0.3, $CHCl_3$);^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.42−7.31 (m, 4H, ArH), 5.51 (d, 1H, $J_{1,2}$ = 5.0 Hz, H-1A), 5.06−5.00 (m, 2H, H-1B, ArCH_2), 4.83 (d, 1H, J_{gem} = 10.1 Hz, ArCH_2), 4.81 (d, 1H, J_{gem} = 12.6 Hz, ArCH_2), 4.71 (d, 1H, J_{gem} = 12.6 Hz, ArCH_2), 4.58 (dd, 1H,

$J_{2,3}$ = 2.4 Hz, $J_{3,4}$ = 7.9 Hz, H-3A), 4.50 (ddd, $J_{4,5a}$ = 2.8 Hz, $J_{3,4}$ = $J_{4,5b}$ = 7.9 Hz, H-4A), 4.38 (dd, 1H, $J_{5,6a}$ = 2.8 Hz, J_{gem} = 12.3 Hz, H-6aB), 4.34 (dd, 1H, $J_{1,2}$ = 5.0 Hz, $J_{2,3}$ = 2.4 Hz, H-4B), 4.29 (dd, 1H, $J_{1,2}$ = 5.0 Hz, $J_{2,3}$ = 2.4 Hz, H-2A), 4.24 (dd, 1H, $J_{2,3}$ = 2.0 Hz, $J_{3,4}$ = 7.9 Hz, H-3B), 4.12−4.10 (m, 1H, H-6bB), 4.06−3.99 (m, 2H, H-2B, H-5B), 3.85−3.76 (m, 2H, H-5aA, H-5bA), 2.02 (s, 3H, C(O)CH_3), 1.52 (s, 3H, CH_3), 1.30 (s, 3H, CH_3), 1.29 (s, 3H, CH_3), 1.19 (s, 3H, CH_3);^{13}C NMR (125 MHz, $CDCl_3$) δ_C 170.9 (C=O), 136.6 (Ar), 135.5 (Ar), 131.6 (Ar), 131.5 (Ar), 129.6 (Ar), 129.5 (Ar), 109.2 (C-1B), 96.3 (C-1A), 83.1 (C-2B), 80.0 (C-2A), 76.1 (C-4B), 71.4 (C-3B), 70.7 (C-3A), 70.6 (C-5B), 69.7 (ArCH_2), 69.1 (ArCH_2), 67.0 (C-5A), 66.8 (C-4A), 63.6 (C-6B), 26.07 (CH_3), 25.82 (CH_3), 24.96 (CH_3), 24.21 (CH_3) 21.0 (C(O)CH_3); HRMS-ESI *m/z* $[M + Na]^+$ calcd for $C_{27}H_{36}NaO_{11}$: 559.2155, found: 559.2164.



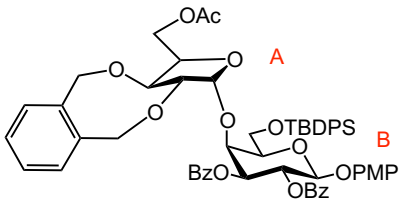
5-*O*-Acetyl-2,3-*O*-xylylene-α-D-xylofuranosyl-(1→3)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (122): R_f 0.3 (2:1, hexane–EtOAc); $[\alpha]_D$ = +35.7 (*c* = 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.42−7.31 (m, 4H, ArH), 5.89 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-1B),

5.20 (d, 1H, $J_{1,2}$ = 4.8 Hz, H-1A), 4.99 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.84 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.80 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.75 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.60 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-2B), 4.47−4.40 (m, 2H, H-4A, H-5B), 4.36 (dd, 1H, J_{gem} = 12.3 Hz, $J_{4,5a}$ = 3.0 Hz, H-5aA), 4.32 (dd, 1H, $J_{2,3}$ = 5.1 Hz, $J_{3,4}$ = 7.6 Hz, H-3A), 4.23−4.13 (m, 4H, H-3B, H-4B, H-5bA, H-6aB), 4.03 (app t, 1H, $J_{1,2}$ = $J_{2,3}$ = 5.1 Hz, H-2A), 3.95 (dd, 1H, J_{gem} = 8.4 Hz, $J_{5,6b}$ = 6.5 Hz, H-6bB), 2.04 (s, 3H, C(O)CH_3), 1.51 (s, 3H, CH_3), 1.44 (s, 3H, CH_3), 1.39 (s, 3H, CH_3), 1.32 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 170.8 (C=O), 131.6 (Ar), 131.4 (Ar), 129.5 (2C, Ar), 111.8 (Ar), 108.8 (Ar), 105.2 (C-1B), 102.1 (C-1A), 83.9 (C-2B), 82.8 (C-2A), 81.28, 81.25 (C-3B, C-4B), 79.6 (C-3A), 76.3, 72.5 (C-4A, C-5B), 69.6 (Ar*C*H_2), 69.0 (Ar*C*H_2), 67.2 (C-6B), 63.5 (C-5A), 26.9 (CH_3), 26.7 (CH_3), 26.3 (CH_3), 25.5 (CH_3), 20.9 (C(O)*C*H_3). HRMS-ESI *m/z* $[M + Na]^+$ calcd for $C_{27}H_{36}NaO_{11}$: 559.2155, found: 559.2164.



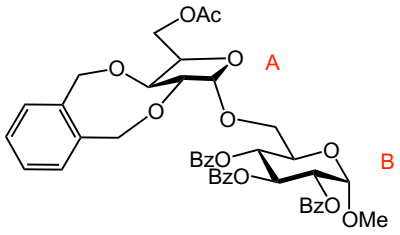
Benzyl 5-*O*-acetyl-2,3-*O*-xylylene-α-D-xylofuranosyl-(1→5)-2,3-*O*-isopropylidene-β-D-ribofuranoside (131): R_f 0.3 (2:1, hexane–EtOAc); $[\alpha]_D$ = −24.5 (*c* = 0.5, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.41−7.27 (m, 9H, ArH), 5.13 (s, 1H, H-1B), 5.03−5.00

(m, 2H, H-1A, ArCH$_2$), 4.83 (d, 1H, J_{gem} = 11.8 Hz, ArCH_2), 4.83 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.79 (dd, 1H, $J_{2,3}$ = 6.0 Hz, $J_{3,4}$ = 1.0 Hz, H-3B), 4.71 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.67 (d, 1H, J_{gem} = 11.8 Hz, ArCH_2), 4.65 (d, 1H, $J_{2,3}$ = 6.0 Hz, H-2B), 4.50−4.43 (m, 2H, H-4A, H-4B), 4.42 (d, 1H, J_{gem} = 11.8 Hz, ArCH_2), 4.39−4.36 (m, 2H, H-3A, H-5bA), 4.12 (dd, 1H, J_{gem} = 12.3 Hz, $J_{4,5a}$ = 8.2 Hz, H-5aA), 4.01 (app t, 1H, $J_{1,2}$ = $J_{2,3}$ = 4.9 Hz, H-2A), 3.75−3.70 (m, 2H, H-5aB, H-5bB), 1.97 (s, 3H, C(O)CH_3), 1.46 (s, 3H, CH$_3$), 1.31 (s, 3H, CH$_3$); ^{13}C NMR (125 MHz, CDCl$_3$) δ_C 170.8 (C=O), 137.1 (Ar), 136.5 (Ar), 135.4 (Ar), 131.6 (Ar), 131.5 (Ar), 129.6 (Ar), 129.5 (Ar), 128.4 (Ar), 127.9 (2C, Ar), 127.8 (2C, Ar), 107.2 (C-1B), 101.9 (C-1A), 85.4 (C-4A or C-4B), 85.3 (C-2B), 83.0 (C-2A), 82.1 (C-3B), 79.7 (C-3A), 76.3 (C-4A or C-4B), 69.7 (ArCH$_2$), 69.6 (C-5B), 69.04 (ArCH$_2$), 69.03 (ArCH$_2$), 63.5 (C-5A), 26.5 (CH$_3$), 25.1 (CH$_3$), 20.9 (C(O)CH$_3$); HRMS-ESI *m/z* [M + Na]$^+$ calcd for $C_{30}H_{36}NaO_{10}$: 579.2206, found: 579.2210.



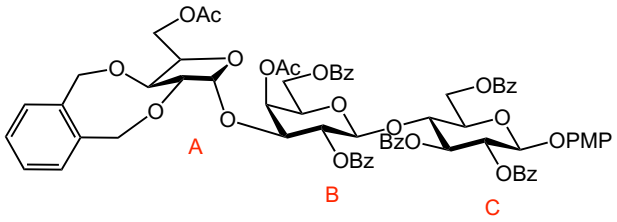
***p*-Methoxyphenyl 5-*O*-acetyl-2,3-*O*-xylylene-α-D-xylofuranosyl-(1→4)-6-*O*-(*tert*-butyldiphenylsilyl)-2,3-di-*O*-benzoyl-β-D-galactopyranoside (132):** R_f 0.3 (4:1, hexane–EtOAc); $[\alpha]_D$ = +45.7 (c = 0.9, CHCl$_3$); ^{1}H NMR (500 MHz, CDCl$_3$) δ_H

8.04−7.96 (m, 4H, ArH), 7.80−7.73 (m, 4H, ArH), 7.54−7.28 (m, 15H, ArH), 7.19−7.12 (m, 1H, ArH), 7.01−6.93 (m, 2H, ArH), 6.76−6.69 (m, 2H, ArH), 5.96 (dd, 1H, $J_{1,2}$ = 8.0 Hz, $J_{2,3}$ = 10.6 Hz, H-2B), 5.24 (dd, 1H, $J_{2,3}$ = 10.6 Hz, $J_{3,4}$ = 3.3 Hz, H-3B), 5.12 (d, 1H, $J_{1,2}$ = 8.0 Hz, H-1B), 5.12 (d, 1H, $J_{1,2}$ = 4.6 Hz, H-1A), 4.85 (d, 1H, J_{gem} = 12.8 Hz, ArCH_2), 4.76−4.66 (m, 2H, ArCH_2), 4.50−4.42 (m, 4H, H-3A, H-4A, H-4B, ArCH_2), 4.15 (dd, 1H, J_{gem} = 10.6 Hz, $J_{5,6a}$ = 6.5 Hz, H-6aB), 4.09 (dd, 1H, J_{gem} = 10.6 Hz, $J_{5,6b}$ = 6.4 Hz, H-6bB), 3.92 (app t, 1H, $J_{5,6a}$ = $J_{5,6b}$ = 6.4 Hz, H-5B), 3.81 (app t, 1H, $J_{1,2}$ = $J_{2,3}$ = 4.8 Hz, H-2A), 3.73 (s, 3H, OCH_3), 3.67 (dd, 1H, J_{gem} = 11.8 Hz, $J_{4,5a}$ = 3.0 Hz, H-5aA), 3.55 (dd, 1H, J_{gem} = 11.8 Hz, $J_{4,5b}$ = 3.8 Hz, H-5bA), 1.71 (s, 3H, C(O)CH_3), 1.12 (s, 9H, 3 x CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 170.4 (C=O), 166.0 (C=O), 165.4 (C=O), 155.3 (Ar), 151.4 (Ar), 137.1 (Ar), 135.7 (Ar), 135.65 (2C, Ar), 135.62 (2C, Ar), 133.4 (Ar), 133.3 (Ar), 133.2 (Ar), 133.1 (Ar), 131.4 (Ar), 131.1 (Ar), 129.9 (Ar), 129.80 (Ar), 129.79 (Ar), 129.6 (2C, Ar), 129.5 (Ar), 129.2 (Ar), 129.1 (Ar), 128.38 (2C, Ar), 128.32 (2C, Ar), 127.83 (2C, Ar), 127.81 (2C, Ar), 118.6 (2C, Ar), 114.4 (2C, Ar), 103.3 (C-1A), 101.0 (C-1B), 82.1 (C-2A), 79.4, 76.0, 75.7, 74.7 (C-3A, C-4A, C-4B, C-5B), 73.8 (C-3B), 69.6 (C-2B), 69.3 (Ar*C*H_2), 69.0 (Ar*C*H_2), 62.2 (C-6B), 62.0 (C-5A), 55.5 (OCH_3), 26.9 (*C*$(CH_3)_3$), 20.7(C(O)*C*H_3), 19.2 (3 x CH_3); HRMS-ESI *m/z* $[M + Na]^+$ calcd for $C_{58}H_{60}NaO_{14}Si$: 1031.3650, found: 1031.3661.



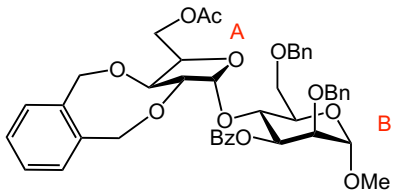
Methyl 5-*O*-acetyl-2,3-*O*-xylylene-α-D-xylofuranosyl-(1→6)-2,3,4-tri-*O*-benzoyl -α-D-glucopyranoside (133): R_f 0.4 (3:2 hexane/EtOAc); $[\alpha]_D$ = +45.3 (c = 0.7, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.01−7.96 (m, 2H, ArH), 7.96−7.92 (m, 2H, ArH), 7.89−7.83 (m, 2H, ArH), 7.53−7.46 (m, 2H, ArH), 7.43−7.27 (m, 11H, ArH), 6.13 (app t, 1H, $J_{2,3}$ = $J_{3,4}$ = 9.8 Hz, H-3B), 5.58 (app t, 1H, $J_{3,4}$ = $J_{4,5}$ = 9.8 Hz, H-4B), 5.29 (dd, 1H, $J_{1,2}$ = 3.6 Hz, $J_{2,3}$ = 9.8 Hz, H-2B), 5.22 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-1B), 4.98−4.91 (m, 2H, H-1A, ArCH_2), 4.79 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.76−4.68 (m, 2H, ArCH_2), 4.47 (ddd, 1H, $J_{4,5a}$ = 2.7 Hz, $J_{3,4}$ = $J_{4,5b}$ = 8.0 Hz, H-4A), 4.36−4.30 (m, 2H, H-3A, H-5aA), 4.27 (ddd, 1H, $J_{4,5}$ = 9.8 Hz, $J_{5,6a}$ = 5.6 Hz, $J_{5,6b}$ = 2.8 Hz, H-5B), 4.07 (dd, 1H, J_{gem} = 12.3 Hz, $J_{4,5a}$ = 8.0 Hz, H-5aA), 3.97 (app t, 1H, $J_{1,2}$ = $J_{2,3}$ = 5.0 Hz, H-2A), 3.92 (dd, 1H, J_{gem} = 11.1 Hz, $J_{5,6a}$ = 5.6 Hz, H-6aB), 3.70 (dd, 1H, J_{gem} = 11.1 Hz, $J_{5,6b}$ = 2.8 Hz, H-6bB), 3.44 (s, 3H, OCH_3), 1.90 (s, 3H, C(O)CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 170.9 (C=O), 165.8 (C=O), 165.8 (C=O), 165.3 (C=O), 136.8 (Ar), 135.5 (Ar), 133.3 (Ar), 133.3 (Ar), 133.0 (Ar), 131.6 (Ar), 131.4 (Ar), 129.9 (2C, Ar), 129.8 (2C, Ar), 129.6 (2C, Ar), 129.5 (Ar), 129.4 (Ar), 129.3 (Ar), 129.1 (Ar), 129.1 (Ar), 128.4 (3C, Ar), 128.2 (2C, Ar), 100.8 (C-1A), 96.8 (C-1B), 82.7 (C-2A), 79.9 (C-3A), 76.2 (C-4A),

72.1 (C-2B), 70.7 (C-3B), 69.7 (C-4B), 69.3 (Ar*C*H_2), 69.3 (Ar*C*H_2), 68.3 (C-6B), 66.2 (C-5B), 63.6 (C-5A), 55.5 (OCH_3), 20.8 (C(O)*C*H_3); HRMS-ESI *m/z* $[M + Na]^+$ calcd for $C_{43}H_{42}NaO_{14}$: 805.2472, found: 805.2479.



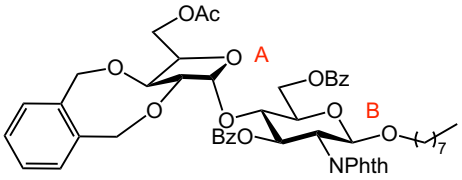
***p*-Methoxyphenyl 5-*O*-acetyl-2,3-*O*-xylylene-α-D-xylofuranosyl-(1→3)-4-*O*-acetyl-2,6-di-*O*-benzoyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-benzoyl-β-D-glucopyranoside (134):** R_f 0.4 (3:2, hexane–EtOAc); $[\alpha]_D$ = +27.3 (*c* = 1.8, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.07−7.99 (m, 6H, ArH), 7.99−7.88 (m, 4H, ArH), 7.61−7.48 (m, 6H, ArH), 7.42−7.30 (m, 11H, ArH), 7.25−7.18 (m, 2H, ArH), 6.89−6.81 (m, 2H, ArH), 6.66−6.60 (m, 2H, ArH), 5.79 (app t, 1H, $J_{2,3} = J_{3,4}$ = 9.3 Hz, H-3C), 5.64 (dd, 1H, $J_{2,3}$ = 9.3 Hz, $J_{1,2}$ = 7.8 Hz, H-2C), 5.37−5.29 (m, 2H, H-2B, H-4B), 5.09 (d, 1H, $J_{1,2}$ = 7.8 Hz, H-1C), 4.97 (d, 1H, $J_{1,2}$ = 4.6 Hz, H-1A), 4.84 (d, 1H, J_{gem} = 13.1 Hz, ArCH_2), 4.68−4.52 (m, 5H, 3(ArCH_2), H-1B, H-5bA), 4.41 (dd, 1H, J_{gem} = 11.9 Hz, $J_{4,5a}$ = 5.6 Hz, H-5aA), 4.20 (app t, 1H, $J_{3,4} = J_{4,5}$ = 9.5 Hz, H-4C), 3.98−3.96 (m, 1H, H-3B), 3.95−3.94 (m, 1H, H-3A), 3.93−3.81 (m, 5H, H-2A, H-4A, H-5C, H-6aC, H-6bC), 3.74−3.60 (m, 6H, H-5B, H-6aB, H-6bB, OCH_3), 2.09 (s, 3H, C(O)CH_3), 1.87 (s, 3H, C(O)CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 165.7 (C=O), 165.6 (C=O), 165.2 (C=O), 164.6 (C=O), 155.6 (C=O), 136.2 (Ar), 135.9 (Ar), 133.4 (2C, Ar), 133.3 (2C, Ar),

133.2 (2C, Ar), 133.1 (2C, Ar), 131.6 (2C, Ar), 131.2 (2C, Ar), 129.85 (2C, Ar), 129.81 (2C, Ar), 129.7 (2C, Ar), 129.66 (2C, Ar), 129.64 (2C, Ar), 129.5 (2C, Ar), 129.3 (2C, Ar), 129.2 (Ar), 128.6 (2C, Ar), 128.5 (2C, Ar), 128.47 (2C, Ar), 128.43 (2C, Ar), 128.2 (2C, Ar), 118.9 (2C, Ar), 114.4 (2C, Ar), 101.1 (C-1B), 100.6 (C-1C), 97.5 (C-1A), 81.8 (C-2A), 79.1 (C-3A), 76.1 (C-4C), 75.8 (C-5C), 73.1 (C-3B), 72.9 (C-3C), 72.8 (C-4A), 71.6 (C-2C), 71.1 (C-5B), 70.9 (C-2B), 69.9 (Ar*C*H_2), 69.0 (Ar*C*H_2), 64.9 (C-4B), 63.1 (C-6C), 62.6 (C-5A), 61.0 (C-6B), 55.5 (OCH_3), 20.7 (2 × C(O)*C*H_3); HRMS-ESI *m/z* $[M + Na]^+$ calcd for $C_{71}H_{66}NaO_{23}$: 1309.3893, found: 1309.3898.



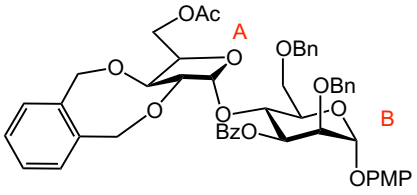
Methyl 5-*O*-acetyl-2,3-*O*-xylylene-α-D-xylofuranosyl-(1→4)-3-*O*-benzoyl-2,6-di-*O*-benzyl-α-D-mannopyranoside (135): R_f 0.3 (2:1, hexane–EtOAc); $[\alpha]_D$ = +23.5 (*c* = 0.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.14−8.08 (m, 2H, ArH), 7.70−7.64 (m, 1H, ArH), 7.56−7.48 (m, 2H, ArH), 7.44−7.37 (m, 2H, ArH), 7.35−7.15 (m, 11H, ArH), 6.55−6.48 (m, 1H, ArH), 5.63 (dd, 1H, $J_{2,3}$ = 3.3 Hz, $J_{3,4}$ = 9.8 Hz, H-3B), 5.23 (d, 1H, $J_{1,2}$ = 5.1 Hz, H-1A), 4.84 (d, 1H, $J_{1,2}$ = 1.8 Hz, H-1B), 4.74 (d, 1H, J_{gem} = 11.9 Hz, ArCH_2), 4.71−4.62 (m, 4H, ArCH_2), 4.61−4.55 (m, 2H, ArCH_2), 4.28−4.07 (m, 6H, H-3A, H-4B, H-5B, H-6aB, H-6bB, ArCH_2), 3.99 (ddd, 1H, $J_{4,5a}$ = 1.8 Hz, $J_{3,4}$ = 9.9 Hz,

$J_{4,5b}$ = 6.0 Hz, H-4A), 3.93 (dd, 1H, $J_{1,2}$ = 1.8 Hz, $J_{2,3}$ = 3.3 Hz, H-2B), 3.87 (dd, 1H, J_{gem} = 10.8 Hz, $J_{4,5a}$ = 1.8 Hz, H-5aA), 3.79 (dd, 1H, J_{gem} = 10.8 Hz, $J_{4,5b}$ = 6.0 Hz, H-5bA), 3.69 (app t, 1H, $J_{1,2}$ = $J_{2,3}$ = 5.0 Hz, H-2A), 3.42 (s, 3H, OCH_3), 1.91 (s, 3H, C(O)CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 170.7 (C=O), 165.3 (C=O), 138.6 (Ar), 137.9 (Ar), 136.6 (Ar), 135.2 (Ar), 132.8 (Ar), 131.4 (Ar), 131.1 (Ar), 130.6 (Ar), 129.7 (2C, Ar), 129.2 (Ar), 129.1 (Ar), 128.5 (2C, Ar), 128.23 (3C, Ar), 128.22 (3C, Ar), 127.7 (3C, Ar), 127.6 (3C, Ar), 127.4 (Ar), 103.3 (C-1A), 98.8 (C-1B), 81.4 (C-2A), 80.3 (C-3A, C-4B or C-5B), 76.10 (C-3A, C-4B or C-5B), 76.06 (C-2B), 74.03 (C-3A, C-4B or C-5B), 73.97 (C-3B), 73.3 (ArCH$_2$), 72.9 (ArCH$_2$), 70.8 (C-4A), 69.5 (ArCH$_2$), 69.3 (ArCH$_2$), 69.1 (C-5A), 63.5 (C-6A), 54.8 (OCH_3), 20.8 (C(O)CH$_3$); HRMS-ESI *m/z* $[M + Na]^+$ calcd for $C_{43}H_{46}NaO_{12}$: 777.2887, found: 777.2880.

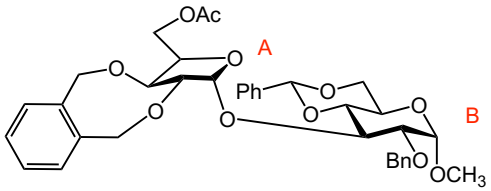


Octyl 5-*O*-acetyl-2,3-*O*-xylylene-α-D-xylofuranosyl-(1→3)-4,6-di-*O*-benzoyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (136): R_f 0.25 (2:1, hexane–EtOAc); $[\alpha]_D$ = +69.0 (*c* = 0.3, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.11−8.05 (m, 2H, ArH), 7.95−7.86 (m, 3H, ArH), 7.76−7.53 (m, 5H, ArH), 7.49−7.43 (m, 2H, ArH), 7.43−7.37 (m, 2H, ArH), 7.25−7.21 (m, 1H, ArH), 7.19−7.15 (m, 1H, ArH), 7.13−7.08 (m, 1H,

ArH), 6.53−6.49 (m, 1H, ArH), 6.15 (app t, 1H, $J_{2,3} = J_{3,4} = 10.9$ Hz, H-3B), 5.49 (d, 1H, $J_{1,2} = 8.4$ Hz, H-1B), 5.11 (d, 1H, $J_{1,2} = 5.1$ Hz, H-1A), 4.76 (dd, 1H, $J_{gem} = 11.9$ Hz, $J_{4,5a} = 1.5$ Hz, H-5aA), 4.64 (d, 1H, $J_{gem} = 12.7$ Hz, ArCH_2), 4.61−4.56 (m, 2H, ArCH_2), 4.51 (dd, 1H, $J_{gem} = 11.9$ Hz, $J_{4,5b} = 7.6$ Hz, H-5bA), 4.46 (ddd, 1H, $J_{4,5a} = 1.5$ Hz, $J_{3,4} = J_{4,5b} = 7.6$ Hz, H-4A), 4.38 (dd, 1H, $J_{1,2} = 8.4$ Hz, $J_{2,3} = 10.9$ Hz, H-2B), 4.26 (dd, 1H, $J_{2,3} = 5.3$ Hz, $J_{3,4} = 7.7$ Hz, H-3A), 4.18−4.12 (m, 1H, H-6aB), 4.10−3.99 (m, 4H, H-3B, H-4B, H-6bB, ArCH_2), 3.82 (dt, 1H, $J_{gem} = 9.8$ Hz, $J = 6.2$ Hz, octyl OCH_2), 3.60 (app t, 1H, $J_{1,2} = J_{2,3} = 5.3$ Hz, H-2A), 3.45 (m, 1H, octyl OCH_2), 1.85 (s, 3H, C(O)CH_3), 1.47−1.31 (m, 2H, octyl), 1.18−1.10 (m, 2H, octyl CH_2), 1.07−0.98 (m, 6H, octyl CH_2), 0.97−0.88 (m, 2H, octyl CH_2), 0.79 (t, 3H, $J = 7.3$ Hz, octyl CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 170.9 (C=O), 166.2 (C=O), 165.4 (C=O), 136.5 (Ar), 135.1 (Ar), 134.0 (Ar), 133.9 (Ar), 133.0 (Ar), 132.9 (Ar), 131.4 (Ar), 131.0 (Ar), 130.2 (Ar), 129.73 (2C, Ar), 129.71 (2C, Ar), 129.6 (Ar), 129.2 (2C, Ar), 129.1 (2C, Ar), 128.5 (2C, Ar), 128.4 (Ar), 123.5 (2C, Ar), 104.0 (C-1A), 98.3 (C-1B), 81.3 (C-2A), 79.9 (C-3A), 77.9 (C-4B or C-3B), 76.7 (C-4A), 73.3 (C-5B), 72.7 (C-4B or C-3B), 70.2 (octyl OCH_2), 69.2 (Ar*C*H_2), 69.1 (Ar*C*H_2), 63.5 (C-5A), 63.1 (C-6B), 55.1 (C-2B), 31.6 (octyl CH_2), 29.3 (octyl CH_2), 29.14 (octyl CH_2), 29.13 (octyl CH_2), 25.8 (octyl CH_2), 22.6 (octyl CH_2), 20.6 (C(O)*C*H_3), 14.0 (octyl *C*H_3); HRMS-ESI *m/z* $[M + Na]^+$ calcd for $C_{51}H_{55}NO_{14}$: 905.3623, found: 905.3627.

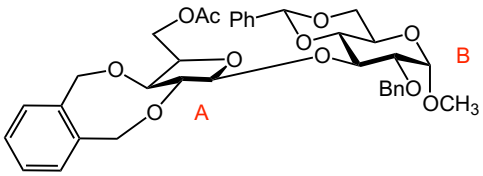


***p*-Methoxyphenyl 5-*O*-acetyl-2,3-*O*-xylylene-α-D-xylofuranosyl-(1→4)-3-*O*-benzoyl-2,6-di-*O*-benzyl-α-D-mannopyranoside (137):** R_f 0.3 (2:1, hexane–EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.14−8.07 (m, 2H, ArH), 7.70−7.64 (m, 1H, ArH), 7.56−7.43 (m, 2H, ArH), 7.34−7.26 (m, 5H, ArH), 7.25−7.00 (m, 10H, ArH), 6.84−6.75 (m, 2H, ArH), 6.50−6.44 (m, 1H, ArH), 5.82 (dd, 1H, $J_{2,3}$ = 3.3 Hz, $J_{3,4}$ = 9.8 Hz, H-3B), 5.49 (d, 1H, $J_{1,2}$ = 1.8 Hz, H-1B), 5.23 (d, 1H, $J_{1,2}$ = 5.1 Hz, H-1A), 4.71−4.63 (m, 2H, H-4A, ArCH_2), 4.63−4.55 (m, 4H, ArCH_2), 4.50 (d, 1H, J_{gem} = 11.5 Hz, ArCH_2), 4.38−4.27 (m, 2H, H-4B, H-5B), 4.23−4.21 (m, 1H, H-3A), 4.16−4.04 (m, 3H, H-2B, H-6aB, H-6bB), 3.85−3.73 (m, 5H, OCH_3, H-5aA, H-5bA), 3.69 (app t, 1H, $J_{1,2}$ = $J_{2,3}$ = 5.1 Hz, H-2A), 1.87 (s, 3H, C(O)CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 170.7 (C=O), 165.5 (C=O), 155.0 (Ar), 150.3 (Ar), 138.5 (Ar), 137.87 (Ar), 136.6 (Ar), 135.1 (Ar), 132.9 (Ar), 131.3 (Ar), 131.1 (Ar), 130.5 (Ar), 129.6 (2C, Ar), 129.2 (Ar), 129.1 (Ar), 128.6 (2C, Ar), 128.23 (3C, Ar), 128.22 (3C, Ar), 127.7 (3C, Ar), 127.5 (3C, Ar), 127.4 (Ar), 103.6 (C-1A), 97.0 (C-1B), 81.5 (C-2A), 80.3 (C-3A, C-4B or C-5B), 77.3 (C-3A, C-4B or C-5B), 76.0 (C-2B), 74.2 (C-3A, C-4B or C-5B), 73.7 (C-3B), 73.2 (ArCH$_2$), 71.3 (ArCH$_2$), 70.83 (C-4A), 69.51 (ArCH$_2$), 69.30 (ArCH$_2$), 69.1 (C-5A), 63.5 (C-6A), 55.6 (OCH_3), 20.8 (C(O)CH$_3$); HRMS-ESI *m/z* [M + Na]$^+$ calcd for $C_{49}H_{50}NaO_{13}$: 869.3149, found: 869.3155.



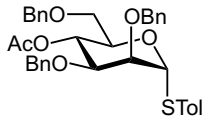
Methyl 5-*O*-acetyl-2,3-*O*-xylylene-α-D-xylofuranosyl-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (138α): R_f 0.25 (2:1, hexane–EtOAc); $[\alpha]_D = -38.2$ (c = 0.3, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.47−7.43 (m, 2H, ArH), 7.39−7.27 (m, 12H, ArH), 5.53 (s, 1H, PhC*H*O_2), 5.46 (d, 1H, $J_{1,2}$ = 4.6 Hz, H-1A), 5.04 (d, 1H, J_{gem} = 12.7 Hz, ArC*H*$_2$), 4.87−4.78 (m, 2H, ArC*H*$_2$), 4.73 (d, 1H, J_{gem} = 12.7 Hz, ArC*H*$_2$), 4.71 (d, 1H, J_{gem} = 11.7 Hz, ArC*H*$_2$), 4.61−4.54 (m, 3H, H-4A, H-1B, ArC*H*$_2$), 4.39 (app t, $J_{2,3} = J_{3,4}$ = 9.4 Hz, H-3B), 4.30−4.20 (m, 3H, H-3A, H-5bA, H-6aB), 4.10 (dd, 1H, J_{gem} = 12.2 Hz, $J_{4,5a}$ = 7.1 Hz, H-5aA), 4.03 (app t, 1H, $J_{1,2} = J_{2,3}$ = 4.9 Hz, H-2A), 3.80 (app td, 1H, $J_{4,5} = J_{5,6a}$ = 9.8 Hz, $J_{5,6b}$ = 4.7 Hz, H-5B), 3.75−3.64 (m, 2H, H-4B, H-6bB), 3.56 (dd, 1H, $J_{1,2}$ = 3.7 Hz, $J_{2,3}$ = 9.5 Hz, H-2B), 3.37 (s, 3H, OCH_3), 1.95 (s, 3H, C(O)C*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 170.9 (C=O), 138.1 (Ar), 137.4 (Ar), 136.6 (Ar), 135.9 (Ar), 131.6 (Ar), 131.3 (Ar), 129.4 (Ar), 129.3 (Ar), 128.9 (2C, Ar), 128.4 (2C, Ar), 128.2 (2C, Ar), 128.0 (2C, Ar), 127.9 (Ar), 126.1 (2C, Ar), 101.3 (Ph*C*HO_2), 100.2 (C-1A), 99.0 (C-1B), 83.1 (C-2A), 82.5 (C-4B), 79.9 (C-3A), 77.4 (C-2B), 75.7 (C-4A), 73.3 (Ar*C*H_2), 72.35 (C-3B), 70.1 (Ar*C*H_2), 69.1 (Ar*C*H_2), 68.9 (C-6B), 63.2

(C-5A), 62.0 (C-5B), 55.2 (OCH_3), 20.9 (C(O)CH_3); HRMS-ESI *m/z* $[M + Na]^+$ calcd for $C_{36}H_{40}NaO_{11}$: 671.2468, found: 671.2474.



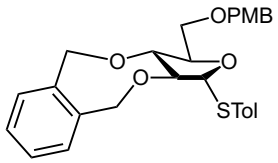
Methyl 5-*O*-acetyl-2,3-*O*-xylylene-β-D-xylofuranosyl-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (138β): R_f 0.27 (2:1, hexane–EtOAc); $[\alpha]_D$ = +20.3 (*c* = 0.2, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.53−7.48 (m, 2H, ArH), 7.42−7.27 (m, 12H, ArH), 5.48 (s, 1H, PhC*H*O_2), 5.34 (d, 1H, $J_{1,2}$ = 2.7 Hz, H-1A), 4.89−4.78 (m, 3H, ArCH_2), 4.74−4.67 (m, 2H, ArCH_2), 4.63−4.57 (m, 2H, H-1B, ArCH_2), 4.41 (dd, 1H, J_{gem} = 11.9 Hz, $J_{4,5a}$ = 3.8 Hz, H-5aA), 4.29 (ddd, 1H, $J_{3,4}$ = 7.0 Hz, $J_{4,5a}$ = 3.8 Hz, $J_{4,5b}$ = 7.0 Hz, H-4A), 4.24 (dd, 1H, $J_{5,6b}$ = 4.7 Hz, J_{gem} = 10.1 Hz, H-6aB), 4.18−4.07 (m, 4H, H-2A, H-3A, H-5bA, H-3B), 3.79 (app td, 1H, $J_{4,5}$ = $J_{5,6a}$ = 9.8 Hz, $J_{5,6b}$ = 4.7 Hz, H-5B), 4.24 (app t, 1H, $J_{5,6b}$ = J_{gem} = 10.3 Hz, H-6bB), 3.53−3.46 (m, 2H, H-2B, H-4B), 3.38 (s, 3H, OCH_3), 1.86 (s, 3H, C(O)CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 170.7 (C=O), 138.2 (Ar), 137.4 (Ar), 136.5 (Ar), 135.7 (Ar), 131.7 (Ar), 131.3 (Ar), 129.6 (Ar), 129.5 (Ar), 128.7 (Ar), 128.4 (2C, Ar), 128.2 (2C, Ar), 128.0 (2C, Ar), 127.9 (Ar), 126.2 (2C, Ar), 108.7 (C-1A), 101.3 (Ph*C*HO_2), 98.9 (C-1B), 87.1 (C-2A or C-3A), 81.1 (C-2A or C-3A), 80.6 (C-2B or C-4B), 79.0 (C-2B or C-4B), 78.4 (C-4A), 76.5 (C-3B), 73.5 (Ar*C*H_2), 69.2 (2 x Ar*C*H_2), 69.0 (C-6B), 64.3 (C-5A), 62.3 (C-5B),

55.3 (OCH_3), 20.9 ($C(O)CH_3$); HRMS-ESI *m/z* $[M + Na]^+$ calcd for $C_{36}H_{40}NaO_{11}$: 671.2468, found: 671.2481.



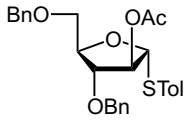
***p*-Tolyl 4-*O*-acetyl-2,3,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (140):** To a solution of **145** (2.86 g, 10.0 mmol) in benzyl chloride (14 mL) at rt was added lithium hydroxide monohydrate (3.35 g, 80.0 mmol). The reaction mixture was stirred for 14 h at 140 °C, cooled to room temperature and then co-evaporated with toluene to remove the benzyl chloride. The resulting crude residue was purified by flash column chromatography (10:1, hexanes–EtOAc) providing the *p*-tolyl 2,3,6-tri-*O*-benzyl-1-thio-*α*-D-mannopyranoside, which was dissolved in pyridine (10 mL) was added acetic anhydride (10 mL) at rt. The solution was stirred for 2 h at rt and then the reaction was quenched by the addition of CH_3OH, followed by co-evaporation with toluene to remove the solvent. The residue was purified by silica gel column chromatography (8:1, hexanes–EtOAc) to afford **140** (2.93 g, 49%) as an oil: R_f 0.5 (4:1, hexanes–EtOAc); $[\alpha]_D$ = +46.8 (*c* = 0.6, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.41−7.23 (m, 17H, ArH), 7.06−7.01 (m, 2H, ArH), 5.52 (d, 1 H, $J_{1,2}$ = 1.9 Hz, H-1), 4.24 (app t, 1 H, $J_{3,4} = J_{4,5}$ = 9.7 Hz, H-4), 4.71 (d, 1H, J_{gem} = 12.3 Hz, ArCH_2), 4.64 (d, 1H, J_{gem} = 12.3 Hz, ArCH_2), 4.58 (d, 1H, J_{gem} = 12.1 Hz, ArCH_2), 4.53 (d, 1H, J_{gem} =

11.8 Hz, ArCH_2), 4.50−4.48 (m, 2H, ArCH_2), 4.41 (ddd, 1H, $J_{4,5}$ = 9.7 Hz, $J_{5,6a}$ = 6.4 Hz, $J_{5,6b}$ = 2.9 Hz, H-5), 4.00 (d, 1H, $J_{1,2}$ = 1.9 Hz, $J_{2,3}$ = 3.1 Hz, H-2), 3.87 (dd, 1H, $J_{2,3}$ = 3.1 Hz, $J_{3,4}$ = 9.5 Hz, H-3), 3.68 (dd, 1H, $J_{5,6a}$ = 6.4 Hz, J_{gem} = 10.9 Hz, H-6a), 3.61 (dd, 1H, $J_{5,6b}$ = 2.9 Hz, J_{gem} = 10.9 Hz, H-6b), 2.31 (s, 3H, ArCH_3), 1.98 (s, 3H, C(O)CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 169.8 (C=O), 138.2 (Ar), 137.9 (Ar), 137.8 (Ar), 132.4 (2C, Ar), 130.0 (Ar), 129.8 (2C, Ar), 128.4 (2C, Ar), 128.3 (2C, Ar), 128.2 (2C, Ar), 127.9 (2C, Ar), 127.75 (Ar), 127.72 (2C, Ar) (2C, Ar), 127.70 (Ar), 127.6 (2C, Ar), 127.4 (2C, Ar), 86.1 (C-1), 77.1 (C-3), 75.7 (C-2), 73.4 (ArCH$_2$), 72.1 (ArCH$_2$), 71.7 (ArCH$_2$), 71.3 (C-5), 69.8 (C-6), 69.0 (C-4), 21.1 (ArCH$_3$), 20.9 (C(O)CH$_3$); HRMS-ESI *m/z* [M + Na]$^+$ calcd for $C_{36}H_{38}NaO_6S$: 621.2287, found: 621.2295.



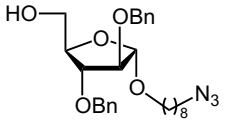
***p*-Tolyl 5-*O*-*p*-methoxybenzyl-1-thio-2,3-*O*-xylylene-α-D-arabinofuranoside (141):** To a solution of **149** (358 mg, 1.00 mmol) in DMF (6.0 mL) at 0 °C were added NaH (60 mg, 1.50 mmol) and PMBCl (173 μL, 1.50 mmol). The solution was stirred for 2 h at rt, and the reaction was then quenched by the addition of satd aq. NH_4Cl. Dilution of the mixture with CH_2Cl_2 provided a solution that was then washed with brine. The organic layer was subsequently dried with anhydrous Na_2SO_4, filtered, concentrated and the residue was purified by silica gel column chromatography (5:1, hexanes–EtOAc) to

give **141** (439 mg, 92%) as a white solid. R_f 0.37 (3:1 hexanes–EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.42−6.84 (m, 12H, ArH), 5.35 (d, 1H, $J_{1,2}$ = 4.5 Hz, H-1), 4.97 (d, 1H, J_{gem} = 12.5 Hz, ArCH_2), 4.85 (d, 1H, J_{gem} = 13.0 Hz, ArCH_2), 4.76 (d, 1H, J_{gem} = 12.5 Hz, ArCH_2), 4.74 (d, 1H, J_{gem} = 13.0 Hz, ArCH_2), 4.52 (d, 1H, J_{gem} = 12.0 Hz, ArCH_2), 4.45 (d, 1H, J_{gem} = 12.0 Hz, ArCH_2), 4.23 (ddd, 1H, $J_{3,4}$ = 8.5 Hz, $J_{4,5a}$ = 2.5 Hz, $J_{4,5b}$ = 4.5 Hz, H-4), 4.01 (dd, 1H, $J_{2,3}$ = 5.0 Hz, $J_{3,4}$ = 8.5 Hz, H-3), 3.95 (app t, 1H, $J_{1,2}$ = 4.5 Hz, $J_{2,3}$ = 5.0 Hz, H-2), 3.81 (s, 3H, OCH_3), 3.67 (dd, 1H, J_{gem} = 11.5 Hz, $J_{4,5a}$ = 2.5 Hz, H-5a), 3.56 (dd, 1H, J_{gem} = 11.5 Hz, $J_{4,5b}$ = 4.5 Hz, H-5b), 2.30 (s, 3H, ArCH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 159.1 (Ar), 137.3 (Ar), 136.1 (Ar), 135.6 (Ar), 132.1 (2C, Ar), 131.7 (Ar), 131.4 (Ar), 130.6 (Ar), 130.3 (Ar), 129.7 (Ar), 129.7 (2C, Ar), 129.5 (2C, Ar), 129.2 (Ar), 113.7 (2C, Ar), 90.9 (C-1), 86.6 (C-2), 81.1 (C-4), 80.0 (C-3), 72.9 (ArCH$_2$), 69.8 (ArCH$_2$), 68.5 (C-5), 68.4 (ArCH$_2$), 55.2 (OCH_3), 21.0 (ArCH$_3$); HRMS-ESI *m/z* $[M + Na]^+$ calcd for $C_{28}H_{30}NaO_5S$: 501.1706, found: 501.1698.



***p*-Tolyl 2-*O*-acetyl-3,5-di-*O*-benzyl-1-thio-α-D-arabinofuranoside (142):** To a solution of **154** (1.0 g, 2.59 mmol) in dry CH_2Cl_2 (10 mL) at 0 °C was added *p*-thiocresol (386 mg, 3.11 mmol). Then, $BF_3{\cdot}OEt_2$ (0.66 mL, 5.18 mmol) was added dropwise to the solution over 5 min. The solution was stirred for 1 h at 0 °C, and then

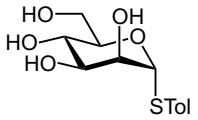
triethylamine (1 mL) was added. After dilution with CH_2Cl_2, the organic layer was washed with a satd. aq. solution of $NaHCO_3$ and dried with anhydrous Na_2SO_4, filtered and concentrated. The resulting oil was purified by silica gel column chromatography (10:1, hexanes–EtOAc) providing **142** (1.13 g, 91%) as a colorless oil: R_f 0.6 (6:1, hexanes–EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.43−7.39 (m, 2H, ArH), 7.36−7.26 (m, 10H, ArH), 7.12−7.07 (m, 2H, ArH), 5.50 (s, 1 H, H-1), 5.29 (d, 1H, $J_{1,2}$ = 1.6 Hz, H-2), 4.73 (d, 1H, J_{gem} = 12.1 Hz, ArCH_2), 4.60−4.52 (m, 2H, ArCH_2), 4.51−4.45 (m, 2H, ArCH_2, H-4), 3.98 (d, 1H, $J_{3,4}$ = 6.0 Hz, H-3), 3.66 (dd, 1H, $J_{4,5a}$ = 4.1 Hz, J_{gem} = 10.9 Hz, H-5a), 3.44 (dd, 1H, $J_{4,5b}$ = 4.6 Hz, J_{gem} = 10.9 Hz, H-5b), 2.32 (s, 3H, ArCH_3), 1.99 (s, 3H, C(O)CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 169.8 (C=O), 138.0 (Ar), 137.5 (2C, Ar), 132.3 (Ar), 130.5 (2C, Ar), 129.7 (2C, Ar), 128.4 (2C, Ar), 128.3 (2C, Ar), 127.9 (Ar), 127.8 (2C, Ar), 127.7 (Ar), 127.6 (2C, Ar), 91.4 (C-1), 83.0 (C-3), 81.97 (C-4 or C-2), 81.92 (C-4 or C-2), 73.4 (Ar*C*H$_2$), 72.2 (Ar*C*H$_2$), 68.8 (C-5), 21.1 (Ar*C*H$_3$), 20.9 (C(O)*C*H$_3$); HRMS-ESI *m/z* [M + Na]$^+$ calcd for $C_{28}H_{30}NaO_5S$: 501.1712, found: 501.1718.



Azidooctyl 2,3-di-*O*-benzyl-α-D-arabinofuranoside (143): To a solution of **156** (4.00 g, 7.3 mmol) in DMF (20 mL) were added NaH (711 mg, 29.5 mmol) and benzyl

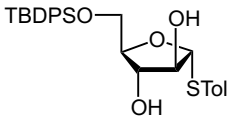
bromide (3.14 g, 18.4 mmol) slowly at 0 °C. After stirring for 2 h at rt, the reaction was quenched by the addition of satd aq. NH_4Cl. Dilution of the mixture with CH_2Cl_2 provided a solution that was then washed with brine. The organic layer was dried with anhydrous Na_2SO_4, filtered and concentrated. The crude product was purified by flash column chromatography (20:1 hexane/EtOAc) to give the crude product. To a solution of the crude product in THF (50 mL) cooled to 0 °C, was added *n*-Bu_4NF (8.0 mL of a 1.0 M solution in THF, 8.0 mmol) under an argon atmosphere. The reaction mixture was stirred for 1 h and then concentrated to an oil, which was purified by chromatography (hexane/EtOAc, 4:1) to give **143** (2.99 g, 93%) as an oil. R_f 0.3 (hexanes/ EtOAc, 3:1); $[\alpha]_D$ = +64.03 (*c* = 1.45, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.41−7.29 (m, 10H, ArH), 5.05 (d, 1H, $J_{1,2}$ = 1.2 Hz, H-1), 4.66−4.52 (m, 4H, 2 ArC*H*$_2$), 4.16 (ddd, 1H, $J_{3,4}$ = 6.6 Hz, $J_{4,5a}$ = 2.8 Hz, $J_{4,5b}$ = 4.1 Hz, H-4), 4.06 (dd, 1H, $J_{1,2}$ = 1.2 Hz, $J_{2,3}$ = 3.1 Hz, H-2), 4.02 (dd, 1H, $J_{2,3}$ = 3.1 Hz, $J_{3,4}$ = 6.6 Hz, H-3), 3.86 (dd, 1H, $J_{4,5a}$ = 2.8 Hz, J_{gem} = 12.0 Hz, H-5a), 3.76−3.65 (m, 2H, H-5b, CH_2-O), 3.43 (dt, 1H, J_{gem} = 9.6 Hz, *J* = 6.5 Hz, CH_2-O), 3.28 (t, 2H, *J* = 7.0 Hz, CH_2-N_3), 1.64−1.60 (m, 4H, 2 (CH_2)), 1.43−1.35 (m, 8H, 4 (CH_2)); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 137.8 (Ar), 137.4 (Ar), 128.4 (2C, Ar), 128.4 (2C, Ar), 127.9 (2C, Ar), 127.8 (Ar), 127.7 (Ar), 106.3 (C-1), 88.1 (C-2), 82.7 (C-3), 81.8 (C-4), 72.3 (Ar*C*H_2), 71.9 (Ar*C*H_2), 67.6 (CH_2-O), 62.2 (C-5), 51.4 (CH_2-N_3), 29.5 (octyl), 29.2 (octyl), 29.1 (octyl), 28.8 (octyl),

26.6 (octyl), 26.0 (octyl); HRMS-ESI *m/z* $[M + Na]^+$ calcd for $C_{27}H_{37}N_3NaO_5$: 506.2625, found: 506.2633.



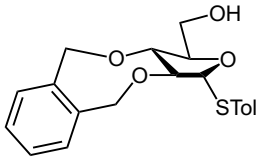
***p*-Tolyl 1-thio-α-D-mannopyranoside (145):** To a solution of D-mannose (3.94 g, 21.9 mmol) in pyridine (20 mL) was added acetic anhydride (20 mL) at rt. The reaction mixture was stirred for 6 h at rt. The reaction was quenched by the addition of CH_3OH, followed by co-evaporation with toluene to remove solvent to afford the crude 1,2,3,4,6-penta-*O*-acetyl-a-D-mannose. To a solution of the crude product in dry CH_2Cl_2 (15 mL) was added *p*-thiocresol (2.85 g, 22.9 mmol) at 0 °C. $BF_3{\cdot}OEt_2$ (5.5 mL, 43.8 mmol) was added dropwise to the solution over 10 min. The solution was stirred for 1 h at 0 °C, followed by the addition of triethylamine (7 mL). After dilution with CH_2Cl_2, the organic layer was washed with a satd. aq. solution of $NaHCO_3$ and dried with anhydrous Na_2SO_4, filtered and concentrated. The resulting oil was purified by flash silica gel column chromatography (3:1, hexanes/EtOAc) providing *p*-Tolyl 2,3,4,5-tetra-acetyl-1- thio-*α*-D-mannopyranoside as yellowish oil. To a solution of *p*-Tolyl 2,3,4,5-tetra-acetyl-1-thio-*α*-D-mannopyranoside in CH_3OH (15 mL) and CH_2Cl_2 (10 mL) was added 1.0 M CH_3ONa in CH_3OH (1 mL). The mixture was stirred for 3 h at rt, neutralized by the addition of Amberlite IR-120 H^+ resin, filtered, and the

filtrate was concentrated. The resulting crude residue was recrystallized to give **145** (5.1 g, 81% over three steps) as white cubic crystals: R_f 0.6 (10:1, CH_2Cl_2/CH_3OH); ^1H NMR (500 MHz, CD_3OD) δ_H 7.39−7.09 (m, 4H, ArH), 5.35 (d, 1 H, $J_{1,2}$ = 1.6 Hz, H-1), 4.85 (m, 1H, H-5), 4.04 (dD, 1H, $J_{1,2}$ = 1.6 Hz, $J_{2,3}$ =2.8 Hz, H-2), 4.09−3.68 (m, 4H, H-3, H-4, H-6a, H-6b), 2.29 (s, 3H, Tosyl CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 138.8 (Ar), 133.4 (2C, Ar), 132.0 (Ar), 130.7 (2C, Ar), 90.7 (C-1), 75.4 (C-3), 73.6, 73.1 (C-2, C-4), 68.6 (C-5), 62.5 (C-6), 21.1 (Tosyl *C*H_3); HRMS-ESI *m/z* $[M + Na]^+$ calcd for $C_{13}H_{18}NaO_5S$: 309.0767, found: 309.0773.



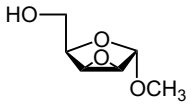
***p*-Tolyl 5-*O*-*tert*-butyldiphenylsilyl-1-thio-α-D-arabinofuranoside (148):** To a solution of **147** (7.7 g, 13.7 mmol) in CH_3OH (25 mL) and CH_2Cl_2 (10 mL) was added 1.0 M CH_3ONa in CH_3OH (1 mL). The mixture was stirred for 3 h at rt, neutralized by the addition of Amberlite IR-120 H^+ resin, filtered, and the filtrate was concentrated. The resulting crude residue was dissolved in pyridine (25 mL), followed by the addition of *tert*-butylchlorodiphenylsilane (3.9 mL, 15.1 mmol) and triethylamine (5.7 mL, 41.1 mmol). The reaction mixture was stirred for 15 h at rt. The reaction was quenched by the addition of CH_3OH, followed by co-evaporation with toluene to remove solvent. The crude residue was diluted with CH_2Cl_2 and washed with 2M HCl, H_2O, satd aq

$NaHCO_3$, and brine. The organic layer was subsequently dried with anhydrous Na_2SO_4, filtered, concentrated and the residue was purified by silica gel column chromatography (4:1 hexanes–EtOAc) to give **148** (6.53 g, 91% over two steps) as an oil. R_f 0.3 (2.5:1 hexanes–EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.73−7.17 (m, 14H, ArH), 5.54 (d, 1H, $J_{1,2}$ = 2.0 Hz, H-1), 4.32 (app t, 1H, $J_{2,3}$ = 2.0 Hz, $J_{3,4}$ = 3.0 Hz, H-3), 4.25 (ddd, 1H, $J_{3,4}$ = 3.0 Hz, $J_{4,5a}$ = 2.5 Hz, $J_{4,5b}$ = 3.0 Hz, H-4), 4.21 (app t, 1H, $J_{1,2}$ = $J_{2,3}$ = 2.0 Hz, H-2), 3.87 (dd, 1H, J_{gem} = 11.5 Hz, $J_{4,5b}$ = 3.0 Hz, H-5b), 3.81 (dd, 1H, J_{gem} = 11.5 Hz, $J_{4,5a}$ = 2.5 Hz, H-5a), 2.32 (s, 3H, tolyl CH_3), 1.04 (s, 9H, TBDPS CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 135.6 (2C, Ar), 135.5 (3C, Ar), 132.5 (3C, Ar), 130.1 (3C, Ar), 130.0 (2C, Ar), 129.8 (3C, Ar), 127.9 (2C, Ar), 127.8 (2C, Ar), 93.0 (C-1), 86.1 (C-2), 81.0 (C-3), 78.7 (C-4), 64.0 (C-5), 26.7 (*t*-Bu), 21.1 (STol CH_3), 19.0 (*t*-Bu).

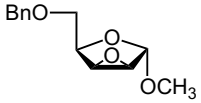


***p*-Tolyl 1-thio-2,3-*O*-xylylene-α-D-arabinofuranoside (149).** To a solution of **148** (5.10 g, 12.6 mmol) in DMF (50 mL) were added NaH (1.10 g, 27.7 mmol) and *α,α'*-dibromo-*o*-xylene (3.66 g, 13.9 mmol) at 0 °C. After stirring for 1.5 h at rt as the reaction was monitored by TLC (R_f 0.40, 50:1 toluene–EtOAc), the reaction was quenched by the addition of satd aq NH_4Cl. Dilution of the mixture with CH_2Cl_2 provided a solution that was then washed with brine. The organic layer was

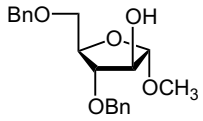
subsequently dried with anhydrous Na_2SO_4, filtered, concentrated. The obtained residue was dissolved in THF (10 mL). To the mixture was added TBAF (1.0 M solution in THF, 9.0 mL, 9.00 mmol) and the mixture was stirred for 3 h at rt. After completion of the reaction, the mixture was diluted with CH_2Cl_2 and washed with 2M HCl, H_2O, satd aq $NaHCO_3$, and brine. The organic layer was subsequently dried with anhydrous Na_2SO_4, filtered, concentrated and the residue was purified by silica gel column chromatography (4:1, hexanes–EtOAc) to give **149** (2.45 g, 54%, over two steps) as an oil. R_f 0.3 (2:1 hexanes–EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.41−7.08 (m, 8H, ArH), 5.34 (d, 1H, $J_{1,2}$ = 4.4 Hz, H-1), 5.00 (d, 1H, J_{gem} = 12.5 Hz, ArC*H*$_2$), 4.86 (d, 1H, J_{gem} = 12.7 Hz, ArC*H*$_2$), 4.80 (d, 1H, J_{gem} = 12.7 Hz, ArC*H*$_2$), 4.76 (d, 1H, J_{gem} = 12.5 Hz, ArC*H2*), 4.16 (ddd, 1H, $J_{3,4}$ = 8.5 Hz, $J_{4,5a}$ = 3.0 Hz, $J_{4,5b}$ = 3.5 Hz, H-4), 4.09 (dd, 1H, $J_{2,3}$ = 5.2 Hz, $J_{3,4}$ = 8.6 Hz, H-3), 3.97 (app t, 1H, $J_{1,2}$ = 4.5 Hz, $J_{2,3}$ = 5.0 Hz, H-2), 3.86 (app dd, 1H, $J_{4,5a}$ = 3.0 Hz, J_{gem} = 12.0 Hz, H-5a), 3.68 (septet, 1H, $J_{4,5b}$ = 3.5 Hz, J_{gem} = 12.0 Hz, H-5b), 2.31 (s, 3H, ArC*H*$_3$), 1.75 (dd, 1H, OH); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 137.7 (Ar), 136.2 (Ar), 135.3 (Ar), 132.4 (2C, Ar), 131.8 (Ar), 131.5 (Ar), 130.5 (Ar), 129.8 (Ar), 129.8 (Ar), 129.7 (2C, Ar), 91.4 (C-1), 86.7 (C-2), 80.7 (C-4), 80.49 (C-3), 70.23 (Ar*C*H$_2$), 68.45 (Ar*C*H$_2$), 61.19 (C-5), 21.17 (Ar*C*H$_3$).



Methyl 2,3-anhydro-α-D-lyxofuranoside (151): A mixture of D-arabinose **150** (5.0 g, 33.3 mmol) and methanol (50 mL) containing 3.0% acetyl chloride was stirred for 5 h; the solution became homogenous after about 2 h. After the addition of triethyl amine, the mixture was stirred for 1 h, and then filtered through Celite. The neutral filtrate was concentrated to a syrup *in vacuo* to get the crude methyl α-D-arabinofuranoside. The crude methyl α-D-arabinofuranoside and triphenylphosphine (10.5 g, 40.0 mmol) were then dissolved in tetrahydrofuran (25 mL), and the solution was cooled to 0 °C. Diisopropylazodicarboxylate (7.9 mL, 40.0 mmol) was added dropwise over a period of 10 min. After complete addition of the reagent, the reaction mixture was warmed to room temperature and was stirred for 1 h. The solution was subsequently concentrated, diluted with Et_2O and filtrated. The solution was then concentrated and purified by chromatography (4:1 hexane-EtOAc) to obtain **151** (4.8 g, 86%) as a white crystalline solid: R_f 0.3 (1:1, hexanes–EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 4.98 (s, 1 H, H-1), 4.17–4.13 (m, 1 H, H-4), 3.91–3.88 (m, 2 H, H-5a, H-5b), 3.75 (dd, 1 H, $J_{1,2}$ = 0.7 Hz, $J_{2,3}$ = 2.9 Hz, H-2), 3.66 (d, 1 H, $J_{2,3}$ = 2.9 Hz, H-3), 3.43 (s, 3 H, OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 102.2 (C-1), 76.2 (C-4), 61.9 (C-5), 55.8 (C-3), 55.6 (OCH_3), 54.1 (C-2); HRMS-ESI *m/z* $[M + Na]^+$ calcd for $C_6H_{10}NaO_4$: 169.0471, found: 169.0472.

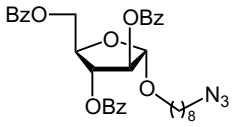


Methyl 2,3-anhydro-5-*O*-benzyl-α-D-lyxofuranoside (152): To a solution of **151** (7.30 g, 50 mmol) in DMF (25 mL) were added NaH (2.88 g, 60 mmol) and benzyl bromide (7.1 mL, 60 mmol) slowly at 0 °C. After stirring for 4 h at rt, the reaction was quenched by the addition of satd aq. NH_4Cl. The mixture was poured into ice-water and extracted with EtOAc, the extract was then washed with brine. The organic layer was dried with anhydrous Na_2SO_4, filtered and concentrated. The crude product was purified by flash column chromatography (7:1, hexane–EtOAc) to give **152** (10 g, 85%) as an oil: R_f 0.3 (4:1, hexanes–EtOAc,); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.41−7.26 (m, 5H, ArH), 4.95 (s, 1H, H-1), 4.62 (d, 1H, J_{gem} = 12.0 Hz, ArCH_2), 4.58 (d, 1H, J_{gem} = 12.0 Hz, ArCH_2), 4.23−4.18 (m, 1 H, H-4), 3.76 (dd, 1 H, $J_{1,2}$ = 0.7 Hz, $J_{2,3}$ = 2.9 Hz, H-2), 3.62−3.68 (m, 3H, H-3, H-5a, H-5b), 3.42 (s, 3H, OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 137.9 (Ar), 128.42 (2C, Ar), 127.79 (2C, Ar), 127.76 (Ar), 102.27 (C-1), 75.08 (C-4), 73.62 (ArCH_2), 68.56 (C-5), 56.24 (C-3), 55.58 (OMe), 54.34 (C-2); HRMS-ESI *m/z* $[M + Na]^+$ calcd for $C_{13}H_{16}NaO_4$: 259.0946, found: 259.0951.



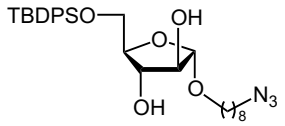
Methyl 3,5-di-*O*-benzyl-α-D-arabinofuranoside (153): To a solution of methyl 5-*O*-benzyl-2,3-anhydro-α-D-lyxofuranoside **152** (2.4 g, 1.0 mmol) dissolved in dry DMF (10 mL) was added 1M sodium benzylate in benzyl alcohol (2.0 mL, 2.0 mmol) The

reaction mixture was stirred at 100 °C for 2.5 h and then cooled and neutralized by the addition of acetic acid. The excess benzyl alcohol was removed by vacuum distillation and the crude oil was purified by chromatography (3:1, hexanes–EtOAc) to yield **153** (3.0 g, 84%) as a colorless oil: R_f 0.4 (2:1, hexanes–EtOAc,); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.37−7.24 (m, 10H, ArH), 4.91 (s, 1H, H-1), 4.69 (d, 1H, J_{gem} = 12.3 Hz, ArCH_2), 4.61 (d, 1H, J_{gem} = 11.9 Hz, ArCH_2), 4.52 (d, 1H, J_{gem} = 12.3 Hz, ArCH_2), 4.47 (d, 1H, J_{gem} = 11.9 Hz, ArCH_2), 4.30−4.22 (m, 1 H, H-4), 4.12 (d, 1 H, $J_{2,OH}$ = 10.9 Hz, H-2), 3.84 (d, 1H, $J_{3,4}$ = 2.8 Hz, H-3), 3.65 (dd, 1H, $J_{4,5a}$ = 2.4 Hz, J_{gem} = 10.4 Hz, H-5a), 3.44 (dd, 1H, $J_{4,5b}$ = 2.4 Hz, J_{gem} = 10.4 Hz, H-5b), 3.41 (s, 3H, OCH_3), 3.27 (s, 1H, OH); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 138.1 (Ar), 137.4 (Ar), 128.9 (2C, Ar), 128.8 (2C, Ar), 128.4 (Ar), 128.3 (Ar), 128.2 (Ar), 110.9 (C-1), 85.3 (C-3), 83.9 (C-4), 78.3 (C-2), 74.1 (Ar*C*H$_2$), 72.5 (Ar*C*H$_2$), 70.1 (C-5), 55.6 (OCH_3); HRMS-ESI *m/z* $[M + Na]^+$ calcd for $C_{20}H_{24}NaO_5$: 367.1521, found: 367.1529.



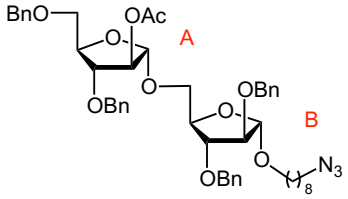
8-Azido-octyl 2,3,5-tri-*O*-benzoyl-α-D-arabinofuranoside (155): To a solution of *p*-tolyl 2,3,5-tri-*O*-benzoyl-1-thio-α-D-arabinofuranoside **147** (1.45 g, 2.6 mmol) and 8-azidooctanol (315 mg, 1.7 mmol) in CH_2Cl_2 (15 mL) was added 4 Å molecular sieves (1.0 g) at rt. After stirring for 1 h and then cooling to 0 °C, NIS (958 mg, 4.3 mmol) and

AgOTf (88 mg, 0.34 mmol) were added to the mixture. After stirring for 1 h at 0 °C as the reaction was monitored by TLC, the reaction mixture was quenched by the addition of Et_3N. The solution was diluted with CH_2Cl_2 and filtered through Celite. The filtrate was then washed with satd aq. $Na_2S_2O_3$ and brine. The organic layer was subsequently dried with anhydrous Na_2SO_4, filtered, concentrated and the residue was purified by silica gel column chromatography (7:1 hexanes–EtOAc) to give **155** (983 mg, 92%) as an oil. R_f 0.5 (4:1, hexanes–EtOAc,); $[\alpha]_D = -6.9$ (c = 0.3, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.11−8.06 (m, 2H, ArH), 8.05−7.98 (m, 4H, ArH), 7.63−7.55 (m, 2H, ArH), 7.53−7.48 (m, 1H, ArH), 7.48−7.43 (m, 2H, ArH), 7.42−7.37 (m, 2H, ArH), 7.34−7.24 (m, 2H, ArH), 5.57 (d, 1H, $J_{3,4}$ = 5.0 Hz, H-3), 5.52 (d, 1H, $J_{1,2}$ = 1.3 Hz, H-1), 5.28 (s, 1H, H-2), 4.83 (dd, 1H, J_{gem} = 11.9 Hz, $J_{4,5b}$ = 3.6 Hz, H-5b), 4.69 (dd, 1H, J_{gem} = 11.9 Hz, $J_{4,5a}$ = 5.0 Hz, H-5a), 4.25 (ddd, 1H, $J_{3,4}$ = 5.0 Hz, $J_{4,5a}$ = 5.0 Hz, $J_{4,5b}$ = 3.6 Hz, H-4), 3.79 (dt, 1H, J_{gem} = 9.6 Hz, J = 6.7 Hz, octyl CH_2O), 3.55 (dt, J_{gem} = 9.6 Hz, J = 6.3 Hz, octyl CH_2O), 3.22 (t, 2H, J = 7.0 Hz, CH_2N_3) 1.64−1.58 (m, 4H, 2 (CH_2)), 1.39−1.31 (m, 8H, 4 (CH_2)); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 166.3 (Ar), 165.8 (Ar), 165.5 (Ar), 133.6 (Ar), 133.5 (Ar), 133.1 (Ar), 123.0 (2C, Ar), 129.9 (2C, Ar), 129.8 (2C, Ar), 129.3 (Ar), 129.1 (Ar), 128.6 (Ar), 128.50 (2C, Ar), 128.4 (2C, Ar), 105.7 (C-2), 82.1 (C-1), 81.1 (C-4), 78.0 (C-3), 67.6 (CH_2O), 63.9 (C-5), 51.5 (CH_2N_3), 29.5 (octyl), 29.3 (octyl), 29.1 (octyl), 28.9 (octyl), 26.7 (octyl), 26.1 (octyl); HRMS-ESI m/z $[M + Na]^+$ calcd for $C_{34}H_{37}N_3NaO_8$: 638.2478, found: 638.2463.



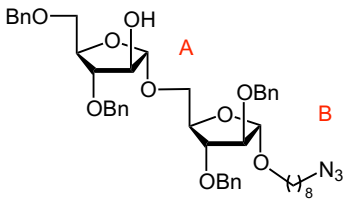
8-Azido-octyl 5-*O*-*tert*-butyldiphenylsilyl-α-D-arabinofuranoside (156): To a solution of **155** (9.5 g, 14.7 mmol) in CH_3OH (75 mL) and CH_2Cl_2 (25 mL) was added 1.0 M CH_3ONa in CH_3OH (2 mL). The mixture was stirred for 3 h at rt, neutralized by the addition of Amberlite IR-120 H^+ resin, filtered, and the filtrate was concentrated. The resulting crude residue was dissolved in pyridine (35 mL), followed by the addition of *tert*-butylchlorodiphenylsilane (4.2 mL, 16.2 mmol) and Et_3N (6.1 mL, 44.1 mmol). The reaction mixture was stirred for 15 h at rt. The reaction was quenched by the addition of CH_3OH, followed by co-evaporation with toluene to remove the solvent. The crude residue was diluted with CH_2Cl_2 and washed with 2M HCl, H_2O, satd aq. $NaHCO_3$, and brine. The organic layer was subsequently dried with anhydrous Na_2SO_4, filtered, concentrated and the residue was purified by silica gel column chromatography (4:1, hexanes–EtOAc) to give **156** (7.23 g, 91% over two steps) as an oil. R_f 0.55 (2:1, hexanes–EtOAc); $[\alpha]_D$ = +46.8 (c = 0.7, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.72−7.64 (m, 4H, ArH), 7.48−7.36 (m, 6H, ArH), 5.08 (s, 1H, H-1), 4.12−4.10 (m, 2H, H-2, H-4), 4.02 (s, 1H, H-3), 3.83 (dd, 1H, J_{gem} = 11.4 Hz, $J_{4,5b}$ = 2.4 Hz, H-5b), 3.78−3.71 (m, 2H, H-5a, octyl CH_2O), 3.47 (dt, 1H, J_{gem} = 9.6 Hz, J = 6.5 Hz, octyl CH_2O), 3.24 (t, 2H, J = 7.0 Hz, CH_2N_3), 3.06 (br. s, 1H, OH), 1.64−1.58 (m, 4H, 2

(CH_2)), 1.39−1.31 (m, 8H, 4 (CH_2)), 1.06 (s, 9H, 3 C(CH_3)$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 136.0 (Ar), 135.7 (2C, Ar), 135.6 (2C, Ar), 131.9 (Ar), 131.8 (Ar), 130.2 (Ar), 130.1 (Ar), 128.0 (Ar), 127.9 (Ar), 123.8 (Ar), 101.1 (C-1), 82.3 (C-2), 78.4 (C-3), 78.2 (C-4), 68.7 (CH_2-O), 65.9 (C-5), 51.8 (CH_2-N_3), 29.8 (octyl), 29.6 (octyl), 29.4 (octyl), 29.2 (octyl), 27.2 (octyl), 27.0 (octyl), 26.3 (C(CH_3)$_3$), 19.6 (C(CH_3)$_3$); HRMS-ESI *m/z* [M + Na]$^+$ calcd for $C_{29}H_{43}N_3NaO_5Si$: 564.2864, found: 564.2851.



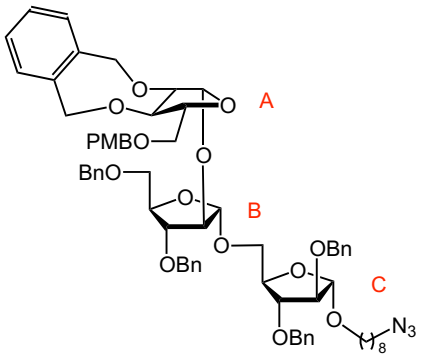
8-Azido-octyl 2-*O*-acetyl-3,5-di-*O*-benzyl-α-D-arabinofuranosyl-(1→5)-2,3-di-*O*-benzyl-α-D-arabinofuranoside (157): To a mixture of donor **142** (215 mg, 0.449 mmol) and acceptor **143** (203 mg, 0.408 mmol) in CH_2Cl_2 (15 mL) was added 4 Å molecular sieves (300 mg) at rt. After stirring for 1 h and then cooling to 0 °C, NIS (158 mg, 0.702 mmol) and AgOTf (17 mg, 0.0702 mmol) were added to the mixture and the reaction was monitored by TLC. After stirring for 1 h at 0 °C, the reaction was quenched by the addition of Et_3N. The solution was diluted with CH_2Cl_2 and filtered through Celite. The filtrate was then washed with satd aq. $Na_2S_2O_3$ and brine. The organic layer was subsequently dried with anhydrous Na_2SO_4, filtered, concentrated and the residue was purified by silica gel column chromatography (6:1, hexane–EtOAc) to give the product

157 as a colorless oil: R_f 0.3 (4:1, hexanes–EtOAc); $[\alpha]_D$ = +79.7 (c = 0.8, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.36−7.20 (m, 20H, ArH), 5.24 (d, 1H, $J_{1,2}$ = 1.4 Hz, H-2A), 5.19 (s, 1H, H-1A), 5.07 (d, 1H, $J_{1,2}$ = 1.5 Hz, H-1B), 4.77 (d, 1H, J_{gem} = 12.1 Hz, $ArCH_2$) 4.64−4.50 (m, 7H, $ArCH_2$), 4.29−4.27 (m, 1H, H-4A), 4.23 (dt, 1H, $J_{3,4}$ = $J_{4,5a}$ = 4.1 Hz, $J_{4,5b}$ = 7.8 Hz, H-4B), 4.10 (dd, 1H, $J_{2,3}$ = 3.5 Hz, $J_{3,4}$ = 6.9 Hz, H-3B), 4.06 (dd, 1H, $J_{1,2}$ = 1.5 Hz, $J_{2,3}$ = 3.5 Hz, H-2B), 3.94 (dd, 1H, $J_{4,5a}$ = 4.3 Hz, J_{gem} = 11.2 Hz, H-5aB), 3.90 (dd, 1H, $J_{2,3}$ = 3.4 Hz, $J_{3,4}$ = 1.6 Hz, H-3A), 3.79−3.72 (m, 2H, H-5bB, octyl CH_2O), 3.65 (dd, 1H, $J_{4,5a}$ = 3.7 Hz, J_{gem} = 10.8 Hz, H-5aA), 3.54 (dd, 1H, $J_{4,5b}$ = 5.0 Hz, J_{gem} = 10.5 Hz, H-5bA), 3.44−3.42 (m, 1H, octyl CH_2-O), 3.28 (t, 2H, J = 7.0 Hz, CH_2N_3), 2.03 (s, 3H, C(O)CH_3), 1.69−1.51 (m, 4H, octyl), 1.48−1.34 (m, 8H, octyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 169.6 (C=O), 138.1 (Ar), 138.0 (Ar), 137.8 (Ar), 137.7 (Ar), 128.37 (2C, Ar), 128.31 (2C, Ar), 128.2 (2C, Ar), 127.85 (2C, Ar), 127.81 (2C, Ar), 127.74 (2C, Ar), 127.72 (2C, Ar), 127.69 (2C, Ar), 127.62 (2C, Ar), 127.5 (2C, Ar), 106.06 (C-1A or C-1B), 106.04 (C-1A or C-1B), 88.5 (C-2B), 83.5 (C-3A), 83.2 (C-3B), 82.2 (C-4A), 81.2 (C-2A), 80.0 (C-4B), 73.3 (ArCH$_2$), 72.2 (ArCH$_2$), 72.1 (ArCH$_2$), 71.8 (ArCH$_2$), 69.3 (C-5A), 67.6 (octyl CH_2O), 65.9 (C-5B), 51.4 (CH_2N_3), 29.4 (octyl), 29.2 (octyl), 29.1 (octyl), 28.8 (octyl), 26.6 (octyl), 26.0 (octyl), 20.8 (C(O)CH$_3$); HRMS-ESI m/z $[M + Na]^+$ calcd for $C_{48}H_{59}N_3NaO_{10}$: 860.4098, found: 860.4087.



8-Azido-octyl 3,5-di-*O*-benzyl-α-D-arabinofuranosyl-(1→5)-2,3-di-*O*-benzyl-α-D-arabinofuranoside (158): To a solution of **157** (200 mg, 0.239 mmol) in CH_3OH (3 mL) and CH_2Cl_2 (2 mL) was added 1.0 M CH_3ONa in CH_3OH (20 uL). The mixture was stirred for 3 h at rt, neutralized by the addition of Amberlite IR-120 H^+ resin, filtered, and the filtrate was concentrated. The residue was purified by silica gel column chromatography (6:1, hexanes–EtOAc) to give **158** (190 mg, 100%) as an oil: R_f 0.5 (2:1, hexanes–EtOAc); $[\alpha]_D$ = +85.9 (c = 0.8, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.43−7.20 (m, 20H, ArH), 5.15 (s, 1H, H-1A), 5.08 (d, 1H, $J_{1,2}$ = 1.9 Hz, H-1B), 4.71−4.63 (m, 2H, $ArCH_2$), 4.61−4.43 (m, 6H, $ArCH_2$), 4.28−4.23 (m, 2H, H-2A, H-4B), 4.21 (dt, $J_{3,4}$ = $J_{4,5a}$ = 3.5 Hz, $J_{4,5b}$ = 6.9 Hz, H-4A), 4.15 (dd, 1H, $J_{2,3}$ = 3.4 Hz, $J_{3,4}$ = 6.9 Hz, H-3B), 4.05 (dd, 1H, $J_{1,2}$ = 1.9 Hz, $J_{2,3}$ = 3.4 Hz, H-2B), 3.95 (dd, 1H, $J_{4,5a}$ = 3.5 Hz, J_{gem} = 11.5 Hz, H-5aA), 3.91 (dd, 1H, $J_{2,3}$ = 1.6 Hz, $J_{3,4}$ = 3.4 Hz, H-3A), 3.79−3.72 (m, 2H, H-5bA, octyl CH_2O), 3.69 (dd, 1H, $J_{4,5a}$ = 2.4 Hz, J_{gem} = 10.5 Hz, H-5aB), 3.54 (dd, 1H, $J_{4,5b}$ = 2.8 Hz, J_{gem} = 10.5 Hz, H-5bB), 3.44−3.42 (m, 1H, octyl CH_2O), 3.34 (d, 1H, J = 9.5 Hz, OH), 3.28 (t, 2H, J = 7.0 Hz, CH_2N_3), 1.73−1.53 (m, 4H, octyl), 1.48−1.34 (m, 8H, octyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 138.2 (Ar), 137.9 (Ar), 137.6 (Ar), 137.1 (Ar), 128.5 (2C, Ar), 128.4 (2C, Ar), 128.3 (2C, Ar), 128.2 (2C,

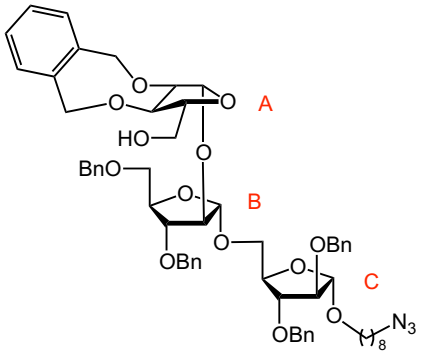
Ar), 127.97 (Ar), 127.93 (2C, Ar), 127.82 (2C, Ar), 127.81 (Ar), 127.7 (2C, Ar), 127.63 (2C, Ar), 127.61 (Ar), 127.5 (Ar), 109.2 (C-1A), 106.0 (C-1B), 88.5 (C-2B), 84.9 (C-3A), 83.1 (C-3B), 82.9 (C-2A), 80.3 (C-4A), 78.0 (C-4B), 73.7 (Ar*C*H_2), 72.2 (Ar*C*H_2), 71.9 (2 Ar*C*H_2), 69.7 (C-5B), 67.5 (CH_2-O), 65.9 (C-5A), 51.4 (CH_2-N_3), 29.4 (octyl), 29.2 (octyl), 29.0 (octyl), 28.8 (octyl), 26.6 (octyl), 26.0 (octyl); HRMS-ESI *m/z* $[M + Na]^+$ calcd for $C_{46}H_{57}N_3NaO_9$: 818.3993, found: 818.3999.



8-Azido-octyl 5-*O*-*p*-methoxybenzyl-2,3-*O*-xylylene-β-D-arabinofuranosyl-(1→2)-3,5-di-*O*-benzyl-α-D-arabinofuranosyl-(1→5)-2,3-di-*O*-benzyl-α-D-arabinofuranoside (159): To a mixture of donor **141** (150 mg, 0.314 mmol) and acceptor **158** (170 mg, 0.210 mmol) in CH_2Cl_2 (15 mL) was added 4 Å molecular sieves (300 mg) at rt. After stirring for 1 h and then cooling to –45 °C, NIS (106 mg, 0.473 mmol) and AgOTf (13.5 mg, 0.0473 mmol) were added to the mixture. The reaction was monitored by TLC, and after stirring for 30 min at –45 °C it was quenched by the addition of Et_3N. The solution was diluted with CH_2Cl_2 and filtered through Celite. The filtrate was then washed with

satd aq. $Na_2S_2O_3$ and brine. The organic layer was subsequently dried with anhydrous Na_2SO_4, filtered, concentrated and the residue was purified by silica gel column chromatography (12:1, toluene–EtOAc) to give **159** (219 mg, 91%, β/α ratio 11:1) as a colorless oil: R_f 0.25 (8:1, toluene–EtOAc); $[\alpha]_D$ = +34.7 (c = 0.9, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.40−7.23 (m, 24H, ArH), 7.16−7.09 (m, 2H, ArH), 6.83−6.76 (m, 2H, ArH), 5.15 (d, 1H, $J_{1,2}$ = 1.9 Hz, H-1C), 5.07 (d, 1H, $J_{1,2}$ = 5.0 Hz, H-1A), 5.02−4.94 (m, 2H, H-1B, ArCH_2), 4.83 (d, 1H, J_{gem} = 12.8 Hz, ArCH_2), 4.81−4.75 (m, 2H, ArCH_2), 4.64 (d, 1H, J_{gem} = 11.8 Hz, ArCH_2), 4.58−4.46 (m, 6H, ArCH_2), 4.45−4.38 (m, 2H, ArCH_2), 4.36−4.30 (m, 2H, H-2C, ArCH_2), 4.20 (ddd, $J_{3,4}$ = 3.7 Hz, $J_{4,5a}$ = 5.4 Hz, $J_{4,5b}$ = 6.4 Hz, H-4C), 4.16 (dt, $J_{3,4}$ = $J_{4,5a}$ = 3.9 Hz, $J_{4,5b}$ = 7.5 Hz, H-4A), 4.12−4.06 (m, 2H, H-3B, H-4B), 4.04 (dd, 1H, $J_{2,3}$ = 6.9 Hz, $J_{3,4}$ = 3.7 Hz, H-3A), 4.02−3.97 (m, 3H, H-2A, H-2B, H-3C), 3.90 (dd, 1H, $J_{4,5a}$ = 4.3 Hz, J_{gem} = 11.4 Hz, H-5aA), 3.76 (s, 3H, OCH_3), 3.72−3.66 (m, 2H, H-5bA, octyl CH_2O), 3.63−3.54 (m, 3H, H-5aB, H-5aC, H-5bC), 3.50 (dd, 1H, $J_{4,5b}$ = 5.4 Hz, J_{gem} = 10.0 Hz, H-5bB), 3.39−3.37 (m, 1H, octyl CH_2O), 3.25 (t, 2H, J = 7.0 Hz, CH_2N_3), 1.64−1.53 (m, 4H, octyl), 1.42−1.29 (m, 8H, octyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 159.0 (Ar), 138.2 (Ar), 138.17 (Ar), 138.13 (Ar), 137.7 (Ar), 136.8 (Ar), 135.8 (Ar), 131.4 (Ar), 131.2 (Ar), 130.2 (Ar), 129.3 (Ar), 129.2 (Ar), 129.1 (2C, Ar), 128.4 (2C, Ar), 128.3 (3C, Ar), 128.29 (2C, Ar), 128.21 (2C, Ar), 127.8 (3C, Ar), 127.73 (2C, Ar), 127.71 (Ar), 127.6 (Ar), 127.56 (Ar), 127.52 (Ar), 127.4 (Ar), 113.6 (Ar), 106.7 (C-1C), 106.0 (C-1B),

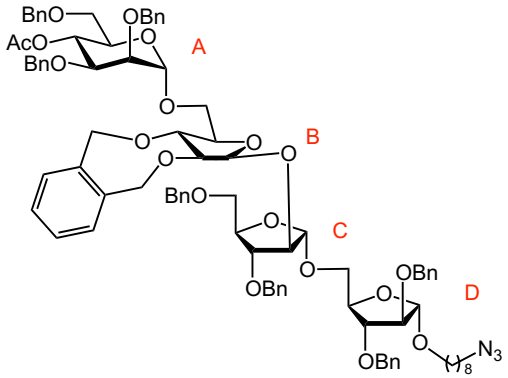
102.8 (C-1A), 88.5 (C-2A), 86.4 (C-2C), 83.8 (C-2B), 83.3 (C-3C), 82.7 (C-3A), 81.9 (C-3B), 81.7 (C-4B), 81.0 (C-4C), 80.1 (C-4A), 73.3 (Ar*C*H_2), 72.5 (Ar*C*H_2), 72.3 (Ar*C*H_2), 72.16 (C-5B), 72.15 (Ar*C*H_2), 71.9 (Ar*C*H_2), 69.8 (C-5C), 69.5 (Ar*C*H_2), 69.2 (Ar*C*H_2), 67.6 (octyl CH_2O), 66.2 (C-5A), 55.2 (OCH_3), 51.4 (CH_2N_3), 29.5 (octyl), 29.2 (octyl), 29.1 (octyl), 28.8 (octyl), 26.6 (octyl), 26.0 (octyl); HRMS-ESI *m/z* [M + Na]$^+$ calcd for $C_{67}H_{79}N_3NaO_{14}$: 1172.5460, found: 1172.5468.



8-Azido-octyl 2,3-*O*-xylylene-β-D-arabinofuranosyl-(1→2)-3,5-di-*O*-benzyl-α-D-arabinofuranosyl-(1→5)-2,3-di-*O*-benzyl-α-D-arabinofuranoside (160): To a solution of **159** (170 mg, 0.148 mmol) in CH_2Cl_2 (7 mL) was added TFA (70 μL). The the reaction was monitored by TLC while the solution was stirred at rt. After 1 h the reaction was quenched by the addition of sat aq. $NaHCO_3$. The mixture was diluted with CH_2Cl_2 and washed with brine. The organic layer was subsequently dried with anhydrous Na_2SO_4, filtered, concentrated and the residue was purified by silica gel column chromatography (3:1 hexanes–EtOAc) to give **160** (144 mg, 93%) as an oil: R_f

0.3 (2:1, hexane–EtOAc); $[\alpha]_D$ = +45.2 (*c* = 0.7, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.58−7.09 (m, 24H, ArH), 5.18 (d, 1H, $J_{1,2}$ = 1.5 Hz, H-1B), 5.09 (d, 1H, $J_{1,2}$ = 5.1 Hz, H-1A), 5.06−4.99 (m, 2H, H-1C, $ArCH_2$), 4.84−4.73 (m, 3H, ArCH_2), 4.66 (d, 1H, J_{gem} = 11.7 Hz, ArCH_2), 4.61−4.52 (m, 4H, ArCH_2), 4.52−4.47 (m, 2H, ArCH_2), 4.37 (dd, 1H, $J_{2,3}$ = 6.7 Hz, $J_{3,4}$ = 5.6 Hz, H-3A), 4.34 (dd, 1H, $J_{1,2}$ = 1.5 Hz, $J_{2,3}$ = 3.7 Hz, H-2B), 4.21−4.16 (m, 2H, H-4C, H-4B), 4.08 (dd, 1H, $J_{2,3}$ = 6.8 Hz, $J_{3,4}$ = 3.7 Hz, H-3B), 4.06−4.02 (m, 2H, H-2C, H-3C), 4.02−3.97 (m, 2H, H-2A, H-4A), 3.91 (dd, 1H, $J_{4,5a}$ = 4.4 Hz, J_{gem} = 11.4 Hz, H-5aC), 3.76−3.65 (m, 3H, H-5bA, H-5bC, octyl CH_2O), 3.65−3.58 (m, 2H, H-5aA, H-5aB), 3.56 (dd, 1H, $J_{4,5a}$ = 4.9 Hz, J_{gem} = 10.9 Hz, H-5bB), 3.41−3.39 (m, 1H, octyl CH_2O), 3.26 (t, 2H, *J* = 7.0 Hz, CH_2N_3), 2.61 (dd, 1H, $J_{5a,OH}$ = 4.3 Hz, $J_{5b,OH}$ = 8.6 Hz, OH), 1.64−1.53 (m, 4H, octyl), 1.42−1.29 (m, 8H, octyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 138.1 (Ar), 138.0 (Ar), 137.9 (Ar), 137.6 (Ar), 137.1 (Ar), 135.5 (Ar), 131.6 (Ar), 131.3 (Ar), 129.5 (Ar), 129.4 (Ar), 128.44 (2C, Ar), 128.40 (2C, Ar), 128.37 (2C, Ar), 128.35 (2C, Ar), 127.92 (2C, Ar), 127.91 (2C, Ar), 127.8 (Ar), 127.76 (2C, Ar), 127.73 (2C, Ar), 127.70 (Ar), 127.6 (Ar), 106.6 (C-1B), 106.1 (C-1C), 102.6 (C-1A), 88.6 (C-2C), 86.8 (C-2B), 84.4 (C-2A), 83.39 (C-4A), 83.35 (C-3C), 82.1 (C-2B), 80.7 (C-4C), 80.4 (C-4B), 80.1 (C-3A), 73.4 (ArCH_2), 72.38 (ArCH_2), 72.30 (ArCH_2), 72.0 (ArCH_2), 69.8 (ArCH_2), 69.4 (C-5B), 68.9 (ArCH_2), 67.6 (octyl CH_2O), 66.4 (C-5A), 63.1 (C-5C), 51.5 (CH_2-N_3), 29.5 (octyl), 29.3 (octyl), 29.1 (octyl),

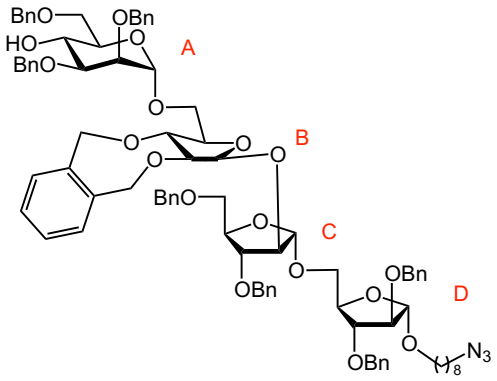
28.8 (octyl), 26.7 (octyl), 26.1 (octyl); HRMS-ESI *m/z* $[M + Na]^+$ calcd for $C_{59}H_{71}N_3NaO_{13}$: 1052.4885, found: 1052.4893.



8-Azido-octyl 4-*O*-acetyl-2,3,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→5)-2,3-*O*-xylylene-β-D-arabinofuranosyl-(1→2)-3,5-di-*O*-benzyl-α-D-arabinofuranosyl-(1→5)-2,3-di-*O*-benzyl-α-D-arabinofuranoside (161): To a mixture of donor **140** (340 mg, 0.568 mmol) and acceptor **160** (370 mg, 0.354 mmol) in CH_2Cl_2–Et_2O 1:2 (12 mL) was added 4 Å molecular sieves (300 mg) at rt. After stirring for 1 h and then cooling to –15 °C, NIS (191 mg, 0.848 mmol) and AgOTf (13.7 mg, 0.0568 mmol) were added to the mixture. The reaction was monitored by TLC while the solution was stirred for 30 min at –15 °C before the reaction was quenched by the addition of Et_3N. The solution was then diluted with CH_2Cl_2 and filtered through Celite. The filtrate was then washed with satd aq. $Na_2S_2O_3$ and brine. The organic layer was subsequently dried with anhydrous Na_2SO_4, filtered, concentrated and the residue was purified by silica gel column chromatography (7:1, hexane–EtOAc) to give **159** (406 mg, 74%, β/α ratio

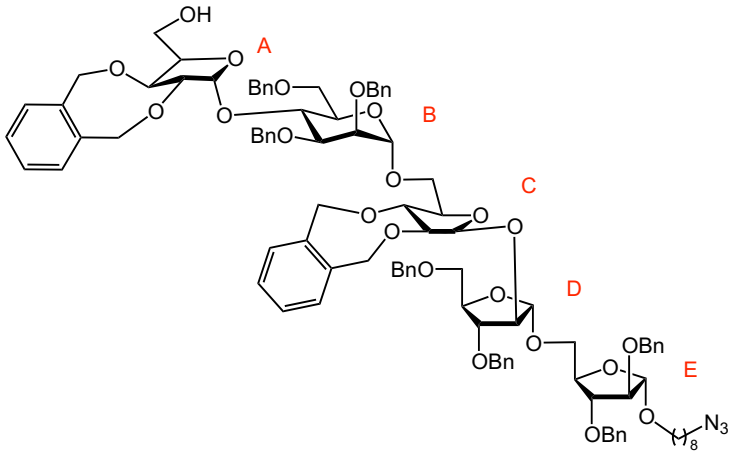
5.5:1) as a colorless oil: R_f 0.5 (2:1, hexane–EtOAc); $[\alpha]_D$ = +32.2 (c = 1.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.39−7.25 (m, 39H, ArH), 5.43 (app t, 1H, $J_{3,4} = J_{4,5}$ = 9.6 Hz, H-4A), 5.16 (s, 1H, H-1C), 5.07 (d, 1H, $J_{1,2}$ = 5.0 Hz, H-1B), 5.01 (s, 1H, H-1D), 4.96 (d, 1H, J_{gem} = 11.7 Hz, ArCH_2), 4.88 (d, 1H, $J_{1,2}$ = 1.9 Hz, H-1A), 4.82−4.74 (m, 2H, ArCH_2), 4.71 (d, 2H, J_{gem} = 12.5 Hz, ArCH_2), 4.69−4.43 (m, 13H, ArCH_2), 4.39 (d, 1H, J_{gem} = 12.1 Hz, ArCH_2), 4.33 (d, 1H, $J_{2,3}$ = 3.3 Hz, H-2C), 4.24−4.15 (m, 2H, H-4C, H-4D), 4.11−4.01 (m, 4H, H-2D, H-3D, H-3B, H-4B), 4.01−3.96 (m, 2H, H-2B, H-3C), 3.95−3.86 (m, 2H, H-5A, H-5aD), 3.83−3.75 (m, 3H, H-2A, H-3A, H-5aC), 3.74−3.69 (m, 2H, octyl CH_2O, H-5bD), 3.67−3.53 (m, 5H, H-5bC, H-5aB, H-5bB, H-6aA, H-6bA), 3.40−3.38 (m, 1H, octyl CH_2O), 3.26 (t, 2H, J = 7.0 Hz, CH_2-N_3), 1.90 (s, 3H, C(O)CH_3), 1.64−1.53 (m, 4H, octyl), 1.39−1.32 (m, 8H, octyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 169.8 (C=O), 138.4 (Ar), 138.28 (Ar), 138.25 (Ar), 138.21 (Ar), 138.1 (Ar), 138.0 (Ar), 137.7 (Ar), 136.8 (Ar), 135.8 (Ar), 131.6 (Ar), 131.1 (Ar), 129.4 (Ar), 128.4 (Ar), 128.35 (Ar), 128.33 (Ar), 128.32 (Ar), 128.30 (Ar), 128.2 (Ar), 127.9 (Ar), 127.8 (Ar), 127.77 (Ar), 127.75 (Ar), 127.71 (Ar), 127.64 (Ar), 127.61 (Ar), 127.59 (Ar), 127.55 (Ar), 127.49 (Ar), 127.46 (Ar), 127.2 (Ar), 106.7 (C-1C), 106.0 (C-1D), 103.0 (C-1B), 98.1 (C-1A), 88.6 (C-2D), 86.7 (C-2C), 83.8, 83.4, 82.6, 82.0, 81.0, (C-2B, C-3C, C-3D, C-3B, C-4B), 80.9, 80.1, (C-4C, C-4D), 77.4, 74.4, (C-2A, C-3A), 73.4 (ArCH$_2$), 73.3 (ArCH$_2$), 72.8 (ArCH$_2$), 72.3 (ArCH$_2$), 72.1 (ArCH$_2$), 71.9 (ArCH$_2$), 71.8 (ArCH$_2$), 70.5 (C-5A), 69.9 (C-5B), 69.7 (C-5C), 69.76 (C-6A), 69.73 (ArCH$_2$),

69.5 (Ar*C*H_2), 69.2 (C-4A), 67.6 (octyl CH_2O), 66.2 (C-5D), 51.4 (CH_2N_3), 29.5 (octyl), 29.3 (octyl), 29.1 (octyl), 28.8 (octyl), 26.7 (octyl), 26.1 (octyl), 20.9 (C(O)*C*H_3); HRMS-ESI *m/z* $[M + Na]^+$ calcd for $C_{88}H_{101}N_3NaO_{19}$: 1526.6927, found: 1526.6938.



8-Azido-octyl 2,3,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→5)-2,3-*O*-xylylene-β-D-arabinofuranosyl-(1→2)-3,5-di-*O*-benzyl-α-D-arabinofuranosyl-(1→5)-2,3-di-*O*-benzyl-α-D-arabinofuranoside (162): To a solution of **161** (200 mg, 0.133 mmol) in CH_3OH (3 mL) and CH_2Cl_2 (2 mL) was added 1.0 M CH_3ONa in CH_3OH (20 μL). The mixture was stirred for 3 h at rt, neutralized by the addition of Amberlite IR-120 H^+ resin, filtered, and the filtrate was concentrated. The residue was purified by silica gel column chromatography (3:1, hexanes–EtOAc) to give **158** (178 mg, 92%) as an oil: R_f 0.35 (5:1, toluene–EtOAc); $[\alpha]_D$ = +27.9 (*c* = 2.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.37−7.16 (m, 39H, ArH), 5.16 (d, 1H, $J_{1,2}$ = 1.2 Hz, H-1C), 5.08 (d, 1H, $J_{1,2}$ = 5.0 Hz, H-1B), 5.02 (d, 1H, $J_{1,2}$ = 1.4 Hz, H-1D), 4.97 (d, 1H, J_{gem} = 12.7 Hz, ArC*H*$_2$), 4.88 (d, 1H, $J_{1,2}$ = 1.8 Hz, H-1A), 4.82−4.76 (m, 2H, ArC*H*$_2$), 4.68 (d, 1H, J_{gem} = 11.7 Hz,

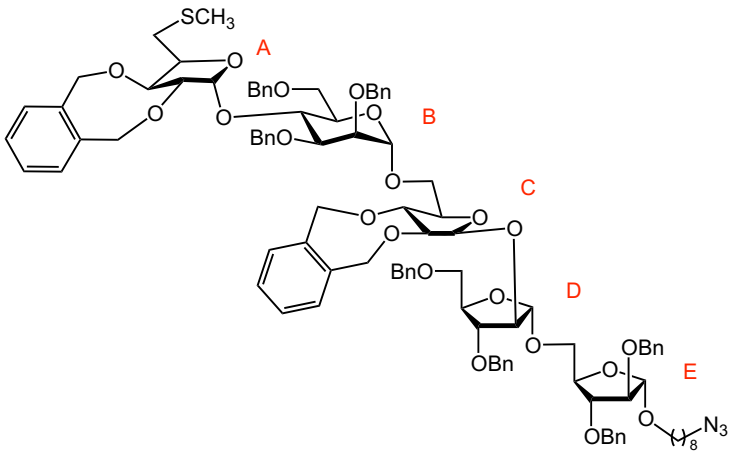
ArCH_2), 4.66−4.43 (m, 14H, ArCH_2), 4.33 (d, 1H, $J_{1,2}$ = 1.2 Hz, $J_{2,3}$ = 3.3 Hz, H-2C), 4.24−4.17 (m, 2H, H-4C, H-4D), 4.13−3.97 (m, 6H, H-2D, H-3D, H-3B, H-4B, H-2B, H-3C), 3.92 (dd, 1H, $J_{4,5a}$ = 4.3 Hz, J_{gem} = 11.4 Hz, H-5aD), 3.84−3.61 (m, 11H, H-2A, H-3A, H-5aC, H-5bC, H-5aB, H-5bB, H-6aA, azidooctyl CH_2-O, H-5bD, H-4A, H-5A), 3.59 (dd, 1H, $J_{5,6a}$ = 5.4 Hz, J_{gem} = 10.9 Hz, H-6bA), 3.40−3.38 (m, 1H, octyl CH_2O), 3.27 (t, 2H, J = 7.0 Hz, CH_2N_3), 1.64−1.53 (m, 4H, octyl), 1.39−1.32 (m, 8H, octyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 138.4 (Ar), 138.28 (Ar), 138.25 (Ar), 138.21 (Ar), 138.1 (Ar), 138.0 (Ar), 137.7 (Ar), 136.8 (Ar), 135.8 (Ar), 131.6 (Ar), 131.1 (Ar), 129.4 (Ar), 128.4 (Ar), 128.35 (Ar), 128.33 (Ar), 128.32 (Ar), 128.30 (Ar), 128.2 (Ar), 127.9 (Ar), 127.8 (Ar), 127.77 (Ar), 127.75 (Ar), 127.71 (Ar), 127.64 (Ar), 127.61 (Ar), 127.59 (Ar), 127.55 (Ar), 127.49 (Ar), 127.46 (Ar), 127.2 (Ar), 106.7 (C-1C), 106.0 (C-1D), 103.0 (C-1B), 98.1 (C-1A), 88.6 (C-2D), 86.7 (C-2C), 83.8, 83.4, 82.6, 82.1, 81.0, (C-2B, C-3C, C-3D, C-3B, C-4B), 80.9, 80.1, (C-4C, C-4D), 79.6, 74.4, (C-2A, C-3A), 73.6 (ArCH$_2$), 73.3 (ArCH$_2$), 72.7 (ArCH$_2$), 72.3 (ArCH$_2$), 72.1 (ArCH$_2$), 71.9 (ArCH$_2$), 71.8 (ArCH$_2$), 70.5 (C-5A), 69.9 (C-5B), 69.7 (C-5C), 69.76 (C-6A), 69.73 (ArCH$_2$), 69.5 (ArCH$_2$), 69.2 (C-4A), 67.6 (octyl CH_2O), 66.2 (C-5D), 51.4 (CH_2N_3), 29.5 (octyl), 29.3 (octyl), 29.1 (octyl), 28.8 (octyl), 26.7 (octyl), 26.1 (octyl); HRMS-ESI *m/z* $[M + Na]^+$ calcd for $C_{86}H_{99}N_3NaO_{18}$: 1484.6821, found: 1484.6829.



8-Azido-octyl 2,3-*O*-xylylene-α-D-xylofuranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→5)-2,3-*O*-xylylene-β-D-arabinofuranosyl-(1→2)-3,5-di-*O*-benzyl-α-D-arabinofuranosyl-(1→5)-2,3-di-*O*-benzyl-α-D-arabinofuranoside (163): To a mixture of donor **114** (81.4 mg, 0.203 mmol) and acceptor **160** (175 mg, 0.120 mmol) in Et_2O (7 mL) was added 4 Å molecular sieves (200 mg) at rt. After stirring for 1 h, NIS (191 mg, 0.848 mmol) and AgOTf (13.7 mg, 0.0568 mmol) were added to the mixture. The reaction was monitored by TLC and after stirring for 2 h at rt, the reaction was quenched by the addition of Et_3N. The solution was diluted with CH_2Cl_2 and filtered through Celite. The filtrate was then washed with satd aq. $Na_2S_2O_3$ and brine. The organic layer was subsequently dried with anhydrous Na_2SO_4, filtered, concentrated and the residue was purified by flash silica gel column chromatography

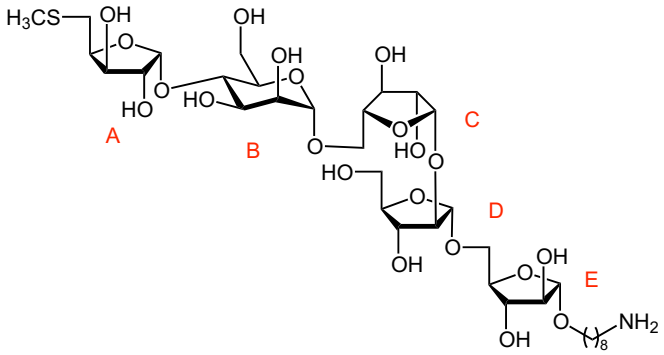
(5:1, hexane–EtOAc) to give a mixture of α- and β-anomer, which could not be separated. To a solution of the mixture in CH_3OH (3 mL) and CH_2Cl_2 (2 mL) was added 1.0 M CH_3ONa in CH_3OH (20 μL). The mixture was stirred for 5 h at rt, neutralized by the addition of Amberlite IR-120 H^+ resin, filtered, and the filtrate was concentrated. The residue was purified by silica gel column chromatography (2:1, hexanes–EtOAc) to give **163** (169 mg, 83% over two steps, α/β 11:1) as an oil: R_f 0.35 (2.5:1, hexane–EtOAc); $[\alpha]_D$ = +26.8 (c = 0.6, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.41−7.23 (m, 43H, ArH), 5.51 (d, 1H, $J_{1,2}$ = 5.0 Hz, H-1A), 5.17 (d, 1H, $J_{1,2}$ = 1.2 Hz, H-1D), 5.08 (d, 1H, $J_{1,2}$ = 5.0 Hz, H-1C), 5.02 (d, 1H, $J_{1,2}$ = 1.4 Hz, H-1E), 4.99−4.96 (m, 2H, ArCH_2), 4.88 (d, 1H, $J_{1,2}$ = 1.8 Hz, H-1B), 4.85−4.47 (m, 20H, ArCH_2), 4.32 (d, 1H, $J_{1,2}$ = 1.2 Hz, $J_{2,3}$ = 3.3 Hz, H-2D), 4.27 (dd, 1H, $J_{2,3}$ = 7.7 Hz, $J_{3,4}$ = 5.6 Hz, H-3A), 4.23−4.21 (m, 1H, H-5B), 4.19 (dt, 1H, $J_{3,4}$ = $J_{4,5a}$ = 4.2 Hz, $J_{4,5b}$ = 7.5 Hz, H-4E), 4.10−3.91 (m, 12H, H-2A, H-3D, H-2C, H-2E, H-5aE, H-3E, H-4A, H-3B, H-4B, H-3C, H-4C, H-4D), 3.80 (dd, 1H, $J_{4,5a}$ = 6.2 Hz, J_{gem} = 10.7 Hz, H-5aD), 3.84−3.61 (m, 10H, H-2B, octyl CH_2-O, H-6aB, H-6bB, H-5bE, H-5bD, H-5aA, H-5bA, H-5aC, H-5bC), 3.41−3.39 (m, 1H, octyl CH_2O), 3.27 (t, 2H, J = 7.0 Hz, CH_2N_3), 2.25 (dd, 1H, J = 5.0 Hz, J = 8.7 Hz, OH), 1.64−1.53 (m, 4H, octyl), 1.39−1.32 (m, 8H, octyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 138.79 (Ar), 138.71 (Ar), 138.4 (Ar), 138.2 (Ar), 138.1 (Ar), 137.7 (Ar), 136.8 (Ar), 136.2 (Ar), 136.0 (Ar), 135.7 (Ar), 131.6 (2C, Ar), 131.5 (2C, Ar), 131.3 (2C, Ar), 131.2 (2C, Ar), 129.55 (2C, Ar), 129.53 (2C, Ar), 129.4 (2C, Ar),

129.3 (2C, Ar), 128.4 (2C, Ar), 128.34 (2C, Ar), 128.32 (2C, Ar), 128.26 (2C, Ar), 128.25 (2C, Ar), 127.9 (2C, Ar), 127.79 (2C, Ar), 127.78 (2C, Ar), 127.76 (2C, Ar), 127.73 (2C, Ar), 127.6 (2C, Ar), 127.59 (2C, Ar), 127.57 (2C, Ar), 127.54 (2C, Ar), 127.4 (2C, Ar), 127.39 (Ar), 127.34 (Ar), 106.7 (C-1D), 106.0 (C-1E), 103.0 (C-1C), 101.9 (C-1A), 97.8 (C-1B), 88.6 (C-2E), 86.7 (C-2D), 83.8, 83.4, 82.6, 82.1, 81.9, 81.1, 81.0 (C-2A, C-3A, C-2C, C-3D, C-3E, C-3C, C-4C), 80.9, 80.3, 80.1 (C-4A, C-4D, C-4E), 77.5, 74.4 (C-2C, C-3C), 73.6 (Ar*C*H_2), 73.3 (Ar*C*H_2), 73.1 (Ar*C*H_2), 72.7 (Ar*C*H_2), 72.3 (Ar*C*H_2), 72.1 (Ar*C*H_2), 71.9 (Ar*C*H_2), 71.4 (Ar*C*H_2), 71.8 (Ar*C*H_2), 70.5 (C-5B), 69.9 (C-5C), 69.7 (C-5D), 69.76 (C-6B), 69.73 (Ar*C*H_2), 69.5 (Ar*C*H_2), 69.2 (C-4B), 67.6 (octyl CH_2O), 66.2 (C-5E), 61.7 (C-5A), 51.4 (CH_2-N_3), 29.5 (octyl), 29.3 (octyl), 29.1 (octyl), 28.8 (octyl), 26.7 (octyl), 26.1 (octyl); HRMS-ESI *m/z* [M + Na]$^+$ calcd for $C_{99}H_{113}N_3NaO_{22}$: 1718.7713, found: 1718.7721.



8-Azido-octyl 5-deoxy-5-methylthio-2,3-*O*-xylylene-α-D-xylofuranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→5)-2,3-*O*-xylylene-β-D-arabinofuranosyl-(1→2)-3,5-di-*O*-benzyl-α-D-arabinofuranosyl-(1→5)-2,3-di-*O*-benzyl-α-D-arabino-furanoside (164): To a solution of **163** (169 mg, 0.1 mmol) in pyridine (3 mL) at 0 °C was added toluenesulfonyl chloride (57 mg, 0.3 mmol). The reaction mixture was stirred at rt for 8 h and then concentrated to a syrup that was purified by flash column chromatography. Then to a solution of the product in CH_3CN (4 mL) was added 18-crown-6 (25 mg) followed by sodium thiomethoxide (17 mg, 0.3 mmol). The reaction mixture was heated at reflux for 10 h and then cooled to rt before being diluted with CH_3CN (8 mL) and filtered through Celite. The filtrate was concentrated to a syrup that was purified by column chromatography (6:1, hexanes–EtOAc) to afford **164** (134 mg, 78%) as an oil. R_f 0.35 (2.5:1, hexane–EtOAc); $[\alpha]_D$ = +45.9 (c = 0.7, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.39−7.23 (m, 43H, ArH), 5.47 (d, 1H, $J_{1,2}$ = 5.0 Hz, H-1A), 5.16 (d, 1H, $J_{1,2}$ = 1.2 Hz, H-1D), 5.07 (d, 1H, $J_{1,2}$ = 5.0 Hz, H-1C), 5.02 (d, 1H, $J_{1,2}$ = 1.4 Hz, H-1E), 4.96−4.93 (m, 2H, $ArCH_2$), 4.88 (d, 1H, $J_{1,2}$ = 1.8 Hz, H-1B), 4.83−4.49 (m, 20H, $ArCH_2$), 4.31 (d, 1H, $J_{1,2}$ = 1.2 Hz, $J_{2,3}$ = 3.3 Hz, H-2D), 4.27−4.14 (m, 4H, H-3A, H-4E, H-4A, H-3E), 4.10−4.02 (m, 5H, H-2E, H-5B, H-4D, H-3B, H-4C), 4.01−3.91 (m, 6H, H-2A, H-3D, H-5aE, H-2C, H-4B, H-3C), 3.83−3.76 (m, 2H, H-5aD, H-5bD), 3.76−3.68 (m, 4H, H-2B, H-5aC, H-5bE, octyl CH_2O), 3.65−3.56 (m, 3H, H-6aB, H-6bB, H-5bC), 3.44−3.36 (m, 1H, octyl CH_2O), 3.27 (t, 2H, J = 7.0 Hz,

CH_2N_3), 2.72 (dd, 1H, $J_{4,5a}$ = 5.1 Hz, J_{gem} = 13.9 Hz, H-5aA), 2.52 (dd, 1H, $J_{4,5b}$ = 7.5 Hz, J_{gem} = 13.9 Hz, H-5bA), 1.64−1.53 (m, 4H, octyl), 1.39−1.32 (m, 8H, octyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 138.79 (Ar), 138.71 (Ar), 138.4 (Ar), 138.2 (Ar), 138.1 (Ar), 137.7 (Ar), 136.8 (Ar), 136.2 (Ar), 136.0 (Ar), 135.7 (Ar), 131.6 (2C, Ar), 131.5 (2C, Ar), 131.3 (2C, Ar), 131.2 (2C, Ar), 129.55 (2C, Ar), 129.53 (2C, Ar), 129.4 (2C, Ar), 129.3 (2C, Ar), 128.4 (2C, Ar), 128.34 (2C, Ar), 128.32 (2C, Ar), 128.26 (2C, Ar), 128.25 (2C, Ar), 127.9 (2C, Ar), 127.79 (2C, Ar), 127.78 (2C, Ar), 127.76 (2C, Ar), 127.73 (2C, Ar), 127.6 (2C, Ar), 127.59 (2C, Ar), 127.57 (2C, Ar), 127.54 (2C, Ar), 127.4 (2C, Ar), 127.39 (Ar), 127.34 (Ar), 106.7 (C-1D), 106.0 (C-1E), 103.0 (C-1C), 101.9 (C-1A), 97.8 (C-1B), 88.6 (C-2E), 86.7 (C-2D), 83.8, 83.4, 82.6, 82.1, 81.9, 81.1, 81.0 (C-2A, C-3A, C-2C, C-3D, C-3E, C-3C, C-4C), 80.9, 80.3, 80.1 (C-4A, C-4D, C-4E), 77.5, 74.4 (C-2C, C-3C), 73.6 (Ar*C*H_2), 73.3 (Ar*C*H_2), 73.1 (Ar*C*H_2), 72.7 (Ar*C*H_2), 72.3 (Ar*C*H_2), 72.1 (Ar*C*H_2), 71.9 (Ar*C*H_2), 71.4 (Ar*C*H_2), 71.8 (Ar*C*H_2), 70.5 (C-5B), 69.9 (C-5C), 69.7 (C-5D), 69.76 (C-6B), 69.73 (Ar*C*H_2), 69.5 (Ar*C*H_2), 69.2 (C-4B), 67.6 (octyl CH_2O), 66.2 (C-5E), 51.4 (CH_2-N_3), 33.9 (C-5A), 29.5 (octyl), 29.3 (octyl), 29.1 (octyl), 28.8 (octyl), 26.7 (octyl), 26.1 (octyl), 16.8 (SCH_3); HRMS-ESI *m/z* $[M + Na]^+$ calcd for $C_{100}H_{115}N_3NaO_{21}S$: 1748.7641, found: 1748.7649.



8-Amine-octyl 5-deoxy-5-methylthio-α-D-xylofuranosyl-(1→4)-α-D-manno-pyranosyl-(1→5)-β-D-arabinofuranosyl-(1→2)-α-D-arabinofuranosyl-(1→5)-α-D-ar-abino-furanoside (139): Sodium was added to freshly collected liquid ammonia (~ 15 mL) at −78 °C until the dark blue color of the solution persisted. Then, a solution of **164** (21 mg) in THF (1 mL) and CH_3OH (10 μL) was added dropwise at −78 °C. After 1.5 h, CH_3OH (3 mL) was added and the solution was concentrated to dryness. The resulting residue was dissolved in H_2O (10 mL), neutralized with Amberlite IR120 H^+ ion-exchange resin, filtered and concentrated. The resulting crude residue was purified by C_{18} chromatography (100% water to 1:8 CH_3OH–water) to give **139**.

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