Synthesis of Ketose-containing Microbial Glycans

by

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Abstract

Molecules that include ketose residues are referred to as ketose-containing glycans. They have been identified in both prokaryotic and eukaryotic organisms where they serve important biological roles. To understand better the biological roles of ketose-containing glycans, chemical synthesis provides a useful tool to access probe molecules. However, there are many challenges that need to be addressed in the synthesis of molecules of this type. This thesis is focused on developing synthetic approaches to glycans with three different ketose residues.

In Chapter 2, the synthesis of 3-deoxy-D-*manno*-oct-2-ulosonic acid (Kdo) and its derivatives are described. In 2013, Whitfield and coworkers identified that the core of capsular polysaccharides (CPS) from *Escherichia coli* K1 and K5, and *Neisseria meningitides* group B, contain alternating β-(2→4)- and β-(2→7)-β-Kdo linkages. However, the biosynthesis of this CPS had not been definitively resolved when I started my thesis research. In this study, one β-Kdo monosaccharide and two disaccharides with either a β-(2→4)- or a β-(2→7)-linkage were synthesized as the probe molecules for biosynthetic studies and high-throughput screens.

Xylulose (Xul) is the second ketose that was studied in this thesis. β-Xylulofuranose (β-Xul*f*) moieties have been identified as components of microbial glycans. However, there have been no reports on synthesizing molecules with this ketose, particularly those containing β-Xul*f* residues. I developed two methods for stereoselective xylulofuranosylation. In Chapter 3, moderate to good β selectivity in xylulofuranosylation was observed with a variety of acceptors using conformationally-restricted donors. In Chapter 4, exclusive β selectivity was obtained using a siloxane-protected donor that hindered the α-face of the furanose ring. Both methods were applied to the synthesis of β-D-Xul*f*-containing glycans that are present in microbial glycans.

In Chapter 5, the third ketose, Fructose (Fru), was investigated. Fru is found in nature primarily in the β-furanose form. Previous studies to synthesize β-Fru*f* glycosides (an example of *cis*-glycosides) have focused on two different strategies: intramolecular aglycone delivery and the use of sterically-hindered donors. The strategy of using conformationally-restricted donors has not been reported although it has been shown to be a powerful method to synthesize *cis*-glycosides of aldofuranoses. Three different conformationally-restricted Fru*f* donors were synthesized and their use in glycosylation reactions provided stereoselectivity totally contrary to my expectation. The unexpected results are discussed in the context of the influence of side chain (hydroxymethyl groups) on stereoselectivity and compared to other related systems (arabinofuranosylation and xylulofuranosylation).

Preface

Chapter 2 – Part of this chapter was published:

Ovchinnikova, O. G.; Doyle, L.; **Huang, B.-S.**; Kimber, M. S.; Lowary, T. L.; Whitfield, C. *J. Biol. Chem.* **2016**, 21519–21530.

The paper was written by our collaborators from the Whitfield laboratory and edited by Professor Lowary and I. My contributions to this paper include the preparation of samples used for characterizing the functionof β-Kdo glycosyltransferases KpsC from *Escherichia coli* in capsule biosynthesis.

Doyle, L.; Ovchinnikova, O. G.; Myler, K,; Mallette, E.; **Huang, B.-S.**; Lowary, T. L.; Kimber, M. S.; Whitfield, C. *Nat. Chem. Biol.* **2019**, 15, 632–640.

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Gao, Z.; Ovchinnikova, O. G.; **Huang, B.-S.**; Liu, F.; Williams, D. E.; Ahderson, R. J.; Lowary, T. L; Whitfield, C.; Withers, S. G. *J. Am. Chem. Soc.* **2019**, *141*, 2201–2204.

The paper was written by our collaborators from the Withers laboratory and edited by Professor Lowary and I. My contributions to this paper include the preparation of samples used for identi-fying potent inhibitors of β-Kdo glycosyltransferases via high-throughput screening assays.

Chapter 3–5 – The work described in this three chapters were done solely by me and have not been published.

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List of Schemes

List of Abbreviations

$[\alpha]_D$	specific rotation (sodium D Line)
Å	Angstrom
Ac	acetyl
AgOTf	silver trifluromethanesulfonate
All	allyl
AllBr	allyl bromide
app	apparent
Ar	aromatic
Ara	arabinose
Ara*f*	arabinofuranose, arabinofuranoside
ax	axial
Bn	benzyl
BnBr	benzyl bromide
BnONa	sodium benzyloxide
br s	broad singlet (NMR spectra)
Bz	benzoyl
BzCl	benzoyl chloride
C. heliozoae	*Chlorellaceae heliozoae*
C. jejuni	*Campylobacter jejuni*
Cbz	benzyloxycarbonyl

ACN	acetonitrile
COSY	correlation sepctroscopy
CPS	capsular polysaccharide
CSA	camphorsulfonic acid
CSA	10-camphorsulfonic acid
CsF	cesium fluoride
d	doublet (NMR spectra)
DABCO	1,4-diazabicyclo[2,2,2]octane
DCE	dichloroethane
ddd	doublet of doublet of doublet (NMR spectra)
DDQ	2,3-dichloro-5,6-dicyano-*p*-benzoquinone
D-Fru	D-fructose
DFT	density functional theory
D-Gal	D-galactose
D-Glc	D-glucose
DIAD	diisopropyl azodicarboxylate
DMAP	4-(dimethylamino)pyridine
DMF	dimethylformamide
DMP	dimethoxypropane
DMSO	dimethyl sulfoxide
DMTST	dimethylthiomethyl sulfonium trifluoromethanesul-

	fonate
dt	doublet of triplet (NMR spectra)
DTBMP	2,6-di-*tert*-butyl-4-methylpyridine
DTBS	di-*tert*-butylsilyl
$DTBS(OTf)_2$	di-*tert*-butylsilyl bis(trifloromethanesulfonate)
E. coli	*Escherichia coli*
eq	equatorial
ESI	electrospray ionization
Et	ethyl
FITC	fluorescein isothiocyanate
Fru	fructose
Fru*f*	fructofuranose, fructofuranoside, fructofuranosyl
Gal	galactose
Gal*f*	galactofuranose, galactofuranoside
gem	geminal
gg	*gauche–gauche*
Glc	glucose
gt	*gauche–trans*
HAD	hydrogen-bond-mediated aglycone delivery
HMBC	heteronuclear multiple bond correlation
HRMS	high-resolution mass spectrometry

Hz	Hertz
IAD	intramolecular aglycone delivery
IBr	iodine monobromide
IDCP	iodonium dicollidine perchlorate
IDCT	iodonium collidine triflate
im	imidazole
*i*Pr	isopropyl
Kdo	3-deoxy-D-manno-oct-2-ulosonic acid
$KMnO_4$	potassium permanganate
Leg	legionaminic acid
LG	leaving group
LPS	lipopolysaccharide
Lyx*f*	lyxofuranose, lyxofuranoside
m	multiplet (NMR spectra)
Me	methyl
MeOTf	trifluoromethanesulfonate
N. meningitidis	*Neisseria meningitides*
Naph	2-methylnaphthyl
NaphBr	2-(bromomethyl)naphthalene
NBS	*N*-bromosuccinimide
n-Bu_2SnO	di-*n*-butyltin oxide

n-BuLi	*n*-butyllithium
NeuNAc	*N*-acetylneuraminic acid
NIS	*N*-iodosuccinimide
NMR	nuclear magnetic resonance
NOESY	Nuclear overhauser effect spectroscopy
Nu	Nucleophile
Ph	phenyl
Phen	4'-methoxyphenacyl
PMB	*p*-methoxybenzyl
PMBz	*p*-methoxybenzoyl
PPh_3	triphenylphosphine
ppm	parts per million
Pse	pseudaminic acid
p-TSA	*para*-toluenesulfonic acid
py	pyridine
q	quartet (NMR spectra)
Quin	2-quinolinecarbonyl
R_f	retention factor
Rha	rhamnose
Rha*p*	rhamnopyranose

Rib*f*	ribofuranose, ribofuranoside
s	singlet (NMR spectra)
TBAF	tetrabutylammonium fluoride
TBAI	tetrabutylammonium iodide
TBDPS	*ter*t-butyldiphenylsilyl
TBDPSCl	*tert*-butyldiphenylsilyl chloride
TBS	*tert*-butyldimethylsilyl
TBSCl	*tert*-butyldimethylsilyl chloride
t-Bu	*tert*-butyl
t-BuOK	potassium *tert*-butoxide
t-BuOLi	Lithium *tert*-butoxide
TES	triethylsilyl
Tf_2O	Trifluoromethanesulfonic anhydride
TFA	trifluoroacetic acid
TfOH	trifluoromethanesulfonic acid
tg	*transgauche*
THF	tetrahydrofuran
$TIPSCl_2$	1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane
TLC	thin layer chromatography
TMS	trimethylsilyl

TMSOTf	trimethylsilyl trifluoromethanesulfonate
Tol	*p*-tolyl
TrCl	trityl chloride
Troc	2,2,2-trichloroethoxycarbonyl
TROESY	transverse rotating frame overhauser enhancement spectroscopy
Ts	toluenesulfonyl
Xul	xylulose
Xul*f*	xylulofuranose, xylulofuranoside, xylulofuranosyl
Xyl*f*	xylofuranose, xylofuranoside
Y. enterocolitica	*Yersinia enterocolitica*

Chapter 1

Introduction

1.1 General introduction of ketose-containing glycans

Glycans are the carbohydrate portion of glycoconjugates such as glycoproteins, glycolipids and proteoglycans. Glycans are composed of a large number of monosaccharide units linked via glycosidic linkages. Monosaccharides can be simply classified into two types based on the position of the carbonyl group: monosaccharides with the carbonyl group at C-1 are called aldoses, e.g., D-glucose (D-Glc) or D-galactose (D-Gal) (**Figure 1.1a**) and those with the carbonyl group at other positions, normally at C-2, are named ketoses, e.g., *N*-acetylneuraminic acid (NeuAc), and D-fructose (D-Fru). (**Figure 1.1b**). The glycans that contain any ketose in the sugar sequence are called ketose-containing glycans.

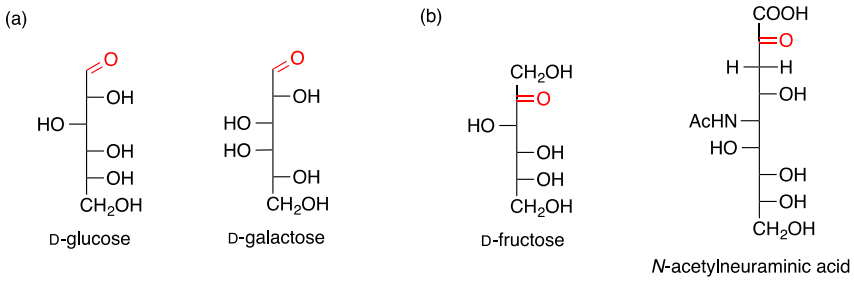


Figure 1.1. (a) Examples of aldoses in the Fischer projection; (b) Examples of ketoses in the Fischer projection.

Ketose-containing glycans have been widely identified in both prokaryotic and eukaryotic cells and have many important biological roles, such as the regulation of lymphocyte homing (sialyl 6-sulfo Lewis X)[1] and neuronal and brain development (gangliosides) in eukaryotic cells[2,3]. Ketose-containing glycans are also expressed in various surface structures of microorganisms, including lipopolysaccharides (LPS), capsular polysaccharides (CPS) as well as N- and

O-linked glycans[4]. These microbial ketose-containing glycans play important roles as virulence factors and can be used as targets for the development of anti-microbial therapeutics and/or vaccines.

To probe the biological functions of these microbial ketose-containing glycans, structurally well-defined and homogenous molecules are needed. However, the isolation of a single glycoform (a molecule consisting of a single glycan) from biological systems is often difficult and impractical. Furthermore, the quantities of glycans obtained from biological systems are often small. Therefore, chemical synthesis provides an alternative method to obtain pure glycans in enough amounts for biological testing. In the following section, I describe the challenges in the synthesis of ketose-containing glycans.

1.2 Challenges in the chemical synthesis of ketose-containing glycans

Although chemical synthesis is a powerful tool for the preparation of glycans, there are still many challenges to be tackled due to the diversity of the oligosaccharides that arise from the different types of glycosidic linkages and sugar compositions. In the chemical synthesis of ketose-containing glycans, there are three major challenges to be addressed: (1) the preparation of rare ketose monosaccharides; (2) the stereoselective glycosylation of ketoses; and (3) the characterization of the anomeric configuration of diastereomers. In the following sections, I provide a few recently developed examples on how to address these challenges. More specific discussions relevant to the work described later in the thesis can be found in the introduction to each chapter.

1.2.1 Chemical synthesis of rare ketose monosaccharides

As is the case with uncommon or rare aldoses, synthetic approaches to rare ketoses is often the first challenge in making ketose-containing glycans. With the exception of NeuAc and D-fructose, all of the other ketoses are defined as rare sugars. Improvements to the methods for the preparation of rare ketoses, such as NeuAc analogues (e.g., legionaminic acid, pseudaminic acid), pentuloses (e.g., xylulose and ribulose) and hexuloses (e.g., psicose, sorbose and tagatose), are still required given the expense of commercial sources. Many chemical[5–21] and enzymatic[22–24] methodologies have been reported to synthesize rare ketoses. In this Section, I will provide some recent synthetic reports as examples.

Many studies have focused on the synthesis of NeuAc, legionaminic acid (Leg) and pseudaminic acid (Pse) and their glycosides, by both chemical[14–21] or enzymatic[23,24] methodologies. Leg, compared to NeuAc, also contains the D-*glycero*-D-*galacto* configuration, but with no hydroxyl group at C-9 and by the replacement of the C–O bond at C-7 by a C–N bond. Pse contains an L-*glycero*-L-*manno* configuration, which differs from NeuAc in the stereochemistry at C-5, C-7 and C-8. Like Leg, Pse is also deoxygenated C-9 and has an O- to N-substitution at C-7 (**Figure 1.2**). In the past few years, synthetic strategies toward Leg and Pse derivatives have been developed, including the synthesis from amino acids[14,16], transformations of NeuAc[17–21] and chemoenzymatic synthesis[23,24].

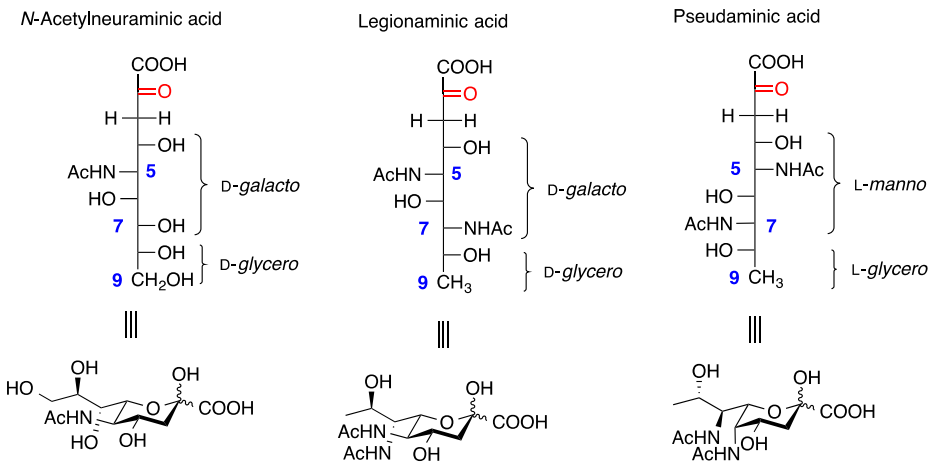
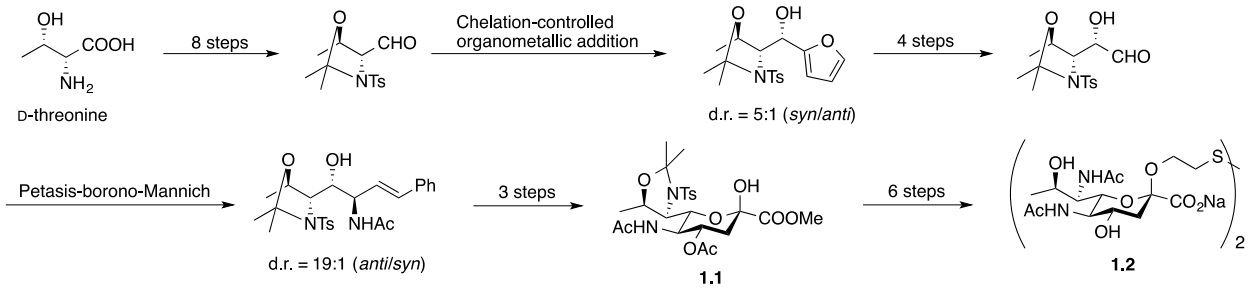
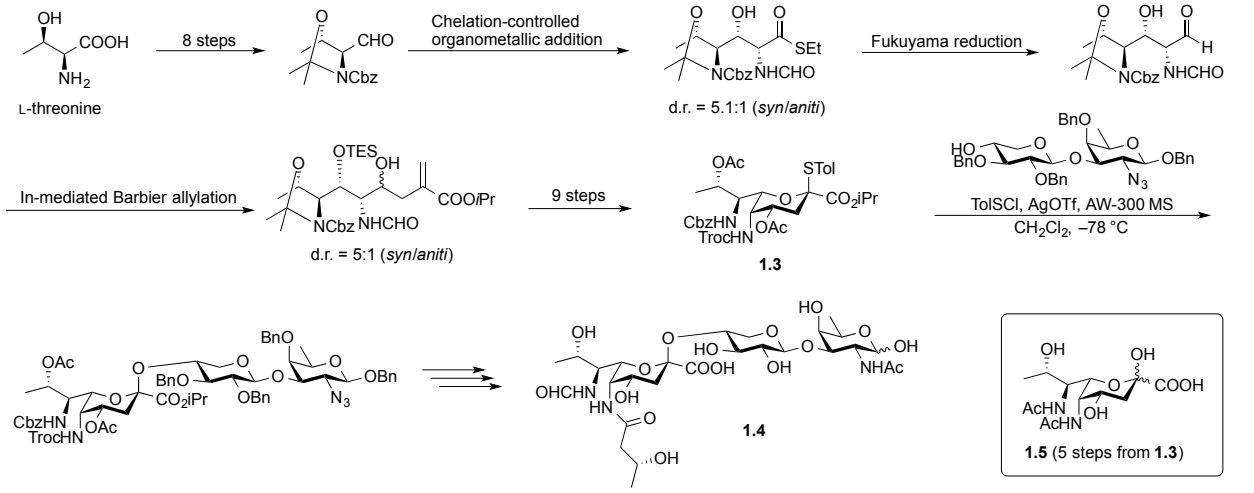


Figure 1.2. Fischer projections and cyclized structures of *N*-acetylneuraminic acid, legionaminic acid and pseudaminic acid.

In 2015, Matthies *et. al.* synthesized the Leg building block **1.1** and linker-functionalized Leg **1.2** via a *de novo* strategy from inexpensive and commercially available D-threonine (**Scheme 1.1**)[14]. The synthesis involved a series of chelation-controlled organometallic additions and a Petasis multicomponent reaction. In 2017, a *de novo* strategy for the synthesis of Pse derivative **1.3** was developed from L-threonine via two chain-elongation reactions by Li and coworkers[16] (**Scheme 1.2**). The Pse derivative **1.3** was used to synthesize the *Pseudomonas aeruginosa* 1244 pilin glycan trisaccharide **1.4** with exclusive α-selectivity, as well as to synthesize Pse (**1.5**). The most challenging issue when using *de novo* approaches from small molecules to synthesize Leg and Pse analogues is the diastereoselectivity in the chain elongation steps.



Scheme 1.1. Synthesis of legionaminic acid building block **1.1** and linker-functionalized legionaminic acid **1.2**.



Scheme 1.2. Synthesis of pseudaminic acid derivative **1.3** and its synthetic applications leading to **1.4** and **1.5**.

The synthesis of Leg[19,20] and Pse[17,18,21] derivatives has also been developed via transformations of NeuAc. As mentioned above, the differences between NeuAc and Leg are the absence of a hydroxyl group the C-9 position and the replacement of a C–O bond by a C–N bond at C-7 (**Figure 1.2**). In 2017, Crich and coworkers[20] synthesized Leg derivative **1.6** (**Figure 1.3a**) from

NeuAc for a study on glycosylation selectivity. The synthetic route involved deoxygenation of the C-9 hydroxyl group and conversion of the C-7 hydroxyl group to an azide by double inversion (**Figure 1.3a**). In 2018, Kiefel and coworkers[19] used the same strategy to synthesize Leg derivative **1.7** and 7-*epi*-Leg derivative **1.8** (**Figure 1.3a**).

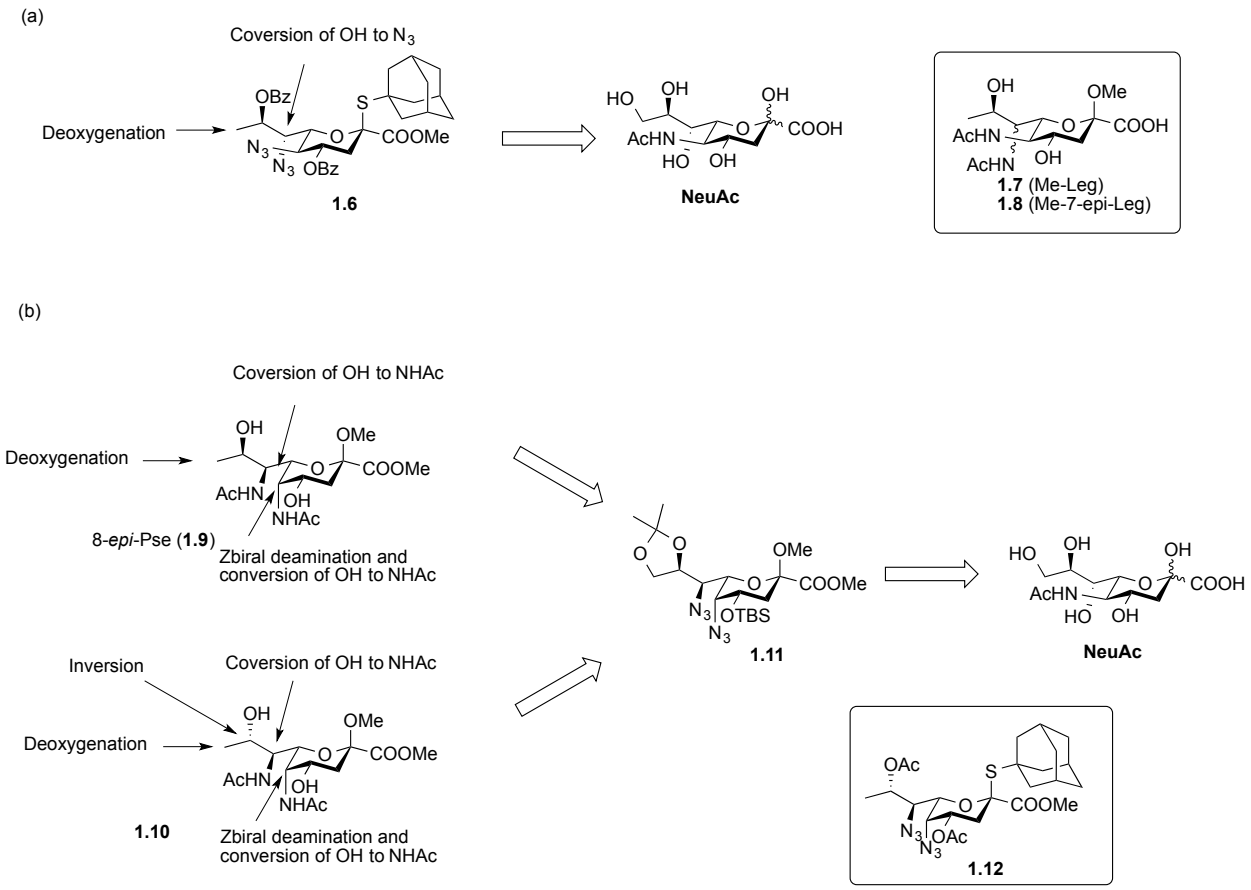


Figure 1.3. (a) Retrosynthetic analysis of synthesizing Leg derivatives **1.6–1.8** from NeuAc. (b) Retrosynthetic analysis of synthesizing Pse derivatives from NeuAc

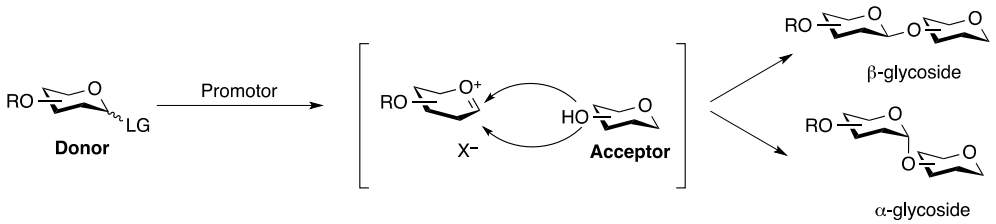
The synthesis of Pse derivatives from NeuAc is complicated because of the inverse configurations at C-5, C-7 and C-8, the absence of a hydroxyl group at C-9 and the replacement of the C–O bond by a C–N bond at C-7 (**Figure 1.2**). Nevertheless, in 2014, Kiefel and coworkers[18] completed the synthesis of 8-*epi*-Pse derivative **1.9** from NeuAc with intermediate **1.11**. The synthetic route involved the deoxygenation of the C-9 hydroxyl group, and the conversion and inversion of the hydroxyl groups at C-5 and C-7 to NHAc groups (**Figure 1.3b**). The Pse derivative **1.10** was also synthesized by Payne and coworkers[17] from **1.11** in eight steps. In 2018, Crich and coworkers[21] synthesized Pse derivative **1.12** from NeuAc using a similar strategy as they used for the Leg analogues (**Figure 1.3b**). The strategy using NeuAc as a starting material usually leads to routes with many steps, due to the multiple hydroxyl groups of NeuAc, which requires many protection/deprotection transformations.

As mentioned above, the first challenge in synthesizing ketose-containing glycans is to prepare the rare ketoses. Once those are obtained, the next challenge is to generate the ketosidic bonds stereoselectively. In the following section, I will provide the most recent investigations on stereoselective ketosidic bond formation.

1.2.2 Recent work on the stereoselectivity of ketose glycosylation

Stereocontrolled formation of many classes of glycosidic bonds is a long-standing challenge in carbohydrate chemistry. The glycosidic linkage is generally formed through the nucleophilic attack of a glycosyl acceptor (normally a hydroxyl group) on the anomeric carbon of an electrophilic intermediate formed from the glycosyl donor. Unlike enzymatic glycosylation, which generates the glycosidic linkage with absolute stereocontrol, chemical glycosylation reac-

tions can often result in the formation of both α- and β-diastereomers (**Scheme 1.3**). Thus, controlling the stereoselectivity is an issue in every glycosylation reaction.



Scheme 1.3. General mechanism of a chemical glycosylation reaction.

For instance, α-selectivity in sialylation reactions is difficult to achieve because of the hindered tertiary C-2 anomeric center, the electron-withdrawing carbonyl group at C-1 and the lack of directing group at C-3. As such, stereocontrolled α-sialylation has been heavily investigated and several different methods have been developed. In nitrile solvent-directed α-sialylation, the stereoselectivity results from formation of a β-sialyl nitrilium ion[25–27], which forms by initial reaction of the electrophilic intermediate with the solvent (**Figure 1.4a**). The *O*4,*N*5-carbonyl systems sialyl donors have also been developed and they show excellent stereocontrolled α-sialylation[28,29] (**Figure 1.4b**). Moreover, the introduction of directing group at either C-1 or C-3 has also been exploited to obtain excellent α-stereoselective sialylation[30–38] (**Figure 1.4c**).

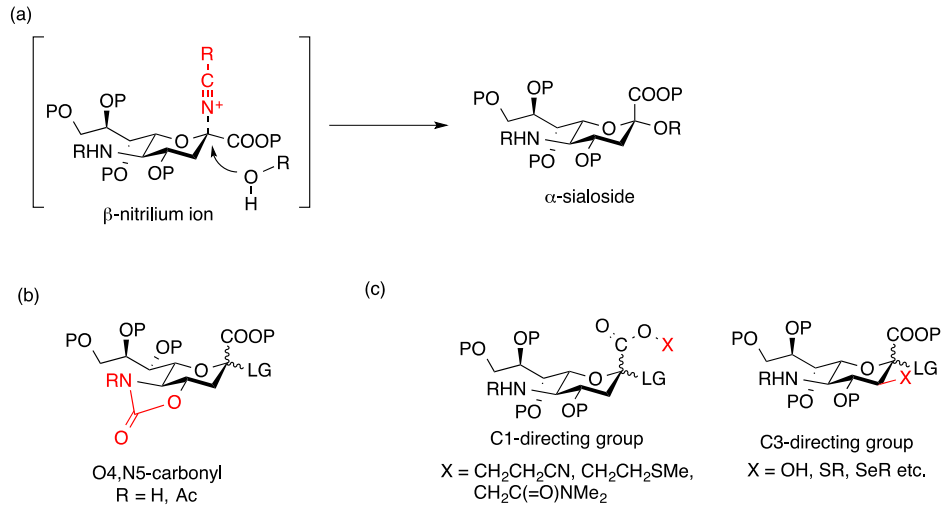


Figure 1.4. (a) Solvent-assisted α-sialylation via the formation of a β-sialyl nitrilium ion; (b) Examples of *O*4,*N*5-carbonyl sialyl donors for α-sialylation; (c) Examples of C-1 or C-3 directing groups that enhance α-sialylation.

Recently, Crich and coworkers[21,39,40] reported that the side chain conformation of NeuAc and its C-5- and C-7-epimers influence the anomeric selectivity and reactivity of glycosyl donors. They used NeuAc donors **1.13** and **1.15**, 7-*epi*-NeuAc donor **1.14** and 5-*epi*-NeuAc donor **1.16** to study the influence of the side chain on glycosylation selectivity (**Figure 1.5**). For both NeuAc derivatives (**1.13** and **1.15**), the *gg*-conformation of the side chain was favored. However the side-chain conformation of epimers **1.14** and **1.16** was changed to the *gt*-conformation[21,39,40] to avoid unfavorable dipolar and steric interactions with the C-5–N-5 bond (**Figure 1.5**).

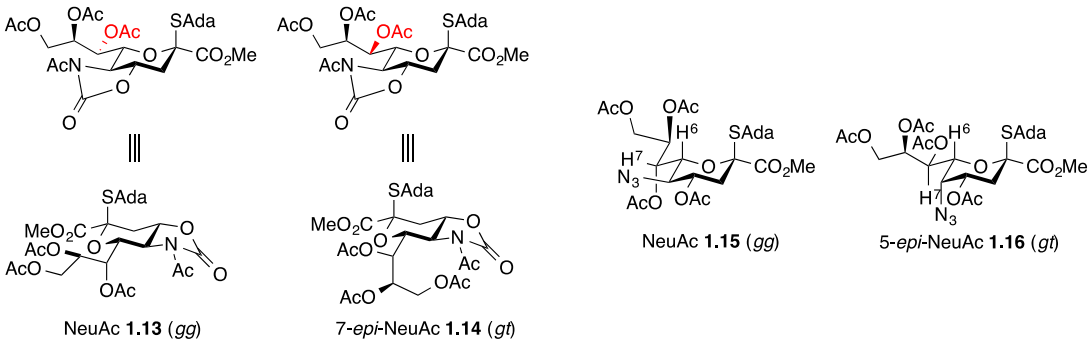


Figure 1.5. Structures of NeuAc donors **1.13** and **1.15**, 7-*epi*-NeuAc donor **1.14** and 5-*epi*-NeuAc donor **1.16**.

With regard to reactivity and stereoselectivity, the natural NeuAc donor (**1.13**) showed more equatorial selectivity and more reactivity than the 7-*epi*-NeuAc donor **1.14**[39]. The greater reactivity of the natural system, with its *gg*-side chain conformation can be explained by the ability of O-7 to stabilize the electrophilic intermediate through space due to the periplanar alignment of the C-7–O-7 bond and the vacant *p*-orbital on C-2 (**Figure 1.6**). Compared to more equatorial selectivity in the natural NeuAc donor (**1.13**), the observed reduced α-selectivity in **1.14** is suggested to result from shielding of the α-face in the *gt*-conformation of the side chain (**Figure 1.6**).

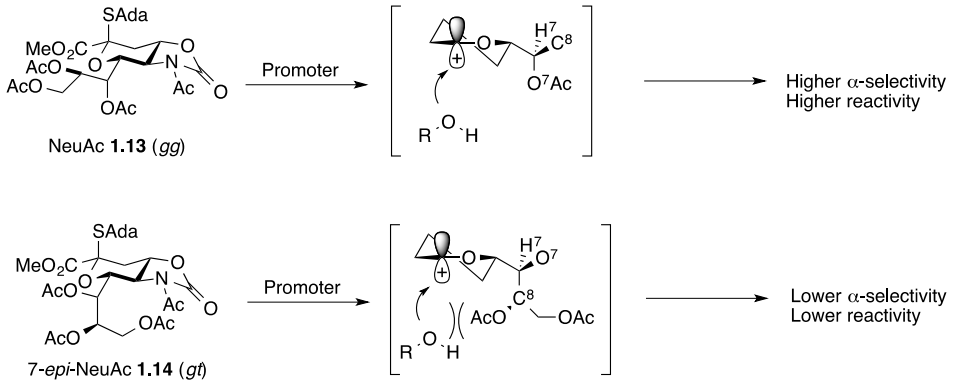


Figure 1.6. Explanation for the influence of side chain conformation on anomeric reactivity and selectivity in **1.13** and **1.14**.

In 2019, Ando and cowokers[41] reported a robust method to obtain complete α-selective sialylation, with a broad substrate scope (**Figure 1.7**). The key feature of their approach is the use of a macrobicyclic NeuAc donor, **1.17**, which has tethers at the C-1 carbonyl group and at the C-5 amino group. The chain length of the tethers was found to influence the reactivity of the donors in glycosylation reactions. Moreover, the 2,2-dichloroalkoxycarbonyl moiety at C-5 could be selectively cleaved to allow installation of different groups on nitrogen. A series of glycosyl acceptors, including simple alcohols and sugar-based alcohols were tested and all gave α-sialosides only.

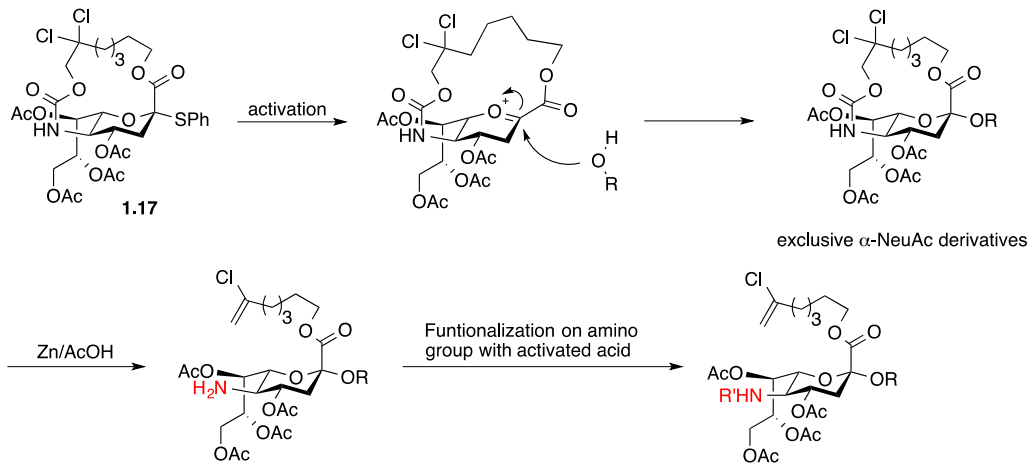


Figure 1.7. Ando's strategy for synthesizing α-sialosides using a bicyclic donor **1.17**.

Other than the reports of α-sialylation previously mentioned, the development of stereocontrolled methodologies for other ketoses, such as ketofuranosylation, is still necessary and important. Additional examples will be discussed in Chapter 2–5. A final challenge in the synthesis of ketose-containing glycoconjugates is the differentiation of diastereomeric glycosides to prove their structure.

1.2.3 Characterization of anomeric configuration in ketosides

The characterization of the anomeric configuration for aldose glycosides is relatively straightforward using the coupling constant ($^3J_{H1,H2}$) of the anomeric proton (H-1) and the adjacent proton (H-2). There are four possible relative relationships between H-1 and H-2, axial–axial (*anti*), equatorial–axial (*gauche,* two possibilities) and equatorial–equatorial (*gauche*) (**Figure 1.8a**). According to the Karplus equation[42], the anomeric configuration can be characterized by the magnitude of the $^3J_{H1,H2}$. For example, in α-glucopyranosides, $^3J_{H1,H2}$ ranges from 3–5 Hz and in β-glucopyranosides it ranges from 7–10 Hz (**Figure 1.8b**). In addition to the $^3J_{H1,H2}$,

the one bond coupling constant ($^{1}J_{C1,H1}$) between the anomeric carbon (C-1) and the anomeric proton (H-1) is a useful method for characterizing anomeric configuration. The $^{1}J_{C1,H1}$ of α-glycosides is larger than that of the β-glycosides due to hyperconjugation between one of the lone pairs of the ring oxygen and the antibonding orbital of the C-1–H-1 bond (**Figure 1.8c**), which leads to a longer C–H bond in β-glycosides.

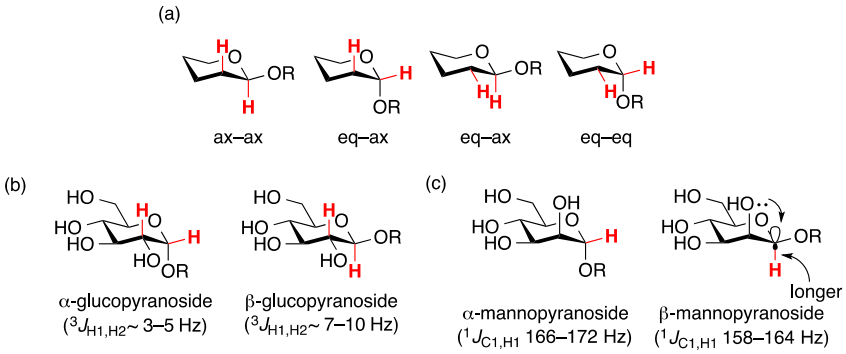


Figure 1.8. (a) Four possible relative relationships between H-1 and H-2 in aldopyranosides; (b) Two anomers of glucopyranosides and their anomeric characterization via $J_{H1,H2}$; (c) Influence of hyperconjugation on the C-1–H-1 bond length.

However, characterizing the anomeric configuration of ketosidic bonds cannot use coupling constants analogous to $^{3}J_{H1,H2}$ and $^{1}J_{C1,H1}$ because of the lack of an anomeric hydrogen. Thus, the use of other NMR experiments is needed to characterize the stereochemistry of products formed in glycosylation reactions leading to ketosides. For example, the three-bond coupling constant between the anomeric carbon and the axial proton at C-3 ($^{3}J_{C1,H3ax}$) can be used to assign the anomeric configuration of sialic acid glycosides (**Figure 1.9**), assuming that the ring has a $^{2}C_{5}$ conformation[43–45]. In the β-anomer, a *gauche* relationship (axial–equatorial) between H-3_{ax} and the C-1 is present and, in the ^{1}H-coupled ^{13}C NMR spectrum, C-1 appears as a broad

singlet ($^3J_{C1,H3ax}$ < 2 Hz). In the α-anomer, these atoms have a *trans*-diaxial relationship and C-1 appears as a doublet ($^3J_{C1,H3ax}$ > 5 Hz).

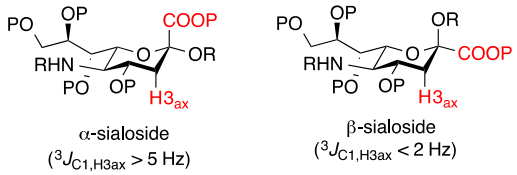


Figure 1.9. Two possible anomers of a sialic acid glycosides and the relationship between C-1 and H-3_{ax}.

1.3 Overview of thesis research

This thesis describes my work on three different projects on the synthesis of ketosidic bonds. A brief summary of the objectives of my thesis is provided below.

1.3.1 Research objective 1 – Synthesis of β-Kdo-containing fragments as probes for Kdo transferases

Just before starting my Ph.D. work, Whitfield and coworkers reported a novel 3-deoxy-D-*manno*-oct-2-ulosinc (Kdo)-containing core structure in the capsular polysaccharides (CPS) in *Escherichia coli* K1 and K5, and *Neisseria meningitis* group B[46]. However, the biological assembly of this structure was not understood. The CPS is an important virulence factor that protects the pathogens against the immune system of the host. Thus, glycosyltransferase inhibitors that block the production of these polysaccharides could be novel drug lead compounds. Understanding how the bacteria assemble this capsular polysaccharide is first needed. The objective of this part of my thesis was to develop chemical methods for making β-Kdo-containing-

oligosaccharides (**Figure 1.10**) that could be used to probe the activity, structure and function of Kdo glycosyltransferases. In Chapter 2, I describe my synthetic work to make these compounds. These compounds were then sent to collaborators for studies focused on understanding the specificity of Kdo glycosyltransferases, the determination of their structures by X-ray crystallography and the identification of inhibitors of these enzymes[47–49].

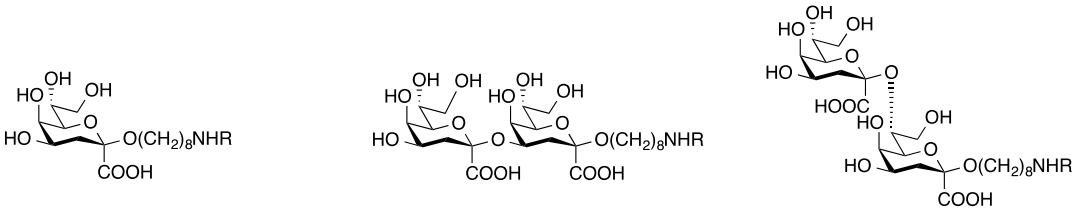


Figure 1.10. Structures of three β-Kdo containing-oligosaccharides synthesized as probes for Kdo glycosyltransferases.

1.3.2 Research objective 2 – Stereoselectivity studies on 2,3-*cis*-ketofuranosylations

The synthesis of 1,2-*cis*-glycosides of aldofuranoses (e.g., β-arabinofuranosides or α-xylofuranosides) has been successfully developed using different powerful methodologies[50–64]. In contrast, very few studies have reported methods for the formation of similar bonds in ketofuranoses (2,3-*cis*-ketofuranosides). The first ketofuranosylation of interest in my research was β-xylulofuranosylation. β-Xylulofuranosyl (β-Xul*f*) moieties are found in microorganisms[65–67]. The development of chemical methods for making oligosaccharides with these residues is necessary to provide probe molecules to understand their biological role. Chapters 3 and 4, describe my work on the synthesis of β-Xul*f* glycosides using three different donors, the conformational-

ly-restricted Xul*f* thioglycosides **1.18** and **1.19**, and siloxane-bridged Xul*f* donor **1.20** (**Figure 1.11**). The two methods were also used for the synthesis of β-Xul*f*-containing glycans.

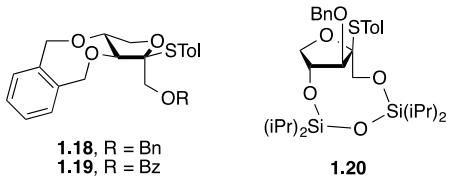


Figure 1.11. Structures of Xul*f* donors **1.18**–**1.20** used in stereoselectivity studies of xylulofuranosylation.

The second ketofuranosylation I studied was β-fructofuranosylation. In earlier studies, the synthesis of β-fructofuranosides with high selectivity had been developed using intramolecular aglycone delivery[51] or by the use of sterically blocking siloxane groups[68]. However, no conformationally-restricted fructofuranose (Fru*f*) donors have been developed. In Chapter 5, the synthesis of four Fru*f* donors **1.21**–**1.24** (**Figure 1.12a**) will be described, as well as their use in glycosylation reactions. In addition, the influence of the side chains at the anomeric carbon and the last carbon of the furanose ring (C-4 or C-5) on stereoselectivity using conformationally-restricted donors of arabinofuranose (Ara*f*) [63], xylulofuranose (Xyl*f*, Chapter 3) and Fru*f* will be further discussed (**Figure 1.12b**).

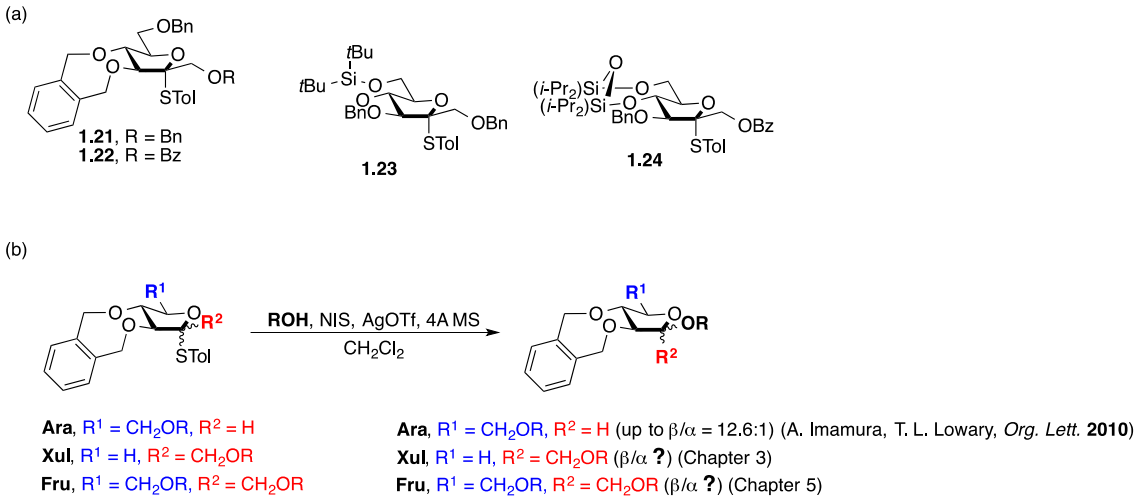


Figure 1.12. (a) Structures of conformationally-restricted Fru*f* donors **1.21**–**1.24** explored for the the synthesis of β-fructofuranosides. (b) Investigation of the influence of side chains on the stereoselectivity via three conformationally-restricted furanosyl donors (Ara*f*, Xul*f* and Fru*f*).

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Chapter 2

Synthesis of β-Kdo Oligosaccharide Fragments as Biochemical Probes

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A portion of this Chapter has been published:

1. Ovchinnikova, O. G.; Doyle, L.; **Huang, B.-S.**; Kimber, M. S.; Lowary, T. L.; Whitfield, C. *J. Biol. Chem.* **2016**, 21519–21530.

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2.1 Background

2.1.1 Biological importance of Kdo olisaccharides

3-Deoxy-D-*manno*-oct-2-ulosonic acid (Kdo) is an unusual eight carbon sugar (**Figure 2.1a**) that has been found as both α- and β-Kdo glycosides (**Figure 2.1b**) in the lipopolysaccharides (LPS) and capsular polysaccharides (CPS) of several different bacterial strains[1]. It has also been found in plants and algae[2].

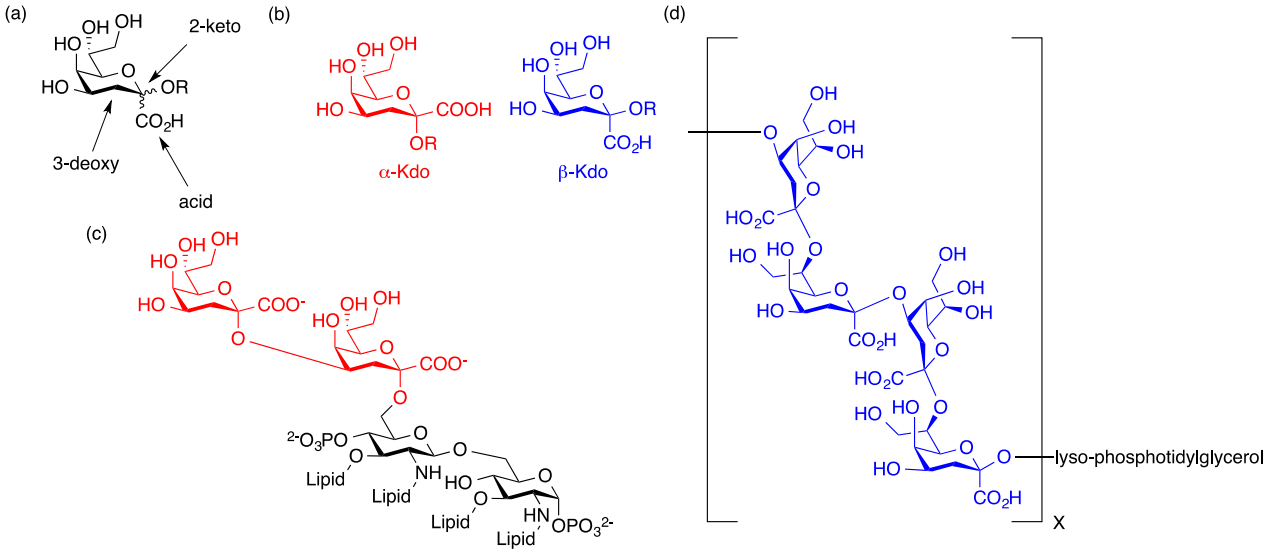


Figure 2.1. (a) Structure of Kdo; (b) α-Kdo and β-Kdo glycosides; (c) The core structure of lipopolysaccharides; (d) The core structure of capsular polysaccharides from *E. coli.* K1, K5 and *N. menigitidis*.

In the LPS of Gram-negative bacteria, α-Kdo is present in the-structurally conserved inner core region, located between lipid A and the *O*-antigenic glycan backbone (**Figure 2.1c**)[1,3]. Recently, β-Kdo was identified in the core of CPS of *Escherichia coli* K1, K5 and *Neisseria meningitides* by Whitfield and coworkers in 2013[4]. The structure of this core motif consists of a *lyso*-

phosphotidylglycerol moiety attached to a polymer of alternating β-(2→4) and β-(2→7)-linked Kdo residues (**Figure 2.1d**). When I started my thesis research, the biosynthesis of this CPS had not been definitively resolved. Because Kdo residues are not found in mammals, Kdo glycosyltransferases are attractive targets for small molecule inhibitors in anti-virulence strategies. Unmasked bacteria, due to their inability to produce Kdo-containing polysaccharides, would be susceptible to host defenses. For this reason, understanding how these molecules are produced is important.

To study the biosynthesis of this alternating β-(2→4) and β-(2→7)-Kdo polymer, we envisioned a strategy where the glycosyltransferases could be probed using molecules obtained by chemical synthesis. There are three major challenges involved in the chemical synthesis of β-Kdo-containing oligosaccharides: (1) Kdo is commercially-available but expensive; therefore, the synthesis of the monosaccharide is required; (2) controlling the stereoselectivity of Kdo glycosylation; and (3) determining the anomeric configuration of Kdo glycosides. The following sections will discuss these three challenges and past developments to overcome them.

2.1.2 Previous approaches in synthesizing Kdo derivatives

As Kdo is a very expensive monosaccharide ($1100/50 mg, Millipore-Sigma), many approaches to synthesize Kdo derivatives chemically have been developed. These approaches use two different starting materials: D-arabinose[5] or D-mannose[6].

The Cornforth reaction was originally applied to the synthesis of Kdo from D-arabinose (**2.1**) and oxalacetic acid (**2.2**) by Ghalambor and Heath[5a,5b] (**Figure 2.2**). As the carbonyl group of aldoses such as D-arabinose is diastereotopic, two isomers are possible in the reaction (D-*manno* and D-*gluco* diastereomers). When applied to the synthesis of Kdo, the Cornforth reaction proceeds by the attack of enolate species **2.3** (generated from **2.2**) on the carbonyl group of **2.1** to

give dicarboxylic acid salt **2.4**. After decarboxylation, the 3-deoxy-*glyc*-2-ulosonic acid salt **2.5** is produced. Although diastereoisomers are generated from the aldol condensation, this approach is a straightforward, reliable and scalable approach to give multi-gram amounts of Kdo in a single step.

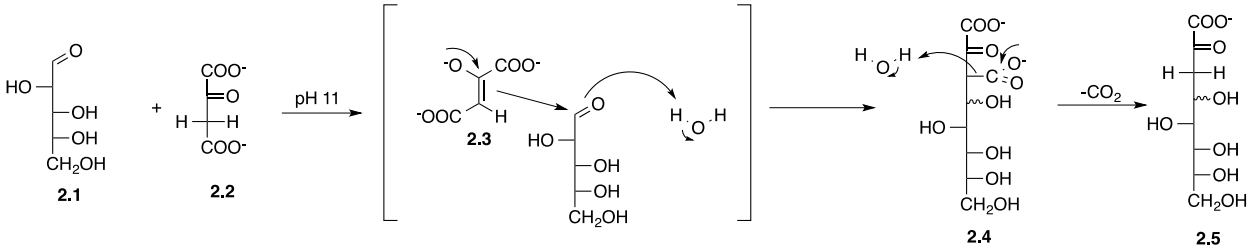
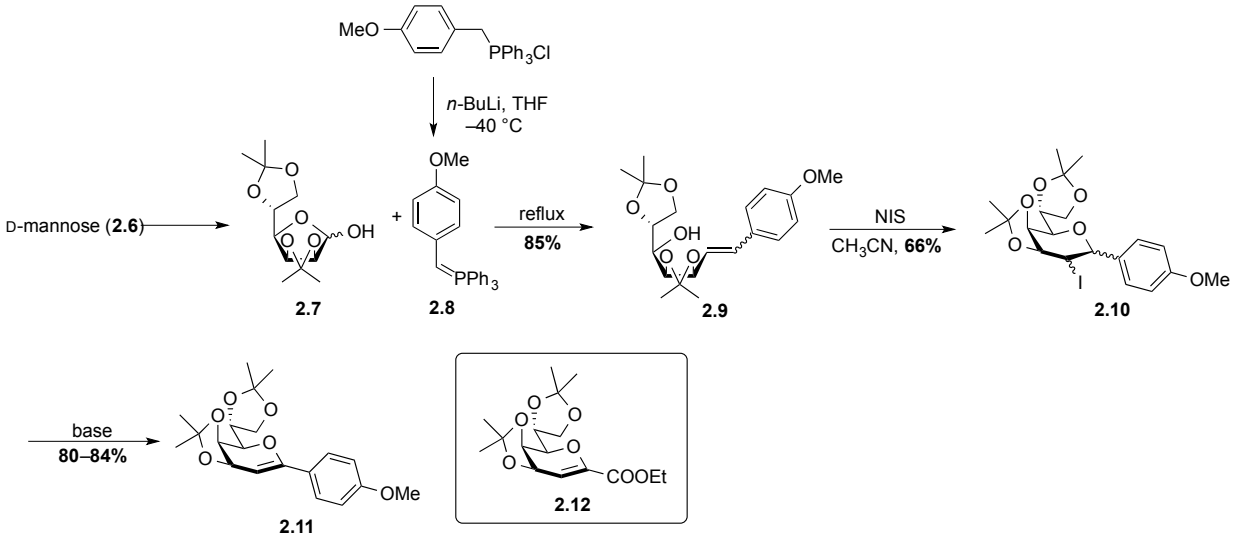


Figure 2.2. Synthesis of Kdo via the Cornforth reaction[5a,5b].

The reported approaches to make Kdo from D-mannose (**2.6**, **Scheme 2.1**) may be more preferred in that no diastereoisomers are produced. All three reported approaches start from 2,3:5,6-di-*O*-isopropylidene mannose, **2.7**. In 2012, the C-aryl glycal **2.11** was developed by Ling[6h] as glycosyl donor to furnish β-Kdo glycosides with high anomeric selectivity and good to excellent yield. Compound **2.11** was synthesized from **2.7** via a Wittig Reaction with **2.8** followed by iodo-etherification and elimination. Before the preparation of C-aryl glycal **2.11**, they initially designed glycal **2.12** as a donor, which did not form a six-member ring in an *N*-iodosuccinimide (NIS)-mediated ring closure process (**Figure 2.3**), instead providing a five-membered ring product. They hypothesized that the substituent on the double bond plays an important role in controlling the regioselectivity of the ring closure. With the electron withdrawing group (–COOEt), carbocation **2.15** should be less stable than the carbocation **2.14** because the positive charge is closer to the electron deficient carbonyl group. Consequently, the C-5 hydroxyl group attacks the **2.14**, which leads to the formation of the five-membered ring cyclic ether

2.16; none of six-membered ring product **2.17** was observed. When they changed the substituent from a methyl ester to an electron-rich aryl group, the positive charge in carbocation **2.15** is stabilized by resonance and this led to the preferred formation of **2.17**.



Scheme 2.1. Ling's approach[6h] to C-aryl glycal **2.10** from D-mannose **2.6**.

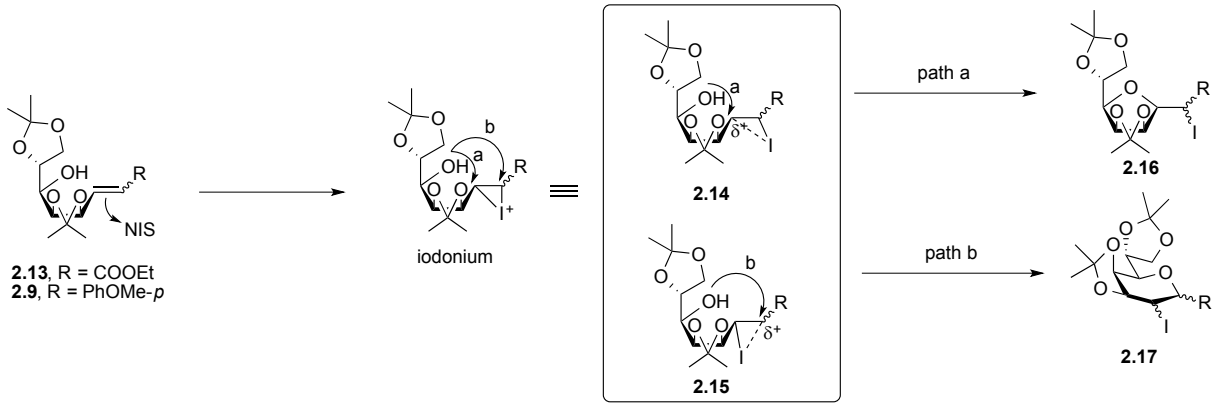
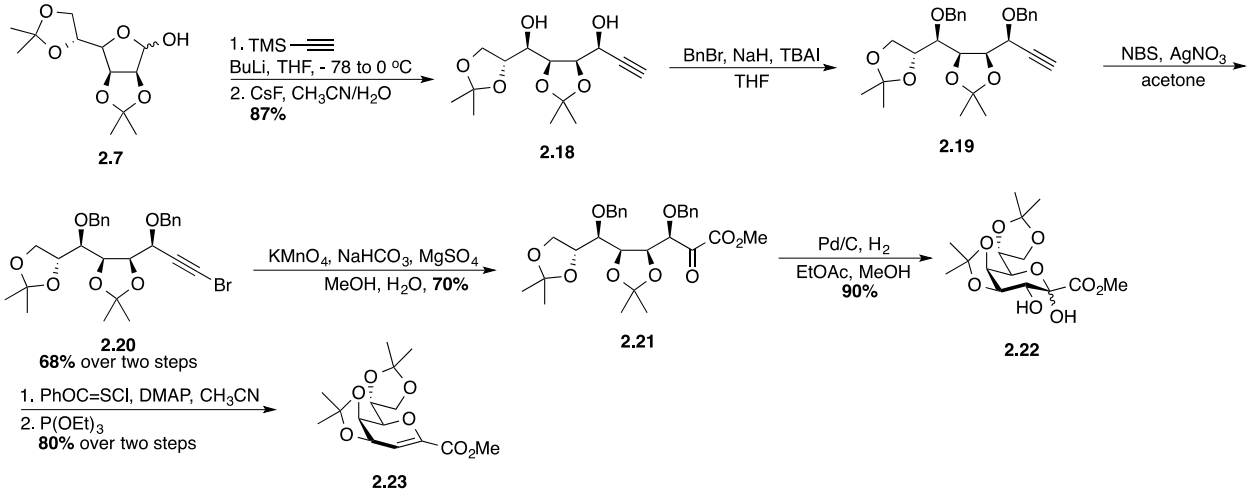


Figure 2.3. Plausible explanation for the regiocontrol observed in the iodo-etherification of **2.9** and **2.13**[6h].

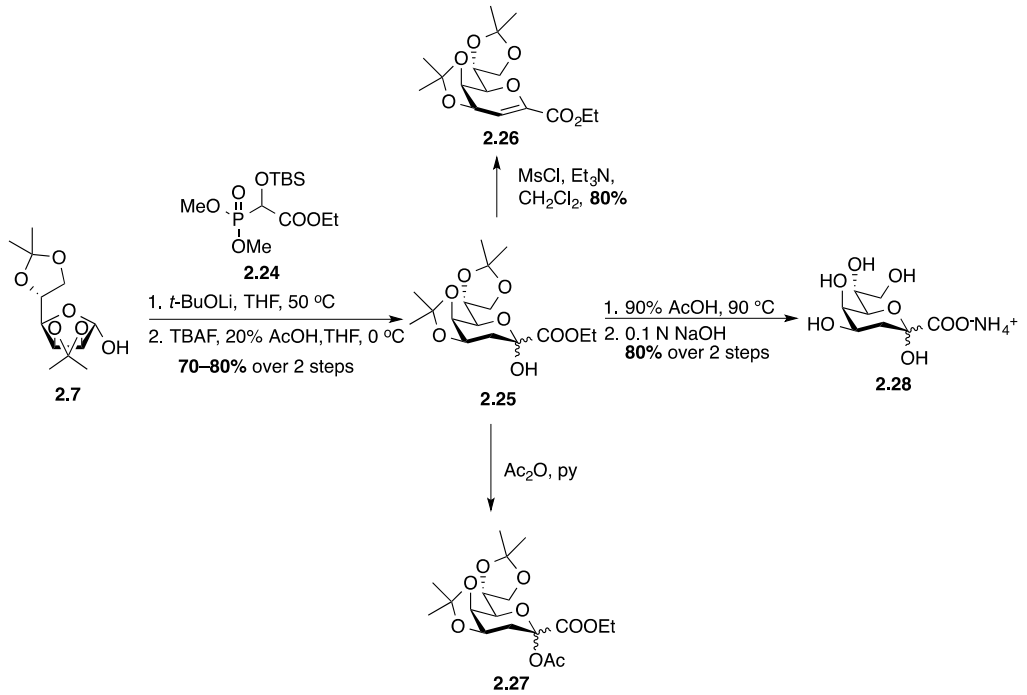
In 2014, Mong and co-workers[6i] developed a synthetic route (**Scheme 2.2**) to glycal **2.23** starting from mannofuranose derivative **2.7**. The carbon chain was elongated by the addition of lithiated trimethylsilylacetylide and desilylation to give alkyne **2.18**. The transformation of **2.18** into bromo-alkyne **2.20**, the precursor of α-keto ester **2.21**, was successfully achieved by the benzylation of the two hydroxyl groups and bromination. The oxidative cleavage of the bromo-alkyne with $KMnO_4$ in methanol and water provided **2.21**. Hydrogenolysis of the two benzyl groups resulted in the instantaneous cyclization of the C-6 hydroxyl group onto the C-2 ketone to generate hemiketal **2.22**. A Corey–Winter reaction on **2.22** furnished Kdo glycal **2.23**. This glycal donor was used in the formation of β-Kdo glycosides; the β-stereocontrol will be discussed in detail in **Section 2.1.3**. Compared to Ling's approach, Mong's methods requires a relatively longer synthetic route to the glycal donor.



Scheme 2.2. Mong's approach[6i] to synthesize glycal **2.23** from **2.7**.

In 2015, Chai and co-workers[6j] developed an efficient method to rapidly synthesize di-*O*-isopropylidene-protected Kdo derivative **2.25** in only two steps from **2.7**. A Horner–Wadsworth–Emmons reaction between **2.7** and phosphate ester **2.24**, followed by the de-silylation gave **2.25**.

This method can be applied to the preparation of **2.25** on a scale of more than 40 g in 70–80% overall yield without intermediate purification. Additionally, compound **2.25** could be transformed rapidly into Kdo glycal **2.26**, the C-2-*O*-acetylated Kdo ester **2.27** and the Kdo ammonium salt **2.28**, in high yield (Scheme 2.3).



Scheme 2.3. Chai's efficient approach[6j] to synthesize Kdo derivatives **2.25**–**2.28** from **2.7**.

2.1.3 Reports of α and β-selectivity in the synthesis of Kdo glycosides

The stereoselectivity of glycosylation is one of the major challenges in the preparation of Kdo glycosides. Unlike many more common sugars, Kdo lacks a stereodirecting group next to the anomeric center, which limits stereochemical control in product formation. In addition, the formation of the 2,3-dehydro product (the glycal ester) is a common problem in glycosylation reactions of Kdo due to the strong deactivation of the anomeric position by the adjacent carboxylic acid group (**Figure 2.4**). As described above in **Section 2.1.1**, both α- and β-Kdo have been

identified in the glycans of several different bacterial strains. Therefore, highly stereoselective methods for the preparation of either α- or β-Kdo glycosides are desired and necessary.

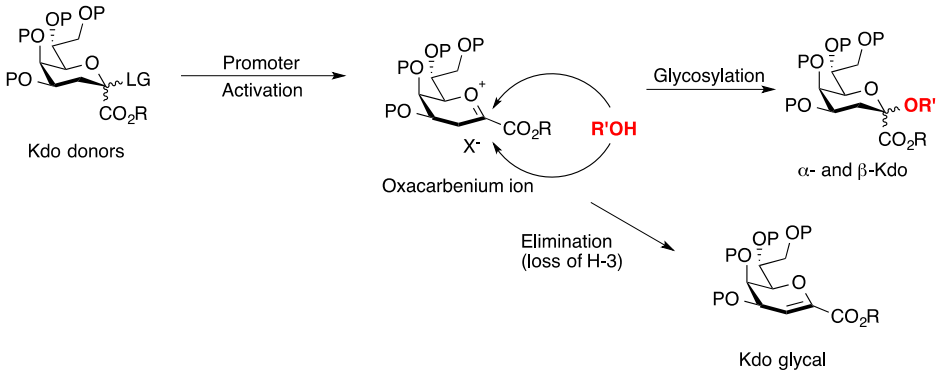


Figure 2.4. Challenges in the stereoselective preparation of Kdo glycosides.

A significant amount of synthetic work on Kdo glycosylation has focused on the synthesis of α-Kdo glycosides as they are more widespread than β-Kdo glycosides. For instance, the use of Kdo fluorides[7], bromides[8], *N*-phenyltrifluoroacetimidates[9], and 3-iodo-fluorides[10] have been exploited to synthesize various α-Kdo-containing glycans (**Figure 2.5a**). Peracetylated[11] and perbenzylated[12] Kdo glycal donors have also been used to synthesize α-Kdo-containing saccahrides via the introduction of a participating group at the C-3 position, which can direct the stereochemistry of the glycosidic bond formation (**Figure 2.5b**). More recently, Yang *et. al.*[13] reported a new method for the stereoselective synthesis of α-Kdo glycosides using 5,7-*O*-DTBS-protected Kdo ethyl thioglycosides **2.29** as glycosyl donors (**Figure 2.5c**). The high stereoselectivity was proposed to arise from the 5,7-*O*-DTBS group, which is similar to the 4,6-*O*-DTBS-protected galactopyranosyl donors **2.30** (**Figure 2.5c**). The highly stereoselective formation of α-galactopyranosides via 4,6-*O*-DTBS-protected donors such as **2.30** results from steric hinderance

from the bulky silyl protecting group, and through-space electron donation[14]. Presumably the same effects play a role in the high α-selectivity in glycosylations with **2.29**.

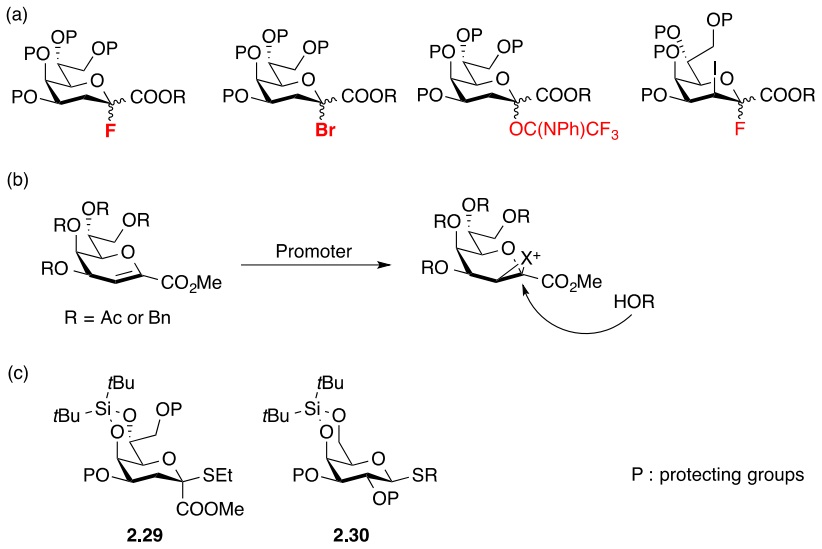


Figure 2.5. (a) Different donors for synthesizing α-Kdo glycosides[7–10]; (b) Kdo glycals for synthesizing α-Kdo glycosides via a participating group at C-3[11,12]; (c) 5,7-*O*-DTBS-protected Kdo dnor **2.29**[13] and 4,6-*O*-DTBS-protected galactose donor **2.30**[14].

Compared to the considerable progress on the synthesis of α-Kdo glycosides, the synthesis of β-Kdo glycosides has been less reported. In 2012, Ling and co-workers exploited the di-*O*-isopropylidene-protected C-aryl glycal **2.11** for the synthesis of β-Kdo glycosides[6h]. Modest to excellent β-selectivity was obtained with various acceptors. To explain the β-selectivity of the reaction, the crystal structure of **2.11** was obtained[6h]. They observed that one of the methyl groups of the 4,5-*O*-isopropylidene ketal is very close to the top face of the glycal double bond. Thus, the selectivity in the NIS-mediated glycosylation could be rationalized (**Figure 2.6**) by a steric shielding effect of this methyl group. The formation of intermediate cyclic iodonium **2.32** would be more favored than the cyclic iodonium **2.31**. The subsequent attack by glycosyl accep-

tor from top face of the intermediate **2.32** produces the observed β-glycosides. Although modest to excellent β-stereoselectivity was obtained, only one sugar acceptor (a primary alcohol) was investigated. Additionally, the transformation of the aryl group into the carboxylic acid and the deiodination of 3-iodo product (**2.33** or **2.34**) are necessary after every glycosylation, which leads to decreased efficiency.

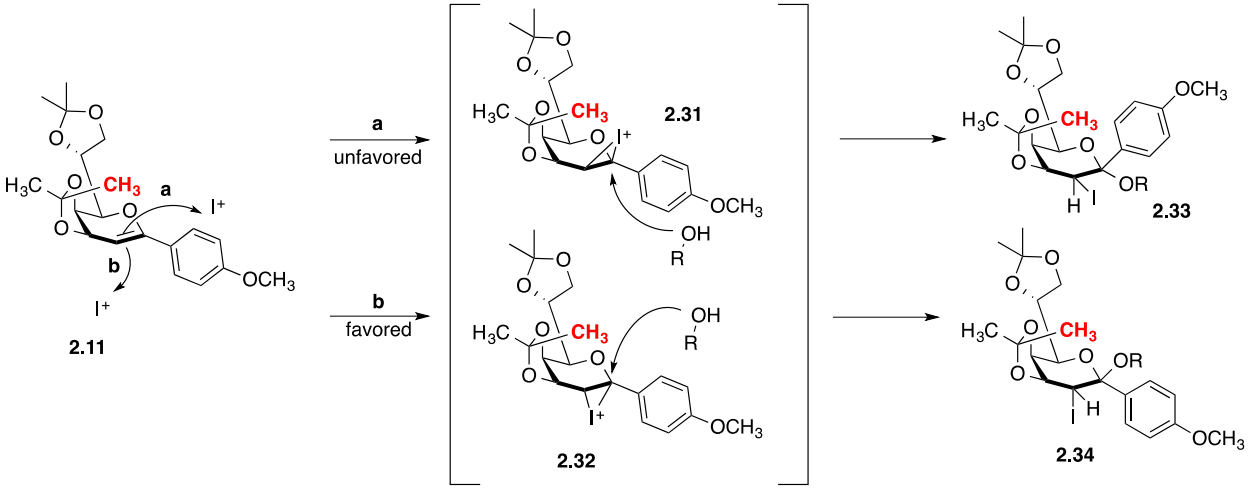
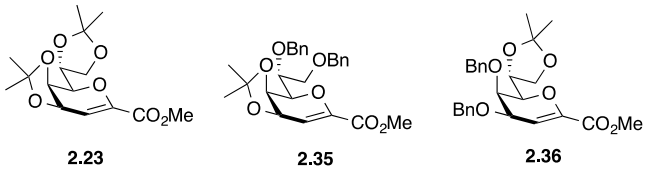


Figure 2.6. Plausible mechanism for the formation of β-Kdo glycosides from glycal donor **2.11**[6h].

In 2014, Mong and co-workers developed a different di-*O*-isopropylidene-protected Kdo glycal, **2.23**, for the synthesis of two trisaccharides from CPS of *Rhizobium fredii* and *Sinorhizobium meliloti*.[6i] As described in the previous paragraph, the 4,5:7,8-di-*O*-isopropylidene ketal protecting group, especially the 4,5-*O*-isopropylidene ketal, was needed for the β-selectivity by the formation of a cyclic iodonium intermediate from the bottom face of sugar ring. They compared the stereoselective influence of the isopropylidene groups in the 4,5:7,8-di-*O*-isopropylidene glycal donor **2.23**, the 4,5-*O*-isopropylidene glycal donor **2.35** and the 7,8-*O*-isopropylidene glycal donor **2.36** (**Figure 2.7**) using methanol as the acceptor. The diastereose-

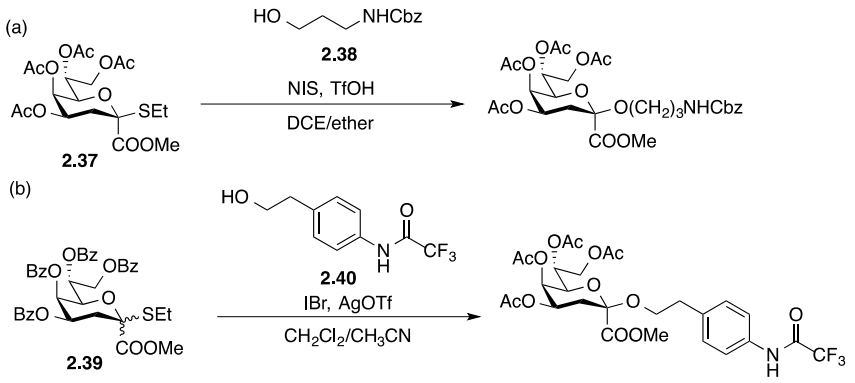
lectivity decreased significantly from a 13:1 β/α ratio for **2.23** to a 6:1 β/α ratio for **2.35**. Replacement of 4,5-*O*-isopropylidene ketal with benzyl ethers (donor **2.36**) led to a reaction with no selectivity (1:1, β/α). These results suggest that the diastereoselectivity is influenced by both ketal protecting groups, but that the 4,5-*O*-isopropylidene ketal has the most impact. Like Ling's method, Mong's approach requires a deiodination step after glycosylation.



2.23 **2.35** **2.36**

Figure 2.7. Three glycal donors **2.23, 2.35** and **2.36**[6i] used to probe the influence of isopropylidene ketals on glycosylation stereoselectivity in Kdo.

Kdo thioglycosides have served as "non-glycal" donors in the synthesis of β-Kdo glycosides. In 1992, van Boom and coworkers[15] were the first to produce β-Kdo glycosides with peracetylated Kdo thioglycoside **2.37** and 3-amino-*N*-[benzyloxy]carbonyl]-1-propanol **2.38** using activation with NIS and triflic acid (**Scheme 2.4a**). Perbenzoylated Kdo thioglycoside **2.39** was studied for the formation of β-Kdo glycosides with 2-(4-trifluoroacetamidophenyl) ethanol **2.40** using IBr–AgOTf as the promoter by Oscarson and co-workers[16] (**Scheme 2.4b**). Complete β-selectivity was reported with the IBr–AgOTf system in a 3:2 mixture of CH_3CN and CH_2Cl_2; this implicate the β-directed effect of the nitrile solvent[17]. However, Oscarson used no sugar acceptors with either peracetylated or perbenzoylated Kdo thioglycosides.



Scheme 2.4. (a) Formation of β-Kdo via peracetylated Kdo thioglycoside donor **2.37**; (b) Formation of β-Kdo via perbenzoylated Kdo thioglycoside donor **2.39**.

In 2016, Gauthier and coworkers[18] developed a novel approach for the stereoselective synthesis of β-Kdo glycosides using long range participation from a 4'-methoxyphenacyl (Phen) auxiliary group at C-1 (**2.41**, **Figure 2.8**). A mechanism was proposed, supported with DFT calculations. Formation of the α-spiro intermediate **2.43**, which results in the formation of β-Kdo glycoside **2.45** is more stable than the β-spiro intermediate **2.42**, which gives the α-Kdo glycoside **2.44**. As such, the formation of the β-glycoside is preferred. Although good β-selectivity was observed by using this auxiliary group, only one sugar-based glycosyl acceptor with primary alcohol was used in the reactions. In addition, the Phen group has to be cleaved after the glycosylation, thereby lowering the synthetic efficiency.

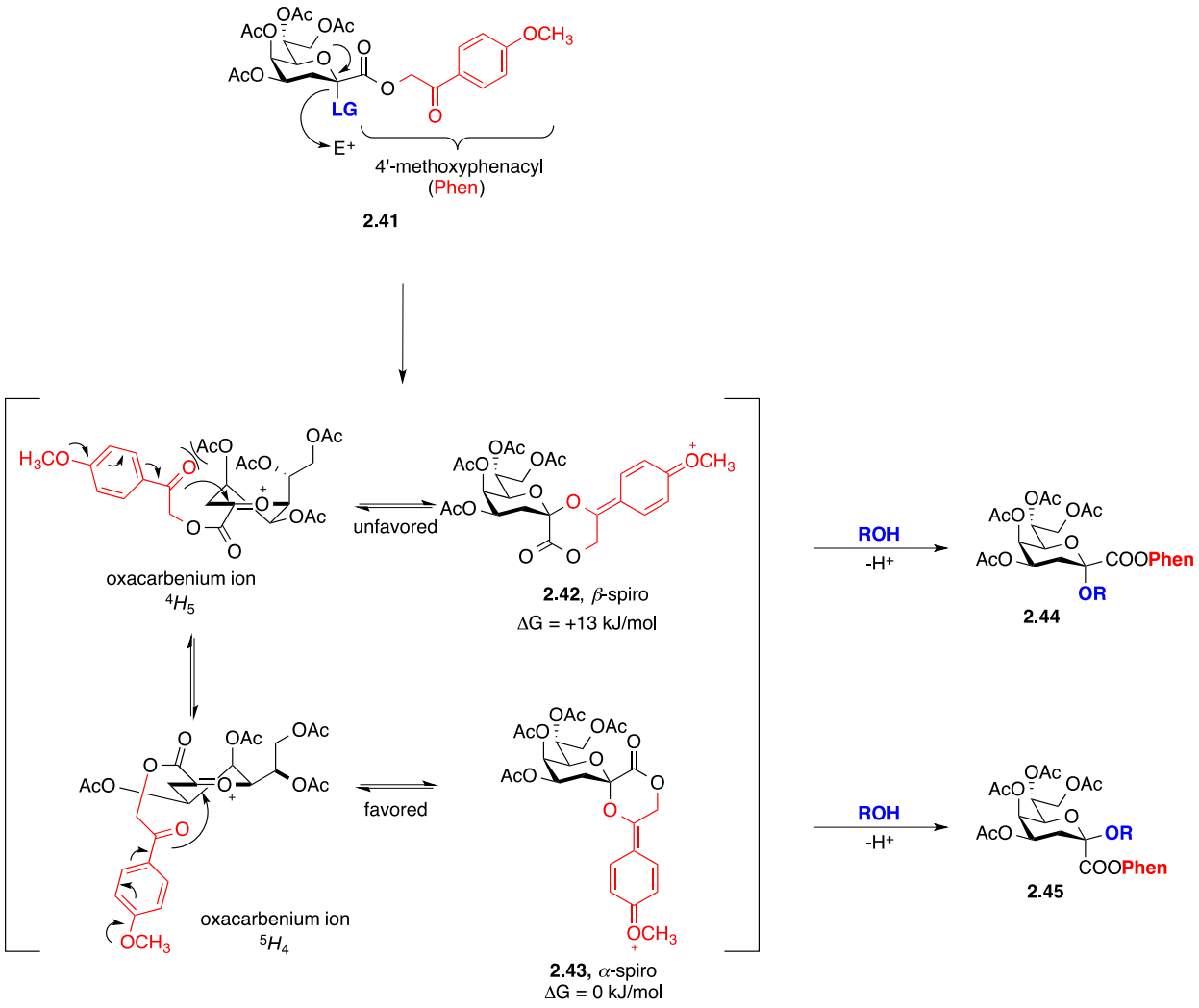


Figure 2.8. Proposed mechanism of the synthesis of β-Kdo glycosides via the Phen auxiliary group at C-1[18].

In 2018, Yang and coworkers reported their efforts on studying the effect of the C5-substituent on the formation of Kdo glycosides[19]. They identified that 5-*O*-benzoyl or acetyl protected Kdo thioglycosides give α-Kdo glycosides, which they attributed to the remote participating effect of the carbonyl group at C-5 (**2.46**) (**Figure 2.9**). On the other hand, β-Kdo glycosides are produced with 5-*O*-2-quinolinecarbonyl or 5-*O*-4-nitropicoloyl donors, presumably via hy-

drogen-bond-mediated aglycone delivery (HAD)[20]. However, they identified that the stereoselectivity via HAD approach was dependent on the acceptor. Complete β-selectivity and good to excellent yields were obtained by the glycosylation of primary alcohols with a 5-Quin-protected Kdo thioglycoside donor **2.47**. In contrast, when disarmed or sterically-congested sugar-based secondary alcohols were used, the same donor produced the α-Kdo glycoside as the predominant or only product. The use of the 5-*O*-4-nitropicoloyl substituted Kdo thioglycoside donor **2.48** gave predominantly the β-Kdo glycoside with more reactive secondary alcohols (**Figure 2.9**). Although the formation of both α-Kdo and β-Kdo glycosides has been reported using Kdo thioglycosides, the undesired formation of glycal products is still the common problem.

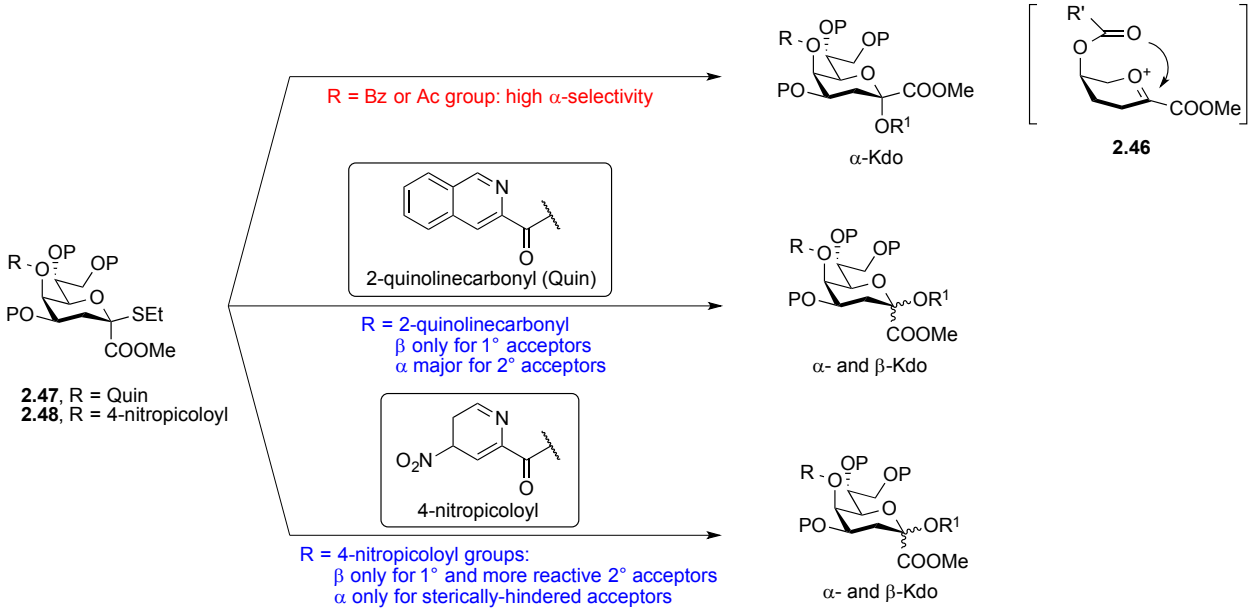


Figure 2.9. The effect of the C5-substituent on the stereoselectivity in Kdo glycosylations[19].

2.1.4 Characterization of anomeric configurations

The anomeric center of a sugar is a stereocenter produced from the intramolecular formation of an acetal (or ketal) of a sugar hydroxyl group and an aldehyde (or ketone) group. Two possible diastereomers at the anomeric center (termed anomers) are possible.

The characterization of anomeric configuration for aldose glycosides is relatively straightforward using the coupling constant ($^3J_{H1,H2}$) of the anomeric proton (H-1) and the adjacent proton (H-2). There are four possible relative relationships between H-1 and H-2, axial–axial (*anti*), equatorial–axial (*gauche,* two possibilities) and equatorial–equatorial (*gauche*) (**Figure 2.10a**). According to the Karplus equation[21], the anomeric configuration can be characterized by the value of the $^3J_{H1,H2}$. For instance, in α-glucopyranosides $^3J_{H1,H2}$ ranges from 3–5 Hz and in β-glucopyranosides 7–10 Hz (**Figure 2.10b**). In addition to the $^3J_{H1,H2}$, the one bond coupling constant ($^1J_{C1,H1}$) between the anomeric carbon (C-1) and the anomeric proton (H-1) is a useful method for characterizing anomeric configuration. The $^1J_{C1,H1}$ of α-glycosides is larger than that of the β-glycosides due to hyperconjugation between one of the lone pairs of the ring oxygen and the antibonding orbital of the C-1–H-1 bond (**Figure 2.10c**), which leads to the longer C–H bond in β-glycosides.

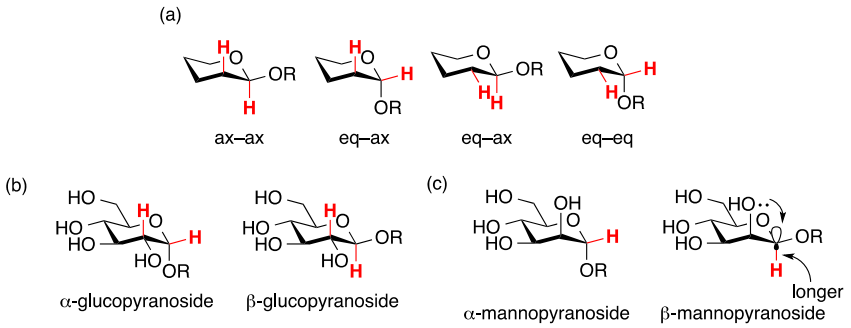


Figure 2.10. (a) Four possible relative relationships between H-1 and H-2; (b) Two anomers of glucopyranosides for anomeric characterization via $J_{H1,H2}$; (c) Influence of C1–H1 bond length due to hyperconjugation with the ring-oxygen lone pair.

The assignment of anomeric configuration in Kdo glycosides is one of the three major challenges in making Kdo-containing glycans. Unlike aldoses, Kdo lacks an anomeric hydrogen; therefore, determining the anomeric configuration of Kdo glycosides is impossible using $^{3}J_{H,H}$ or $^{1}J_{C,H}$ involving this proton. However, Unger *et al.*[22] identified that the three-bond coupling constant between the anomeric carbon and the axial proton at C-3 ($^{3}J_{C1,H3ax}$) can be used to assign the anomeric configuration of Kdo glycosides, assuming that the ring has a $^{5}C_{2}$ conformation (**Figure 2.11**). A *gauche* relationship (axial–equatorial) between H-3_{ax} and the C-1 is present in in α-anomer and, in the ^{1}H coupled ^{13}C spectrum, C-1 appears as a broad singlet ($^{3}J_{C1,H3ax} < 2$ Hz); in the β-anomer, these atoms have a *trans*-diaxial relationship and C-1 appears as a doublet ($^{3}J_{C1,H3ax} > 5$ Hz).

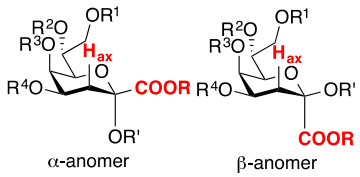


Figure 2.11. Two possible anomers and corresponding relationships between C-1 and H-3_{ax}.

2.1.5 Target molecules and purpose

As mentioned in **Section 2.1.1**, and in Chapter 1, Kdo is not found in mammalian glycans. Therefore, Kdo-transferases are possible targets for drug discovery to inhibit growth of bacteria. In this Chapter, we describe the synthesis of Kdo-containing oligosaccharides **2.49**–**2.51** and their derivatives (**Figure 2.12**), which are fragments of CPS of *E.coli* K1, K5, and *N. menigitides*. The purposes of these tagged-fragments are: (1) to serve as probes in understanding the function of Kdo glycosyltransferases in CPS assembly; (2) to investigate structure–activity relationships between Kdo glycosyltransferases and their ligands; and (3) to develop an assay that can used to efficiently search for inhibitors of Kdo glycosyltransferases.

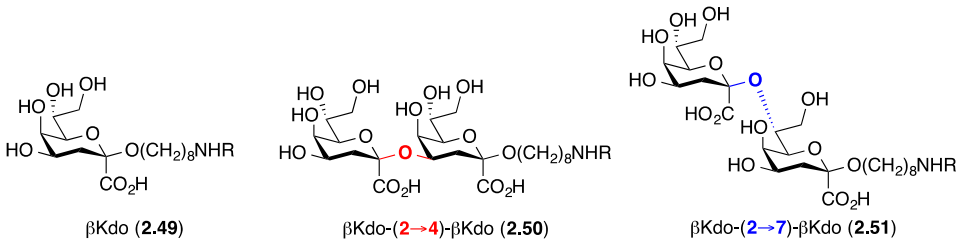


Figure 2.12. Target molecules **2.49**–**2.51**.

2.2 Results and Discussion

2.2.1 Initial attempts to target molecules

To synthesize target molecules **2.49**–**2.51**, we initially chose an approach using glycal **2.23** and glycosyl acceptors **2.53** and **2.54** (**Figure 2.13**). As discussed above (**Section 2.1.2**), with **2.23** in hand, our target molecules could be assembled by the NIS-mediated glycosylation of the acceptors. The di-*O*-isopropylidene ketal is needed to ensure the β-selectivity by steric shielding of one methyl group. Due to this hindrance, I^+ prefers to approach **2.23** from the bottom face of

the ring, resulting in the formation of an intermediate cyclic iodonium that subsequently undergoes nucleophilic attack from the top face to produce β-glycosides.

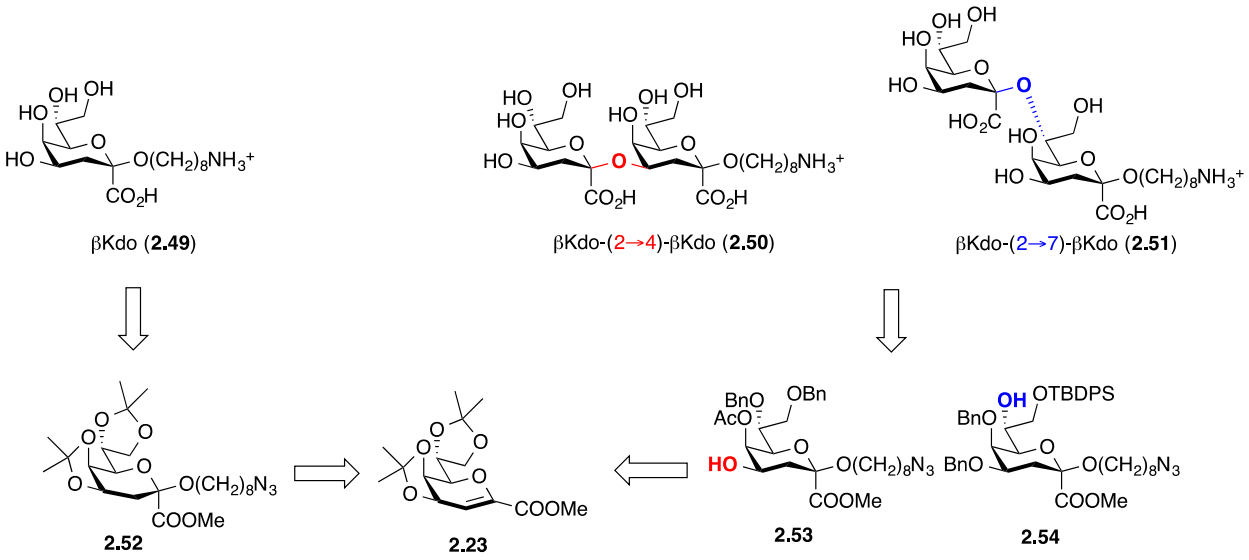
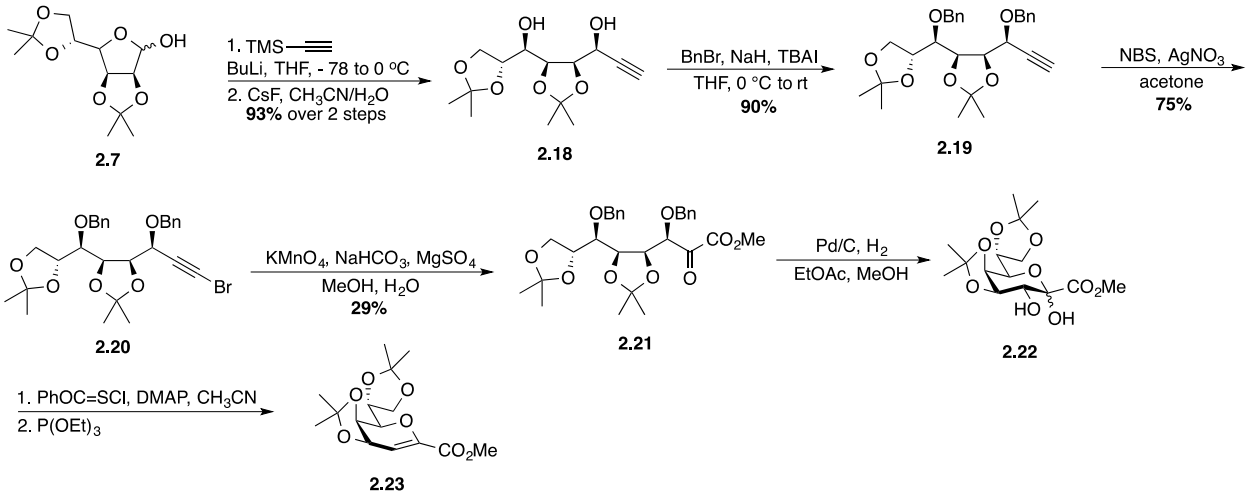


Figure 2.13. Retrosynthesis of target molecules **2.49**–**2.51** from glycal **2.23**.

The first consideration was how to access Kdo given its high commercial price. As discussed in **Section 2.1.2**, there are several synthetic approaches to Kdo derivatives[5,6]. When I started this work, the most efficient approach, developed by Chai, had not yet been reported. Therefore, I attempted to reproduce the Mong's approach to make glycal **2.23** as it appeared to be the most straightforward route[6h].

My efforts to reproduce Mong's synthesis (**Scheme 2.5**) began by treating D-mannose (**2.6**) with concentrated sulfuric acid in acetone to furnish 2:3:5,6-di-*O*-isoproylidene mannose (**2.7**)[23]. The next step was carbon chain elongation by treating **2.7** with trimethylsilylacetylide and *n*-BuLi and then desilylation to afford the alkyne derivative **2.18**. Subsequent benzylation of the hydroxyl groups and bromination transformed **2.18** into the bromo-alkyne derivative **2.20**. These steps could all be reproduced with acceptable yield. I then attempted the oxidative cleavage of

bromoalkyne **2.20** with $KMnO_4$ in methanol and water; however, I could only obtain **2.21** in low yield, and sometimes the reaction was not reproducible. Due to the irreproducibility of oxidative cleavage step, I abandoned the use of this method.



Scheme 2.5. Attempt to synthesize Kdo glycal **2.23** using Mong's approach[6h].

After abandoning Mong's approach, I considered other methods. Impressed by the reported β-exclusive selectivity from Kdo thioglycosides reported by van Boom[15] and Oscarson[16], I decided to explore synthesizing **2.49**–**2.51** from peracetylated Kdo thioglycoside donor **2.37** and acceptors **2.56**–**2.57**, which could be obtained from mannose derivative **2.7** (**Figure 2.14**).

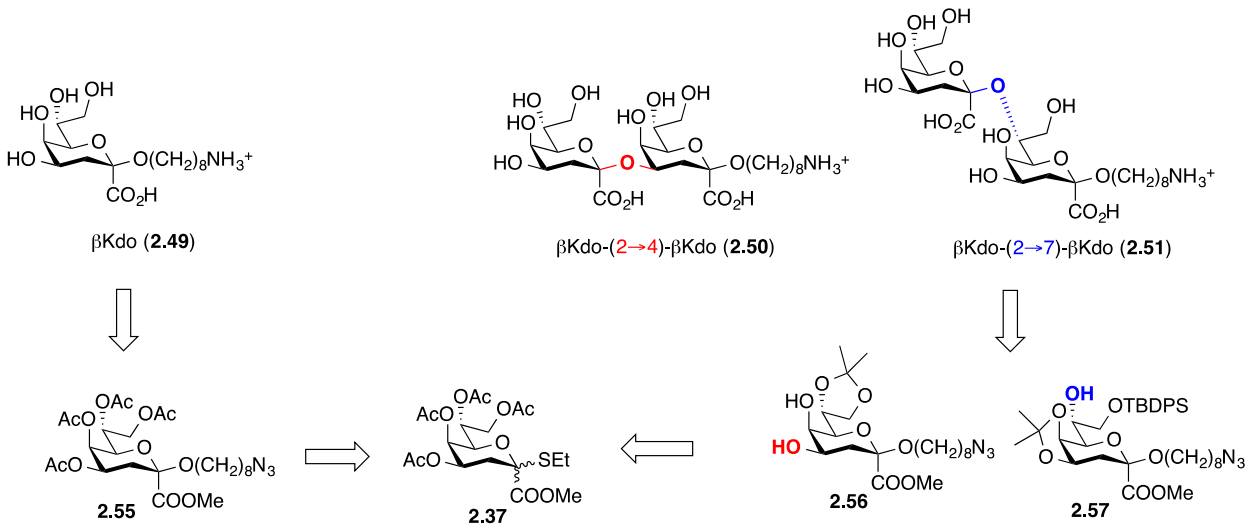
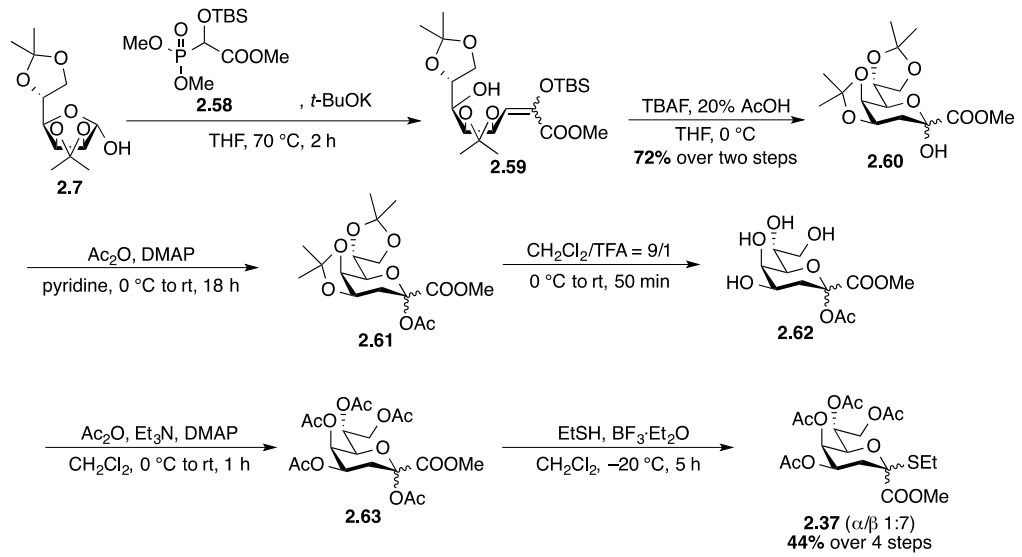


Figure 2.14. Retrosynthesis of **2.49**–**2.51** via Kdo thioglycoside **2.37**.

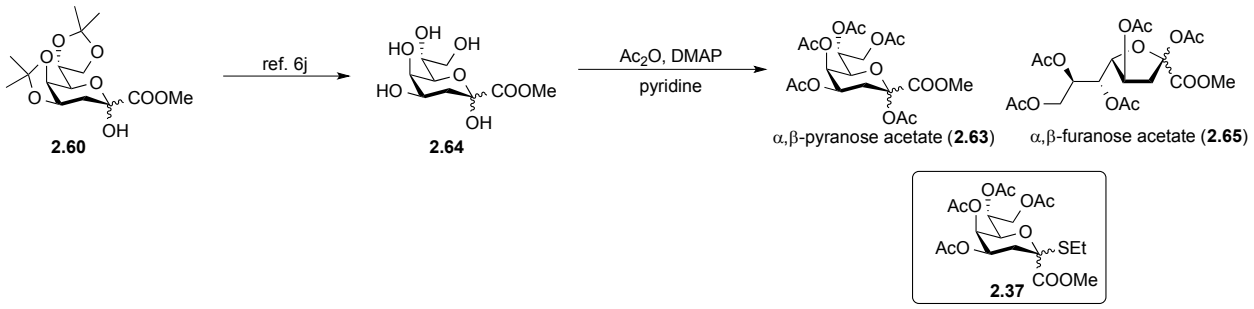
2.2.2 Synthesis of Kdo donor 2.56 and acceptors 2.58 and 2.59

The synthesis of thioglycoside **2.37** (**Scheme 2.6**) started with the preparation of Kdo methyl ester **2.60**, as reported by Chai and co-workers[6j]. The method was reproducible and could be done on large scale; compound **2.60** could be synthesized in 72% overall yield from **2.7**. Once prepared, **2.60** was treated with acetic anhydride and 4-dimethylaminopyrdine (DMAP) in pyridine for 18 h to afford **2.61**. Without purification, both isopropylidene ketals in **2.61** were then removed using 10% trifluoracetic acid (TFA) in dichloromethane. The solution was co-evaporated with toluene to remove TFA *in vacuo* and, without any purification, the residue was then acetylated with acetic anhydride, triethylamine and DMAP in dichloromethane to afford **2.63**. The Kdo thioglcyoside donor **2.37** was prepared by the thioglycosylation of **2.63** with ethanethiol. Compound **2.37** was obtained in 44% yield over four steps from **2.60**.



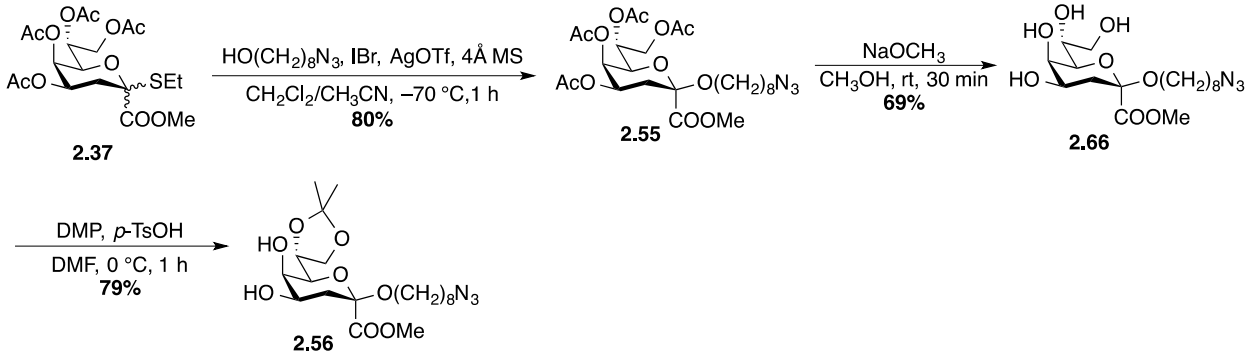
Scheme 2.6. Synthesis of Kdo thioglycoside donor **2.37**.

I also explored synthesizing peracetylated Kdo donor **2.37** by not acetylating **2.60** before removal of the ketals as this would reduce the number of steps (**Scheme 2.7**). The conversion of **2.60** into **2.64** was possible in quantitative yield using the reported acidic conditions[6j]. However, when the acetylation of **2.64** was performed using standard conditions (acetic anhydride, pyridine), a mixture of α,β-pyranose acetates **2.63** and α,β-furanose acetates **2.65** was observed with the furanoses being the major species. This has been reported previously in the acetylation of unprotected Kdo[27]. Therefore, the preparation of **2.37** was done via a four-step procedure illustrated in **Scheme 2.6**.



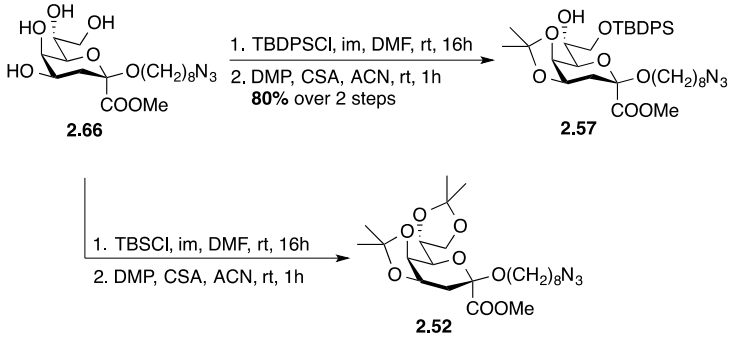
Scheme 2.7. Attempt to synthesize **2.37** using a shorter route.

With the Kdo donor **2.37** in hand, the synthesis of Kdo acceptor **2.56** (**Scheme 2.8**) began by its treatment with 8-azidooctanol, IBr and AgOTf[16] in a mixture of dichloromethane and acetonitrile. This reaction provided the β-Kdo glycoside **2.66** in 80% yield; none of the α-glycoside was detected. The stereochemistry at the anomeric carbon of **2.55** was determined by the $^{3}J_{C1,H3ax}$ value (6.7 Hz) as measured using a proton-coupled ^{13}C NMR experiment. The Kdo glycoside **2.55** was then deacetylated with a catalytic amount of sodium methoxide in methanol to afford a 69% yield of Kdo glycoside **2.66** ($^{3}J_{C1,H3ax}$ = 6.7 Hz). To synthesize **2.56**, an isopropylidene ketal was selectively introduced at O-7 and O-8 by the reaction of **2.66** with dimethoxypropane and *p*-toluenesulfonic acid to the desired diol in 79% yield[15].



Scheme 2.8. Synthesis of 4,5-diol Kdo acceptor **2.56**.

The synthesis of Kdo acceptor **2.57** was also achieved from the Kdo glycoside **2.66** (**Scheme 2.9**). We initially attempted to synthesize this compound by first protecting O-8 as a *t*-butyldimethylsilyl (TBS) ether and then introduction of the ketal on O-4 and O-5. However, under these conditions, only the di-*O*-isopropyline-protected Kdo glycoside **2.52** was obtained due to cleavage of the TBS group under the acidic reaction conditions. Therefore, the more acid-stable *t*-butyldiphenylsilyl (TBDPS) group was used as the protecting group for O-8. Thus, **2.66** was treated with TBDPSCl and imidazole in DMF to afford a silylated intermediate, which was then reacted with dimethoxypropane and 10-camphorsulfonic acid in CH_3CN to give **2.57** in 80% yield over the two steps.

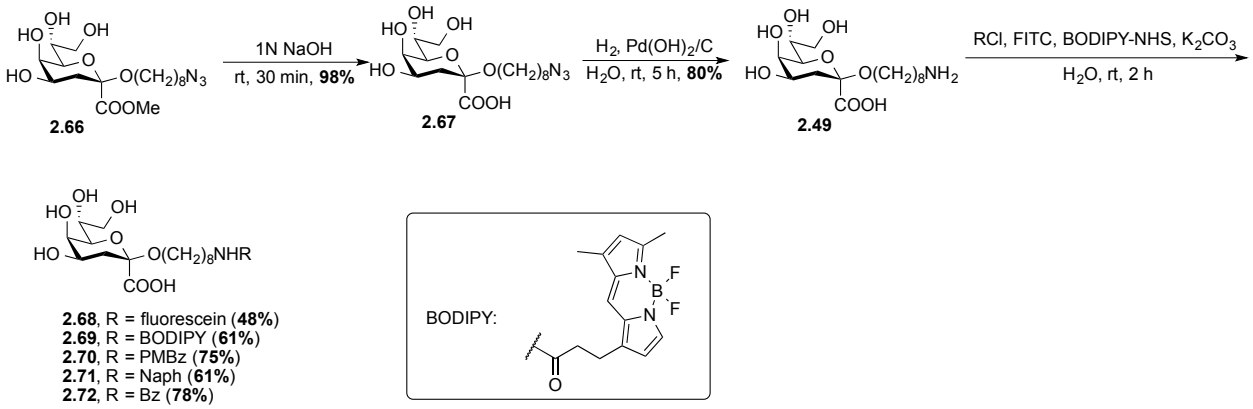


Scheme 2.9. Synthesis of 7-OH Kdo acceptor **2.57**.

2.2.3 Synthesis of monosaccharide 2.49 and its derivatives 2.68–2.72

The synthesis of Kdo monosaccharide **2.49** (**Scheme 2.10**) began with hydrolysis of Kdo methyl ester **2.66** under basic conditions to afford **2.67**, which was then reduced to amine **2.49** in 80% yield over two steps. Using the amine-functionality, several tags were introduced to provide substrates for biosynthetic and screening studies[28]. These derivatives included one (**2.68**) produced by reaction of **2.49** with fluorescein isothiocyanate (FITC), one (**2.69**) produced by the reaction with BODIPY NHS ester, and others formed by reaction with different acyl chlorides giv-

ing *p*-methoxybenzamide derivative **2.70**, naphthylamide derivative **2.71**, and benzamide derivative **2.72**. All of these compounds could be prepared from **2.49** in modest to good yield (48–78%).

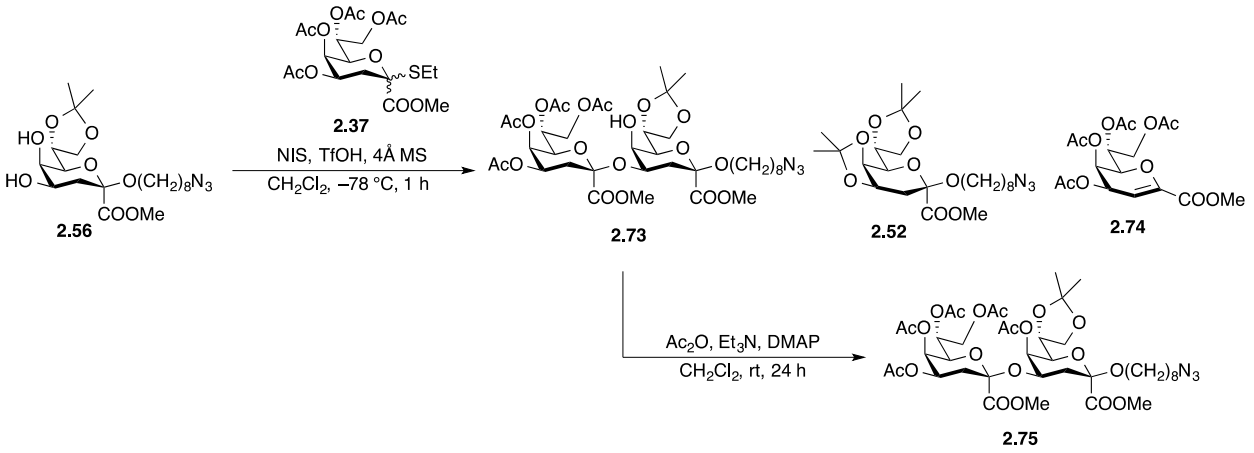


Scheme 2.10. Synthesis of Kdo monosaccharide **2.49** and its derivatives **2.68–2.72**.

2.2.4 Synthesis of β-(2→4)-linked disaccharide 2.50 and its fluorescein-conjugate 2.78

As shown in **Scheme 2.11**, the synthesis of the β-(2→4)-linked disaccharide **2.50** was initially attempted by the coupling of Kdo donor **2.37** and diol acceptor **2.56** using NIS and triflic acid (TfOH). Three major products were identified in this reaction: (1) the desired β-(2→4)-linked disaccharide **2.73** (41%); (2) the elimination product **2.74**; and (3) the di-*O*-isopropylidene-ketal protected Kdo monosaccharide **2.52**. Thus, although the glycosylation of diol **2.56** was regioselective, as anticipated, other products were formed. The regioselective formation of the glycosidic bond at the O-4 position was supported by the ^{1}H NMR spectra of the compound (**2.75**) obtained after the acetylation of the C-5 hydroxyl group in **2.73**. The chemical shift of H-5 in **2.75** appeared at 5.37 ppm, which is more downfield compared to the H-5 of **2.73** (4.03 ppm). The stereochemistry of both anomeric centers was determined to be β by a proton-

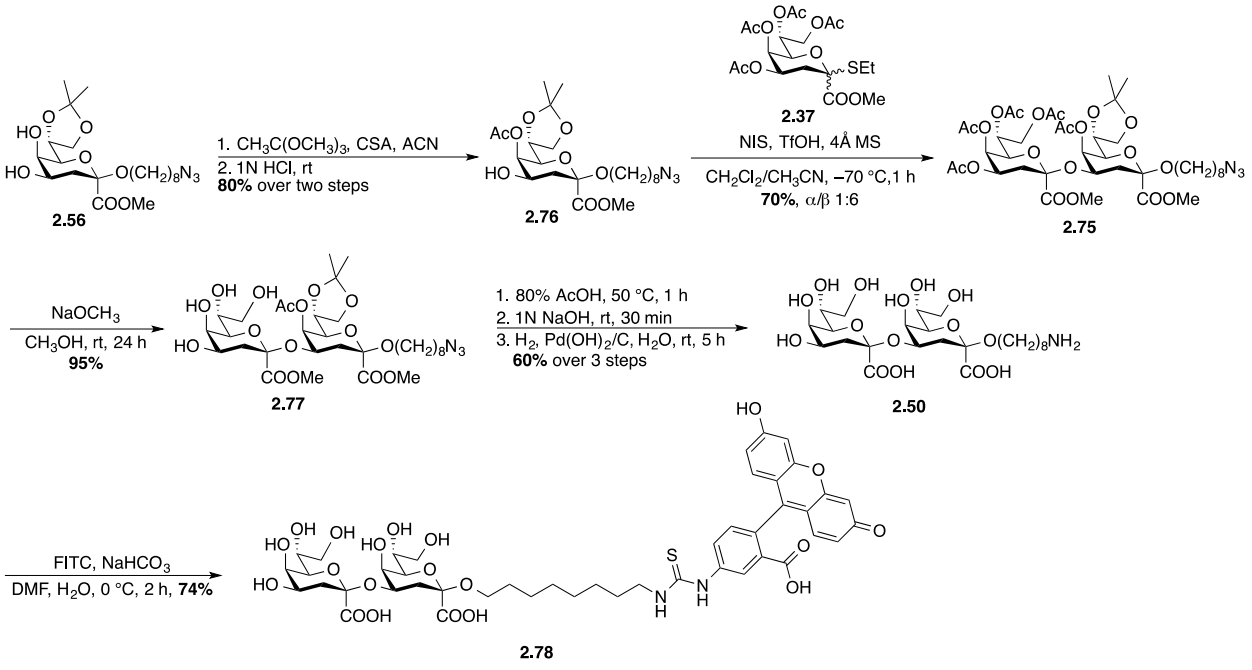
coupled ^{13}C NMR experiment on **2.73** ($^{3}J_{C1,H3ax}$ = 6.5 Hz and $^{3}J_{C1',H3'ax}$ = 6.5 Hz). The alkene product **2.74** came from the elimination of the electrophilic intermediate generated upon activation of **2.37** and its formation was not unexpected, due to the stability of the α,β-unsaturated ester. However, the generation of the di-*O*-isopropylidene-ketal protected monosaccharide **2.52** was unexpected and, to the best of my knowledge, has not been reported previously in glycosylation reactions of Kdo derivatives of this type. Presumably, under the acidic conditions of the glycosylation, the 7,8-*O*-isopropylidene-ketal in **2.56** (or **2.73**) is transferred to another molecule of **2.56** to afford **2.52**. We did not, however, detect any products that lacked a 7,8-*O*-isopropylidene-ketal, which would be expected if this transfer process were to occur.



Scheme 2.11. Attempts to synthesize the β-(2→4)-linked disaccharide **2.73**.

To tackle this problem, I chose to protect the C-5 hydroxyl group so that formation of an isopropylidene ketal was not possible. Thus, diol **2.56** was converted into glycosyl acceptor **2.76** via an orthoester intermediate (**Scheme 2.12**). Glycosylation of **2.76** using peracetylated Kdo donor **2.37** provided the desired disaccharide **2.75** in 70% yield in a 1:6 α:β ratio, together with a 42% yield of glycal **2.74**. The yield of disaccharide **2.75** was calculated using the acceptor **2.56**

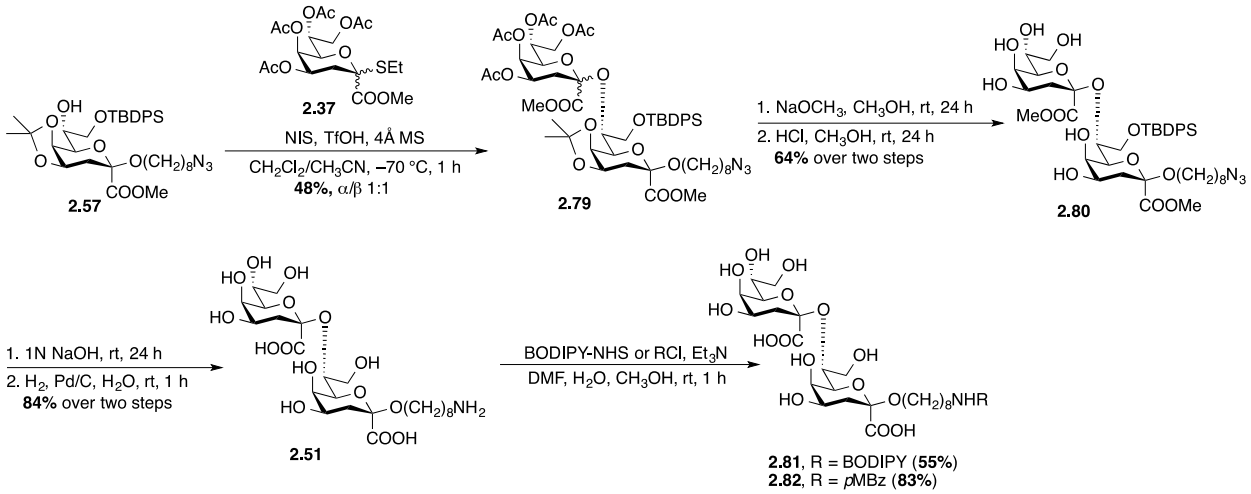
as the limiting reagent and the yield of glycal **2.74** was calculated based on the donor. With the fully-protected β-(2→4)-linked disaccharide **2.75** in hand, the acetates were cleaved by methanolysis to produce **2.77** in 95% yield. As shown in the structure of **2.77**, the acetate at the O-5 position of the reducing-end residue of **2.77** was not removed, even when extra sodium methoxide was added or the reaction time was prolonged. I nevertheless proceeded to carry the disaccharide forward. Cleavage of the isopropylidene ketal in **2.77** was carried out under acidic conditions. Then treatment with 1 N sodium hydroxide cleaved both the Kdo methyl esters and also removed the acetate ester that has been resistant to methanolysis in **2.77**. Finally, the azide was reduced to generate amine **2.50**. The material could be obtained in 60% overall yield in three steps from **2.77**. To generate a probe for use in biosynthetic studies[28], amine **2.50** was conjugated to fluorescein via reaction with FITC to afford, in 74% yield, disaccharide **2.78**.



Scheme 2.12. Synthesis of β-(2→4)-linked disaccharide **2.50** and its fluorescein-conjugate **2.78**.

2.2.5 Synthesis of β-(2→7)-linked disaccharides 2.51 and its derivatives 2.81 and 2.82

In the synthesis of the β-(2→7)-linked disaccharide **2.51** (**Scheme 2.13**), the coupling reaction of donor **2.37** and acceptor **2.57** was performed by treating with NIS and TfOH. Both α/β anomers and the elimination product **2.74** were observed. Unfortunately, the desired β anomer **2.79** and the glycal **2.74** were not separable by chromatography. The mixture was therefore deacetylated with sodium methoxide to remove the acetates. At this stage, the mixture was still inseparable, but most of deprotected glycal could be removed because of its insolubility in ethyl acetate. Thus, trituration of the solid with ethyl acetate led to extraction of the deacetylated disaccharide. After the removal of the isopropylidene ketal under acidic conditions, disaccharide **2.80** was isolated in 64% yield over two steps following the glycosylation. The methyl esters in disaccharide **2.80** were then hydrolyzed and the azide reduced to give, in 84% over two steps, amine **2.51**. The stereochemistry of the Kdo residues in **2.51** was determined using a proton-coupled ^{13}C NMR experiment ($^{3}J_{C1,H3ax}$ = 5.5 Hz and $^{3}J_{C1',H3'ax}$ = 5.8 Hz). This disaccharide was converted to the corresponding BODIPY derivative **2.81** and *p*-methoxybenzamide derivative **2.82**, in 55% and 83% yield, respectively using standard transformations.



Scheme 2.13. Synthesis of β-(2→7)-linked disaccharide **2.51** and its derivatives **2.81** and **2.82**.

2.2.6 Synthesis of orthogonally-protected Kdo donors 2.85 and acceptor 2.88 for the synthesis of molecules with longer Kdo chains

My original goals were not only to synthesize the three Kdo-containing glycans **2.49**–**2.51** and their derivatives, which is described above. We also wanted to access molecules with longer Kdo chains with alternating β-(2→4) and β-(2→7)-linkages. To date, there has only been one report on the synthesis of oligomers of β-linked Kdo residues longer than a disaccharide[6i]. We thus targeted trisaccharides **2.83** and **2.84 (Figure 2.15**) for synthesis. To reduce the number of steps after every glycosylation when accessing these oligosaccharides, the orthogonally-protected Kdo donor **2.85** and acceptors **2.88** and **2.89** were designed.

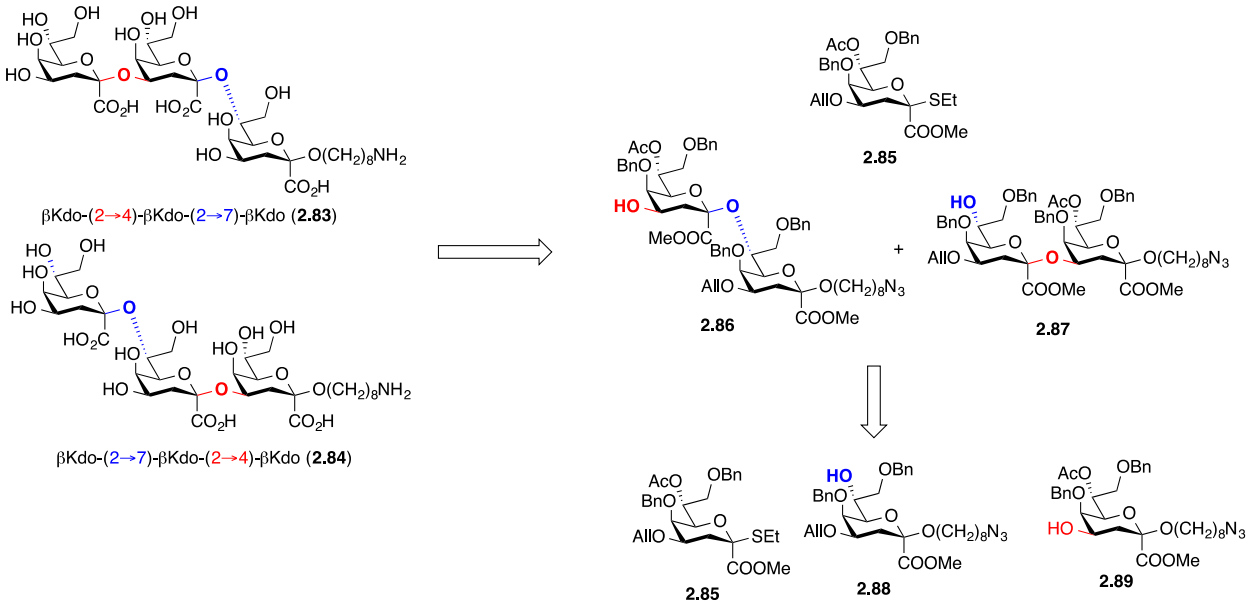
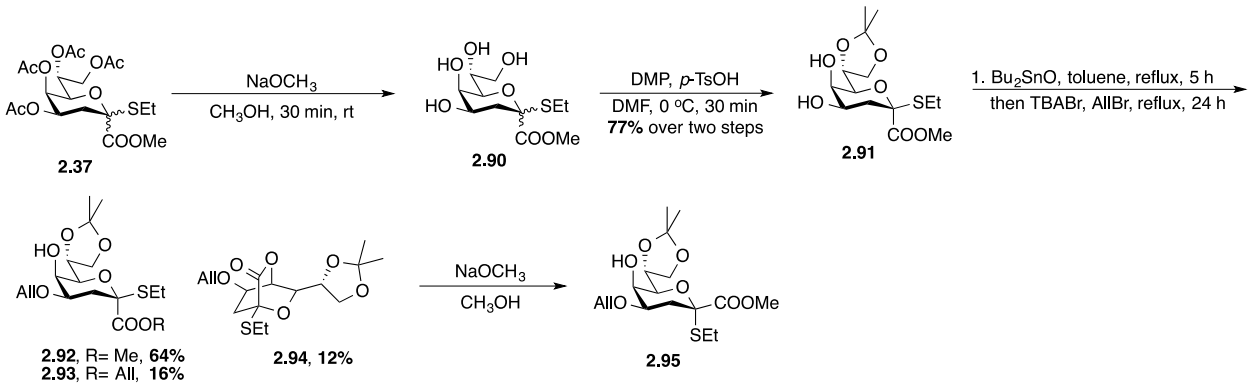


Figure 2.15. Retrosynthesis of trisaccharides **2.83** and **2.84**.

I first attempted the synthesis of trisaccharide **2.83**, which required access to **2.85** and **2.88**. As shown in **Scheme 2.14**, the synthesis of **2.85** and **2.88** started from the Kdo glycosyl donor **2.37**. The preparation of the fully-deprotected thioglycoside **2.90** was achieved by treat-

ment with sodium methoxide in methanol. An isopropylidene ketal was then introduced onto O-7 and O-8 by the reaction of **2.90** with dimethoxypropane and *p*-toluenesulfonic acid to give **2.91** in 77% overall yield from **2.37**. The β anomer of **2.91** could be partially purified column chromatography in a small-scale reaction. However, its purification was very difficult on large scale due to the similarity of its R_f value with that of the α-isomer (<0.02 difference, hexane–EtOAc 1:1). Fortunately, the α and β anomers were easily separated after regioselective allylation of the C-4 hydroxyl group. During this reaction, the methyl ester of α-Kdo thioglycoside **2.91** spontaneously lactonized with the C-5 hydroxyl group to give **2.94**, whereas the β-thioglycoside did not (**Figure 2.16**)[31]. Thus, when the α/β mixture of **2.91** was treated first with *n*-Bu_2SnO and then AllBr and TBABr at reflux in toluene, **2.92** and **2.94** were produced in 64% and 12%, respectively. In this reaction, not only were **2.92** and **2.94** observed, but also the trans-esterification product **2.93** was obtained in 16% yield. Using 1D ^1H and 2D HMBC NMR experiments, I confirmed the structure of **2.94**. The chemical shift of H-5 (δ_{H5} 4.99 ppm) of **2.94** was more downfield than H-5 of **2.95** (δ_{H5} ~4.06 ppm). I propose the deshielding results from the C-1 carbonyl group in the lactone. In addition, there was a correlation identified between C-1 and H-5 of **2.94** in the 2D HMBC spectrum. Moreover, when **2.94** was treated with sodium methoxide in methanol, compound **2.95**, with the α-stereochemistry ($^3J_{C1,H3ax}$ = 2.2 Hz) was obtained.



Scheme 2.14. Synthesis of **2.92** from **2.37**.

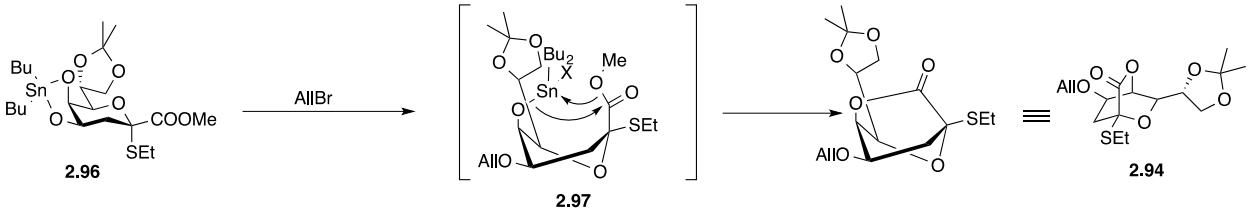
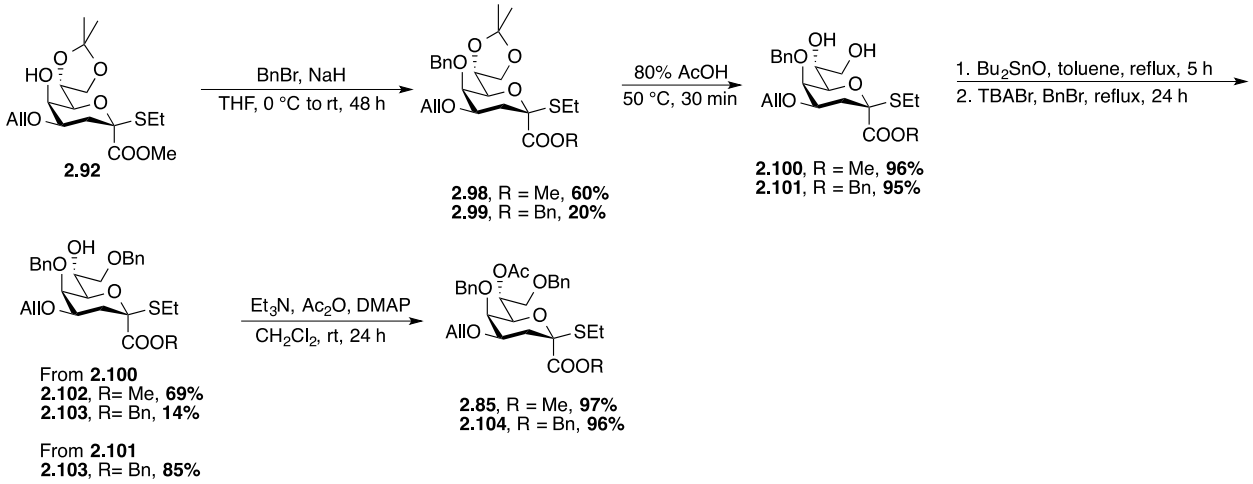


Figure 2.16. Plausible mechanism of latonizationof **2.96** during O-4 allylation[31].

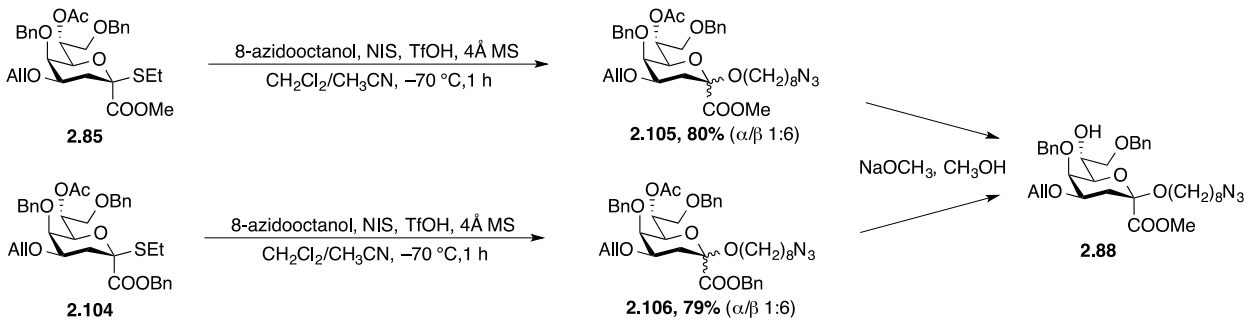
The C-5 hydroxyl group in thioglycoside **2.92** was then benzylated in the presence of BnBr and NaH in THF to afford both the desired compound **2.98** and the trans-esterified product **2.99** in 60% and 20% yield, respectively. I propose that the trans-esterification occurs from the reaction of the methyl ester with benzyl alcohol present either in the benzyl bromide or generated during the reaction under the basic reaction conditions. The isopropylidene ketal of both **2.98** and **2.99** was removed under acidic condition (4:1 acetic acid–water) to afford **2.100** and **2.101** in 96% and 95% yield, respectively. Regioselective benzylation of the C-8 hydroxyl group of methyl ester **2.100** was performed by first treatment with *n*-Bu_2SnO and then BnBr and TBABr in toluene at reflux to obtain both **2.102** and trans-esterified benzyl ester product **2.103** in 83% total yield. Application of the same method to benzyl ester **2.101** gave an 85% of **2.103**. The C-7 hy-

droxyl group of both **2.102** and **2.103** was then acetylated upon reaction with acetic anhydride, triethylamine, and DMAP to afford orthogonally-protected Kdo thioglycosides **2.85** and **2.104** in 97% and 96%, respectively (**Scheme 2.15**).



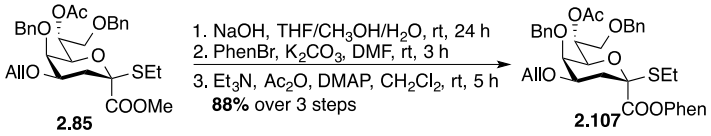
Scheme 2.15. Synthesis of orthogonally-protected Kdo thioglycosides **2.85** and **2.104** from **2.92**.

With both orthogonally-protected Kdo thioglycosides **2.85** and **2.104** in hand, the synthesis of the C-7 unprotected Kdo acceptor **2.88** started from the coupling of Kdo thioglycoside **2.85** (or **2.104**) with 8-azidooctanol promoted by NIS and AgOTf. This reaction afforded Kdo glycosides **2.105** or **2.106** in 80% and 79% yield, respectively (**Scheme 2.16**). Unfortunately, compared to the β-exclusive coupling reaction of peracetylated Kdo thioglycoside **2.37** with 8-azidooctanol, I only obtained a 1:6 α:β ratio in the reactions with thioglycosides **2.85** and **2.104**. Fortunately, the anomers from both reactions could be easily separated by column chromatography. After deacetylation of the β-anomers of **2.105** and **2.106** with sodium methoxide in methanol, the C-7 unprotected Kdo glycosyl acceptor **2.88** was obtained in 96% and 95%, respectively.



Scheme 2.16. Synthesis of the C-7 unprotected Kdo acceptor **2.88** from **2.85** (or **2.104**).

Around the time that I was completing the synthesis of **2.85** and **2.104**, the use of a long-range participating 4-methoxyphenacyl (Phen) auxiliary group at the C-1 position was reported to increase β-selectivity in Kdo glycosylation[18]. Thus, I decided to explore this auxiliary group in my work. It was straightforward to prepare a suitable donor (**2.107**) from **2.85** in 88% yield over three steps (**Scheme 2.17**).

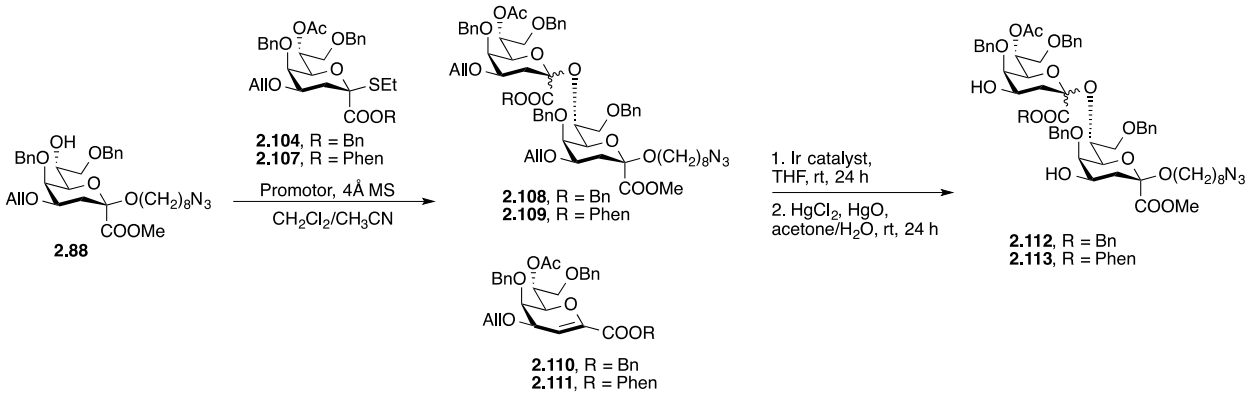


Scheme 2.17. Synthesis of 4-methoxyphenacyl-protected Kdo thioglyoside donor **2.107**.

2.2.7 Approach to a β-(2→7)-linked Kdo-disaccharide using orthogonally-protected Kdo donor 2.104 and limitations

In exploring the use of an orthogonally-protected Kdo derivative in glycosylations, I initially investigated **2.104**. I first looked at its reaction with glycosyl acceptor **2.88** and promotion by NIS and TfOH at –70 °C. Unfortunately, the reaction showed undesired α-selectivity (8:1 α:β) and moderate yield (48%) of the disaccharide product, **2.108** (**Table 2.1**, entry 1). The α/β

anomers of **2.108** could not be separated after glycosylation, but fortunately they were separable after the removal of the two allyl groups to afford **2.112**. The characterization of anomeric configuration **2.112** was done by using proton-coupled ^{13}C NMR experiment ($^{3}J_{C1',H3'ax}$ = 0 Hz for the α-isomer of **2.112** and $^{3}J_{C1',H3'ax}$ = 6.7 Hz for the β-isomer).



Entry	Donor (equiv)	Promotor	Temp. (°C)	Yield (α/β)
1	**2.104** (2.0)	NIS, TfOH	–70	**48%** (8:1)
2	**2.107** (1.0)	NIS, AgOTf	–25	**20%** (1:1)
3	**2.107** (2.0)	NIS, AgOTf	–25	**45%** (1:1)
4	**2.107** (2.0)	NIS, AgOTf	–70 to –40	**42%** (1:1)
5	**2.107** (2.0)	NIS, TfOH	–70	**70%** (1:1)

Table 2.1. Approach to β-(2→7)-linked disaccharide using orthogonally protected donors **2.104** and **2.107**.

Due to the undesired α-selectivity (8:1 α/β) for donor **2.104**, the coupling reaction of donor **2.107**, which contains the reportedly stereodirecting Phen auxiliary, and acceptor **2.88** was performed. The reaction was optimized to give a 70% yield of disaccharide **2.109** when using the NIS and TfOH activator system at –70 °C (**Table 2.1**, entry 5). Although there was no selectivity in this coupling reaction, the α/β ratio was neverless significantly improved compared to the use of donor **2.104** (from 8:1 to 1:1 α/β); the yield was also higher. However, a large amount of glycal **2.111** was observed (46%). The yield of disaccharide **2.109** was calculated based on the

acceptor **2.88** as the limiting reagent and the yield of glycal **2.111** was based on the donor. Deallylation of **2.109** gave **2.113**, the anomers of which were separated and characterized (α-isomer: $^{3}J_{C1'\text{-}H3'ax}$ = 0 Hz; β-isomer: $^{3}J_{C1'\text{-}H3'ax}$ = 6.7 Hz). To further prove the anomeric configuration, the protecting groups on both anomers of **2.113** were completely removed and the anomeric configurations of both anomers of **2.51** were determined. The values were consistent with the stereochemistry determined for **2.113**. Although the use of these orthogonally protected donor gave the desired products, the sterereoselectivities of the glycosylation was poor for the desired β-anomer and the separations of diastereomers from the reactions was difficult. Therefore, I decided not move forward on the synthesis of the molecules with longer Kdo chains (trisaccharides **2.83** and **2.84**) using donors **2.85**, **2.104** and **2.107**.

2.3 Summary

In this chapter I described the synthesis of three Kdo-containing glycans, **2.49**–**2.51** from the peracetylated Kdo thioglycoside **2.37** and two Kdo glycosyl acceptors, **2.57** and **2.76**. Monosaccharide **2.49** was obtained exclusively as the β-glycoside via reaction with 8-azidooctanol under reported conditions[13] (IBr–AgOTf), followed by the removal of all protecting groups. Disaccharides **2.50** and **2.51** were synthesized from glycosylation of **2.37** with **2.76** (or **2.57**), followed by global deprotection. Although the stereoselectivity was poor to moderate in the synthesis of the disaccharides, the desired β anomers could be purified by column chromatography. The anomeric configuration of all Kdo glycosides was characterized using proton-coupled ^{13}C NMR experiments the $^{3}J_{C1,H3ax}$, of the α-Kdo glycosides appears as a broad singlet (< 2 Hz), and the β-Kdo glycosides as a doublet ($^{3}J_{C1,H3ax}$ > 5 Hz). The target molecules **2.49**–**2.51** were further at-

tached different tags at the reducing end for biosynthetic studies[28,30] and in the development of assays to screen for potential inhibitors of the Kdo glycosyltransferase KpsC[29].

The synthesis of trisaccharides **2.83** and **2.84** was attempted via the orthogonally-protected donors **2.85**, **2.104** and **2.107**. The design of orthogonally-protected donors was to reduce the number of steps after every glycosylation when accessing these oligosaccharides. However, the steroselectivity of the glycosylation and the isolation of diastereomers from the glycosylation were the issues using this approach. A 6:1 β:α ratio was observed in the glycosylation of orthogonally-protected donors **2.85** and **2.104** with 8-azidooctanol, whereas the exclusive β-selectivity was found with the peracetylated donor **2.37**. The stereoselectivity of the reaction for the formation of β-(2→7)-disaccharides **2.108** and **2.109** was also unsatisfying (1:8 β:α ratio for **2.108** and 1:1 β:α ratio for **2.109**). Moreover, the isolation of the diastereomeric disaccharides **2.108** and **2.109** was not possible using column chromatography. Therefore, the synthesis of trisaccharides **2.83** and **2.84** using orthogonally-protected donors **2.85**, **2.104** and **2.107** was ceased.

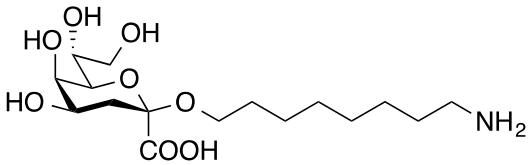
2.4 Experimental Data

2.4.1 General experiment methods

Reactions were carried out in oven-dried glassware. 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 oxide under nitrogen. Unless stated otherwise, all reactions were carried out at rt under a positive pressure of argon and were monitored by TLC on silica gel 60 F_{254} (0.25 mm, E. Merck). Spots were detected under UV light or by charring with 10% H_2SO_4, in EtOH. Unless otherwise indicated,

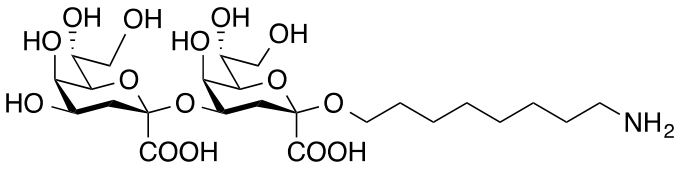
all column chromatography was performed on silica gel 60 (40–60 μm). The ratio between silica gel and crude product ranged from 100 to 50:1 (w/w). Optical rotations were measured at 22 ± 2 °C at the sodium D line (589 nm) and are in units of deg·mL(dm·g)$^{-1}$. ^{1}H NMR spectra were recorded at 500 or 700 MHz, and chemical shifts are referenced to $CHCl_3$ (7.26 ppm, $CDCl_3$), HOD (4.78 ppm, CD_3OD) or HOD (4.78 ppm, D_2O). ^{13}C NMR spectra were recorded at 125 or 175 MHz, and ^{13}C chemical shifts were referenced to internal $CDCl_3$ (77.23 ppm, $CDCl_3$) , external CD_3OD (48.9 ppm, CD_3OD) or external dioxane (67.40 ppm, D_2O). In the processing of reaction mixtures, solutions of organic solvents were washed with equal amounts of aqueous solutions. Organic solutions were concentrated under vacuum at < 40 ºC (bath). Electrospray mass spectra were recorded on samples suspended in mixtures of THF with CH_3OH and added NaCl.

2.4.2 Experimental details for new compounds



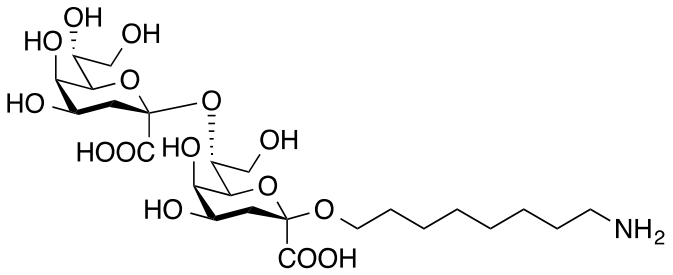
(8-Aminooctyl 3-deoxy-β-D-*manno*-2-octulopyranosid)onic acid (2.49). To a solution of **2.67** (82 mg, 0.209 mmol) in H_2O (2.1 mL) was added $Pd(OH)_2/C$ (82 mg). The flask was then flushed with H_2 gas and the mixture was stirred 5 h under H_2 atmosphere at room temperature. After 5 h, the reaction mixture was filtered through Celite to remove $Pd(OH)_2/C$ and the filtrate was concentrated. The resulting residue was purified by column chromatography (7:2:1, EtOAc–CH_3OH–H_2O) to give **2.49** (61.2 mg, 80%) as a white amorphous solid. $[\alpha]^{25}_{D}$ +21.3 (*c* 2.0, H_2O); R_f 0.18 (5:2:1:0.5, EtOAc–CH_3OH–H_2O–AcOH); ^{1}H NMR (D_2O, 500 MHz) δ_H 4.03–3.93 (m, 3H, H-5, H-7, H-8a), 3.83–3.78 (m, 2H, H-4, H-8b), 3.76 (dt, 1H, *J* = 9.3, 6.9 Hz, octyl

OCH_2), 3.68 (d, 1H, J = 9.3 Hz, H-6), 3.48 (dt, 1H, J = 9.3, 6.9 Hz, octyl OCH_2), 3.03 (t, 2H, J = 6.9 Hz, CH_2N), 2.47 (dd, 1H, J = 12.2, 4.8 Hz, H-3$_{eq}$), 1.84 (t, 1H, J = 12.2 Hz, H-3$_{ax}$), 1.75–1.66 (m, 2H, octyl CH_2), 1.64–1.56 (m, 2H, octyl CH_2), 1.46–1.34 (m, 8H, octyl CH_2); ^{13}C NMR (D_2O, 125 MHz) δ_C 174.9 (C-1, $J_{C1\text{-}H3ax}$ = 5.8 Hz), 102.1 (C-2), 74.3 (C-6), 70.0 (C-5), 68.5 (C-4), 66.3 (C-7), 65.8 (O*C*H$_2$), 65.1 (C-8), 40.6 (*C*H$_2$N), 35.8 (C-3), 29.8 (octyl *C*H$_2$), 29.0 (octyl *C*H$_2$), 28.9 (octyl *C*H$_2$), 27.8 (octyl *C*H$_2$), 26.4 (octyl *C*H$_2$), 25.9 (octyl *C*H$_2$); HRMS (ESI) calcd. for $C_{16}H_{31}NO_8$ $[M+H]^+$ 366.2122 found 366.2123.



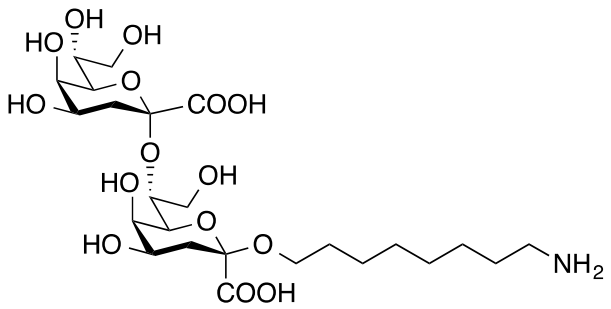
[8-Aminooctyl 3-deoxy-4-*O*-(3-deoxy-β-D-*manno*-2-octulopyranosyl)onic acid]-β-D-*manno*-2-octulopyranosid]onic acid (2.50). A mixture of **2.77** (15.1 mg, 0.021 mmol) in 80% AcOH (1.0 mL) was stirred at 50 °C. After 1 h, the reaction mixture was cooled and co-evaporated with toluene under reduced pressure. The resulting residue was directly added 1N NaOH (1.0 mL) at room temperature. After 30 min, the mixture was neutralized by the addition of Amberlite IR-120 H^+ resin. The mixture was then filtered and concentrated under reduced pressure. To the resulting residue was added $Pd(OH)_2/C$ at room temperature. The flask was then flushed with H_2 gas and the mixture was stirred 5 h under H_2 atmosphere at room temperature. After 5 h, the reaction mixture was filtered through Celite to remove $Pd(OH)_2/C$ and the filtrate was concentrated. The resulting residue was purified by column chromatography (3:2:1, EtOAc–CH_3OH–H_2O) to give **2.50** (7.4 mg, 60% over three steps) as a colorless amorphous solid. $[\alpha]^{25}_D$ +2.4 (*c* 0.2, H_2O); R_f 0.22 (3:2:1:0.5, EtOAc–CH_3OH–H_2O–AcOH); ^{1}H NMR (D_2O, 500 MHz) δ_H 4.13–4.05 (m, 4H, H-4, H-5, H-7, H-8), 4.02 (s, 1H, H-5'), 3.94–3.83 (m, 3H, H-7', H-8'a, H-8b), 3.78–3.71 (m,

3H, H-4', H-6, H-8'b), 3.68 (dt, 1H, J = 9.6, 6.8 Hz, octyl OCH_2), 3.56 (d, 1H, J = 9.1 Hz, H-6'), 3.41 (dt, 1H, J = 9.6, 6.8 Hz, octyl OCH_2), 2.98 (t, 2H, J = 7.6 Hz, CH_2N), 2.36 (dd, 1H, J = 12.5, 5.0 Hz, H-3_{eq}'), 2.15 (dd, 1H, J = 13.3, 5.3 Hz, H-3_{eq}), 1.88 (t, 1H, J = 13.3 Hz, H-3_{ax}'), 1.81 (t, 1H, J = 12.5 Hz, H-3_{ax}), 1.68–1.60 (m, 2H, octyl CH_2), 1.57–1.49 (m, 2H, octyl CH_2), 1.40–1.28 (m, 8H, octyl CH_2); ^{13}C NMR (D_2O, 125 MHz) δ_C 176.7 (C-1), 174.7 (C-1'), 102.0 (C-2), 101.0 (C-2'), 74.1 (C-6'), 73.2 (C-6), 71.4 (C-4'), 71.2 (C-7'), 69.9 (C-7), 67.3 (C-4), 66.6 (C-5), 65.7 (octyl OCH_2), 63.9 (C-8'), 64.3 (2C, C-5, C-4), 63.3 (C-8), 40.4 (CH_2N), 35.4 (C-3), 34.7 (C-3'), 29.8 (octyl CH_2), 29.0 (octyl CH_2), 28.9 (octyl CH_2), 27.6 (octyl CH_2), 26.3 (octyl CH_2), 25.9 (octyl CH_2); HRMS (ESI) calcd. for $C_{24}H_{42}NO_{15}$ $[M–H]^-$ 584.2560 found 584.2559.



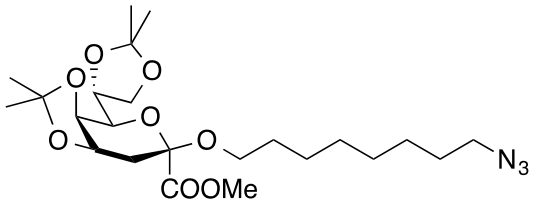
[8-Aminooctyl 3-deoxy-7-*O*-(3-deoxy-β-D-*manno*-2-octulopyranosyl)onic acid]-β-D-*manno*-2-octulopyranosid]onic acid (2.51β). To a solution of **2.80** (10.1 mg, 0.011 mmol) in H_2O (1 mL) was added 1N NaOH (0.5 mL) at room temperature. After 24 h, the reaction mixture was neutralized with the addition of Amberlite IR-120 H^+ resin. The mixture was filtered and the filtrate concentrated under reduced pressure. The residue was then dissolved in H_2O (1 mL) and Pd/C was added (14 mg) at room temperature. The flask was then flushed with H_2 gas and the mixture was stirred 1 h under H_2 atmosphere at room temperature. After 1 h, the reaction mixture was filtered through Celite to remove Pd/C and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatography (3:2:1 EtOAc–CH_3OH–H_2O) followed by size exclusion column chromatography (LH-20) using the eluant (1:1, CH_3OH–H_2O)

to give **2.51β** (5.5 mg, 84% over two steps) as a colorless oil. $[\alpha]^{25}_{D}$ +27.1 (*c* 0.3, H_2O); R_f 0.24 (3:2:1:0.5 EtOAc–CH_3OH–H_2O–AcOH); ^{1}H NMR (D_2O, 500 MHz) δ_H 4.47–4.43 (m, 1H, H-7), 4.07 (d, 1H, $J_{5,4}$ = 2.9 Hz, H-5), 4.04–3.97 (m, 3H, H-5', H-7', H-8'a), 3.94 (dd, 1H, $J_{8a,7}$ = 2.9 Hz, J_{gem} = 13.1 Hz, H-8a), 3.85–3.72 (m, 5H, H-4, H-8b, H-4', H-8'b, octyl OCH_2), 3.66 (d, 1H, $J_{6,7}$ = 9.1 Hz, H-6), 3.52 (d, 1H, *J* = 9.1 Hz, H-6'), 3.48 (dt, 1H, *J* = 9.4, 6.8 Hz, octyl OCH_2), 3.04 (t, 2H, *J* = 7.7 Hz, CH_2N), 2.49 (dd, 1H, *J* = 12.1, 4.7 Hz, H-3$_{eq}$'), 2.15 (dd, 1H, *J* = 12.0, 4.6 Hz, H-3$_{eq}$), 1.88 (app t, 1H, *J* = 12.1 Hz, H-3$_{ax}$'), 1.84 (app t, 1H, *J* = 12.0 Hz, H-3$_{ax}$), 1.74–1.66 (m, 2H, octyl CH_2), 1.63–1.55 (m, 2H, octyl CH_2), 1.46–1.33 (m, 8H, octyl CH_2); ^{13}C NMR (D_2O, 125 MHz) δ_C 174.99 (C-1, $J_{C1,H3ax}$ = 5.5 Hz), 174.94 (C-1', $J_{C1',H3'ax}$ = 5.8 Hz), 102.0 (C-2), 101.3 (C-2'), 74.4 (C-6'), 73.1 (C-6), 72.1 (C-7), 70.2 (C-7'), 68.50 (C-4), 68.46 (C-4'), 66.3 (C-5'), 65.9 (C-5), 65.7 (octyl O*C*H_2), 65.1 (C-8'), 63.0 (C-8), 40.5 (CH_2N), 35.7 (C-3), 35.4 (C-3'), 29.7 (octyl *C*H_2), 28.84 (octyl *C*H_2), 28.78 (octyl *C*H_2), 27.6 (octyl *C*H_2), 26.3 (octyl *C*H_2), 25.8 (octyl *C*H_2); HRMS (ESI) calcd. for $C_{24}H_{42}NO_{15}$ $[M–H]^-$ 584.2560; found 584.2559.

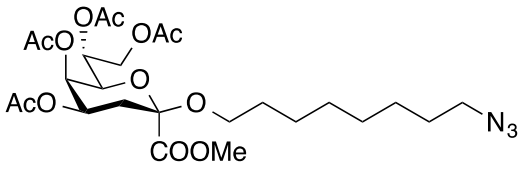


[8-Aminooctyl 3-deoxy-7-*O*-(3-deoxy-α-D-manno-2-octulopyranosyl)onic acid]-β-D-*manno*-2-octulopyranosid]onic acid (2.51α). To a solution of **2.113α** (20.7 mg, 0.0176 mmol) in H_2O (3.0 mL) was added 1N NaOH (1.0 mL) at room temperature. After 24 h, the reaction mixture was neutralized with the addition of Amberlite IR-120 H^+ resin. The mixture was filtered and the filtrate concentrated under reduced pressure. The residue was then dissolved in H_2O (1 mL) and Pd/C was added (50 mg) at room temperature. The flask was then flushed with H_2 gas and the

mixture was stirred 1 h under H_2 atmosphere at room temperature. After 1 h, the reaction mixture was filtered through Celite to remove Pd/C and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatography (3:2:1 EtOAc–CH_3OH–H_2O) followed by size exclusion column chromatography (LH-20) using the eluant (1:1, CH_3OH–H_2O) to give **2.51α** (4.2 mg, 41% over two steps) as a colorless oil. $[\alpha]^{25}_D$ +42.5 (*c* 0.4, H_2O); R_f 0.21 (3:2:1:0.5 EtOAc–CH_3OH–H_2O–AcOH); ^{1}H NMR (D_2O, 500 MHz) δ_H 4.19 (ddd, 1H, $J_{4,5}$ = 3.0 Hz, $J_{4,3eq}$ = 4.6 Hz, $J_{4,3ax}$ = 12.3 Hz, H-4), 4.12 (d, 1H, $J_{5,4}$ = 3.0 Hz, H-5), 4.09 (d, 1H, *J* = 2.4 Hz, H-5'), 4.06–4.02 (m, 1H, H-7), 4.00–3.92 (m, 3H, H-7', H-8a, H-8'a), 3.90–3.85 (m, 1H, H-8b), 3.84–3.70 (m, 5H, H-4', H-6, H-6', H-8'b, octyl OC*H*$_2$), 3.46 (dt, 1H, *J* = 9.4, 6.8 Hz, octyl OC*H*$_2$), 3.04 (t, 2H, *J* = 7.7 Hz, *CH*$_2$N), 2.46 (dd, 1H, $J_{3'eq,4}$ = 4.9 Hz, J_{gem} = 12.5 Hz, H-3$_{eq}$'), 2.19 (dd, 1H, $J_{3eq,4}$ = 4.6 Hz, J_{gem} = 12.3 Hz, H-3$_{eq}$), 1.85 (app t, 1H, $J_{gem} = J_{3ax,4}$ = 12.3 Hz, H-3$_{ax}$), 1.82 (app t, 1H, $J_{gem} = J_{3'ax,4}$ = 12.5 Hz, H-3'$_{ax}$), 1.74–1.66 (m, 2H, octyl C*H*$_2$), 1.61–1.54 (m, 2H, octyl C*H*$_2$), 1.45–1.33 (m, 8H, octyl C*H*$_2$); ^{13}C NMR (D_2O, 125 MHz) δ_C 175.8 (C-1', $J_{C'1,H3'ax}$ = 0 Hz), 174.92 (C-1, $J_{C1,H3ax}$ = 6.0 Hz), 103.3 (C-2'), 102.0 (C-2), 74.5 (C-6), 73.1 (C-6'), 72.9 (C-7'), 71.4 (C-7), 67.9 (C-4'), 67.6 (C-5'), 66.6 (C-5 or C-4), 66.2 (C-4 or C-5), 65.7 (octyl O*C*H$_2$), 63.8 (C-8 or C-8'), 63.0 (C-8 or C-8'), 40.5 (CH_2N), 36.3 (C-3), 36.0 (C-3'), 29.7 (octyl *C*H$_2$), 28.84 (octyl *C*H$_2$), 28.79 (octyl *C*H$_2$), 27.5 (octyl *C*H$_2$), 25.3 (octyl *C*H$_2$), 25.8 (octyl *C*H$_2$); HRMS (ESI) calcd. for $C_{24}H_{42}NO_{15}$ $[M–H]^-$ 584.2560; found 584.2557.

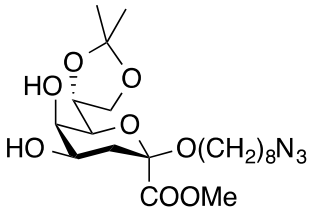


Methyl (8-azidooctyl 3-deoxy-4,5,7,8-di-*O*-isopropylidene-β-D-*manno*-2-octulopyranosid)-onate (2.52). This was a side product from the TBS protection and isopropylidenation of **2.66** and the side product from the glycosylation of **2.37** and **2.56**. The compound **2.52** was a colorless oil. $[\alpha]^{25}_{D}$ –14.4 (*c* 1.0, $CHCl_3$); R_f 0.25 (1:4 hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 4.47 (app dt, 1H, $J_{4,3a} = J_{4,3b} = 4.3$ Hz, $J_{4,5} = 7.4$ Hz, H-4), 4.30–4.22 (m, 3H, H-5, H-7, H-8a), 4.09 (dd, 1H, $J_{8b,7} = 6.0$ Hz, $J_{gem} = 8.4$ Hz, H-8b), 3.75 (s, 3H, COOCH_3), 3.65 (dt, 1H, $J = 9.3$, 6.7 Hz, octyl OCH_2), 3.45 (dd, 1H, $J_{6,5} = 2.0$ Hz, $J_{gem} = 6.7$ Hz, H-6), 3.26 (dt, 1H, $J = 9.3$, 6.7 Hz, octyl OCH_2), 3.22 (t, 2H, $J = 6.9$ Hz, CH_2N$_3$), 2.23 (dd, 1H, $J_{3a,4} = 4.3$ Hz, $J_{gem} = 12.0$ Hz, H-3a), 1.90 (dd, 1H, $J_{3b,4} = 4.3$ Hz, $J_{gem} = 12.0$ Hz, H-3b), 1.59–1.48 (m, 4H, octyl CH_2), 1.48 (s, 3H, (CH_3)$_2$C), 1.40 (s, 3H, (CH_3)$_2$C), 1.36–1.24 (m, 14H, (CH_3)$_2$C, octyl CH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 170.7 (C-1), 109.49 (CH$_3$)$_2$*C*), 109.44 (CH$_3$)$_2$*C*), 98.6 (C-2, $^1J_{C1,H3ax} = 0$ Hz), 74.0 (C-7), 73.7 (C-6), 71.5 (C-5), 70.3 (C-4), 67.1 (C-8), 64.5 (octyl O*C*H$_2$), 52.4 (COO*C*H$_3$), 51.6 (*C*H$_2$N$_3$), 33.2 (C-3), 29.9 (octyl *C*H$_2$), 29.4 (octyl *C*H$_2$), 29.2 (octyl *C*H$_2$), 29.0 (octyl *C*H$_2$), 27.2 (*C*H$_3$)$_2$C), 26.80 (*C*H$_3$)$_2$C), 26.77 (octyl *C*H$_2$), 26.1 (octyl *C*H$_2$), 25.4 (*C*H$_3$)$_2$C), 25.3 (*C*H$_3$)$_2$C); HRMS (ESI) calcd. for $C_{23}H_{39}N_3NaO_8$ $[M+Na]^+$ 508.2629 found 508.2627.



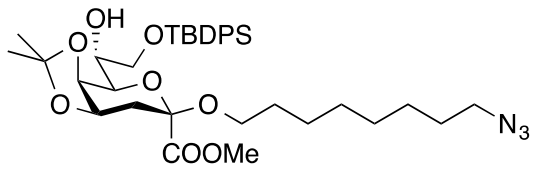
Methyl (8-azidooctyl 4,5,7,8-tetra-*O*-acetyl-3-deoxy-β-D-*manno*-2-octulopyranosid)-onate (2.55). A mixture of **2.37** (133 mg, 0.286 mmol), 8-azidooctanol (58.8 mg, 0.344 mmol) and 4Å molecular sieve in CH_2Cl_2/CH_3CN (2.9 mL) was stirred under Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –70 °C and then IBr (118 mg, 0.572 mmol) and silver triflate (14.7 mg, 0.0573 mmol) were added at –70 °C. After 1 h, triethylamine was added to the reaction mixture. The reaction was warmed to room temperature and then a small amount of H_2O was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The mixture was dried with $MgSO_4$ and then filtered and concentrated under reduced pressure. The resulting mixture was filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography (2:1 hexane–EtOAc) to give **2.55** (131 mg, 0.229 mmol, 80%) as a colorless oil. $[\alpha]^{25}_D$ +34.0 (*c* 2.1, $CHCl_3$); R_f 0.32 (2:1 hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 5.30–5.27 (m, 1H, H-5) 5.18 (ddd, 1H, $J_{7,6}$ = 9.6 Hz, $J_{7.8a}$ = 4.3 Hz, $J_{7,8b}$ = 2.8 Hz, H-7), 4.88 (ddd, 1H, $J_{4,3eq}$ = 5.0 Hz, $J_{4,3ax}$ = 12.6 Hz, $J_{4,5}$ = 3.1 Hz, H-4), 4.40–4.33 (m, 2H, H-8a, H-8b), 4.18 (dd, 1H, $J_{6,5}$ = 1.4 Hz, $J_{6,7}$ = 9.6 Hz, H-6), 3.81 (s, 3H, COOC*H*$_3$), 3.74 (dt, 1H, *J* = 9.4, 6.6 Hz, octyl OC*H*$_2$), 3.29 (dt, 1H, *J* = 9.4, 6.6 Hz, octyl OC*H*$_2$), 3.26 (t, 2H, *J* = 7.3 Hz, CH_2N_3), 2.36 (dd, 1H, $J_{3eq,4}$ = 5.0 Hz, J_{gem} = 12.6 Hz, H-3$_{eq}$), 2.12 (s, 3H, COC*H*$_3$), 2.11 (app t, 1H, $J_{3ax,4} = J_{gem}$ = 12.6 Hz, H-3$_{ax}$), 2.10 (s, 3H, COC*H*$_3$), 2.01 (s, 3H, COC*H*$_3$), 1.98 (s, 3H, COC*H*$_3$), 1.66–1.54 (m, 4H, octyl C*H*$_2$), 1.40–1.28 (m, 8H, octyl C*H*$_2$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 170.7 (Ac), 170.5 (Ac), 169.9 (Ac), 169.8 (Ac), 168.4 (C-1, $J_{C1\text{-}H3ax}$ = 6.7 Hz), 99.4 (C-2), 70.6 (C-6), 68.1 (C-7), 67.1 (C-4), 64.7 (octyl O*C*H$_2$), 64.1 (C-5), 62.4 (C-8), 52.7

(COO*C*H$_3$), 51.5 (*C*H$_2$N$_3$), 32.4 (C-3), 29.5 (octyl *C*H$_2$), 29.1 (octyl *C*H$_2$), 29.0 (octyl *C*H$_2$), 28.8 (octyl *C*H$_2$), 26.6 (octyl *C*H$_2$), 25.8 (octyl *C*H$_2$), 20.8 (CO*C*H$_3$), 20.7 (3C, CO*C*H$_3$); HRMS (ESI) calcd. for $C_{25}H_{39}N_3O_{12}$ $[M+H]^+$ 574.2551 found 574.2542.



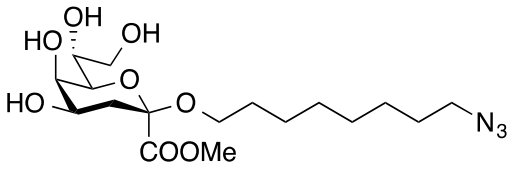
Methyl (8-azidooctyl 3-deoxy-7,8-*O*-isopropylidene-β-D-*manno*-2-octulopyranosid)-onate (2.56). To a solution of **2.66** (72.0 mg, 0.178 mmol) in DMF (2.0 mL) was added 2,2-dimethoxypropane (33.0 μL, 27.8 mg, 0.266 mmol) and *p*-toluenesulfonic acid (3.0 mg, 0.018 mmol) at 0 °C. After 1 h, the reaction mixture was neutralized by the addition of triethylamine. The reaction mixture was then diluted with EtOAc and washed with H_2O. The aqueous layers were extracted with EtOAc, and the combined organic layers were dried and concentrated under reduced pressure. The resulting residue was purified by column chromatography (1:1 hexane–EtOAc) to give **2.56** (62.5 mg, 79%) as a colorless oil. $[\alpha]^{25}_D$ +15.9 (*c* 0.3, $CHCl_3$); R_f 0.23 (1:1 hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 4.34 (ddd, 1H, $J_{7,6}$ = 10.8 Hz, $J_{7,8a}$ = 6.1 Hz, $J_{7,8b}$ = 5.0 Hz, H-7), 4.18 (dd, 1H, $J_{8a,7}$ = 6.1 Hz, J_{gem} = 8.5 Hz, H-8a), 4.11 (dd, 1H, $J_{8b,7}$ = 5.0 Hz, J_{gem} = 8.5 Hz, H-8b), 3.96 (br s, 1H, H-5), 3.81 (s, 3H, COOC*H$_3$*), 3.72 (dt, 1H, *J* = 9.2, 6.7 Hz, octyl OC*H$_2$*), 3.71–3.67 (m, 1H, H-4), 3.52 (dd, 1H, 1H, $J_{6,5}$ = 1.2 Hz, $J_{6,7}$ = 10.8 Hz, H-6), 3.31 (dt, 1H, *J* = 9.2, 6.7 Hz, octyl OC*H$_2$*), 3.27 (t, 2H, *J* = 6.9 Hz, C*H$_2$*N$_3$), 2.72 (br s, 1H, 5-OH), 2.57 (d, 1H, *J* = 7.2 Hz, 4-OH), 2.44 (dd, 1H, $J_{3eq,4}$ = 4.6 Hz, J_{gem} = 12.8 Hz, H-3$_{eq}$), 1.95 (app t, 1H, $J_{3ax,4}$ = J_{gem} = 12.5 Hz, H-3$_{ax}$), 1.64–1.50 (m, 4H, octyl C*H$_2$*), 1.42 (s, 3H, (C*H$_3$*)$_2$C), 1.39 (s, 3H, (C*H$_3$*)$_2$C), 1.38–1.28 (m, 8H, octyl C*H$_2$*); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 169.3 (C-1), 109.8 ((CH$_3$)$_2$*C*), 99.6 (C-2), 75.9 (C-6), 73.5 (C-7), 67.7 (C-8), 67.3 (C-4), 66.5 (C-5), 64.5

(octyl O*C*H$_2$), 52.7 (COO*C*H$_3$), 51.6 (*C*H$_2$N$_3$), 35.5 (C-3), 29.6 (octyl *C*H$_2$), 29.1 (octyl *C*H$_2$), 29.0 (octyl *C*H$_2$), 28.8 (octyl *C*H$_2$), 26.8 (octyl *C*H$_2$), 26.6 ((*C*H$_3$)$_2$C), 25.8 ((*C*H$_3$)$_2$C), 25.2(octyl *C*H$_2$); HRMS (ESI) calcd. for $C_{20}H_{35}N_3NaO_8$ $[M+Na]^+$ 468.2316 found 468.2319.



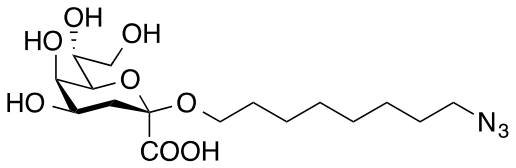
Methyl (8-azidooctyl 8-*O*-*tert*-butyldiphenylsilyl-3-deoxy-4,5-*O*-isopropylidene-β-D-*manno*-2-octulopyranosid)-onate (**2.57**). To a solution of **2.66** (270 mg, 0.67 mmol) in DMF (6.7 mL) was added imidazole (68.0 mg, 1.00 mmol) and TBDPSCl (225 μL, 238 mg, 0.87 mmol) at 0 ºC. The reaction mixture was warmed to room temperature and after 16 h the excess TBDPSCl was quenched by the addition of CH_3OH. The reaction mixture was concentrated and then diluted with EtOAc and washed with H_2O. The resulting organic layer was washed with satd. aq. $NaHCO_3$, dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was then dissolved in acetonitrile (6.7 mL) and 10-camphorsulfonic acid (47 mg, 0.201 mmol) and 2,2-dimethoxypropane (107 μL, 91 mg, 0.87 mmol) were added at room temperature. After 1 h, triethylamine was added. The reaction mixture was concentrated and the resulting residue was purified by column chromatography (4:1 hexane–EtOAc) to give **2.57** (366 mg, 80%) as a colorless oil. $[\alpha]^{25}_D$ +15.9 (*c* 0.3, $CHCl_3$); R_f 0.24 (4:1 hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.74–7.68 (m, 4H, ArH), 7.46–7.42 (m, 2H, ArH), 7.42–7.36 (m, 4H, ArH), 4.43 (dt, 1H, $J_{4,3a} = J_{4,3b} = 5.0$ Hz, $J_{4,5} = 7.0$ Hz, H-4), 4.32 (dd, 1H, $J_{5,4} = 7.0$ Hz, $J_{5,6} = 2.0$ Hz, H-5), 4.06 (ddd, 1H, $J_{7,6} = 8.0$ Hz, $J_{7,8a} = 4.0$ Hz, $J_{7,8b} = 6.5$ Hz, H-7), 4.00 (dd, 1H, $J_{8a,7} = 4.0$, $J_{gem} = 10.5$ Hz, H-8a), 3.84 (dd, 1H, $J_{8b,7} = 6.5$ Hz, $J_{gem} = 10.5$ Hz, H-8b), 3.69 (dd, $J_{6,5} = 2.0$ Hz, $J_{6,7} = 8.0$ Hz, 1H, H-6), 3.65 (s, 3H, COOC*H*$_3$), 3.58 (dt, 1H, $J = 9.5$, 6.5 Hz, octyl OC*H*$_2$), 3.27–3.24 (m, 3H, octyl OC*H*$_2$, C*H*$_2$N$_3$), 2.10 (d, 2H, $J = 5.0$ Hz, H-3a, H-3b), 1.62–1.55 (m, 4H, octyl

CH_2), 1.51 (s, 3H, C(CH_3)$_2$), 1.36 (s, 3H, C(CH_3)$_2$), 1.36–1.27 (m, 8H, octyl CH_2), 1.09 (s, 9H, C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 170.1 (C-1), 135.6 (Ar), 133.3 (Ar), 133.2 (Ar), 129.8 (Ar), 129.7 (Ar), 127.7 (Ar), 109.2((CH$_3$)$_2$*C*), 98.5 (C-2), 72.0 (C-6), 71.1 (C-5), 70.7 (C-7), 70.5 (C-4), 65.4 (C-8), 64.2 (octyl O*C*H$_2$), 52.1 (COO*C*H$_3$), 51.5 (*C*H$_2$N$_3$), 33.8 (C-3), 29.7 (octyl *C*H$_2$), 29.2 (octyl *C*H$_2$), 29.1 (octyl *C*H$_2$), 28.8 (octyl *C*H$_2$), 27.0 (octyl *C*H$_2$), 26.9 ((*C*H$_3$)$_2$C), 26.7 ((*C*H$_3$)$_2$C), 26.5 ((*C*H$_3$)$_3$C), 26.4 (octyl *C*H$_2$), 19.3 (CH$_3$)$_3$*C*); HRMS (ESI) calcd. for $C_{36}H_{53}N_3NaO_8Si$ $[M+Na]^+$ 706.3494; found 706.3490.

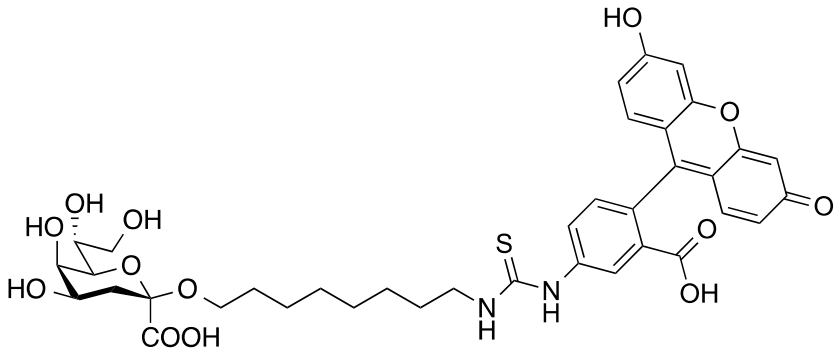


Methyl (8-azidooctyl 3-deoxy-β-D-*manno*-2-octulopyranosid)-onate (2.66). To a solution of **2.55** (133 mg, 0.232 mmol) in CH_3OH (2.3 mL) was added sodium methoxide (1.0 mg, 0.023 mmol) at room temperature. After 30 min, the reaction mixture was neutralized by the addition of Amberlite IR-120 H^+ resin. The mixture was then filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography (1:6 CH_3OH–CH_2Cl_2) to give **2.66** (61 mg, 0.150 mmol, 69%) as a colorless oil. $[\alpha]^{25}_D$ +32.0 (*c* 3.0, CH_3OH); R_f 0.22 (1:6 CH_3OH–CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 3.92–3.87 (m, 2H, H-5, H-7), 3.82 (dd, 1H, $J_{8a,7}$ = 3.0 Hz, J_{gem} = 12.0 Hz, H-8a), 3.78 (s, 3H, COOCH_3), 3.71 (dt, 1H, J = 9.2, 6.5 Hz, octyl OCH_2), 3.66 (dd, 1H, $J_{8b,7}$ = 6.6 Hz, J_{gem} = 12.0 Hz, H-8b), 3.56 (ddd, 1H, $J_{4,3eq}$ = 4.4 Hz, $J_{4,3ax}$ = 12.5 Hz, $J_{4,5}$ = 2.8 Hz, H-4), 3.22 (dd, 1H, $J_{6,5}$ = 1.1 Hz, $J_{6,7}$ = 8.8 Hz, H-6), 3.31 (dt, 1H, J = 9.2, 6.5 Hz, octyl OCH_2), 3.27 (t, 2H, J = 6.9 Hz, CH_2N$_3$), 2.29 (dd, 1H, $J_{3eq,4}$ = 4.8 Hz, J_{gem} = 12.5 Hz, H-3$_{eq}$), 1.98 (app t, 1H, $J_{3ax,4}$ = J_{gem} = 12.5 Hz, H3$_{ax}$), 1.61–1.54 (m, 2H, octyl CH_2), 1.53–1.46 (m, 2H, octyl CH_2), 1.41–1.29 (m, 8H, octyl CH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 171.0

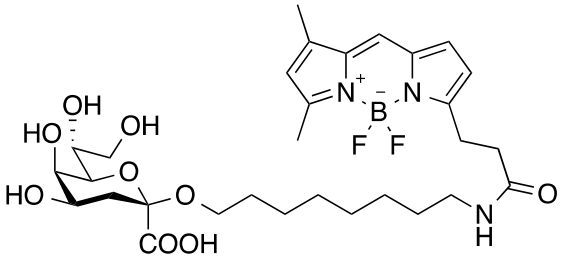
(C-1), 100.8 (C-2, $^{1}J_{C1,H3ax}$ = 6.5 Hz), 76.0 (C-6), 71.0 (C-7), 68.6 (C-4), 67.0 (C-5), 65.5 (C-8), 65.0 (octyl O*C*H$_2$), 52.9 (COO*C*H$_3$), 52.4 (*C*H$_2$N$_3$), 35.7 (C-3), 30.7 (octyl *C*H$_2$), 30.2 (octyl *C*H$_2$), 30.1 (octyl *C*H$_2$), 29.9 (octyl *C*H$_2$), 27.7 (octyl *C*H$_2$), 26.9 (octyl *C*H$_2$); HRMS (ESI) calcd. for $C_{17}H_{31}N_3NaO_8$ $[M+Na]^+$ 428.2003 found 428.2001.



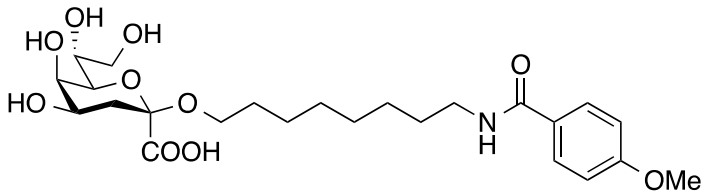
(8-Azidooctyl 3-deoxy-β-D-*manno*-2-octulopyranosid)onic acid (2.67). To a solution of **2.66** (102 mg, 0.251 mmol) in H_2O (2.5 mL) was added 1N sodium hydroxide (1 mL). After 30 min, the reaction mixture was neutralized by the addition of Amberlite IR-120 H^+ resin until the solution was pH 7. The mixture was passed through the filter paper and the solution was concentrated under reduced pressure. The resulting residue was purified by column chromatography (7:2:1, EtOAc–CH_3OH–H_2O) to give **2.67** (96.5 mg, 98%) as an amorphous solid. $[\alpha]^{25}_D$ +2.7 (*c* 0.3, H_2O); R_f 0.32 (7:2:1:0.5, EtOAc–CH_3OH–H_2O–AcOH); ^{1}H NMR (D_2O, 500 MHz) δ_H 4.03–3.96 (m, 3H, H-5, H-7, H-8a), 3.85–3.79 (m, 2H, H-4, H-8b), 3.77 (dt, 1H, *J* = 9.3, 7.1 Hz, octyl OC*H*$_2$), 3.69 (d, 1H, *J* = 9.2 Hz, H-6), 3.48 (dt, 1H, *J* = 9.3, 7.1 Hz, octyl OC*H*$_2$), 3.38 (t, 2H, *J* = 7.0 Hz, 1H, C*H*$_2$N$_3$), 2.48 (dd, 1H, $J_{3eq,4}$ = 4.7 Hz, J_{gem} = 12.1 Hz, H-3$_{eq}$), 1.85 (app t, 1H, $J_{3ax,4}$ = J_{gem} = 12.1 Hz, H-3$_{ax}$), 1.71–1.64 (m, 2H, octyl C*H*$_2$), 1.64–1.57 (m, 2H, octyl C*H*$_2$), 1.47–1.35 (m, 8H, octyl C*H*$_2$); ^{13}C NMR (D_2O, 125 MHz) δ_C 174.9 (C-1), 102.1 (C-2), 74.3 (C-6), 70.0 (C-5), 68.5 (C-7), 66.3 (C-4), 65.9 (octyl O*C*H$_2$), 65.1 (C-8), 52.2 (*C*H$_2$N$_3$), 35.7 (C-3), 29.9 (octyl *C*H$_2$), 29.3 (octyl *C*H$_2$), 29.1 (octyl *C*H$_2$), 28.9 (octyl *C*H$_2$), 26.8 (octyl *C*H$_2$), 26.0 (octyl *C*H$_2$); HRMS (ESI) calcd. for $C_{16}H_{28}N_3O_8$ $[M–H]^–$ 390.1882 found 390.1874.



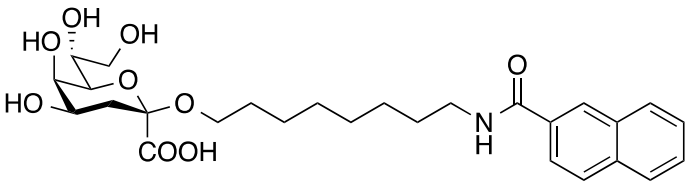
8-Aminooctyl 3-deoxy-β-D-*manno*-2-octulopyranosidonic acid, FITC conjugate (2.68). To a solution of **2.49** (4.0 mg, 11 μmol) in H_2O (1.0 mL) and DMF (0.05 mL) at 0 °C was added sodium bicarbonate (2.8 mg, 0033 mmol) and FITC (5.2 mg, 13.2 μmol). After stirring at 0 °C for 2 h, the reaction mixture was concentrated under reduced pressure. The resulting residue was purified by column chromatography (7:2:1, EtOAc–CH_3OH–H_2O) and size exclusion chromatography (Sephadex LH-20, 1:1, CH_2Cl_2–CH_3OH) to give **2.68** (4.0 mg, 48%) as an orange amorphous solid. $[\alpha]^{25}_D$ +2.7 (*c* 0.3, H_2O); R_f 0.20 (7:2:1:0.5, EtOAc–CH_3OH–H_2O–HOAc) ^{1}H NMR (D_2O, 700 MHz) δ_H 7.80 (s, 1H, Ar), 7.71–7.59 (m, 1H, Ar), 7.49–7.28 (m, 3H, Ar), 6.94–6.67 (m, 4H, Ar), 4.04–3.91 (m, 3H, H-5, H-7, H-8a), 3.85–3.61 (m, 6H, H-4, H-6, H-8b, OCH_2, CH_2N), 3.53–3.44 (m, 1H, OCH_2), 2.48 (dd, 1H, J = 12.5, 4.2 Hz, H-3_{eq}), 1.84 (app t, 1H, J = 12.5 Hz, H-3_{ax}), 1.72–1.60 (m, 2H, octyl CH_2), 1.59–1.51 (m, 2H, octyl CH_2), 1.43–1.27 (m, 8H, octyl CH_2); ^{13}C NMR (D_2O, 125 MHz) δ_C 174.0 (C=O), 158.3, 138.6, 131.8, 131.5, 131.2, 126.0, 125.0, 121.6, 114.6, 103.4, 101.1, 73.3, 69.0, 67.5, 65.4, 64.9, 64.2, 45.1, 34.8, 29.0, 28.4, 28.2, 26.1, 25.1; HRMS (ESI) calcd. for $C_{37}H_{41}N_2O_{13}S$ $[M–H]^-$ 753.2329 found 753.2328.



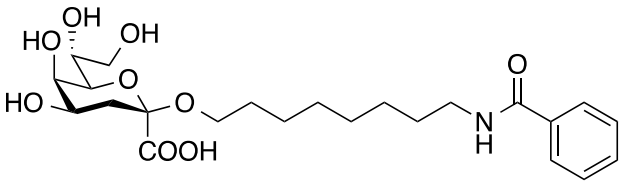
8-Aminooctyl 3-deoxy-β-D-*manno*-2-octulopyranosidonic acid, BODIPY conjugate (2.69). To a solution of **2.49** (9.4 mg, 25.7 μmol) in H_2O (1.0 mL) and DMF (0.05 mL) at 0 °C was added potassium bicarbonate (10.7 mg, 77 μmol) and BODIPY NHS ester (10.0 mg, 25.7 μmol). After stirring at 0 °C for 2 h, the reaction mixture was concentrated under reduced pressure. The resulting residue was purified by column chromatography (7:2:1, EtOAc–CH_3OH–H_2O) and size exclusion chromatography (Sephadex LH-20, 1:1, CH_2Cl_2–CH_3OH) to give **2.69** (10.1 mg, 61%) as a blue amorphous solid. $[\alpha]^{25}_D$ +1.6 (*c* 0.1, H_2O); R_f 0.20 (7:2:1:0.5, EtOAc–CH_3OH–H_2O–HOAc) ^{1}H NMR (D_2O, 700 MHz) δ_H 7.58 (s, 1H, ArH), 7.17 (d, 1H, *J* = 4.0 Hz, ArH), 6.49 (d, 1H, *J* = 4.0 Hz, ArH), 6.42 (s, 1H, ArH), 4.07–3.97 (m, 3H, H-5, H-7, H-8a), 3.88–3.70 (m, 4H, H-4, H-6, H-8b, OC*H*$_2$), 3.50–3.41 (m, 1H, OC*H*$_2$), 3.30 (app t, 2H, *J* = 6.8 Hz, C*H*$_2$), 3.19 (app t, 2H, *J* = 6.4 Hz, C*H*$_2$N), 2.77 (app t, 2H, *J* = 6.8 Hz, C*H*$_2$), 2.62 (s, 3H, C*H*$_3$), 2.52 (dd, 1H, *J* = 12.2, 4.6 Hz, H-3$_{eq}$), 2.37 (s, 3H, C*H*$_3$), 1.87 (app t, 1H, *J* = 12.2 Hz, H-3$_{ax}$), 1.59–1.05 (m, 12H, octyl C*H*$_2$); ^{13}C NMR (D_2O, 125 MHz) δ_C 175.5 (C=O), 174.8 (C=O), 162.4 (Ar), 156.5 (Ar), 147.4 (Ar), 136.3 (Ar), 134.2 (Ar), 129.7 (Ar), 125.8 (Ar), 121.6 (Ar), 122.0 (Ar), 117.8 (Ar), 102.1 (C-2), 74.2 (C-6), 70.0 (C-7), 68.5 (C-4), 66.3 (C-5), 65.8 (O*C*H$_2$), 65.1 (C-8), 40.2 (*C*H$_2$), 35.8 (C-3), 30.0 (*C*H$_2$), 29.5 (octyl *C*H$_2$), 29.4 (octyl *C*H$_2$), 29.2 (octyl *C*H$_2$), 26.8 (octyl *C*H$_2$), 26.2 (octyl *C*H$_2$), 25.5 (octyl *C*H$_2$), 15.2 (*C*H$_3$), 11.5 (*C*H$_3$); HRMS (ESI) calcd. for $C_{30}H_{43}$[11B]$F_2N_3O_9$ $[M–H]^-$ 638.3066 found 638.3087.



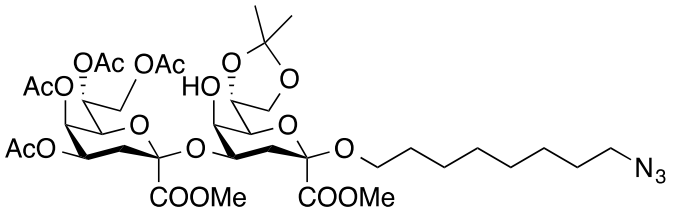
(8-Anisoylamidooctyl 3-deoxy-β-D-*manno*-2-octulopyranosid)onic acid (2.70). To a solution of **2.49** (26.6 mg, 0.073 mmol) in H_2O (1.0 mL) was added potassium carbonate (30.1 mg, 0.218 mmol) and *p*-anisoyl chloride (18.6 mg, 0.109 mmol) at room temperature. After 24 h, the reaction mixture was concentrated under reduced pressure. The resulting residue was purified by column chromatography (7:2:1, EtOAc–CH_3OH–H_2O) to give **2.70** (27.3 mg, 75%) as a white amorphous solid. $[\alpha]^{25}_D$ +6.0 (*c* 2.0, H_2O); R_f 0.16 (7:2:1:0.5, EtOAc–CH_3OH–H_2O–AcOH); ^{1}H NMR (CD_3OD, 500 MHz) δ_H 7.79–7.75 (m, 2H, ArH), 6.98–6.94 (m, 2H, ArH), 3.92–3.86 (m, 3H, H-5, H-7, H-8a), 3.83 (s, 3H, OC*H*$_3$), 3.71 (dt, 1H, *J* = 9.2, 7.2 Hz, octyl OC*H*$_2$), 3.68–3.62 (m, 2H, H-4, H-8b), 3.56 (d, 1H, *J* = 9.0 Hz, H-6), 3.43 (dt, 1H, *J* = 9.2, 7.2 Hz, octyl OC*H*$_2$), 3.33 (t, 2H, *J* = 7.2 Hz, C*H*$_2$N), 2.42 (dd, 1H, $J_{3eq,4}$ = 4.6 Hz, J_{gem} = 12.4 Hz, H-3$_{eq}$), 1.86 (app t, 1H, $J_{3ax,4} = J_{gem}$ = 12.4 Hz, H-3$_{ax}$), 1.63–1.55 (m, 2H, octyl C*H*$_2$), 1.55–1.48 (m, 2H, octyl C*H*$_2$), 1.40–1.29 (m, 8H, octyl C*H*$_2$); ^{13}C NMR (CD_3OD, 125 MHz) δ_C 169.8 (C=O), 163.8 (Ar), 130.1 (2C, Ar), 128.0 (Ar), 114.7 (2C, Ar), 75.1 (C-6), 70.8 (C-7), 69.4 (C-4), 67.2 (C-5), 65.8 (C-8), 65.1 (octyl O*C*H$_2$), 55.9 (O*C*H$_3$), 41.0 (*C*H$_2$N), 36.4 (C-3), 30.9 (octyl *C*H$_2$), 30.6 (octyl *C*H$_2$), 30.5 (octyl *C*H$_2$), 30.4 (octyl *C*H$_2$), 28.1 (octyl *C*H$_2$), 27.1 (octyl *C*H$_2$); HRMS (ESI) calcd. for $C_{24}H_{36}NO_{10}$ $[M–H]^+$ 498.2345 found 498.2337.



[8-(2-Naphthyl)amidooctyl 3-deoxy-β-D-*manno*-2-octulopyranosid]onic acid (2.71). To a solution of **2.49** (14.0 mg, 0.038 mmol) in H_2O (1.0 mL) was added potassium carbonate (15.9 mg, 0.115 mmol) and 2-naphthoyl chloride (11.0 mg, 0.058 mmol) at room temperature. After 24 h, the reaction mixture was concentrated under reduced pressure. The resulting residue was purified by column chromatography (7:2:1, EtOAc–CH_3OH–H_2O) to give **2.71** (23.5 mg, 61%) as a white amorphous solid. $[\alpha]^{25}_D$ +25.2 (*c* 0.5, CH_3OH); R_f 0.17 (7:2:1:0.5, EtOAc–CH_3OH–H_2O–AcOH); ^{1}H NMR (CD_3OD, 500 MHz) δ_H 8.34 (br s, 1H, ArH), 7.98–7.88 (m, 3H, ArH), 7.86 (dd, J = 8.7, 1.9 Hz, 1H, ArH), 7.58–7.52 (m, 2H, ArH), 3.93–3.86 (m, 3H, H-5, H-7, H-8a), 3.72 (dt, 1H, J = 9.1, 6.8 Hz, octyl OCH_2), 3.69–3.62 (m, 2H, H-4, H-8b), 3.56 (d, 1H, $J_{6,7}$ = 8.7 Hz, H-6), 3.43 (dt, 1H, J = 9.1, 6.8 Hz, octyl OCH_2), 3.41 (t, 2H, J = 7.3 Hz, octyl CH_2N), 2.43 (dd, 1H, $J_{3eq,4}$ = 4.5 Hz, J_{gem} = 12.0 Hz, H-3_{eq}), 1.87 (app t, 1H, $J_{3ax,4}$ = J_{gem} = 12.0 Hz, H-3_{ax}), 1.69–1.60 (m, 2H, octyl CH_2), 1.56–1.48 (m, 2H, octyl CH_2), 1.44–1.29 (m, 8H, octyl CH_2); ^{13}C NMR (CD_3OD, 125 MHz) δ_C 170.2 (C=O), 136.2 (Ar), 134.1 (Ar), 133.1 (Ar), 130.0 (Ar), 129.3 (Ar), 128.8 (Ar), 128.7 (Ar, 2C), 127.8 (Ar), 124.9 (Ar), 75.1 (C-6), 70.8 (C-7), 69.4 (C-4), 67.2 (C-5), 65.8 (C-8), 65.1 (octyl OCH_2), 41.2 (CH_2N), 36.4 (C-3), 30.9 (octyl CH_2), 30.5 (2C, octyl CH_2), 30.4 (octyl CH_2), 28.1 (octyl CH_2), 27.1 (octyl CH_2); HRMS (ESI) calcd. for $C_{27}H_{36}NO_9$ $[M–H]^-$ 518.2386 found 518.2389.

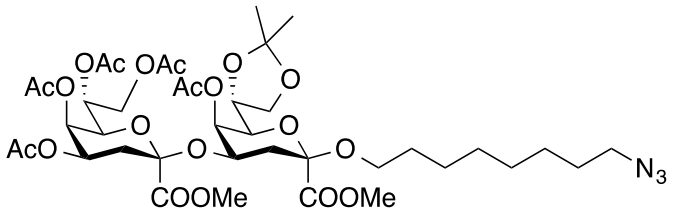


(8-Benzoylamidooctyl 3-deoxy-β-D-*manno*-2-octulopyranosid)onic acid (2.72). To a solution of **2.49** (22.0 mg, 0.060 mmol) in H_2O (1.0 mL) was added potassium carbonate (25.0 mg, 0.181 mmol) and benzoyl chloride (10.5 μL, 12.7 mg, 0.090 mmol) at room temperature. After 24 h, the reaction mixture was concentrated under reduced pressure. The resulting residue was purified by column chromatography (7:2:1, EtOAc–CH_3OH–H_2O) to give **2.72** (22.0 mg, 78%) as a white amorphous solid. $[\alpha]^{25}_D$ +23.8 (*c* 0.9, H_2O); R_f 0.14 (7:2:1:0.5, EtOAc–CH_3OH–H_2O–AcOH); ^{1}H NMR (D_2O, 500 MHz) δ_H 7.82–7.77 (m, 2H, ArH), 7.69–7.65 (m, 1H, ArH), 7.58 (t, 2H, J = 7.7 Hz, ArH), 4.01 (d, 1H, $J_{5,4}$ = 2.7 Hz, H-5), 4.00–3.93 (m, 2H, H-7, H-8a), 3.83–3.78 (m, 2H, H-4, H-8b), 3.75 (dt, 1H, J = 9.1, 6.6 Hz, octyl OCH_2), 3.69 (d, 1H, $J_{6,7}$ = 8.9 Hz, H-6), 3.47 (dt, 1H, J = 9.1, 6.6 Hz, octyl OCH_2), 3.43 (t, 2H, J = 6.9 Hz, 2H, CH_2N), 2.48 (dd, 1H, $J_{3eq,4}$ = 4.9 Hz, J_{gem} = 12.3 Hz, H-3$_{eq}$), 1.84 (app t, 1H, $J_{3ax,4}$ = J_{gem} = 12.3 Hz, H-3$_{ax}$), 1.71–1.62 (m, 2H, octyl CH_2), 1.62–1.55 (m, 2H, octyl CH_2), 1.46–1.31 (m, 8H, octyl CH_2); ^{13}C NMR (D_2O, 125 MHz) δ_C 174.9 (C-1, $J_{C1\text{-}H3ax}$ = 5.9 Hz), 171.8 (C=O), 134.9 (Ar), 132.9 (Ar), 129.7 (2C, Ar), 127.9 (2C, Ar), 102.1 (C-2), 74.3 (C-6), 70.0 (C-7), 68.5 (C-4), 66.3 (C-5), 65.8 (octyl O*C*H$_2$), 65.1 (C-8), 41.0 (*C*H$_2$N), 35.8 (C-3), 29.9 (octyl *C*H$_2$), 29.3 (3C, octyl *C*H$_2$), 27.0 (octyl *C*H$_2$), 26.0 (octyl *C*H$_2$); HRMS (ESI) calcd. for $C_{23}H_{34}NO_9$ $[M–H]^-$ 468.2239 found 468.2234.



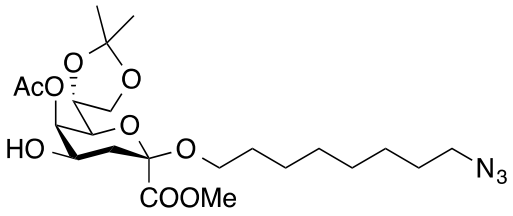
Methyl {(8-Azidooctyl 3-deoxy-7,8-*O*-isopropylidene-4-*O*-[methyl 4,5,7,8-tetra-*O*-acetyl-3-deoxy-β-D-manno-2-octulopyranosyl]onate)-β-D-*manno*-2-octulopyranosid}onate (2.73). A mixture of **2.37** (18 mg, 0.048 mmol) and **2.56** (18 mg, 0.0404 mmol) and 4Å molecular sieves (50 mg) in CH_2Cl_2–CH_3CN (1.0 mL, 2:3) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –70 °C before AgOTf (31 mg, 0.121 mmol) and IBr (16.7 mg, 0.0809 mmol) were added at –70 °C. After 1 h, triethylamine was added to the reaction mixture. The reaction was warmed to room temperature and then a small amount of H_2O was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The mixture was dried with $MgSO_4$ and then filtered and concentrated under reduced pressure. The mixture was filtered and concentrated under reduced pressure and the resulting residue was purified by column chromatography (hexane–EtOAc) to give **2.73** (13.7 mg, 41%) as a colorless oil. R_f 0.28 (4:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 5.26 (br s, 1H, H-5'), 5.09 (ddd, 1H, $J_{7',6'}$ = 9.6 Hz, $J_{7',8'a}$ = 3.3 Hz, $J_{7',8'b}$ = 1.8 Hz, H-7'), 4.83 (ddd, 1H, $J_{4',3'eq}$ = 4.6 Hz, $J_{4',3'ax}$ = 13.2 Hz, $J_{4',5'}$ = 3.0 Hz, H-4'), 4.66 (dd, 1H, $J_{8'a,7'}$ = 3.3 Hz, J_{gem} = 12.6 Hz, H-8'a), 4.37 (ddd, $J_{7,6}$ = 8.6 Hz, $J_{7,8a}$ = 6.0 Hz, $J_{7,8b}$ = 4.8 Hz, 1H, H-7), 4.27 (dd, 1H, $J_{6',5'}$ = 1.4 Hz, $J_{6',7'}$ = 9.6 Hz, H-6'), 4.16–4.08 (m, 2H, H-8a, H-8b), 4.04–4.01 (m, 1H, H-5), 3.91 (dd, 1H, $J_{8'b,7'}$ = 1.8 Hz, J_{gem} = 12.6 Hz, H-8'b), 3.87–3.76 (m, 7H, COOC*H*$_3$, H-4), 3.70 (dt, 1H, J = 9.1, 6.6 Hz, octyl OC*H*$_2$), 3.52 (d, 1H, $J_{6,7}$ = 8.6 Hz, H-6), 3.35 (dt, 1H, J = 9.1, 6.6 Hz, octyl OC*H*$_2$), 3.24 (t, 2H, J = 6.9 Hz, C*H*$_2$N$_3$), 2.36 (dd, 1H, J_{gem} = 12.6, $J_{3'eq,4'}$ = 4.6 Hz, H-3'$_{eq}$), 2.21 (br s, 1H, OH), 2.12 (s, 3H, COC*H*$_3$), 2.11 (s, 3H, COC*H*$_3$), 2.16–2.02 (m, 3H, H-3$_{eq}$, H-3'$_{ax}$, H-3$_{ax}$), 2.00 (s, 3H, COC*H*$_3$),

1.97 (s, 3H, COCH_3), 1.61–1.48 (m, 4H, octyl CH_2), 1.41 (s, 3H, (CH_3)$_2$C), 1.38–1.25 (m, 11H, octyl CH_2, (CH_3)$_2$C); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 170.6 (C=O), 170.4 (C=O), 170.05 (C=O), 170.0 (C=O), 169.0 (C-1', $J_{C1'\text{-}H3'ax}$ = 6.9 Hz), 168.2 (C-1, $J_{C1\text{-}H3ax}$ = 6.5 Hz), 109.7 ((CH$_3$)$_2$*C*), 100.1 (C-2'), 99.6 (C-2), 75.1 (C-6), 73.3 (C-7), 71.7 (C-4), 70.6 (C-6'), 68.5 (C-7'), 67.6 (C-8), 67.0 (C-4'), 66.8 (C-5), 64.2 (octyl O*C*H$_2$), 64.1 (C-5'), 61.4 (C-8'), 53.1 (COO*C*H$_3$), 52.6 (COO*C*H$_3$), 51.7 (*C*H$_2$N$_3$), 32.8 (C-3 or C-3'), 32.6 (C-3' or C-3), 29.7 (octyl *C*H$_2$), 29.3 (octyl *C*H$_2$), 29.2 (octyl *C*H$_2$), 29.0 (octyl *C*H$_2$), 26.8 (2C, octyl *C*H$_2$, (*C*H$_3$)$_2$C), 26.0 (octyl *C*H$_2$), 25.5 ((*C*H$_3$)$_2$C), 21.0 (CO*C*H$_3$), 20.92 (CO*C*H$_3$), 20.90 (2C, CO*C*H$_3$); HRMS (ESI) calcd. for $C_{37}H_{57}N_3NaO_{19}$ $[M+Na]^+$ 870.3484 found 870.3486.



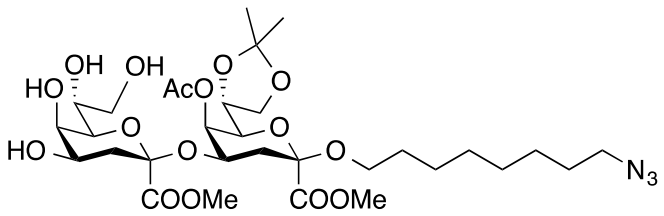
Methyl {(8-Azidooctyl 5-*O*-acetyl-3-deoxy-7,8-*O*-isopropylidene-4-*O*-[methyl 4,5,7,8-tetra-*O*-acetyl-3-deoxy-β-D-manno-2-octulopyranosyl]onate)-β-D-*manno*-2-octulopyranosid}onate (2.75). A mixture of **2.37** (57.0 mg, 0.123 mmol) and **2.76** (50.0 mg, 0.112 mmol) and 4Å molecular sieve (100 mg) in CH_2Cl_2–CH_3CN (5.0 mL, 2:3) was stirred under Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –70 °C and NIS (33.2 mg, 0.148 mmol) and TfOH (1.1 μL, 1.8 mg, 0.0123 mmol) were added at –70 °C. After stirring for 1 h, triethylamine was added to the reaction mixture. The reaction was warmed to room temperature and then a small amount of H_2O was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The mixture was dried with $MgSO_4$ and then filtered and concentrated under reduced pressure. The resulting mixture was filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography (4:1, hexane–

EtOAc) to give **2.75** (69.8 mg, 70%) as a colorless oil. $[\alpha]^{25}_{D}$ +135.8 (*c* 3.0, $CHCl_3$); R_f 0.28 (4:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 5.35 (d, 1H, $J_{5',4'}$ = 2.8 Hz, H-5'), 5.30 (d, 1H, $J_{5,4}$ = 2.8 Hz, H-5), 5.26–5.21 (m, 2H, H-4', H-7'), 4.71 (dd, 1H, J_{gem} = 12.1 Hz, $J_{8'a,7}$ = 2.8 Hz, H-8'a), 4.17 (dd, 1H, $J_{6',5'}$ = 1.5 Hz, $J_{6',7'}$ = 9.6 Hz, H-6'), 4.14–4.12 (m, 1H, H-4), 4.11–4.03 (m, 4H, H-7, H-8a, H-8b, H-8'b), 3.85 (s, 3H, COOC*H*$_3$), 3.81 (s, 3H, COOC*H*$_3$), 3.73 (dt, 1H, *J* = 9.0, 6.6 Hz, octyl OC*H*$_2$), 3.52 (d, 1H, $J_{6,7}$ = 7.5 Hz, H-6), 3.35 (dt, 1H, *J* = 9.0, 6.6 Hz, octyl OC*H*$_2$), 3.27 (t, 2H, *J* = 7.0 Hz, C*H*$_2$N$_3$), 2.44 (dd, 1H, $J_{3eq,4}$ = 4.9 Hz, J_{gem} = 12.6 Hz, H-3$_{eq}$), 2.16 (s, 3H, COC*H*$_3$), 2.14–2.09 (m, 2H, H-3'$_{eq}$, H-3'$_{ax}$), 2.08 (s, 3H, COC*H*$_3$), 2.07 (s, 3H, COC*H*$_3$), 2.07 (m, 1H, H-3$_{ax}$), 2.01 (s, 3H, COC*H*$_3$), 2.00 (s, 3H, COC*H*$_3$), 1.64–1.58 (m, 2H, octyl C*H*$_2$), 1.57–1.51 (m, 2H, octyl C*H*$_2$), 1.40 (s, 3H, (C*H*$_3$)$_2$C), 1.39–1.29 (m, 11H, octyl C*H*$_2$, (C*H*$_3$)$_2$C); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 170.6 (C=O), 170.4 (C=O), 170.0 (C=O), 169.7 (C=O), 169.6 (C=O), 168.8 (C-1', $J_{C1\text{-}H3ax}$ = 6.5 Hz), 167.0, 109.5 ((CH$_3$)$_2$*C*), 99.3 (C-2'), 98.6 (C-2), 74.4 (C-6), 73.1 (C-7), 69.7 (C-6'), 68.8 (C-4), 67.7 (C-7'), 67.0 (C-8), 66.2 (C-5), 66.1 (C-4'), 64.3 (2C, C-5', octyl O*C*H$_2$), 62.1 (C-8'), 52.8 (COO*C*H$_3$), 52.7 (COO*C*H$_3$), 51.5 (*C*H$_2$N$_3$), 34.2 (C-3), 31.9 (C-3'), 29.6 (octyl *C*H$_2$), 29.2 (octyl *C*H$_2$), 29.1 (octyl *C*H$_2$), 28.8 (octyl *C*H$_2$), 26.9 ((*C*H$_3$)$_2$C), 26.7 (octyl *C*H$_2$), 25.8 (octyl *C*H$_2$), 25.2 ((*C*H$_3$)$_2$C), 20.9 (CO*C*H$_3$), 20.8 (2C, CO*C*H$_3$), 20.7 (2C, CO*C*H$_3$); HRMS (ESI) calcd. for $C_{39}H_{59}N_3NaO_{20}$ $[M+Na]^+$ 912.3584 found 912.3598.



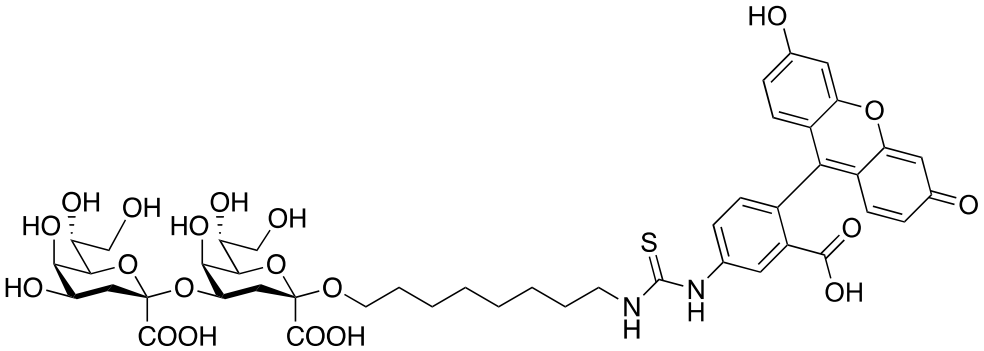
Methyl (8-Azidooctyl 5-*O*-acetyl-3-deoxy-7,8-*O*-isopropylidene-β-D-*manno*-2-octulopyranosid)-onate (2.76). To a solution of **2.56** (900 mg, 2.02 mmol) in acetonitrile (20 mL) was added trimethylorthoacetate (386 μL, 364 mg, 3.03 mmol) and 10-camphorsulphonic acid (94 mg, 0.404 mmol) at room temperature. After 30 min, the reaction mixture was neutralized by the addition of triethylamine. The reaction mixture was then diluted with EtOAc and washed with H_2O. The aqueous layers were extracted with EtOAc, and the combined organic layers were further washed with 1N HCl. The resulting organic layer was washed with satd. aq. $NaHCO_3$, dried with $MgSO_4$, filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography (2:1, hexane–EtOAc) to give **2.76** (788 mg, 80% over two steps) as a colorless oil. $[\alpha]^{25}_D$ +6.8 (*c* 0.8, $CHCl_3$); R_f 0.31 (2:1 hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 5.26 (d, 1H, $J_{5,4}$ = 2.6 Hz, H-5), 4.16–4.08 (m, 3H, H-7, H-8a, H-8b), 3.91–3.84 (m, 1H, H-4), 3.80 (s, 3H, COOC*H*$_3$), 3.70 (dt, 1H, *J* = 9.5, 6.8 Hz, octyl OC*H*$_2$), 3.68 (d, 1H, $J_{6,7}$ = 7.9 Hz, H-6), 3.30 (dt, 1H, *J* = 9.5, 6.8 Hz, octyl OC*H*$_2$), 3.25 (t, 2H, *J* = 6.8 Hz, C*H*$_2$N$_3$), 2.43 (dd, 1H, $J_{3eq,4}$ = 4.5 Hz, J_{gem} = 12.8 Hz, H-3$_{eq}$), 2.40–2.37 (m, 1H, OH), 2.18 (s, 3H, COC*H*$_3$), 1.92 (app t, 1H, $J_{3ax,4} = J_{gem}$ = 12.8 Hz, H-3$_{ax}$), 1.63–1.51 (m, 4H, octyl C*H*$_2$), 1.40 (s, 3H, (C*H*$_3$)$_2$C), 1.34 (s, 3H, (C*H*$_3$)$_2$C), 1.40–1.28 (m, 8H, octyl C*H*$_2$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 172.4 (C=O), 169.0 (C-1), 109.6 ((CH$_3$)$_2$*C*), 99.6 (C-2), 74.5 (C-6), 73.0 (C-7), 68.9 (C-8), 67.4 (C-4), 67.2 (C-5), 64.5 (octyl OC*H*$_2$), 52.7 (COO*C*H$_3$), 51.6 (*C*H$_2$N$_3$), 34.9 (C-3), 29.6 (octyl *C*H$_2$), 29.2 (octyl *C*H$_2$), 29.1 (octyl *C*H$_2$), 28.8 (octyl *C*H$_2$), 26.9 (octyl *C*H$_2$), 26.7

((CH_3)$_2$C), 25.8 ((CH_3)$_2$C), 25.2(octyl CH_2) 21.0 (COCH_3); HRMS (ESI) calcd. for $C_{22}H_{37}N_3NaO_9$ $[M+Na]^+$ 510.2422 found 510.2423.



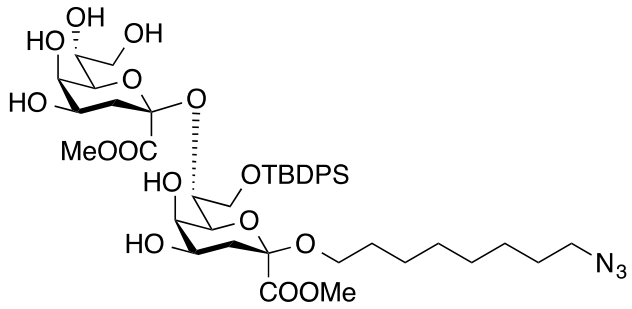
Methyl {(8-Azidooctyl 5-*O*-acetyl-3-deoxy-7,8-*O*-isopropylidene-4-*O*-[methyl 3-deoxy-β-D-*manno*-2-octulopyranosyl]onate)-β-D-*manno*-2-octulopyranosid}onate (2.77). To a solution of **2.75** (40.0 mg, 0.044 mmol) in CH_3OH (1.0 mL) was added sodium methoxide (0.2 mg, 4.4 μmol) at room temperature. After 24 h, the reaction mixture was neutralized by the addition of Amberlite IR-120 H^+ resin. The mixture was filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography (1:15, CH_3OH–CH_2Cl_2) to give **2.77** (30.5 mg, 95%) as a colorless amorphous solid. $[\alpha]^{25}_D$ +27.5 (*c* 1.0, $CHCl_3$); R_f 0.21 (1:15, CH_3OH–CH_2Cl_2); ^{1}H NMR (CD_3OD, 500 MHz) δ_H 5.36 (d, 1H, $J_{5,4}$ = 2.7 Hz, H-5), 4.19 (ddd, 1H, $J_{4,3eq}$ = 4.6 Hz, $J_{4,3ax}$ = 13.0 Hz, $J_{4,5}$ = 2.7 Hz, H-4), 4.11–4.00 (m, 3H, H-7, H-8a, H-8b), 3.90 (ddd, 1H, $J_{7',6'}$ = 8.7, $J_{7',8'a}$ = 3.0 Hz, $J_{7',8'b}$ = 5.7 Hz, 1H, H-7') 3.87 (d, 1H, $J_{5',4'}$ = 2.8 Hz, H-5'), 3.82 (s, 3H, COOCH_3), 3.79 (s, 3H, COOCH_3), 3.76 (dd, 1H, *J* = 11.6, 3.0 Hz, H-8'a), 3.69 (dt, 1H, *J* = 9.0, 6.3 Hz, octyl OCH_2), 3.66 (d, *J* = 8.0 Hz, 1H, H-6), 3.64–3.58 (m, 2H, H-4', H-8'b), 3.44 (d, 1H, *J* = 8.7 Hz, 1H, H-6'), 3.31 (dt, 1H, *J* = 9.0, 6.3 Hz, octyl OCH_2), 3.27 (t, 2H, *J* = 6.9 Hz, CH_2N$_3$), 2.29 (dd, 1H, $J_{3'eq,4}$ = 4.8 Hz, J_{gem} = 12.5 Hz, H-3$_{eq}$'), 2.18 (dd, 1H, $J_{3'ax,4}$ = 4.8 Hz, J_{gem} = 13.0 Hz, H-3$_{eq}$), 2.12 (s, 3H, COCH_3), 1.90 (app t, 1H, J_{gem} = $J_{3ax,4}$ = 13.0 Hz, 1H, H-3$_{ax}$), 1.80 (app t, 1H, J_{gem} = $J_{3'ax,4}$ = 12.5 Hz, H-3$_{ax}$'), 1.62–1.55 (m, 2H, octyl CH_2), 1.54–1.46 (m, 2H, octyl CH_2), 1.41–1.27 (m, 8H, octyl CH_2), 1.37 (s, 3H, (CH_3)$_2$C), 1.29 (s, 3H, (CH_3)$_2$C); ^{13}C NMR (CD_3OD, 125 MHz) δ_C 172.0 (C=O), 170.7 (C-1), 170.1 (C-1'), 110.8

(($CH_3)_2C$), 100.8 (C-2), 100.7 (C-2'), 76.5 (C-6'), 75.9 (C-6), 74.5 (C-7), 70.7 (C-7'), 70.1 (C-5), 69.1 (C-4), 68.4 (C-4'), 68.1 (C-8), 67.5 (C-5'), 65.2 (octyl OCH_2), 65.0 (C-8'), 53.2 (CH_2N_3), 53.1 (COOCH_3), 52.5 (COOCH_3), 35.5 (C-3'), 35.3 (C-3), 30.6 (octyl CH_2), 30.2 (2C, octyl CH_2), 29.9 (octyl CH_2), 27.8 (octyl CH_2), 27.3 (octyl CH_2), 26.9 (($CH_3)_2$C), 25.4 (($CH_3)_2$C), 20.9 (COCH_3); HRMS (ESI) calcd. for $C_{31}H_{51}N_3NaO_{16}$ $[M+Na]^+$ 744.3162 found 744.3164.



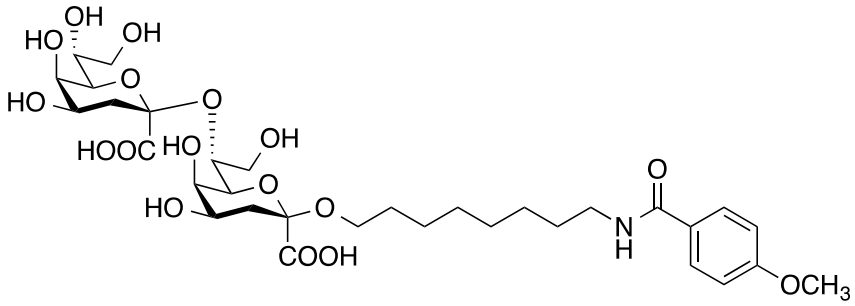
8-Aminooctyl [3-deoxy-4-*O*-(3-deoxy-β-D-*manno*-2-octulopyranosyl)onic acid]-β-D-*manno*-2-octulopyranosidonic acid, FITC conjugate (2.78). To a solution of amine **2.50** (3.5 mg, 5.9 μmol) in H_2O (1.0 mL) and DMF (0.05 mL) at 0 °C was added sodium bicarbonate (1.7 mg, 0.021 mmol) and FITC (3.5 mg, 8.9 μmol). After stirring at 0 °C for 2 h, the reaction mixture was concentrated under reduced pressure. The resulting residue was purified by column chromatography (5:2:1, EtOAc–CH_3OH–H_2O) and size exclusion chromatography (Sephadex LH-20, 1:1, CH_2Cl_2–CH_3OH) to give **2.78** (2.8 mg, 74%) as an orange amorphous solid. $[\alpha]^{25}_D$ +2.7 (*c* 0.1, H_2O); R_f 0.24 (5:2:1:0.5, EtOAc–CH_3OH–H_2O–HOAc) ^{1}H NMR (D_2O, 700 MHz) δ_H 7.95 (s, 1H, Ar), 7.76–7.67 (m, 1H, Ar), 7.38 (d, 1H, J = 8.4 Hz, Ar), 7.35–7.25 (m, 2H, Ar), 6.71–6.63 (m, 4H, Ar), 4.12–4.07 (ddd, 1H, J = 11.7, 5.0, 2.8 Hz, H-4), 4.05 (br s, 1H, H-5), 3.99 (br s, 1H, H-5'), 3.98–3.96 (m, 1H, H-7), 3.93–3.83 (m, 4H, H-8a, H-7', H-8'a, H-8b), 3.76–3.59 (m, 6H, H-4', H-6, H-8'b, OCH_2, CH_2N), 3.57 (d, 1H, J = 8.5 Hz, H-6'), 3.44–3.38 (m, 1H, OCH_2), 2.35 (dd, 1H, J = 12.2, 4.7 Hz, H-3_{eq}'), 2.14 (dd, 1H, J = 13.5, 5.0 Hz, H-3_{eq}), 1.87 (app t, 1H, J

= 12.2 Hz, H-3_{ax}'), 1.78 (app t, 1H, J = 13.5 Hz, H-3_{ax}), 1.70–1.60 (m, 2H, octyl CH_2), 1.59–1.50 (m, 2H, octyl CH_2), 1.41–1.29 (m, 8H, octyl CH_2); HRMS (ESI) calcd. for $C_{45}H_{53}N_2O_{20}S$ [M–H]$^-$ 973.2918 found 973.2922.



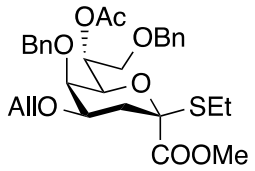
Methyl {(8-Azidooctyl 8-*O*-*tert*-butyldiphenyl-3-deoxy-7-*O*-[methyl 3-deoxy-β-D-*manno*-2-octulopyranosyl]onate)-β-D-*manno*-2-octulopyranosid}onate (**2.80**). A mixture of thioglycoside **2.37** (30.0 mg, 0.0439 mmol) and **2.57** (81.5 mg, 0.175 mmol) and 4Å molecular sieves (100 mg) in CH_2Cl_2–CH_3CN (2:3, 1.5 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –70 °C and then NIS (79.0 mg, 0.351 mmol) and TfOH (0.39 μL, 0.66 mg, 4.39 μmol) were added. After stirring at –70 °C for 1 h, trimethylamine was added to the reaction mixture. The reaction was warmed to room temperature and then a small amount of H_2O was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The mixture was dried with $MgSO_4$ and then filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography (4:1, hexane–EtOAc) to give a mixture of **2.79** and **2.74**. To a solution of the mixture of **2.74** and **2.79** (19.5 mg, 0.018 mmol) in CH_3OH (1.0 mL) was added sodium methoxide (0.1 mg, 1.8 μmol) at room temperature. After 24 h, the reaction mixture was neutralized by the addition of Amberlite IR-120 H^+ resin. The mixture was filtered and the filtrate concentrated under reduced pressure. The residue was triturated with EtOAc to remove most of deacetylated glycal **2.74** that was formed in the previous glycosylation step. The glycal is insoluble in EtOAc. The solution was filtered and the filtrate

was concentrated under reduced pressure. The residue was then dissolved in CH_3OH (2.0 mL) and treated with 1N HCl (0.5 mL) at room temperature. After 24 h, the reaction mixture was diluted with CH_2Cl_2 and washed with satd. aq. $NaHCO_3$ and H_2O. The organic layer was then dried with $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure and the residue was purified by column chromatography (1:9 CH_3OH–EtOAc) to give **2.80** (10.1 mg, 64% over two steps) as a colorless oil. $[\alpha]^{25}_D$ +21.8 (*c* 0.17, CH_3OH); R_f 0.17 (1:9 CH_3OH–EtOAc); ^1H NMR (CD_3OD, 500 MHz) δ_H 7.74–7.69 (m, 4H, ArH), 7.46–7.32 (m, 6H, ArH), 4.37 (dt, 1H, $J_{7,6}$ = 8.0 Hz, $J_{7,8a}$ = $J_{7,8b}$ = 2.5 Hz, H-7), 4.15 (d, 1H, $J_{6,7}$ = 8.0 Hz, H-6), 4.01 (d, 1H, $J_{5,4}$ = 3.0 Hz, H-5), 3.94–3.83 (m, 3H, H-8a, H-6', H-7'), 3.79–3.75 (m, 1H, H-8'a), 3.72–3.64 (m, 3H, H-4, H-8b, octyl OC*H*$_2$), 3.63 (s, 3H, COOC*H*$_3$), 3.62–3.54 (m, 2H, H-4', H-8'b), 3.40-3.35 (m, 5H, H-5', COOC*H*$_3$, octyl OC*H*$_2$), 3.23 (t, 2H, *J* = 7.0 Hz, C*H*$_2$N$_3$), 2.47 (dd, 1H, *J* = 12.5, 4.5 Hz, H-3$_{eq}$'), 2.18 (dd, 1H, *J* = 12.5, 4.5 Hz, H-3$_{eq}$), 2.09 (app t, 1H, *J* = 12.5 Hz, H-3$_{ax}$'), 2.03 (app t, 1H, *J* = 12.5 Hz, H-3$_{ax}$), 1.62–1.44 (m, 4H, octyl C*H*$_2$), 1.38–1.22 (m, 8H, octyl C*H*$_2$), 1.05 (s, 9H, C(C*H*$_3$)$_3$); ^{13}C NMR (CD_3OD, 125 MHz) δ_C 171.0 (C-1), 170.0 (C-1'), 137.0 (Ar), 136.9 (Ar), 135.1 (Ar), 134.7 (Ar), 130.8 (Ar), 130.7 (Ar), 128.8 (Ar), 128.6 (Ar), 100.9 (C-2), 100.5 (C-2'), 76.1 (C-5'), 74.7 (C-6), 74.4 (C-7), 71.7 (C-7'), 68.4 (C-4'), 68.2 (C-4), 67.21 (C-5), 67.17 (C-6'), 65.07 (C-8'), 65.00 (octyl O*C*H$_2$), 64.0 (C-8), 53.0 (COO*C*H$_3$), 53.7 (COO*C*H$_3$), 52.4 (CH$_2$N$_3$), 36.4 (C-3), 35.8 (C-3'), 30.8 (octyl *C*H$_2$), 30.22 (octyl *C*H$_2$), 30.19 (octyl *C*H$_2$), 29.9 (octyl *C*H$_2$), 27.8 (octyl *C*H$_2$), 27.5 (octyl *C*H$_2$), 26.9 (C(*C*H$_3$)$_3$), 20.3 (*C*(CH$_3$)$_3$); HRMS (ESI) calcd. for $C_{42}H_{63}N_3NaO_{15}Si$ $[M+Na]^+$ 900.3920; found 900.3912.



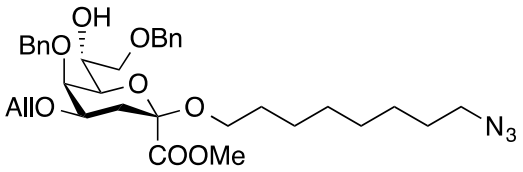
[8-Aniosoylamidooctyl 3-deoxy-7-*O*-(3-deoxy-β-D-*manno*-2-octulopyranosyl)onic acid]-β-D-*manno*-2-octulopyranosid]onic acid (2.82). To a solution of **2.51** (10.0 mg, 0.0171 mmol) in H_2O (1 mL) was added potassium carbonate (9.4 mg, 0.0683 mmol) and *p*-anisoyl chloride (4.4 mg, 0.0256 mmol) at room temperature. After stirring for 24 h, the reaction mixture was concentrated under reduced pressure. The resulting residue was purified by column chromatography (5:2:1 EtOAc–CH_3OH–H_2O) followed by size exclusion column chromatography (LH-20) using the eluant (1:1, CH_3OH–H_2O) to give **2.82** (10.2 mg, 83%) as an amorphous solid. $[\alpha]^{25}_D$ +10.6 (*c* 0.1, H_2O); R_f 0.15 (5:2:1:0.5 EtOAc–CH_3OH–H_2O–AcOH); ^{1}H NMR (D_2O, 700 MHz) δ_H 7.78 (d, 2H, *J* = 8.9 Hz, ArH), 7.11 (d, 2H, *J* = 8.9 Hz, ArH), 4.45–4.43 (m, 1H, H-7), 4.05 (d, 1H, *J* = 2.6 Hz, H-5), 4.01–3.97 (m, 3H, H-5', H-7', H-8'a), 3.94–3.91 (m, 4H, OC*H*$_3$, H-8a), 3.85–3.70 (m, 5H, H-4, H-8b, H-4', H-8'b, OC*H*$_2$), 3.65 (d, 1H, *J* = 9.4 Hz, H-6), 3.51 (d, 1H, *J* = 8.8 Hz, H-6'), 3.45 (dt, 1H, *J* = 9.1, 6.9 Hz, OC*H*$_2$), 3.40 (t, 2H, *J* = 7.7 Hz, C*H*$_2$N), 2.48 (dd, 1H, *J* = 12.1, 4.6 Hz, H-3$_{eq}$'), 2.46 (dd, 1H, *J* = 12.1, 4.6 Hz, H-3$_{eq}$), 1.90 (app t, 1H, *J* = 12.1 Hz, H-3$_{ax}$'), 1.83 (app t, 1H, *J* = 12.1 Hz, H-3$_{ax}$), 1.67–1.61 (m, 2H, octyl C*H*$_2$), 1.60–1.54 (m, 2H, octyl C*H*$_2$), 1.44–1.31 (m, 8H, octyl C*H*$_2$); ^{13}C NMR (D_2O, 125 MHz) δ_C 174.88 (C-1 or C-1'), 174.81 (C-1' or C-1), 171.0 (C=O), 162.6 (Ar), 129.8 (Ar), 127.3 (Ar), 114.9 (Ar), 101.9 (C-2), 101.3 (C-2'), 74.3 (C-6'), 73.0 (C-6), 71.9 (C-7), 70.1 (C-7'), 68.40 (C-4 or C-4'), 68.36 (C-4' or C-4), 66.2 (C-5'), 65.78 (C-5), 65.71 (octyl O*C*H$_2$), 64.9 (C-8'), 63.0 (C-8), 56.4 (O*C*H$_3$), 40.8 (*C*H$_2$N), 35.6 (C-3), 35.1 (C-3'), 29.8 (octyl *C*H$_2$), 29.18 (octyl *C*H$_2$), 29.14 (octyl *C*H$_2$), 29.11

(octyl CH_2), 26.9 (octyl CH_2), 25.9 (octyl CH_2); HRMS (ESI) calcd. for $C_{32}H_{48}NO_{17}$ $[M–H]^-$ 718.2928; found 718.2915.



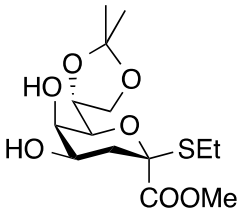
Methyl (Ethyl 7-*O*-acetyl-4-*O*-allyl-5,8-di-*O*-benzyl-3-deoxy-2-thio-β-D-*manno*-oct-2-ulopyranoside)onate (2.85). To a solution of **2.102** (120 mg, 0.232 mmol) in CH_2Cl_2 (2.3 mL) was added triethylamine (38.7 μL, 0.279 mmol), acetic anhydride (24.1 μL, 0.256 mmol) and DMAP (2.8 mg, 0.0232 mmol) sequentially. After 30 min, CH_3OH (1 mL) was added to the reaction mixture and then the solutioin was concentrated under reduced pressure. The residue was diluted with EtOAc and washed with H_2O. The organic layers were dried with $MgSO_4$ and then filtered. The filtrate was concentrated under reduced pressure and the residue was purified by column chromatography (8:1, hexane–EtOAc) to give **2.85** (125 mg, 97%) as an oil. $[\alpha]^{25}_D$ –21.6 (*c* 1.1, $CHCl_3$); R_f 0.27 (8:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.38–7.22 (m, 10H, ArH), 5.96–5.87 (m, 1H, OCH_2CH=CH_2), 5.38–5.28 (m, 2H, OCH_2CH=CH_2, H-7), 5.23–5.20 (m, 1H, OCH_2CH=CH_2), 4.89 (d, 1H, J_{gem} = 11.0 Hz, ArCH_2), 4.56 (s, 2H, ArCH_2), 4.53 (d, 1H, J = 11.0 Hz, ArCH_2), 4.14–4.07 (m, 1H, OCH_2CH=CH_2), 4.04–4.01 (m, 1H, OCH_2CH=CH_2), 3.90 (dd, 1H, $J_{8,7}$ = 2.5 Hz, J_{gem} = 11.2 Hz, H-8a), 3.80 (br s, 1H, H-5), 3.77–3.71 (m, 5H, H-6, H-8b, OCH_3), 3.45 (ddd, 1H, $J_{4,3ax}$ = 12.0 Hz, $J_{4,3eq}$ = 4.0, $J_{4,5}$ = 2.4 Hz, H-4), 2.73 (dq, 1H, J = 7.6 Hz, J_{gem} = 12.5 Hz, SCH_2), 2.65–2.55 (m, 2H, H-3_{eq}, SCH_2), 2.30 (app t, 1H, $J_{3ax,4}$ = J_{gem} = 12.0 Hz, H-3_{ax}), 1.99 (s, 3H, COCH_3), 1.18 (app t, 3H, J = 7.6 Hz, SCH_2CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 169.9 (C-1, $J_{C1\text{-}H3ax}$ = 8.4 Hz), 169.7 (C=O), 138.5 (Ar), 138.4 (Ar), 134.6 (OCH_2CH=CH_2), 128.6 (2C, Ar), 128.4 (2C, Ar), 128.3 (2C, Ar), 127.8 (2C, Ar), 127.66 (Ar), 127.65 (Ar), 117.1 (OCH_2CH=CH_2), 84.5 (C-2), 76.5 (C-4), 74.7 (C-6), 74.2 (ArCH_2), 73.4

(Ar*C*H_2), 71.0 (C-5), 70.8 (C-7), 69.5 (O*C*H_2CH=CH_2), 68.4 (C-8), 52.7 (O*C*H_3), 33.1 (C-3), 23.5 (S*C*H_2), 21.2 (CO*C*H_3), 14.4 (SCH_2*C*H_3); HRMS (ESI) calcd. for $C_{30}H_{42}NO_8S$ $[M+NH_4]^+$ 576.2626 found 576.2619.



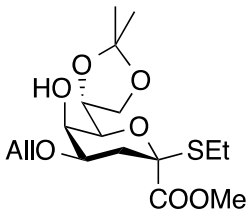
Methyl (8-Azidooctyl 4-*O*-allyl-5,8-di-*O*-benzyl-3-deoxy-β-D-*manno*-oct-2-ulopyranoside)onate (2.88). To a solution of **2.106** (80 mg, 0.107 mmol) in CH_3OH (1.0 mL) was added sodium methoxide (0.43 mg, 0.0107 mmol) at room temperature. After 24 h, the reaction mixture was neutralized with the addition of IR-120 H^+ and then filtered. The filtrate was concentrated and the resulting residue was purified by column chromatography (4:1, hexane–EtOAc) to give **2.88** (63.5 mg, 95%) as a colorless oil. $[\alpha]^{25}_D$ +20.7 (*c* 1.3, $CHCl_3$); R_f 0.20 (4:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.43–7.25 (m, 10H, ArH), 5.92–5.84 (m, 1H, OCH_2CH=CH_2), 5.30–5.25 (m, 1H, OCH_2CH=CH_2), 5.19–5.15 (m, 1H, OCH_2CH=CH_2), 4.92 (d, 1H, J_{gem} = 11.7 Hz, ArCH_2), 4.71 (d, 1H, J_{gem} = 11.7 Hz, ArCH_2), 4.60 (d, 1H, J_{gem} = 11.7 Hz, ArCH_2), 4.56 (d, 1H, J_{gem} = 11.7 Hz, ArCH_2), 4.11–4.04 (m, 1H, H-7), 4.03 (m, 2H, OCH_2CH=CH_2), 4.00 (br s, 1H, H-5), 3.79 (dd, 1H, $J_{8a,7}$ = 3.1 Hz, J_{gem} = 9.8 Hz, H-8a), 3.74 (s, 3H, COOCH_3), 3.68–3.60 (m, 2H, OCH_2, H-8b), 3.55 (dd, 1H, $J_{6.5}$ = 1.1 Hz, $J_{6,7}$ = 8.8 Hz, H-6), 3.42 (ddd, 1H, $J_{4,3eq}$ = 4.2 Hz, $J_{4,3ax}$ = 12.6 Hz, $J_{4,5}$ = 2.5 Hz, H-4), 3.29 (app dt, 1H, *J* = 9.1, 6.8 Hz, OCH_2), 3.23 (t, 2H, *J* = 7.0 Hz, CH_2N_3), 2.43 (dd, 1H, $J_{3eq,4}$ = 4.2 Hz, J_{gem} = 12.6 Hz, H-3_{eq}), 2.36 (d, 1H, $J_{OH,7}$ = 5.2 Hz, 7-OH), 2.25 (app t, 1H, $J_{3ax,4}$ = J_{gem} = 12.6 Hz, H-3_{ax}), 1.99 (s, 3H, COCH_3), 1.64–1.48 (m, 4H, octyl CH_2), 1.38–1.25 (m, 8H, octyl CH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 169.8 (C-1, $J_{C1\text{-}H3ax}$ = 6.9 Hz), 139.2 (Ar), 138.3 (Ar), 134.7 (OCH_2*C*H=CH_2), 128.6 (2C, Ar), 128.4 (2C, Ar), 128. 3 (2C, Ar), 127.93 (2C, Ar), 127.88 (Ar), 127.7 (Ar), 117.0

($OCH_2CH{=}CH_2$), 99.9 (C-2), 76.0 (C-4), 75.1 (C-6), 74.3 ($ArCH_2$), 73.6 ($ArCH_2$), 71.6 (C-8), 70.9 (C-5), 69.4 ($OCH_2CH{=}CH_2$), 68.4 (C-7), 64.3 (OCH_2), 52.4 ($COOCH_3$), 51.6 (CH_2N_3), 32.9 (C-3), 29.8 (octyl CH_2), 29.4 (octyl CH_2), 29.33 (octyl CH_2), 29.28 (octyl CH_2), 26.8 (octyl CH_2), 26.0 (octyl CH_2); HRMS (ESI) calcd. for $C_{34}H_{47}NaN_3O_8$ $[M+Na]^+$ 648.3255 found 648.3252.



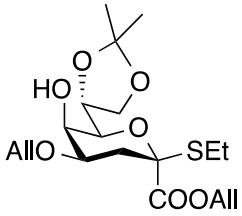
Methyl (Ethyl 3-deoxy-7,8-*O*-isopropylidene-2-thio-β-D-*manno*-oct-2-ulopyranoside)onate (2.91β). To a solution of **2.37** (138 mg, 0.466 mmol) in CH_3OH (4.7 mL) was added sodium methoxide (1.9 mg, 0.0466 mmol) at room temperature. After stirring for 30 min, the reaction mixture was neutralized by addition of Amberlite IR-120 H^+ resin. The mixture was filtered and concentrated. To a solution of residue in DMF (4.7 mL) was added 2,2-dimethoxypropane (68.5 μL, 58 mg, 0.559 mmol) and *p*-toluenesulfonic acid (8.0 mg, 0.0466 mmol) at room temperature. After 30 min, the reaction mixture was neutralized by the addition of triethylamine. The reaction mixture was then diluted with EtOAc and washed with H_2O. The aqueous layer was extracted with EtOAc, and the combined organic layers were dried and concentrated under reduced pressure. The resulting residue was purified by column chromatography (1:1 to 1:2 hexane–EtOAc) to give **2.91β** (118 mg, 77%) as a white amorphous solid. $[\alpha]^{25}_D$ +18.8 (*c* 1.3, $CHCl_3$) for **2.91β**; R_f 0.16 for **2.91β** (1:1 hexane–EtOAc); R_f 0.14 for **2.91α** (1:1 hexane–EtOAc); Data for **2.91β**: ^1H NMR ($CDCl_3$, 500 MHz) δ_H 4.26 (app dt, 1H, $J_{7,6}$ = 8.4 Hz, $J_{7,8a} = J_{7,8b}$ = 5.2 Hz, H-7), 4.10–4.03 (m, 2H, H-8a, H-8b), 3.89 (br s, 1H, H-5), 3.72 (s, 3H, $COOCH_3$), 3.58–3.50 (m, 3H, H-4, OH), 3.22 (d, 1H, $J_{6,7}$ = 8.4 Hz, 1H, H-6), 2.67 (dq, 1H, *J* =

12.4, 7.6 Hz, SCH_2), 2.51 (dq, 1H, J = 12.4, 7.6 Hz, SCH_2), 2.45 (dd, 1H, $J_{3eq,4}$ = 4.0 Hz, J_{gem} = 12.0 Hz, H-3_{eq}), 1.95 (app t, 1H, $J_{3ax,4}$ = J_{gem} = 12.0 Hz, H-3_{ax}), 1.33 (s, 3H, (CH_3)$_2$C), 1.30 (s, 3H, (CH_3)$_2$C)), 1.13 (t, 3H, J = 9.5 Hz, SCH$_2$CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 169.6 (C-1, $J_{C1,H3ax}$ = 8.2 Hz), 109.7 ((CH$_3$)$_2$*C*), 84.0 (C-2), 77.7 (C-6), 72.9 (C-7), 67.5 (C-8), 67.2 (C-4), 66.2 (C-5), 52.8 (COO<u>C</u>H$_3$), 35.4 (C-3), 26.9 ((*C*H$_3$)$_2$C)), 25.1 ((*C*H$_3$)$_2$C)), 23.4 (S*C*H$_2$), 14.4 (SCH$_2$*C*H$_3$); HRMS (ESI) calcd. for $C_{14}H_{24}NaO_7S$ $[M+Na]^+$ 359.1135 found 359.1131.



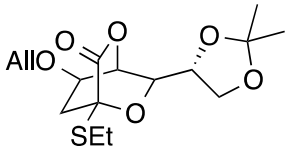
Methyl (Ethyl 4-*O*-allyl-3-deoxy-7,8-*O*-isopropylidene-2-thio-β-D-*manno*-oct-2-ulopyranoside)onate (2.92). To a solution of **2.91** (84 mg, 0.250 mmol) in toluene (25 mL) was added di-*n*-butyltin oxide (93 mg, 0.375 mmol) at room temperature and then the solution was heated at reflux for 5 h. The solution was cooled to room temerpature and to this mixture was then added tetrabutylammonium bromide (37 mg, 0.250 mmol) and allyl bromide (26 μL, 36 mg, 0.300 mmol). The mixture was then heated at reflux and, after 24 h, the reaction mixture was concentrated. The residue was diluted with EtOAc and washed with 10% KF solution and then brine before being dried ($MgSO_4$) and filtered. The filtrate was concentrated and the resulting residue was purified by column chromatography (4:1, hexane–EtOAc) to give **2.92** (60 mg, 64%) as a colorless oil, transesterifed product **2.93** (16 mg, 16%) as a colorless oil and lactone **2.94** (10.3 mg, 12%) as a colorless oil. Data for **2.92**: $[\alpha]^{25}_D$ +32.5 (*c* 1.7, $CHCl_3$); R_f 0.21 (4:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 5.91 (ddt, 1H, J = 17.3, 10.4, 5.7 Hz, OCH$_2$C*H*=CH$_2$), 5.28 (dq, 1H, J = 17.0, 1.5 Hz, 1H, OCH$_2$CH=CH_2), 5.20 (dq, 1H, J = 10.4, 1.5 Hz, OCH$_2$CH=CH_2), 4.39 (ddd, 1H, $J_{7,6}$ = 8.5 Hz, $J_{7,8a}$ = 6.2 Hz, $J_{7,8b}$ = 5.2 Hz, H-7), 4.15 (dd,

1H, $J_{8a,7}$ = 6.2 Hz, J_{gem} = 8.7 Hz, H-8a), 4.11–4.06 (m, 4H, H-5, H-8b, OC*H*$_2$CH=CH$_2$), 3.81 (s, 3H, COOC*H*$_3$), 3.41 (ddd, 1H, $J_{4,3eq}$ = 5.0 Hz, $J_{4,3ax}$ = 12.4 Hz, $J_{4,5}$ = 3.2 Hz, H-4), 3.28–3.25 (d, 1H, $J_{6,7}$ = 8.5 Hz, H-6), 2.76 (dq, 1H, *J* = 12.6, 7.6 Hz, SC*H*$_2$), 2.60 (dq, 1H, *J* = 12.6, 7.6 Hz, SC*H*$_2$), 2.45 (dd, 1H, $J_{3eq,4}$ = 5.0 Hz, J_{gem} = 12.4 Hz, H-3$_{eq}$), 2.21 (br s, 1H, OH), 2.05 (app t, 1H, $J_{3ax,4}$ = J_{gem} = 12.4 Hz, H-3$_{ax}$), 1.40 (s, 3H, (C*H*$_3$)$_2$C), 1.36 (s, 3H, (C*H*$_3$)$_2$C), 1.20 (t, 3H, *J* = 7.6 Hz, SCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 169.7 (C-1, $J_{C1,3ax}$ = 8.1 Hz), 134.3 (OCH$_2$*C*H=CH$_2$), 117.8 (OCH$_2$CH=*C*H$_2$), 109.7 ((CH$_3$)$_2$*C*)), 84.1 (C-2), 77.6 (C-6), 73.9 (C-4), 73.0 (C-7), 69.3 (O*C*H$_2$CH=CH$_2$), 67.8 (C-8), 64.0 (C-5), 52.9 (Me), 32.8 (C-3), 27.0 ((*C*H$_3$)$_2$C), 25.3 ((*C*H$_3$)$_2$C), 23.5 (S*C*H$_2$), 14.5 (SCH$_2$*C*H$_3$); HRMS (ESI) calcd. for $C_{17}H_{28}NaO_7S$ $[M+Na]^+$ 399.1448 found 399.1445.

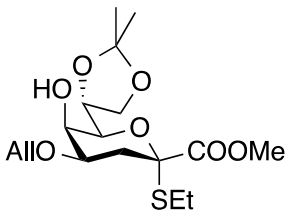


Allyl (Ethyl 4-*O*-allyl-3-deoxy-7,8-*O*-isopropylidene-2-thio-β-D-*manno*-oct-2-ulopyranoside)onate (2.93). $[\alpha]^{25}_D$ –18.7 (*c* 1.0, $CHCl_3$); R_f 0.16 (4:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 5.91 (ddt, 1H, *J* = 17.2, 10.5, 5.9, Hz, OCH$_2$C*H*=CH$_2$), 5.86 (ddt, 1H, *J* = 17.2, 10.4, 5.6, Hz, OCH$_2$C*H*=CH$_2$), 5.37 (dq, 1H, *J* = 17.2, 1.6 Hz, OCH$_2$CH=C*H*$_2$), 5.27 (dq, 1H, *J* = 10.4, 1.2 Hz, OCH$_2$CH=C*H*$_2$), 5.25 (dq, 1H, *J* = 17.2, 1.6 Hz, OCH$_2$CH=C*H*$_2$), 5.16 (dq, 1H, *J* = 10.4, 1.2 Hz, OCH$_2$CH=C*H*$_2$), 4.68 (ddt, 1H, *J* = 13.0, 5.9, 1.3 Hz, OC*H*$_2$CH=CH$_2$), 4.63 (ddt, 1H, *J* = 13.0, 5.9, 1.3 Hz, OC*H*$_2$CH=CH$_2$), 4.35 (ddd, 1H, $J_{7,6}$ = 8.5 Hz, $J_{7,8a}$ = 6.3 Hz, $J_{7,8b}$ = 5.1 Hz, H-7), 4.10 (dd, 1H, $J_{8a,7}$ = 6.3 Hz, J_{gem} = 8.5 Hz, H-8a), 4.05 (dd, 1H, $J_{8b,7}$ = 5.1 Hz, J_{gem} = 8.5 Hz, H-8b), 4.05–4.03 (m, 2H, OC*H*$_2$CH=CH$_2$), 4.02–4.00 (m, 1H, H-5), 3.39 (ddd, 1H, $J_{4,3ax}$ = 12.5 Hz, $J_{4,3eq}$ = 4.6 Hz, $J_{4,5}$ = 2.9 Hz, H-4), 3.24 (d, 1H, $J_{6,7}$ = 8.5 Hz, H-6), 2.74 (dq, 1H,

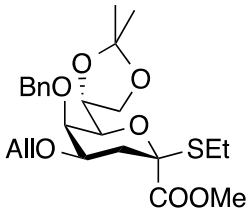
J = 12.5, 7.5 Hz, SCH_2), 2.57 (dq, 1H, J = 12.5, 7.5 Hz, 1H, SCH_2), 2.52 (dd, 1H, $J_{3eq,4}$ = 4.6 Hz, J_{gem} = 12.5 Hz, H-3$_{eq}$), 2.32 (m, 1H, OH), 2.03 (app t, 1H, $J_{3,ax}$ = J_{gem} = 12.5 Hz, H-3$_{ax}$), 1.36 (s, 3H, (CH_3)$_2$C), 1.33 (s, 3H, (CH_3)$_2$C), 1.17 (t, 3H, J = 7.4 Hz, SCH$_2$CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 168.9 (C-1, $J_{C1\text{-}H3ax}$ = 8.0 Hz), 134.3 (OCH$_2$*C*H=CH$_2$), 131.5 (OCH$_2$*C*H=CH$_2$), 119.7 (OCH$_2$CH=*C*H$_2$), 117.7 (OCH$_2$CH=*C*H$_2$), 109.5 ((CH$_3$)$_2$*C*), 84.0 (C-2), 77.5 (C-6), 73.8 (C-4), 73.0 (C-7), 69.2 (O*C*H$_2$CH=CH$_2$), 67.6 (C-8), 66.4 (O*C*H$_2$CH=CH$_2$), 64.0 (C-5), 32.7 (C-3), 26.9 ((*C*H$_3$)$_2$C), 25.3 ((*C*H$_3$)$_2$C), 23.4 (S*C*H$_2$), 14.4 (SCH$_2$*C*H$_3$); HRMS (ESI) calcd. for $C_{19}H_{30}NaO_7S$ $[M+Na]^+$ 425.4918 found 425.4917.



Ethyl 4-*O*-Allyl-1,5-anhydro-3-deoxy-7,8-*O*-isopropylidene-2-thio-α-D-*manno*-oct-2-ulopyranoside)onate (2.94). $[\alpha]^{25}_D$ –25.0 (*c* 1.0, $CHCl_3$); R_f 0.30 (4:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 5.88 (ddt, 1H, J = 17.2, 10.4, 5.7, Hz, OCH$_2$C*H*=CH$_2$), 5.29 (dq, 1H, J = 17.4, 1.4 Hz, OCH$_2$CH=CH_2), 5.22 (dq, 1H, J = 10.4, 1.4 Hz, OCH$_2$CH=CH_2), 4.98 (d, 1H, $J_{5,4}$ = 2.1 Hz, H-5), 4.13–4.06 (m, 3H, H-7, H-8a, OCH_2CH=CH$_2$), 4.04–3.95 (m, 2H, H-8b, OCH_2CH=CH$_2$), 3.86 (dt, 1H, J = 8.6, 2.1 Hz, H-4), 3.66 (d, 1H, $J_{6,7}$ = 8.6 Hz, H-6), 2.86–2.70 (m, 3H, SCH_2, H-3a), 2.08 (d, 1H, J = 14.7 Hz, H-3b), 1.40 (s, 3H, (CH_3)$_2$C), 1.34 (s, 3H, (CH_3)$_2$C), 1.26 (t, 3H, J = 7.7 Hz, SCH$_2$CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 168.0 (C-1), 133.8 (OCH$_2$*C*H=CH$_2$), 118.2 (OCH$_2$CH=*C*H$_2$), 110.2 ((CH$_3$)$_2$*C*), 83.0 (C-2), 75.2 (C-6), 73.8 (C-5), 72.6 (C-7), 71.9 (C-4), 69.6 (O*C*H$_2$CH=CH$_2$), 66.8 (C-8), 40.1 (C-3), 27.1 ((*C*H$_3$)$_2$C), 25.2 ((*C*H$_3$)$_2$C), 23.1 (S*C*H$_2$), 14.8 (SCH$_2$*C*H$_3$); HRMS (ESI) calcd. for $C_{16}H_{24}NaO_6S$ $[M+Na]^+$ 367.1186 found 367.1183.

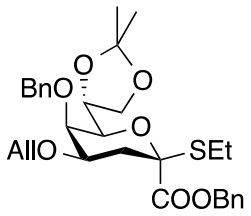


Methyl (Ethyl 4-*O*-allyl-3-deoxy-7,8-*O*-isopropylidene-2-thio-α-D-*manno*-oct-2-ulopyranoside)onate (2.95). To a solution of **2.94** (10.3 mg, 0.0299 mmol) in CH_3OH (1.0 mL) was added sodium methoxide (0.5 mg, 0.478 mmol) at room temperature. After 2 h, the reaction mixture was then neutralized by the addition of Amberlite IR-120 H^+ resin. The mixture was passed through filter paper and the filtrate was concentrated and the resulting residue was purified by column chromatography (2:1, hexane–EtOAc) to give **2.95** (10.7 mg, 95%) as an oil. $[\alpha]^{25}_D$ +136.9 (*c* 3.3, $CHCl_3$); R_f 0.27 (2:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 5.87 (ddt, 1H, *J* = 17.2, 10.3, 5.6, Hz, OCH_2CH=CH_2), 5.27 (dq, 1H, *J* = 17.3, 1.6 Hz, OCH_2CH=CH_2), 5.18 (dq, 1H, *J* = 10.4, 1.6 Hz, OCH_2CH=CH_2), 4.42 (ddd, 1H, $J_{7,6}$ = 7.5 Hz, $J_{7,8a}$ = 6.2 Hz, $J_{7,8b}$ = 5.4 Hz, H-7), 4.12 (dd, 1H, $J_{8a,7}$ = 6.2 Hz, J_{gem} = 8.8 Hz, H-8a), 4.10–4.02 (m, 3H, H-5,OCH_2CH=CH_2), 3.95 (dd, 1H, $J_{8b,7}$ = 5.4 Hz, J_{gem} = 8.8 Hz, H-8b), 3.87 (dd, 1H, $J_{6,5}$ = 1.1 Hz, $J_{6,7}$ = 7.5 Hz, H-6), 3.85–3.80 (m, 1H, H-4), 3.74 (s, 3H, $COOCH_3$), 2.57 (dq, 1H, *J* = 12.2, 7.2 Hz, SCH_2), 2.48 (dq, 1H, *J* = 12.2, 7.2 Hz, SCH_2), 2.29 (br s, 1H, OH), 2.21–2.12 (m, 2H, H-3_{eq}, H-3_{ax}), 1.41 (s, 3H, $(CH_3)_2C$), 1.36 (s, 3H, $(CH_3)_2C$), 1.16 (t, 3H, *J* = 7.5 Hz, SCH_2CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 169.4 (C-1, $J_{C1,H3ax}$ = 2.2 Hz), 134.4 (OCH_2CH=CH_2), 117.8 (OCH_2CH=CH_2), 109.4 ($(CH_3)_2C$), 85.0 (C-2), 74.0 (C-7), 73.4 (C-4), 72.2 (C-6), 69.5 (OCH_2CH=CH_2), 67.3 (C-8), 64.5 (C-5), 52.8 ($COOCH_3$), 32.1 (C-3), 27.1 ($(CH_3)_2C$), 25.7 ($(CH_3)_2C$), 22.6 (SCH_2), 14.4 (SCH_2CH_3); HRMS (ESI) calcd. for $C_{17}H_{28}NaO_7S$ $[M+Na]^+$ 399.1448 found 399.1445.



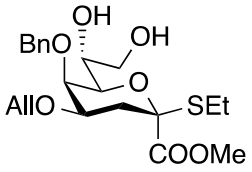
Methyl (Ethyl 4-*O*-Allyl-5-*O*-benzyl-3-deoxy-7,8-*O*-isopropylidene-2-thio-β-D-*manno*-oct-2-ulopyranoside)onate (2.98). To a solution of **2.92** (76 mg, 0.201 mmol) in THF (2 mL) was added benzyl bromide (29.1 μL, 42.0 mg, 0.245 mmol) and sodium hydride at 0 °C and then the mixture was warmed to room temperature. After 24 h, CH_3OH (2 mL) was added to the reaction mixture and then the solution concentrated under reduced pressure. The residue was diluted with EtOAc and washed with brine and H_2O. The organic layer was dried with $MgSO_4$ and then filtered. The filtrate was concentrated and the resulting residue was purified by column chromatography (8:1, hexane–EtOAc) to give **2.98** (60 mg, 64%) as a colorless oil and trans-esterified product **2.99** (20 mg, 18%) as a colorless oil. $[\alpha]^{25}_D$ +1.9 (*c* 1.0, $CHCl_3$); R_f 0.22 (8:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 700 MHz) δ_H 7.39 (d, 2H, J = 7.4 Hz, ArH), 7.30 (m, 2H, ArH), 7.25 (m, 1H, ArH), 5.87 (ddt, 1H, J = 17.2, 10.4, 5.3 Hz, OCH_2CH=CH_2), 5.27 (dd, 1H, J = 16.9, 1.6 Hz, OCH_2CH=CH_2), 5.17 (dd, 1H, J = 10.2, 1.6 Hz, OCH_2CH=CH_2), 4.88 (d, 1H, J_{gem} = 11.8 Hz, $ArCH_2$), 4.69 (d, 1H, J_{gem} = 11.8 Hz, $ArCH_2$), 4.33 (app dt, 1H, $J_{7,6}$ = 8.6 Hz, $J_{7,8a}$ = $J_{7,8b}$ = 6.0 Hz, H-7), 4.11 (dd, 1H, $J_{8a,7}$ = 6.0 Hz, J_{gem} = 8.3 Hz, H-8a), 4.05–3.97 (m, 3H, H-8b, OCH_2CH=CH_2), 3.90 (br s, 1H, H-5), 3.79 (s, 3H, $COOCH_3$), 3.37 (ddd, 1H, $J_{4,3eq}$ = 3.9 Hz, $J_{4,3ax}$ = 12.0 Hz, $J_{4,5}$ = 2.6 Hz, H-4), 3.29 (dd, 1H, $J_{6,5}$ = 0.9 Hz, $J_{6,7}$ = 8.6 Hz, H-6), 2.71 (dq, 1H, J = 12.5, 7.3 Hz, SCH_2), 2.57 (dq, 1H, J = 12.5, 7.3 Hz, SCH_2), 2.55 (dd, 1H, $J_{3eq,4}$ = 3.9 Hz, J_{gem} = 12.4 Hz, H-3_{eq}), 2.27 (app t, 1H, $J_{3ax,4}$ = J_{gem} = 12.0 Hz, H-3_{ax}), 1.38 (s, 3H, $(CH_3)_2C$), 1.33 (s, 3H, $(CH_3)_2C$), 1.13 (t, 3H, J = 7.5 Hz, SCH_2CH_3); ^{13}C NMR ($CDCl_3$, 175 MHz) δ_C 169.9 (C=O, $J_{C1\text{-}H3ax}$ = 8.7 Hz), 139.0 (Ar), 134.5 (OCH_2CH=CH_2), 128.12 (2C, Ar), 128.06 (2C, Ar), 127.3

(Ar), 116.8 ($OCH_2CH=CH_2$), 109.2 ($(CH_3)_2C$), 84.3 (C-2), 78.5 (C-6), 75.7 (C-5), 74.4 ($ArCH_2$), 72.8 (C-7), 71.7 (C-5), 69.2 ($OCH_2CH=CH_2$), 67.7 (C-8), 52.6 (Me), 33.2 (C-3), 26.8 ($(CH_3)_2C$), 25.2 ($(CH_3)_2C$), 23.3 (SCH_2), 14.3 (SCH_2CH_3); HRMS (ESI) calcd. for $C_{24}H_{34}NaO_7S$ $[M+Na]^+$ 489.1917 found 489.1923.



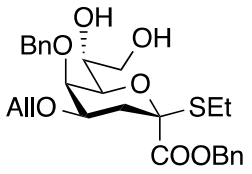
Benzyl (Ethyl 4-*O*-Allyl-5-*O*-benzyl-3-deoxy-7,8-*O*-isopropylidene-2-thio-β-D-*manno*-oct-2-ulopyranoside)onate (2.99). $[\alpha]^{25}_D$ +7.8 (*c* 1.8, $CHCl_3$); R_f 0.27 (8:1, hexane–EtOAc); ^1H NMR ($CDCl_3$, 500 MHz) δ_H 7.44–7.40 (m, 4H, ArH), 7.38–7.33 (m, 3H, ArH), 7.32–7.28 (m, 2H, ArH), 7.27–7.24 (m, 1H, ArH), 5.85 (ddt, 1H, *J* = 17.1, 10.5, 5.4 Hz, $OCH_2CH=CH_2$), 5.25 (m, 2H, $ArCH_2$), 5.24 (dq, 1H, *J* = 17.3, 1.7 Hz, $OCH_2CH=CH_2$), 5.15 (dd, 1H, *J* = 10.5, 1.7 Hz, $OCH_2CH=CH_2$), 4.92 (d, 1H, J_{gem} = 11.9 Hz, $ArCH_2$), 4.72 (d, 1H, J_{gem} = 11.9 Hz, $ArCH_2$), 4.36 (app dt, 1H, $J_{7,6}$ = 8.6 Hz, $J_{7,8a} = J_{7,8b}$ = 6.1 Hz, H-7), 4.11 (dd, 1H, $J_{8a,7}$ = 6.1 Hz, J_{gem} = 8.4 Hz, H-8a), 4.04 (dd, 1H, $J_{8b,7}$ = 6.1 Hz, J_{gem} = 8.6 Hz, H-8b), 3.98 (ddt, 1H, *J* = 13.0, 5.2, 1.6 Hz, $OCH_2CH=CH_2$), 3.92 (ddt, 1H, *J* =13.0, 5.2, 1.6 Hz, $OCH_2CH=CH_2$), 3.90–3.87 (m, 1H, H-5), 3.36–3.31 (m, 2H, H-4, H-6), 2.71 (dq, 1H, *J* = 12.4, 7.6 Hz, SCH_2), 2.62 (ddd, 1H, $J_{3eq,4}$ = 4.0 Hz, J_{gem} = 12.4 Hz, H-3_{eq}), 2.52 (dq, 1H, *J* = 12.4, 7.6 Hz, SCH_2), 2.32 (app t, 1H, $J_{3ax,4} = J_{gem}$ = 12.4 Hz, H-3_{ax}), 1.39 (s, 3H, $(CH_3)_2C$), 1.36 (s, 3H, $(CH_3)_2C$), 1.15 (t, 3H, *J* = 7.5 Hz, SCH_2CH_3); ^{13}C NMR ($CDCl_3$, 175 MHz) δ_C 168.8 (C=O, $J_{C1\text{-}H3ax}$ = 8.3 Hz), 138.8 (Ar), 135.1 (Ar), 134.3 ($OCH_2CH=CH_2$), 128.46 (2C, Ar), 128.42 (Ar), 128.38 (2C, Ar), 127.9 (2C, Ar) 127.9 (2C, Ar), 127.1 (Ar), 116.4 ($OCH_2CH=CH_2$), 108.9 ($(CH_3)_2C$), 84.1 (C-2), 78.2 (C-6), 75.6 (C-4), 74.2 ($ArCH_2$), 72.7 (C-7), 71.6 (C-5), 68.9 ($OCH_2CH=CH_2$), 67.4 (C-8), 67.1 ($ArCH_2$), 33.0 (C-3),

26.6 ((*C*H$_3$)$_2$C), 25.1 ((*C*H$_3$)$_2$C), 23.0 (S*C*H$_2$), 14.1 (SCH$_2$*C*H$_3$); HRMS (ESI) calcd. for $C_{30}H_{38}NaO_7S$ $[M+Na]^+$ 565.2230 found 565.2227.



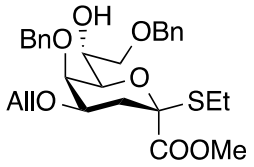
Methyl (Ethyl 4-*O*-Allyl-5-*O*-benzyl-3-deoxy-2-thio-β-D-*manno*-oct-2-ulopyranoside)onate (2.100). A solution of **2.98** (18 mg, 0.0331 mmol) in 4:1 AcOH–H_2O (1.0 mL) was stirred at 50 °C. After 30 min, the reaction mixture was cooled to room temperature and then diluted with EtOAc and washed with H_2O twice. The organic layer was then washed with satd. aq. $NaHCO_3$. The organic layer was then dried with $MgSO_4$ and filtered. The filtrate was concentrated and the resulting residue was purified by column chromatography (1:1, hexane–EtOAc) to give **2.100** (16 mg, 96%) as a colorless oil. $[\alpha]^{25}_D$ –22.9 (*c* 1.5, $CHCl_3$); R_f 0.15 (1:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.43–7.39 (m, 2H, ArH), 7.37–7.32 (m, 2H, ArH), 7.31–7.27 (m, 1H, ArH), 5.90 (ddt, 1H, *J* = 17.2, 10.5, 5.4 Hz, OCH$_2$C*H*=CH$_2$), 5.29 (dq, 1H, *J* = 17.4, 1.8 Hz, OCH$_2$CH=C*H$_2$*), 5.20 (dq, 1H, *J* = 10.5, 1.8 Hz, OCH$_2$CH=C*H$_2$*), 4.93 (d, 1H, J_{gem} = 11.8 Hz, ArC*H$_2$*), 4.71 (d, 1H, J_{gem} = 11.8 Hz, ArC*H$_2$*), 4.05 (m, 2H, OC*H$_2$*CH=CH$_2$), 4.01–3.96 (m, 2H, H-5, H-8a), 3.89–3.83 (m, 1H, H-7), 3.81 (s, 3H, COOC*H$_3$*), 3.68 (ddd, 1H, *J* = 12.1, 10.0, 2.1 Hz, H-8b), 3.38 (ddd, 1H, $J_{4,3eq}$ = 4.2 Hz, $J_{4,3ax}$ = 12.0 Hz, $J_{4,5}$ = 2.5 Hz, H-4), 3.23 (dd, 1H, $J_{6,5}$ = 0.9 Hz, $J_{6,7}$ = 9.0 Hz, H-6), 2.72 (dq, 1H, *J* = 12.4, 7.8 Hz, SC*H$_2$*), 2.70–2.67 (m, 1H, 8-OH), 2.59–2.54 (m, 1H, H-3$_{eq}$), 2.55 (dq, 1H, *J* = 12.4, 7.8 Hz, SC*H$_2$*), 2.31 (app t, 1H, $J_{3ax,4}$ = J_{gem} = 12.0 Hz, H-3$_{ax}$), 1.71 (d, 1H, *J* = 8.6 Hz, 7-OH), 1.19 (t, 3H, *J* = 7.4 Hz, SCH$_2$C*H$_3$*); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 170.8 (C-1, $J_{C1\text{-}H3ax}$ = 8.3 Hz), 138.7 (Ar), 134.4 (OCH$_2$*C*H=CH$_2$), 128.5 (2C, Ar), 128.4 (2C, Ar), 127.8 (Ar), 117.1 (OCH$_2$CH=*C*H$_2$), 84.0 (C-2), 76.4 (C-6), 76.2 (C-4),

74.0 (Ar*C*H_2), 69.7 (C-5), 69.4 (O*C*H_2CH=CH_2), 69.3 (C-7), 64.1 (C-8), 53.1 (COO*C*H_3), 33.1 (C-3), 23.3 (S*C*H_2), 14.0 (SCH_2*C*H_3); HRMS (ESI) calcd. for $C_{21}H_{30}NaO_7S$ $[M+Na]^+$ 449.1604 found 449.1598.



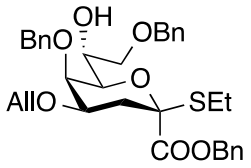
Benzyl (Ethyl 4-*O*-Allyl-5-*O*-benzyl-3-deoxy-2-thio-β-D-*manno*-oct-2-ulopyranoside)onate (2.101). A solution of **2.99** (60 mg, 0.128 mmol) in 4:1 AcOH–H_2O (1 mL) was stirred at 50 °C. After 30 min, the reaction mixture was cooled to room temperature and then diluted with EtOAc and washed with H_2O twice. The organic layer was then washed with satd. aq. $NaHCO_3$. The organic layer was dried with $MgSO_4$, filtered, concentrated and the resulting residue was purified by column chromatography (1:1, hexane–EtOAc) to give **2.101** (50 mg, 95%) as a colorless oil. $[\alpha]^{25}_D$ –10.8 (*c* 1.8, $CHCl_3$); R_f 0.22 (1:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.42–7.26 (m, 10H, ArH), 5.83 (ddt, 1H, *J* = 17.2, 10.5, 5.3 Hz, 1H, OCH$_2$C*H*=CH$_2$), 5.29 (d, 1H, J_{gem} = 12.1 Hz, ArCH$_2$), 5.21 (dq, 1H, *J* = 17.2, 1.7 Hz, OCH$_2$CH=C*H*$_2$), 5.17 (d, 1H, J_{gem} = 12.1 Hz, ArCH$_2$), 5.12 (dq, 1H, *J* = 10.5, 1.7 Hz, OCH$_2$CH=C*H*$_2$), 4.91 (d, 1H, J_{gem} = 11.8 Hz, ArC*H*$_2$), 4.70 (d, 1H, J_{gem} = 11.8 Hz, ArC*H*$_2$), 3.96 (ddt, 1H, *J* = 13.0, 5.4, 1.6 Hz, OC*H*$_2$CH=CH$_2$), 3.96–3.92 (m, 2H, H-5, H-8a), 3.91 (ddt, 1H, *J* = 13.0, 5.4, 1.6 Hz, OC*H*$_2$CH=CH$_2$), 3.88–3.82 (m, 1H, H-7), 3.66 (app dt, 1H, *J* = 10.0, 2.3 Hz, H-8b), 3.29 (ddd, 1H, $J_{4,3eq}$ = 4.2 Hz, $J_{4,3ax}$ = 12.4 Hz, $J_{4,5}$ = 2.5 Hz, H-4), 3.23 (dd, 1H, $J_{6,5}$ = 0.8 Hz, $J_{6,7}$ = 8.9 Hz, 1H, H-6), 2.74 (dd, 1H, *J* = 10.0, 4.3 Hz, 8-OH), 2.67 (dq, 1H, *J* = 12.1, 7.6 Hz, SC*H*$_2$), 2.59 (dd, 1H, $J_{3eq,4}$ = 4.2 Hz, J_{gem} = 12.4 Hz, H-3$_{eq}$), 2.44 (dq, 1H, *J* = 12.1, 7.6 Hz, SC*H*$_2$), 2.30 (app t, 1H, $J_{3ax,4}$ = J_{gem} = 12.4 Hz, H-3$_{ax}$), 1.88 (d, 1H, *J* = 8.2 Hz, 7-OH), 1.12 (t, 3H, *J* = 7.3 Hz, SCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz)

δ_C 170.2 (C-1, $J_{C1\text{-}H3ax}$ = 8.0 Hz), 138.9 (Ar), 135.2 (Ar), 134.5 ($OCH_2CH{=}CH_2$), 128.92 (2C, Ar), 128.85 (Ar), 128.7 (2C, Ar), 128.6 (2C, Ar), 128.5 (2C, Ar), 127.9 (Ar), 117.1 ($OCH_2CH{=}CH_2$), 84.2 (C-2), 76.5 (C-6), 76.4 (C-4), 74.1 ($ArCH_2$), 70.0 (C-5), 69.5 ($OCH_2CH{=}CH_2$), 69.4 (C-7), 68.0 ($ArCH_2$), 64.2 (C-8), 33.3 (C-3), 23.3 (SCH_2), 14.0 (SCH_2CH_3); HRMS (ESI) calcd. for $C_{27}H_{34}NaO_7S$ $[M+Na]^+$ 525.1917 found 525.1913.



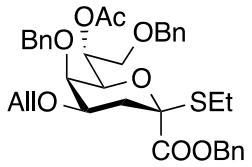
Methyl (Ethyl 4-*O*-allyl-5,8-di-*O*-benzyl-3-deoxy-2-thio-β-D-*manno*-oct-2-ulopyranoside)onate (2.102) To a solution of **2.100** (71 mg, 0.166 mmol) in toluene (25 mL) was added di-*n*-butyltin oxide (60 mg, 0.241 mmol) and the solution was heated to reflux. After 5 h tetrabutylammonium bromide (51.8 mg, 0.161 mmol) and benzyl bromide (33 mg, 23 μL, 0.193 mmol) were added at room temperature and the solution was continued to heat at reflux for 24 h. The reaction mixture was cooled to room temperature and then concentrated under reduced pressure. The residue was diluted with EtOAc and washed with 10% KF solution and then brine before being dried ($MgSO_4$) and filtered. The filtrate was concentrated and the resulting residue was purified by column chromatography (4:1, hexane–EtOAc) to give **2.102** (59 mg, 69%) as a colorless oil and **2.103** (14 mg, 14%) as a colorless oil. Data for **2.102**: $[\alpha]^{25}_D$ +18.8 (*c* 1.3, $CHCl_3$); R_f 0.18 (4:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.43–7.37 (m, 2H, ArH), 7.37–7.25 (m, 8H, ArH), 5.88 (ddt, 1H, *J* = 17.2, 10.5, 5.4 Hz, $OCH_2CH{=}CH_2$), 5.28 (dq, 1H, *J* = 17.2, 1.7 Hz, $OCH_2CH{=}CH_2$), 5.18 (dq, 1H, *J* = 10.4, 1.7 Hz, 1H, $OCH_2CH{=}CH_2$), 4.91 (d, 1H, J_{gem} = 11.3 Hz, $ArCH_2$), 4.72 (d, 1H, J_{gem} = 11.3 Hz, $ArCH_2$), 4.62 (d, 1H, J_{gem} = 11.7 Hz, $ArCH_2$), 4.56 (d, 1H, J_{gem} = 11.7 Hz, $ArCH_2$), 4.10–3.98 (m, 4H, H-5, H-7, $OCH_2CH{=}CH_2$), 3.80

(dd, 1H, $J_{8a,7}$ = 3.0 Hz, J_{gem} = 10.0 Hz, H-8a), 3.77 (s, 3H, COOC*H*$_3$), 3.62 (dd, 1H, $J_{8b,7}$ = 6.1 Hz, J_{gem} = 10.0 Hz, H-8b), 3.38 (ddd, 1H, $J_{4,3eq}$ = 4.2 Hz, $J_{4,3ax}$ = 12.0 Hz, $J_{4,5}$ = 2.1 Hz, H-4), 3.35 (d, 1H, $J_{6,7}$ = 8.6 Hz, H-6), 2.69 (dq, 1H, J = 12.5, 7.5 Hz, 1H, SC*H*$_2$), 2.60–2.52 (m, 2H, H-3, SC*H*$_2$), 2.29 (app t, 1H, $J_{3ax,4}$ = J_{gem} = 12.0 Hz, H-3$_{ax}$), 2.25 (d, 1H, $J_{OH,7}$ = 5.2 Hz, 7-OH), 1.17 (t, 3H, J = 7.6 Hz, 3H, SCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 169.9 (C-1, $J_{C1\text{-}H3ax}$ = 8.3 Hz), 139.0 (Ar), 138.1 (Ar), 134.5 (OCH$_2$*C*H=CH$_2$), 128.4 (2C, Ar), 128.34 (2C, Ar), 128.32 (2C, Ar), 127.8 (2C, Ar), 127.7 (Ar), 127.6 (Ar), 116.9 (OCH$_2$CH=*C*H$_2$), 84.2 (C-2), 76.8 (C-6), 76.0 (C-4), 74.2 (Ar*C*H$_2$), 73.5 (Ar*C*H$_2$), 71.4 (C-8), 70.6 (C-5), 69.3 (O*C*H$_2$CH=CH$_2$), 68.1 (C-7), 52.5 (COO*C*H$_3$), 33.3 (C-3), 23.3 (S*C*H$_2$), 14.2 (SCH$_2$*C*H$_3$); HRMS (ESI) calcd. for $C_{28}H_{36}NaO_7S$ $[M+Na]^+$ 539.2074 found 539.2069.



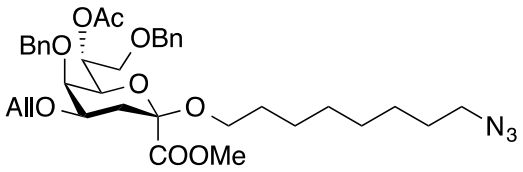
Benzyl (Ethyl 4-*O*-allyl-5,8-di-*O*-benzyl-3-deoxy-2-thio-β-D-*manno*-oct-2-ulopyranoside)onate (2.103). $[\alpha]^{25}_D$ +3.0 (*c* 1.3, $CHCl_3$); R_f 0.27 (4:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.44–7.26 (m, 15H, ArH), 5.84 (ddt, 1H, J = 17.2, 10.5, 5.3 Hz, 1H, OCH$_2$C*H*=CH$_2$), 5.29 (d, 1H, J_{gem} = 12.2 Hz, ArC*H*$_2$), 5.23 (dq, 1H, J = 17.4, 1.5 Hz, 1H, OCH$_2$CH=C*H*$_2$), 5.15 (d, 1H, J_{gem} = 12.2 Hz, ArC*H*$_2$), 5.14 (dq, 1H, J = 10.4, 1.5 Hz, 1H, OCH$_2$CH=C*H*$_2$), 4.91 (d, 1H, J_{gem} = 11.5 Hz, ArC*H*$_2$), 4.73 (d, 1H, J_{gem} = 11.5 Hz, ArC*H*$_2$), 4.58 (d, 1H, J_{gem} = 11.8 Hz, ArC*H*$_2$), 4.52 (d, 1H, J_{gem} = 11.8 Hz, ArC*H*$_2$), 4.12–4.05 (m, 1H, H-7), 3.98 (br s, 1H, H-5), 3.94 (ddt, 1H, J = 13.1, 7.8, 1.6 Hz, OC*H*$_2$CH=CH$_2$), 3.91 (ddt, 1H, J = 13.1, 7.8, 1.6 Hz, OC*H*$_2$CH=CH$_2$), 3.78 (dd, 1H, $J_{8a,7}$ = 2.9 Hz, J_{gem} = 9.8 Hz, H-8a), 3.52 (dd, 1H, $J_{8b,7}$ = 6.9 Hz, J_{gem} = 9.8 Hz, H-8b), 3.36 (d, 1H, $J_{6,7}$ = 8.9 Hz, H-6), 3.32 (ddd, 1H, $J_{4,3eq}$ = 4.3

Hz, $J_{4,3ax}$ = 12.2 Hz, $J_{4,5}$ = 2.6 Hz, H-4), 2.66 (dq, 1H, J = 12.4, 7.7 Hz, SCH_2), 2.60 (dd, 1H, $J_{3eq,4}$ = 4.3 Hz, J_{gem} = 12.2 Hz, H-3_{eq}), 2.49 (dq, 1H, J = 12.4, 7.7 Hz, SCH_2), 2.31 (app t, 1H, $J_{3ax,4}$ = J_{gem} = 12.2 Hz, H-3_{ax}), 2.30 (d, 1H, $J_{OH,7}$ = 5.0 Hz, 7-OH), 1.13 (t, 3H, J = 7.5 Hz, SCH_2CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_H 169.1 (C-1, $J_{C1\text{-}H3ax}$ = 8.3 Hz), 139.0 (Ar), 138.1 (Ar), 135.4 (Ar), 134.5 ($OCH_2CH{=}CH_2$), 128.7 (2C, Ar), 128.6 (Ar), 128.5 (2C, Ar), 128.4 (2C, Ar), 128.31 (2C, Ar), 128.29 (2C, Ar), 127.9 (2C, Ar), 127.7 (Ar), 127.6 (Ar), 116.8 ($OCH_2CH{=}CH_2$), 84.2 (C-2), 76.8 (C-6), 76.1 (C-4), 74.2 ($ArCH_2$), 73.4 ($ArCH_2$), 71.6 (C-8), 70.7 (C-5), 69.3 ($OCH_2CH{=}CH_2$), 68.1 (C-7), 67.3 ($ArCH_2$), 33.3 (C-3), 23.2 (SCH_2), 14.1 (SCH_2CH_3); HRMS (ESI) calcd. for $C_{34}H_{40}NaO_7S$ $[M+Na]^+$ 615.2387 found 615.2379.



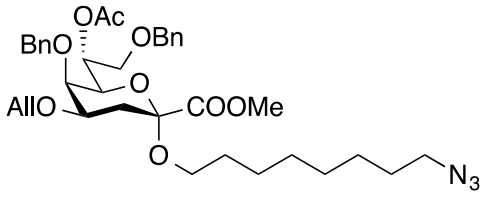
Benzyl (Ethyl 7-*O*-acetyl-4-*O*-allyl-5,8-di-*O*-benzyl-3-deoxy-2-thio-β-D-*manno*-oct-2-ulopyranoside)onate (2.104). To a solution of **2.103** (75 mg, 0.127 mmol) in CH_2Cl_2 (1.5 mL) was added triethylamine (21.0 mL, 0.152 mmol), acetic anhydride (13.1 mL, 0.139 mmol) and DMAP (1.6 mg, 0.0127 mmol) sequentially. After 24 h, CH_3OH (1.0 mL) was added to the reaction mixture and the solution was concentrated under reduced pressure. The residue was diluted with EtOAc and washed with H_2O. The organic layer was dried with $MgSO_4$ and then filtered. The filtrate was concentrated under reduced pressure and the residue was purified by column chromatography (8:1, hexane, EtOAc) to give **2.104** (77 mg, 96%) as an oil. $[\alpha]^{25}_D$ –14.5 (*c* 1.0, $CHCl_3$); R_f 0.30 (8:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 700 MHz) δ_H 7.39–7.27 (m, 14H, ArH), 7.27–7.23 (m, 1H, ArH), 5.83 (ddt, 1H, J = 17.2, 10.7, 5.4 Hz, $OCH_2CH{=}CH_2$), 5.30 (d, 1H, J_{gem} = 12.5 Hz, $ArCH_2$), 5.27 (ddd, 1H, $J_{7,6}$ = 8.3 Hz, $J_{7,8a}$ = 2.5 Hz, $J_{7,8b}$ = 5.3 Hz, H-7), 5.21 (dq, 1H, J = 17.1, 1.5 Hz, $OCH_2CH{=}CH_2$), 5.12 (dq, 1H, J = 10.0, 1.5 Hz, $OCH_2CH{=}CH_2$), 5.10 (d, 1H,

J_{gem} = 12.5 Hz, ArCH_2), 4.86 (d, 1H, J_{gem} = 10.8 Hz, ArCH_2), 4.53–4.49 (m, 2H, ArCH_2), 4.49 (d, 1H, J_{gem} = 10.8 Hz, ArCH_2), 3.98 (ddt, 1H, J = 12.9, 5.7, 1.5 Hz, OCH_2CH=CH$_2$), 3.88 (ddt, 1H, J = 12.9, 5.7, 1.5 Hz, OCH_2CH=CH$_2$), 3.86 (dd, 1H, $J_{8a,7}$ = 2.5 Hz, J_{gem} = 11.3 Hz, H-8a), 3.75 (br s, 1H, H-5), 3.74 (d, 1H, $J_{6,7}$ = 8.3 Hz, H-6), 3.67 (dd, 1H, $J_{8b,7}$ = 5.3 Hz, J_{gem} = 11.3 Hz, H-8b), 3.34 (ddd, 1H, $J_{4,3eq}$ = 12.1 Hz, $J_{4,3ax}$ = 3.5 Hz, $J_{4,5}$ = 2.4 Hz, H-4), 2.65 (dq, 1H, J = 12.4, 7.4 Hz, SCH_2), 2.59 (dd, 1H, $J_{3eq,4}$ = 3.5 Hz, J_{gem} = 12.1 Hz, H-3$_{eq}$), 2.47 (dq, 1H, J = 12.4, 7.4 Hz, SCH_2), 2.28 (app t, 1H, $J_{3ax,4}$ = J_{gem} = 12.1 Hz, H-3$_{ax}$), 1.96 (s, 3H, COCH_3), 1.10 (t, 3H, J = 7.7 Hz, SCH$_2$CH_3); ^{13}C NMR ($CDCl_3$, 175 MHz) δ_C 169.7 (C=O), 168.8 (C-1, $J_{C1\text{-}H3ax}$ = 8.4 Hz), 138.34 (Ar), 138.31 (Ar), 135.4 (Ar), 134.3 (OCH$_2$*C*H=CH$_2$), 128.64 (2C, Ar), 128.57 (Ar), 128.50 (2C, Ar), 128.47 (2C, Ar), 128.24 (2C, Ar), 128.17 (2C, Ar), 127.8 (2C, Ar), 127.51 (Ar), 127.47 (Ar), 116.8 (OCH$_2$CH=*C*H$_2$), 84.3 (C-2), 76.4 (C-4), 74.7 (C-6), 74.1 (Ar*C*H$_2$), 73.2 (Ar*C*H$_2$), 71.0 (C-5), 70.6 (C-7), 69.3 (C-8), 68.4 (O*C*H$_2$CH=CH$_2$), 67.3 (Ar*C*H$_2$), 32.9 (C-3), 23.3 (S*C*H$_2$), 21.1 (CO*C*H$_3$), 14.1 (SCH$_2$*C*H$_3$); HRMS (ESI) calcd. for $C_{36}H_{46}NO_8S$ $[M+NH_4]^+$ 652.2939 found 652.2940.

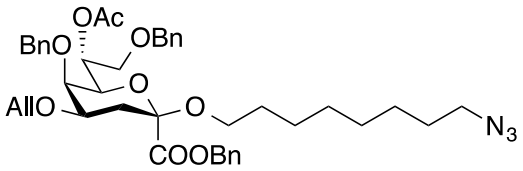


Methyl (8-Azidooctyl 7-*O*-acetyl-4-*O*-allyl-5,8-di-*O*-benzyl-3-deoxy-β-D-*manno*-oct-2-ulopyranoside)onate (2.105β). A mixture of **2.85** (716 mg, 1.28 mmol) and 8-azidooctanol (329 mg, 1.92 mmol) and 4Å molecular sieves (1.0 g) in CH_2Cl_2–CH_3CN (2:3, 25.0 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –70 °C and then NIS (346 mg, 1.54 mmol) and TfOH (11.3 μL, 0.128 mmol) were added. After stirring at –70 °C for 1 h, trimethylamine was added to the reaction mixture. The reaction was warmed to room temperature and then a small amount of H_2O was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$

until the solution was colorless. The mixture was filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography (15:1 to 8:1, hexane–EtOAc) to give **2.105β** (591 mg, 69%) as a colorless oil and **2.105α** (94 mg, 11%) as a colorless oil. Data for **2.105β**: R_f 0.27 (8:1, hexane–EtOAc); $[\alpha]^{25}_D$ –0.8 (*c* 2.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.37–7.23 (m, 10H, ArH), 5.95–5.86 (m, 1H, OCH_2CH=CH_2), 5.33–5.25 (m, 2H, OCH_2CH=CH_2, H-7), 5.22–5.17 (m, 1H, OCH_2CH=CH_2), 4.89 (d, 1H, J_{gem} = 11.0 Hz, ArCH_2), 4.59–4.48 (m, 3H, ArCH_2), 4.12–4.07 (m, 2H, OCH_2CH=CH_2), 3.95 (dd, 1H, $J_{6,5}$ = 1.0 Hz, $J_{6,7}$ = 8.4 Hz, H-6), 3.87 (dd, 1H, $J_{8,7}$ = 2.4 Hz, J_{gem} = 11.1 Hz, H-8a), 3.78 (br s, 1H, H-5), 3.76–3.70 (m, 4H, H-8b, OCH_3), 3.64 (app dt, 1H, *J* = 9.1, 6.8 Hz, octyl OCH_2), 3.50 (ddd, 1H, $J_{4,3ax}$ = 12.4 Hz, $J_{4,3eq}$ = 3.9 Hz, $J_{4,5}$ = 2.1 Hz, H-4), 3.33 (app dt, 1H, *J* = 9.1, 6.8 Hz, octyl OCH_2), 3.23 (app t, 2H, *J* = 6.9 Hz, octyl CH_2N_3), 2.44 (dd, 1H, $J_{3eq,4}$ = 3.9 Hz, J_{gem} = 12.4 Hz, H-3_{eq}), 2.25 (app t, 1H, $J_{3ax,4}$ = J_{gem} = 12.4 Hz, H-3_{ax}), 2.00 (s, 3H, $COCH_3$), 1.63–1.47 (m, 4H, octyl CH_2), 1.38–1.22 (m, 8H, octyl CH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 169.9 (C=O), 169.7 (C-1, $J_{C1\text{-}H3ax}$ = 6.9 Hz), 138.7 (Ar), 138.5 (Ar), 134.7 (OCH_2CH=CH_2), 128.52 (2C, Ar), 128.46 (2C, Ar), 128.39 (2C, Ar), 127.8 (2C, Ar), 127.71 (Ar), 127.68 (Ar), 117.1 (OCH_2CH=CH_2), 100.1 (C-2), 76.4 (C-4), 74.3 (ArCH_2), 73.4 (ArCH_2), 73.0 (C-6), 71.2 (2C, C-5, C-7), 69.6 (OCH_2CH=CH_2), 68.5 (C-8), 64.4 (octyl OCH_2), 52.5 (OCH_3), 51.7 (octyl CH_2N_3), 32.5 (C-3), 29.8 (octyl CH_2), 29.4 (octyl CH_2), 29.3 (octyl CH_2), 29.0 (octyl CH_2), 26.8 (octyl CH_2), 26.0 (octyl CH_2), 21.3 ($COCH_3$); HRMS (ESI) calcd. for $C_{36}H_{49}N_3NaO_9$ $[M+Na]^+$ 690.3361 found 690.3356.

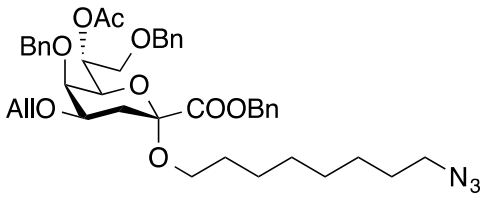


Methyl (8-Azidooctyl 7-*O*-acetyl-4-*O*-allyl-5,8-di-*O*-benzyl-3-deoxy-α-D-*manno*-oct-2-ulopyranoside)onate (2.105α). R_f 0.32 (8:1, hexane–EtOAc); $[\alpha]^{25}_D$ –5.9 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz) δ_H 7.37–7.22 (m, 10H, ArH), 5.98–5.87 (m, 1H, OCH_2CH=CH_2), 5.35–5.26 (m, 2H, OCH_2CH=CH_2, H-7), 5.21–5.16 (m, 1H, OCH_2CH=CH_2), 4.88 (d, 1H, J_{gem} = 11.1 Hz, $ArCH_2$), 4.55–4.43 (m, 3H, $ArCH_2$), 4.14–4.03 (m, 2H, OCH_2CH=CH_2), 3.99 (d, 1H, $J_{6,7}$ = 9.1 Hz, H-6), 3.93 (ddd, 1H, $J_{4,3ax}$ = 12.3 Hz, $J_{4,3eq}$ = 4.2 Hz, $J_{4,5}$ = 2.3 Hz, H-4), 3.88–3.80 (m, 3H, H-5, H-8a, H-8b), 3.75 (s, 3H, $COOCH_3$), 3.52 (app dt, 1H, *J* = 9.1, 6.8 Hz, octyl OCH_2), 3.24 (app t, 2H, *J* = 6.9 Hz, octyl CH_2N_3), 3.19 (app dt, 1H, *J* = 9.1, 6.8 Hz, octyl OCH_2), 2.44 (dd, 1H, $J_{3eq,4}$ = 4.2 Hz, J_{gem} = 12.3 Hz, H-3_{eq}), 2.25 (app t, 1H, $J_{3ax,4}$ = J_{gem} = 12.3 Hz, H-3_{ax}), 1.98 (s, 3H, $COCH_3$), 1.65–1.52 (m, 2H, octyl CH_2), 1.47–1.38 (octyl CH_2), 1.36–1.14 (m, 8H, octyl CH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 169.8 (C=O), 168.9 (C-1, $J_{C1\text{-}H3ax}$ = 0 Hz), 138.6 (Ar), 138.3 (Ar), 134.9 (OCH_2CH=CH_2), 128.7 (2C, Ar), 128.5 (2C, Ar), 128.4 (2C, Ar), 127.74 (Ar), 127.70 (Ar), 127.6 (2C, Ar), 116.7 (OCH_2CH=CH_2), 99.1 (C-2), 75.5 (C-4), 74.2 ($ArCH_2$), 73.4 ($ArCH_2$), 71.23 (C-5), 71.18 (C-7), 70.2 (C-6), 69.7 (OCH_2CH=CH_2), 68.0 (C-8), 63.7 (octyl OCH_2), 52.6 (OCH_3), 51.6 (octyl CH_2N_3), 33.1 (C-3), 29.7 (octyl CH_2), 29.5 (octyl CH_2), 29.2 (octyl CH_2), 29.0 (octyl CH_2), 26.9 (octyl CH_2), 26.1 (octyl CH_2), 21.3 ($COCH_3$); HRMS (ESI) calcd. for $C_{36}H_{49}N_3NaO_9$ $[M+Na]^+$ 690.3361 found 690.3361.



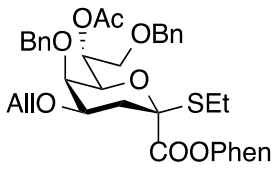
Benzyl (Ethyl 7-*O*-acetyl-4-*O*-allyl-5,8-di-*O*-benzyl-3-deoxy-β-D-*manno*-oct-2-ulopyranoside)onate (2.106β). A mixture of **2.104** (130 mg, 0.219 mmol) and 8-azidooctanol (315 mg, 0.496 mmol) and 4Å molecular sieves (500 mg) in CH_2Cl_2–CH_3CN (1:1, 5.0 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –70 °C and then NIS (59 mg, 0.263 mmol) and TfOH (1.9 μL, 0.0213 mmol) were added. After stirring at –70 °C for 1 h, trimethylamine was added to the reaction mixture. The reaction was warmed to room temperature and then a small amount of H_2O was added, followed by solid $Na_2S_2O_3 \cdot H_2O$ until the solution was colorless. The mixture was filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography (15:1 to 8:1, hexane–EtOAc) to give **2.106β** (110 mg, 68%) as a colorless oil and **2.106α** (18 mg, 11%) as a colorless oil. Data for **2.106β**: $[\alpha]^{25}_D$ +1.1 (*c* 2.3, $CHCl_3$); R_f 0.29 (4:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.38–7.22 (m, 15H, ArH), 5.88–5.80 (m, 1H, OCH_2CH=CH_2), 5.30–5.19 (m, 3H, OCH_2CH=CH_2, H-7, ArCH_2), 5.15–5.09 (m, 2H, OCH_2CH=CH_2, ArCH_2), 4.87 (d, 1H, J_{gem} = 11.1 Hz, ArCH_2), 4.54 (d, 1H, J_{gem} = 11.1 Hz, ArCH_2), 4.50–4.46 (m, 2H, ArCH_2), 3.99–3.94 (m, 2H, H-6, OCH_2CH=CH_2), 3.92–3.85 (m, 2H, H-8a, OCH_2CH=CH_2), 3.75 (br s, 1H, H-5), 3.69 (dd, 1H, $J_{8b,7}$ = 5.4 Hz, J_{gem} = 11.4 Hz, H-8b), 3.62 (app dt, 1H, *J* = 9.1, 6.8 Hz, octyl OCH_2), 3.36 (ddd, 1H, $J_{4,3eq}$ = 4.1 Hz, $J_{4,3ax}$ = 12.6 Hz, $J_{4,5}$ = 2.2 Hz, H-4), 3.26–3.21 (m, 3H, octyl OCH_2, octyl CH_2N_3), 2.44 (dd, 1H, $J_{3eq,4}$ = 4.1 Hz, J_{gem} = 12.6 Hz, H-3_{eq}), 2.23 (app t, 1H, $J_{3ax,4} = J_{gem}$ = 12.6 Hz, H-3_{ax}), 1.99 (s, 3H, COCH_3), 1.60–1.53 (m, 2H, octyl CH_2), 1.49–1.42 (m, 2H, octyl CH_2), 1.35–1.19 (m, 8H, octyl CH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 169.9 (C=O),

168.8 (C-1, $J_{C1\text{-}H3ax}$ = 6.9 Hz), 138.63 (Ar), 138.56 (Ar), 135.6 (Ar), 134.6 ($OCH_2CH{=}CH_2$), 128.82 (2C, Ar), 128.75 (Ar), 128.73 (2C, Ar), 128.6 (2C, Ar), 128.43 (2C, Ar), 128.37 (2C, Ar), 127.9 (2C, Ar), 127.7 (Ar), 127.6 (Ar), 116.9 ($OCH_2CH{=}CH_2$), 99.9 (C-2), 76.4 (C-4), 74.3 ($ArCH_2$), 73.4 ($ArCH_2$), 73.2 (C-6), 71.3 (C-5), 71.2 (C-7), 69.5 ($OCH_2CH{=}CH_2$), 68.6 (C-8), 67.2 ($ArCH_2$), 64.4 (octyl OCH_2), 51.7 (octyl CH_2N_3), 32.7 (C-3), 29.8 (octyl CH_2), 29.4 (octyl CH_2), 29.2 (octyl CH_2), 29.0 (octyl CH_2), 26.8 (octyl CH_2), 26.0 (octyl CH_2), 21.3 ($COCH_3$); HRMS (ESI) calcd. for $C_{42}H_{57}N_4O_9$ $[M+NH_4]^+$ 761.4120 found 761.4125.



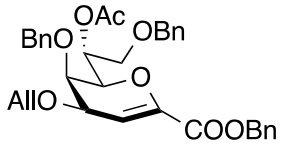
Benzyl (8-Azidooctyl 7-*O*-acetyl-4-*O*-allyl-5,8-di-*O*-benzyl-3-deoxy-α-D-*manno*-oct-2-ulopyranoside)onate (2.106α). $[\alpha]^{25}_D$ –0.02 (*c* 1.0, $CHCl_3$); R_f 0.32 (4:1, hexane–EtOAc); ^1H NMR ($CDCl_3$, 500 MHz) δ_H 7.40–7.21 (m, 15H, ArH), 5.98–5.87 (m, 1H, $OCH_2CH{=}CH_2$), 5.34–5.27 (m, 2H, $OCH_2CH{=}CH_2$, H-7), 5.21–5.17 (m, 3H, $OCH_2CH{=}CH_2$, $ArCH_2$), 4.88 (d, 1H, J_{gem} = 11.0 Hz, $ArCH_2$), 4.51 (d, 1H, J_{gem} = 11.0 Hz, $ArCH_2$), 4.48–4.42 (m, 2H, $ArCH_2$), 4.14–4.04 (m, 2H, $OCH_2CH{=}CH_2$), 3.99 (dd, 1H, $J_{6,5}$ = 1.0 Hz, $J_{6,7}$ = 9.0 Hz, H-6), 3.96 (ddd, 1H, $J_{4,3ax}$ = 12.2 Hz, $J_{4,3eq}$ = 4.7 Hz, $J_{4,5}$ = 2.2 Hz, H-4), 3.88–3.81 (m, 3H, H-5, H-8a, H-8b), 3.49 (app dt, 1H, *J* = 9.1, 6.8 Hz, octyl OCH_2), 3.23 (app t, 2H, *J* = 6.9 Hz, octyl CH_2N_3), 3.14 (app dt, 1H, *J* = 9.1, 6.8 Hz, octyl OCH_2), 2.25 (dd, 1H, $J_{3eq,4}$ = 4.7 Hz, J_{gem} = 12.2 Hz, H-3_{eq}), 2.18 (app t, 1H, $J_{3ax,4} = J_{gem}$ = 12.2 Hz, H-3_{ax}), 1.99 (s, 3H, $COCH_3$), 1.66–1.52 (m, 2H, octyl CH_2), 1.40–1.08 (m, 10H, octyl CH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 169.9 (C=O), 168.1 (C-1, $J_{C1\text{-}H3ax}$ = 0 Hz), 138.7 (Ar), 138.3 (Ar), 135.7 (Ar), 134.8 ($OCH_2CH{=}CH_2$), 128.7 (2C, Ar), 128.6 (2C, Ar), 128.5 (3C, Ar), 128.4 (2C, Ar), 128.3 (2C, Ar), 127.73 (Ar), 127.67 (Ar), 127.61 (2C, Ar), 116.8

($OCH_2CH=CH_2$), 99.0 (C-2), 75.5 (C-4), 74.2 (ArCH_2), 73.4 (ArCH_2), 71.3 (2C, C-5, C-7), 70.2 (C-6), 69.7 ($OCH_2CH=CH_2$), 68.1 (C-8), 67.1 (ArCH_2), 63.7 (OCH_2), 51.6 (CH_2N_3), 33.0 (C-3), 29.6 (octyl CH_2), 29.5 (octyl CH_2), 29.2 (octyl CH_2), 29.0 (octyl CH_2), 26.8 (octyl CH_2), 26.1 (octyl CH_2), 21.3 ($COCH_3$); HRMS (ESI) calcd. for $C_{42}H_{57}N_4O_9$ $[M+NH_4]^+$ 761.4120 found 761.4126.



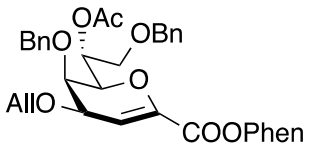
4'-Methoxyphenacyl (Ethyl 7-*O*-acetyl-4-*O*-allyl-5,8-di-*O*-benzyl-3-deoxy-2-thio-β-D-*manno*-oct-2-ulopyranoside)onate (2.107). To a solution of **2.85** (500 mg, 0.708 mmol) in a mixture of THF–CH_3OH–H_2O (1:1:1, 30 mL) was added 1N NaOH (5 mL) at room temperature. After strring for 24 h, the reaction mixture was neutralized by the addition of Amberlite IR-120 H^+ and then filtered and concentrated under reduced pressure. The residue was dried *in vacuo* for 24 h. The residue was then dissolved in DMF (30 mL) and potassium carbonate (mg 163 mg, 1.18 mmol) and PhenBr (270 mg, 1.18 mmol) were added at room temperature. After 3 h, CH_3OH was added and the reaction mixture was diluted with EtOAc and washed with H_2O to remove DMF. The organic layer was dried with $MgSO_4$, then filtered and concentrated. The residue was dried *in vacuo* for 4 h. To a solution of the residue in CH_2Cl_2 (30 mL) was added Et_3N (163 μL, 1.18 mmol), Ac_2O (89 μL, 0.945 mmol) and DMAP (9.6 mg, 0.0708 mmol). After stirring for 5 h, CH_3OH was added and the solution was concentrated. The residue was purified by column chromatography (8:1, hexane–EtOAc) to give **2.107** (480 mg, 88% over three steps) as a colorless oil. $[\alpha]^{25}_D$ –8.2 (*c* 1.0, $CHCl_3$); R_f 0.25 (8:1, hexane–EtOAc); ^1H NMR ($CDCl_3$, 500 MHz) δ_H 7.87–7.83 (m, 2H, ArH), 7.43–7.39 (m, 2H, ArH), 7.36–7.32 (m, 2H, ArH), 7.31–7.26 (m, 3H, ArH), 7.23–7.15 (m, 3H, ArH), 7.00–6.96 (m, 2H, ArH), 6.01–5.93 (m, 1H,

$OCH_2CH{=}CH_2$), 5.40–5.31 (m, 3H, H-7, $OCH_2CH{=}CH_2$, Phen OCH_2CO), 5.24 (d, 1H, J_{gem} = 16.0 Hz, Phen OCH_2CO), 5.20–5.17 (m, 1H, $OCH_2CH{=}CH_2$), 4.95 (d, 1H, J_{gem} = 11.0 Hz, $ArCH_2$), 4.59 (d, 1H, J_{gem} = 11.0 Hz, $ArCH_2$), 4.55 (d, 1H, J_{gem} = 11.9 Hz, $ArCH_2$), 4.49 (d, 1H, J_{gem} = 11.9 Hz, $ArCH_2$), 4.21–4.11 (m, 2H, $OCH_2CH{=}CH_2$), 4.08 (d, 1H, $J_{6,7}$ = 8.7 Hz, H-6), 4.00 (ddd, 1H, $J_{4,3eq}$ = 4.0 Hz, $J_{4,3ax}$ = 11.9 Hz, $J_{4,5}$ = 2.3 Hz, H-4), 3.94–3.88 (m, 5H, H-8a, H-5, OCH_3), 3.75 (dd, 1H, J_{gem} = 11.3 Hz, $J_{8b,7}$ = 5.4 Hz, H-8b), 2.79 (dq, 1H, J = 12.4, 7.7 Hz, SCH_2), 2.73–2.65 (m, 2H, $H\text{-}3_{eq}$, SCH_2), 2.39 (app t, 1H, $J_{gem} = J_{3ax,4}$ = 11.9 Hz, $H\text{-}3_{ax}$), 2.00 (s, 3H, $COCH_3$), 1.22 (t, 3H, J = 7.7 Hz, SCH_2CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 189.7 (Phen OCH_2CO), 169.9 (C=O), 169.1 (C-1, $J_{C1\text{-}H3ax}$ = 8.2 Hz), 164.3 (Ar), 138.7 (Ar), 138.6 (Ar), 134.8 ($OCH_2CH{=}CH_2$), 131.0 (Ar), 130.18 (Ar), 130.15 (2C, Ar), 128.7 (2C, Ar), 128.3 (3C, Ar), 127.64 (2C, Ar), 127.60 (Ar), 127.4 (Ar), 116.8 ($OCH_2CH{=}CH_2$), 114.23 (Ar), 114.22 (Ar), 84.4 (C-2), 76.6 (C-4), 74.9 (C-6), 74.2 ($ArCH_2$), 73.2 ($ArCH_2$), 71.3 (C-5), 70.7 (C-7), 69.7 ($OCH_2CH{=}CH_2$), 68.9 (C-8), 66.6 (Phen OCH_2CO), 55.7 (OCH_3), 33.6 (C-3), 23.5 (SCH_2), 21.3 ($COCH_3$), 14.3 (SCH_2CH_3); HRMS (ESI) calcd. for $C_{38}H_{44}NaO_{10}S$ $[M+Na]^+$ 715.2533 found 715.2534.



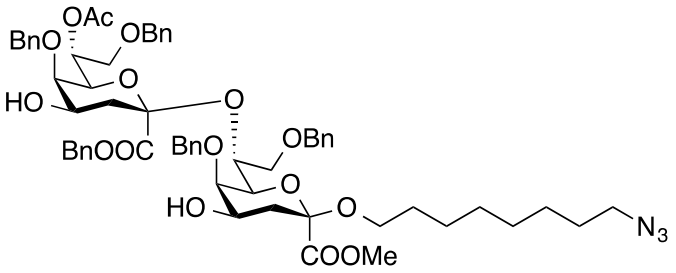
Benzyl (7-*O*-Acetyl-4-*O*-allyl-2,6-anhydro-5,8-di-*O*-benzyl-3-deoxy-D-*manno*-oct-2-enosonate (2.110). This compound was a side product from glycosylation of **2.88** and **2.104**; it is an oil $[\alpha]^{25}_D$ –3.1 (*c* 0.8, $CHCl_3$); R_f 0.27 (8:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.40–7.22 (m, 15H, ArH) 6.09 (app t, 1H, $J_{3,4} = J_{3,5}$ = 2.0 Hz, H-3), 5.98–5.90 (m, 1H, $OCH_2CH{=}CH_2$), 5.39–5.17 (m, 5H, H-7, $OCH_2CH{=}CH_2$, $ArCH_2$), 4.90 (d, 1H, J_{gem} = 11.1 Hz, $ArCH_2$), 4.61 (d, 1H, J_{gem} = 11.1 Hz, $ArCH_2$), 4.48 (s, 2H, $ArCH_2$), 4.37 (ddd, 1H, $J_{5,3}$ = 2.0 Hz,

$J_{5,4}$ = 3.1 Hz, $J_{5,6}$ = 1.3 Hz, H-5), 4.26 (app dt, 1H, $J_{6,4} = J_{6,5}$ = 1.2 Hz, $J_{6,7}$ = 9.0 Hz, H-6), 4.22–4.18 (m, 1H, OCH_2CH=CH_2), 4.13–4.08 (m, 1H, OCH_2CH=CH_2), 3.93 (ddd, 1H, $J_{4,3}$ = 2.1 Hz, $J_{4,5}$ = 3.1 Hz, $J_{4,6}$ = 1.0 Hz, H-4), 3.87 (dd, 1H, $J_{8a,7}$ = 2.3 Hz, J_{gem} = 11.3 Hz, H-8a), 3.83 (dd, 1H, $J_{8b,7}$ = 3.4 Hz, J_{gem} = 11.3 Hz, H-8b), 1.96 (s, 3H, $COCH_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 169.8 (C=O), 161.8 (C-1), 143.9 (C-2), 138.4 (Ar), 138.2 (Ar), 135.7 (Ar), 134.4 ($OCH_2CH=CH_2$), 128.7 (3C, Ar), 128.52 (3C, Ar), 128.49 (2C, Ar), 128.47 (2C, Ar), 128.38 (Ar), 127.9 (Ar), 127.81 (2C, Ar), 127.78 (Ar), 117.5 ($OCH_2CH=CH_2$), 110.0 (C-3), 75.1 (C-6), 74.5 (ArCH_2), 74.3 (C-5), 73.7 (ArCH_2), 70.7 (C-7), 70.4 ($OCH_2CH=CH_2$), 67.9 (C-8), 67.7 (C-4), 67.0 ($ArCH_2$), 21.3 ($COCH_3$); HRMS (ESI) calcd. for $C_{34}H_{36}NaO_8$ $[M+Na]^+$ 595.2302 found 595.2301.



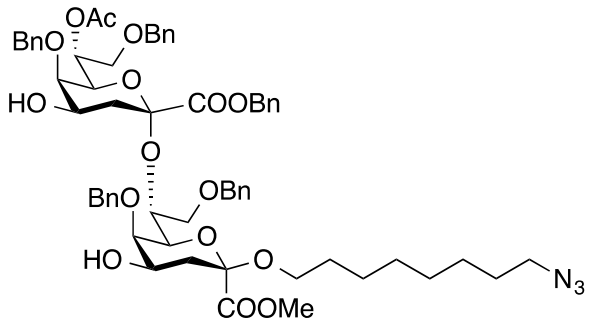
4'-Methoxyphenacyl (7-*O*-Acetyl-4-*O*-allyl-2,6-anhydro-5,8-di-*O*-benzyl-3-deoxy-D-*manno*-oct-2-enosonate (2.111). This compound was a side product from glycosylation of **2.88** and **2.107**; it is an oil $[\alpha]^{25}_D$ –44.1 (*c* 0.5, $CHCl_3$); R_f 0.24 (8:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.93–7.88 (m, 2H, ArH), 7.37–7.21 (m, 10H, ArH), 6.97–6.93 (m, 2H, ArH), 6.22 (app t, 1H, $J_{3,4} = J_{3,5}$ = 2.1 Hz, H-3), 5.99–5.91 (m, 1H, $OCH_2CH=CH_2$), 5.42 (d, 1H, J_{gem} = 15.9 Hz, Phen OCH_2CO), 5.37–5.26 (m, 3H, H-7, $OCH_2CH=CH_2$, Phen OCH_2CO), 5.25–5.21 (m, 1H, $OCH_2CH=CH_2$), 4.93 (d, 1H, J_{gem} = 11.0 Hz, ArCH_2), 4.63 (d, 1H, J_{gem} = 11.0 Hz, ArCH_2), 4.52 (s, 2H, ArCH_2), 4.42 (ddd, 1H, $J_{5,3}$ = 2.0 Hz, $J_{5,4}$ = 3.7 Hz, $J_{5,6}$ = 1.2 Hz, H-5), 4.31 (app dt, 1H, $J_{6,4} = J_{6,5}$ = 1.2 Hz, $J_{6,7}$ = 9.0 Hz, H-6), 4.25–4.20 (m, 1H, OCH_2CH=CH_2), 4.14–4.09 (m, 1H, OCH_2CH=CH_2), 3.95 (ddd, 1H, $J_{4,3}$ = 2.0 Hz, $J_{4,5}$ = 3.7 Hz, $J_{4,6}$ = 1.2 Hz, H-4), 3.90–3.82 (m, 5H, H-8a, H-8b, OCH_3), 1.98 (s, 3H, $COCH_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 190.2 (Phen

OCH_2CO), 169.8 (C=O), 164.3 (Ar), 161.3 (C-1), 143.3 (C-2), 138.4 (Ar), 138.3 (Ar), 134.4 ($OCH_2CH=CH_2$), 130.4 (2C, Ar), 128.7 (2C, Ar), 128.52 (2C, Ar), 128.50 (2C, Ar), 127.91 (2C, Ar), 127.87 (Ar), 127.73 (Ar), 127.5 (Ar), 117.5 ($OCH_2CH=CH_2$), 114.3 (2C, Ar), 110.9 (C-3), 75.3 (C-6), 74.5 ($ArCH_2$), 74.3 (C-5), 73.7 ($ArCH_2$), 70.7 (C-7), 70.4 ($OCH_2CH=CH_2$), 67.9 (2C, C-8, C-4), 66.4 (Phen OCH_2CO), 55.7 (OCH_3), 21.3 ($COCH_3$); HRMS (ESI) calcd. for $C_{36}H_{38}NaO_{10}$ $[M+Na]^+$ 653.2357 found 653.2357.



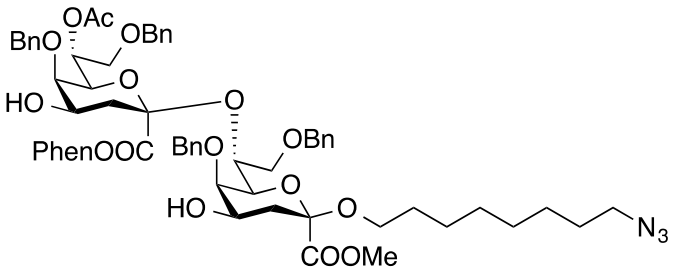
Methyl {8-Azidoooctyl 5,8-di-*O*-benzyl-3-deoxy-7-*O*-[benzyl 7-*O*-acetyl-5,8-di-*O*-benzyl-3-deoxy-β-D-*manno*-2-octulopyranosyl]onate}-β-D-*manno*-2-octulopyranosid}onate (2.112β). To a solution of **2.109** (100 mg, 0.084 mmol) in THF (10.0 mL), degassed under vaccum, and stirred under an Ar atmosphere, (1,5-cyclooctadiene) bis-(methyldiphenylphosphine)iridium I hexafluorophosphate catalyst (3.5 mg, 0.0041 mmol) was added, followed by further degassing of the mixture. The suspension was stirred for 30 min at 0 ºC, and the catalyst was then activated with hydrogen. At this point, the solution became nearly colorless. The excess of hydrogen gas was removed by exchange of Ar gas. The reaction mixture was then stirred for 24 h at room temperature under an Ar atmosphere. The solvent was then evaporated, and the residue was dissolved in acetone–H_2O (9:1, 10.0 mL). To the solution was added HgO (27 mg, 0.125 mmol) and $HgCl_2$ (34 mg, 0.383 mmol). After stirring for 24 h at room temperature, the solvent was evaporated and the residue was diluted with EtOAc and washed with 10% KI solution, satd. aq. $Na_2S_2O_3$, and H_2O. The organic layer was then dried over $MgSO_4$, filtered and concentrated un-

der reduced pressure. The resulting residue was purified by column chromatography (2:1, hexane–EtOAc) to give **2.112α** (65 mg, 69%) as colorless oil and **2.112β** (8.1 mg, 9%) as colorless oil. Data for **2.112β**: $[\alpha]^{25}_{D}$ –2.5 (*c* 0.3, $CHCl_3$); R_f 0.25 (1:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.38–7.22 (m, 25H, ArH), 5.24 (ddd, 1H, $J_{7',6'}$ = 8.3 Hz, $J_{7',8'a}$ = 5.6 Hz, $J_{7',8'b}$ = 2.6 Hz, H-7'), 5.09 (d, 1H, J_{gem} = 12.3 Hz, ArCH_2), 4.79 (d, 1H, J_{gem} = 11.5 Hz, ArCH_2), 4.75 (d, 1H, J_{gem} = 11.5 Hz, ArCH_2), 4.57–4.41 (m, 6H, H-7, ArH), 4.40 (br s, 2H, ArH), 3.98 (dd, 1H, $J_{6',5'}$ = 1.0 Hz, $J_{6',7'}$ = 8.3 Hz H-6'), 3.91–3.87 (m, 2H, H-6, H-8a), 3.81–3.76 (m, 2H, H-5, H-8'a), 3.69–3.52 (m, 9H, H-4, H-8b, H-4', H-5', H-8'b, octyl OCH_2, COOCH_3), 3.33 (dt, 1H, *J* = 9.4, 6.7 Hz, octyl OCH_2), 3.22 (t, 2H, *J* = 6.9 Hz, octyl CH_2N_3), 2.50 (dd, 1H, $J_{3eq,4}$ = 4.8 Hz, J_{gem} = 12.7 Hz, H-3$_{eq}$'), 2.35 (dd, 1H, $J_{3eq,4}$ = 4.8 Hz, J_{gem} = 12.4 Hz, H-3$_{eq}$), 2.09 (app t, 1H, $J_{3ax,4}$ = J_{gem} = 12.7 Hz, H-3$_{ax}$'), 2.05 (s, 3H, COCH_3), 1.92 (app t, 1H, $J_{3ax,4}$ = J_{gem} = 12.4 Hz, H-3$_{ax}$), 1.60–1.46 (m, 4H, octyl CH_2), 1.37–1.24 (m, 8H, octyl CH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 170.0 (C=O), 169.5 (C-1), 168.4 (C-1', $J_{C1',H3'ax}$ = 6.6 Hz), 138.9 (Ar), 138.8 (Ar), 138.4 (Ar), 138.1 (Ar), 135.5 (Ar), 128.77 (2C, Ar), 128.75 (2C, Ar), 128.73 (2C, Ar), 128.63 (Ar), 128.57 (2C, Ar), 128.54 (2C, Ar), 128.4 (2C, Ar), 128.2 (3C, Ar), 127.88 (2C, Ar), 127.87 (Ar), 127.83 (2C, Ar), 127.7 (Ar), 127.62 (2C, Ar), 127.57 (Ar), 99.7 (C-2'), 99.1 (C-2), 75.8 (Ar*C*H$_2$), 75.5 (C-6), 75.3 (Ar*C*H$_2$), 74.8 (C-5'), 74.6 (C'5), 73.53 (C-6), 73.50 (Ar*C*H$_2$), 73.3 (Ar*C*H$_2$), 72.8 (C-7), 70.9 (C-7'), 69.0 (C-8'), 68.5 (C-8), 68.4 (C-4' or C-4), 68.3 (C-4' or C-4), 67.6 (Ar*C*H$_2$), 64.3 (octyl O*C*H$_2$), 52.3 (COO*C*H$_3$), 51.7 (octyl *C*H$_2$N$_3$), 37.0 (C-3), 36.1 (C-3'), 29.9 (octyl CH$_2$), 29.4 (octyl CH$_2$), 29.3 (octyl CH$_2$), 29.0 (octyl CH$_2$), 26.8 (octyl CH$_2$), 26.0 (octyl CH$_2$), 21.3 (CO*C*H$_3$); HRMS (ESI) calcd. for $C_{62}H_{75}N_3NaO_{16}$ $[M+Na]^+$ 1140.5040 found 1140.5041.



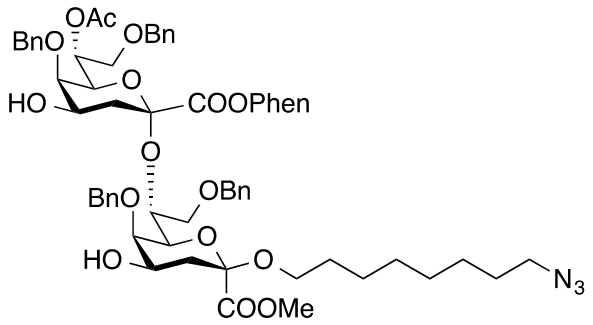
Methyl {8-Azidoooctyl 5,8-di-*O*-benzyl-3-deoxy-7-*O*-[benzyl 7-*O*-acetyl-5,8-di-*O*-benzyl-3-deoxy-α-D-*manno*-2-octulopyranosyl]onate}-β-D-*manno*-2-octulopyranosid}onate (2.112α). $[\alpha]^{25}_{D}$ +22.1 (*c* 1.0, $CHCl_3$); R_f 0.21 (1:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.38–7.22 (m, 25H, ArH), 5.51 (app dt, 1H, $J_{7',6'} = J_{7',8'b} = 7.5$ Hz, $J_{7',8'a} = 2.4$ Hz, H-7'), 5.03 (d, 1H, $J_{gem} = 12.8$ Hz, ArCH_2), 4.96 (d, 1H, $J_{gem} = 12.8$ Hz, ArCH_2), 4.74–4.69 (m, 2H, ArCH_2), 4.58–4.54 (m, 2H, H-6', ArCH_2), 4.52–4.45 (m, 2H, H-7, ArCH_2), 4.42–4.34 (m, 4H, ArCH_2), 4.09–3.98 (m, 2H, H-4', H-8a), 3.98 (dd, 1H, $J_{8'a,7'} = 2.4$ Hz, $J_{gem} = 11.3$ Hz H-8'a), 3.96–3.55 (m, 9H, H-5, H-6, H-8b, H-5', H-8'b, octyl OCH_2, COOCH_3), 3.54–3.46 (m, 1H, H-4), 3.30 (dt, 1H, J = 9.2, 6.6 Hz, octyl OCH_2), 3.23 (t, 2H, J = 6.9 Hz, octyl CH_2N_3), 2.28–2.23 (m, 2H, H-3_{eq}, H-3_{eq}'), 2.05–2.00 (m, 4H, H-3'$_{ax}$, COCH_3), 1.91 (app t, 1H, $J_{3ax,4} = J_{gem} = 12.3$ Hz, H-3_{ax}), 1.63–1.47 (m, 4H, octyl CH_2), 1.37–1.24 (m, 8H, octyl CH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 170.3 (C=O), 169.5 (C-1), 168.0 (C-1', $J_{C1',H3'ax} = 0$ Hz), 138.7 (Ar), 138.6 (Ar), 138.44 (Ar), 138.39 (Ar), 135.3 (Ar), 128.8 (Ar), 128.53 (Ar), 128.50 (Ar), 128.44 (Ar), 128.24 (Ar), 128.22 (Ar), 128.17 (Ar), 128.1 (Ar), 128.0 (Ar), 127.74 (Ar), 127.67 (Ar), 99.5 (C-2'), 98.3 (C-2), 76.3 (C-5), 75.9 (C-5'), 75.7 (ArCH$_2$), 75.5 (C-6), 75.3 (ArCH$_2$), 74.0 (C-6'), 73.4 (ArCH$_2$), 73.0 (ArCH$_2$), 71.8 (C-7), 71.3 (C-7'), 70.5 (C-8), 69.8 (C-8'), 68.1 (C-4), 67.3 (ArCH$_2$), 67.0 (C-4'), 64.3 (octyl OCH$_2$), 52.5 (COOCH$_3$), 51.7 (octyl CH$_2$N$_3$), 36.6 (C-3), 35.7 (C-3'), 29.9 (octyl CH$_2$), 29.4 (oc-

tyl CH_2), 29.3 (octyl CH_2), 29.0 (octyl CH_2), 26.9 (octyl CH_2), 26.1 (octyl CH_2), 21.4 ($COCH_3$); HRMS (ESI) calcd. for $C_{62}H_{75}N_3NaO_{16}$ $[M+Na]^+$ 1140.5040 found 1140.5040.



Methyl {8-Azidoooctyl 5,8-di-*O*-benzyl-3-deoxy-7-*O*-[4'-methoxyphenacyl 7-*O*-acetyl-5,8-di-*O*-benzyl-3-deoxy-β-D-*manno*-2-octulopyranosyl]onate}-β-D-*manno*-2-octulopyranosid}onate (2.113β). To a solution of **2.109** (320 mg, 0.0319 mmol) in THF (30.0 mL), degassed under vaccum, and stirred under an Ar atmosphere, (1,5-cyclooctadiene) bis-(methyldiphenylphosphine)iridium I hexafluorophosphate catalyst (10.8 mg, 0.128 mmol) was added, followed by further degassing of the mixture. The suspension was stirred for 30 min at 0 ºC, and the catalyst was then activated with hydrogen. At this point, the solution became nearly colorless. The excess of hydrogen gas was removed by exchange of Ar gas. The reaction mixture was then stirred for 24 h at room temperature under Ar atmosphere. The solvent was then evaporated, and the residue was dissolved in acetone–H_2O (9:1, 30.0 mL). To the solution was then added HgO (86 mg, 0.383 mmol) and $HgCl_2$ (104 mg, 0.383 mmol). After stirring for 24 h at room temperature, the solvent was evaporated and the residue was diluted with EtOAc and washed with 10% KI solution, satd. aq. $Na_2S_2O_3$, and H_2O. The organic layer was then dried over $MgSO_4$, filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography (2:1, hexane–EtOAc) to give **2.113α** (145 mg, 43%) as colorless oil and **2.113β** (155 mg, 45%) as colorless oil. Data for **2.113β**: $[\alpha]^{25}_D$ –1.5 (*c* 1.1, $CHCl_3$); R_f 0.38 (1:1, hexane–EtOAc); ^1H NMR ($CDCl_3$, 500 MHz) δ_H 7.59–7.53 (m, 2H, ArH), 7.40–7.14

(m, 20H, ArH), 6.92–6.87 (m, 2H, ArH), 5.32 (ddd, 1H, $J_{7',6'}$ = 8.5 Hz, $J_{7',8'a}$ = 5.7 Hz, $J_{7',8'b}$ = 2.4 Hz, H-7'), 4.90–4.84 (m, 2H, OCH_2CO, ArCH_2), 4.66–4.60 (m, 3H, OCH_2CO, ArCH_2), 4.56 (d, 1H, J_{gem} = 10.9 Hz, ArCH_2), 4.51–4.44 (m, 3H, H-7, ArCH_2), 4.41–4.34 (m, 2H, ArCH_2), 4.29–4.21 (m, 2H, H-4', H-6'), 3.93 (dd, 1H, $J_{8a,7}$ = 2.2 Hz, J_{gem} = 11.0 Hz, H-8a), 3.90 (dd, 1H, $J_{6,5}$ = 0.9 Hz, $J_{6,7}$ = 6.5 Hz, H-6), 3.88 (s, 3H, OCH_3), 3.86–3.79 (m, 3H, H-5, H-5', H-8'a), 3.74–3.63 (m, 4H, H-4, H-8b, H-8'b, octyl OCH_2), 3.57 (s, 3H, COOCH_3), 3.35 (dt, 1H, J = 9.4, 6.7 Hz, octyl OCH_2), 3.22 (t, 2H, J = 6.9 Hz, octyl CH_2N$_3$), 2.67 (dd, 1H, $J_{3'eq,4}$ = 4.6 Hz, J_{gem} = 12.3 Hz, H-3'$_{eq}$), 2.38 (dd, 1H, $J_{3eq,4}$ = 4.7 Hz, J_{gem} = 12.4 Hz, H-3$_{eq}$), 2.18 (app t, 1H, $J_{3ax,4}$ = J_{gem} = 12.3 Hz, H-3'$_{ax}$), 2.06 (s, 3H, COCH_3), 1.94 (app t, 1H, $J_{3ax,4}$ = J_{gem} = 12.4 Hz, H-3$_{ax}$), 1.84 (d, 1H, $J_{OH,4'}$ = 8.3 Hz, 4'-OH), 1.74 (d, 1H, $J_{OH,4}$ = 9.5 Hz, 4-OH), 1.60–1.48 (m, 4H, octyl CH_2), 1.36–1.24 (m, 8H, octyl CH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 190.0 (Phen CH_2*C*O), 170.0 (C=O), 169.4 (C-1, $J_{C1,H3ax}$ = 6.6 Hz), 168.1 (C-1', $J_{C1',H3'ax}$ = 6.1 Hz), 164.3 (Ar), 139.1 (Ar), 138.9 (Ar), 138.5 (Ar), 138.3 (Ar), 130.2 (2C, Ar), 128.7 (2C, Ar), 128.6 (2C, Ar), 128.46 (2C, Ar), 128.45 (2C, Ar), 128.35 (2C, Ar), 128.1 (2C, Ar), 128.0 (Ar), 127.8 (Ar), 127.7 (2C, Ar), 127.64 (2C, Ar), 127.59 (Ar), 127.57 (Ar), 126.9 (Ar), 114.1 (2C, Ar), 99.7 (C-2'), 99.1 (C-2), 75.7 (Ar*C*H$_2$), 75.5 (C-5), 75.4 (Ar*C*H$_2$), 74.9 (C-5' or C-6), 74.8 (C-5' or C-6), 73.7 (C-6'), 73.4 (Ar*C*H$_2$), 73.2 (Ar*C*H$_2$), 72.8 (C-7), 70.8 (C-7'), 69.3 (C-8'), 68.6 (C-8), 68.4 (C-4' or C-4), 68.2 (C-4' or C-4), 66.5 (Phen O*C*H$_2$CO), 64.3 (octyl O*C*H$_2$), 55.8 (OCH_3), 52.3 (COO*C*H$_3$), 51.6 (octyl *C*H$_2$N$_3$), 37.6 (C-3), 36.1 (C-3'), 29.9 (octyl CH$_2$), 29.4 (octyl CH$_2$), 29.2 (octyl CH$_2$), 29.0 (octyl CH$_2$), 26.8 (octyl CH$_2$), 26.1 (octyl CH$_2$), 21.4 (CO*C*H$_3$); HRMS (ESI) calcd. for $C_{64}H_{77}N_3NaO_{18}$ $[M+Na]^+$ 1198.5094 found 1198.5118.



Methyl {8-Azidoooctyl 5,8-di-*O*-benzyl-3-deoxy-7-*O*-[4'-methoxyphenacyl 7-*O*-acetyl-5,8-di-*O*-benzyl-3-deoxy-α-D-*manno*-2-octulopyranosyl]onate}-β-D-*manno*-2-octulopyranosid}onate (2.113α). $[\alpha]^{25}_{D}$ +13.5 (*c* 1.0, $CHCl_3$); R_f 0.36 (1:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.77–7.73 (m, 2H, ArH), 7.38–7.18 (m, 20H, ArH), 6.95–6.90 (m, 2H, ArH), 5.51 (dd, 1H, $J_{7',6'} = J_{7',8'b} = 7.4$ Hz, $J_{7',8'a} = 2.4$ Hz, H-7'), 4.99 (d, 1H, $J_{gem} = 16.0$ Hz, OCH_2CO), 4.94 (d, 1H, $J_{gem} = 16.0$ Hz, OCH_2CO), 4.85 (d, 1H, $J_{gem} = 11.9$ Hz, ArCH_2), 4.75 (d, 1H, $J_{gem} = 11.3$ Hz, ArCH_2), 4.66 (d, 1H, $J_{gem} = 11.9$ Hz, ArCH_2), 4.60–4.54 (m, 2H, H-7, ArCH_2), 4.53–4.44 (m, 2H, H-6', ArCH_2), 4.44–4.37 (m, 3H, ArCH_2), 4.14–4.06 (m, 2H, H-4, H-8a), 3.95 (dd, 1H, $J_{8'a,7} = 2.4$ Hz, $J_{gem} = 11.3$ Hz, H-8'a), 3.91 (dd, 1H, $J_{6,5} = 1.0$ Hz, $J_{6,7} = 4.8$ Hz, H-6), 3.87 (s, 3H, OCH_3), 3.80–3.72 (m, 5H, H-4, H-5, H-8b, H-5', H-8'b), 3.67–3.63 (m, 4H, octyl OCH_2, COOCH_3), 3.34 (dt, 1H, $J = 9.4$, 6.7 Hz, octyl OCH_2), 3.23 (t, 2H, $J = 6.9$ Hz, octyl CH_2N$_3$), 2.36 (dd, 1H, $J_{3'eq,4} = 4.8$ Hz, $J_{gem} = 12.6$ Hz, H-3'$_{eq}$), 2.30 (dd, 1H, $J_{3'eq,4} = 4.6$ Hz, $J_{gem} = 12.6$ Hz, H-3'$_{eq}$), 2.18 (app t, 1H, $J_{3'ax,4} = J_{gem} = 12.6$ Hz, H-3'$_{ax}$), 2.05 (s, 3H, COCH_3), 1.94 (app t, 1H, $J_{3ax,4} = J_{gem} = 12.6$ Hz, H-3$_{ax}$), 1.80 (d, 1H, $J_{OH,4} = 9.7$ Hz, 4-OH), 1.67 (d, 1H, $J_{OH,4'} = 9.7$ Hz, 4'-OH), 1.60–1.49 (m, 4H, octyl CH_2), 1.38–1.27 (m, 8H, octyl CH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 189.9 (Phen CH_2CO), 170.3 (C=O), 169.5 (C-1, $J_{C1,H3ax} = 6.6$ Hz), 167.6 (C-1', $J_{C1',H3'ax} = 0$ Hz), 164.3 (Ar), 138.9 (Ar), 138.58 (Ar), 138.55 (Ar), 138.48 (Ar), 130.2 (2C, Ar), 128.76 (2C, Ar), 128.7 (2C, Ar), 128.46 (2C, Ar), 128.44 (2C, Ar), 128.29 (2C, Ar), 128.27

(2C, Ar), 128.1 (Ar), 127.84 (Ar), 127.79 (2C, Ar), 127.7 (Ar), 127.67 (2C, Ar), 127.65 (Ar), 127.2 (Ar), 114.1 (2C, Ar), 99.5 (C-2'), 98.6 (C-2), 76.3 (C-5 or C-5'), 76.1 (C-5 or C-5'), 75.8 (Ar*C*H_2), 75.3 (Ar*C*H_2), 75.2 (C-6), 74.1 (C-6'), 73.3 (Ar*C*H_2), 73.0 (Ar*C*H_2), 72.0 (C-7), 71.5 (C-7'), 70.7 (C-8), 69.6 (C-8'), 67.9 (C-4'), 67.0 (C-4), 66.5 (Phen O*C*H_2CO), 64.3 (octyl O*C*H_2), 55.7 (OC*H*$_3$), 52.5 (COO*C*H_3), 51.7 (octyl *C*H_2N_3), 37.4 (C-3), 35.9 (C-3'), 29.9 (octyl CH_2), 29.4 (octyl CH_2), 29.3 (octyl CH_2), 29.0 (octyl CH_2), 26.9 (octyl CH_2), 26.1 (octyl CH_2), 21.4 (CO*C*H_3); HRMS (ESI) calcd. for $C_{64}H_{77}N_3NaO_{18}$ $[M+Na]^+$ 1198.5094 found 1198.5118.

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Chapter 3

Development of Conformationally-Restricted Xylulose Thioglycoside Donors for β-Selective Xylulofuranosylation and Their Synthetic Applications

3.1 Background

3.1.1 Natural occurrence of xylulose-containing glycans

Xylulose (Xul) is a rare ketopentose that contains five carbon atoms and a ketone functionality at its C-2 position (**Figure 3.1a**). This monosaccharide can only exist in the open-chain and furanose ring forms. Both β-D-xylulofuranosides (β-D-Xul*f*) and α-D-xylulofuranosides (α-D-Xul*f*) (**Figure 3.1b**) are components of essential glycans in microorganisms. For instance, β-D-Xul*f* has been identified in the O-chain of lipopolysaccharide (LPS) of *Yersinia enterocolitica* serovars O:5 and O:5,27, which is identical to the O-antigens of *Escherichia coli* O97[1] (**Figure 3.1c**). β-D-Xul*f* has also been found in N-linked glycans of chloroviruses (**Figure 3.1c**)[2]. Moreover, both β-D-Xul*f* and α-D-Xul*f* have been found in the capsular polysaccharide (CPS) of *Campylobacter jejuni* RM1221 (**Figure 3.1c**)[3]. To my best knowledge, there are no reports of synthesizing xylulose-containing glycans, particularly β-D-Xul*f*-containing glycans.

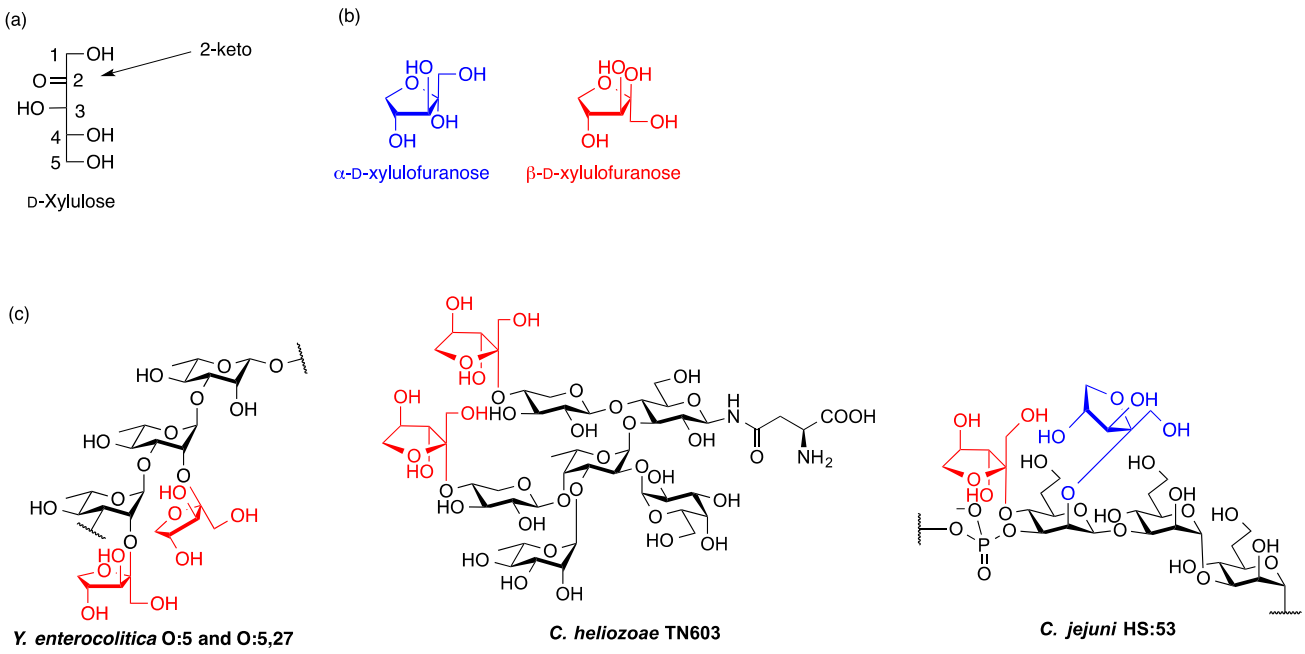


Figure 3.1. (a) Fischer projection of D-xylulose. (b) Cyclic forms of D-xylulofuranose. (c) Examples of natural Xul*f*-containing glycans.

3.1.2 Methodologies for 1,2-*cis*-aldofuranosylation and 2,3-*cis*-ketofuranosylation

Stereoselective glycosidic bond formation in furanosides is a general challenge, particularly those where the target is a 1,2-*cis*-furanoside, *e.g.,* β-arabinofuranosides (β-Ara*f*)[4] α-galactofuranosides (α-Gal*f*)[5], α-xylofuranosides (α-Xyl*f*)[6] and β-fructofuranosides (β-Fru*f*)[7] (**Figure 3.2a**). The inherent flexibility in furanose rings often leads to small energy differences between competing transition states, and a mixture of 1,2-*cis*- and 1,2-*trans*-furanosides are often observed (**Figure 3.2b**). The formation of 1,2-*trans* furanosides is relatively easy to achieve via the use of a participating acyl group on O-2 (**Figure 3.2c**). Therefore, although there are many examples of 1,2-*trans*-furanoside bond formation in the literature[8] here I will only discuss methods for 1,2-*cis*-furanosylation.

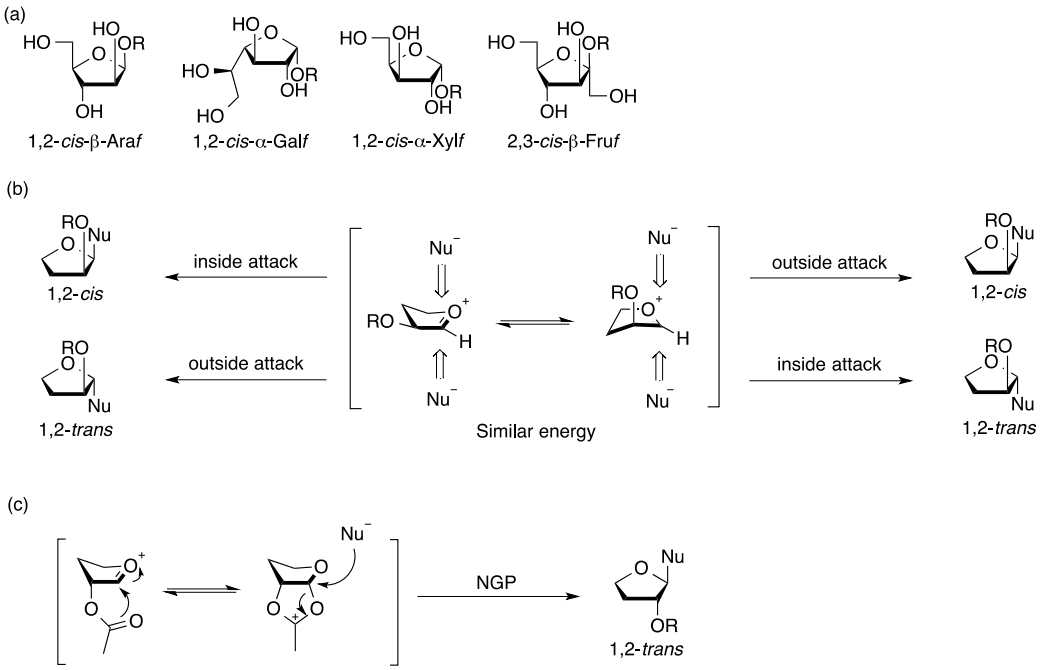
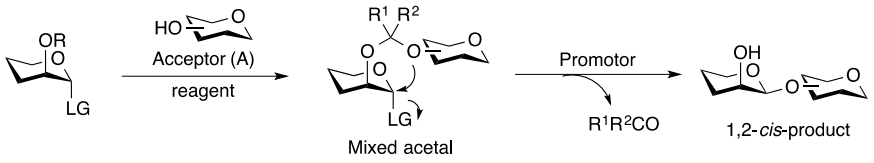


Figure 3.2. (a) Examples of common 1,2-*cis*-furanosides. (b) General mechanism for the formation of a mixture of 1,2-*cis*- and 1,2-*trans*-furanosides without a participating group at C-2. (c) Mechanism for the formation of 1,2-*trans*-furanosides with a participating group at C-2.

There is currently no general method to achieve the stereocontrolled preparation of 1,2-*cis*-furanosides. As mentioned above, in the absence of neighboring group participation, the conformational flexibility of the furanose ring leads to a number of reaction pathways with similar transition state energies, and results in a mixture of anomers. Methodologies that have been investigated for 1,2-*cis*-furanoside synthesis include the use of indirect methods such as intramolecular aglycone delivery[9] and oxidation–reduction[10]. Direct methods, including hydrogen bond-mediated aglycone delivery[11] and the use of conformationally-restricted donors[12], have also been developed. In the following sections, I will discuss the concept behind and examples of each of these methodologies.

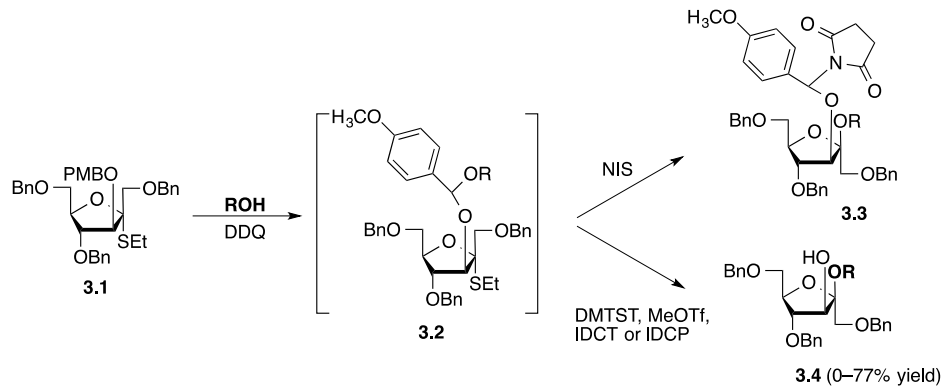
3.1.2.1 Intramolecular aglycone delivery (IAD)

IAD is an indirect glycosylation method first developed by Hindsgaul and coworkers for synthesizing 1,2-*cis*-mannopyranosides[9]. This strategy normally uses a functional group at C-2 to which the glycosyl acceptor is tethered to generate a mixed acetal (or ketal) in the first step. Then, in the second step, the glycosyl acceptor is delivered intramolecularly from the same side as the C-2 substituent to provide the 1,2-*cis* glycoside (**Scheme 3.1**).



Scheme 3.1. General mechanism of intramolecular aglycone delivery.

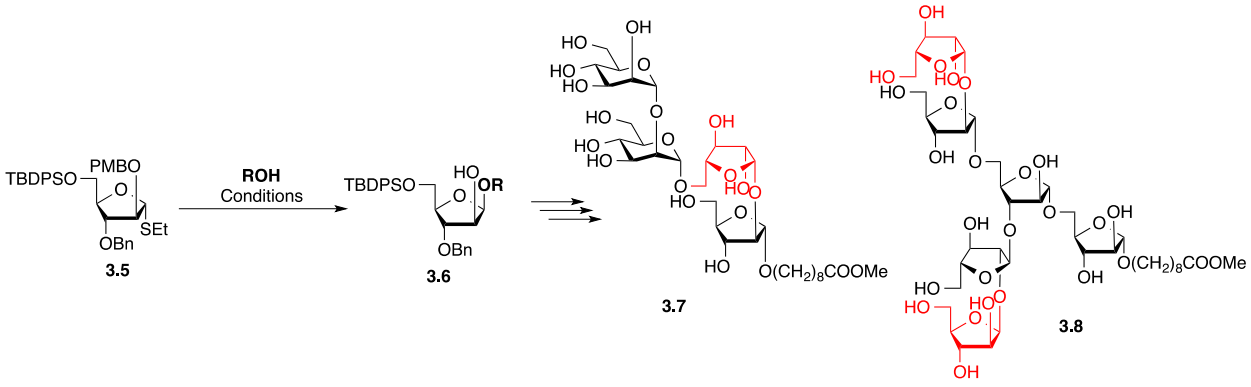
IAD was first applied by Oscarson and coworkers to the preparation of 1,2-*cis*-furanosides in the synthesis of β-fructofuranosides using a PMB ether on O-2[13]. During treatment of glycosyl donor **3.1** and the alcohol acceptor (**ROH**) with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ), the PMB ether precursor was oxidized to the corresponding oxacarbenium ion, which then reacted with the acceptor to generate the mixed acetal **3.2**. After activation of the thioglycoside, β-fructofuranosides **3.4** were obtained as the exclusive glycoside product (**Scheme 3.2**).



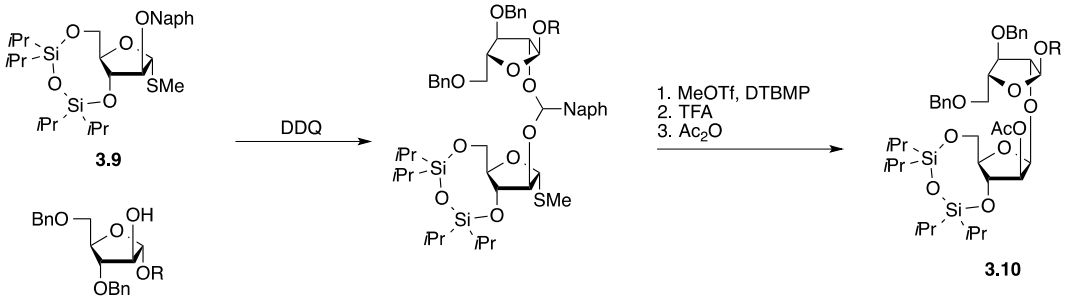
Scheme 3.2. Synthesis of 2,3-*cis*-fructofuranosides via IAD using PMB group as tether.

The activation promoter in the glycosylation step affected the yield, but there was no significant trend observed. When methyl trifluoromethanesulfonate (MeOTf), dimethylthiomethyl sulfonium trifluoromethanesulfonate (DMTST), iodonium collidine triflate (IDCT) and iodonium dicollidine perchlorate (IDCP) were used, the fructofuranoside **3.4** was obtained in different yields. *N*-iodosuccinimide (NIS) could not be used in this case, as the very stable succinimide side product **3.3** was formed and could not be converted into the glycoside (**Scheme 3.2**).

The construction of β-arabinofuranosides using the IAD strategy was first reported by Prandi and coworkers[14]. The use of arabinofuranosyl donors with a PMB ether on the O-2 position (*e.g.,* **3.5**) and different acceptors successfully generated β-Ara*f*-containing glycan fragments of mycobacterial glycans **3.7** and **3.8**[14] (**Scheme 3.3**). Donors containing a 2-naphthylmethyl group (Nap) on the O-2 position (*e.g.,* **3.9**) were later developed for the synthesis of β-Ara*f* glycosides (*e.g.,* **3.10**, **Scheme 3.4**)[15]. In 2011, Nap-directed IAD was applied to the preparation of a 22-residue arabinan fragment of mycobacterial arabinogalactan[15b].



Scheme 3.3. PMB-IAD strategy to synthesize 1,2-*cis*-β-Ara*f*-containing glycan fragments **3.7** and **3.8** of mycobacterial glycans.

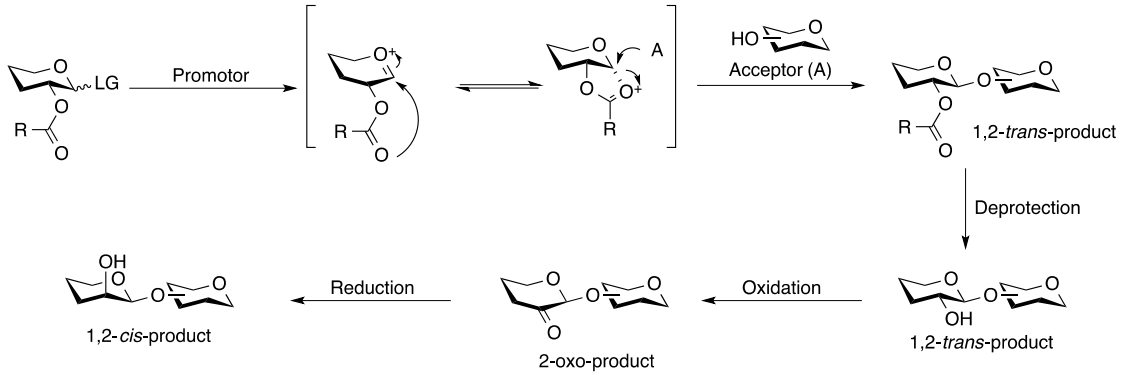


Scheme 3.4. β-Arabinofuranosylation via the Nap IAD strategy.

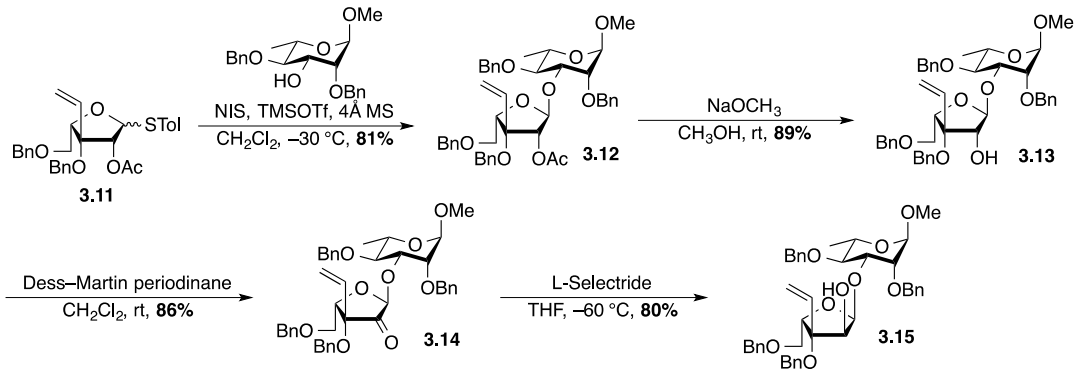
3.1.2.2 Oxidation–reduction

The oxidation–reduction strategy[10] is an indirect method for making *cis*-glycosides. It involves first the formation of a 1,2-*trans*-glycosidic bond via anchimeric assistance from a group at O-2, followed by O-2 deprotection and an oxidation–reduction protocol to afford the 1,2-*cis*-glycoside (**Scheme 3.5**). The strategy was first applied to 1,2-*cis*-furanosides by Field and coworkers[16] in their synthesis of a rare aceric acid-containing disaccharide (**3.15**), which is a component of Rhamnogalacturonan II (RGII) (**Scheme 3.6**), a plant polysaccharide. The 1,2-

trans-furanoside **3.12** was obtained stereoselectively from donor **3.11** via acetyl participation; deprotection of the acetyl group afforded alcohol **3.13**. Then a two step oxidation–reduction process was performed using Dess–Martin oxidation to give the 2-oxo product **3.14**, which was reduced from the less hindered face by L-selectride to give 1,2-*cis* disaccharide **3.15**.



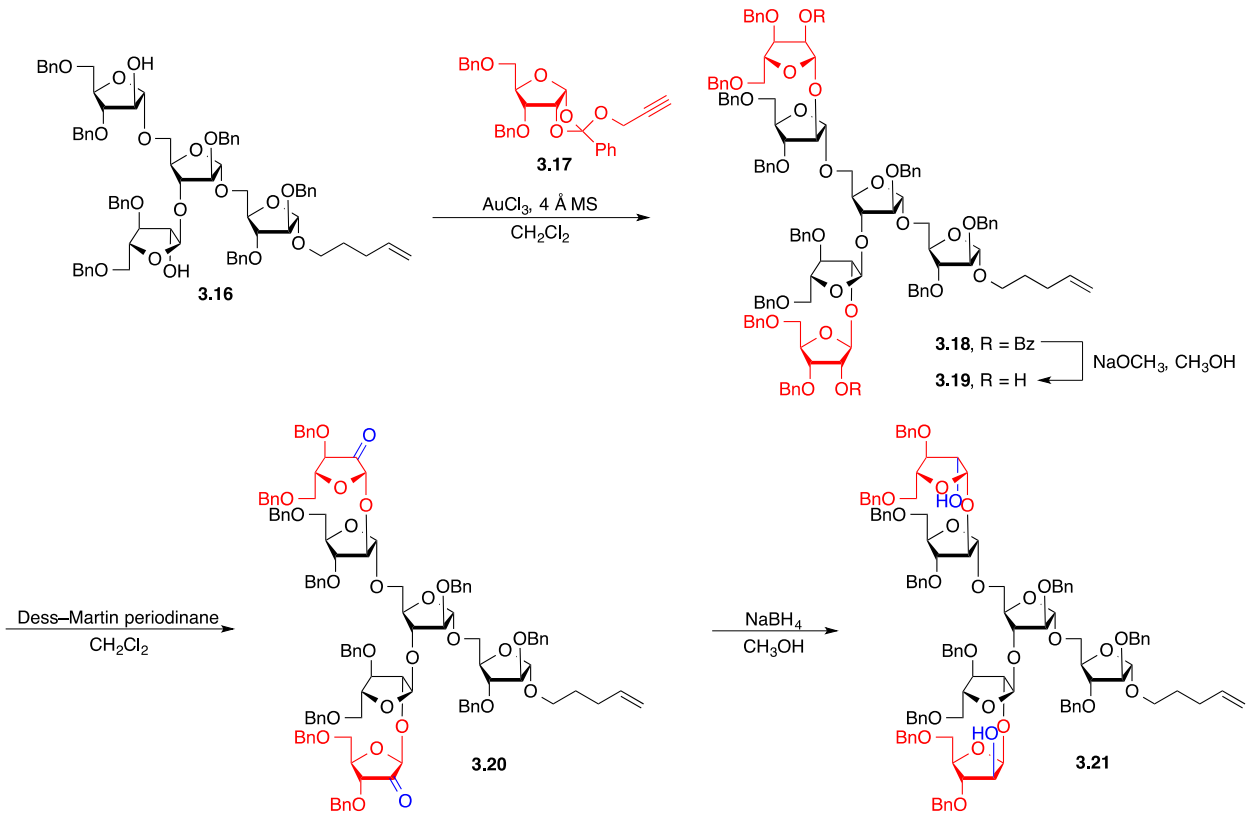
Scheme 3.5. General process for making 1,2-*cis*-glycosidic bonds via an oxidation–reduction strategy.



Scheme 3.6. Synthesis of 1,2-*cis*-disaccharide **3.15** via an oxidation–reduction strategy.

In 2013, Hotha and coworkers extended this strategy to the synthesis of the protected 1,2-*cis*-Ara*f*-containing hexasaccharide **3.21**, a protected derivative of a fragment of *Mycobacterium tuberculosis* arabinogalactan (**Scheme 3.7**)[17]. Hexasaccharide **3.18**, with two 1,2-*trans*-β-ribofuranosyl motifs, was synthesized by the coupling reaction of tetrasaccharide **3.16** and ribo-

furanosyl orthoester **3.17**. Subsequently, hexasaccharide **3.18** was saponified under Zemplén conditions to afford hexasaccharide diol **3.19**. Oxidation of the hydroxyl groups with Dess–Martin periodinane and reduction of the product **3.20** by $NaBH_4$ afforded hexasaccharide **3.21** with two β-Ara*f* motifs.



Scheme 3.7. Synthesis of a protected derivative of the β-Ara*f*-containing hexasaccharide **3.21** from *M. tuberculosis* arabinogalactan via an oxidation–reduction strategy.

The next year, the Hotha group successfully extended this methodology to generate three out of four *cis*-pentofuranosides **3.26–3.28** except for α-xylofuranoside **3.29** (**Figure 3.3a**)[18]. The conversion of 1,2-*trans*-furanosides to 1,2-*cis*-furanosides is the key step. As shown in **Figure 3.3b**, the stereoselective outcome was explained based on different steric environments

around the carbonyl group of the C-2-ulose derivatives. In three cases (**3.22** to **3.26**, **3.23** to **3.27** and **3.24** to **3.28**), the hydride successfully attacked from the less hindered face of the ring to afford the 1,2-*cis*-furanoside in the reduction step. However, in case of the α-lyxofuranoside (α-Lyx*f*, **3.25**) to α-xylofuranoside (α-Xyl*f*, **3.29**) conversion, the benzyl groups on O-3 and O-5 prevent hydride attack on the carbonyl group from the top face of the ring. Thus, the reduction gives back the starting material (**Figure 3.3b**).

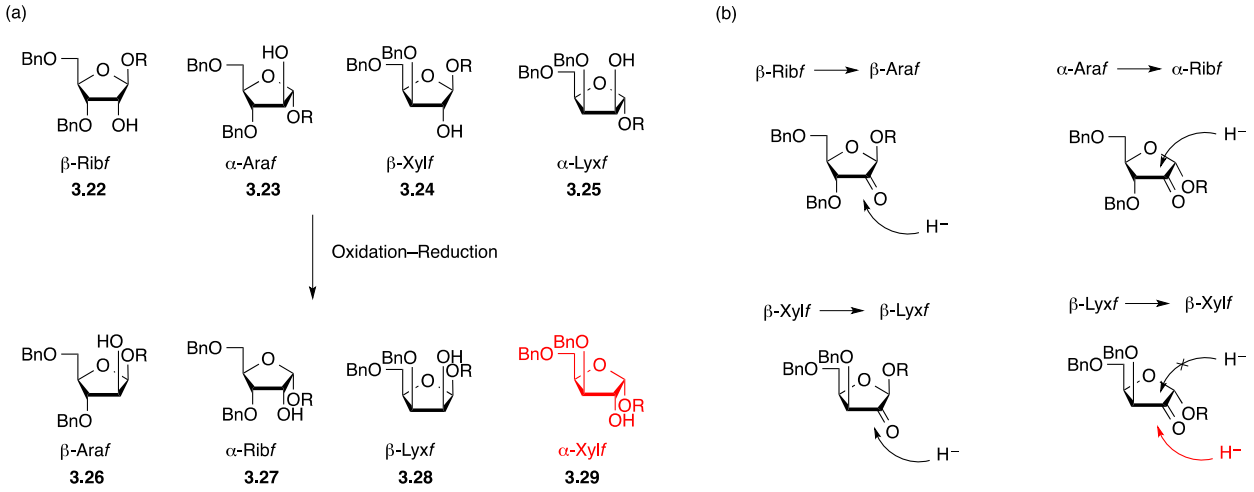
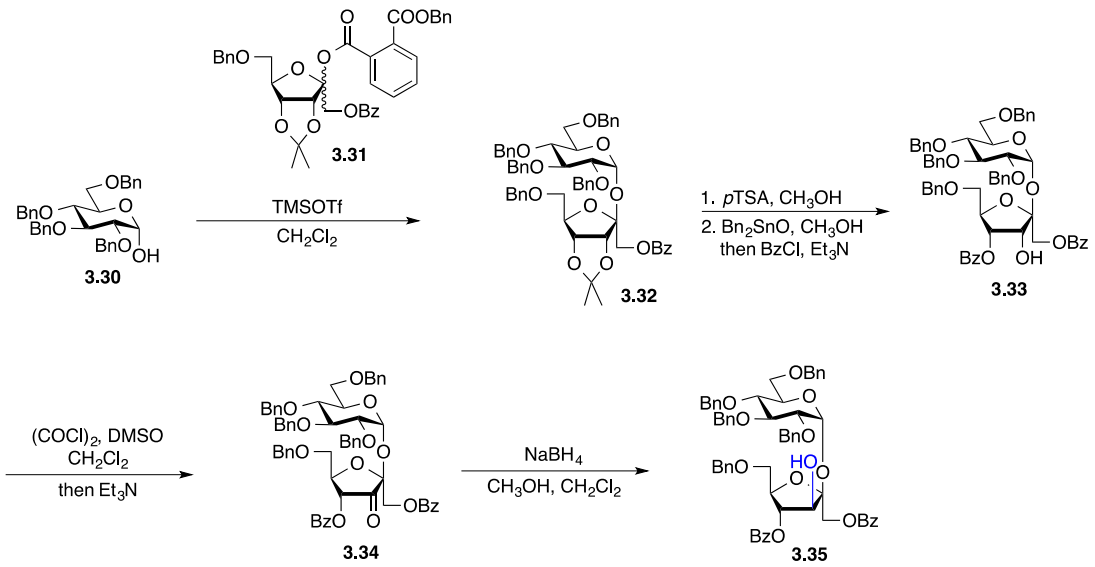


Figure 3.3. (a) Generation of three out of four *cis*-pentofuranosides **3.26**–**3.28** via an oxidation–reduction strategy. (b) Explanation of the diastereoselectivity in the reduction step.

The oxidation–reduction method was also applied to the synthesis of 2,3-*cis*-ketofuranosyl residues by Uenishi and Ueda[19]. Using the 3,4-isopropylidene-protecteed D-psicofuransyl donor **3.31**, the 2,3-*trans* disaccharide **3.32** was obtained, although an anomeric mixture at the glucopyranosyl moiety was obtained. After deprotection of the isopropylidene ketal and selective benzoylation of O-4 to afford disaccharide **3.33**, the redox process was executed by Swern oxidation and $NaBH_4$ reduction to give disaccharide **3.35** (**Scheme 3.8**).

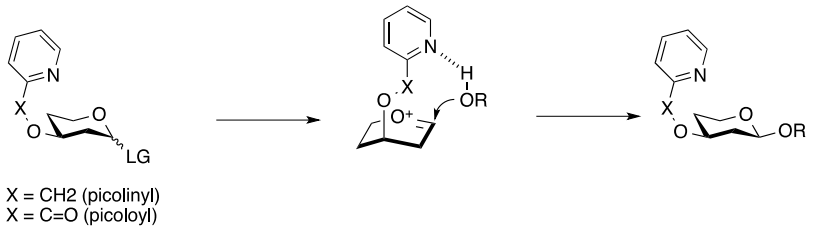


Scheme 3.8. Synthesis of 2,3-*cis*-disaccharide **3.35** via an oxidation–reduction strategy.

As outlined above, this two-step strategy was successfully applied in many cases to the formation of 1,2-*cis*-furanosides. However, the steric bulk around the carbonyl group is the biggest factor to be considered. For instance, the generation of α-Xyl*f* glycosides was unattainable from α-Lyx*f* glycosides due to steric hindrance[18]. Moreover, the efficiency of the stereoselective reduction in the case of larger furanose-containing oligosaccharide or polysaccharides might be an issue, as well as the simultaneous stereoselective reduction of several 2-ulose residues.

3.1.2.3 Hydrogen-bond-mediated aglycone delivery (HAD)

The HAD methodology was developed by Demchenko and coworkers for making 1,2-*cis*- and 1,2-*trans*-glycosides in pyranosides[11]. The concept of this strategy is based on the formation of an intermolecular hydrogen bond between the glycosyl donor and acceptor, which directs the nucleophilic attack of the acceptor preferentially from the same face of the ring as the directing group (**Scheme 3.9**). High yields and good stereoselectivity have been obtained using the proper combination of directing group and location on the donor, usually a picolinyl or picoloyl group installed on O-3, O-4 or O-6.



Scheme 3.9. The basis of the HAD methodology developed by Demchenko and coworkers.

This strategy was applied to the stereoselective synthesis of β-D- and β-L-arabinofuranosides by Yang and coworkers[20]. Several directing groups attached to O-5 and glycosylation methods were examined and it was shown that 2-quinolinecarbonyl (Quin)-substituted D- and L-arabinfuranosyl thiogycosides **D-3.36** and **L-3.36** gave high to excellent β-selectivity (7:1 to 1:0 β:α ratio) with a range of acceptors (**Figure 3.4a**). The proposed mechanism involves tethering of the alcohol, via a H-bond, to the donor and, upon activation of thioglycoside, the formation of intermediate **3.37** (**Figure 3.4b**). The tethering directs the nucleophilic attack leading to the β-Ara*f* linkage. This methodology was applied to the synthesis of octasaccharide **3.38**,

an oligosaccharide related to mycobacterial lipoarabinomannan, with excellent stereoselectively in the formation of the β-linked Ara*f* linkages (**Figure 3.4c**).

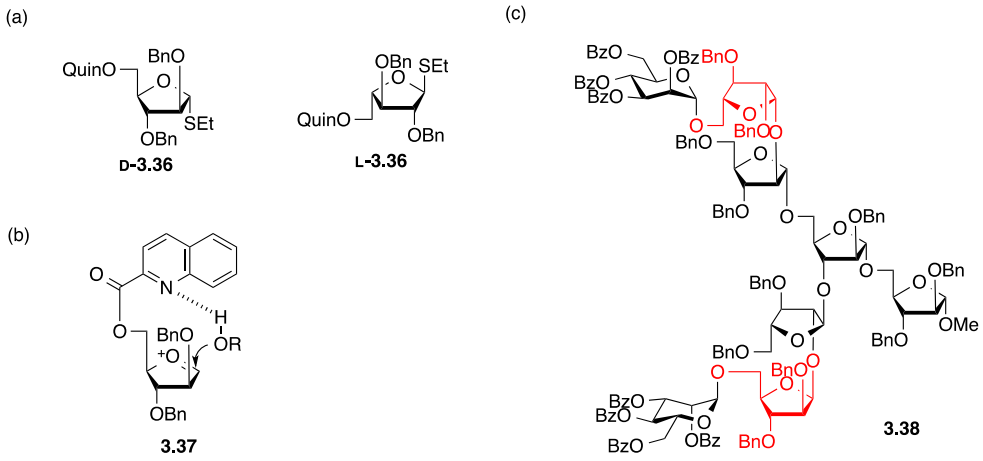
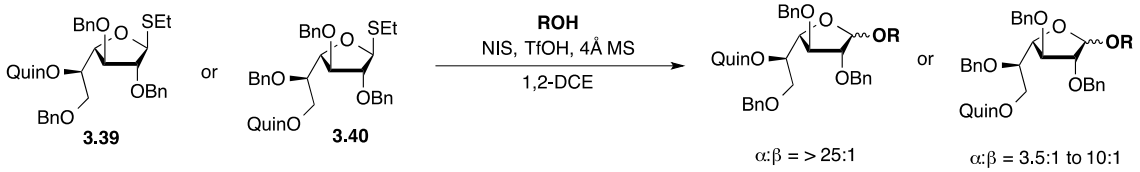
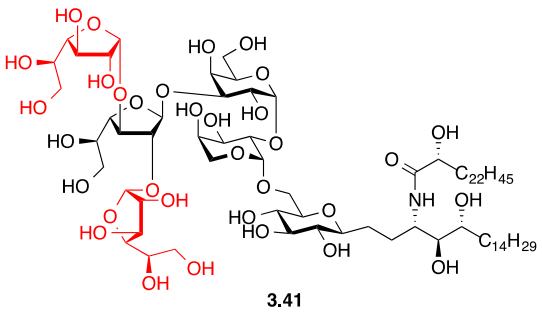


Figure 3.4. (a) 5-*O*-Quin-substituted D- and L-arabinofuranosyl thioglycosides **D-3.36** and **L-3.36** that provide high β-selectivity via HAD. (b) Proposed HAD glycosylation intermediate **3.37**. (c) Octasaccharide **3.38** synthesized by Yang and coworkers using HAD.

In 2016, Yang and coworkers applied the HAD approach to introduce α-D-Gal*f* glycosides using 5-*O*-Quin-protected Gal*f* donor **3.39** and 6-*O*-Quin-protected Gal*f* donor **3.40** (**Scheme 3.10**)[21]. These donors were used in the synthesis of vesparioside B (**3.41**, **Figure 3.5**), a complex glycosphingolipid from the Caribbean sponge *Spheciospongia vesparia*[21].



Scheme 3.10. Glycosylation of Quin-substituted Gal*f* thioglycoside donors **3.39** and **3.40**.

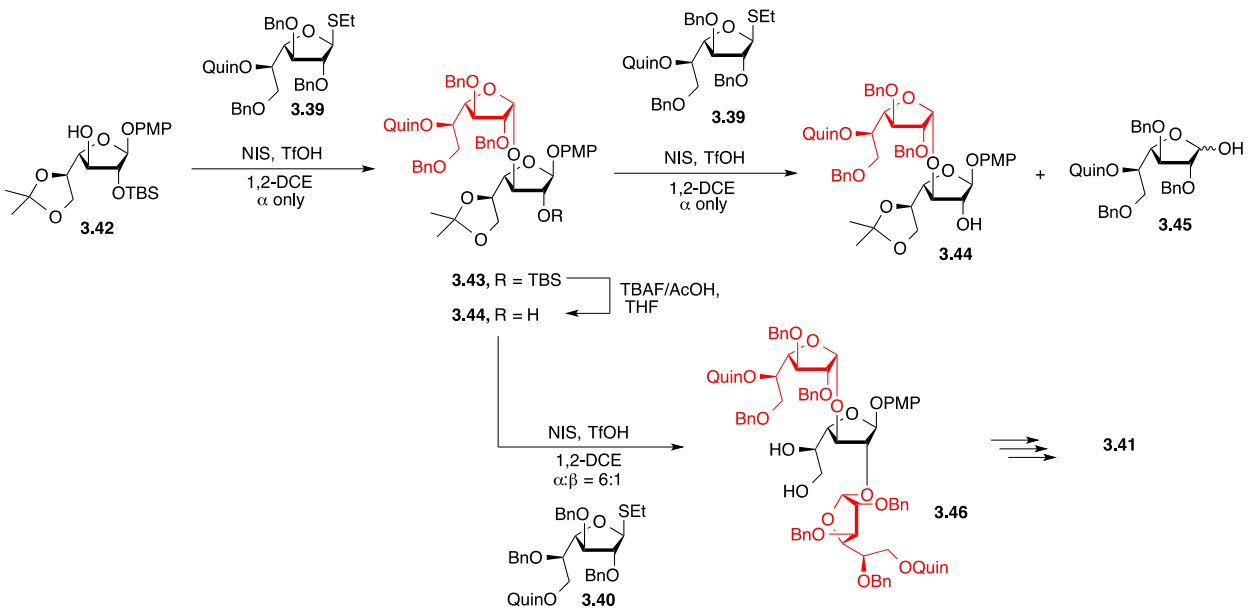


3.41

Figure 3.5. The glycosphingolipid vesparioside B **3.41** synthesized by Yang and coworkers.

The glycosylation stereoselectivity was investigated using NIS and TfOH activation conditions in dichloroethane with both 5-*O*-Quin-protected Gal*f* donor **3.39** and 6-*O*-Quin-protected Gal*f* donor **3.40** and a variety of glycosyl acceptors (**Scheme 3.10**). Their results showed that the use of the 5-*O*-Quin-protected donor **3.39** led to a better yield of the product and greater 1,2-*cis* stereoselectivity, compared to the use of the 6-*O*-Quin-protected donor **3.40**.

The key steps in the synthesis of **3.41** were two HAD glycosylations (**Scheme 3.11**). The first 1,2-*cis*-Gal*f* moiety was installed as the exclusive product using donor **3.39** and acceptor **3.42** to afford disaccharide **3.43**. However, the second 1,2-*cis*-Gal*f* moiety could not be installed by the coupling disaccharide alcohol **3.44** and donor **3.39**. Only unreacted **3.44** and the donor hydrolysis product (**3.45**) were observed. However, the 6-*O*-Quin-substituted donor **3.40** could be reacted with **3.44** to afford trisaccharide **3.46** to give a separable 6:1 α:β mixture of products in favor of the desired α-isomer. Trisaccharide **3.46** was then converted to the target molecule **3.41**.



Scheme 3.11. Installation of two Gal*f* moieties via Quin-substituted Gal*f* donors **3.39** and **3.40**.

3.1.2.4 Conformationally-restricted donors

Woerpel and coworker's work[22] on the synthesis of furanose *C*-glycosides, from which they developed the "inside attack" model (**Figure 3.6a**), influenced thoughts on the synthesis of *O*-furanosides. However, the development of methods that results in the formation of single intermediate in the reaction is the fundamental challenge. To address this problem, the use of conformationally-restricted donors has been exploited in O-furanosylation. In this approach, a protecting group is introduced to provide a conformationally-restricted intermediate (an oxacarbenium ion or a related electrophile) that preferentially reacts with an alcohol via "inside attack" (**Figure 3.6b**).

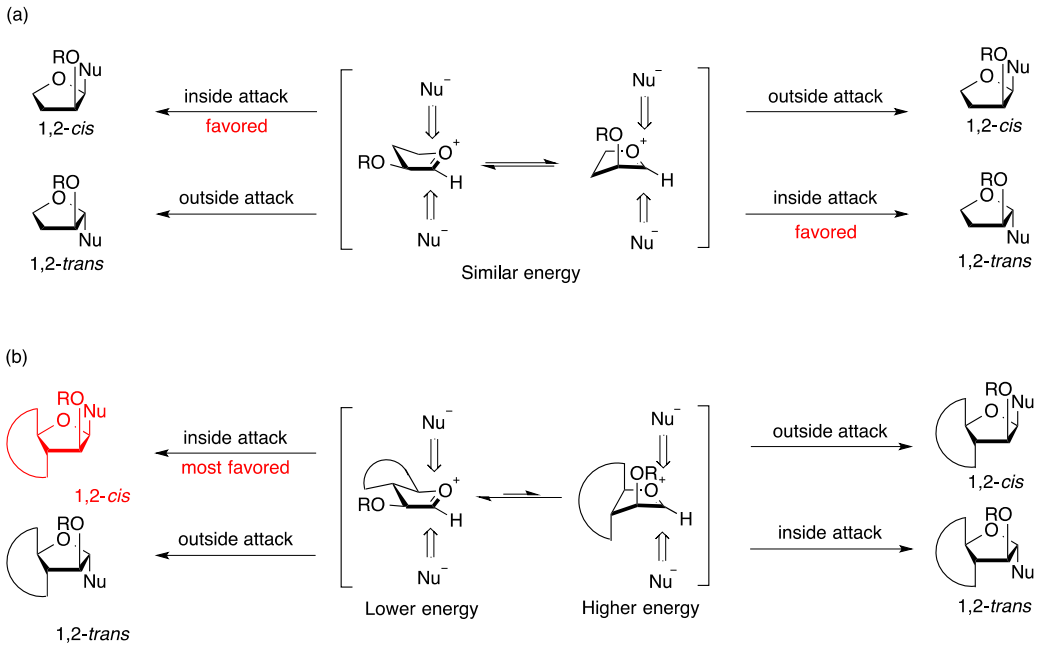
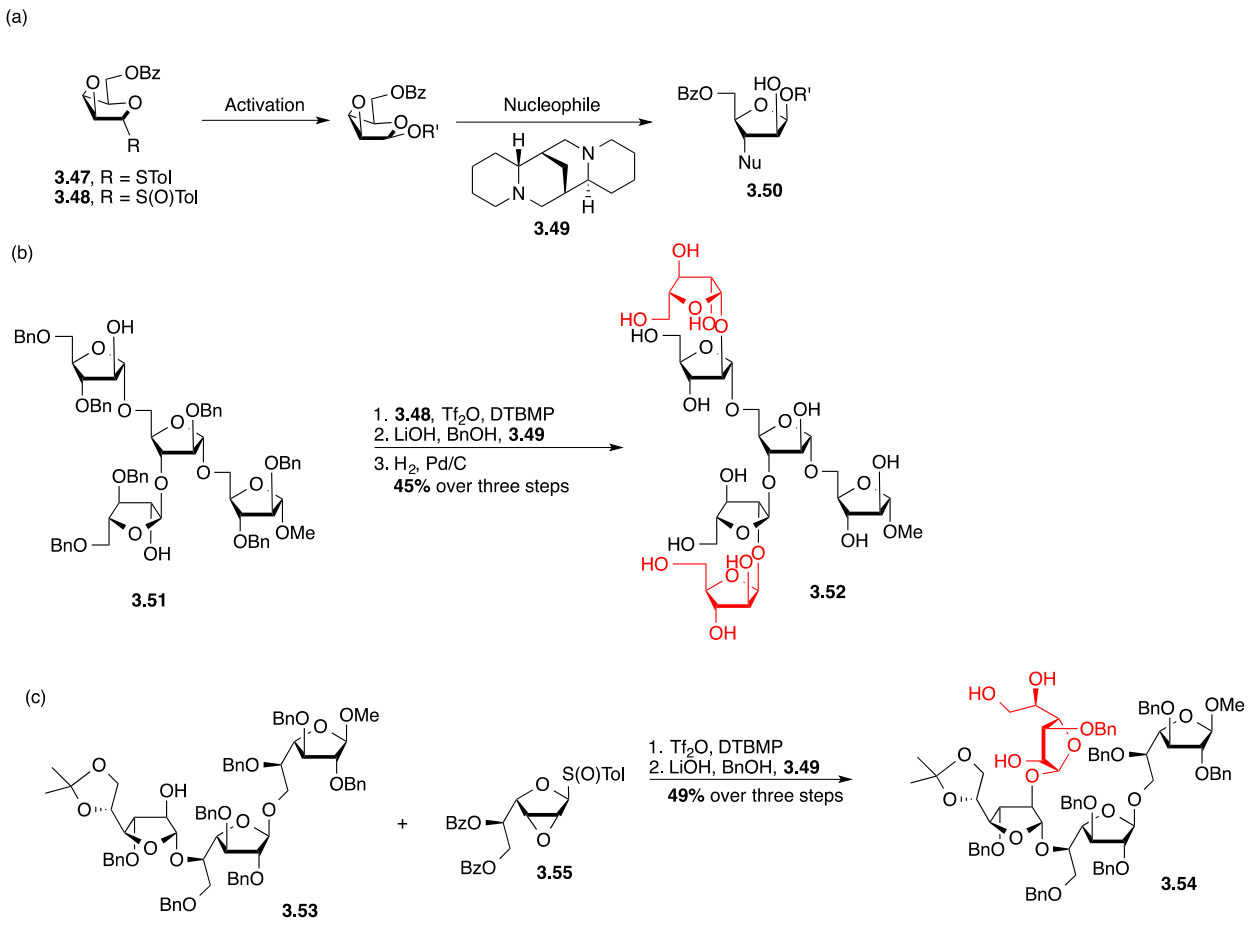


Figure 3.6. (a) "Inside attack" model developed by Woerpel and coworkers for *C*-furanosylation[22a]. (b) Plausible mechanism of furanosylation using conformationally-restricted donors[22b].

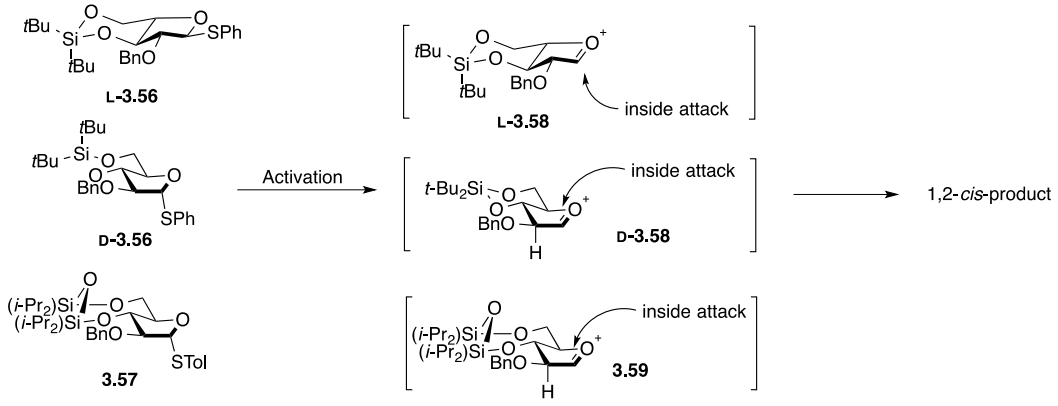
The first conformationally-restricted donors, 2,3-anhydro-lyxofuranosyl thioglycoside **3.47** and glycosyl sulfoxide **3.48**, were developed by Lowary and coworkers for the synthesis of β-Ara*f* glycosides **3.50**[23] (**Scheme 3.12a**). Glycosylation of a range of alcohols and subsequent opening of the epoxide ring by nucleophiles afforded β-arabinofuranosides **3.50** in excellent yield. This methodology was applied successfully to the synthesis of arabinofuranosyl hexasaccharide **3.52** (**Scheme 3.12b**). Furthermore, this methodology was extended to synthesize α-galactofuranosyl tetrasaccharide **3.54** using 2,3-anhydrosugar donors **3.55** with excellent stereoselectivity[24] (**Scheme 3.12c**).



Scheme 3.12. (a) Synthesis of 1,2-*cis*-β-arabinofuranosides **3.50** via 2,3-anhydrosugars **3.47** and **3.48**. (b) Synthesis of the hexasaccharide **3.52** via 2,3-anhydro sulfoxide **3.48**. (c) Synthesis of protected tetrasaccharide **3.54** with an α-galactofuranosyl moiety via 2,3-anhydro sulfoxide **3.55**.

Later examples of conformationally-restricted donors were developed by Boons and coworkers[12], and soon after by the Ito[25] and Crich groups[26]. In this work, donors D-**3.56** or L-**3.56** and **3.57**, with a silyl acetal (DTBS) or siloxane spanning O-3 and O-5 in Ara*f* rings (**Scheme 3.13**) were used. Density functional-theory calculations[12] supported the "inside attack" model developed by Woerpel and coworkers. The proposed mechanism is that a conformationally-restricted intermediate (*e.g.,* D-**3.58**, L-**3.58** or D-**3.59**) is generated and then nucleophilic attack

by the glycosyl acceptor from "inside" occurs. This is due to eclipsing interactions with H-2 when the nucleophile attacks from the "outside" (**Scheme 3.13**).



Scheme 3.13. Plausible mechanism of generating β-Ara*f* glycosides (1,2-*cis*-glycosides) using conformationally-restricted donors D-**3.56**, L-**3.56** and **3.57**.

The preparation of other furanosides (*e.g.,* β-D-fructofuranosides) using 3,5-*O*-protected conformationally-restricted donors has not been reported. The application of this approach to fructofuranosylation using thioglycosides protected with a silyl acetal or siloxane group (*e.g.,* **3.60** and **3.61**) will be discussed in Chapter 5 (**Figure 3.7**).

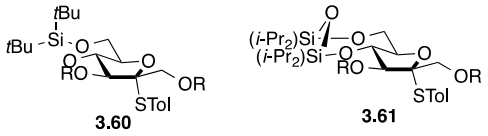
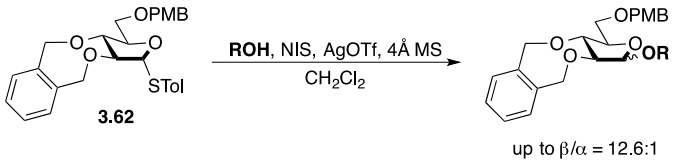


Figure 3.7. Fru*f* donors **3.60** and **3.61** explored in Chapter 5.

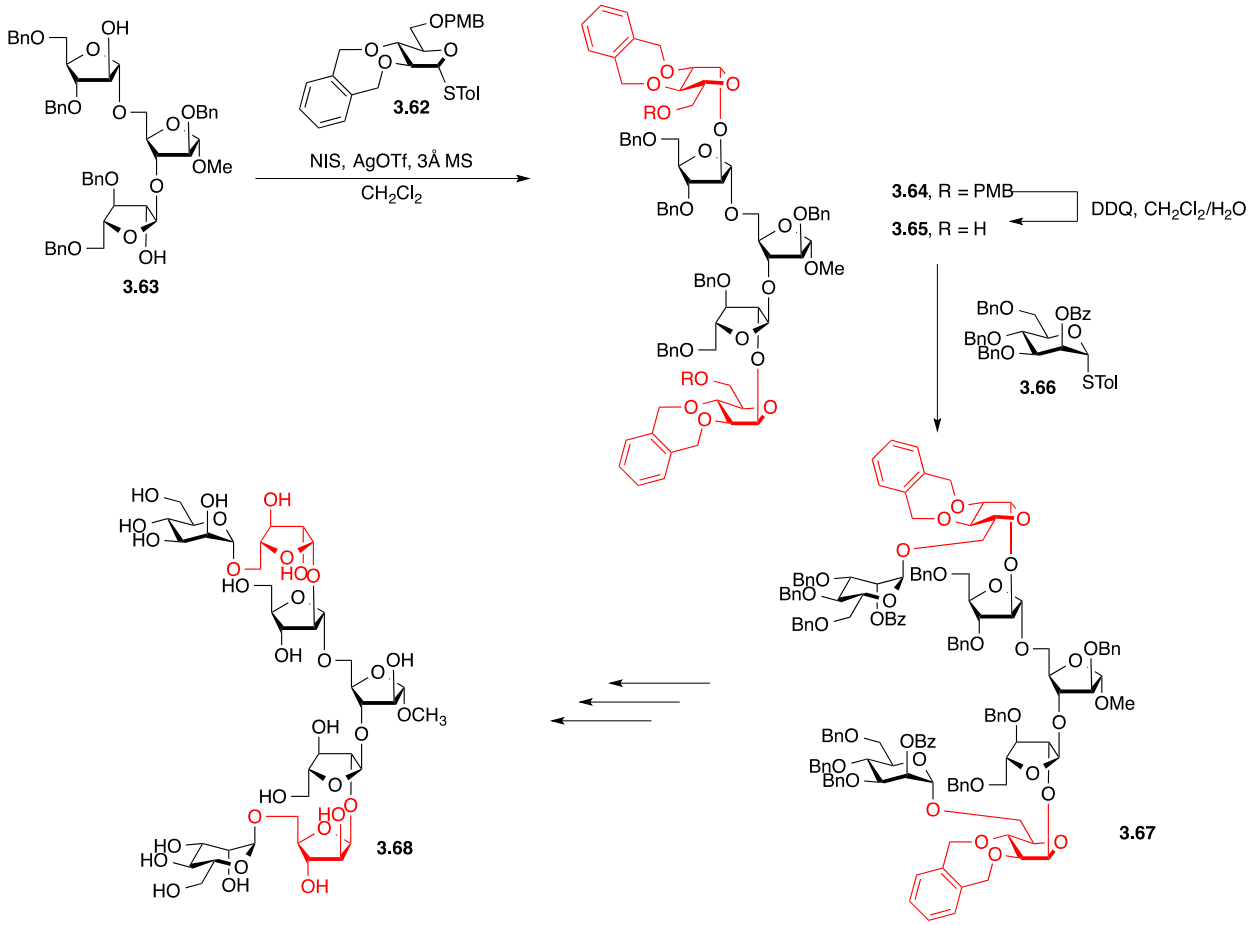
Although 3,5-*O*-protected Ara*f* donors are powerful reagents for the highly stereoselective preparation of β-arabinofuranosides, a limitation of them is that several post-glycosylation steps are needed for the further modification of this residue. In particular, β-Ara*f* residues are often found in nature modified at O-5. For the ease of manipulating the O-5 position of the β-D-

Ara*f* residue, another conformationally-restricted Ara*f* donor, **3.62**, which has a xylylene bis-ether across O-2 and O-3, was developed in our group (**Scheme 3.14**). Donor **3.62** gives good to excellent stereoselectivity with a variety of acceptors, providing a convenient route to β-Ara*f* glycosides[27].



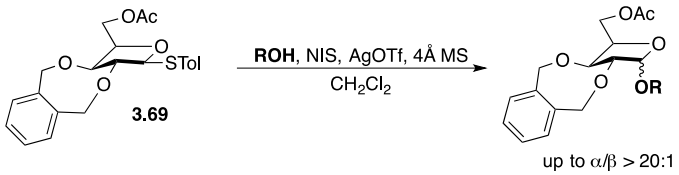
Scheme 3.14. Stereoselective β-arabinofuranosylation using the 2,3-*O*-xylylene-protected donor **3.62**.

Donor **3.62** was applied to the preparation of heptasaccharide **3.68**, in which the O-5 position of both β-Ara*f* residues are attached to mannopyranose residues (**Scheme 3.15**)[27]. Excellent stereoselectivity was obtained in the coupling reaction of **3.62** and trisaccharide diol **3.63** to afford pentasaccharide **3.64**. Removal of the PMB group allowed further glycosylation of pentasaccharide **3.65** with glycosyl donor **3.66** to afford heptasaccharide **3.67**, which provided the target glycan **3.68** after global deprotection.



Scheme 3.15. Synthesis of heptasaccharide **3.68** via conformationally-restricted donor **3.62**.

The extension of this strategy to the synthesis of α-D-xylofuranosides has been reported[28]. In this case, the xylylene bis-ether was also installed across the O-2 and O-3 positions, leading to xylofuranosyl thioglycoside **3.69**. This donor provided modest to excellent α-selectivity (**Scheme 3.16**) and it was particularly useful in the synthesis of the α-D-xylofuranosyl-(1→4)-α-D-mannopyranose linkage. This is a key structural motif present in some mycobacterial polysaccharides[29]. Computational studies supported the hypothesis that α-xylofuranosides were obtained via "inside-attack" of the alcohol on an electrophilic intermediate[28].



Scheme 3.16. Stereoselectivity in xylofuranosylation using 2,3-*O*-xylylene-protected donor **3.69**.

With the success of using xylylene bis-ether protected donors in 1,2-*cis*-arabinofuranosylation[27] and 1,2-*cis*-xylofuranosylation[28], I wanted to extend this method to two ketofuranose cases: β-D-xylulofuranosylation and β-D-fructofuranosylation. These two sugars (D-Xul*f* and D-Fru*f*) have a *trans*-diol at the C-3 and C-4 positions, which is similar to the structure of D-Ara*f* (**Figure 3.8**). My work on extending this methodology to synthesize β-Xul*f* glycosides is described in Chapter 3. My investigations on synthesizing β-Fru*f* glycosides are detailed in Chapter 5. It should be noted that these studies allowed me to understand the influence of the hydroxymethyl groups on glycosylation strereoselectivity (**Figure 3.8**). Ara*f* and Xul*f* have a single hydroxymethyl group, but at different locations on the ring, whereas Fru*f* has two of these groups.

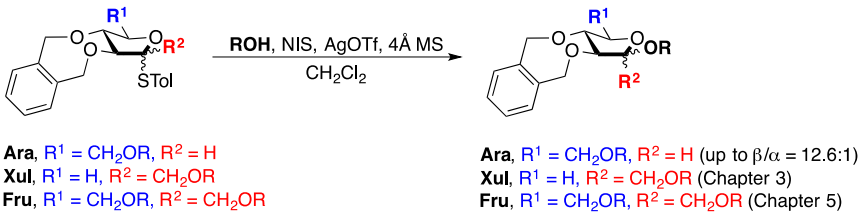
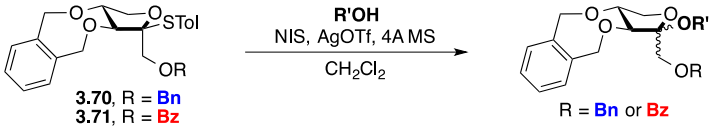


Figure 3.8. Comparison of conformationally-restricted donors in Ara*f*, Xul*f* and Fru*f* rings.

3.1.3 Research Objective

As mentioned in **Section 3.1.1**, β-D-Xul*f* residues have been identified in several different microorganisms, but there are no papers that report the chemical synthesis of these natural oligosaccharide fragments. In this chapter, I describe my work on constructing the conformationally-restricted xylylene-protected donors **3.70** and **3.71** (**Scheme 3.17**) to: (1) develop methodology for β-selective xylulofuranosylation; (2) study the influence of the xylylene group and O-1 protecting group on xylulofuranosylation stereoselectivity; and (3) apply the methodology to the synthesis of the repeating unit of the LPS O-antigen from *Y. enterocolitica* O:5/O:5,27.



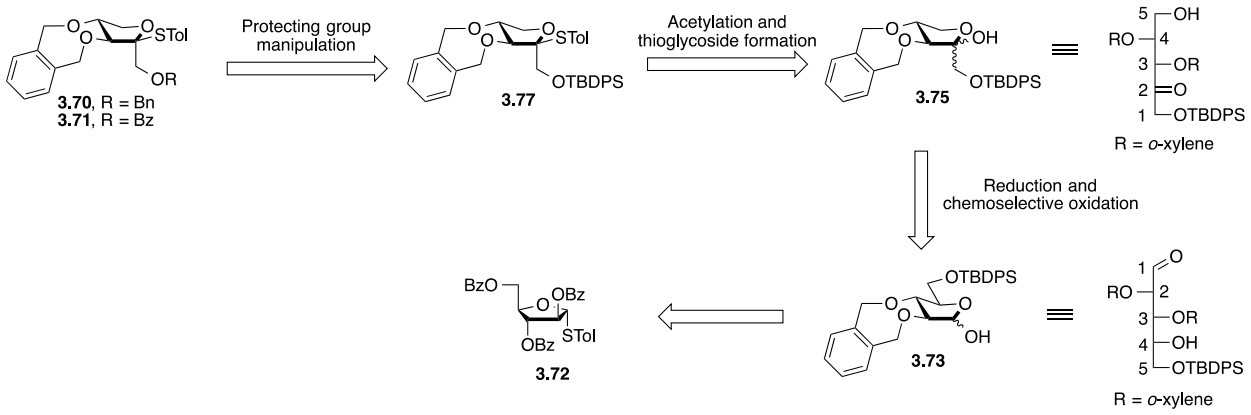
Scheme 3.17. Use of D-Xul*f* thioglycosides **3.70** and **3.71** in glycosylation reactions.

3.2 Results and Discussion

3.2.1 Retrosynthetic analysis and synthetic approach to xylylene-protected donors 3.70 and 3.71

To study the stereoselectivity of xylulofuranosylation, conformationally-restricted 3,4-*O*-xylylene-protected thioglycosides **3.70** and **3.71** were designed (**Scheme 3.18**). As described in **Section 3.1.2.4**, the 3,4-*O*-xylylene group will restrict the conformation of the Xul*f* ring, which is expected to lead to the formation of β-xylulofuranosides. To synthesize **3.70** and **3.71**, a route was designed from perbenzoylated Ara*f* thioglycoside **3.72**[30]. As shown in **Scheme 3.18**, the C-2 and C-3 configuration of arabinose is identical to the C-4 and C-3 configuration of xylulose. Therefore, the xylylene group can be installed on an Ara*f* derivative following the literature[27].

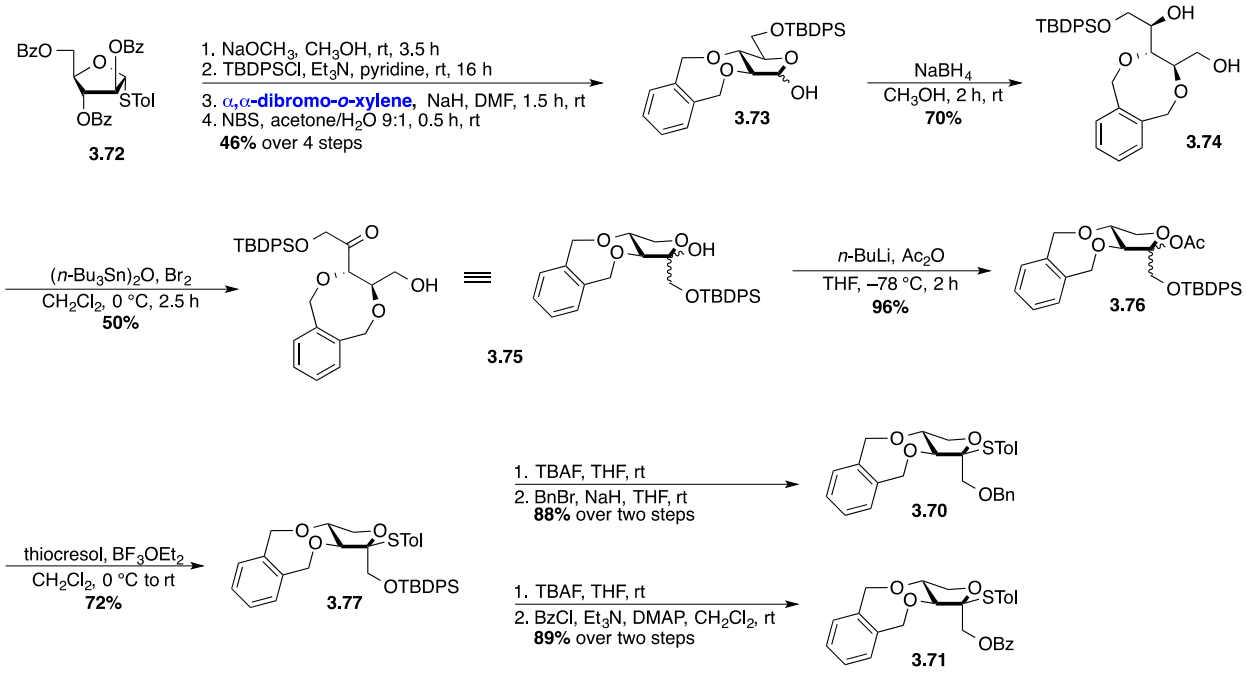
The C-1 aldehyde of arabinose could then be reduced to an alcohol (to become C-5 of Xul) and the C-4 hydroxyl group of arabinose could be oxidized to a ketone (to become C-2 of Xul) providing **3.75**. Conversion of **3.75** into **3.70** and **3.71** via thioglycoside **3.77** is anticipated to be straightforward.



Scheme 3.18. Retrosynthetic analysis of **3.70** and **3.71** and carbon atom numbering of xylulose and arabinose.

The synthesis of **3.70** and **3.71** began from perbenzoylated thioglycoside **3.72**[30] (**Scheme 3.19**), which was converted into hemiacetal **3.73** via a four-step procedure (deacylation, the installation of an TBDPS ether on O-5, xylylene protection on O-2 and O-3 and finally hydrolysis) in 46% overall yield. The hemiacetal **3.73** was then reduced, in 70% yield, to diol **3.74** upon treatment with sodium borohydride. A key step was the selective oxidation of the secondary alcohol of **3.74** with $(n\text{-}Bu_3Sn)_2O$ and bromine[31] to afford xylulose derivative **3.66** in 50% yield. After this, the acetylation of **3.75** using normal conditions (Ac_2O and pyridine) was attempted. However, only O-5 acetylation of the open chain form of **3.75** was observed. Thus, an acetylation procedure[32] using *n*-BuLi and Ac_2O was tested, and **3.76** was successfully obtained in 96% yield. Finally, thioglycoside **3.77** was prepared in 72% yield from **3.76**. Only the β-thioglycoside

was isolated, which we found encouraging as it suggested that these donors would indeed be β-selective. Conversion of **3.77** into **3.70** and **3.71** proceeded without incident using standard transformations.



Scheme 3.19. Synthesis of xylylene-protected xylulose donors **3.70** and **3.71**.

3.2.2 Stereoselectivity xylulofuranosylation using donors 3.70 and 3.71

The stereoselectivity study began with the coupling of 3,4-*O*-xylylene-protected xylulothioglycoside **3.70** with cyclohexanol **3.78**. All glycosylations were conducted in dichloromethane using *N*-iodosuccinimide (NIS) and silver triflate (AgOTf) as the promoter (**Table 3.1**). First, the effect of acceptor concentration on reaction stereoselectivity was studied. At 1.0 M (Entry 1), the reaction was slightly α-selectivity; at lower concentration (0.1 and 0.03 M, entries 2 and 3, respectively), very slight β-selectivity was observed. In all cases, the yield was excellent

(82–92%). The selectivity was slightly sensitive to temperature with the best β-selectivity being seen at –78 °C (Entries 3–5).

Entry	Conc. (M)	Temp. (°C)	Yield[a] (α/β)[b]
1	1	–78	87% (2.6:1)
2	0.1	–78	83% (0.9:1)
3	0.03	–78	82% (0.9:1)
4	0.03	25	87% (1.1:1)
5	0.03	–40	92% (1.1:1)

[a]Total yield of α/β mixture
[b]α/β ratio was determined by ^{1}H NMR of mixture or isolated mass of both anomers

Table 3.1. Reaction condition optimization of glycosylation of **3.70** with cyclohexanol **3.78**.

Based on these results, we carried out the rest of the glycosylations with an acceptor concentration of 0.03M at –78 °C. The coupling of **3.70** with various acceptors (**3.80**–**3.85**, **Figure 3.9**) was next examined. Acceptors **3.80**–**3.83** are commercially available; acceptor **3.84** was synthesized from xylose (below) and **3.85** was synthesized from rhamnose following a literature procedure[33].

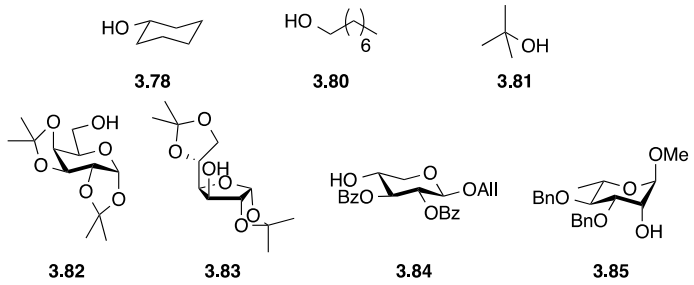
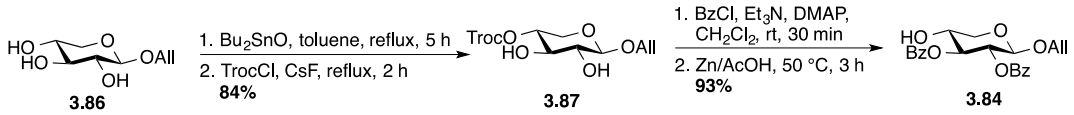


Figure 3.9. Acceptors used in glycosylations with donors **3.70** and **3.71**.

The synthesis of xylose acceptor **3.84** is shown in **Scheme 3.20**. Fischer glycosylation of D-xylose and allyl alcohol was performed as reported[34] to afford triol **3.86**. Selective Troc protection of the C-4 hydroxyl group in **3.86**, via the formation of a stannylidene acetal, afforded diol **3.87** in 84% yield. Benzoylation under standard conditions and Troc deprotection upon treatment with Zn/AcOH provided acceptor **3.84** in 93% over two steps.



Scheme 3.20. Synthesis of xylose acceptor **3.84**.

With the acceptors in hand, the coupling reactions were executed with the optimized reaction conditions: 0.03 M of acceptor, –78 °C. As shown in **Figure 3.10**, the glycosylation of simple alcohols (**3.78**, **3.80** and **3.81**) showed almost no selectivity (glycosides **3.79**, **3.88** and **3.89**). In coupling with sugar-derived acceptors (**3.82**–**3.85**), increased β-selectivity (glycosides **3.91**–**3.93**) was observed when the reactions were conducted with secondary alcohols (**3.83**–**3.85**) but the selectivity was low with primary carbohydrate alcohols (**3.82**).

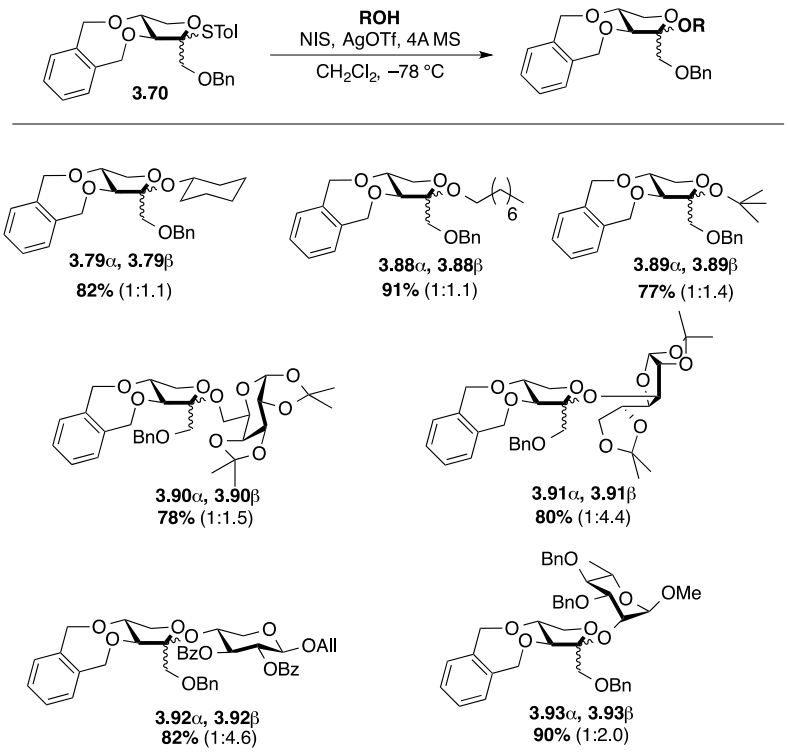
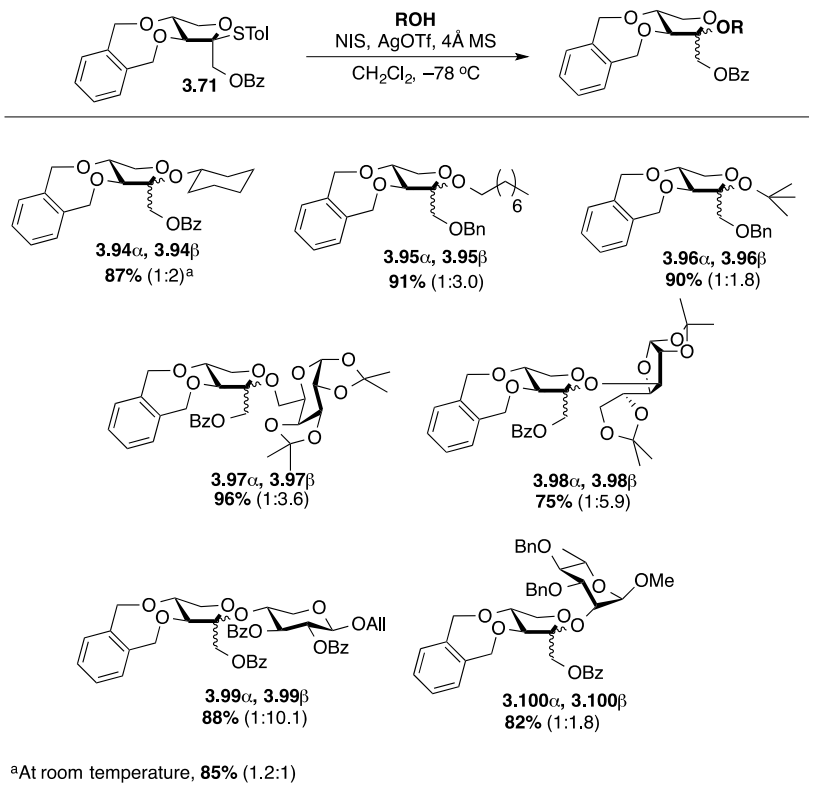


Figure 3.10. Products resulting from the glycosylation of acceptors **3.78** and **3.80–3.85** with donor **3.70**.

Although β-selectivity was observed, especially for alcohols **3.84** and **3.85**, the moderate stereoselectivity was still not satisfactory. An O-1 benzoyl group in fructofuranosides was reported to have a neighboring group participation effect leading to β-selectivity[35]. Therefore, the effect of O-1 protecting group in the Xul*f* donor was also studied (**Figure 3.11**). For almost all of the acceptors (**3.78**, **3.80–3.85**), the use of O-1 benzoylated donor **3.71** gave the product in excellent yield and with higher β-selectivity compared to the O-1 benzylated donor **3.70**. This β-selectivity is presumably due to neighboring group participation, where the α-spiro intermediate **3.103** is more favored than the β-spiro intermediate **3.101** because of the anomeric effect and steric clashing between the H-2 and the two H-1's. (**Figure 3.12**).



[a]At room temperature, **85%** (1.2:1)

Figure 3.11. Products resulting from the glycosylation of acceptors **3.78** and **3.80–3.85** with donor **3.71**.

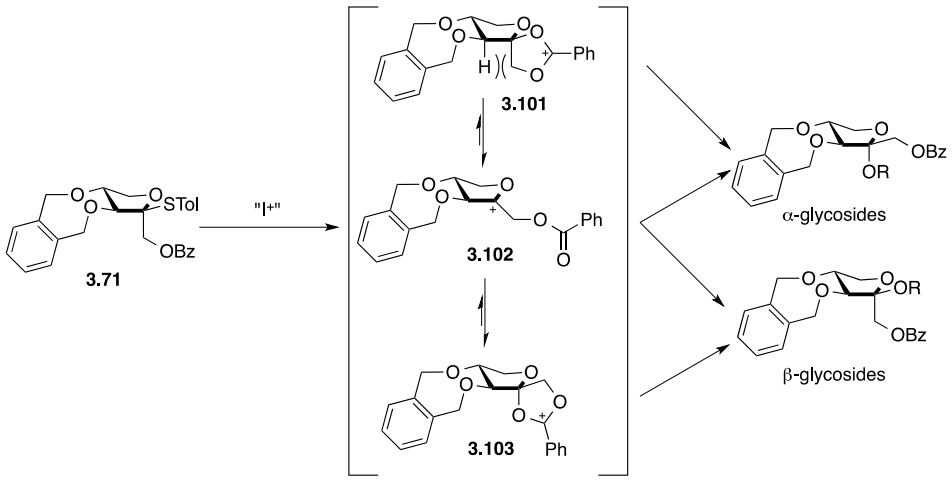
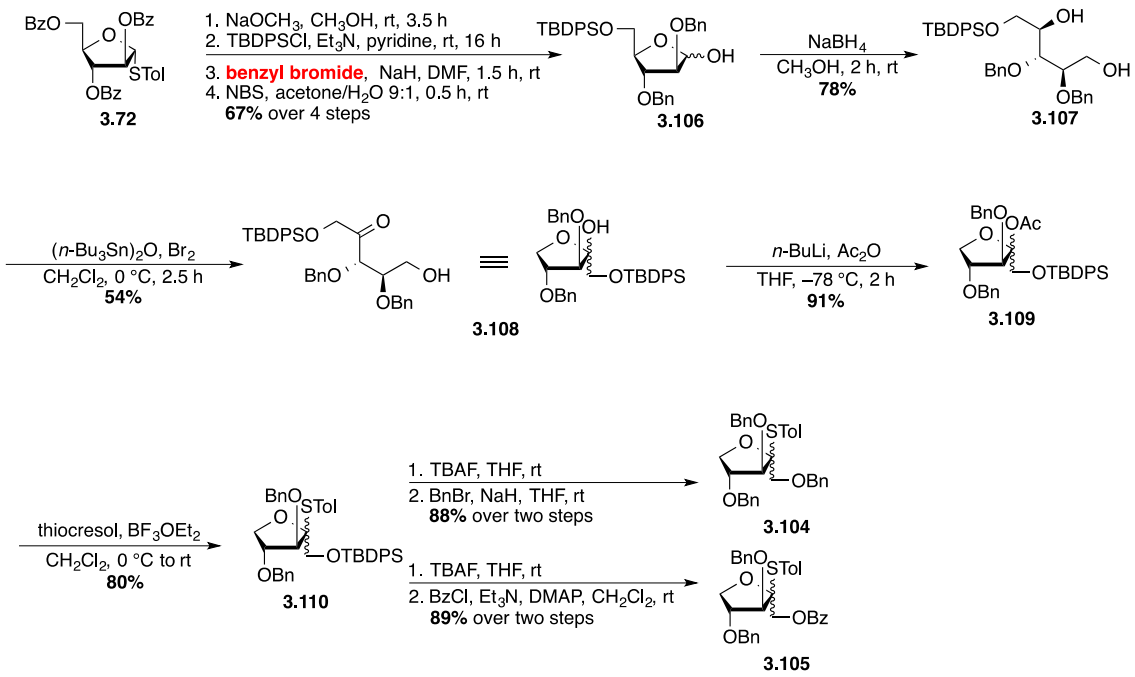


Figure 3.12. Plausible mechanism for increasing β-selectivity via neighboring group participation in Xul*f* donors with an O-1 benzoate ester.

Although moderate to good stereoselectivity was observed in these cases, the stereoselectivity using the xylylene group was still not as high as the other two sugars investigated earlier (Ara*f* and Xyl*f*). To investigate the effect of the xylylene group on the stereoselectivity of the glycosylations, 3,4-di-*O*-benzylated donors **3.104** and **3.105** were also synthesized (**Scheme 3.21**). The synthetic route to these compounds was the same as that used for synthesizing the xylylene-protected donors. Starting from **3.72**, hemiacetal **3.106** was obtained in 67% yield after four steps. Treatment of **3.106** with sodium borohydride gave diol **3.107** (78%), which was subjected to selective oxidation of the secondary alcohol to afford xylulose derivative **3.108** in 54% yield. After acetylation and thioglycosylation, xylulose thioglycoside **3.110** was obtained in 72% yield over two steps. Without any incident, a benzyl or benzoyl group was installed at O-1 in **3.110** in two steps to afford **3.104** and **3.105**, in 88% and 89% yield, respectively.



Scheme 3.21. Synthesis of 3,4-di-*O*-benzylated xylulose donors **3.104** and **3.105**.

The influence of the xylylene group on stereoselectivity was examined for two acceptors (**Figure 3.13**). Glycosylation of **3.84** and **3.85** with 3,4-di-*O*-benzylated donors **3.104** and **3.105** were carried out and the results were compared to those using donors **3.70** and **3.71**. For both acceptors, the 3,4-di-*O*-benzylated donors **3.104** and **3.105** gave α-selectivity or no selectivity (disaccharides **3.111–3.114**). Thus, the increased β-selectivity observed in the coupling reaction of xylylene-protected donors **3.70** and **3.71**, leading to disaccharides **3.92**, **3.93**, **3.99** and **3.100**, appears to arise from the presence of the cyclic xylylene protecting group.

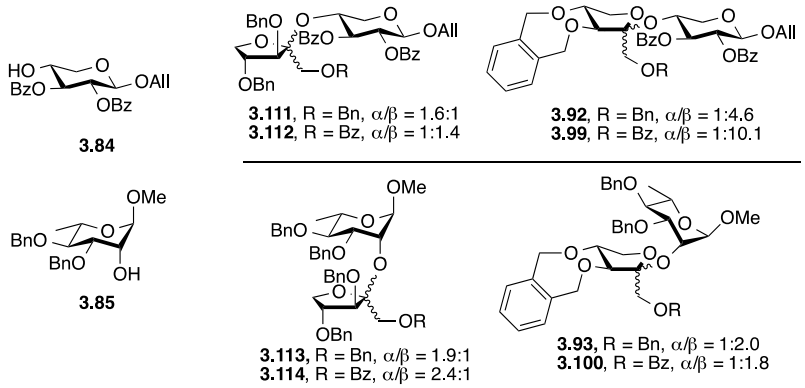


Figure 3.13. Comparison of the xylylene group and two benzyl groups on stereoselectivity in glycosylations of **3.84** and **3.85**.

3.2.3 Characterization of anomeric configuration

One of the key challenges in this study was to determine the stereoselectivity of the glycosylations. Ketosides lack an anomeric hydrogen atom; thus, determining the stereochemistry at this center could not be done using the $^{3}J_{H1,H2}$ or $^{1}J_{C1,H1}$ magnitude. In this study, the stereochemistry of products was confirmed by the chemical shift of anomeric carbon in the ^{13}C NMR spectrum[36] (**Table 3.2**), as well as a correlation between H-1 and H-3 in the 2D ^{1}H–^{1}H TROESY spectrum (**Figure 3.14a**). Higher field (105–108 ppm) C-2 resonances were assigned as β-

xylulofuranosides based on the correlation of H-1 and H-3 in the ^{1}H–^{1}H TROESY spectra. Signals for C-2 at lower field (108–110 ppm) were assigned as α-xylulofuranosides, because in the TROESY spectrum of these molecules a correlation between H-1 and H-3 was lacking. These assignments were further supported by an X-ray structure of a crystalline solid **3.115β** (**Figure 3.14b**). For **3.115β**, the resonance of C-2 was at 106.8 ppm. In the other isomer, which was by inference the α-anomer, the C-2 resonance appeared at 109.6 ppm.

	Chemical Shift of C-2_{xul} (ppm)			Chemical Shift of C-2_{xul} (ppm)	
Compound #	α	β	Compound #	α	β
3.79	109.4	107.1	**3.96**	109.5	106.0
3.88	108.5	106.4	**3.97**	108.2	105.2
3.89	110.3	107.6	**3.98**	108.2	105.9
3.90	108.5	106.3	**3.99**	–	105.6
3.91	110.0	107.2	**3.100**	108.8	105.6
3.92	109.6	106.8	**3.111**	108.8	105.2
3.93	109.3	107.2	**3.112**	108.8	105.6
3.94	108.2	105.4	**3.113**	108.5	105.9
3.95	107.9	105.1	**3.114**	107.8	105.0
			3.115	109.6	106.8

Table 3.2. C-2 chemical shift of all xylulofuranosides synthesized in this study.

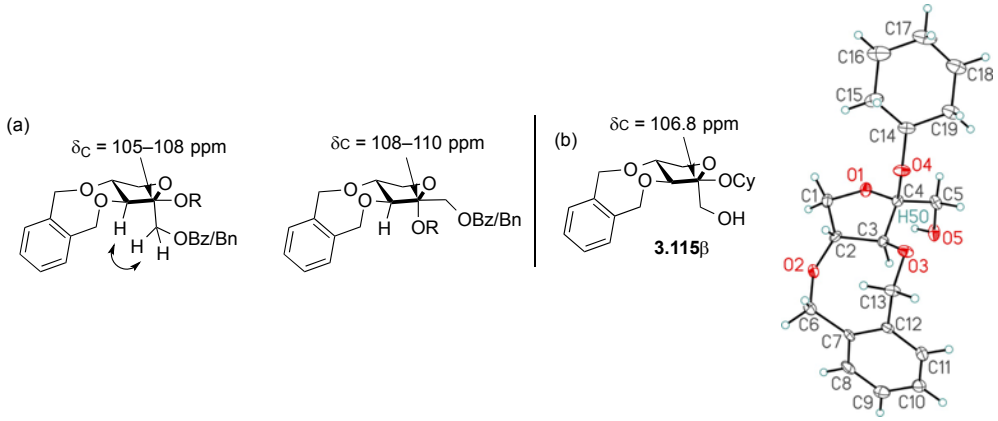
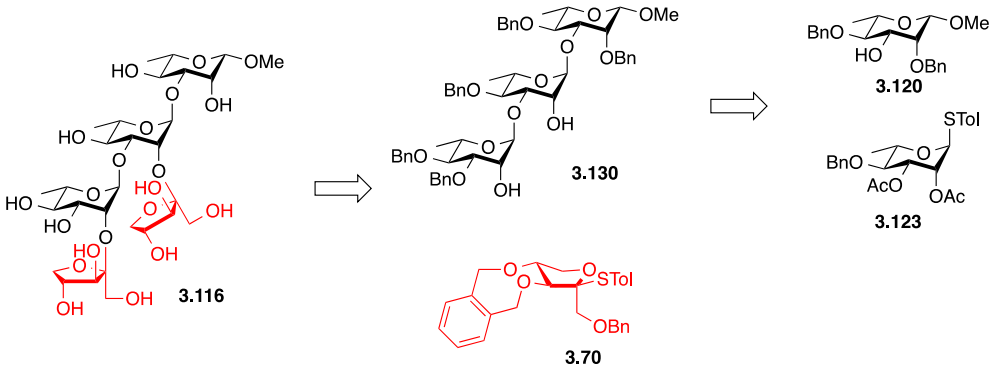


Figure 3.14. (a) NMR spectroscopic data used to differentiate glycoside products. (b) X-ray structure of **3.115β**.

3.2.4 Application of conformationally-restricted Xul*f* donor 3.70 in the synthesis of the pentasaccharide repeating unit from *Y. enterocolitica* O:5/O:5,27

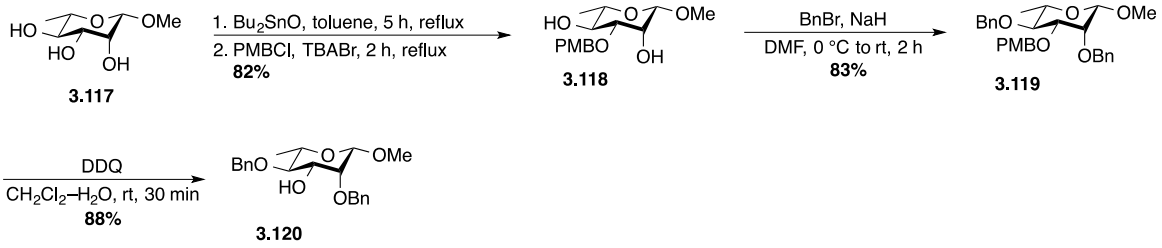
Having the optimized glycosylation method, the synthesis of the repeating unit of the lipopolysaccharide O-antigen from *Y. enterocolitica* O:5/O:5,27, which contains two β-Xul*f* residues, was carried out. The synthetic route originally designed to the target (**3.116**, **Scheme 3.22**), involved the introduction of both β-Xul*f* residues in a single step using a trisaccharide acceptor **3.130** with two free hydroxyl groups and glycosyl donor **3.70** (prepared as described in **Section 3.2.1**). Here, the use of **3.70**, instead of **3.71**, was because the similar selectivity was seen for both donors in the model cases (**3.93** and **3.100**) and a single step was required for deprotection at the end. The synthesis of trisaccharide acceptor **3.130** could come from two rhamnose substrates, **3.120** and **3.123**.



Scheme 3.22. Original retrosynthesis for synthesizing pentasaccharide **3.116**.

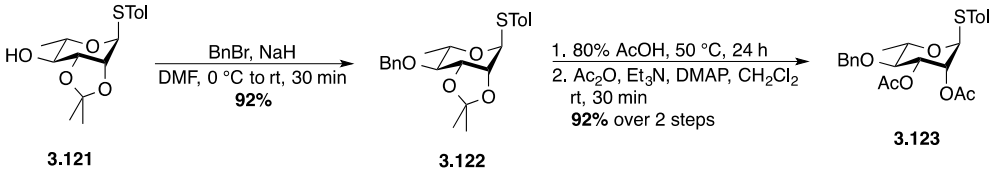
To synthesize acceptor **3.120**, methyl glycoside **3.117** was synthesized following the literature procedure[37] by the reaction of L-rhamnose with di-*n*-butyltin oxide, giving the 1,2-*O*-*cis*-stannylene acetal, and then treatment with methyl iodide. This sequence gave **3.117** in 71% overall yield. Next (**Scheme 3.23**), a PMB ether was installed at the O-3 position of **3.117** via

organotin-mediated regioselective protection to obtain, in 82% yield, methyl 3-*O*-*p*-methoxylbenzyl-β-L-rhamnopyranoside (**3.118**)[37]. After benzylation of the C-2 and C-4 hydroxyl groups, affording an 83% yield of **3.119**, the PMB ether was cleaved by treatment with DDQ in a mixture of CH_2Cl_2 and H_2O to give **3.120**. The final compound **3.120** was obtained in 88% yield from **3.119**.



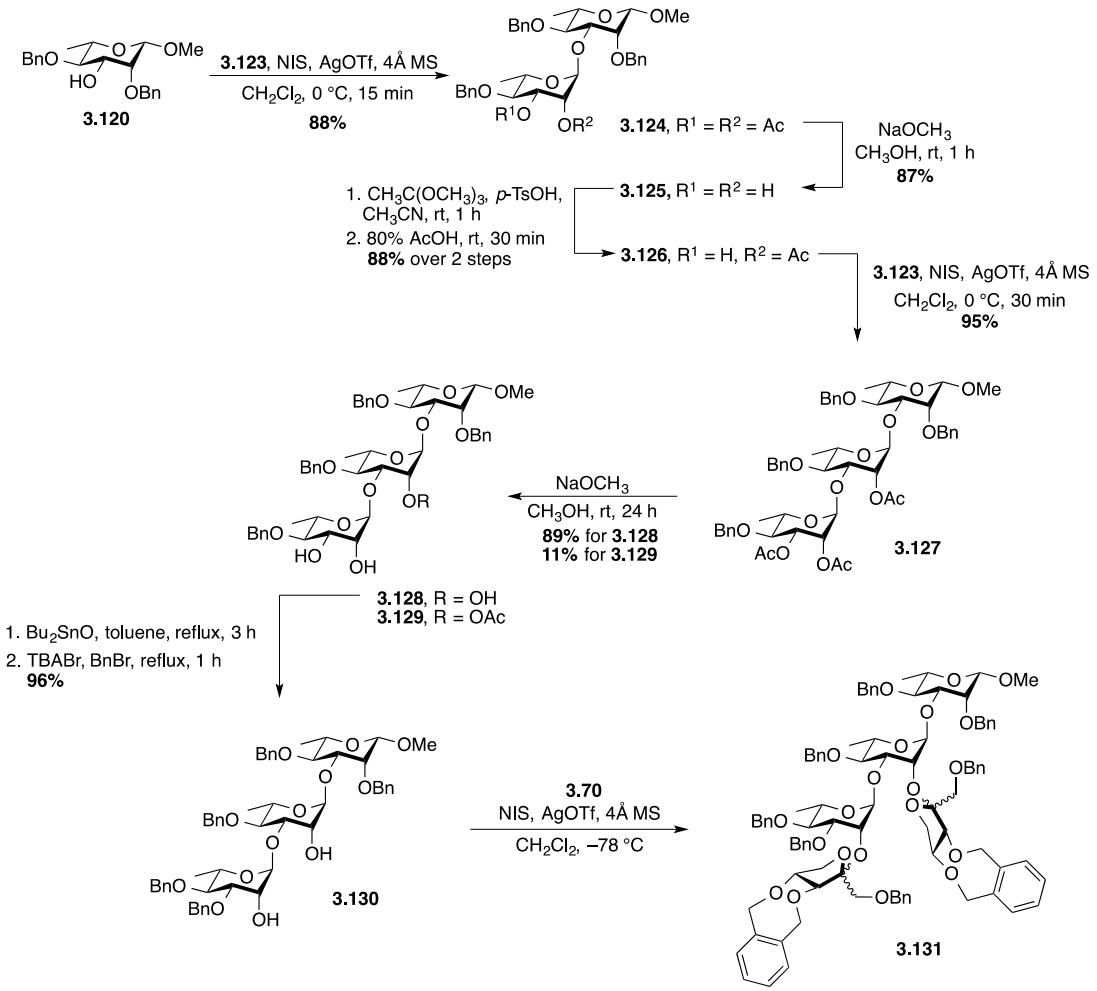
Scheme 3.23. Synthesis of methyl β-L-rhamnopyranoside acceptor **3.120**.

As illustrated in **Scheme 3.24**, the rhamnose thioglycoside donor **3.123** was synthesized from known **3.121**[38]. Thioglycoside **3.121** was benzylated to afford **3.122**[39] and then the isopropylidene ketal was cleaved by acidic hydrolysis. Acetylation of the C-2 and C-3 hydroxyl groups provided thioglycoside **3.123** in 85% overall yield over the three steps from **3.121**.



Scheme 3.24. Synthesis of rhamnose thioglycoside donor **3.123**.

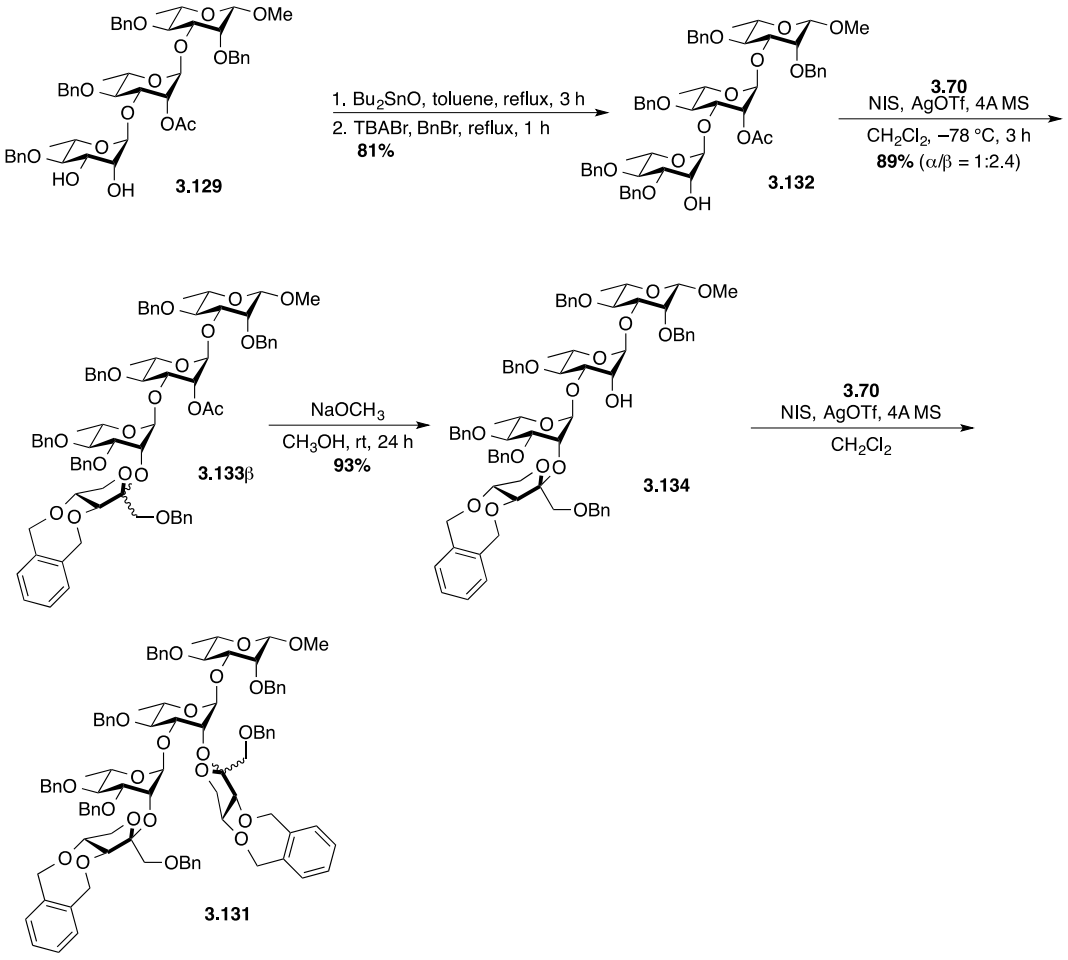
Having synthesized the monosaccharide acceptor **3.120** and monosaccharide donor **3.123**, their coupling reaction was executed by treatment with the NIS–AgOTf promoter system to afford, in 88% yield, disaccharide **3.124** (**Scheme 3.25**). After Zemplén deacetylation and installation of an acetate ester on the C-3 hydroxyl group of the non-reducing end residue via an ortho-ester intermediate, the disaccharide acceptor **3.126** was synthesized in 77% overall yield. Next, trisaccharide **3.127** was obtained in 95% yield from the coupling of acceptor **3.126** and donor **3.123**. Deacetylation of **3.127** was performed to afford trisaccharide **3.128** in 89% yield. I also observed a trisaccharide side product, **3.129**, in 11% yield. Presumably this is due to the acetate ester on the internal monosaccharide residue being slow to cleave due to steric hindrance. Triol **3.128** was then treated with di-*n*-butyltin oxide followed by BnBr to afford an 96% yield of trisaccharide acceptor **3.130**, with two free hydroxyl groups. Glycosylation of **3.130** with thioglycoside **3.70** using the optimized reaction conditions provided pentasaccharide products as determined by mass spectrometric analysis. However, by NMR spectroscopy, all four possible stereoisomers ($\alpha\alpha$, $\alpha\beta$, $\beta\alpha$, $\beta\beta$) were formed and they were inseparable by column chromatography. This result led us to abandon this approach and instead install the Xul*f* residues one-by-one.



Scheme 3.25. Synthesis of trisaccharide acceptor **3.130** and an attempt to synthesize pentasaccharide **3.131**.

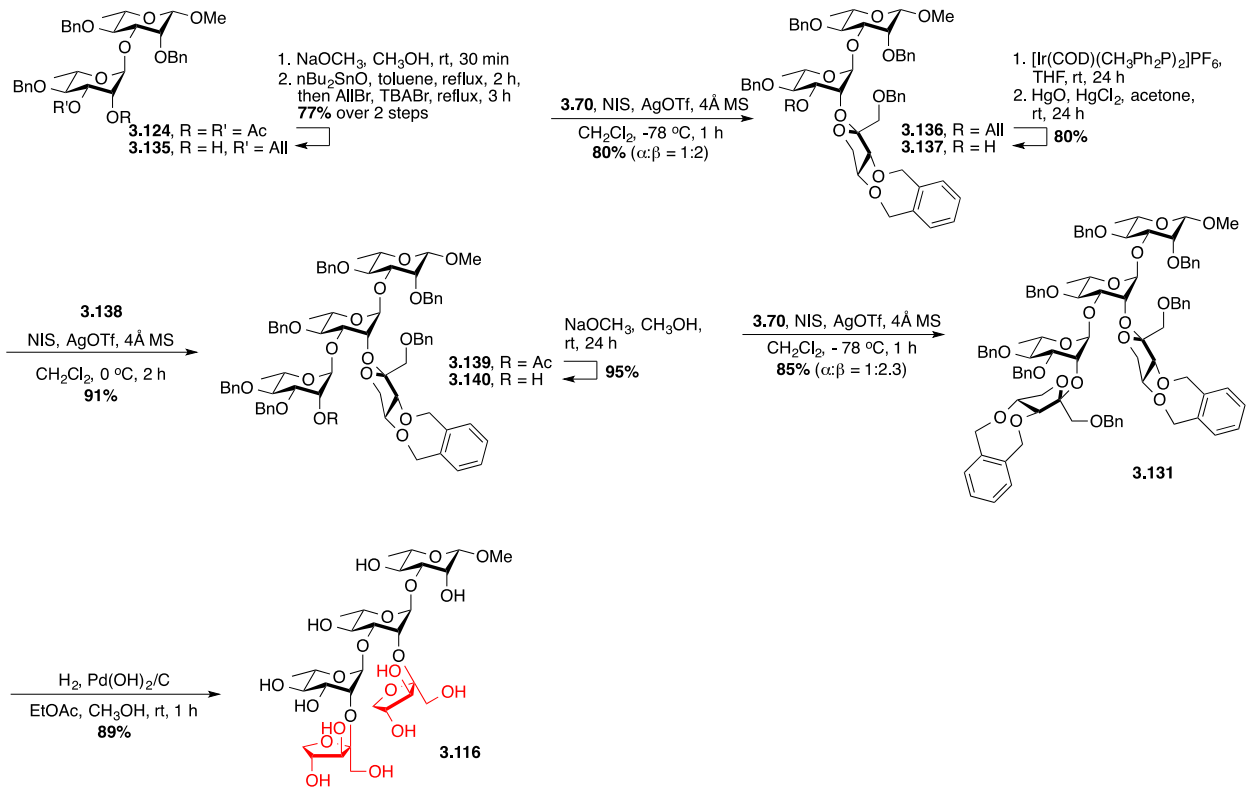
As mentioned above, the desired ββ-xylulofuranosyl pentasaccharide **3.131** could not be isolated from the mixture obtained after the installation of two Xul*f* residues onto trisaccharide **3.130** in a single step. I, therefore, synthesized another trisaccharide acceptor (**3.132**) with only one free hydroxyl group. This compound was prepared from **3.129**, the side product of the Zemplén deacetylation of **3.127** (**Scheme 3.26**), via an organotin-mediated regioselective benzylation in 81% yield. After the benzylation, the first Xul*f* residue was installed to afford tetrasaccharide **3.133** in excellent yield (89%) but with moderate selectivity (α/β = 1:2.4). The iso-

mers were separable by column chromatography, despite having small difference of R_f value (<0.03). The acetyl group of tetrasaccharide **3.133**β was then smoothly removed by Zemplén deacetylation to afford tetrasaccharide acceptor **3.134** in 93% yield. The coupling between **3.134** and Xul*f* thioglycoside **3.70** led to a mixture of products that could not be separated. Moreover, the NMR spectrum of the mixture showed that the major product of this last coupling was the α-Xul*f* glycoside (C2 of the newly introduced residue: 110.17 ppm). Thus, I redesigned the approach a second time.



Scheme 3.26. First attempt to synthesize **3.131** via introducing Xul*f* residues in separate steps.

Due to the undesired stereoselectivity in the introduction of the second Xul*f* residue, I hypothesized that the nature of glycosyl acceptor influenced the stereoselectivity in the glycosylation. Based on the results from the monosaccharide test acceptor (**3.85**, **Figure 3.10**), I considered that disaccharide acceptor **3.135** would give better results as it was more similar to the monosaccharide acceptor **3.85**. Thus (**Scheme 3.27**), the two acetyl groups of disaccharide **3.124** were removed by Zemplén deacetylation, and the resulting diol was regioselectively allylated via an organotin intermediate to afford disaccharide acceptor **3.135** with a C-2' hydroxyl group. The coupling reaction between **3.135** with **3.70** was executed using the optimized conditions to afford trisaccharide **3.136** in 80% yield (α/β = 1:2.0). This selectivity was comparable to what was observed for monosaccharaide acceptor **3.85**. Next, trisaccharide acceptor **3.137**, which was obtained by removal of the allyl group of trisaccharide **3.136**, was coupled with rhamnose thioglycoside **3.138**[39] to afford the desired tetrasaccharide **3.139**. After deacetylation of tetrasaccharide **3.139**, the tetrasaccharide acceptor **3.140** was obtained in 95% and then coupled with Xul*f* thioglycoside **3.70** to afford the fully-protected pentasaccharide **3.131** in 85% yield with similar stereoselectivity as the previous glycosylation (α/β = 1:2.3). The target molecule, the pentasaccharide repeating unit of *Y. enterocolitica* O:5 and O:5/27 LPS was afforded in excellent yield by hydrogenation of **3.131**. The stereochemistry of rhamnopyranoside residues in pentasaccharide **3.116** were identified by their $^{1}J_{C1,H1}$ magnitudes. The value for the β-rhamnopyranoside was 159.3 Hz and both α-rhamnopyranosides were 175.7 Hz, which is consistent with these assignments. The stereochemistry of the two Xul*f* residues were identified by the chemical shift of their C-2 resonances, which appeared at 106.01 and 106.07 ppm (105.78 and 105.91 ppm in literature[1b,1c]) and were assigned as β-xylulofuranosides.



Scheme 3.27. Successful synthesis of pentasaccharide **3.116**.

3.3 Conclusion

Xylulose thioglycoside donors **3.70** and **3.71** were synthesized and investigated for their ability to stereoselectively introduce β-Xul*f* residues into oligosaccharides. The donors were designed based on the concept that restricting the conformation of the electrophilic intermediate produced upon activation of the thioglycoside would lead to preferential 1,2-*cis* glycoside formation. The three major achievements are: (1) Donors **3.70** and **3.71** were successfully synthesized in ten steps from arabinose; (2) Moderate to good β selectivity in the xylulofuranosylation was observed with a variety of acceptors using donors containing a xylylene group at the O-3 and O-4 positions and a benzoyl group at O-1; (3) Characterization of the anomeric configuration

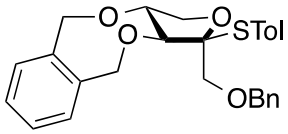
of all xylulofuranosides was achieved by the chemical shift of C-2, accompanied with 2D ^{1}H–^{1}H TROESY spectra and an X-ray structure of **3.115β**. Finally, the conformationally-restricted thioglycoside donor **3.70** was successfully used in the synthesis of the pentasaccharide repeating unit of *Y. enterocolitica* O:5/O:5,27 LPS.

3.4 Experimental Data

3.4.1 General experimental methods

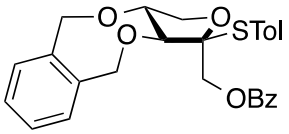
Reactions were carried out in oven-dried glassware. All reagents used were purchased from commercial sources and were used without further purification unless noted. Solvents used in reactions were purified by successive passage through columns of alumina and copper oxide catalyst under nitrogen. Unless stated otherwise, all reactions were carried out at room temperature under a positive pressure of argon and were monitored by TLC on silica gel 60 F_{254} (0.25 mm, E. Merck). Spots were detected under UV light or by charring with 10% H_2SO_4, in EtOH. Unless otherwise indicated, all column chromatography was performed on silica gel 60 (40–60 μm). The ratio between silica gel and crude product ranged from 100 to 50:1 (w/w). Optical rotations were measured at 22 ± 2 °C at the sodium D line (589 nm) and are in units of deg·mL(dm·g)$^{-1}$. ^{1}H NMR spectra were recorded at 500 or 700 MHz, and chemical shifts are referenced to either $CHCl_3$ (7.26 ppm, $CDCl_3$) or HOD (4.78 ppm, D_2O). ^{13}C NMR spectra were recorded at 125 or 175 MHz, and ^{13}C chemical shifts were referenced to internal $CDCl_3$ (77.23 ppm, $CDCl_3$), external dioxane (67.40 ppm, D_2O). In the processing of reaction mixtures, solutions of organic solvents were washed with equal amounts of aqueous solutions. Organic solutions were concentrated under vacuum at < 40 ºC (bath). Electrospray mass spectra were recorded on samples suspended in mixtures of THF with CH_3OH and added NaCl.

3.4.2 Experimental details and data for new compounds



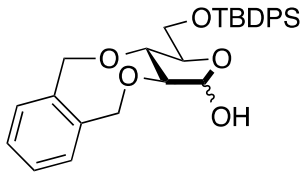
Tolyl 1-*O*-benzyl-2-thio-3,4-*O*-xylylene-β-D-xylulofuranoside (3.70). To a solution of **3.77** (159 mg, 0.267 mmol) in tetrahydrofuran (2.7 mL) was added 1M tetrabutylammonium fluoride (399 μL, 0.399 mmol) at 0 °C. After 4 h, the reaction mixture was added satd aq $NaHCO_3$ and then the solution was extracted with EtOAc. The organic layer was then washed with water and brine. The organic layer was dried with $MgSO_4$ and then filtered. The filtrate was concentrated and dried *in vacuo*. To a solution of the resulting residue in DMF (2.7 mL) was added benzyl bromide (54.8 mg, 38.0 μL, 0.320 mmol) and 60% NaH (12.8 mg, 0.320 mmol) at room temperature. After 1 h, CH_3OH was added. The mixture was concentrated and then diluted with CH_2Cl_2, and then washed with brine and water. The organic layers were dried with $MgSO_4$ and then filtered. The filtrate was concentrated under reduced pressure and then purified by column chromatography (8:1, hexane–EtOAc) to give **3.70** (105 mg, 88% over two steps) as a colorless oil. $[\alpha]^{25}_D$ –18.7 (*c* 0.7, $CHCl_3$); R_f 0.41 (4:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.48–7.38 (m, 4H, Ar), 7.38–7.34 (m, 2H, Ar), 7.31–7.24 (m, 3H, Ar), 7.14–7.10 (m, 2H, Ar), 7.10–7.06 (m, 2H, Ar), 5.04 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.93 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.85 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.78 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.58 (dd, 1H, $J_{5a,4}$ = 7.7 Hz, J_{gem} = 9.8 Hz, H-5a), 4.54–4.49 (m, 2H, H-4, ArCH_2), 4.48 (d, 1H, $J_{3,4}$ = 4.8 Hz, H-3), 4.33 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 3.94 (dd, 1H, $J_{5b,4}$ = 3.2 Hz, J_{gem} = 9.8 Hz, H-5b), 3.69 (d, 1H, J_{gem} = 11.3 Hz, H-1a), 3.41 (d, 1H, J_{gem} = 11.3 Hz, H-1b), 2.33 (s, 3H, ArCH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.6 (Ar), 138.1 (Ar), 136.4 (Ar), 136.3 (2C, Ar), 135.7 (Ar), 131.7 (Ar), 131.5

(Ar), 129.7 (Ar), 129.65 (Ar), 129.4 (2C, Ar), 128.3 (2C, Ar), 127.7 (2C, Ar), 127.5 (Ar), 126.8 (Ar), 98.2 (C-2), 83.8 (C-3), 81.4 (C-4), 73.3 (Ar*C*H_2), 70.9 (C-5), 70.3 (C-1), 69.5 (Ar*C*H_2), 68.8 (Ar*C*H_2), 21.2 (CH_3); HRMS (ESI) calcd. for $C_{27}H_{28}NaO_4S$ $[M+Na]^+$ 471.1601; found 471.1598.



Tolyl 1-*O*-benzoyl-2-thio-3,4-*O*-xylylene-β-D-xylulofuranoside (3.71). To a solution of **3.77** (106 mg, 0.178 mmol) in tetrahydrofuran (1.8 mL) was added 1M tetrabutylammonium fluoride (266 μL, 0.266 mmol) at 0 °C. After 4 h, the reaction mixture was added to satd aq $NaHCO_3$ and then extracted with EtOAc. The organic layer was then washed with brine and water. The organic layer was dried with $MgSO_4$ and then filtered. The filtrate was concentrated and dried *in vacuo*. To a solution of the resulting residue in CH_2Cl_2 (1.8 mL) was added Et_3N (21.6 mg, 29.5 μL, 0.213 mmol), benzoyl chloride (30.0 mg, 24.7 μL, 0.213 mmol) and DMAP (2.2 mg, 0.0178 mmol) at room temperature. After 1 h, CH_3OH was added and the mixture was concentrated and then diluted with CH_2Cl_2, washed with brine and water. The organic layers were dried with $MgSO_4$ and then filtered. The filtrate was concentrated under reduced pressure and then purified by column chromatography (8:1, hexane–EtOAc) to give **3.71** (73 mg, 89% over two steps) as a colorless oil. $[\alpha]^{25}_D$ –78.1 (*c* 0.5, $CHCl_3$); R_f 0.51 (4:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.84–7.80 (m, 2H, ArH), 7.56–7.50 (m, 1H, ArH), 7.43–7.34 (m, 8H, ArH), 7.14–7.09 (m, 2H, ArH), 5.06 (d, 1H, J_{gem} = 12.5 Hz, ArCH_2), 4.89 (d, 1H, J_{gem} = 12.5 Hz, ArCH_2), 4.86 (d, 1H, J_{gem} = 12.5 Hz, ArCH_2), 4.79 (d, 1H, J_{gem} = 12.5 Hz, ArCH_2), 4.61 (dd, 1H, $J_{5a,4}$ = 7.9, J_{gem} = 9.7 Hz, H-5a), 4.56 (ddd, 1H, $J_{4,3}$ = 4.6 Hz, $J_{4,5a}$ = 7.9 Hz, $J_{4,5b}$ = 3.0 Hz, H-4), 4.43 (d, 1H, J_{gem} = 12.0 Hz, H-1a), 4.38 (d, 1H, J_{gem} = 12.0 Hz, H-1b), 4.35 (d, 1H, $J_{3,4}$ = 4.6 Hz, H-3), 3.92 (dd,

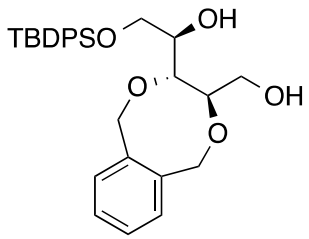
1H, $J_{5b,4}$ = 3.0 Hz, J_{gem} = 9.7 Hz, H-5b), 2.33 (s, 3H, ArCH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 165.8 (C=O), 139.1 (Ar), 136.6 (Ar), 136.5 (2C, Ar), 135.2 (Ar), 133.0 (Ar), 131.8 (Ar), 131.4 (Ar), 129.9 (Ar), 129.8 (2C, Ar), 129.72 (2C, Ar), 129.67 (2C, Ar), 128.3 (2C, Ar), 126.0 (Ar), 96.5 (C-2), 84.1 (C-4), 81.6 (C-3), 71.1 (C-5), 69.5 (ArCH_2), 69.1 (ArCH_2), 64.5 (C-1), 21.1 (ArCH_3); HRMS (ESI) calcd. for $C_{27}H_{26}NaO_5S$ $[M+Na]^+$ 485.1393; found 485.1397.



5-*O*-*t*-butyldiphenylsilyl-2,3-*O*-xylylidene-α/β-D-arabinose (3.73). To a solution of the **3.72**[30] (10.0 g, 17.6 mmol) in CH_3OH (88.0 mL) was added sodium methoxide (70.4 mg, 1.76 mmol) at room temperature. After stirring for 3.5 h, sodium methoxide was neutralized by the addition of Amberlite IR-120 H^+ resin. The mixture was then filtered and the filtrate was concentrated under reduced pressure and dried *in vacuo*. To a solution of the resulting residue in pyridine (52 mL) was added TBDPSCl (5.4 g, 5.1 mL, 19.4 mmol) and Et_3N (5.3 g, 7.3 mL, 52.8 mmol) at 0 ºC. After stirring for 16 h at room temperature, the CH_3OH was added and the solution was co-evaporated with toluene. The crude residue was diluted with CH_2Cl_2 and washed with 1N HCl, water, satd aq $NaHCO_3$ and brine. The organic layers were dried with $MgSO_4$ and filtered. The filtrate was then concentrated under reduced pressure and dried *in vacuo*. The residue was then dissolved in DMF (88 mL), followed by addition of 60% NaH (1.76 g, 44.0 mol) and α,α'-dibromo-*o*-xylylene (5.1 g, 19.4 mmol) at 0 ºC. After stirring for 1.5 h at room temperature, satd aq NH_4Cl was added. Dilution of the mixture with CH_2Cl_2 provided a solution that was washed with water and brine. The organic layer was dried with $MgSO_4$, filtered and the filtrate was concentrated. The obtained residue was dissolved in mixture of acetone and water (80.0 mL, 9:1),

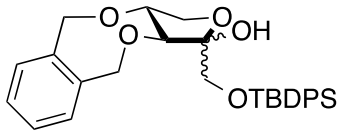
followed by addition of *N*-bromosuccinimide (4.7 g, 26.4 mmol) at room temperature. After stirring for 30 min at room temperature, the mixture was concentrated. The crude residue was then diluted with CH_2Cl_2 and washed with water and brine. The organic layer was then dried over $MgSO_4$ and concentrated. The resulting residue was purified by column chromatography (4:1, hexane–EtOAc) to give an inseparable α/β mixture of **3.73** (4.0 g, 46% over four steps, α:β = 1.6:1) as a white foam; R_f 0.27 (4:1, hexane–EtOAc); Data for **3.73α**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.68–7.62 (m, 4H, ArH), 7.55–7.52 (m, 1H, ArH), 7.45–7.34 (m, 9H, ArH), 5.36 (d, 1H, $J_{1,2}$ = 2.5 Hz, H-1), 4.94 (d, 1H, J_{gem} = 12.5 Hz, ArCH_2), 4.71 (d, 1H, J_{gem} = 12.5 Hz, ArCH_2), 4.21 (ddd, 1H, $J_{4,3}$ = 8.3 Hz, $J_{4,5a}$ = 2.4 Hz, $J_{4,5b}$ = 3.9 Hz, H-4), 4.16 (dd, 1H, $J_{3,2}$ = 5.2 Hz, $J_{3,4}$ = 8.3 Hz, H-3), 4.00 (dd, 1H, $J_{2,1}$ = 2.5 Hz, $J_{2,3}$ = 5.2 Hz, H-2), 3.87 (dd, 1H, $J_{5a,4}$ = 2.4 Hz, J_{gem} = 11.5 Hz, H-5a), 3.75 (dd, 1H, $J_{5b,4}$ = 3.9 Hz, J_{gem} = 11.5 Hz, H-5b), 2.80 (br s, 1H, OH), 1.01 (s, 9H, C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 135.8 (Ar), 135.7 (2C, Ar), 135.6 (Ar), 131.77 (Ar), 131.74 (Ar), 131.45 (Ar), 131.44 (Ar), 129.71 (2C, Ar), 129.66 (Ar), 129.64 (Ar), 127.89 (Ar), 127.87 (Ar), 127.70 (2C, Ar), 127.67 (2C, Ar), 102.4 (C-1), 88.3 (C-2), 81.7 (C-4), 80.8 (C-3), 69.9 (Ar*C*H$_2$), 68.5 (Ar*C*H$_2$), 63.1 (C-5), 26.8 ((*C*H$_3$)$_3$C) 19.3 ((CH$_3$)$_3$*C*); Data for **3.73β**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.68–7.62 (m, 4H, ArH), 7.45–7.34 (m, 10H, ArH), 5.28 (dd, 1H, $J_{1,2}$ = 5.3 Hz, $J_{1,OH}$ = 7.8 Hz, H-1), 4.99 (d, 1H, J_{gem} = 12.5 Hz, ArCH_2), 4.95 (d, 1H, J_{gem} = 12.5 Hz, ArCH_2), 4.90 (d, 1H, J_{gem} = 12.5 Hz, ArCH_2), 4.71 (d, 1H, J_{gem} = 12.5 Hz, ArCH_2), 4.26 (app t, 1H, $J_{3,2}$ = $J_{3,4}$ = 5.3 Hz, H-3), 4.16 (app t, 1H, $J_{2,1}$ = $J_{2,3}$ = 5.3 Hz, H-2), 4.13 (d, 1H, $J_{OH,1}$ = 7.8 Hz, OH), 4.04 (app dt, 1H, $J_{4,3}$ = 5.3 Hz, $J_{4,5a}$ = $J_{4,5b}$ = 3.4 Hz, H-4), 3.79 (dd, 1H, $J_{5a,4}$ = 3.4 Hz, J_{gem} = 11.2 Hz, H-5a), 3.61 (dd, 1H, $J_{5b,4}$ = 3.4 Hz, J_{gem} = 11.2 Hz, H-5b), 1.00 (s, 9H, (CH_3)$_3$C); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 136.3 (Ar), 136.2 (Ar), 136.1 (Ar), 135.9 (Ar), 133.5 (Ar), 133.4 (Ar), 132.5 (Ar), 132.3 (Ar), 130.0 (Ar), 129.9 (Ar), 97.6 (C-1), 83.7 (C-4), 83.6 (C-

2), 80.0 (C-3), 69.4 (Ar*C*H_2), 68.7 (Ar*C*H_2), 64.7 (C-5), 26.8 ((*C*H_3)$_3$C), 19.2 ((CH$_3$)$_3$*C*); HRMS (ESI) calcd. for $C_{29}H_{34}NaO_5Si$ $[M+Na]^+$ 513.2068; found 513.2061.

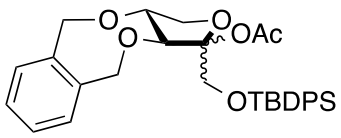


5-*O*-*t*-butyldiphenylsilyl-2,3-*O*-xylylidene-D-arabinitol (3.74). To a solution of **3.73** (250 mg, 0.508 mmol) in CH_3OH (5 mL) was added sodium borohydride (19.2 mg, 0.508 mmol) at room temperature. After stirring for 2 h, the reaction mixture was added to 1N HCl (10 mL) and then extracted with EtOAc. The organic layer was then washed with water and brine. The organic layer was dried with $MgSO_4$ and then filtered. The filtrate was concentrated and the resulting residue was purified by column chromatography (1:1, hexane–EtOAc) to give **3.74** (175.1 mg, 70%) as a white foam. $[\alpha]^{25}_D$ –28.7 (*c* 1.1, $CHCl_3$); R_f 0.35 (1:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 700 MHz) δ_H 7.75–7.71 (m, 2H, ArH), 7.70–7.68 (m, 2H, ArH), 7.51–7.40 (m, 6H, ArH), 7.24–7.21 (m, 2H, ArH), 7.11–7.07 (m, 1H, ArH), 7.06–7.02 (m, 1H, ArH), 5.10 (d, 1H, J_{gem} = 14.0 Hz, ArCH_2), 5.03 (d, 1H, J_{gem} = 14.0 Hz, ArCH_2), 5.00 (d, 1H, J_{gem} = 14.0 Hz, ArCH_2), 4.82 (d, 1H, J_{gem} = 14.0 Hz, ArCH_2), 3.94 (dd, 1H, $J_{5a,4}$ = 4.2 Hz, J_{gem} = 10.5 Hz, H-5a), 3.91 (dd, 1H, $J_{5b,4}$ = 5.6 Hz, J_{gem} = 10.5 Hz, H5-b), 3.91–3.82 (m, 1H, H-1a), 3.75–3.72 (m, 2H, H-2, H-4), 3.68–3.63 (m, 1H, H-1b), 3.26 (dd, 1H, *J* = 9.1, 7.0 Hz, H-3), 2.96 (d, 1H, *J* = 5.6 Hz, OH), 2.84 (br s, 1H, OH), 1.14 (s, 9H, (CH_3)$_3$C); ^{13}C NMR ($CDCl_3$, 175 MHz) δ_C 136.95 (Ar), 136.92 (Ar), 135.7 (2C, Ar), 135.65 (2C, Ar), 133.03 (Ar), 133.02 (Ar), 130.05 (Ar), 130.03 (Ar), 128.4 (Ar), 128.3 (Ar), 127.98 (2C, Ar), 127.96 (2C, 127.5 (2C, Ar), 84.2 (C-2), 82.0 (C-3), 75.1 (Ar*C*H_2),

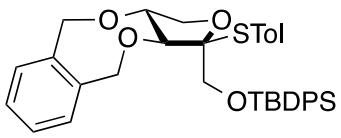
74.9 (Ar*C*H_2), 72.4 (C-4), 64.5 (C-5), 63.7 (C-1), 26.9 ((*C*H_3)$_3$C) 19.2 ((CH$_3$)$_3$*C*); HRMS (ESI) calcd. for $C_{29}H_{36}NaO_5Si$ $[M+Na]^+$ 515.2224; found 515.2217.



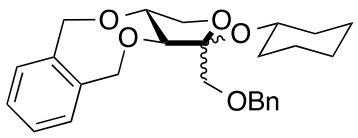
1-*O*-*tert*-butyldiphenylsilyl-3,4-*O*-xylylene-α/β-D-xylulofuranose (3.75). To a solution of **3.74** (75.1 mg, 0.152 mmol) in CH_2Cl_2 (4 mL) was added bis(tri-*n*-butyltin) oxide (116 μL, 136 mg, 0.229 mmol) at 0 ºC, followed by bromine (11.7 μL, 36.5 mg, 0.229 mmol) dropwise. After stirring for 2 h, the reaction mixture was concentrated. The resulting residue was purified by column chromatography (CH_2Cl_2, then 4:1, hexane–EtOAc) to give **3.75** (40 mg, 50%, α/β = 1:10) as a colorless oil; R_f 0.32 (2:1, hexane–EtOAc); Data for **3.75β**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.67–7.62 (m, 4H, ArH), 7.45–7.35 (m, 10H, ArH), 5.05 (d, 1H, J_{gem} = 12.4 Hz, ArC*H*$_2$), 4.88 (d, 1H, J_{gem} = 12.9 Hz, ArC*H*$_2$), 4.82 (d, 1H, J_{gem} = 12.4 Hz, ArC*H*$_2$), 4.78 (d, 1H, J_{gem} = 12.9 Hz, ArC*H*$_2$), 4.42 (app dt, 1H, $J_{4,3}$ = $J_{4,5b}$ = 4.6 Hz, $J_{4,5a}$ = 7.8 Hz, H-4), 4.35 (dd, 1H, $J_{5a,4}$ = 7.8 Hz, J_{gem} = 9.5 Hz, H5-a), 4.05 (d, 1H, $J_{3,4}$ = 4.6 Hz, H-3), 3.80 (dd, 1H, $J_{5b,4}$ = 4.6 Hz, J_{gem} = 9.5 Hz, H-5b), 3.69 (d, 1H, J_{gem} = 10.4 Hz, H-1a), 3.67 (s, 1H, OH), 3.61 (d, 1H, J_{gem} = 10.4 Hz, H-1b), 1.01 (s, 9H, (C*H*$_3$)$_3$C); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 136.7 (Ar), 135.9 (Ar), 135.81 (2C, Ar), 135.79 (2C, Ar), 135.7 (Ar), 133.22 (Ar), 133.18 (Ar), 131.8 (Ar), 131.7 (Ar), 130.0 (Ar), 129.9 (2C, Ar), 129.8 (Ar), 127.9 (3C, Ar), 104.0 (C-2), 81.7 (C-3), 81.0 (C-4), 70.3 (C-5), 69.2 (Ar*C*H_2), 69.1 (Ar*C*H_2), 65.9 (C-1), 26.7 ((*C*H_3)$_3$C), 19.2 ((CH$_3$)$_3$*C*); HRMS (ESI) calcd. for $C_{29}H_{34}NaO_5Si$ $[M+Na]^+$ 513.2068; found 513.2068.



2-*O*-acetyl-1-*O*-*tert*-butyldiphenyl-3,4-*O*-xylylene-α/β-D-xylulofuranose (3.76). To a solution of **3.75** (4.34 g, 8.85 mmol) in tetrahydrofuran (88.5 mL) was added acetic anhydride (1.0 mL, 1.08 g, 10.6 mmol) at room temperature. The mixture was then cooled to –78 ºC and *n*-butyllithium (6.63 mL, 10.6 mmol) was added dropwise. After stirring for 2 h, the reaction mixture was added satd aq $NaHCO_3$ and then extracted with EtOAc. The organic layer was then washed with brine and water. The organic layer was dried with $MgSO_4$ and then filtered. The filtrate was concentrated and the resulting residue was purified by column chromatography (8:1, hexane–EtOAc) to give **3.76** (4.50 g, 96%, α/β = 1:10) as a yellow oil. R_f 0.45 (4:1, hexane–EtOAc); Data for **3.76β**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.63–7.60 (m, 2H, ArH), 7.52–7.49 (m, 2H, ArH), 7.45–7.34 (m, 10H, ArH), 5.13 (d, 1H, J_{gem} = 12.4 Hz, ArCH_2), 4.94 (app dt, 1H, $J_{4,3}$ = $J_{4,5b}$ = 5.2 Hz, $J_{4,5a}$ = 8.3 Hz, H-4), 4.87 (d, 1H, J_{gem} = 12.9 Hz, ArCH_2), 4.80 (d, 1H, J_{gem} = 12.9 Hz, ArCH_2), 4.78 (d, 1H, J_{gem} = 12.4 Hz, ArCH_2), 4.59 (app t, 1H, $J_{5a,4}$ = J_{gem} = 8.3 Hz, H-5a), 4.57 (d, 1H, $J_{3,4}$ = 5.2 Hz, H-3), 3.89 (dd, 1H, $J_{5b,4}$ = 5.2 Hz, J_{gem} = 8.3 Hz, H-5b), 3.75 (d, 1H, J_{gem} = 10.6 Hz, H-1a), 3.60 (d, 1H, J_{gem} = 10.6 Hz, H-1b), 2.01 (s, 3H, CH_3CO), 0.89 (s, 9H, (CH_3)$_3$C); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 169.1 (C=O), 137.7 (Ar), 135.5 (2C, Ar), 134.8 (Ar), 133.0 (Ar), 132.96 (Ar), 131.7 (Ar), 131.2 (Ar), 129.7 (Ar), 129.64 (Ar), 129.62 (Ar), 129.5 (Ar), 127.66 (2C, Ar), 127.64 (2C, Ar), 127.61 (Ar), 127.58 (Ar), 109.4 (C-2), 82.7 (C-4), 80.5 (C-3), 73.9 (C-5), 70.1 (Ar*C*H$_2$), 68.1 (Ar*C*H$_2$), 64.2 (C-1), 26.5 ((*C*H$_3$)$_3$C), 21.8 (*C*H$_3$CO), 19.2 ((CH$_3$)$_3$*C*); HRMS (ESI) calcd. for $C_{31}H_{40}NO_6Si$ $[M+NH_4]^+$ 550.2619; found 550.2616.

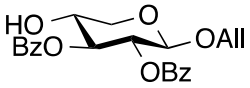


Tolyl 1-*O*-*tert*-butyldiphenyl-2-thio-3,4-*O*-xylylene-β-D-xylulofuranoside (3.77). To a solution of **3.76** (132 mg, 0.248 mmol) and thiocresol (36.9 mg, 0.297 mmol) in CH_2Cl_2 (2.5 mL) was added boron trifluoride diethyl etherate (39.8 μL, 0.322 mmol) at 0 °C. After stirring for 2 h, the reaction mixture was added to satd aq $NaHCO_3$ and then extracted with EtOAc. The organic layer was then washed with brine and water. The organic layer was dried with $MgSO_4$ and then filtered. The filtrate was concentrated and the resulting residue was purified by column chromatography (8:1, hexane–EtOAc) to give **3.77** (106 mg, 72%) as a yellow oil. $[\alpha]^{25}_D$ –29.6 (*c* 2.2, $CHCl_3$); R_f 0.57 (4:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.53–7.50 (m, 2H, ArH), 7.47–7.44 (m, 2H, ArH), 7.42–7.37 (m, 5H, ArH), 7.36–7.31 (m, 3H, ArH), 7.25–7.21 (m, 2H, ArH), 7.20 (d, 2H, J = 7.8 Hz, ArH), 6.95 (d, 2H, J = 7.8 Hz, ArH), 5.07 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.89 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.83 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.81 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.63–4.61 (m, 1H, H-3), 4.60–4.52 (m, 2H, H-4, H-5a), 3.93–3.88 (m, 1H, H-5b), 3.85 (d, 1H, J_{gem} = 11.4 Hz, H-1a), 3.61 (d, 1H, J_{gem} = 11.4 Hz, H-1b), 2.28 (s, 3H, ArCH_3), 0.88 (s, 9H, (CH_3)$_3$C); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.2 (Ar), 136.8 (Ar), 136.0 (2C, Ar), 135.6 (2C, Ar), 135.5 (2C, Ar), 134.8 (Ar), 133.5 (Ar), 133.1 (Ar), 131.7 (Ar), 131.4 (Ar), 129.8 (Ar), 129.7 (Ar), 129.5 (Ar), 129.3 (Ar), 129.2 (2C, Ar), 127.8 (Ar), 127.6 (2C, Ar), 127.5 (2C, Ar), 98.7 (C-2), 82.7 (C-4), 81.9 (C-3), 71.0 (C-5), 69.4 (ArCH_2), 69.1(ArCH_2), 64.5 (C-1), 26.6 ((CH_3)$_3$C), 21.1 (ArCH_3), 19.3 ((CH_3)$_3$*C*); HRMS (ESI) calcd. for $C_{36}H_{40}NaO_4SSi$ $[M+Na]^+$ 619.2309; found 619.2298.



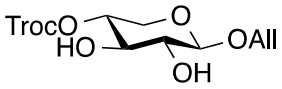
Cyclohexyl 1-*O*-benzyl-3,4-*O*-xylylene-α-D-xylulofuranoside (3.79α) and Cyclohexyl 1-*O*-benzyl-3,4-*O*-xylylene-β-D-xylulofuranoside (3.79β). A mixture of **3.70** (56 mg, 0.156 mmol), **3.78** (18.7 mg, 0.187 mmol) and 4Å molecular sieves in CH_2Cl_2 (6.2 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –78 °C before *N*-iodosuccinimide (42.1 mg, 0.187 mmol) and silver triflate (4.0 mg, 0.0156 mmol) were added. After stirring at –78 °C for 2 h, triethylamine was added. The reaction mixture was warmed to room temperature and then a small amount of water was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The solution was then dried over $MgSO_4$, filtered and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatography (9:1, hexane–EtOAc) to give **3.79α** (21.0 mg, 40%) as a colorless oil and **3.79β** (23.0 mg, 44%) as a colorless oil. Data for **3.79α**: $[\alpha]^{25}_D$ +47.8 (*c* 2.1, $CHCl_3$); R_f 0.33 (9:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.41–7.35 (m, 3H, ArH), 7.35–7.29 (m, 5H, ArH), 7.29–7.26 (m, 1H, ArH), 4.92 (d, 1H, J_{gem} = 12.0 Hz, ArCH_2), 4.91 (d, 1H, J_{gem} = 12.0 Hz, ArCH_2), 4.77 (d, 1H, J_{gem} = 12.0 Hz, ArCH_2), 4.76 (d, 1H, J_{gem} = 12.0 Hz, ArCH_2), 4.59 (d, 1H, J_{gem} = 12.0 Hz, ArCH_2), 4.56 (d, 1H, J_{gem} = 12.0 Hz, ArCH_2), 4.20 (dt, 1H, $J_{4,3}$ = 5.2 Hz, $J_{4,5a}$ = $J_{4,5b}$ = 8.1 Hz, H-4), 4.07 (app t, 1H, $J_{5a,4}$ = J_{gem} = 8.1 Hz, H-5a), 4.05 (d, 1H, $J_{3,4}$ = 5.2 Hz, H-3), 3.76 (app t, 1H, $J_{5b,4}$ = J_{gem} = 8.1 Hz, H-5b), 3.68–3.62 (m, 1H, cyclohexyl OC*H*), 3.63 (d, 1H, J_{gem} = 10.5 Hz, H-1a), 3.50 (d, 1H, J_{gem} = 10.5 Hz, H-1b), 1.83–1.76 (m, 1H, cyclohexyl CH_2), 1.73-1.61 (m, 3H, cyclohexyl CH_2), 1.52–1.44 (m, 1H, cyclohexyl CH_2), 1.30–1.07 (m, 5H, cyclohexyl CH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.8 (Ar), 136.7 (Ar), 136.3 (Ar), 131.8 (Ar), 131.6 (Ar), 129.66 (Ar), 129.63 (Ar), 128.4 (2C, Ar), 127.9 (2C, Ar), 127.6 (Ar), 109.4 (C-2),

87.5 (C-3), 81.4 (C-4), 73.7 (Ar*C*H$_2$), 71.2 (cyclohexyl O*C*H), 70.1 (C-1), 69.8 (Ar*C*H$_2$), 69.3 (Ar*C*H$_2$), 68.8 (C-5), 35.0 (cyclohexyl *C*H$_2$), 34.6 (cyclohexyl *C*H$_2$), 25.7 (cyclohexyl *C*H$_2$), 24.9 (2C, cyclohexyl *C*H$_2$); HRMS (ESI) calcd. for $C_{26}H_{32}NaO_5$ $[M+Na]^+$ 447.2142; found 447.2145. Data for **3.79β**: $[\alpha]^{25}_D$ +11.8 (*c* 2.8, $CHCl_3$); R_f 0.15 (9:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.41–7.33 (m, 4H, ArH), 7.33–7.24 (m, 3H, ArH), 7.21–7.17 (m, 2H, ArH), 5.05 (d, 1H, J_{gem} = 12.8 Hz, ArC*H*$_2$), 4.85 (d, 1H, J_{gem} = 12.8 Hz, ArC*H*$_2$), 4.81 (d, 1H, J_{gem} = 12.8 Hz, ArC*H*$_2$), 4.79 (d, 1H, J_{gem} = 12.8 Hz, ArC*H*$_2$), 4.59 (d, 1H, J_{gem} = 12.2 Hz, ArC*H*$_2$), 4.44 (d, 1H, J_{gem} = 12.2 Hz, ArC*H*$_2$), 4.20 (ddd, 1H, $J_{4,3}$ = 5.4 Hz, $J_{4,5a}$ = 7.2 Hz, $J_{4,5b}$ = 3.9 Hz, H-4), 4.23 (dd, 1H, $J_{5a,4}$ = 7.2 Hz, J_{gem} = 9.4 Hz, H-5a), 4.20 (d, 1H, $J_{3,4}$ = 5.4 Hz, H-3), 3.76 (dd, 1H, $J_{5b,4}$ = 3.9 Hz, J_{gem} = 9.4 Hz, H-5b), 3.67 (app tt, 1H, *J* = 10.8, 4.1 Hz, cyclohexyl OC*H*), 3.53 (s, 2H, H-1), 1.80–1.74 (m, 1H, cyclohexyl C*H*$_2$), 1.73–1.65 (m, 3H, cyclohexyl C*H*$_2$), 1.56–1.48 (m, 1H, cyclohexyl C*H*$_2$), 1.44–1.29 (m, 2H, cyclohexyl C*H*$_2$), 1.28–1.14 (m, 2H, cyclohexyl C*H*$_2$), 1.12–1.02 (m, 1H, cyclohexyl C*H*$_2$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.3 (Ar), 137.0 (Ar), 136.3 (Ar), 131.8 (Ar), 131.5 (Ar), 129.51 (Ar), 129.47 (Ar), 128.5 (2C, Ar), 127.8 (2C, Ar), 127.7 (Ar), 107.1 (C-2), 82.9 (C-3), 81.2 (C-4), 73.6 (Ar*C*H$_2$), 71.0 (2C, cyclohexyl O*C*H, C-5), 70.0 (Ar*C*H$_2$), 69.1 (2C, C-1, Ar*C*H$_2$), 35.1 (cyclohexyl *C*H$_2$), 34.7 (cyclohexyl *C*H$_2$), 25.6 (cyclohexyl *C*H$_2$), 25.3 (cyclohexyl *C*H$_2$), 25.2 (cyclohexyl *C*H$_2$); HRMS (ESI) calcd. for $C_{26}H_{32}NaO_5$ $[M+Na]^+$ 447.2142; found 447.2144.

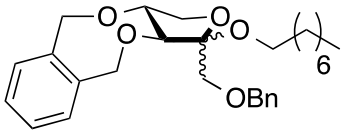


Allyl 2,3-di-*O*-benzoyl-β-D-xylopyranoside (3.84). To a solution of **3.87** (119 mg, 0.326 mmol) in dichloromethane (3 mL) was added triethylamine (98.8 mg, 135 μL, 0.977 mmol), benzoyl chloride (137.2 mg, 113 μL, 0.977 mmol) and DMAP (4.0 mg, 0.0326 mmol), and the mixture

was stirred for 30 min at room temperature. After completion of the reaction, the benzoyl chloride was quenched by the addition of CH_3OH and the solution was concentrated under reduced pressure. The residue was then diluted with CH_2Cl_2 and washed with 1N HCl, H_2O, satd aq $NaHCO_3$ and brine. The organic layers were dried with $MgSO_4$ and then filtered. The filtrate was then concentrated for the next step. To a solution of the residue in acetic acid (3 mL) was added activated zinc dust (2.4 g) and the reaction mixture was stirred at 50 °C for 3 h. After completion of the reaction, the reaction mixture was cooled and then passed through Celite. The filtrate was then diluted with CH_2Cl_2 and washed with water, satd aq $NaHCO_3$ and brine. The organic layer was dried with $MgSO_4$ and then filtered. The filtrate was then concentrated under reduced pressure. The resulting residue was purified by column chromatography (3:1, hexane–EtOAc) to give **3.84** (120 mg, 93% over two steps) as a white foam. $[\alpha]^{25}_D$ +69.6 (*c* 0.6, $CHCl_3$); R_f 0.15 (4:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 8.05–7.98 (m, 4H, ArH), 7.58–7.52 (m, 2H, ArH), 7.45–7.38 (m, 4H, ArH), 5.84 (dddd, 1H, *J* = 16.6, 10.6, 6.0, 5.0 Hz, $OCH_2C\mathit{H}{=}CH_2$), 5.40 (dd, 1H, $J_{2,1}$ = 6.2 Hz, $J_{2,3}$ = 8.1 Hz, H-2), 5.32–5.25 (m, 2H, $OCH_2CH{=}C\mathit{H}_2$, H-3), 5.17 (dq, 1H, *J* = 10.6, 1.2 Hz, $OCH_2CH{=}C\mathit{H}_2$), 4.78 (d, 1H, $J_{1,2}$ = 6.2 Hz, H-1), 4.34 (ddt, 1H, *J* = 13.4, 5.0, 1.6 Hz, $OC\mathit{H}_2CH{=}CH_2$), 4.24 (dd, 1H, $J_{5a,4}$ = 4.7 Hz, J_{gem} = 12.0 Hz, H-5a), 4.13 (ddt, 1H, *J* = 13.4, 6.0, 1.6 Hz, $OC\mathit{H}_2CH{=}CH_2$), 4.05–3.99 (m, 1H, H-4), 3.55 (dd, 1H, $J_{5b,4}$ = 8.0 Hz, J_{gem} = 12.0 Hz, H-5b), 3.08 (d, 1H, $J_{OH,4}$ = 5.8 Hz, OH); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 167.3 (*C*=O), 165.2 (*C*=O), 133.7 ($OCH_2\mathit{C}H{=}CH_2$), 133.6 (Ar), 133.4 (Ar), 130.1 (2C, Ar), 129.8 (2C, Ar), 129.4 (Ar), 129.0 (Ar), 128.52 (2C, Ar), 128.49 (2C, Ar), 117.7 ($OCH_2CH{=}\mathit{C}H_2$), 99.4 (C-1), 75.7 (C-3), 70.5 (C-2), 69.6 ($O\mathit{C}H_2CH{=}CH_2$), 68.8 (C-4), 64.6 (C-5); HRMS (ESI) calcd. for $C_{22}H_{22}NaO_7$ $[M+Na]^+$ 421.1258; found 421.1261.

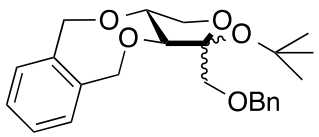


Allyl 4-*O*-2,2,2-trichloroethoxycarbonyl-β-D-xylopyranoside (3.87). To a solution of **3.86**[34] (74 mg, 0.389 mmol) in toluene (20 mL) was added *n*-Bu_2SnO (145 mg, 0.584 mmol) at room temperature and the reaction mixture was stirred at reflux. After 5 h, the reaction mixture was cooled to room temperature and 2,2,2-trichloroethyl chloroformate (123.6 mg, 80.3 μL, 0.584 mmol) and CsF (88.6 mg, 0.584 mmol) were added. The reaction mixture was continuely stirred at reflux for 2 h. The solution was cooled to room temperature and then concentrated under reduced pressure. The resulting residue was purified by column chromatography (3:1, hexane–EtOAc) to give **3.87** (119 mg, 84%) as a colorless oil. $[\alpha]^{25}_D$ –37.8 (*c* 1.4, $CHCl_3$); R_f 0.55 (1:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 5.93 (dddd, 1H, J = 16.7, 10.3, 6.3, 5.4 Hz, $OCH_2CH{=}CH_2$), 5.32 (dq, 1H, J = 17.1, 1.6 Hz, $OCH_2CH{=}CH_2$), 5.25 (dq, 1H, J = 10.3, 1.6 Hz, $OCH_2CH{=}CH_2$), 4.82 (d, 1H, J_{gem} = 11.8 Hz, Troc CH_2), 4.81–4.76 (m, 1H, H-4), 4.76 (d, 1H, J_{gem} = 11.8 Hz, Troc CH_2), 4.46 (d, 1H, $J_{1,2}$ = 6.3 Hz, H-1), 4.35 (ddt, 1H, J = 12.7, 5.3, 1.4 Hz, $OCH_2CH{=}CH_2$), 4.18 (dd, 1H, $J_{5a,4}$ = 4.7 Hz, J_{gem} = 12.1 Hz, H-5a), 4.13 (ddt, 1H, J = 12.7, 5.3, 1.3 Hz, $OCH_2CH{=}CH_2$), 3.84 (dt, 1H, $J_{3,2} = J_{3,4}$ = 7.8 Hz, $J_{3,OH}$ = 4.6 Hz, H-3), 3.55 (ddd, 1H, $J_{2,1}$ = 6.3 Hz, $J_{2,3}$ = 7.8 Hz, $J_{2,OH}$ = 4.6 Hz, H-2), 3.47 (dd, 1H, $J_{5b,4}$ = 8.1 Hz, J_{gem} = 12.1 Hz, H-5b), 3.10 (d, 1H, $J_{OH,3}$ = 4.6 Hz, OH), 2.80 (d, 1H, $J_{OH,2}$ = 4.6 Hz, OH); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 153.5 (C=O), 133.5 ($OCH_2CH{=}CH_2$), 118.7 ($OCH_2CH{=}CH_2$), 101.5 (C-1), 77.5 (Troc CH_2), 75.7 (C-4), 72.5 (C-2), 72.2 (C-3), 70.3 ($OCH_2CH{=}CH_2$), 61.4 (C-5); HRMS (ESI) calcd. for $C_{11}H_{15}Cl_3NaO_7$ $[M+Na]^+$ 386.9776; found 386.9772.



Octyl 1-*O*-benzyl-3,4-*O*-xylylidene-α-D-xylulofuranoside (3.88α) and **Octyl 1-*O*-benzyl-3,4-*O*-xylylidene-β-D-xylulofuranoside (3.88β)**. A mixture of **3.70** (27.4 mg, 0.0611 mmol), **3.80** (9.5 mg, 11.6 μL, 0.0733 mmol), and 4Å molecular sieves in CH_2Cl_2 (2.4 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –78 °C and then *N*-iodosuccinimide (16.5 mg, 0.0733 mmol) and silver triflate (1.6 mg, 6.11 μmol) were added. After stirring for 1 h at –78 °C, triethylamine was added. The reaction was warmed to room temperature and then a small amount of water was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The solution was then dried over $MgSO_4$, filtered and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatography (15:1, hexane–EtOAc) to give **3.88α** (12.2 mg, 44%) as a colorless oil and **3.88β** (13.0 mg, 47%) as a colorless oil. Data for **3.88α**: $[\alpha]^{25}_D$ +56.2 (*c* 1.2, $CHCl_3$); R_f 0.61 (4:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.41–7.31 (m, 8H, ArH), 7.30–7.26 (m, 1H, ArH), 4.92 (d, 1H, J_{gem} = 12.5 Hz, ArCH_2), 4.91 (d, 1H, J_{gem} = 12.5 Hz, ArCH_2), 4.77 (d, 1H, J_{gem} = 12.5 Hz, ArCH_2), 4.76 (d, 1H, J_{gem} = 12.5 Hz, ArCH_2), 4.58 (d, 1H, J_{gem} = 12.2 Hz, ArCH_2), 4.56 (d, 1H, J_{gem} = 12.2 Hz, ArCH_2), 4.16 (app dt, 1H, $J_{4,3}$ = 5.0 Hz, $J_{4,5a}$ = $J_{4,5b}$ = 8.1 Hz, H-4), 4.07 (d, 1H, $J_{3,4}$ = 5.0 Hz, H-3), 4.04 (app t, 1H, $J_{5a,4}$ = 8.1 Hz, J_{gem} = 8.4 Hz, H-5a), 3.69 (app t, 1H, $J_{5b,4}$ = 8.1 Hz, J_{gem} = 8.4 Hz, H-5b), 3.59 (d, 1H, J_{gem} = 10.5 Hz, H-1a), 3.53 (d, 1H, J_{gem} = 10.5 Hz, H-1b), 3.46 (app t, 2H, *J* = 6.9 Hz, octyl OCH_2), 1.53–1.45 (m, 2H, octyl CH_2), 1.33–1.20 (m, 10H, octyl CH_2), 0.87 (t, 3H, *J* = 7.1 Hz, octyl CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.6 (Ar), 136.6 (Ar), 136.1 (Ar), 131.7 (Ar), 131.5 (Ar), 129.6 (Ar), 129.5 (Ar), 128.2 (2C, Ar), 127.8 (2C, Ar), 127.5 (Ar), 108.5 (C-2), 86.8 (C-3), 81.4 (C-4), 73.5 (Ar*C*H$_2$), 69.8 (Ar*C*H$_2$), 69.1 (Ar*C*H$_2$),

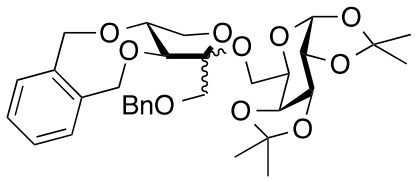
68.6 (C-1), 68.2 (C-5), 61.7 (octyl O*C*H$_2$), 31.9 (octyl *C*H$_2$), 30.1 (octyl *C*H$_2$), 29.4 (octyl *C*H$_2$), 29.3 (octyl *C*H$_2$), 26.2 (octyl *C*H$_2$), 22.7 (octyl *C*H$_2$), 14.2 (octyl *C*H$_3$); HRMS (ESI) calcd. for $C_{28}H_{38}NaO_5$ $[M+Na]^+$ 477.2611; found 477.2616. Data for **3.88β**: $[\alpha]^{25}_D$ +14.6 (*c* 1.3, $CHCl_3$); R_f 0.48 (4:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.42–7.35 (m, 4H, ArH), 7.33–7.26 (m, 3H, ArH), 7.24–7.20 (m, 2H, ArH), 5.01 (d, 1H, J_{gem} = 12.8 Hz, ArC*H*$_2$), 4.90 (d, 1H, J_{gem} = 12.8 Hz, ArC*H*$_2$), 4.81 (d, 1H, J_{gem} = 12.8 Hz, ArC*H*$_2$), 4.76 (d, 1H, J_{gem} = 12.8 Hz, ArC*H*$_2$), 4.59 (d, 1H, J_{gem} = 12.2 Hz, ArC*H*$_2$), 4.48 (d, 1H, J_{gem} = 12.2 Hz, ArC*H*$_2$), 4.34 (ddd, 1H, $J_{4,5b}$ = 4.0 Hz, $J_{4,3}$ = 5.2 Hz, $J_{4,5a}$ = 7.6 Hz, H-4), 4.20 (d, 1H, $J_{3,4}$ = 5.2 Hz, H-3), 4.15 (dd, 1H, $J_{5a,4}$ = 7.6 Hz, J_{gem} = 9.6 Hz, H-5a), 3.79 (dd, 1H, $J_{5b,4}$ = 4.0 Hz, J_{gem} = 9.6 Hz, H-5b), 3.56 (d, 1H, J_{gem} = 10.8 Hz, H-1a), 3.54 (d, 1H, J_{gem} = 10.8 Hz, H-1b), 3.52 (app dt, 1H, *J* = 9.1, 7.6 Hz, OC*H*$_2$), 3.41 (app dt, 1H, *J* = 9.1, 7.6 Hz, OC*H*$_2$), 1.58–1.49 (m, 2H, octyl C*H*$_2$), 1.31–1.19 (m, 10H, octyl C*H*$_2$), 0.87 (t, 3H, *J* = 7.0 Hz, octyl C*H*$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.1 (Ar), 136.5 (Ar), 136.4 (Ar), 131.6 (Ar), 131.5 (Ar), 129.5 (2C, Ar), 128.4 (2C, Ar), 127.7 (2C, Ar), 127.6 (Ar), 106.4 (C-2), 83.2 (C-3), 80.8 (C-4), 73.4 (Ar*C*H$_2$), 70.8 (C-5), 69.8 (Ar*C*H$_2$), 68.6 (Ar*C*H$_2$), 68.2 (C-1), 61.7 (octyl O*C*H$_2$), 31.9 (octyl *C*H$_2$), 30.2 (octyl *C*H$_2$), 29.4 (octyl *C*H$_2$), 29.3 (octyl *C*H$_2$), 26.1 (octyl *C*H$_2$), 22.7 (octyl *C*H$_2$), 14.1 (octyl *C*H$_3$); HRMS (ESI) calcd. for $C_{28}H_{38}NaO_5$ $[M+Na]^+$ 477.2611; found 477.2619.



***tert*-Butyl 1-*O*-benzyl-3,4-*O*-xylylidene-α-D-xylulofuranoside (3.89α)** and ***tert*-Butyl 1-*O*-benzyl-3,4-*O*-xylylidene-β-D-xylulofuranoside (3.89β)**. A mixture of the **3.70** (24.1 mg, 0.0537 mmol), **3.81** (4.8 mg, 0.0644 mmol), and 4Å molecular sieves in CH_2Cl_2 (2.14 mL) was stirred

under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –78 °C and *N*-iodosuccinimide (14.5 mg, 0.0644 mmol) and silver triflate (1.4 mg, 5.37 μmol) were added and slowly warmed to –60 °C. After stirring for 4 h at –60 °C, triethylamine was added. The reaction was warmed to room temperature and then a small amount of water was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The solution was then dried over $MgSO_4$, filtered and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatography (10:1, hexane–EtOAc) to give **3.89α** (6.7 mg, 31%) and **3.89β** (9.8 mg, 46%), both as colorless oils. Data for **3.89α**: $[\alpha]^{25}_D$ +24.6 (*c* 0.7, $CHCl_3$); R_f 0.31 (6:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.41–7.37 (m, 3H, ArH), 7.34–7.25 (m, 6H, ArH), 4.93 (d, 1H, J_{gem} = 12.9 Hz, ArCH_2), 4.90 (d, 1H, J_{gem} = 12.9 Hz, ArCH_2), 4.80 (d, 1H, J_{gem} = 12.9 Hz, ArCH_2), 4.75 (d, 1H, J_{gem} = 12.9 Hz, ArCH_2), 4.54 (d, 1H, J_{gem} = 11.9 Hz, ArCH_2), 4.50 (d, 1H, J_{gem} = 11.9 Hz, ArCH_2), 4.27 (app dt, 1H, $J_{4,3}$ = 5.9 Hz, $J_{4,5a}$ = $J_{4,5b}$ = 8.0 Hz, H-4), 4.15 (d, 1H, $J_{3,4}$ = 5.9 Hz, H-3), 4.13 (dd, 1H, $J_{5a,4}$ = 8.0 Hz, J_{gem} = 8.4 Hz, H-5a), 3.78 (dd, 1H, $J_{5b,4}$ = 8.0 Hz, J_{gem} = 8.4 Hz, H-5b), 3.60 (d, 1H, J_{gem} = 10.0 Hz, H-1a), 3.49 (d, 1H, J_{gem} = 10.0 Hz, H-1b), 1.25 (s, 9H, (CH_3)$_3$C); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.9 (Ar), 136.8 (Ar), 136.6 (Ar), 131.8 (Ar), 131.4 (Ar), 129.59 (Ar), 129.55 (Ar), 128.3 (2C, Ar), 127.8 (2C, Ar), 127.5 (Ar), 110.3 (C-2), 88.8 (C-3), 80.5 (C-4), 76.0 (CH_3)$_3$*C*), 73.4 (Ar*C*H$_2$), 72.0 (C-1), 69.6 (C-5), 69.2 (Ar*C*H$_2$), 69.0 (Ar*C*H$_2$), 30.7 (3C, (*C*H$_3$)$_3$C); HRMS (ESI) calcd. for $C_{24}H_{30}NaO_5$ $[M+Na]^+$ 421.1985; found 421.1984. Data for **3.89β**: $[\alpha]^{25}_D$ +25.2 (*c* 1.0, $CHCl_3$); R_f 0.16 (6:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.40–7.20 (m, 7H, ArH), 7.22–7.17 (m, 2H, ArH), 5.06 (d, 1H, J_{gem} = 12.9 Hz, ArCH_2), 4.83 (s, 2H, ArCH_2), 4.81 (d, 1H, J_{gem} = 12.9 Hz, ArCH_2), 4.59 (d, 1H, J_{gem} = 12.1 Hz, ArCH_2), 4.46 (d, 1H, J_{gem} = 12.1 Hz, ArCH_2), 4.39 (ddd, 1H, $J_{4,3}$ = 6.0 Hz, $J_{4,5a}$ = 7.6 Hz, $J_{4,5b}$ = 4.4 Hz, H-4), 4.22 (dd, 1H, $J_{5a,4}$ = 7.6 Hz, J_{gem} = 9.5 Hz,

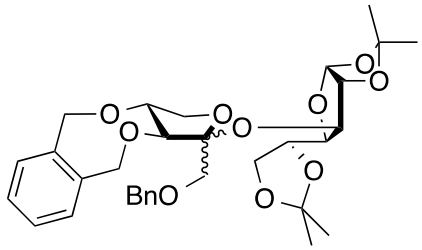
H-5a), 4.19 (d, 1H, $J_{3,4}$ = 6.0 Hz, H-3), 3.74 (dd, 1H, $J_{5b,4}$ = 4.4 Hz, J_{gem} = 9.5 Hz, H-5b), 3.71 (d, 1H, J_{gem} = 10.4 Hz, H-1a), 3.57 (d, 1H, J_{gem} = 10.4 Hz, H-1b), 1.29 (s, 9H, $(CH_3)_3C$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.2 (Ar), 136.8 (Ar), 136.7 (Ar), 131.7 (Ar), 131.0 (Ar), 129.2 (Ar), 129.1 (Ar), 128.3 (2C, Ar), 127.7 (2C, Ar), 127.5 (Ar), 107.6 (C-2), 83.4 (C-3), 80.7 (C-4), 75.6 $(CH_3)_3C$), 73.4 ($ArCH_2$), 70.4 (C-1), 70.0 (2C, C-5, $ArCH_2$), 69.0 ($ArCH_2$), 31.0 (3C, $(CH_3)_3C$); HRMS (ESI) calcd. for $C_{24}H_{30}NaO_5$ $[M+Na]^+$ 421.1985; found 421.1983.



1-*O*-benzyl-3,4-*O*-xylylidene-α-D-xylulofuranosyl-(2→6)-1,2,3,4-di-*O*-isopropylidene-α-D-galactopyranose (3.90α) and **1-*O*-benzyl-3,4-*O*-xylylidene-β-D-xylulofuranosyl-(2→6)-1,2,3,4-di-*O*-isopropylidene-α-D-galactopyranose (3.90β)**. A mixture of **3.70** (18.9 mg, 0.0421 mmol), **3.82** (10.4 mg, 0.0506 mmol), and 4Å molecular sieves in CH_2Cl_2 (1.7 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –78 °C and *N*-iodosuccinimide (11.4 mg, 0.0506 mmol) and silver triflate (1.1 mg, 4.21 μmol) were added. After stirring for 1 h at –78 °C, triethylamine was added. The reaction was warmed to room temperature and then a small amount of water was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The solution was then dried over $MgSO_4$, filtered and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatography (10:1, hexane–EtOAc) to give **3.90α** (7.6 mg, 31%) and **3.90β** (11.5 mg, 47%) both as colorless oils. Data for **3.90α**: $[\alpha]^{25}_D$ +15.4 (*c* 0.8, $CHCl_3$); R_f 0.47 (2:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.41–7.31 (m, 8H, ArH), 7.30–7.26 (m, 1H, ArH), 5.51 (d, 1H, $J_{1,2}$ = 4.9 Hz, H-1), 4.94 (d, 1H, J_{gem} = 12.6 Hz, $ArCH_2$), 4.90 (d, 1H, J_{gem} = 12.6 Hz, $ArCH_2$), 4.78

(d, 1H, J_{gem} = 12.6 Hz, ArCH_2), 4.77 (d, 1H, J_{gem} = 12.6 Hz, ArCH_2), 4.59 (d, 1H, J_{gem} = 12.2 Hz, ArCH_2), 4.56 (dd, 1H, $J_{3,2}$ = 2.4 Hz, $J_{3,4}$ = 7.9 Hz, H-3), 4.55 (d, 1H, J_{gem} = 12.2 Hz, ArCH_2), 4.28 (dd, 1H, $J_{2,1}$ = 4.9 Hz, $J_{2,3}$ = 2.4 Hz, H-2), 4.22 (dd, 1H, $J_{4,3}$ = 7.9 Hz, $J_{4,5}$ = 1.9 Hz, H-4), 4.17–4.13 (m, 2H, H-3', H-4'), 4.05–4.01 (m, 1H, H-5'a), 3.91 (app dt, 1H, $J_{5,4}$ = 1.9 Hz, $J_{5,6a}$ = $J_{5,6b}$ = 6.3 Hz, H-5), 3.80–3.73 (m, 2H, H-6a, H-5'b), 3.70 (dd, 1H, $J_{6b,5}$ = 6.3 Hz, J_{gem} = 10.3 Hz, H-6b), 3.63 (d, 1H, J_{gem} = 10.7 Hz, H-1'a), 3.58 (d, 1H, J_{gem} = 10.7 Hz, H-1'b), 1.52 (s, 3H, (CH_3)$_2$C), 1.42 (s, 3H, (CH_3)$_2$C), 1.33 (s, 3H, (CH_3)$_2$C), 1.32 (s, 3H, (CH_3)$_2$C); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.5 (Ar), 136.6 (Ar), 135.9 (Ar), 131.7 (Ar), 131.5 (Ar), 129.54 (Ar), 129.48 (Ar), 128.2 (2C, Ar), 127.7 (2C, Ar), 127.4 (Ar), 109.1 ((CH$_3$)$_2$*C*), 108.8 ((CH$_3$)$_2$*C*), 108.5 (C-2'), 96.3 (C-1), 87.1 (C-3'), 81.2 (C-4'), 73.6 (Ar*C*H$_2$), 71.0 (C-4), 70.7 (C-2), 70.6 (C-3), 69.6 (Ar*C*H$_2$), 69.2 (Ar*C*H$_2$), 69.1 (C-1'), 68.3 (C-5'), 67.3 (C-5), 60.9 (C-6), 26.1 ((*C*H$_3$)$_2$C), 26.0 ((*C*H$_3$)$_2$C), 25.0 ((*C*H$_3$)$_2$C), 24.4 ((*C*H$_3$)$_2$C); HRMS (ESI) calcd. for $C_{32}H_{40}NaO_{10}$ $[M+Na]^+$ 607.2514; found 607.2507. Data for **3.90β**: $[\alpha]^{25}_D$ –14.6 (*c* 0.4, $CHCl_3$); R_f 0.27 (2:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.44–7.35 (m, 4H, ArH), 7.33–7.25 (m, 3H, ArH), 7.24–7.21 (m, 2H, ArH), 5.39 (d, 1H, $J_{1,2}$ = 5.0 Hz, H-1), 5.01 (d, 1H, J_{gem} = 12.8 Hz, ArCH_2), 4.91 (d, 1H, J_{gem} = 12.8 Hz, ArCH_2), 4.83 (d, 1H, J_{gem} = 12.8 Hz, ArCH_2), 4.77 (d, 1H, J_{gem} = 12.8 Hz, ArCH_2), 4.58 (d, 1H, J_{gem} = 12.6 Hz, ArCH_2), 4.55 (dd, 1H, $J_{3,2}$ = 2.2 Hz, $J_{3,4}$ = 7.9 Hz, H-3), 4.51 (d, 1H, J_{gem} = 12.6 Hz, ArCH_2), 4.39–4.31 (m, 2H, H-4', H-5'a), 4.27 (dd, 1H, $J_{2,1}$ = 5.0 Hz, $J_{2,3}$ = 2.2 Hz, H-2), 4.22 (dd, 1H, $J_{4,3}$ = 7.9 Hz, $J_{4,5}$ = 1.9 Hz, H-4), 4.20 (d, 1H, $J_{3',4'}$ = 4.8 Hz, H-3'), 4.00 (ddd, 1H, $J_{5,4}$ = 1.9 Hz, $J_{5,6a}$ = 5.9 Hz, $J_{5,6b}$ = 8.7 Hz, H-5), 3.81 (app t, 1H, $J_{6a,5}$ = J_{gem} = 8.7 Hz, H-6a), 3.76 (dd, 1H, $J_{5b',4}$ = 3.1 Hz, J_{gem} = 8.6 Hz, H-5'b), 3.57 (s, 2H, H-1'a, H-1'b), 3.55 (dd, 1H, $J_{6b,5}$ = 5.9 Hz, J_{gem} = 8.7 Hz, H-6b), 1.53 (s, 3H, (CH_3)$_2$C), 1.42 (s, 3H, (CH_3)$_2$C), 1.32 (s, 3H, (CH_3)$_2$C), 1.28 (s, 3H, (CH_3)$_2$C); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.0

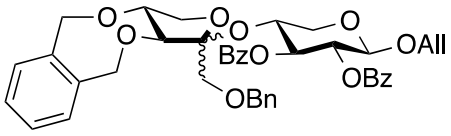
(Ar), 136.4 (Ar), 136.3 (Ar), 131.5 (Ar), 131.4 (Ar), 129.4 (2C, Ar), 128.3 (2C, Ar), 127.7 (2C, Ar), 127.6 (Ar), 108.8 ($(CH_3)_2C$), 108.4 ($(CH_3)_2C$), 106.3 (C-2'), 96.1 (C-1), 83.3 (C-3'), 80.7 (C-4'), 73.4 ($ArCH_2$), 70.8 (C-2), 70.7 (C-5'), 70.5 (C-4), 70.4 (C-3), 69.6 ($ArCH_2$), 68.7 ($ArCH_2$), 68.1 (C-1'), 66.2 (C-5), 59.8 (C-6), 26.1 ($(CH_3)_2C$), 26.0 ($(CH_3)_2C$), 24.9 ($(CH_3)_2C$), 24.4 ($(CH_3)_2C$); HRMS (ESI) calcd. for $C_{32}H_{40}NaO_{10}$ $[M+Na]^+$ 607.2514; found 607.2502.



1-*O*-benzyl-3,4-*O*-xylylidene-α-D-xylulofuranosyl-(2→3)-1,2,5,6-di-*O*-isopropylidene-α-D-glucopyranose (3.91α) and **1-*O*-benzyl-3,4-*O*-xylylidene-β-D- xylulofuranosyl-(2→3)-1,2,3,4-di-*O*-isopropylidene-α-D-glucopyranose (3.91β)**. A mixture of the **3.70** (25.1 mg, 0.0560 mmol), **3.83** (17.5 mg, 0.0671 mmol), and 4Å molecular sieves in CH_2Cl_2 (2.24 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –78 °C and *N*-iodosuccinimide (15.1 mg, 0.0671 mmol) and silver triflate (1.4 mg, 5.60 μmol) were added. After stirring for 1 h at –78 °C, triethylamine was added. The reaction was warmed to room temperature and then a small amount of water was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The solution was then dried over $MgSO_4$, filtered and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatography (8:1, hexane–EtOAc) to give **3.91α** (4.8 mg, 15%) and **3.91β** (21.1 mg, 65%) both as colorless oils. Data for **3.91α**: $[\alpha]^{25}_D$ +35.1 (*c* 0.5, $CHCl_3$); R_f 0.25 (4:1, hexane–EtOAc); ^1H NMR ($CDCl_3$, 500 MHz) δ_H 7.42–7.27 (m, 9H, ArH), 5.82 (d, 1H, $J_{1,2}$ = 3.7 Hz, H-1), 4.95 (d, 1H, J_{gem} = 12.8 Hz, $ArCH_2$), 4.88 (d, 1H, J_{gem} = 12.8 Hz, $ArCH_2$), 4.76 (d, 2H, J_{gem} = 12.8 Hz,

ArCH_2), 4.55 (d, 1H, J_{gem} = 11.7 Hz, ArCH_2), 4.52 (d, 1H, J_{gem} = 11.7 Hz, ArCH_2), 4.41 (d, 1H, $J_{2,1}$ = 3.7 Hz, H-2), 4.32–4.15 (m, 5H, H-3, H-4, H-5, H-4', H-5'a), 4.05 (d, 1H, $J_{3'4'}$ = 5.9 Hz, H-3'), 3.96–3.91 (m, 2H, H-6a, H-6b), 3.74 (dd, 1H, J= 8.0, 8.7 Hz, H-5'b), 3.65 (d, 1H, J_{gem} = 10.8 Hz, H-1'a), 3.54 (d, 1H, J_{gem} = 10.8 Hz, H-1'b), 1.45 (s, 3H, (CH_3)$_2$C), 1.35 (s, 3H, (CH_3)$_2$C), 1.25 (s, 6H, (CH_3)$_2$C); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.4 (Ar), 136.3 (Ar), 136.0 (Ar), 131.5 (2C, Ar), 129.69 (Ar), 129.66 (Ar), 128.3 (2C, Ar), 127.63 (2C, Ar), 127.55 (Ar), 111.7 ((CH$_3$)$_2$*C*), 110.0 (C-2'), 108.5 ((CH$_3$)$_2$*C*), 105.1 (C-1), 86.6 (C-3'), 84.3 (C-2), 81.0 (C-4'), 80.5 (C-4), 75.9 (C-3), 73.7 (Ar*C*H$_2$), 73.1 (C-5), 69.7 (2C, C-1', C-5'), 69.5 (Ar*C*H$_2$), 68.9 (Ar*C*H$_2$), 66.2 (C-6), 26.9 ((*C*H$_3$)$_2$C), 26.6 ((*C*H$_3$)$_2$C), 26.4 ((*C*H$_3$)$_2$C), 25.3 ((*C*H$_3$)$_2$C); HRMS (ESI) calcd. for $C_{32}H_{40}NaO_{10}$ $[M+Na]^+$ 607.2514; found 607.2514. Data for **3.91β**: $[\alpha]^{25}_D$ +1.9 (*c* 1.0, $CHCl_3$); R_f 0.17 (4:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.43–7.26 (m, 7H, ArH), 7.24–7.21 (m, 2H, ArH), 5.87 (d, 1H, $J_{1,2}$ = 3.8 Hz, H-1), 4.99 (d, 1H, J_{gem} = 12.6 Hz, ArCH_2), 4.87 (d, 1H, J_{gem} = 12.6 Hz, ArCH_2), 4.81 (d, 1H, J_{gem} = 12.6 Hz, ArCH_2), 4.77 (d, 1H, J_{gem} = 12.6 Hz, ArCH_2), 4.57 (d, 1H, J_{gem} = 12.3 Hz, ArCH_2), 4.53 (d, 1H, J_{gem} = 12.3 Hz, ArCH_2), 4.51 (d, 1H, $J_{2,1}$ = 3.8 Hz, H-2), 4.44 (dd, 1H, $J_{5'a,4'}$ = 7.9 Hz, J_{gem} = 9.0 Hz, H-5'a), 4.41–4.35 (m, 1H, H-4'), 4.33 (d, 1H, $J_{3,4}$ = 3.5 Hz, H-3), 4.31–4.25 (m, 1H, H-5), 4.16 (d, 1H, $J_{3',4'}$ = 5.5 Hz, H-3'), 4.15 (dd, 1H, $J_{4,3}$ = 3.5 Hz, $J_{4,5}$ = 7.4 Hz, H-4), 4.04 (dd, 1H, $J_{6a,5}$ = 6.2 Hz, J_{gem} = 8.5 Hz, H-6a), 3.96 (dd, 1H, $J_{6b,5}$ = 6.6 Hz, J_{gem} = 8.5 Hz, H-6b), 3.72 (dd, 1H, $J_{5'b,4'}$ = 4.8 Hz, J_{gem} = 9.0 Hz, H-5'b), 3.57 (d, 1H, J_{gem} = 10.6 Hz, H-1'a), 3.46 (d, 1H, J_{gem} = 10.6 Hz, H-1'b), 1.47 (s, 3H, (CH_3)$_2$C), 1.39 (s, 3H, (CH_3)$_2$C), 1.26 (s, 3H, (CH_3)$_2$C), 1.24 (s, 3H, (CH_3)$_2$C); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 137.8 (Ar), 136.5 (Ar), 136.2 (Ar), 131.5 (Ar), 131.4 (Ar), 129.59 (Ar), 129.55 (Ar), 128.4 (2C, Ar), 127.8 (Ar), 127.70 (2C, Ar), 111.4 ((CH$_3$)$_2$*C*), 108.9 ((CH$_3$)$_2$*C*), 107.2 (C-2'), 105.0 (C-1), 84.9 (C-2), 83.9 (C-3'), 81.2 (C-4), 80.7 (C-4'), 74.6 (C-3),

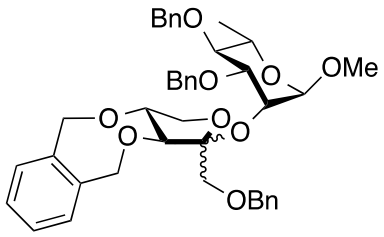
73.5 (Ar*C*H_2), 72.4 (C-5), 70.7 (C-5') 70.4 (C-1'), 69.4 (Ar*C*H_2), 69.1 (Ar*C*H_2), 67.3 (C-6), 26.9 ((*C*H_3)$_2$C), 26.7 ((*C*H_3)$_2$C), 26.4 ((*C*H_3)$_2$C), 25.5 ((*C*H_3)$_2$C); HRMS (ESI) calcd. for $C_{32}H_{40}NaO_{10}$ $[M+Na]^+$ 607.2514; found 607.2518.



Allyl 1-*O*-benzyl-3,4-*O*-xylylidene-α-D-xylulofuranosyl-(2→4)-2,3-di-*O*-benzoyl-β-D-xylopyranoside (3.92α) and **Allyl 1-*O*-benzyl-3,4-*O*-xylylidene-β-D-xylulofuranosyl-(2→4)-2,3-di-*O*-benzoyl-β-D-xylopyranoside (3.92β)**. A mixture of **3.70** (24.0 mg, 0.0535 mmol), **3.84** (17.8 mg, 0.0446 mmol), and 4Å molecular sieves in CH_2Cl_2 (1.8 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –78 ºC and *N*-iodosuccinimide (14.4 mg, 0.0642 mmol) and silver triflate (1.4 mg, 5.35 μmol) were added. After stirring for 1 h at –78 ºC, triethylamine was added. The reaction was warmed to room temperature and then a small amount of water was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The solution was then dried over $MgSO_4$, filtered and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatography (8:1, Hexane–EtOAc) to give **3.92α** (5.0 mg, 15%) as a colorless oil and **3.92β** (23.2 mg, 72%) as a colorless oil. Data for **3.92α**: $[\alpha]^{25}_D$ +73.1 (*c* 0.5, $CHCl_3$); R_f 0.63 (2:1, Hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 700 MHz) δ_H 7.97–7.95 (m, 2H, ArH), 7.94–7.92 (m, 2H, ArH), 7.52–7.48 (m, 2H, ArH), 7.39–7.33 (m, 6H, ArH), 7.32–7.30 (m, 1H, ArH), 7.28–7.26 (m, 1H, ArH), 7.25–7.21 (m, 3H, ArH), 7.16–7.13 (m, 2H, ArH), 5.83 (m, 1H, OCH_2CH=CH_2), 5.48 (app t, 1H, $J_{3,2} = J_{3,4}$ = 8.1 Hz, H-3), 5.26 (dd, 1H, $J_{2,1}$ = 6.5 Hz, $J_{2,3}$ = 8.1 Hz, H-2), 5.23 (dq, 1H, J = 17.1, 1.6 Hz, OCH_2CH=CH_2), 5.12 (dq, 1H, J = 10.5, 1.6 Hz, OCH_2CH=CH_2), 4.85 (d, 1H,

J_{gem} = 12.7 Hz, ArCH_2), 4.78 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.70 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.68 (d, 1H, $J_{1,2}$ = 6.5 Hz, H-1), 4.64 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.33 (s, 2H, ArCH_2), 4.29 (ddt, 1H, J = 13.0, 5.0, 1.4 Hz, OCH_2CH=CH$_2$), 4.24 (app dt, 1H, $J_{4,5a}$ = 4.9 Hz, $J_{4,3}$ = $J_{4,5b}$ = 8.1 Hz, H-4), 4.15–4.10 (m, 2H, H-5a, H-4'), 4.08 (ddt, 1H, J = 13.0, 6.1, 1.4 Hz, OCH_2CH=CH$_2$), 4.05 (app t, 1H, $J_{5'a,4'}$ = J_{gem} = 8.0 Hz, H-5'a), 4.02 (d, 1H, $J_{3',4'}$ = 5.7 Hz, H-3'), 3.70 (app t, 1H, $J_{5'b,4'}$ = J_{gem} = 8.0 Hz, H-5'b), 3.50 (d, 1H, J_{gem} = 10.5 Hz, H-1'a), 3.44 (d, 1H, J_{gem} = 10.5 Hz, H-1'b), 3.50 (dd, 1H, $J_{5b,4}$ = 8.1 Hz, J_{gem} = 11.8 Hz, H-5b); ^{13}C NMR ($CDCl_3$, 175 MHz) δ_C 165.7 (C=O), 165.5 (C=O), 138.3 (Ar), 136.5 (Ar), 135.9 (Ar), 133.7 (OCH$_2$*C*H=CH$_2$), 132.99 (Ar), 132.98 (Ar), 131.6 (Ar), 131.5 (Ar), 129.90 (Ar), 129.87 (Ar), 129.8 (Ar), 129.7 (Ar), 129.6 (Ar), 129.5 (Ar), 128.3 (Ar), 128.2 (Ar), 127.6 (Ar), 127.4 (Ar), 117.5 (OCH$_2$CH=*C*H$_2$), 109.6 (C-2'), 99.5 (C-1), 88.2 (C-3'), 80.8 (C-4'), 73.4 (Ar*C*H$_2$), 72.4 (C-3), 71.3 (C-2), 69.6 (C-1'), 69.58 (O*C*H$_2$CH=CH$_2$), 69.44 (Ar*C*H$_2$), 69.35 (Ar*C*H$_2$), 68.92 (C-5'), 68.86 (C-4), 64.6 (C-5); HRMS (ESI) calcd. for $C_{42}H_{42}NaO_{11}$ $[M+Na]^+$ 745.2619; found 745.2623. Data for **3.92β**: $[\alpha]^{25}_D$ +25.6 (*c* 2.3, $CHCl_3$); R_f 0.53 (2:1, Hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 700 MHz) δ_H 7.94 (d, 2H, J = 8.1 Hz, ArH), 7.87 (d, 2H, J = 8.1 Hz, ArH), 7.50–7.45 (m, 2H, ArH), 7.39–7.32 (m, 6H, ArH), 7.31–7.27 (m, 4H, ArH), 7.22–7.20 (m, 1H, ArH), 7.20–7.17 (m, 2H, ArH), 5.82–5.76 (m, 1H, OCH$_2$C*H*=CH$_2$), 5.61 (app t, 1H, $J_{3,2}$ = $J_{3,4}$ = 8.8 Hz, H-3), 5.31 (dd, 1H, $J_{2,1}$ = 7.4 Hz, $J_{2,3}$ = 8.8 Hz, H-2), 5.22 (dq, 1H, J = 17.1, 1.6 Hz, OCH$_2$CH=CH_2), 5.12 (dq, 1H, J = 10.4, 1.6 Hz, OCH$_2$CH=CH_2), 4.84 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.67 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.66 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.65 (d, 1H, $J_{1,2}$ = 7.4 Hz, H-1), 4.53 (d, 1H, J_{gem} = 12.4 Hz, ArCH_2), 4.51 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.47 (d, 1H, J_{gem} = 12.4 Hz, ArCH_2), 4.29 (ddt, 1H, J = 13.6, 5.1, 1.6 Hz, OCH_2CH=CH$_2$), 4.24 (app dt, 1H, $J_{4,3}$ = 8.8 Hz, $J_{4,5a}$ = $J_{4,5b}$ = 5.1 Hz, H-4), 4.10–4.04 (m, 3H, H-5a, H-3', OCH_2CH=CH$_2$), 4.03–3.97 (m,

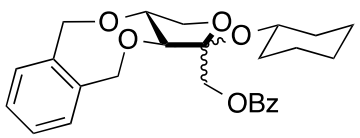
2H, H-5'a, H-4'), 3.54–3.47 (m, 3H, H-5b, H-1'a, H-5'b), 3.38 (d, 1H, J_{gem} = 10.7 Hz, H-1'b); ^{13}C NMR ($CDCl_3$, 175 MHz) δ_C 165.6 (C=O), 165.4 (C=O), 137.7 (Ar), 136.5 (Ar), 136.0 (Ar), 133.6 ($OCH_2CH{=}CH_2$), 133.13 (Ar), 133.06 (Ar), 131.4 (Ar), 131.3 (Ar), 129.8 (Ar), 129.67 (Ar), 129.64 (Ar), 129.55 (Ar), 129.4 (Ar), 129.3 (Ar), 128.44 (Ar), 128.43 (Ar), 128.3 (Ar), 127.7 (Ar), 127.66 (Ar), 117.5 ($OCH_2CH{=}CH_2$), 106.8 (C-2'), 100.0 (C-1), 83.0 (C-3'), 80.2 (C-4'), 73.4 ($ArCH_2$), 73.0 (C-3), 71.8 (C-2), 70.4 (C-5'), 70.1 (C-1'), 69.8 ($OCH_2CH{=}CH_2$), 69.3 ($ArCH_2$), 69.0 ($ArCH_2$), 67.8 (C-4), 65.3 (C-5); HRMS (ESI) calcd. for $C_{42}H_{42}NaO_{11}$ $[M+Na]^+$ 745.2626; found 745.2619.



Methyl 1-*O*-benzyl-3,4-*O*-xylylidene-α-D-xylulofuranosyl-(2→2)-3,4-di-*O*-benzyl-α-L-rhamnopyranoside (3.93α) and **Methyl 1-*O*-benzyl-3,4-*O*-xylylidene-β-D-xylulofuranosyl-(2→2)-3,4-di-*O*-benzyl-α-L-rhamnopyranoside (3.93β)**. A mixture of **3.70** (21.8 mg, 0.0485 mmol), **3.85** (14.5 mg, 0.0404 mmol), and 4Å molecular sieves in CH_2Cl_2 (1.35 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –78 °C and *N*-iodosuccinimide (13.1 mg, 0.0582 mmol) and silver triflate (1.2 mg, 4.85 μmol) were added. After stirring for 2 h at –78 °C, triethylamine was added. The reaction was warmed to room temperature and then a small amount of water was added, followed by solid $Na_2S_2O_3{\cdot}5H_2O$ until the solution was colorless. The solution was then dried over $MgSO_4$, filtered and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatography (8:1, hexane–EtOAc) to give **3.93α** (8.2 mg, 30%) and **3.93β** (16.5 mg, 60%) both as

colorless oils. Data for **3.93α**: $[\alpha]^{25}_{D}$ +36.4 (*c* 0.1, $CHCl_3$); R_f 0.27 (4:1, hexane–EtOAc); ^1H NMR ($CDCl_3$, 500 MHz) δ_H 7.39–7.18 (m, 19H, ArH), 4.95 (d, 1H, J_{gem} = 11.2 Hz, ArCH_2), 4.89 (d, 1H, J_{gem} = 12.3 Hz, ArCH_2), 4.79 (d, 1H, J_{gem} = 13.0 Hz, ArCH_2), 4.71 (d, 1H, J_{gem} = 12.3 Hz, ArCH_2), 4.69 (d, 1H, $J_{1,2}$ = 1.7 Hz, H-1), 4.68 (d, 1H, J_{gem} = 12.1 Hz, ArCH_2), 4.64 (d, 1H, J_{gem} = 13.0 Hz, ArCH_2), 4.63 (d, 1H, J_{gem} = 11.2 Hz, ArCH_2), 4.55 (d, 1H, J_{gem} = 11.9 Hz, ArCH_2), 4.53 (d, 1H, J_{gem} = 11.9 Hz, ArCH_2), 4.52 (d, 1H, J_{gem} = 12.1 Hz, ArCH_2), 4.32 (dd, 1H, $J_{2,1}$ = 1.7 Hz, $J_{2,3}$ = 3.2 Hz, H-2), 4.21 (d, 1H, $J_{3'4'}$ = 5.5 Hz, H-3'), 4.09–4.04 (m, 1H, H-4'), 4.00 (app t, 1H, $J_{5'a,4'}$ = J_{gem} = 8.5 Hz, H-5'a), 3.88 (app t, 1H, $J_{5'b,4'}$ = J_{gem} = 8.5 Hz, H-5'b), 3.76 (dd, 1H, $J_{3,2}$ = 3.2 Hz, $J_{3,4}$ = 9.6 Hz, H-3), 3.67 (d, 1H, J_{gem} = 10.8 Hz, H-1'a), 3.64–3.58 (m, 1H, H-5), 3.56 (d, 1H, J_{gem} = 10.8 Hz, H-1'b), 3.48 (app t, 1H, $J_{4,3}$ = $J_{4,5}$ = 9.6 Hz, H-4), 3.22 (s, 3H, OCH_3), 1.28 (d, 3H, $J_{6,5}$ = 6.3 Hz, H-6); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.8 (Ar), 138.4 (Ar), 137.1 (Ar), 135.7 (Ar), 131.6 (Ar), 131.5 (Ar), 129.5 (Ar), 129.4 (Ar), 128.33 (Ar), 128.26 (Ar), 128.1 (Ar), 127.8 (Ar), 127.7 (Ar), 127.5 (Ar), 127.3 (Ar), 109.3 (C-2'), 101.0 (C-1, $J_{C1,H1}$ = 171.8 Hz), 88.1 (C-3'), 80.3 (C-4'), 79.8 (C-4), 79.1 (C-3), 75.1 (Ar*C*H_2), 73.9 (Ar*C*H_2), 71.8 (Ar*C*H_2), 71.3 (C-1'), 69.44 (C-2), 69.35 (Ar*C*H_2), 69.2 (Ar*C*H_2), 68.9 (C-5'), 67.9 (C-5), 54.7 (O*C*H_3), 18.1 (C-6); HRMS (ESI) calcd. for $C_{41}H_{46}NaO_9$ $[M+Na]^+$ 705.3034; found 705.3021. Data for **3.93β**: $[\alpha]^{25}_{D}$ +12.2 (*c* 0.3, $CHCl_3$); R_f 0.14 (4:1, hexane–EtOAc); ^1H NMR ($CDCl_3$, 500 MHz) δ_H 7.40–7.24 (m, 17H, ArH), 7.15–7.11 (m, 2H, ArH), 5.04 (d, 1H, J_{gem} = 13.3 Hz, ArCH_2), 4.89 (d, 1H, J_{gem} = 13.0 Hz, ArCH_2), 4.87 (d, 1H, J_{gem} = 11.2 Hz, ArCH_2), 4.82 (d, 1H, J_{gem} = 13.0 Hz, ArCH_2), 4.80 (d, 1H, J_{gem} = 13.3 Hz, ArCH_2), 4.64–4.58 (m, 3H, H-1, ArCH_2), 4.58 (d, 1H, J_{gem} = 11.2 Hz, ArCH_2), 4.47 (d, 1H, J_{gem} = 12.1 Hz, ArCH_2), 4.46–4.43 (m, 1H, H-4'), 4.31 (d, 1H, J_{gem} = 12.1 Hz, ArCH_2), 4.27 (d, 1H, $J_{3'4'}$ = 6.5 Hz, H-3'), 4.22 (dd, 1H, $J_{5'a,4'}$ = 8.1 Hz, J_{gem} = 9.4 Hz, H-5'a), 4.09 (dd, 1H, $J_{2,1}$ = 1.7 Hz, $J_{2,3}$ = 3.0 Hz, H-2), 3.79 (dd, 1H, $J_{5'b,4}$

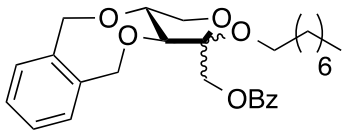
= 5.6 Hz, J_{gem} = 9.4 Hz, H-5'b), 3.76 (dd, 1H, $J_{3,2}$ = 3.0 Hz, $J_{3,4}$ = 9.1 Hz, H-3), 3.65–3.58 (m, 1H, H-5), 3.55 (s, 2H, H-1'a, H-1'b), 3.49 (app t, 1H, $J_{4,3}$ = $J_{4,5}$ = 9.1 Hz, H-4), 3.27 (s, 3H, OCH_3), 1.26 (d, 3H, $J_{6,5}$ = 6.1 Hz, H-6); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.8 (Ar), 138.7 (Ar), 138.2 (Ar), 136.8 (Ar), 136.6 (Ar), 131.6 (Ar), 131.1 (Ar), 129.3 (Ar), 129.2 (Ar), 128.34 (Ar), 128.32 (Ar), 128.0 (Ar), 127.9 (Ar), 127.59 (Ar), 127.57 (Ar), 127.51 (Ar), 127.48 (Ar), 107.2 (C-2'), 100.3 (C-1, $J_{C1,H1}$ = 172.1 Hz), 82.2 (C-3'), 80.4 (C-4), 79.8 (C-4'), 78.9 (C-3), 74.9 (ArCH$_2$), 73.3 (ArCH$_2$), 72.4 (ArCH$_2$), 70.5 (C-5'), 69.6 (C-2), 69.5 (ArCH$_2$), 69.2 (ArCH$_2$), 69.0 (C-1'), 67.9 (C-5), 54.7 (OCH$_3$), 18.1 (C-6); HRMS (ESI) calcd. for $C_{41}H_{46}NaO_9$ $[M+Na]^+$ 705.3034; found 705.3026.



Cyclohexyl 1-*O*-benzoyl-3,4-*O*-xylylidene-α-D-xylulofuranoside (**3.94α**) and **Cyclohexyl 1-*O*-benzoyl-3,4-*O*-xylylidene-β-D-xylulofuranoside** (**3.94β**). A mixture of **3.71** (48 mg, 0.104 mmol), **3.78** (12.5 mg, 13.0 μL, 0.125 mmol), and 4Å molecular sieves in CH_2Cl_2 (4.2 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –78 °C and *N*-iodosuccinimide (28.0 mg, 0.125 mmol) and silver triflate (2.7 mg, 10.4 μmol) were added. After stirring for 4 h at –78 °C, triethylamine was added. The reaction was warmed to room temperature and then a small amount of water was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The solution was then dried over $MgSO_4$, filtered and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatography (9:1, hexane–EtOAc) to give **3.94α** (13.7 mg, 29%) as a colorless oil and **3.94β** (27.3 mg, 58%) as a colorless oil. Data for **3.94α**: $[\alpha]^{25}_D$ +17.8 (*c* 0.4, $CHCl_3$); R_f 0.29

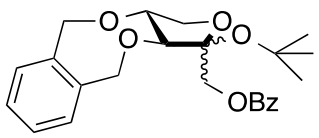
(9:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.97–7.94 (m, 2H, Ar), 7.57–7.52 (m, 1H, Ar), 7.42–7.30 (m, 5H, Ar), 7.25–7.23 (m, 1H, Ar), 4.94 (d, 1H, J_{gem} = 12.4 Hz, ArCH_2), 4.84 (d, 1H, J_{gem} = 12.4 Hz, ArCH_2), 4.76 (d, 1H, J_{gem} = 12.4 Hz, ArCH_2), 4.73 (d, 1H, J_{gem} = 12.4 Hz, ArCH_2), 4.45 (d, 1H, J_{gem} = 11.8 Hz, H-1a), 4.41 (d, 1H, J_{gem} = 11.8 Hz, H-1b), 4.17 (ddd, 1H, $J_{4,3}$ = 5.5 Hz, $J_{4,5a}$ = 7.7 Hz, $J_{4,5b}$ = 8.8 Hz, H-4), 4.10 (d, 1H, $J_{3,4}$ = 5.5 Hz, H-3), 4.06 (dd, 1H, $J_{5a,4}$ = 7.7 Hz, J_{gem} = 8.8 Hz, H-5a), 3.80 (app t, 1H, $J_{5b,4}$ = J_{gem} = 8.8 Hz, H-5b), 3.76–3.69 (m, 1H, cyclohexyl OC*H*), 1.80–1.64 (m, 4H, cyclohexyl CH_2), 1.52–1.46 (m, 1H, cyclohexyl CH_2), 1.36–1.19 (m, 1H, cyclohexyl CH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 166.1 (C=O), 136.7 (Ar), 136.0 (Ar), 133.0 (Ar), 131.8 (Ar), 131.6 (Ar), 130.6 (Ar), 129.83 (2C, Ar), 129.77 (Ar), 129.67 (Ar), 128.5 (2C, Ar), 108.6 (C-2), 88.3 (C-3), 81.1 (C-4), 71.2 (cyclohexyl O*C*H), 69.7 (Ar*C*H$_2$), 68.9 (Ar*C*H$_2$), 68.5 (C-5), 62.8 (C-1), 35.0 (cyclohexyl *C*H$_2$), 34.4 (cyclohexyl *C*H$_2$), 25.5 (cyclohexyl *C*H$_2$), 24.65 (cyclohexyl *C*H$_2$), 24.63 (cyclohexyl *C*H$_2$); HRMS (ESI) calcd. for $C_{26}H_{30}NaO_6$ $[M+Na]^+$ 461.1935; found 461.1940. Data for **3.94β**: $[\alpha]^{25}_D$ +12.9 (*c* 0.9, $CHCl_3$); R_f 0.19 (9:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.89–7.84 (m, 2H, Ar), 7.58–7.53 (m, 1H, Ar), 7.43–7.37 (m, 2H, Ar), 7.37–7.30 (m, 3H, Ar), 7.28–7.25 (m, 1H, Ar), 5.06 (d, 1H, J_{gem} = 12.9 Hz, ArCH_2), 4.85–4.77 (m, 3H, ArCH_2), 4.61 (d, 1H, J_{gem} = 11.8 Hz, H-1a), 4.47 (ddd, 1H, $J_{4,3}$ = 5.1 Hz, $J_{4,5a}$ = 7.7 Hz, $J_{4,5b}$ = 3.8 Hz, H-4), 4.26 (dd, 1H, $J_{5a,4}$ = 7.7 Hz, J_{gem} = 9.8 Hz, H-5a), 4.21 (d, 1H, J_{gem} = 11.8 Hz, H-1b), 4.11 (d, 1H, $J_{3,4}$ = 5.1 Hz, H-3), 3.81–3.76 (m, 1H, cyclohexyl OC*H*), 3.76 (dd, 1H, $J_{5b,4}$ = 3.8 Hz, J_{gem} = 9.8 Hz, H-5b), 1.86–1.70 (m, 4H, cyclohexyl CH_2), 1.59–1.36 (m, 4H, cyclohexyl CH_2), 1.30–1.20 (m, 2H, cyclohexyl CH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 165.9 (C=O), 137.0 (Ar), 135.7 (Ar), 133.2 (Ar), 131.7 (Ar), 131.6 (Ar), 130.0 (Ar), 129.9 (2C, Ar), 129.57 (Ar), 129.55 (Ar), 128.5 (2C, Ar) 105.4 (C-2), 83.5 (C-3), 81.3 (C-4), 71.0 (2C, cyclohexyl O*C*H, C-5), 69.7 (Ar*C*H$_2$), 69.1 (Ar*C*H$_2$), 62.8 (C-1), 34.6 (cy-

clohexyl CH_2), 34.5 (cyclohexyl CH_2), 25.4 (cyclohexyl CH_2), 25.1 (cyclohexyl CH_2), 25.0 (cyclohexyl CH_2); HRMS (ESI) calcd. for $C_{26}H_{30}NaO_6$ $[M+Na]^+$ 461.1935; found 461.1930.



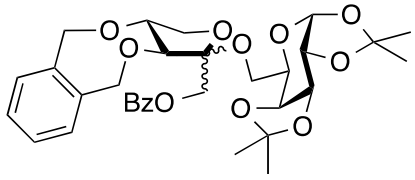
Octyl 1-*O*-benzoyl-3,4-*O*-xylylidene-α-D-xylulofuranoside (**3.95α**) and **Octyl 1-*O*-benzoyl-3,4-*O*-xylylidene-β-D-xylulofuranoside** (**3.95β**). A mixture of the **3.71** (19.9 mg, 0.0430 mmol), **3.80** (6.7 mg, 0.0516 mmol), and 4Å molecular sieves in CH_2Cl_2 (1.72 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –78 °C and *N*-iodosuccinimide (11.6 mg, 0.0516 mmol) and silver triflate (1.1 mg, 4.30 μmol) were added. After stirring for 1 h at –78 °C, triethylamine was added. The reaction was warmed to room temperature and then a small amount of water was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The solution was then dried over $MgSO_4$, filtered and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatography (15:1, hexane–EtOAc) to give **3.95α** (4.5 mg, 23%) and **3.95β** (13.3 mg, 68%) both as colorless oils. Data for **3.95α**: $[\alpha]^{25}_D$ +62.9 (*c* 0.5, $CHCl_3$); R_f 0.14 (15:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.99–7.95 (m, 2H, ArH), 7.58–7.52 (m, 1H, ArH), 7.44–7.32 (m, 5H, ArH), 7.29–7.26 (m, 1H, ArH), 4.95 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.87 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.77 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.74 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.47 (d, 1H, J_{gem} = 11.7 Hz, H-1a), 4.40 (d, 1H, J_{gem} = 11.7 Hz, H-1b), 4.18 (ddd, 1H, $J_{4,3}$ = 5.3 Hz, $J_{4,5a}$ = 7.8 Hz, $J_{4,5b}$ = 8.8 Hz, H-4), 4.11 (d, 1H, $J_{3,4}$ = 5.3 Hz, H-3), 4.07 (dd, 1H, $J_{5a,4}$ = 7.8 Hz, J_{gem} = 8.8 Hz, H-5a), 3.74 (app t, 1H, $J_{5b,4}$ = J_{gem} = 8.8 Hz, H-5b), 3.55 (app dt, 1H, J = 6.8, 9.2 Hz, octyl OCH_2), 3.48 (app dt, 1H, J = 6.8, 9.2 Hz, octyl OCH_2), 1.56–1.47 (m, 2H, octyl CH_2), 1.33–1.18 (m, 10H, octyl CH_2), 0.86 (t, 3H, J = 7.2 Hz, octyl CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 166.1

(C=O), 136.5 (Ar), 135.9 (Ar), 132.9 (Ar), 131.7 (Ar), 131.5 (Ar), 130.4 (Ar), 129.72 (2C, Ar), 129.68 (Ar), 129.58 (Ar), 128.4 (2C, Ar), 107.9 (C-2), 87.6 (C-3), 81.1 (C-4), 69.8 (ArCH_2), 68.9 (ArCH_2), 68.3 (C-5), 62.1 (C-1), 61.8 (octyl OCH_2), 31.9 (octyl CH$_2$), 30.1 (octyl CH$_2$), 29.4 (octyl CH$_2$), 29.3 (octyl CH$_2$), 26.2 (octyl CH$_2$), 22.7 (octyl CH$_2$), 14.1 (octyl CH$_3$); HRMS (ESI) calcd. for $C_{28}H_{36}NaO_6$ $[M+Na]^+$ 491.2404; found 491.2412. Data for **3.95β**: $[\alpha]^{25}_D$ +21.4 (*c* 1.3, $CHCl_3$); R_f 0.09 (15:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.92–7.87 (m, 2H, ArH), 7.58–7.53 (m, 1H, ArH), 7.44–7.29 (m, 6H, ArH), 5.03 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.88 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.82 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.78 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.59 (d, 1H, J_{gem} = 11.8 Hz, H-1a), 4.39 (ddd, 1H, $J_{4,3}$ = 4.9 Hz, $J_{4,5a}$ = 7.5 Hz, $J_{4,5b}$ = 3.7 Hz, H-4), 4.30 (d, 1H, J_{gem} = 11.8 Hz, H-1b), 4.18 (dd, 1H, $J_{5a,4}$ = 7.5 Hz, J_{gem} = 9.9 Hz, H-5a), 4.14 (d, 1H, $J_{3,4}$ = 4.9 Hz, H-3), 3.78 (dd, 1H, $J_{5b,4}$ = 3.7 Hz, J_{gem} = 9.9 Hz, H-5b), 3.62 (app dt, 1H, J = 7.5, 9.2 Hz, octyl OCH_2), 3.54 (app dt, 1H, J = 6.6, 9.2 Hz, octyl OCH_2), 1.65–1.54 (m, 2H, octyl CH_2), 1.35–1.18 (m, 10H, octyl CH_2), 0.87 (t, 3H, J = 7.2 Hz, octyl CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 165.9 (C=O), 136.6 (Ar), 135.8 (Ar), 133.1 (Ar), 131.6 (Ar), 131.4 (Ar), 129.9 (Ar), 129.8 (2C, Ar), 129.5 (2C, Ar), 128.4 (2C, Ar), 105.1 (C-2), 83.7 (C-3), 81.0 (C-4), 71.0 (C-5), 69.7 (ArCH$_2$), 68.9 (ArCH$_2$), 62.4 (C-1), 62.0 (octyl OCH$_2$), 31.9 (octyl CH$_2$), 30.1 (octyl CH$_2$), 29.4 (octyl CH$_2$), 29.3 (octyl CH$_2$), 26.1 (octyl CH$_2$), 22.7 (octyl CH$_2$), 14.1 (octyl CH$_3$); HRMS (ESI) calcd. for $C_{28}H_{38}NaO_5$ $[M+Na]^+$ 491.2404; found 491.2411.



***tert*-Butyl 1-*O*-benzoyl-3,4-*O*-xylylidene-α-D-xylulofuranoside (3.96α)** and ***tert*-Butyl 1-*O*-benzoyl-3,4-*O*-xylylidene-β-D-xylulofuranoside (3.96β).** A mixture of **3.70** (23.2 mg, 0.0502 mmol), **3.81** (4.5 mg, 0.0602 mmol), and 4Å molecular sieves in CH_2Cl_2 (2.01 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –78 °C and *N*-iodosuccinimide (13.5 mg, 0.0602 mmol) and silver triflate (1.3 mg, 5.02 μmol) were added and slowly warmed to –60 °C. After stirring for 6 h at –60 °C, triethylamine was added. The reaction was warmed to room temperature and then a small amount of water was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The solution was then dried over $MgSO_4$, filtered and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatography (10:1, hexane–EtOAc) to give **3.96α** (6.6 mg, 32%) and **3.96β** (11.9 mg, 58%) both as colorless oils. Data for **3.96α**: $[\alpha]^{25}_D$ +36.8 (*c* 0.7, $CHCl_3$); R_f 0.51 (4:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.90–7.86 (m, 2H, ArH), 7.56–7.50 (m, 1H, ArH), 7.40–7.34 (m, 3H, ArH), 7.33–7.29 (m, 2H, ArH), 7.27–7.24 (m, 1H, ArH), 4.97 (d, 1H, J_{gem} = 12.8 Hz, ArCH_2), 4.83 (d, 1H, J_{gem} = 12.8 Hz, ArCH_2), 4.75 (d, 1H, J_{gem} = 12.8 Hz, ArCH_2), 4.74 (d, 1H, J_{gem} = 12.8 Hz, ArCH_2), 4.49 (d, 1H, J_{gem} = 11.2 Hz, H-1a), 4.37 (d, 1H, J_{gem} = 11.2 Hz, H-1b), 4.21–4.13 (m, 2H, H-3, H-4), 4.07 (dd, 1H, $J_{5a,4}$ = 7.6 Hz, J_{gem} = 8.2 Hz, H-5a), 3.83 (app t, 1H, $J_{5b,4}$ = J_{gem} = 8.2 Hz, H-5b), 1.32 (s, 9H, (CH_3)$_3$C); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 166.0 (C=O), 136.8 (Ar), 135.8 (Ar), 132.7 (Ar), 131.6 (Ar), 131.3 (Ar), 130.5 (Ar), 129.6 (2C, Ar), 129.5 (Ar), 129.4 (Ar), 128.3 (2C, Ar), 109.5 (C-2), 90.4 (C-3), 80.0 (C-4), 76.4 ((CH$_3$)$_3$*C*), 69.4 (Ar*C*H$_2$), 69.1 (Ar*C*H$_2$), 68.7 (C-5), 64.8 (C-1), 30.9 (3C, (*C*H$_3$)$_3$C); HRMS

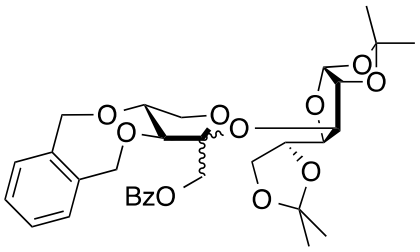
(ESI) calcd. for $C_{24}H_{28}NaO_6$ $[M+Na]^+$ 435.1778; found 435.1782. Data for **3.96β**: $[\alpha]^{25}_D$ +20.2 (*c* 1.2, $CHCl_3$); R_f 0.29 (4:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.86–7.81 (m, 2H, ArH), 7.57–7.52 (m, 1H, ArH), 7.41–7.28 (m, 5H, ArH), 7.26–7.23 (m, 1H, ArH), 5.08 (d, 1H, J_{gem} = 12.9 Hz, ArCH_2), 4.84 (d, 1H, J_{gem} = 12.9 Hz, ArCH_2), 4.81 (d, 1H, J_{gem} = 12.9 Hz, ArCH_2), 4.80 (d, 1H, J_{gem} = 12.9 Hz, ArCH_2), 4.79 (d, 1H, J_{gem} = 11.6 Hz, H-1a), 4.42 (ddd, 1H, $J_{4,3}$ = 5.8 Hz, $J_{4,5a}$ = 7.5 Hz, $J_{4,5b}$ = 4.3 Hz, H-4), 4.27 (d, 1H, J_{gem} = 11.6 Hz, H-1a), 4.25 (dd, 1H, $J_{5a,4}$ = 7.5 Hz, J_{gem} = 9.6 Hz, H-5a), 4.08 (d, 1H, $J_{3,4}$ = 5.8 Hz, H-3), 3.72 (dd, 1H, $J_{5b,4}$ = 4.3 Hz, J_{gem} = 9.6 Hz, H-5b), 1.37 (s, 9H, (CH_3)$_3$C); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 165.9 (C=O), 137.0 (Ar), 136.0 (Ar), 133.0 (Ar), 131.5 (Ar), 131.1 (Ar), 129.9 (Ar), 129.7 (2C, Ar), 129.3 (Ar), 129.2 (Ar), 128.4 (2C, Ar), 106.0 (C-2), 83.8 (C-3), 81.0 (C-4), 76.2 ((CH$_3$)$_3$*C*), 70.2 (C-5), 69.8 (Ar*C*H$_2$), 69.2 (Ar*C*H$_2$), 64.0 (C-1), 31.0 (3C, (*C*H$_3$)$_3$C); HRMS (ESI) calcd. for $C_{24}H_{28}NaO_6$ $[M+Na]^+$ 435.1780; found 435.1778.



1-*O*-benzoyl-3,4-*O*-xylylidene-α-D-xylulofuranosyl-(2→6)-1,2,3,4-di-*O*-isopropylidene-α-D-galactopyranose (3.97α) and **1-*O*-benzoyl-3,4-*O*-xylylidene-β-D-xylulofuranosyl-(2→6)-1,2,3,4-di-*O*-isopropylidene-α-D-galactopyranose (3.97β)**. A mixture of **3.71** (22.1 mg, 0.0478 mmol), **3.82** (14.9 mg, 0.0573 mmol), and 4Å molecular sieves in CH_2Cl_2 (1.91 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –78 °C and *N*-iodosuccinimide (12.9 mg, 0.0573 mmol) and silver triflate (1.2 mg, 4.78 μmol) were added. After stirring for 1 h at –78 °C, triethylamine was added. The reaction was warmed to

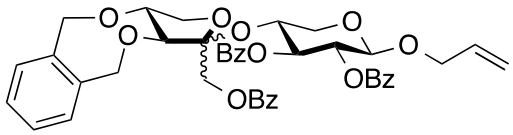
room temperature and then a small amount of water was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The solution was then dried over $MgSO_4$, filtered and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatography (10:1, hexane–EtOAc) to give **3.97α** (6.0 mg, 21%) and **3.97β** (21.6 mg, 76%) both as colorless oils. Data for **3.97α**: $[\alpha]^{25}_D$ +10.0 (*c* 0.6, $CHCl_3$); R_f 0.47 (2:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 8.00–7.95 (m, 2H, ArH), 7.56–7.51 (m, 1H, ArH), 7.43–7.31 (m, 5H, ArH), 7.26–7.23 (m, 1H, ArH), 5.49 (d, 1H, $J_{1,2}$ = 5.0 Hz, H-1), 4.95 (d, 1H, J_{gem} = 12.6 Hz, ArCH_2), 4.85 (d, 1H, J_{gem} = 12.6 Hz, ArCH_2), 4.76 (d, 1H, J_{gem} = 12.6 Hz, ArCH_2), 4.73 (d, 1H, J_{gem} = 12.6 Hz, ArCH_2), 4.54 (dd, 1H, $J_{3,2}$ = 2.5 Hz, $J_{3,4}$ = 8.0 Hz, H-3), 4.49 (d, 1H, J_{gem} = 11.8 Hz, H-1'a), 4.40 (d, 1H, J_{gem} = 11.8 Hz, H-1'b), 4.27 (dd, 1H, $J_{2,1}$ = 5.0 Hz, $J_{2,3}$ = 2.5 Hz, H-2), 4.24 (dd, 1H, $J_{4,3}$ = 8.0 Hz, $J_{4,5}$ = 2.0 Hz, H-4), 4.19–4.13 (m, 2H, H-3', H-4'), 4.07 (dd, 1H, $J_{5'a,4}$ = 7.4 Hz, J_{gem} = 8.4 Hz, H-5'a), 3.88 (ddd, 1H, $J_{5,4}$ = 2.0 Hz, $J_{5,6a}$ = 7.0 Hz, $J_{5,6b}$ = 6.2 Hz, H-5), 3.77 (app t, 1H, $J_{5b,4} = J_{gem}$ = 8.4 Hz, H-5'b), 3.76 (dd, 1H, $J_{6a,5}$ = 7.0 Hz, J_{gem} = 9.7 Hz, H-6a), 3.72 (dd, 1H, $J_{6b,5}$ = 6.2 Hz, J_{gem} = 9.7 Hz, H-6b), 1.48 (s, 3H, (CH_3)$_2$C), 1.37 (s, 3H, (CH_3)$_2$C), 1.31 (s, 3H, (CH_3)$_2$C), 1.22 (s, 3H, (CH_3)$_2$C); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 166.1 (C=O), 136.6 (Ar), 135.7 (Ar), 132.8 (Ar), 131.7 (Ar), 131.5 (Ar), 130.5 (Ar), 129.8 (2C, Ar), 129.7 (Ar), 129.6 (Ar), 128.3 (2C, Ar), 109.2 ((CH$_3$)$_2$*C*), 108.6 ((CH$_3$)$_2$*C*), 108.2 (C-2'), 96.4 (C-1), 87.6 (C-3'), 81.1 (C-4'), 70.9 (C-2), 70.7 (C-4), 70.6 (C-3), 69.7 (Ar*C*H$_2$), 68.9 (Ar*C*H$_2$), 68.4 (C-5'), 66.9 (C-5), 62.2 (C-1'), 60.6 (C-6), 26.1 ((*C*H$_3$)$_2$C), 26.0 ((*C*H$_3$)$_2$C), 25.0 ((*C*H$_3$)$_2$C), 24.4 ((*C*H$_3$)$_2$C); HRMS (ESI) calcd. for $C_{32}H_{38}NaO_{11}$ $[M+Na]^+$ 621.2306; found 621.2307. Data for **3.97β**: $[\alpha]^{25}_D$ –22.4 (*c* 1.0, $CHCl_3$); R_f 0.27 (2:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.92–7.88 (m, 2H, ArH), 7.57–7.52 (m, 1H, ArH), 7.43–7.28 (m, 6H, ArH), 5.50 (d, 1H, $J_{1,2}$ = 5.0 Hz, H-1), 5.00 (d, 1H, J_{gem} = 12.6 Hz, ArCH_2), 4.87 (d, 1H, J_{gem} = 12.6 Hz, ArCH_2), 4.80 (d,

1H, J_{gem} = 12.6 Hz, ArCH_2), 4.77 (d, 1H, J_{gem} = 12.6 Hz, ArCH_2), 4.60 (d, 1H, J_{gem} = 11.8 Hz, H-1'a), 4.56 (dd, 1H, $J_{3,2}$ = 2.1 Hz, $J_{3,4}$ = 8.0 Hz, H-3), 4.40–4.35 (m, 2H, H-4', H-5'a), 4.33 (d, 1H, J_{gem} = 11.8 Hz, H-1'b), 4.27 (dd, 1H, $J_{2,1}$ = 5.0 Hz, $J_{2,3}$ = 2.1 Hz, H-2), 4.24 (dd, 1H, $J_{4,3}$ = 8.0 Hz, $J_{4,5}$ = 1.8 Hz, H-4), 4.14 (d, 1H, $J_{3',4'}$ = 4.4 Hz, H-3'), 4.04 (ddd, 1H, $J_{5,4}$ = 1.8 Hz, $J_{5,6a}$ = 7.8 Hz, $J_{5,6b}$ = 6.0 Hz, H-5), 3.87 (dd, 1H, $J_{6a,5}$ = 7.8 Hz, J_{gem} = 9.6 Hz, H-6a), 3.78–3.73 (m, 1H, H-5'b), 3.70 (dd, 1H, $J_{6b,5}$ = 6.0 Hz, J_{gem} = 9.6 Hz, H-6b), 1.51 (s, 3H, (CH_3)$_2$C), 1.42 (s, 3H, (CH_3)$_2$C), 1.31 (s, 3H, (CH_3)$_2$C), 1.29 (s, 3H, (CH_3)$_2$C); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 165.8 (C=O), 136.6 (Ar), 135.8 (Ar), 133.0 (Ar), 131.6 (Ar), 131.4 (Ar), 129.9 (Ar), 129.8 (2C, Ar), 129.5 (2C, Ar), 128.3 (2C, Ar), 109.0 ((CH$_3$)$_2$*C*), 108.5 ((CH$_3$)$_2$*C*), 105.2 (C-2'), 96.2 (C-1), 83.7 (C-3'), 80.9 (C-4'), 71.0 (C-5'), 70.8 (C-2), 70.7 (C-4), 70.6 (C-3), 69.6 (Ar*C*H$_2$), 69.0 (Ar*C*H$_2$), 66.4 (C-5), 62.6 (C-1'), 60.3 (C-6), 26.12 ((*C*H$_3$)$_2$C), 26.06 ((*C*H$_3$)$_2$C), 24.9 ((*C*H$_3$)$_2$C), 24.5 ((*C*H$_3$)$_2$C); HRMS (ESI) calcd. for $C_{32}H_{38}NaO_{11}$ $[M+Na]^+$ 621.2306; found 621.2304.



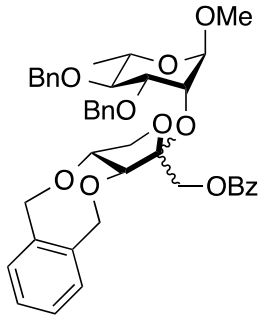
1-*O*-benzoyl-3,4-*O*-xylylidene-α-D-xylulofuranosyl-(2→3)-1,2,5,6-di-*O*-isopropylidene-α-D-glucopyranose (3.98α) and **1-*O*-benzoyl-3,4-*O*-xylylidene-β-D-xylulofuranosyl-(2→6)-1,2,3,4-di-*O*-isopropylidene-α-D-galactopyranose (3.98β)**. A mixture of the **3.71** (23.7 mg, 0.0512 mmol), **3.83** (16.0 mg, 0.0615 mmol), and 4Å molecular sieves in CH_2Cl_2 (2.04 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –78 °C and *N*-iodosuccinimide (13.8 mg, 0.0615 mmol) and silver triflate (1.3 mg, 5.12 μmol) were added. After stirring for 1 h at –78 °C, triethylamine was added. The reaction was warmed

to room temperature and then a small amount of water was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The solution was then dried over $MgSO_4$, filtered and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatography (4:1, hexane–EtOAc) to give an inseparable mixture of **3.98α** and **3.98β** (23.0 mg, 75%, α/β = 1:5.9) as a colorless oil. R_f 0.30 (3:1, hexane–EtOAc). Data for major isomer, **3.98β**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.98–7.93 (m, 2H, ArH), 7.62–7.56 (m, 1H, ArH), 7.48–7.32 (m, 5H, ArH), 7.31–7.28 (m, 1H, ArH), 5.90 (d, 1H, $J_{1,2}$ = 3.8 Hz, H-1), 4.98 (d, 1H, J_{gem} = 12.6 Hz, ArCH_2), 4.88 (d, 1H, J_{gem} = 12.5 Hz, ArCH_2), 4.78 (d, 1H, J_{gem} = 12.6 Hz, ArCH_2), 4.77 (d, 1H, J_{gem} = 12.6 Hz, ArCH_2), 4.58 (d, 1H, $J_{2,1}$ = 3.8 Hz, H-2), 4.55 (d, 1H, J_{gem} = 11.6 Hz, H-1'a), 4.51 (dd, 1H, $J_{6a,5}$ = 8.1 Hz, J_{gem} = 9.5 Hz, H-6a), 4.43 (d, 1H, $J_{3,4}$ = 3.5 Hz, H-3), 4.41 (m, 1H, H-4'), 4.35–4.30 (m, 1H, H-5), 4.29 (d, 1H, J_{gem} = 11.6 Hz, H-1'b), 4.19 (dd, 1H, $J_{4,3}$ = 3.5 Hz, $J_{4,5}$ = 7.0 Hz, H-4), 4.17 (d, 1H, $J_{3',4'}$ = 5.6 Hz, H-3'), 4.08 (dd, 1H, $J_{5'b,4'}$ = 8.4 Hz, J_{gem} = 6.3 Hz, H-5'a), 4.00 (dd, 1H, $J_{5'b,4'}$ = 8.4 Hz, J_{gem} = 6.3 Hz, H-5'b), 3.74 (dd, 1H, $J_{6b,5}$ = 4.9 Hz, J_{gem} = 9.5 Hz, H-6b), 1.48 (s, 3H, (CH_3)$_2$C), 1.42 (s, 3H, (CH_3)$_2$C), 1.28 (s, 3H, (CH_3)$_2$C), 1.27 (s, 3H, (CH_3)$_2$C); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 165.8 (C=O), 136.4 (Ar) 135.7 (Ar), 133.2 (Ar), 131.5 (Ar), 131.3 (Ar), 129.8 (2C, Ar), 129.59 (Ar), 129.58 (Ar), 128.4 (2C, Ar), 111.6 ((CH$_3$)$_2$*C*), 109.0 ((CH$_3$)$_2$*C*), 105.9 (C-2'), 105.0 (C-1), 84.8 (C-2), 83.9 (C-3'), 81.2 (C-4), 80.6 (C-4'), 74.8 (C-3), 72.3 (C-5), 70.9 (C-6), 69.3 (Ar*C*H$_2$), 69.1 (Ar*C*H$_2$), 67.3 (C-5'), 64.4 (C-1'), 26.8 ((*C*H$_3$)$_2$C), 26.7 ((*C*H$_3$)$_2$C), 26.3 ((*C*H$_3$)$_2$C), 25.5 ((*C*H$_3$)$_2$C); HRMS (ESI) calcd. for $C_{32}H_{38}NaO_{11}$ $[M+Na]^+$ 621.2306; found 621.2304.



Allyl 1-*O*-benzoyl-3,4-*O*-xylylidene-α-D-xylulofuranosyl-(2→4)-2,3-di-*O*-benzoyl-β-D-xylopyranoside (3.99α) and **Allyl 1-*O*-benzoyl-3,4-*O*-xylylidene-β-D-xylulofuranosyl-(2→4)-2,3-di-*O*-benzoyl-β-D-xylopyranoside (3.99β)**. A mixture of **3.71** (65.0 mg, 0.140 mmol), **3.84** (46.7 mg, 0.117 mmol), and 4Å molecular sieves in CH_2Cl_2 (3.9 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –78 °C and *N*-iodosuccinimide (38.0 mg, 0.169 mmol) and silver triflate (3.6 mg, 14.0 μmol) were added. After stirring for 30 min at –78 °C, triethylamine was added. The reaction was warmed to room temperature and then a small amount of water was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The solution was then dried over $MgSO_4$, filtered and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatography (4:1, hexane–EtOAc) to give an inseparable mixture of **3.99α** and **3.99β** (76.0 mg, 88%, α/β = 1:10.1) as a colorless oil. R_f 0.42 (2:1, hexane–EtOAc). Data for major isomer, **3.99β**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.98–7.87 (m, 6H, ArH), 7.58–7.45 (m, 3H, ArH), 7.44–7.27 (m, 8H, ArH), 7.25–7.21 (m, 1H, ArH), 7.14–7.10 (m, 1H, ArH), 5.89–5.76 (m, 1H, OCH_2CH=CH_2), 5.67 (app t, 1H, $J_{3,2} = J_{3,4}$ = 8.4 Hz, H-3), 5.35 (dd, 1H, $J_{2,1}$ = 7.0 Hz, $J_{2,3}$ = 8.4 Hz, H-2), 5.24 (dq, 1H, J = 17.3, 1.6 Hz, OCH_2CH=CH_2), 5.13 (dq, 1H, J = 10.4, 1.6 Hz, OCH_2CH=CH_2), 4.83 (d, 1H, J_{gem} = 12.8 Hz, $ArCH_2$), 4.72 (d, 1H, $J_{1,2}$ = 7.0 Hz, H-1), 4.67 (d, 1H, J_{gem} = 12.8 Hz, $ArCH_2$), 4.62 (d, 1H, J_{gem} = 12.8 Hz, $ArCH_2$), 4.55 (d, 1H, J_{gem} = 12.8 Hz, $ArCH_2$), 4.45 (d, 1H, J_{gem} = 11.8 Hz, H-1'a), 4.31 (ddt, 1H, J = 13.3, 5.0, 1.6 Hz, OCH_2CH=CH_2), 4.27–4.19 (m, 3H, H-4, H-5a, H-1'b), 4.15–4.01 (m, 4H, H-5'a, H-3', H-4', OCH_2CH=CH_2), 3.63 (dd, 1H, $J_{5b,4}$ = 8.5 Hz, J_{gem} = 11.5 Hz, H-5b), 3.51 (dd, 1H, $J_{5'b,4'}$ = 4.9 Hz, J_{gem} = 9.5 Hz, H-5'b); ^{13}C NMR

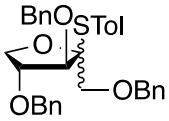
($CDCl_3$, 125 MHz) δ_C 165.7 (C=O), 165.4 (C=O), 165.3 (C=O), 136.5 (Ar),135.5 (Ar), 133.6 ($OCH_2CH=CH_2$), 133.20 (Ar), 133.18 (Ar), 131.4 (Ar), 131.3 (Ar), 129.83 (2C, Ar), 129.76 (2C, Ar), 129.70 (2C, Ar), 129.62, (Ar), 129.58 (Ar), 129.5 (Ar), 129.44 (Ar), 129.40 (Ar), 128.45 (2C, Ar), 128.43 (2C, Ar), 128.3 (2C, Ar), 117.5 ($OCH_2CH=CH_2$), 105.6 (C-2'), 99.8 (C-1), 83.3 (C-3'), 80.4 (C-4'), 72.8 (C-3), 71.6 (C-2), 70.5 (C-5'), 69.7 ($OCH_2CH=CH_2$), 69.18 ($ArCH_2$), 69.14 ($ArCH_2$), 68.1 (C-4), 64.9 (C-5), 64.0 (C-1'); HRMS (ESI) calcd. for $C_{42}H_{40}NaO_{12}$ $[M+Na]^+$ 759.2412; found 759.2403.



Methyl 1-*O*-benzoyl-3,4-*O*-xylylidene-α-D-xylulofuranosyl-(2→2)-3,4-di-*O*-benzyl-α-L-rhamnopyranoside (3.100α) and **Methyl 1-*O*-benzoyl-3,4-*O*-xylylidene-β-D-xylulofuranosyl-(2→2)-3,4-di-*O*-benzyl-α-L-rhamnopyranoside (3.100β)**. A mixture of **3.71** (24.0 mg, 0.0519 mmol), **3.85** (15.5 mg, 0.0432 mmol), and 4Å molecular sieves in CH_2Cl_2 (1.50 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –78 °C and *N*-iodosuccinimide (14.0 mg, 0.0623 mmol) and silver triflate (1.3 mg, 5.19 μmol) were added. After stirring for 2 h at –78 °C, triethylamine was added. The reaction was warmed to room temperature and then a small amount of water was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The solution was then dried over $MgSO_4$, filtered and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatography (4:1, hexane–EtOAc) to give **3.100α** (9.0 mg, 30%) as a colorless oil and **3.100β** (15.8

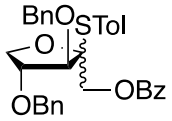
mg, 52%) as a colorless oil. Data for **3.100α**: $[\alpha]^{25}_{D}$ +28.8 (*c* 0.2, $CHCl_3$); R_f 0.58 (2:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.95–7.91 (m, 2H, ArH), 7.57–7.52 (m, 1H, ArH), 7.41–7.21 (m, 16H, ArH), 4.97 (d, 1H, J_{gem} = 11.2 Hz, ArCH_2), 4.90 (d, 1H, J_{gem} = 12.5 Hz, ArCH_2), 4.74 (d, 1H, J_{gem} = 12.5 Hz, ArCH_2), 4.72 (d, 1H, J_{gem} = 11.9 Hz, ArCH_2), 4.70 (d, 1H, J_{gem} = 12.5 Hz, ArCH_2), 4.66 (d, 1H, J_{gem} = 11.2 Hz, ArCH_2), 4.65 (d, 1H, $J_{1,2}$ = 1.8 Hz, H-1), 4.61 (d, 1H, J_{gem} = 12.5 Hz, ArCH_2), 4.59 (d, 1H, J_{gem} = 11.9 Hz, ArCH_2), 4.56 (d, 1H, J_{gem} = 11.7 Hz, H-1'a), 4.32 (dd, 1H, $J_{2,1}$ = 1.8 Hz, $J_{2,3}$ = 3.2 Hz, H-2), 4.35 (d, 1H, J_{gem} = 11.7 Hz, H-1'b), 4.30 (d, 1H, $J_{3'4'}$ = 5.6 Hz, H-3'), 4.10–4.04 (m, 1H, H-4'), 4.00 (app t, 1H, $J_{5'a,4'}$ = J_{gem} = 8.8 Hz, H-5'a), 3.90 (app t, 1H, $J_{5'b,4}$ = J_{gem} = 8.8 Hz, H-5'b), 3.82 (dd, 1H, $J_{3,2}$ = 3.2 Hz, $J_{3,4}$ = 9.5 Hz, H-3), 3.66 (dq, 1H, $J_{5,4}$ = 9.5 Hz, $J_{5,6}$ = 6.3 Hz, H-5), 3.53 (app t, 1H, $J_{4,3}$ = $J_{4,5}$ = 9.5 Hz, H-4), 3.23 (s, 3H, OCH_3), 1.32 (d, 3H, $J_{6,5}$ = 6.3 Hz, H-6); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 166.0 (C=O), 138.71 (Ar), 138.68 (Ar), 137.1 (Ar), 135.4 (Ar), 132.9 (Ar), 131.6 (Ar), 131.4 (Ar), 130.2 (Ar), 129.7 (2C, Ar), 129.6 (Ar), 129.4 (Ar), 128.4 (3C, Ar), 128.3 (2C, Ar), 128.1 (2C, Ar), 127.7 (2C, Ar), 127.6 (Ar), 127.4 (Ar), 108.8 (C-2'), 100.9 (C-1, $J_{C1,H1}$ = 171.6 Hz), 88.5 (C-3'), 79.9 (C-4'), 79.7 (C-4), 78.9 (C-3), 75.1 (Ar*C*H$_2$), 72.1 (Ar*C*H$_2$), 69.7 (C-2), 69.3 (Ar*C*H$_2$), 69.04 (Ar*C*H$_2$), 69.03 (C-5'), 68.0 (C-5), 64.5 (C-1'), 54.6 (O*C*H$_3$), 18.0 (C-6); HRMS (ESI) calcd. for $C_{41}H_{44}NaO_{10}$ $[M+Na]^+$ 719.2827; found 719.2830. Data for **3.100β**: $[\alpha]^{25}_{D}$ –2.9 (*c* 0.2, $CHCl_3$); R_f 0.40 (2:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.91–7.85 (m, 2H, ArH), 7.55–7.50 (m, 1H, ArH), 7.41–7.22 (m, 16H, ArH), 5.08 (d, 1H, J_{gem} = 12.8 Hz, ArCH_2), 4.89–4.80 (m, 4H, ArCH_2), 4.76 (d, 1H, J_{gem} = 11.4 Hz, ArCH_2), 4.69–4.64 (m, 2H, H-1, H-1'a), 4.60 (d, 1H, J_{gem} = 11.4 Hz, ArCH_2), 4.59 (d, 1H, J_{gem} = 11.4 Hz, ArCH_2), 4.51 (ddd, 1H, $J_{4',3'}$ = 6.4 Hz, $J_{4'5'a}$ = 7.9 Hz, $J_{4',5'b}$ = 5.5 Hz, H-4'), 4.28 (d, 1H, J_{gem} = 11.9 Hz, H-1'b), 4.24 (d, 1H, $J_{5'a,4'}$ = 7.9 Hz, J_{gem} = 9.6 Hz, H-5'a), 4.18–4.14 (m, 2H, H-2, H-3'), 3.84 (dd, 1H, $J_{3,2}$ = 2.9 Hz,

$J_{3,4}$ = 9.4 Hz, H-3), 3.74 (dd, 1H, $J_{5'b,4'}$ = 5.5 Hz, J_{gem} = 9.6 Hz, H-5'b), 3.65 (app dq, 1H, $J_{5,4}$ = 9.4 Hz, $J_{5,6}$ = 6.2 Hz, H-5), 3.53 (app t, 1H, $J_{4.3} = J_{4.5}$ = 9.4 Hz, H-4), 3.29 (s, 3H, OCH_3), 1.27 (d, 3H, $J_{6,5}$ = 6.2 Hz, H-6); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 165.8 (C=O), 138.7 (Ar), 138.4 (Ar), 136.7 (Ar), 136.2 (Ar), 132.9 (Ar), 131.4 (Ar), 131.2 (Ar), 129.9 (Ar), 129.7 (2C, Ar), 129.4 (Ar), 129.2 (Ar), 129.0 (2C, Ar), 128.29 (2C, Ar), 128.28 (2C, Ar), 128.1 (2C, Ar), 128.0 (2C, Ar), 127.54 (Ar), 127.47 (Ar), 105.9 (C-2'), 100.2 (C-1, $J_{C1,H1}$ = 172.1 Hz), 82.9 (C-3'), 80.2 (C-4), 80.0 (C-4'), 78.6 (C-3), 74.9 (Ar*C*H_2), 72.6 (Ar*C*H_2), 70.5 (C-5'), 70.0 (C-2), 69.5 (Ar*C*H_2), 69.2 (Ar*C*H_2), 68.0 (C-5), 62.8 (C-1'), 54.7 (O*C*H_3), 18.1 (C-6); HRMS (ESI) calcd. for $C_{41}H_{44}NaO_{10}$ $[M+Na]^+$ 719.2827; found 719.2831.



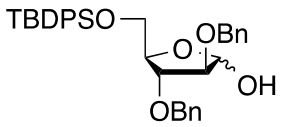
***p*-Tolyl 1,3,4-tri-*O*-benzyl-2-thio-α/β-D-xylulofuranoside (3.104)**. To a solution of **3.110** (116 mg, 0.173 mmol) in THF (1.7 mL) was added tetrabutylammonium fluoride (259 µL, 0.259 mmol) at room temperature and the mixture was stirred for 4 h. After the completion of the reaction, the reaction mixture was added satd aq NH_4Cl and extracted with EtOAc. The organic layer was then washed with water and brine. The organic layers were dried with $MgSO_4$ and then filtered. The filtrate was concentrated and dried *in vacuo*. To a solution of the resulting residue in DMF (1.7 mL) was added benzyl bromide (90.4 mg, 62.8 µL, 0.207 mmol), followed by the addition of sodium hydride (21.1 mg, 0.207 mmol) at room temperature and the mixture was stirred for 2 h. After the completion of the reaction, CH_3OH was added and the solution was concentrated under reduced pressure. The resulting residue was purified by column chromatography (8:1, hexane–EtOAc) to give an inseparable α/β mixture of **3.104** (80 mg, 88%, α/β = 1:7) as a color-

less oil. R_f 0.27 (8:1, hexane–EtOAc); Data for **3.104α**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.43–7.25 (m, 17H, ArH), 7.09–7.06 (m, 2H, ArH), 4.76 (d, 1H, J_{gem} = 11.8 Hz, ArCH_2), 4.62 (d, 1H, J_{gem} = 11.8 Hz, ArCH_2), 4.53 (d, 1H, J_{gem} = 11.8 Hz, ArCH_2), 4.51 (d, 1H, J_{gem} = 11.8 Hz, ArCH_2), 4.46–4.40 (m, 2H, ArCH_2), 4.24 (app dt, 1H, $J_{4,3}$ = 4.6 Hz, $J_{4,5a}$ = $J_{4,5b}$ = 7.4 Hz, H-4), 4.14 (dd, 1H, $J_{5a,4}$ = 7.4 Hz, J_{gem} = 8.9 Hz, H-5a), 4.09 (d, 1H, $J_{3,4}$ = 4.6 Hz, H-3), 3.95–3.91 (m, 1H, H-5b), 3.59 (d, 1H, J_{gem} = 10.0 Hz, H-1a), 3.46 (d, 1H, J_{gem} = 10.0 Hz, H-1b), 2.34 (s, 3H, ArCH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 96.6 (C-2), 88.5 (C-3), 83.3 (C-4), 73.4 (ArCH$_2$), 72.5 (ArCH$_2$), 70.1 (C-1), 69.4 (C-5), 21.4 (ArCH$_3$); Data for **3.104β**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.43–7.25 (m, 17H, ArH), 7.10 (d, 2H, J = 8.2 Hz, ArH), 4.80 (d, 1H, J_{gem} = 11.8 Hz, ArCH_2), 4.60 (d, 1H, J_{gem} = 11.8 Hz, ArCH_2), 4.55 (d, 1H, J_{gem} = 11.8 Hz, ArCH_2), 4.50 (d, 1H, $J_{3,4}$ = 3.7 Hz, H-3), 4.46 (d, 1H, J_{gem} = 11.8 Hz, ArCH_2), 4.43 (d, 1H, J_{gem} = 11.8 Hz, ArCH_2), 4.42 (dd, 1H, $J_{5a,4}$ = 6.2 Hz, J_{gem} = 9.5 Hz, H-5a), 4.37 (d, 1H, J_{gem} = 11.8 Hz, ArCH_2), 4.37–4.33 (m, 1H, H-4), 3.94 (dd, 1H, $J_{5b,4}$ = 3.0 Hz, J_{gem} = 9.5 Hz, H-5b), 3.66 (d, 1H, J_{gem} = 10.9 Hz, H-1a), 3.45 (d, 1H, J_{gem} = 10.9 Hz, H-1b), 2.35 (s, 3H, ArCH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.5 (Ar), 138.1 (Ar), 138.0 (Ar), 137.9 (Ar), 136.5 (2C, Ar), 129.3 (2C, Ar), 128.44 (2C, Ar), 128.37 (2C, Ar), 128.3 (2C, Ar), 128.0 (2C, Ar), 127.9 (2C, Ar), 127.8 (2C, Ar), 127.77 (Ar), 127.75 (Ar), 127.6 (Ar), 127.3 (Ar), 98.3 (C-2), 86.0 (C-3), 84.2 (C-4), 73.5 (ArCH$_2$), 72.9 (ArCH$_2$), 71.9 (C-1), 71.7 (ArCH$_2$), 69.5 (C-5), 21.3 (ArCH$_3$); HRMS (ESI) calcd. for $C_{33}H_{34}NaO_4S$ $[M+Na]^+$ 549.2070; found 549.2067.



***p*-Tolyl 3,4-di-*O*-benzyl-1-*O*-benzoyl-2-thio-α/β-D-xylulofuranoside (3.105)**. To a solution of **3.110** (143 mg, 0.212 mmol) in THF (2.1 mL) was added tetrabutylammonium fluoride (318 μL, 0.318 mmol) at room temperature and the mixture was stirred for 4 h. After the completion of the reaction, the reaction mixture was added satd aq NH_4Cl and extracted with EtOAc. The organic layer was then washed with H_2O and brine. The organic layers were dried with $MgSO_4$ and then filtered. The filtrate was concentrated and dried *in vacuo*. To a solution of the resulting residue in CH_2Cl_2 (2.1 mL) was added triethylamine (25.7 mg, 35.2 μL, 0.254 mmol), benzoyl chloride (35.8 mg, 29.6 μL, 0.254 mmol) and *N*,*N*-dimethylaminopyridine (2.6 mg, 0.0212 mmol) at room temperature and the mixture was stirred for 1 h. After the completion of the reaction, excess benzoyl chloride was quenched by the addition of CH_3OH and then concentrated under reduced pressure. The resulting residue was purified by column chromatography (8:1, hexane–EtOAc) to give an inseparable α/β mixture of **3.105** (102 mg, 89%, α/β = 1:7) as a colorless oil. R_f 0.30 (8:1, hexane–EtOAc); Data for **3.105α**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 8.05–8.01 (m, 2H, ArH), 7.54–7.50 (m, 2H, ArH), 7.49–7.43 (m, 2H, ArH), 7.41–7.24 (m, 11H, ArH), 7.14–7.10 (m, 2H, ArH), 4.73–4.56 (m, 3H, ArCH_2), 4.53–4.37 (m, 3H, ArCH_2, H-1a, H-1b), 4.27 (app dt, 1H, $J_{4,3}$ = 4.7 Hz, $J_{4,5a}$ = $J_{4,5b}$ = 7.2 Hz, H-4), 4.21 (dd, 1H, $J_{5b,4}$ = 7.2 Hz, J_{gem} = 8.9 Hz, H-5a), 4.19 (d, 1H, $J_{3,4}$ = 4.7 Hz, H-3), 4.04 (dd, 1H, $J_{5b,4}$ = 7.2 Hz, J_{gem} = 8.9 Hz, H-5b), 2.34 (s, 3H, ArCH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 165.8 (C=O), 94.8 (C-2), 88.7 (C-3), 82.9 (C-4), 73.0 (ArCH$_2$), 72.4 (ArCH$_2$), 69.0 (C-5), 64.0 (C-1), 21.3 (ArCH$_3$); Data for **3.105β**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 8.00–7.95 (m, 2H, ArH), 7.54–7.50 (m, 2H, ArH), 7.45 (d, 2H, J = 8.0 Hz, ArH), 7.41-7.24 (m, 11H, ArH), 7.13 (d, 2H, J = 8.0 Hz, ArH), 4.84 (d, 1H, J_{gem} = 12.2 Hz, ArCH_2),

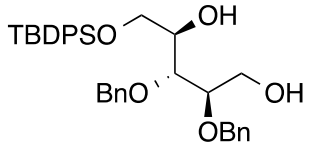
4.67 (d, 1H, J_{gem} = 12.2 Hz, ArCH_2), 4.50 (s, 2H, ArCH_2), 4.47 (dd, 1H, $J_{5a,4}$ = 5.8, J_{gem} = 9.8 Hz, H-5a), 4.45–4.40 (m, 3H, H-1a, H-3, H-4), 4.38 (d, 1H, J_{gem} = 11.9 Hz, H-1b), 3.99 (dd, 1H, $J_{5b,4}$ = 2.8 Hz, J_{gem} = 9.8 Hz, H-5b), 2.34 (s, 3H, ArCH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 165.9 (C=O), 139.0 (Ar), 137.7 (Ar), 137.7 (Ar), 137.4 (Ar), 136.6 (2C, Ar), 133.0 (Ar), 130.6 (Ar), 129.8 (2C, Ar), 129.6 (2C, Ar), 128.9 (Ar), 128.5 (2C, Ar), 128.4 (2C, Ar), 128.3 (2C, Ar), 128.0 (2C, Ar), 127.92 (Ar), 127.88 (Ar), 127.78 (Ar), 96.5 (C-2), 85.9 (C-3), 84.1 (C-4), 73.1 (ArCH$_2$), 71.9 (ArCH$_2$), 69.7 (C-5), 65.6 (C-1), 21.3 (ArCH$_3$); HRMS (ESI) calcd. for $C_{33}H_{32}NaO_5S$ $[M+Na]^+$ 563.1863; found 563.1870.



2,3-di-*O*-benzyl-5-*O*-*tert*-butyldiphenylsilyl-α/β-D-arabinofuranose (3.106). To a solution of **3.72** (4 g, 7.15 mmol) in CH_3OH (35.7 mL) was added sodium methoxide (38.6 mg, 0.715 mmol) at room temperature. The reaction mixture was stirred for 3.5 h at room temperature, then neutralized by addition of Amberlite IR-120 H^+ resin, filtered, and filtrate was concentrated. The resulting crude residue was dissolved in pyridine (27 mL), followed by the addition of TBDPSCl (2.03 mL, 7.85 mmol) and triethylamine (2.98 mL, 21.4 mmol). After stirring for 16 h at room temperature, CH_3OH was added, followed by co-evaporation with toluene. The crude residue was diluted with CH_2Cl_2 and washed with 1N HCl, H_2O, satd aq $NaHCO_3$ and brine. The organic layer was dried with $MgSO_4$ and then filtered, and the filtrate was concentrated and dried *in vacuo*. The resulting crude residue was then dissolved in DMF (27 mL), followed by the addition of benzyl bromide (2.68 g, 1.87 mL, 15.7 mmol) and 60% NaH (713 mg, 17.9 mmol). The reaction mixture was stirred for 2 h, satd aq NH_4Cl was added, and the solution was diluted with CH_2Cl_2.

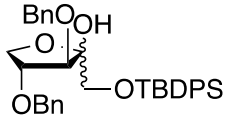
The organic layer was then washed with H_2O, satd aq $NaHCO_3$ and brine. The organic layer was subsequently dried with $MgSO_4$ and then filtered. The filtrate was then concentrated and dried *in vacuo*. The resulting crude residue was then dissolved in the mixture of acetone and H_2O (27 mL, 9:1), followed by the addition of *N*-bromosuccinimide (2.54 g, 14.3 mmol). The reaction mixture was stirred for 1 h at room temperature, then evaporated. The resulting residue was then diluted with CH_2Cl_2, and washed with satd aq $NaHCO_3$, H_2O, and brine. The organic layer was dried with $MgSO_4$ and then filtered. The filtrate was concentrated and the resulting residue was purified by column chromatography (4:1, hexane–EtOAc) to give an α/β mixture of **3.106** (2.72 g, 67%, α/β = 2:1) as a colorless oil. R_f 0.29 (4:1, hexane–EtOAc); Data for **3.106α**: ^{1}H NMR ($CDCl_3$, 700 MHz) δ_H 7.71–7.65 (m, 4H, ArH), 7.47–7.26 (m, 16H, ArH), 5.37 (dd, 1H, $J_{1,2}$ = 1.4 Hz, $J_{1,OH}$ = 8.8 Hz, H-1), 4.62 (d, 1H, J_{gem} = 12.1 Hz, ArCH_2), 4.57 (d, 1H, J_{gem} = 12.1 Hz, ArCH_2), 4.53 (d, 1H, J_{gem} = 12.1 Hz, ArCH_2), 4.49 (d, 1H, J_{gem} = 12.1 Hz, ArCH_2), 4.45 (ddd, 1H, $J_{4,3}$ = 2.8 Hz, $J_{4,5a}$ = 5.2 Hz, $J_{4,5b}$ = 7.7 Hz, H-4), 4.14–4.12 (m, 1H, H-3), 4.01 (d, 1H, $J_{2,1}$ = 1.4 Hz, H-2), 3.84 (dd, 1H, $J_{5a,4}$ = 5.2 Hz, J_{gem} = 10.5 Hz, H-5a), 3.75 (dd, 1H, $J_{5b,4}$ = 7.7 Hz, J_{gem} = 10.5 Hz, H-5b), 3.34 (d, 1H, $J_{OH,1}$ = 8.8 Hz, OH), 1.09 (s, 9H, (CH_3)$_3$C); ^{13}C NMR ($CDCl_3$, 175 MHz) δ_C 135.7 (Ar), 135.63 (Ar), 135.61 (3C, Ar), 129.8 (Ar), 129.7 (Ar), 128.55 (2C, Ar), 128.48 (2C, Ar), 128.1 (Ar), 128.0 (Ar), 127.9 (Ar), 127.83 (Ar), 127.81 (Ar), 127.75 (2C, Ar), 127.73 (2C, Ar), 127.71 (2C, Ar), 127.67 (2C, Ar), 101.2 (C-1), 86.1 (C-2), 84.0 (C-4), 82.3 (C-3), 72.0 (Ar*C*H$_2$), 71.7 (Ar*C*H$_2$), 64.0 (C-5), 26.90 ((*C*H$_3$)$_3$C) 19.29 ((CH$_3$)$_3$*C*); Data for **3.106β**: ^{1}H NMR ($CDCl_3$, 700 MHz) δ_H 7.71–7.65 (m, 4H, ArH), 7.47–7.26 (m, 16H, ArH), 5.40 (dd, 1H, $J_{1,2}$ = 4.3 Hz, $J_{1,OH}$ = 10.0 Hz, H-1), 4.67 (d, 1H, J_{gem} = 12.1 Hz, ArCH_2), 4.58 (d, 1H, J_{gem} = 12.1 Hz, ArCH_2), 4.57 (d, 1H, J_{gem} = 12.1 Hz, ArCH_2), 4.56 (d, 1H, J_{gem} = 12.1 Hz, ArCH_2), 4.25 (app t, 1H, $J_{3,2}$ = $J_{3,4}$ = 4.3 Hz, H-3), 4.08 (app dt, 1H, $J_{4,3}$ = 4.3 Hz, $J_{4,5a}$ = $J_{4,5b}$ = 5.0 Hz, H-4),

4.04 (app t, 1H, $J_{2,1} = J_{2,3}$ = 4.3 Hz, H-2), 3.80 (dd, 1H, $J_{5a,4}$ = 5.0 Hz, J_{gem} = 11.2 Hz, H-5a), 3.78 (d, 1H, $J_{OH,1}$ = 10.0 Hz, OH), 3.75–3.72 (m, 1H, H-5b), 1.10 (s, 9H, $(CH_3)_3C$); ^{13}C NMR ($CDCl_3$, 175 MHz) δ_C 137.8 (Ar), 137.43 (2C, Ar), 137.35 (2C, Ar), 137.33 (Ar), 133.4 (2C, Ar), 133.3 (2C, Ar), 132.9 (Ar), 132.8 (Ar), 129.94 (2C, Ar), 129.86 (2C, Ar), 128.5 (2C, Ar), 128.4 (2C, Ar), 127.8 (2C, Ar), 127.7 (2C, Ar), 96.4 (C-1), 83.7 (C-2), 82.1 (C-4), 81.9 (C-3), 72.3 (ArCH_2), 71.9 (ArCH_2), 64.7 (C-5), 26.91 ($(CH_3)_3C$), 19.25 ($(CH_3)_3C$); HRMS (ESI) calcd. For $C_{35}H_{40}NaO_5Si$ $[M+Na]^+$ 591.2537; found 591.2539.



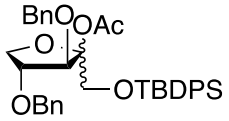
5-*O*-*t*-butyldiphenylsilyl-2,3-di-*O*-benzyl-D-arabinitol (3.107). To a solution of **3.106** (2.72 g, 4.78 mmol) in CH_3OH (35 mL) was added sodium borohydride (198 mg, 5.26 mmol) at room temperature. After stirring for 2 h at room temperature, 1N HCl was added to the reaction mixture and then the solution was extracted with EtOAc. The organic layer was then washed with satd aq $NaHCO_3$, H_2O and brine. The organic layer was dried with $MgSO_4$ and then filtered. The filtrate was concentrated and the resulting residue was purified by column chromatography (2:1, hexane–EtOAc) to give **3.107** (2.12 g, 78%) as a colorless oil. $[\alpha]^{25}_D$ –6.2 (*c* 2.7, $CHCl_3$); R_f 0.37 (1:1, hexane–EtOAc); ^1H NMR ($CDCl_3$, 500 MHz) δ_H 7.70–7.64 (m, 4H, ArH), 7.48–7.43 (m, 2H, ArH), 7.42–7.36 (m, 4H, ArH), 7.34–7.25 (m, 8H, ArH), 7.22–7.18 (m, 2H, ArH), 4.65 (d, 1H, J_{gem} = 11.6, ArCH_2), 4.62 (d, 1H, J_{gem} = 11.6 Hz, ArCH_2), 4.61 (d, 1H, J_{gem} = 11.3 Hz, ArCH_2), 4.57 (d, 1H, J_{gem} = 11.3 Hz, ArCH_2), 3.98–3.92 (m, 1H, H-4), 3.88–3.77 (m, 6H, H-1a, H-1b, H-2, H-3, H-5a, H-5b), 3.06 (d, 1H, *J* = 5.3 Hz, OH), 2.30 (br s, 1H, OH) 1.10 (s, 9H, $(CH_3)_3C$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.1 (Ar), 137.9 (Ar), 135.84 (2C, Ar), 135.78 (2C,

Ar), 133.3 (Ar), 133.2 (Ar), 130.06 (2C, Ar), 130.05 (2C, Ar), 128.7 (2C, Ar), 128.6 (2C, Ar), 128.4 (2C, Ar), 128.3 (2C, Ar), 128.10 (Ar), 128.07 (Ar), 128.00 (2C, Ar), 79.6 (C-2), 78.6 (C-3), 73.7 (Ar*C*H_2), 72.8 (Ar*C*H_2), 71.6 (C-4), 64.9 (C-5), 61.7 (C-1), 26.9 ((*C*H_3)$_3$C) 19.3 ((CH$_3$)$_3$*C*); HRMS (ESI) calcd. for $C_{35}H_{42}NaO_5Si$ $[M+Na]^+$ 593.2694; found 593.2695.



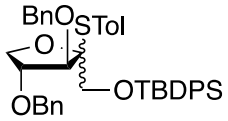
3,4-Di-*O*-benzyl-1-*O*-*tert*-butyldiphenylsilyl-α/β-D-xylulofuranose (3.108). To a solution of **3.107** (2.12 g, 3.71 mmol) in CH_2Cl_2 (90 mL) was added bis(tri-*n*-butyltin) oxde (2.83 mL, 3.31 g, 5.58 mmol) at 0 ºC, followed by bromine (285 μL, 889 mg, 5.58 mmol) dropwise. After stirring for 2 h, the reaction mixture was concentrated. The resulting residue was purified by column chromatography (2:1, hexane–EtOAc) to give an inseparable α/β mixture of **3.108** (1.14 g, 54%, α/β = 1:7) as a colorless oil. R_f 0.34 (2:1, hexane–EtOAc): Data for **3.108α**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.76–7.65 (m, 4H, ArH), 7.45–7.27 (m, 16H, ArH), 4.74–4.69 (m, 1H, ArCH_2), 4.57–4.53 (m, 3H, ArCH_2), 4.18–4.11 (m, 1H, H-5a), 4.08–4.04 (m, 3H, H-3, H-4, H-5b), 3.94–3.90 (m, 2H, H-1a, OH), 3.85–3.79 (m, 1H, H-1b), 1.08 (s, 9H, (CH_3)$_3$C); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 105.6 (C-2), 86.0 (C-3), 81.7 (C-4), 72.4 (Ar*C*H_2), 72.0 (Ar*C*H_2), 70.9 (C-5), 65.1 (C-1), 26.9 ((*C*H_3)$_3$C) 19.29 ((CH$_3$)$_3$*C*); Data for **3.108β**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.76–7.65 (m, 4H, ArH), 7.45–7.27 (m, 16H, ArH), 4.70 (d, 1H, J_{gem} = 11.6 Hz, ArCH_2), 4.54 (d, 1H, J_{gem} = 11.6 Hz, ArCH_2), 4.47 (s, 2H, ArCH_2), 4.22–4.20 (m, 1H, H-4), 4.18–4.11 (m, 2H, H-3, H-5a), 4.03 (s, 1H, OH), 3.85–3.79 (m, 1H, H-5b), 3.76 (d, 1H, J_{gem} = 10.9 Hz, H-1a), 3.73 (d, 1H, J_{gem} = 10.9 Hz, H-1b), 1.07 (s, 9H, (CH_3)$_3$C); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 137.7 (Ar), 137.2 (Ar), 135.7 (2C, Ar), 135.64 (2C, Ar), 133.3 (Ar), 133.1 (Ar), 129.70 (2C, Ar), 129.68 (2C, Ar), 128.5

(2C, Ar), 128.46 (2C, Ar), 128.1 (2C, Ar), 128.0 (2C, Ar), 127.8 (2C, Ar), 127.9 (2C, Ar), 103.3 (C-2), 82.9 (C-3), 82.7 (C-4), 73.1 (Ar*C*H_2), 71.6 (Ar*C*H_2), 69.2 (C-5), 66.5 (C-1), 26.9 (($C$$H_3$)$_3$C) 19.33 (($CH_3$)$_3$*C*); HRMS (ESI) calcd. for $C_{35}H_{40}NaO_5Si$ $[M+Na]^+$ 591.2537; found 591.2539.



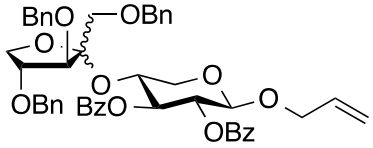
2-*O*-acetyl-3,4-di-*O*-benyl-1-*O*-*tert*-butyldiphenylsilyl-α/β-D-xylulofuranose (3.109). To a solution of the **3.108** (1.14 g, 2.00 mmol) in tetrahydrofuran (20.0 mL) was added acetic anhydride (227 μL, 245 mg, 2.40 mmol) at room temperaturree. The mixture was cooled to –78 ºC and *n*-butyllithium (6.63 mL, 10.6 mmol) was added dropwise. After stirring for 2 h, satd aq NH_4Cl was added and the mixture was extracted with EtOAc. The organic layer was then washed with brine and water. The organic layer was dried with $MgSO_4$ and then filtered. The filtrate was concentrated and the resulting residue was purified by column chromatography (4:1, hexane–EtOAc) to give an inseparable α/β mixture of **3.109** (1.11 g, 91%, α/β = 1:7) as a yellow oil. R_f 0.31 (4:1, hexane–EtOAc); Data for major isomer, **3.109β**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.70–7.67 (m, 4H, ArH), 7.46–7.40 (m, 2H, ArH), 7.39–7.28 (m, 14H, ArH), 4.68 (d, 1H, J_{gem} = 11.5 Hz, ArCH_2), 4.58–4.51 (m, 4H, H-3, H-4, 2 x ArCH_2), 4.50–4.43 (m, 2H, H-5a, ArCH_2), 4.22–4.20 (m, 1H, H-4), 3.95 (d, 1H, J_{gem} = 11.0 Hz, H-1a), 3.90–3.85 (m, 2H, H-1b, H-5b), 1.99 (s, 3H, CH_3CO), 1.08 (s, 9H, (CH_3)$_3$C); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 169.1 (C=O), 138.1 (Ar), 138.0 (Ar), 135.75 (2C, Ar), 135.72 (2C, Ar), 133.2 (Ar), 133.0 (Ar), 129.84 (Ar), 129.80 (Ar), 128.42 (2C, Ar), 128.39 (2C, Ar), 127.78 (2C, Ar), 127.75 (2C, Ar), 127.71 (2C, Ar), 127.66 (2C, Ar), 127.63 (2C, Ar), 108.6 (C-2), 84.4 (C-3), 84.0 (C-4), 72.8 (Ar*C*H_2), 72.6 (C-5), 71.9 (Ar*C*H_2),

65.8 (C-1), 26.9 ((*C*H$_3$)$_3$C) 21.9 (*C*H$_3$CO), 19.33 ((CH$_3$)$_3$*C*); HRMS (ESI) calcd. for $C_{37}H_{42}NaO_6Si$ $[M+Na]^+$ 633.2643; found 633.2643.



***p*-Tolyl 3,4-di-*O*-benyl-1-*O*-*tert*-butyldiphenylsilyl-2-thio-α/β-D-xylulofuranoside (3.110).** To a solution of **3.109** (403 mg, 0.661 mmol) and thiocresol (98.3 mg, 0.791 mmol) in dichloromethane (6.6 mL) was added boron trifluoride diethyl etherate (106 μL, 0.859 mmol) at 0 °C. After stirring for 1 h, to the reaction mixture was added satd aq $NaHCO_3$ and then the solution was extracted with EtOAc. The organic layer was then washed with brine and water. The organic layer was dried with $MgSO_4$ and then filtered. The filtrate was concentrated and the resulting residue was purified by column chromatography (8:1, hexane–EtOAc) to give an inseparable α/β mixture of **3.110** (357 mg, 80%, α/β = 1:7) as a yellow oil. R_f 0.23 (8:1, hexane–EtOAc); Data for **3.110α**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.66–7.61 (m, 4H, ArH), 7.45–7.24 (m, 14H, ArH), 7.02 (d, 2H, J = 8.5 Hz, ArH), 4.82 (d, 1H, J_{gem} = 12.0 Hz, ArCH_2), 4.75 (d, 1H, J_{gem} = 12.0 Hz, ArCH_2), 4.67–4.60 (m, 1H, ArCH_2), 4.57–4.51 (m, 2H, H-4, ArCH_2), 4.22 (dd, 1H, J = 7.5, 8.4 Hz, H-5a), 4.18 (d, 1H, J = 6.0 Hz, H-3), 3.93–3.91 (m, 1H, H-1a), 3.86-3.81 (m, 1H, H-5b), 3.70 (d, 1H, J_{gem} = 10.7 Hz, H-1b), 2.33 (s, 3H, CH_3), 1.01 (s, 9H, (CH_3)$_3$C); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 96.0 (C-2), 88.1 (C-3), 82.2 (C-4), 73.1 (Ar*C*H$_2$), 72.4 (Ar*C*H$_2$), 69.6 (C-5), 65.0 (C-1), 26.7 ((*C*H$_3$)$_3$C) 21.2 (Ar*C*H$_3$), 19.4 ((CH$_3$)$_3$*C*); Data for **3.110β**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.61–7.57 (m, 4H, ArH), 7.45–7.24 (m, 14H, ArH), 6.98 (d, 2H, J = 8.5 Hz, ArH), 4.87 (d, 1H, J_{gem} = 12.0 Hz, ArCH_2), 4.65 (d, 1H, J_{gem} = 12.0 Hz, ArCH_2), 4.64 (d, 1H, $J_{3,4}$ = 3.4 Hz, H-3), 4.50 (d, 1H, J_{gem} = 12.0 Hz, ArCH_2), 4.45 (d, 1H, J_{gem} = 12.0 Hz, ArCH_2), 4.41–4.36 (m,

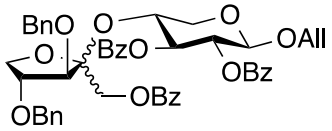
2H, H-4, H-5a), 3.96–3.91 (m, 1H, H-5b), 3.87 (d, 1H, J_{gem} = 11.2 Hz, H-1a), 3.73 (d, 1H, J_{gem} = 11.2 Hz, H1-b), 2.33 (s, 3H, CH_3), 1.06 (s, 9H, $(CH_3)_3C$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.02 (Ar), 137.98 (Ar), 137.9 (Ar), 136.0 (2C, Ar), 135.8 (2C, Ar), 135.7 (2C, Ar), 129.6 (Ar), 129.4 (Ar), 129.1 (2C, Ar), 128.4 (2C, Ar), 127.9 (2C, Ar), 127.72 (Ar), 127.69 (Ar), 127.66 (2C, Ar), 127.6 (2C, Ar), 127.5 (Ar), 99.0 (C-2), 85.5 (C-3), 84.1 (C-4), 73.0 (ArCH_2), 71.5 (ArCH_2), 69.7 (C-5), 65.6 (C-1), 26.9 ($(CH_3)_3C$), 21.2 (ArCH_3), 19.4 ($(CH_3)_3C$); HRMS (ESI) calcd. for $C_{42}H_{46}NaO_4SSi$ $[M+Na]^+$ 697.2778; found 697.2788.



Allyl 1,3,4-tri-*O*-benzyl-α-D-xylulofuranosyl-(2→4)-2,3-di-*O*-benzoyl-β-D-xylopyranoside (3.111α) and **Allyl 1,3,4-tri-*O*-benzyl-α-D-xylulofuranosyl-(2→4)-2,3-di-*O*-benzoyl-β-D-xylopyranoside (3.111β)**. A mixture of the **3.104** (28.0 mg, 0.0530 mmol), **3.84** (17.7 mg, 0.0440 mmol), and 4Å molecular sieves in CH_2Cl_2 (1.50 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –78 °C and *N*-iodosuccinimide (14.3 mg, 0.0636 mmol) and silver triflate (1.4 mg, 5.3 μmol) were added. After stirring for 1 h at –78 °C, triethylamine was added. The reaction was warmed to room temperature and then a small amount of water was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The solution was then dried over $MgSO_4$, filtered and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatography (4:1, hexane–EtOAc) to give **3.111α** (18.9 mg, 53%) as a colorless oil and **3.111β** (11.8 mg, 33%) as a colorless oil. Data for **3.111α**: $[\alpha]^{25}_D$ +6.6 (*c* 1.0, $CHCl_3$); R_f 0.32 (4:1, hexane–EtOAc); ^1H NMR ($CDCl_3$, 500 MHz) δ_H 7.99–7.96 (m, 2H, ArH), 7.94–7.91 (m, 2H, ArH), 7.51–7.43 (m,

2H, ArH), 7.37–7.31 (m, 4H, ArH), 7.30–7.26 (m, 5H, ArH), 7.25–7.23 (m, 3H, ArH), 7.22–7.19 (m, 3H, ArH), 7.13–7.08 (m, 4H, ArH), 5.82 (m, 1H, OCH_2CH=CH_2), 5.59 (dd, 1H, $J_{3,2}$ = 8.7 Hz, $J_{3,4}$ = 7.9 Hz, H-3), 5.33 (dd, 1H, $J_{2,1}$ = 6.7 Hz, $J_{2,3}$ = 8.7 Hz, H-2), 5.25 (dq, 1H, J = 17.2, 1.6 Hz, OCH_2CH=CH_2), 5.14 (dq, 1H, J = 10.4, 1.6 Hz, OCH_2CH=CH_2), 4.70 (d, 1H, $J_{1,2}$ = 6.7 Hz, H-1), 4.54 (d, 1H, J_{gem} = 12.1 Hz, $ArCH_2$), 4.43 (d, 1H, J_{gem} = 12.1 Hz, $ArCH_2$), 4.39 (d, 1H, J_{gem} = 12.1 Hz, $ArCH_2$), 4.36 (d, 1H, J_{gem} = 12.1 Hz, $ArCH_2$), 4.31 (ddt, 1H, J = 13.2, 4.9, 1.6 Hz, OCH_2CH=CH_2), 4.27–4.21 (m, 2H, H-4, H-5a), 4.20 (s, 2H, $ArCH_2$), 4.13–4.03 (m, 4H, H-3', H-4', H-5'a, OCH_2CH=CH_2), 3.78 (dd, 1H, $J_{5'b,4'}$ = 9.0 Hz, J_{gem} = 11.7 Hz, H-5'b), 3.51 (s, 2H, H-1'), 3.43 (dd, 1H, $J_{5b,4}$ = 9.9 Hz, J_{gem} = 13.3 Hz, H-5b); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 165.6 (C=O), 165.3 (C=O), 138.8 (Ar), 137.9 (Ar), 137.8 (Ar), 133.7 (OCH_2CH=CH_2), 133.01 (Ar), 132.98 (Ar), 129.9 (2C, Ar), 129.83 (2C, Ar), 129.77 (Ar), 129.7 (Ar), 128.4 (Ar), 128.30 (Ar), 128.29 (Ar), 128.2 (Ar), 127.80 (Ar), 127.77 (Ar), 127.75 (Ar), 127.65 (Ar), 127.5 (Ar), 117.47 (OCH_2CH=CH_2), 108.8 (C-2'), 99.7 (C-1), 88.4 (C-3'), 81.9 (C-4'), 73.4 ($ArCH_2$), 72.8 (C-3), 72.6 ($ArCH_2$), 72.0 (C-2), 71.4 ($ArCH_2$), 70.2 (C-1'), 69.6 (C-5'), 68.9 (OCH_2CH=CH_2), 68.3 (C-4), 64.9 (C-5); HRMS (ESI) calcd. for $C_{48}H_{48}NaO_{11}$ $[M+Na]^+$ 823.3089; found 823.3103. Data for **3.111β**: $[\alpha]^{25}_D$ –18.1 (*c* 1.0, $CHCl_3$); R_f 0.27 (4:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 8.01–7.93 (m, 4H, ArH), 7.51–7.44 (m, 2H, ArH), 7.38–7.22 (m, 17H, ArH), 7.11–7.06 (m, 2H, ArH), 5.80 (m, 1H, OCH_2CH=CH_2), 5.62 (app t, 1H, $J_{3,2}$ = $J_{3,4}$ = 8.7 Hz, H-3), 5.34 (dd, 1H, $J_{2,1}$ = 7.0 Hz, $J_{2,3}$ = 8.7 Hz, H-2), 5.24 (dq, 1H, J = 17.3, 1.7 Hz, OCH_2CH=CH_2), 5.13 (dq, 1H, J = 10.4, 1.7 Hz, OCH_2CH=CH_2), 4.70 (d, 1H, $J_{1,2}$ = 7.0 Hz, H-1), 4.69 (d, 1H, J_{gem} = 12.4 Hz, $ArCH_2$), 4.54 (d, 1H, J_{gem} = 12.4 Hz, $ArCH_2$), 4.48 (d, 1H, J_{gem} = 12.4 Hz, $ArCH_2$), 4.47 (d, 1H, J_{gem} = 12.4 Hz, $ArCH_2$), 4.31 (ddt, 1H, J = 13.3, 5.0, 1.7 Hz, OCH_2CH=CH_2), 4.29–4.24 (m, 1H, H-4), 4.15–4.08 (m, 3H, H-5a, OCH_2CH=CH_2, $ArCH_2$), 4.07 (d, 1H, $J_{3',4'}$ = 5.7 Hz, H-3'),

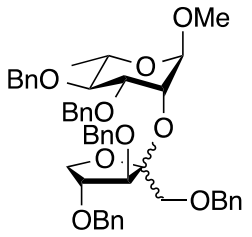
4.05–3.98 (m, 2H, H-4', ArCH_2), 3.78 (dd, 1H, $J_{5'a,4'}$ = 6.5 Hz, J_{gem} = 9.2 Hz, H-5'a), 3.53 (d, 1H, J_{gem} = 10.7 Hz, H-1'a), 3.51 (dd, 1H, $J_{5b,4}$ = 12.2 Hz, J_{gem} = 13.7 Hz, H-5b), 3.44 (dd, 1H, $J_{5'b,4'}$ = 5.4 Hz, J_{gem} = 9.2 Hz, H-5'b), 3.40 (d, 1H, J_{gem} = 10.7 Hz, H-1'b); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 165.5 (C=O), 165.4 (C=O), 138.5 (Ar), 137.9 (Ar), 137.5 (Ar), 133.6 (OCH$_2$*C*H=CH$_2$), 133.11 (Ar), 133.06 (Ar), 129.9 (Ar), 129.8 (Ar), 129.6 (Ar), 128.5 (Ar), 128.43 (Ar), 128.39 (Ar), 128.34 (Ar), 128.31 (Ar), 128.2 (Ar), 127.9 (Ar), 127.84 (Ar), 127.82 (Ar), 127.8 (Ar), 127.75 (Ar), 127.7 (Ar), 127.65 (Ar), 127.5 (Ar), 127.5 (Ar), 117.5 (OCH$_2$CH=*C*H$_2$), 105.2 (C-2'), 99.96 (C-1), 83.8 (C-3'), 82.4 (C-4'), 73.6 (Ar*C*H$_2$), 73.2 (C-3), 72.4 (Ar*C*H$_2$), 72.0 (Ar*C*H$_2$), 71.8 (C-2), 70.5 (C-1'), 69.8 (C-5'), 69.4 (O*C*H$_2$CH=CH$_2$), 68.0 (C-4), 65.2 (C-5); HRMS (ESI) calcd. for $C_{48}H_{48}NaO_{11}$ $[M+Na]^+$ 823.3089; found 823.3100.



Allyl 1-*O*-benzoyl-3,4-di-*O*-benzyl-α-D-xylulofuranosyl-(2→4)-2,3-di-*O*-benzoyl-β-D-xylopyranoside (3.112α) and **Allyl 1-*O*-benzoyl-3,4-di-*O*-benzyl-β-D-xylulofuranosyl-(2→4)-2,3-di-*O*-benzoyl-β-D-xylopyranoside (3112β)**. A mixture of **3.105** (45.1 mg, 0.0830 mmol), **3.84** (27.7 mg, 0.070 mmol), and 4Å molecular sieves in CH_2Cl_2 (2.3 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –78 °C and *N*-iodosuccinimide (22.8 mg, 0.0996 mmol) and silver triflate (4.3 mg, 16.6 μmol) were added. After stirring for 1.5 h at –78 °C, triethylamine was added. The reaction was warmed to room temperature and then a small amount of water was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The solution was then dried over $MgSO_4$, filtered and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatog-

raphy (4:1, hexane–EtOAc) to give an inseparable mixture of **3.112α** and **3.112β** (50.2 mg, 88%, α/β = 1:1.2) as a colorless oil. R_f 0.31 (4:1, hexane–EtOAc). ^{1}H NMR ($CDCl_3$, 700 MHz) δ_H 8.02–7.99 (m, 2H, ArH), 7.99–7.96 (m, 2H, ArH), 7.93–7.87 (m, 4H, ArH), 7.72–7.69 (m, 2H, ArH), 7.66–7.63 (m, 2H, ArH), 7.57–7.54 (m, 1H, ArH), 7.52–7.43 (m, 4H, ArH), 7.41–7.23 (m, 21H, ArH), 7.22–7.19 (m, 2H, ArH), 7.18–7.09 (m, 6H, ArH), 7.09–7.05 (m, 2H, ArH), 7.03–7.00 (m, 2H, ArH), 5.84–5.75 (m, 2H, OCH_2CH=CH_2(α), OCH_2CH=CH_2(β)), 5.67 (app t, 1H, $J_{3,2}$ = 8.5 Hz, $J_{3,4}$ = 8.5 Hz, H-3(β)), 5.63 (app t, 1H, $J_{3,2}$ = $J_{3,4}$ = 9.1 Hz, H-3(α)), 5.37 (dd, 1H, $J_{2,1}$ = 6.8 Hz, $J_{2,3}$ = 8.5 Hz, H-2(β)), 5.31 (dd, 1H, $J_{2,1}$ = 7.3 Hz, $J_{2,3}$ = 9.1 Hz, H-2(α)), 5.27–5.20 (m, 2H, OCH_2CH=CH_2(α), OCH_2CH=CH_2(β)), 5.15–5.10 (m, 2H, OCH_2CH=CH_2(α), OCH_2C=CH_2(β)), 4.74 (d, 1H, $J_{1,2}$ = 6.8 Hz, H-1(β)), 4.69 (d, 1H, J_{gem} = 12.1 Hz, ArCH_2(β)), 4.64 (d, 1H, $J_{1,2}$ = 7.3 Hz, H-1(α)), 4.61 (d, 1H, J_{gem} = 12.1 Hz, ArCH_2(β)), 4.55 (d, 1H, J_{gem} = 12.1 Hz, ArCH_2(α)), 4.52 (d, 1H, J_{gem} = 12.1 Hz, H-1'a(α)), 4.43–4.39 (m, 2H, ArCH_2(α), H-1(β)), 4.37–4.27 (m, 6H, OCH_2CH=CH_2(α), OCH_2CH=CH_2(β), H-4(α), H-4(β), ArCH_2(α), ArCH_2(β)), 4.24–4.17 (m, 5H, H-1'b(α), H-1'b(β), H-5a(α), H-5b(β), H-5'a(β)), 4.15–4.07 (m, 6H, H-3'(α), H-3'(β), H-4'(α), OCH_2CH=CH_2(α), OCH_2CH=CH_2(β), ArCH_2(β)), 4.06–4.03 (m, 1H, H-4'(β)), 4.01–3.98 (m, 2H, H-5'b(α), ArCH_2(α)), 3.90 (dd, 1H, $J_{5'a,4'}$ = 6.3 Hz, J_{gem} = 8.0 Hz, H-5'a (β)), 3.61 (dd, 1H, $J_{5b,4}$ = 8.8 Hz, J_{gem} = 11.9 Hz, H-5b(β)), 3.51 (dd, 1H, J = 5.3, 8.8 Hz, H-5'b (β)), 3.41 (dd, 1H, $J_{5b,4}$ = 9.0 Hz, J_{gem} = 11.8 Hz, H-5b(α)); ^{13}C NMR ($CDCl_3$, 175 MHz) δ_C 165.7 (C=O), 165.5 (C=O), 165.4 (C=O), 165.3 (C=O), 165.28 (C=O), 165.2 (C=O), 137.9 (Ar), 137.69 (Ar), 137.67 (Ar), 136.9 (Ar), 133.66 (OCH_2CH=CH_2), 133.65 (OCH_2CH=CH_2), 133.25 (Ar), 133.22 (Ar), 133.1 (Ar), 133.0 (Ar), 132.9 (Ar), 132.7 (Ar), 129.89 (Ar), 129.86 (Ar), 129.8 (Ar), 129.7 (Ar), 129.6 (Ar), 129.57 (Ar), 129.5 (Ar), 129.45 (Ar), 128.8 (Ar), 128.5 (Ar), 128.44 (Ar), 128.4 (Ar), 128.31 (Ar), 128.28 (Ar), 128.24 (Ar),

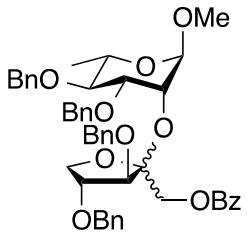
128.0 (Ar), 127.97 (Ar), 127.89 (Ar), 127.85 (Ar), 127.8 (Ar), 127.79 (Ar), 127.7 (Ar), 127.5 (Ar), 117.51 ($OCH_2CH=\mathit{C}H_2$), 118.43 ($O\mathit{C}H_2CH=CH_2$), 108.7 (C-2'(α)), 104.0 (C-2'(β)), 100.1 (C-1(α)), 99.8 (C-1(β)), 86.5 (C-3'(α)), 83.0 (C-4'(α)), 82.1 (C-3'(β), 81.3 (C-4'(β)), 73.0 ($Ar\mathit{C}H_2$), 72.9 (H-3(α)), 72.87 (H-3(β)), 72.79 ($Ar\mathit{C}H_2$), 72.5 ($Ar\mathit{C}H_2$) 72.3 (H-5'(α)), 72.1 (H-2(α)), 71.7 ($Ar\mathit{C}H_2$), 71.6 (H-2(β)), 69.7(H-5'(β)), 69.68 ($O\mathit{C}H_2CH=CH_2$), 69.66 ($O\mathit{C}H_2CH=CH_2$), 68.7 (H-4(α)), 67.9 (H-4(β)), 65.5 (H-5(α)), 64.9 (H-5(β)), 63.8 (H-1'(β)), 62.3 (H-1'(α)); HRMS (ESI) calcd. for $C_{29}H_{36}NaO_5Si$ $[M+H]^+$ 837.2887; found 837.2884.



Methyl 1,3,4-tri-*O*-benzyl-α-D-xylulofuranosyl-(2→2)-3,4-di-*O*-benzyl-α-L-rhamnopyranoside (3.113α) and **Methyl 1,3,4-tri-*O*-benzyl-β-D-xylulofuranosyl-(2→2)-3,4-di-*O*-benzyl-α-L-rhamnopyranoside (3.113β)**. A mixture of **3.104** (30.9 mg, 0.0586 mmol), **3.85** (17.5 mg, 0.0488 mmol), and 4Å molecular sieves in CH_2Cl_2 (1.63 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –78 °C and *N*-iodosuccinimide (15.8 mg, 0.0703 mmol) and silver triflate (1.5 mg, 5.86 μmol) were added. After stirring for 1 h at –78 °C, triethylamine was added. The reaction was warmed to room temperature and then a small amount of water was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The solution was then dried over $MgSO_4$, filtered and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatography (10:1, hexane–EtOAc) to give **3.113α** (18.2 mg, 49%) as a colorless oil and **3.113β** (9.5 mg, 26%) as a colorless oil. Data for **3.113α**: $[\alpha]^{25}_D$ +21.9 (*c* 0.2, $CHCl_3$); R_f 0.26 (4:1, hexane–

EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.40–7.24 (m, 25H, ArH), 4.87 (d, 1H, J_{gem} = 11.6 Hz, ArCH_2), 4.81 (d, 1H, $J_{1,2}$ = 1.7 Hz, H-1), 4.78 (d, 1H, J_{gem} = 11.6 Hz, ArCH_2), 4.69 (d, 1H, J_{gem} = 12.0 Hz, ArCH_2), 4.65–4.56 (m, 3H, ArCH_2), 4.55 (d, 1H, J_{gem} = 12.0 Hz, ArCH_2), 4.53 (d, 1H, J_{gem} = 12.0 Hz, ArCH_2), 4.46 (d, 1H, J_{gem} = 11.6 Hz, ArCH_2), 4.42 (d, 1H, J_{gem} = 12.0 Hz, ArCH_2), 4.35 (dd, 1H, $J_{2,1}$ = 1.7 Hz, $J_{2,3}$ = 3.1 Hz, H-2), 4.25 (d, 1H, $J_{3',4'}$ = 3.7 Hz, H-3'), 4.16–4.09 (m, 2H, H-4', H-5'a), 4.02–3.95 (m, 1H, H-5'b), 3.83 (dd, 1H, $J_{3,2}$ = 3.1 Hz, $J_{3,4}$ = 9.4 Hz, H-3), 3.74 (d, 1H, J_{gem} = 10.8 Hz, H-1'a), 3.68 (d, 1H, J_{gem} = 10.8 Hz, H-1'b), 3.67–3.63 (m, 1H, H-5), 3.55 (app t, 1H, $J_{4,3}$ = $J_{4,5}$ = 9.4 Hz, H-4), 3.28 (s, 3H, OCH_3), 1.32 (d, 3H, $J_{6,5}$ = 6.3 Hz, H-6); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.9 (Ar), 138.8 (Ar), 138.4 (Ar), 138.2 (Ar), 138.0 (Ar), 128.4 (3C, Ar), 128.34 (2C, Ar), 128.29 (2C, Ar), 128.2 (2C, Ar), 127.96 (2C, Ar), 127.93 (2C, Ar), 127.92 (2C, Ar), 127.70 (2C, Ar), 127.69 (2C, Ar), 127.67 (Ar), 127.6 (Ar), 127.5 (Ar), 127.3 (Ar), 108.5 (C-2'), 100.9 (C-1, $J_{C1,H1}$ = 172.8 Hz), 88.2 (C-3'), 82.5 (C-4'), 80.1 (C-4), 79.5 (C-3), 75.2 (Ar*C*H_2), 73.9 (Ar*C*H_2), 72.6 (Ar*C*H_2), 72.0 (Ar*C*H_2), 71.9 (Ar*C*H_2), 70.0 (C-5'), 69.3 (C-1'), 68.9 (C-2), 68.1 (C-5), 54.5 (O*C*H_3), 18.1 (C-6); HRMS (ESI) calcd. for $C_{47}H_{52}NaO_9$ $[M+Na]^+$ 783.3504; found 783.3501. Data for **3.113β**: $[\alpha]^{25}_D$ –4.7 (*c* 0.3, $CHCl_3$); R_f 0.20 (4:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.36–7.20 (m, 25H, ArH), 4.79 (d, 1H, J_{gem} = 11.5 Hz, ArCH_2), 4.77 (d, 1H, J_{gem} = 10.6 Hz, ArCH_2), 4.72 (d, 1H, $J_{1,2}$ = 1.9 Hz, H-1), 4.65 (d, 1H, J_{gem} = 11.6 Hz, ArCH_2), 4.62 (d, 1H, J_{gem} = 11.6 Hz, ArCH_2), 4.61 (d, 1H, J_{gem} = 11.7 Hz, ArCH_2), 4.53 (d, 1H, J_{gem} = 11.7 Hz, ArCH_2), 4.48 (d, 1H, J_{gem} = 11.5 Hz, ArCH_2), 4.47 (d, 1H, J_{gem} = 12.4 Hz, ArCH_2), 4.44 (d, 1H, J_{gem} = 10.6 Hz, ArCH_2), 4.39–4.34 (m, 2H, H-4', ArCH_2), 4.32 (d, 1H, $J_{3',4'}$ = 5.0 Hz, H-3'), 4.24 (dd, 1H, $J_{2,1}$ = 1.9 Hz, $J_{2,3}$ = 3.0 Hz, H-2), 4.16 (dd, 1H, $J_{5'a,4'}$ = 6.4 Hz, J_{gem} = 9.4 Hz, H-5'a), 3.83 (dd, 1H, $J_{5'b,4'}$ = 7.0 Hz, J_{gem} = 9.4 Hz, H-5'b), 3.81 (dd, 1H, $J_{3,2}$ = 3.0 Hz, $J_{3,4}$ = 9.3 Hz, H-3), 3.69 (d, 1H, J_{gem} = 10.8 Hz, H-1'a), 3.66

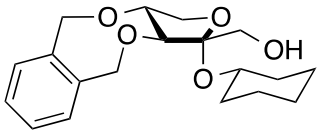
(d, 1H, J_{gem} = 10.8 Hz, H-1'b), 3.66–3.61 (m, 1H, H-5), 3.52 (app t, 1H, $J_{4,3} = J_{4,5}$ = 9.3 Hz, H-4), 3.31 (s, 3H, O*C*H$_3$), 1.28 (d, 3H, $J_{6,5}$ = 6.3 Hz, H-6); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 139.0 (Ar), 138.7 (Ar), 138.2 (Ar), 137.9 (Ar), 128.42 (2C, Ar), 128.37 (2C, Ar), 128.35 (2C, Ar), 128.31 (2C, Ar), 128.2 (2C, Ar), 127.89 (2C, Ar), 127.86 (2C, Ar), 127.8 (2C, Ar), 127.71 (Ar), 127.68 (Ar), 127.61 (2C, Ar), 127.55 (Ar), 127.53 (2C, Ar), 127.4 (Ar), 127.3 (Ar), 105.9 (C-2'), 100.3 (C-1, $J_{C1,H1}$ = 171.4 Hz), 84.3 (C-3'), 82.9 (C-4'), 80.6 (C-4), 79.1 (C-3), 75.2 (Ar*C*H$_2$), 73.5 (Ar*C*H$_2$), 72.4 (Ar*C*H$_2$), 71.9 (Ar*C*H$_2$), 71.8 (Ar*C*H$_2$), 70.4 (C-1'), 69.8 (C-2), 69.7 (C-5'), 68.0 (C-5), 54.7 (O*C*H$_3$), 18.0 (C-6); HRMS (ESI) calcd. for $C_{47}H_{52}NaO_9$ $[M+Na]^+$ 783.3504; found 783.3505.



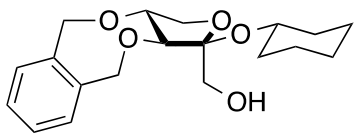
Methyl 1-*O*-benzoyl-3,4-di-*O*-benzyl-α-D-xylulofuranosyl-(2→2)-3,4-di-*O*-benzyl-α-L-rhamnopyranoside (3.114α) and **Methyl 1-*O*-benzoyl-3,4-di-*O*-benzyl-β-D-xylulofuranosyl-(2→2)-3,4-di-*O*-benzyl-α-L-rhamnopyranoside (3.114β)**. A mixture of **3.105** (36.2 mg, 0.0669 mmol), **3.85** (20.0 mg, 0.0558 mmol), and 4Å molecular sieves in CH_2Cl_2 (1.86 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –78 ºC and *N*-iodosuccinimide (18.1 mg, 0.0803 mmol) and silver triflate (1.7 mg, 6.69 μmol) were added. After stirring for 2 h at –78 ºC, triethylamine was added. The reaction was warmed to room temperature and then a small amount of water was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The solution was then dried over $MgSO_4$, filtered and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chroma-

tography (4:1, hexane–EtOAc) to give an inseparable mixture of **3.114α** and **3.114β** (34.0 mg, 78%, α/β = 2.4:1) as a colorless oil; R_f 0.28 (4:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 8.09–8.05 (m, 2H, ArH(α)), 8.03–7.99 (m, 2H, ArH(β)), 7.60–7.56 (m, 1H, ArH(α)), 7.56–7.51 (m, 1H, ArH(β)), 7.47–7.42 (m, 3H, ArH), 7.40–7.20 (m, 41H, ArH), 4.94 (d, 1H, J_{gem} = 11.7 Hz, ArCH_2(β)), 4.89 (d, 1H, J_{gem} = 11.2 Hz, ArCH_2(α)), 4.77–4.74 (m, 3H, ArCH_2(α), ArCH_2(β), H-1'a(β)), 4.73–4.71 (m, 1H, H-1a(β)), 4.67–4.62 (m, 3H, ArCH_2(α), ArCH_2(β), H-1a(α)), 4.61 (d, 1H, J_{gem} = 11.6 Hz, H-1'a(α)), 4.60 (d, 1H, J_{gem} = 11.9 Hz, ArCH_2(α)), 4.55–4.38 (m, 12H, 4 x ArCH_2(α), 5 x ArCH_2(β), H-2(α), H-1'b(β), H-4'(β)), 4.33 (d, 1H, $J_{3',4'}$ = 4.5 Hz, H-3'(α)), 4.31–4.29 (m, 2H, H-2(β), H-3'(β)), 4.22–4.18 (m, 1H, H-5'a(β)), 4.14 (app dt, 1H, $J_{4',3'}$ = 4.5 Hz, $J_{4',5'a}$ = $J_{4',5'b}$ = 6.5 Hz, H-4'(α)), 4.08 (dd, 1H, $J_{5'a,4'}$ = 6.5 Hz, J_{gem} = 9.4 Hz, H-5'a(α)), 4.01 (dd, 1H, $J_{5'b,4'}$ = 6.5 Hz, J_{gem} = 9.4 Hz, H-5'b(α)), 3.89–3.83 (m, 3H, H-3(α), H-3(β), H-5'b(β)), 3.67–3.63 (m, 2H, H-5(α), H-5(β)), 3.59–3.52 (m, 2H, H-4(α), H-4(β)), 3.32 (s, 3H, OCH_3(β)), 3.23 (s, 3H, OCH_3(α)), 1.31 (d, 3H, $J_{6,5}$ = 6.2 Hz, H-6(α)), 1.29 (d, 3H, $J_{6,5}$ = 6.2 Hz, H-6(β)); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 166.0 (C=O), 165.9 (C=O), 138.73 (Ar), 138.65 (Ar), 138.4 (Ar), 138.3 (Ar), 137.89 (Ar), 137.88 (Ar), 137.83 (Ar), 133.02 (Ar), 132.99 (Ar), 130.07 (Ar), 129.84 (Ar), 129.80 (Ar), 129.77 (Ar), 128.5 (Ar), 128.4 (Ar), 128.31 (Ar), 128.28 (Ar), 128.2 (Ar), 128.0 (Ar), 127.9 (Ar), 127.83 (Ar), 127.79 (Ar), 127.7 (Ar), 127.6 (Ar), 127.56 (Ar), 127.52 (Ar), 127.49 (Ar), 127.48 (Ar), 127.46 (Ar), 127.4 (Ar), 107.8 (C-2'(α)), 105.0 (C-2'(β)), 100.9 (C-1(α), $J_{C1,H1}$ = 171.6 Hz), 100.3 (C-1(β), $J_{C1,H1}$ = 171.6 Hz), 88.3 (C-3'(α)), 84.5 (C-3'(β)), 83.0 (C-4'(β)), 81.8 (C-4'(α)), 80.7 (C-4(β)), 80.3 (C-4(α)), 79.2 (C-3(α)), 78.7 (C-3(β)), 75.1 (2C, ArCH$_2$(α), ArCH$_2$(β)), 72.9 (ArCH$_2$(β)), 72.5 (ArCH$_2$(α)), 72.4 (ArCH$_2$(α)), 72.1 (ArCH$_2$(β)), 72.0 (ArCH$_2$(β)), 71.9 (ArCH$_2$(α)), 70.3 (C-2(β)), 70.2 (C-5'(α)), 70.0 (C-5'(β)), 69.4 (C-2(α)), 68.1 (C-5(α)), 68.0 (C-5(β)), 64.1 (C-1'(β)), 63.6 (C-1'(α)), 54.65 (OCH$_3$(β)),

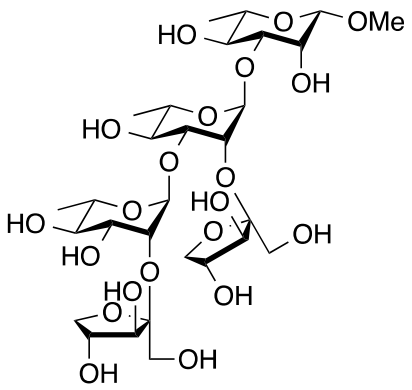
54.60 (O*C*H$_3$(α)), 18.05 (C-6(α)), 18.0 (C-6(β)); HRMS (ESI) calcd. for $C_{47}H_{50}NaO_{10}$ $[M+Na]^+$ 797.3296; found 797.3283.



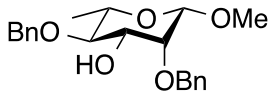
Cyclohexyl 3,4-*O*-xylylidene-α-D-xylulofuranoside (3.115α). To a solution of **3.94α** (13.7 mg, 0.0312 mmol) in CH_3OH (1.0 mL) was added sodium methoxide (0.13 mg, 0.00312 mmol) at room temperature. After stirring at room temperature for 30 min, the reaction mixture was neutralized by the addition of Amberlite IR-120 H^+ resin. The mixture was then filtered and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatography (3:1, hexane–EtOAc) to give **3.115α** (8.8 mg, 84%) as a colorless oil. $[\alpha]^{25}_D$ +105.1 (*c* 0.9, $CHCl_3$); TLC (2:1, hexane–EtOAc) R_f 0.37; ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.43–7.38 (m, 2H, ArH), 7.37–7.33 (m, 2H, ArH), 4.95 (d, 1H, J_{gem} = 12.7 Hz, ArC*H*$_2$), 4.91 (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} = 12.7 Hz, ArC*H*$_2$), 4.12 (ddd, 1H, $J_{4,3}$ = 5.0, $J_{4,5a}$ = 7.7 Hz, $J_{4,5b}$ = 9.0 Hz, H-4), 4.08 (d, 1H, $J_{3,4}$ = 5.0 Hz, H-3), 4.03 (dd, 1H, $J_{5a,4}$ = 7.7 Hz, J_{gem} = 8.4 Hz, H-5a), 3.76 (dd, 1H, $J_{5b,4}$ = 9.0 Hz, J_{gem} = 8.4 Hz, H-5b), 3.70–3.57 (m, 3H, cyclohexyl OC*H*, H-1a, H-1b), 2.66 (app t, 1H, $J_{OH,H1a}$ = $J_{OH,H1b}$ = 7.0 Hz, OH), 1.84–1.64 (m, 4H, cyclohexyl C*H*$_2$), 1.54–1.46 (m, 1H, cyclohexyl C*H*$_2$), 1.35–1.17 (m, 4H, cyclohexyl C*H*$_2$), 1.16–1.06 (m, 1H, cyclohexyl C*H*$_2$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 136.2 (Ar), 135.8 (Ar), 132.0 (Ar), 131.8 (Ar), 130.1 (Ar), 130.0 (Ar), 109.6 (C-2), 89.9 (C-3), 81.7 (C-4), 70.7 (cyclohexyl O*C*H), 69.8 (Ar*C*H$_2$), 68.9 (Ar*C*H$_2$), 68.1 (C-5), 62.3 (C-1), 35.1 (cyclohexyl *C*H$_2$), 34.5 (cyclohexyl *C*H$_2$), 25.5 (cyclohexyl *C*H$_2$), 24.8 (2C, cyclohexyl *C*H$_2$); HRMS (ESI) calcd. for $C_{19}H_{26}NaO_5$ $[M+Na]^+$ 357.1672; found 357.1667.



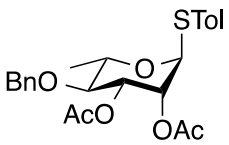
Cyclohexyl 3,4-*O*-xylylidene-β-D-xylulofuranoside (3.115β). To a solution of **3.94β** (27.3 mg, 0.0623 mmol) in CH_3OH (1.0 mL) was added sodium methoxide (0.25 mg, 0.00623 mmol) at room temperature. After stirring at room temperature for 30 min, the reaction mixture was neutralized by the addition of Amberlite IR-120 H^+ resin. The mixture was then filtered and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatography (2:1, hexane–EtOAc) to give **3.115β** (19.8 mg, 95%) as a colorless oil. **3.115β** was dissolved with minimal EtOAc, then slowly diffused with hexanes to obtain colorless crystal for X-ray crystallography. $[\alpha]^{25}_D$ –7.3 (*c* 0.3, $CHCl_3$); R_f 0.27 (2:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.40–7.32 (m, 4H, ArH), 5.05 (d, 1H, J_{gem} = 12.9 Hz, ArCH_2), 4.88 (d, 1H, J_{gem} = 12.9 Hz, ArCH_2), 4.86 (d, 1H, J_{gem} = 12.9 Hz, 1H, ArCH_2), 4.77 (d, 1H, J_{gem} = 12.9 Hz, ArCH_2), 4.39 (ddd, $J_{4,3}$ = 5.1 Hz, $J_{4,5a}$ = 7.7 Hz, $J_{4,5b}$ = 4.0 Hz, H-4), 4.23 (dd, 1H, $J_{5a,4}$ = 7.7 Hz, J_{gem} = 9.3 Hz, H-5a), 4.13 (d, 1H, $J_{3,4}$ = 5.1 Hz, H-3), 3.75 (dd, 1H, $J_{5b,4}$ = 4.0 Hz, J_{gem} = 9.3 Hz, H-5b), 3.67–3.60 (m, 3H, cyclohexyl OC*H*, H-1a, H-1b), 1.85–1.80 (m, 1H, cyclohexyl CH_2), 1.78–1.67 (m, 4H, cyclohexyl CH_2), 1.56–1.49 (m, 1H, cyclohexyl CH_2), 1.47–1.31 (m, 2H, cyclohexyl CH_2), 1.29–1.16 (m, 1H, CH_2), 1.14–1.03 (m, 1H, cyclohexyl CH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 136.4 (Ar), 136.1 (Ar), 131.6 (2C, Ar), 129.53 (Ar), 129.51 (Ar), 106.8 (C-2), 84.0 (C-3), 80.9 (C-4), 71.0 (C-5), 70.8 (cyclohexyl O*C*H), 70.1 (Ar*C*H_2), 68.8 (Ar*C*H_2), 62.5 (C-1), 34.8 (cyclohexyl *C*H_2), 34.4 (cyclohexyl *C*H_2), 25.4 (cyclohexyl *C*H_2), 25.1 (cyclohexyl *C*H_2), 25.0 (cyclohexyl *C*H_2); HRMS (ESI) calcd. for $C_{19}H_{26}NaO_5$ $[M+Na]^+$ 357.1672; found 357.1669.



Methyl β-D-xylulofuranosyl-(2→2)-α-L-rhamnopyranosyl-(1→3)-[β-D-xylulofuranosyl -(2→2)]-α-L-rhamnopyranosyl-(1→3)-β-L-rhamnopyranoside (**3.116**). To a solution of **3.131** (10.3 mg, 6.56 μmol) in EtOAc–CH_3OH (1:1, 1.0 mL) was added $Pd(OH)_2/C$ (20 mg) at room temperature. The reaction mixture was stirred under an H_2 atmosphere by exchange of three cycles of vacuum/H_2. After stirring for 1 h, the reaction mixture was filtered and the filtrate was concentrated under reduced pressure. The resulting residue was purified by gel filtration chromatography (Sephadex, LH-20) with 1:1 CH_3OH–H_2O as the eluent to give **3.116** (4.3 mg, 89%) as a colorless oil. $[\alpha]^{25}_D$ –9.7 (*c* 0.4, H_2O); R_f 0.21 (10:2:1:0.5, EtOAc–CH_3OH–H_2O–AcOH); ^{1}H NMR (D_2O, 500 MHz) δ 5.32 (br s, 1H), 5.15 (m, 1H), 4.62 (br s, 1H), 4.49–4.43 (m, 2H), 4.36–4.33 (m, 1H), 4.30–4.27 (m, 1H), 4.21–4.08 (m, 5H), 3.94–3.68 (m, 12H), 3.64–3.52 (m, 2H), 3.58 (s, 3H, OCH_3), 3.51–3.45 (m), 1.40 (d, 3H, *J* = 6.4 Hz), 1.38 (d, 3H, *J* = 6.4 Hz), 1.36 (d, 3H, *J* = 6.4 Hz); ^{13}C NMR (D_2O, 125 MHz) δ 106.07 (C-2), 106.01 (C-2), 101.9 (C-1', $J_{C1',H1'}$ = 175.7 Hz), 101.83 (C-1, $J_{C1,H1}$ = 159.3 Hz), 101.75 (C-1'', $J_{C1'',H1''}$ = 175.7 Hz), 80.2, 79.5, 78.3, 75.6, 75.0, 73.5, 73.0, 72.9, 72.8, 71.90, 71.87, 71.27, 71.23, 71.19, 70.4, 70.33, 70.25, 61.5, 57.8 (OCH_3), 17.7, 17.5, 17.3; HRMS (ESI) calcd. for $C_{29}H_{50}NaO_{21}$ $[M+Na]^+$ 757.2737; found 757.2740.

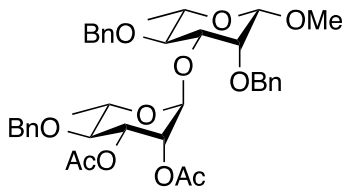


Methyl 2,4-di-*O*-benzyl-β-L-rhamnopyranoside (3.120). To a solution of **3.119**[37] (688 mg, 1.44 mmol) in CH_2Cl_2–H_2O (9:1, 15 mL) was added DDQ (489 mg, 2.16 mmol) at room temperature and the reaction mixture was stirred for 30 min. After the completion of reaction, the reaction mixture was diluted with EtOAc and washed with satd aq $NaHCO_3$ and brine. The organic layer was then dried with $MgSO_4$, filtered and the filtrate was concentrated. The resulting residue was purified by column chromatography (4:1, hexane–EtOAc) to give **3.120** (454 mg, 88%) as a colorless oil. $[\alpha]^{25}_D$ +95.4 (*c* 0.7, $CHCl_3$); R_f 0.31 (4:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.43–7.27 (m, 10H, ArH), 5.08 (d, 1H, J_{gem} = 11.9 Hz, ArCH_2), 4.93 (d, 1H, J_{gem} = 11.0 Hz, ArCH_2), 4.64 (d, 1H, J_{gem} = 11.0 Hz, ArCH_2), 4.63 (d, 1H, J_{gem} = 11.9 Hz, ArCH_2), 4.37 (d, 1H, $J_{1,2}$ = 0.8 Hz, H-1), 3.83 (dd, 1H, $J_{2,1}$ = 0.8 Hz, $J_{2,3}$ = 3.7 Hz, H-2), 3.64 (ddd, 1H, $J_{3,2}$ = 3.7 Hz, $J_{3,4}$ = 8.9 Hz, $J_{3,OH}$ = 9.8 Hz, H-3), 3.56 (s, 3H, OCH_3), 3.32 (app dq, 1H, $J_{5,6}$ = 6.1 Hz, $J_{5,4}$ = 8.9 Hz, H-5), 3.28 (app t, 1H, $J_{4,3}$ = $J_{4,5}$ = 8.9 Hz, H-4), 2.41 (d, 1H, $J_{OH,3}$ = 9.8 Hz, OH), 1.41 (d, 3H, $J_{6,5}$ = 6.1 Hz, H-6); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.48 (Ar), 138.46 (Ar), 128.5 (2C, Ar), 128.4 (2C, Ar), 128.2 (2C, Ar), 128.0 (2C, Ar), 127.9 (Ar), 127.7 (Ar), 102.7 (C-1, $J_{C1, H1}$ = 153.1 Hz), 82.2 (C-4), 78.1 (C-2), 75.1 (ArCH_2), 75.0 (ArCH_2), 74.0 (C-3), 71.4 (C-5), 57.1 (OCH_3), 18.0 (C-6); HRMS (ESI) calcd. for $C_{21}H_{26}NaO_5$ $[M+Na]^+$ 381.1672; found 381.1680.



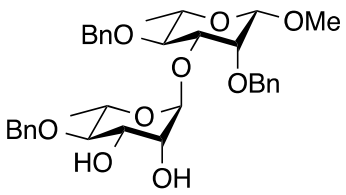
***p*-Tolyl 2,3-di-*O*-acetyl-4-*O*-benzyl-1-thio-α-L-rhamnopyranoside (3.123)**. To a solution of **3.121**[39] (70 mg, 0.175 mmol) in CH_2Cl_2 (2 mL) was added triethylamine (44.2 mg, 60.6 µL,

0.437 mmol), acetic anhydride (44.6 mg, 41.3 μL, 0.437 mmol) and 4-dimethylaminopyridine (2.1 mg, 0.0175 mmol) and the reaction mixture was stirred for 30 min. Excess acetic anhydride was quenched by the addition of CH_3OH and the solution was then concentrated under reduced pressure. The resulting residue was purified by column chromatography (4:1, hexane–EtOAc) to give **3.123** (71.5 mg, 92%) as a colorless syrup. $[\alpha]^{25}_D$ –111.3 (*c* 1.0, $CHCl_3$); R_f 0.63 (2:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 700 MHz) δ_H 7.37–7.33 (m, 4H, ArH), 7.32–7.27 (m, 3H, ArH), 7.12 (d, 1H, J = 8.1 Hz, ArH), 5.49 (dd, 1H, $J_{2,1}$ = 1.7 Hz, $J_{2,3}$ = 3.4 Hz, H-2), 5.32 (dd, 1H, $J_{3,2}$ = 3.4 Hz, $J_{3,4}$ = 9.6 Hz, H-3), 5.29 (d, 1H, $J_{1,2}$ = 1.7 Hz, H-1), 4.72 (d, 1H, J_{gem} = 11.3 Hz, ArCH_2), 4.66 (d, 1H, J_{gem} = 11.3 Hz, ArCH_2), , 4.31 (app dq, 1H, $J_{5,4}$ = 9.6 Hz, $J_{5,6}$ = 6.3 Hz, H-5), 3.57 (app t, 1H, $J_{4,3}$ = $J_{4,5}$ = 9.6 Hz, H-4), 2.32 (s, 3H, ArCH_3), 2.12 (s, 3H, CH_3CO), 1.99 (s, 3H, CH_3CO), 1.36 (d, 3H, $J_{6,5}$ = 6.3 Hz, H-6); ^{13}C NMR ($CDCl_3$, 175 MHz) δ_C 170.0 (C=O), 169.8 (C=O), 138.06 (Ar), 138.05 (Ar), 132.6 (2C, Ar), 129.9 (2C, Ar), 129.8 (Ar), 128.5 (2C, Ar), 127.9 (Ar), 127.7 (2C, Ar), 86.1 (C-1, $J_{C1,H1}$ = 172.3 Hz), 79.0 (C-4), 75.1 (ArCH$_2$), 71.9 (C-3), 71.9 (C-2), 69.1 (C-5), 21.1 (ArCH$_3$), 21.0 (CH$_3$CO), 20.9 (CH$_3$CO), 17.9 (C-6); HRMS (ESI) calcd. for $C_{24}H_{28}NaO_6S$ $[M+Na]^+$ 467.1499; found 467.1496.

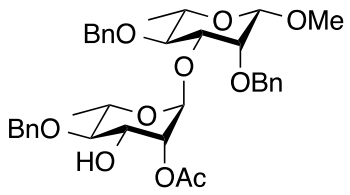


Methyl 2,3-di-*O*-acetyl-4-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-2,4-di-*O*-benzyl-β-L-rhamnopyranoside (3.124). A mixture of the **3.120** (45.4 mg, 0.102 mmol) and **3.123** (33.3 mg, 0.093 mmol) and 4Å molecular sieves in CH_2Cl_2 (1.0 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to 0 °C and *N*-iodosuccinimide (27.5

mg, 0.122 mmol) and silver triflate (2.6 mg, 0.0102 mmol) were added. After stirring for 15 min, triethylamine was added. The reaction mixture was warmed to room temperature and then a small amount of water was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The solution was then dried over $MgSO_4$, filtered and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatography (4:1, hexane–EtOAc) to give **3.124** (55.5 mg, 88%) as a colorless oil. $[\alpha]^{25}_D$ +4.6 (*c* 0.9, $CHCl_3$); R_f 0.27 (4:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 700 MHz) δ_H 7.50–7.47 (m, 2H, ArH), 7.36–7.28 (m, 9H, ArH), 7.27–7.24 (m, 3H, ArH), 7.19–7.15 (m, 1H, ArH), 5.41 (dd, 1H, $J_{2',1'}$ = 1.9 Hz, $J_{2',3'}$ = 3.5 Hz, H-2'), 5.39 (dd, 1H, $J_{3',2'}$ = 3.5 Hz, $J_{3',4'}$ = 9.7 Hz, H-3'), 5.05 (d, 1H, J_{gem} = 12.2 Hz, ArCH_2), 5.04 (d, 1H, $J_{1',2'}$ = 1.9 Hz, H-1'), 4.83 (d, 1H, J_{gem} = 11.0 Hz, ArCH_2), 4.78 (d, 1H, J_{gem} = 12.2 Hz, ArCH_2), 4.66 (d, 2H, J_{gem} = 11.0 Hz, ArCH_2), 4.58 (d, 1H, J_{gem} = 11.0 Hz, ArCH_2) 4.34 (br s, 1H, H-1), 3.81 (d, 1H, $J_{2,3}$ = 1.8 Hz, H-2), 3.75 (app dq, 1H, $J_{5',6'}$ = 6.2 Hz, $J_{5',4'}$ = 9.7 Hz, H-5'), 3.68–3.66 (m, 2H, H-3, H-4), 3.53 (s, 3H, OCH_3), 3.44 (app t, $J_{4',3'}$ = $J_{4',5'}$ = 9.7 Hz, H-4'), 3.33 (app dq, 1H, $J_{5,6}$ = 6.3 Hz, $J_{5,4}$ = 9.3 Hz, H-5), 2.05 (s, 3H, CH_3CO), 1.97 (s, 3H, CH_3CO), 1.38 (d, 3H, $J_{6,5}$ = 6.3 Hz, H-6), 1.21 (d, 3H, $J_{6',5'}$ = 6.3 Hz, H-6'); ^{13}C NMR ($CDCl_3$, 175 MHz) δ_C 169.74 (C=O), 169.65 (C=O), 138.5 (Ar), 138.3 (Ar), 138.1 (Ar), 128.33 (2C, Ar), 128.31 (2C, Ar), 128.25 (2C, Ar), 128.0 (2C, Ar), 127.9 (2C, Ar), 127.6 (2C, Ar), 127.4 (2C, Ar), 102.6 (C-1, $J_{C1,H1}$ = 153.5 Hz), 99.5 (C-1', $J_{C1',H1'}$ = 175.6 Hz), 80.6 (C-3), 80.5 (C-4), 78.6 (C-4'), 77.6 (C-2), 75.4 (Ar*C*H$_2$), 74.6 (Ar*C*H$_2$), 74.2 (Ar*C*H$_2$), 72.0 (C-5), 71.5 (C-3'), 70.3 (C-2'), 68.2 (C-5'), 57.1 (OCH_3), 20.9 (*C*H$_3$CO), 20.8 (*C*H$_3$CO), 17.93 (C-6), 17.90 (C-6'); HRMS (ESI) calcd. for $C_{38}H_{46}NaO_{11}$ $[M+Na]^+$ 701.2932; found 701.2932.

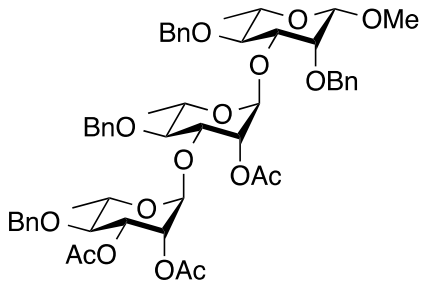


Methyl 4-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-2,4-di-*O*-benzyl-β-L-rhamnopyranoside (3.125). To a solution of **3.124** (48 mg, 0.076 mmol) in CH_3OH (1 mL) was added sodium methoxide (0.3 mg, 7.6 μmol) and the reaction mixture was stirred at room temperature for 1 h. The reaction mixture was then neutralized by the addition of Amberlite IR-120 H^+ resin. The reaction mixture was filtered and then concentrated under reduced pressure. The resulting residue was purified by column chromatography (1:1, hexane–EtOAc) to give **3.125** (39 mg, 87%) as a colorless oil. $[\alpha]^{25}_D$ +31.9 (*c* 0.3, $CHCl_3$); R_f 0.23 (1:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.44–7.40 (m, 2H, ArH), 7.38–7.27 (m, 12H, ArH), 7.23–7.18 (m, 1H, ArH), 5.06 (d, 1H, $J_{1',2'}$ = 1.4 Hz, H-1'), 5.00 (d, 1H, J_{gem} = 12.3 Hz, ArCH_2), 4.74–4.65 (m, 5H, ArCH_2), 4.35 (s, 1H, H-1), 3.87 (app dt, 1H, $J_{2',1'}$ = 1.4 Hz, $J_{2',3'} = J_{2',OH}$ = 3.6 Hz, H-2'), 3.83 (ddd, 1H, $J_{3',2'}$ = 3.6 Hz, $J_{3',4'}$ = 9.4 Hz, $J_{3',OH'}$ = 4.9 Hz, H-3'), 3.78 (d, 1H, $J_{2,3}$ = 2.5 Hz, H-2), 3.69–3.64 (m, 2H, H-3, H-5'), 3.61 (app t, 1H, $J_{4,3} = J_{4,5}$ = 9.6 Hz, H-4), 3.52 (s, 3H, OCH_3), 3.33 (app dq, 1H, $J_{5,4}$ = 9.6 Hz, $J_{5,6}$ = 6.2 Hz, H-5), 3.29 (app t, $J_{4',3'} = J_{4',5'}$ = 9.4 Hz, H-4'), 2.22 (d, 1H, $J_{OH,3'}$ = 4.9 Hz, OH), 2.02 (d, 1H, $J_{OH,2'}$ = 3.6 Hz, OH), 1.39 (d, 3H, $J_{6,5}$ = 6.2 Hz, H-6), 1.22 (d, 3H, $J_{6',5'}$ = 6.2 Hz, H-6'); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.8 (Ar), 138.5 (Ar), 138.2 (Ar), 128.6 (4C, Ar), 128.2 (2C, Ar), 127.9 (4C, Ar), 127.8 (2C, Ar), 127.75 (2C, Ar), 127.4 (Ar), 102.6 (C-1, $J_{C1,H1}$ = 153.1 Hz), 101.5 (C-1', $J_{C1',H1'}$ = 172.3 Hz), 81.5 (C-4'), 81.3 (C-4), 80.2 (C-3), 78.0 (C-2), 75.6 (ArCH_2), 74.7 (ArCH_2), 74.3 (ArCH_2), 72.1 (C-5), 71.3 (C-2'), 71.2 (C-3'), 67.9 (C-5'), 57.2 (OCH_3), 18.0 (2C, C-6, C-6'); HRMS (ESI) calcd. for $C_{34}H_{42}NaO_9$ $[M+Na]^+$ 617.2721; found 617.2734.



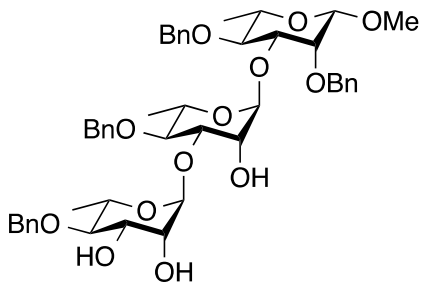
Methyl 2-*O*-acetyl-4-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-2,4-di-*O*-benzyl-β-L-rhamnopyranoside (3.126). To a solution of **3.125** (35.5 mg, 0.060 mmol) in acetonitrile (1.0 mL) was added triethyl orthoacetate (8.6 mg, 9.2 mL, 0.072 mmol) and *p*-toluenesulfonic acid (1.0 mg, 6.0 μmol) at room temperature. After stirring for 1 h, triethylamine was added and the solution was concentrated. The residue was then dried *in vacuo* for 30 min. The residue was then dissolved in 80% aq AcOH and stirred for 30 min at room temperature. The reaction mixture was then diluted with EtOAc and washed with water, satd aq $NaHCO_3$ and brine. The organic layer was then dried with $MgSO_4$, filtered and the filtrate was concentrated. The resulting residue was purified by column chromatography (4:1, hexane–EtOAc) to give **3.126** (31.3 mg, 88%) as a colorless oil. $[\alpha]^{25}_D$ +18.1 (*c* 1.7, $CHCl_3$); R_f 0.21 (4:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 700 MHz) δ_H 7.44–7.41 (m, 2H, ArH), 7.37–7.26 (m, 12H, ArH), 7.22–7.18 (m, 1H, ArH), 5.23 (dd, 1H, $J_{2',1'}$ = 1.7 Hz, $J_{2',3'}$ = 3.6 Hz, H-2'), 5.05 (d, 1H, $J_{1',2'}$ = 1.7 Hz, H-1'), 5.02 (d, 1H, J_{gem} = 12.2 Hz, ArCH_2), 4.83 (d, 1H, J_{gem} = 11.1 Hz, ArCH_2), 4.77 (d, 1H, J_{gem} = 11.3 Hz, ArCH_2), 4.70 (d, 1H, J_{gem} = 12.3 Hz, ArCH_2), 4.65 (d, 1H, J_{gem} = 11.3 Hz, ArCH_2), 4.63 (d, 1H, J_{gem} = 11.1 Hz, ArCH_2), 4.33 (d, 1H, $J_{1,2}$ = 0.5 Hz, H-1), 4.02 (app dt, 1H, $J_{3',2'} = J_{3',OH}$ = 3.9 Hz, $J_{3',4'}$ = 8.9 Hz, H-3'), 3.78 (dd, 1H, $J_{2,1}$ = 0.5 Hz, $J_{2,3}$ = 2.9 Hz, H-2), 3.70 (app dq, 1H, $J_{5',6'}$ = 6.3 Hz, $J_{5',4'}$ = 9.5 Hz, H-5'), 3.67 (dd, 1H, $J_{3,2}$ = 2.8 Hz, $J_{3,4}$ = 9.5 Hz, H-3), 3.63 (app t, 1H, $J_{4,3} = J_{4,5}$ = 9.5 Hz, H-4), 3.51 (s, 3H, OCH_3), 3.31 (app dq, $J_{5,6}$ = 6.3 Hz, $J_{5,4}$ = 9.1 Hz, H-5), 3.30 (app t, $J_{4',3'} = J_{4',5'}$ = 9.4 Hz, H-4'), 2.07 (s, 3H, CH_3CO), 2.02 (d, 1H, $J_{OH,\,3'}$ = 3.9 Hz, OH), 1.35 (d, 3H, $J_{6,5}$ = 6.2 Hz, H-6), 1.24 (d, 3H, $J_{6',5'}$ = 6.2 Hz, H-6'); ^{13}C NMR ($CDCl_3$, 175 MHz) δ_C 170.6

(C=O), 138.7 (Ar), 138.5 (Ar), 138.1 (Ar), 128.5 (2C, Ar), 128.4 (2C, Ar), 128.2 (2C, Ar), 128.1 (2C, Ar), 127.8 (Ar), 127.7 (2C, Ar), 127.3 (Ar), 102.5 (C-1), 99.3 (C-1'), 81.4 (C-4'), 80.8 (C'4), 80.1 (C-3), 78.0 (C-2), 75.4 (Ar*C*H_2), 74.8 (Ar*C*H_2), 74.4 (Ar*C*H_2), 72.6 (C-2'), 72.1 (C-5), 70.2 (C-3'), 68.1 (C-5'), 57.1 (OCH_3), 21.0 (*C*H_3CO), 18.01 (C-6), 17.96 (C-6)'; HRMS (ESI) calcd. for $C_{36}H_{44}NaO_{10}$ $[M+Na]^+$ 659.2827; found 659.2826.



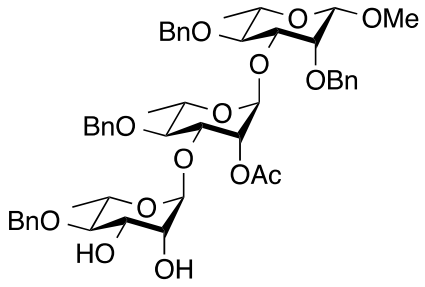
Methyl 2,3-di-*O*-acetyl-4-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-acetyl-4-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-2,4-di-*O*-benzyl-β-L-rhamnopyranoside (3.127). A mixture of **3.123** (34.1 mg, 0.0767 mmol), **3.126** (40.7 mg, 0.0639 mmol) and 4Å molecular sieves in CH_2Cl_2 (2.0 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to 0 °C and and then *N*-iodosuccinimide (20.7 mg, 0.0920 mmol) and silver triflate (2.0 mg, 7.7 μmol) were added. After stirring for 30 min, triethylamine was added. The solution was warmed to room temperature and then a small amount of water was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The solution was then dried over $MgSO_4$, filtered and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatography (4:1, hexane–EtOAc) to give **3.127** (58.1 mg, 95%) as a colorless syrup. $[\alpha]^{25}_D$ –8.0 (*c* 0.9, $CHCl_3$); R_f 0.37 (4:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 700 MHz) δ_H 7.44–7.41 (m, 2H, ArH), 7.38–7.35 (m, 2H, ArH), 7.34–7.30 (m, 6H, ArH), 7.30–7.26 (m, 9H, ArH), 7.18–7.15 (m, 1H, ArH), 5.34 (dd, 1H, $J_{2',1'}$ = 1.7 Hz, $J_{2',3'}$ = 3.3 Hz, H-2'), 5.31

(dd, 1H, $J_{2'',1''}$ = 2.0 Hz, $J_{2'',3''}$ = 3.2 Hz, H-2''), 5.27 (dd, 1H, $J_{3'',2''}$ = 3.2 Hz, $J_{3'',4''}$ = 9.6 Hz, H-3''), 5.07 (d, 1H, $J_{1',2'}$ = 1.5 Hz, H-1'), 5.04 (d, 1H, J_{gem} = 12.1 Hz, ArCH_2), 4.93 (d, 1H, $J_{1'',2''}$ = 1.8 Hz, H-1''), 4.90 (d, 1H, J_{gem} = 10.8 Hz, ArCH_2), 4.80 (d, 1H, J_{gem} = 11.2 Hz, ArCH_2), 4.68 (d, 1H, J_{gem} = 12.1 Hz, ArCH_2), 4.67 (d, 1H, J_{gem} = 11.6 Hz, ArCH_2), 4.62 (d, 1H, J_{gem} = 11.6 Hz, ArCH_2), 4.61 (d, 1H, J_{gem} = 11.2 Hz, ArCH_2), 4.57 (d, 1H, J_{gem} = 10.8 Hz, ArCH_2), 4.33 (br s, 1H, H-1), 4.08 (dd, 1H, $J_{3',2'}$ = 3.4 Hz, $J_{3',4'}$ = 9.6 Hz, H-3'), 3.90 (app dq, 1H, $J_{5'',6''}$ = 6.4 Hz, $J_{5'',4''}$ = 9.6 Hz, H-5''), 3.79 (d, 1H, $J_{2,3}$ = 2.8 Hz, H-2), 3.70 (app dq, 1H, $J_{5',6'}$ = 6.4 Hz, $J_{5',4'}$ = 9.7 Hz, H-5'), 3.67 (dd, 1H, $J_{3,2}$ = 2.8 Hz, $J_{3,4}$ = 9.4 Hz, H-3), 3.63 (app t, 1H, $J_{4,3} = J_{4,5}$ = 9.4 Hz, H-4), 3.52 (s, 3H, OCH_3), 3.46 (app t, 1H, $J_{4'',3''} = J_{4'',5''}$ = 9.4 Hz, H-4''), 3.45 (app t, $J_{4',3'} = J_{4',5'}$ = 9.4 Hz, H-4'), 3.30 (app dq, 1H, $J_{5,6}$ = 6.2 Hz, $J_{5,4}$ = 9.4 Hz, H-5), 2.14 (s, 3H, CH_3CO), 2.06 (s, 3H, CH_3CO), 1.95 (s, 3H, CH_3CO), 1.32 (d, 3H, $J_{6,5}$ = 6.2 Hz, H-6), 1.24 (d, 3H, $J_{6'',5''}$ = 6.4 Hz, H-6''), 1.21 (d, 3H, $J_{6',5'}$ = 6.4 Hz, H-6'); ^{13}C NMR ($CDCl_3$, 175 MHz) δ_C 170.1 (C=O), 169.9 (C=O), 169.8 (C=O), 138.7 (Ar), 138.24 (Ar), 138.23 (Ar), 138.0 (Ar), 128.5 (2C, Ar), 128.39 (2C, Ar), 128.36 (2C, Ar), 128.25 (2C, Ar), 128.2 (2C, Ar), 127.81 (Ar), 127.76 (2C, Ar), 127.75 (2C, Ar), 127.72 (Ar), 127.70 (2C, Ar), 127.5 (Ar), 127.3 (Ar), 102.6 (C-1, $J_{C1,H1}$ = 155.3 Hz), 99.4 (C-1'', $J_{C1'',H1''}$ = 174.9 Hz), 99.2 (C-1', $J_{C1',H1'}$ = 174.9 Hz), 80.6 (C-3), 80.5 (C-4), 80.3 (C-4'), 78.4 (C-4''), 78.1 (C-2), 76.8 (C-3'), 75.5 (ArCH$_2$), 75.2 (ArCH$_2$), 74.41 (ArCH$_2$), 74.39 (ArCH$_2$), 72.1 (C-2'), 72.0 (C-5), 71.4 (C-3''), 70.4 (C-2''), 68.5 (C-5''), 68.4 (C-5'), 57.1 (OCH$_3$), 21.0 (CH$_3$CO), 20.9 (CH$_3$CO), 20.8 (CH$_3$CO), 17.93 (C-6), 17.91 (2C, C-6', C-6''); HRMS (ESI) calcd. for $C_{53}H_{64}NaO_{16}$ $[M+Na]^+$ 979.4087; found 979.4094.



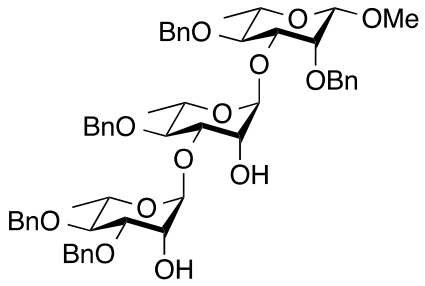
Methyl 4-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-2,4-di-*O*-benzyl-β-L-rhamnopyranoside (3.128). To a solution of **3.127** (58.1 mg, 0.0607 mmol) in CH_3OH (2.0 mL) was added sodium methoxide (1 mg, 0.0243 mmol) and the reaction mixture was stirred for 1 day. The reaction mixture was then neutralized by the addition of Amberlite IR-120 H^+ resin. The mixture was then filtered and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatography (4:1, hexane–EtOAc) to give **3.128** (46.0 mg, 89%) as a colorless oil and **3.129** (7.1 mg, 11%) as a colorless oil. $[\alpha]^{25}_{D}$ +0.8 (*c* 1.0, $CHCl_3$); R_f 0.33 (2:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 700 MHz) δ_H 7.45–7.42 (m, 2H, ArH), 7.38–7.26 (m, 17H, ArH), 7.20–7.17 (m, 1H, ArH), 5.08 (d, 1H, $J_{1',2'}$ = 1.4 Hz, H-1'), 5.03 (d, 1H, J_{gem} = 12.1 Hz, ArCH_2), 5.02 (d, 1H, $J_{1'',2''}$ = 1.8 Hz, H-1''), 4.75 (d, 1H, J_{gem} = 11.0 Hz, ArCH_2), 4.72 (s, 2H, ArCH_2), 4.70 (d, 1H, J_{gem} = 12.1 Hz, ArCH_2), 4.64 (d, 1H, J_{gem} = 11.0 Hz, ArCH_2), 4.63 (d, 1H, J_{gem} = 11.0 Hz, ArCH_2), 4.59 (d, 1H, J_{gem} = 11.0 Hz, ArCH_2), 4.35 (br s, 1H, H-1), 3.98–3.96 (m, 1H, H-2'), 3.94 (dd, 1H, $J_{3',2'}$ = 3.5 Hz, $J_{3',4'}$ = 9.4 Hz, H-3'), 3.88–3.84 (m, 1H, H-3''), 3.83–3.81 (m, 1H, H-2''), 3.79 (d, 1H, $J_{2,3}$ = 2.6 Hz, H-2), 3.78 (app dq, 1H, $J_{5'',6''}$ = 6.4 Hz, $J_{5'',4''}$ = 9.3 Hz, H-5''), 3.67 (dd, 1H, $J_{3,2}$ = 2.6 Hz, $J_{3,4}$ = 9.6 Hz, H-3), 3.66 (app dq, 1H, $J_{5',6'}$ = 6.3 Hz, $J_{5',4'}$ = 9.5 Hz, H-5'), 3.62 (app t, 1H, $J_{4,3}$ = $J_{4,5}$ = 9.6 Hz, H-4), 3.52 (s, 3H, OCH_3), 3.39 (app t, 1H, $J_{4',3'}$ = $J_{4',5'}$ = 9.5 Hz, H-4'), 3.34 (app t, $J_{4'',3''}$ = $J_{4'',5''}$ = 9.3 Hz, H-4''), 3.33 (app dq, 1H, $J_{5,6}$ = 6.2 Hz, $J_{5,4}$ = 9.4 Hz, H-5), 2.29 (d, 1H, $J_{OH,3''}$ = 5.2 Hz, 3''-OH), 2.11 (d, 1H, $J_{OH,2''}$ = 3.8 Hz, 2''-OH), 2.06 (d, 1H, $J_{OH,2'}$ = 3.0 Hz, 2'-OH), 1.37 (d, 3H, $J_{6,5}$ = 6.2

Hz, H-6), 1.27 (d, 3H, $J_{6'',5''}$ = 6.4 Hz, H-6''), 1.19 (d, 3H, $J_{6',5'}$ = 6.3 Hz, H-6'); ^{13}C NMR ($CDCl_3$, 175 MHz) δ_C 138.7 (Ar), 138.4 (Ar), 138.1 (Ar), 138.0 (Ar), 128.7 (2C, Ar), 128.6 (2C, Ar), 128.4 (2C, Ar), 128.2 (2C, Ar), 128.1 (Ar), 128.04 (2C, Ar), 127.96 (2C, Ar), 127.94 (Ar), 127.8 (2C, Ar), 127.7 (Ar), 127.6 (2C, Ar), 127.4 (Ar), 102.6 (C-1, $J_{C1,H1}$ = 154.5 Hz), 101.5 (C-1', $J_{C1',H1'}$ = 172.5 Hz), 101.1 (C-1'', $J_{C1'',H1''}$ = 172.5 Hz), 81.4 (C-4''), 80.8 (C-4), 80.6 (C-4'), 80.5 (C-3), 78.9 (C-3'), 78.3 (C-2), 75.5 (ArCH_2), 75.20 (ArCH_2), 75.18 (ArCH_2), 74.4 (ArCH_2), 72.0 (C-5), 71.4 (C-2''), 71.3 (C-3''), 71.2 (C-2'), 68.2 (C-5''), 68.1 (C-5'), 57.2 (OCH_3), 18.1 (C-6), 17.94 (C-6''), 17.87 (C-6'); HRMS (ESI) calcd. for $C_{47}H_{58}NaO_{13}$ $[M+Na]^+$ 853.3770; found 853.3761.



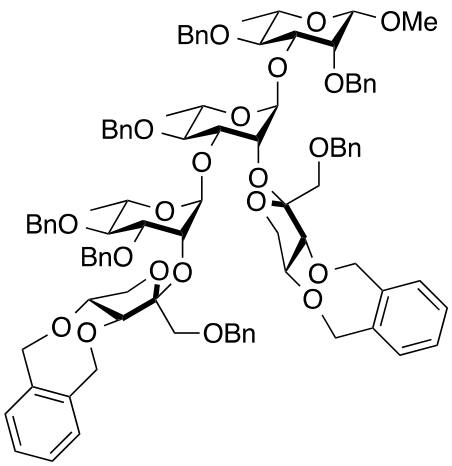
Methyl 4-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-acetyl-4-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-2,4-di-*O*-benzyl-β-L-rhamnopyranoside (3.129). $[\alpha]^{25}_D$ –2.4 (*c* 1.0, $CHCl_3$); R_f 0.46 (2:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 700 MHz) δ_H 7.44–7.42 (m, 2H, ArH), 7.38–7.24 (m, 17H, ArH), 7.19–7.16 (m, 1H, ArH), 5.29 (dd, 1H, $J_{2',1'}$ = 1.9 Hz, $J_{2',3'}$ = 3.3 Hz, H-2'), 5.06–5.03 (m, 2H, H-1', ArCH_2), 4.94 (d, 1H, $J_{1'',2''}$ = 1.5 Hz, H-1''), 4.91 (d, 1H, J_{gem} = 10.9 Hz, ArCH_2), 4.73 (d, 1H, J_{gem} = 11.6 Hz, ArCH_2), 4.69 (d, 1H, J_{gem} = 11.4 Hz, ArCH_2), 4.67 (d, 1H, J_{gem} = 12.4 Hz, ArCH_2), 4.63 (d, 1H, J_{gem} = 11.4 Hz, ArCH_2), 4.60–4.57 (m, 2H, ArCH_2), 4.33 (bs, 1H, H-1), 4.08 (d, 1H, $J_{3',2'}$ = 3.3 Hz, $J_{3',4'}$ = 9.4 Hz, H-3'), 3.82–3.76 (m, 4H, H-2, H-2'', H-3'', H-5''), 3.70 (dq, 1H, $J_{5',6'}$ = 6.3 Hz, $J_{5',4'}$ = 9.4 Hz, H-5'), 3.67–3.61 (m, 2H,

H-3, H-4), 3.51 (s, 3H, OCH_3), 3.39 (app t, 1H, $J_{4',3'} = J_{4',5'}$ = 9.4 Hz, H-4'), 3.31–3.28 (m, 2H, H-5, H-4''), 2.17 (d, 1H, $J_{OH,3''}$ = 5.0 Hz, 3''-OH), 2.08 (s, 3H, COCH_3), 2.00 (d, 1H, $J_{OH,2''}$ = 3.7 Hz, 2''-OH), 1.31 (d, 3H, $J_{6,5}$ = 6.2 Hz, H-6), 1.24 (d, 3H, $J_{6'',5''}$ = 6.4 Hz, H-6''), 1.20 (d, 3H, $J_{6',5'}$ = 6.3 Hz, H-6'); ^{13}C NMR ($CDCl_3$, 175 MHz) δ_C 170.1 (C=O), 138.9 (Ar), 138.50 (Ar), 138.45 (Ar), 138.2 (Ar), 128.8 (2C, Ar), 128.7 (2C, Ar), 128.60 (2C, Ar), 128.59 (2C, Ar), 128.4 (Ar), 128.2 (3C, Ar), 128.0 (Ar), 127.9 (Ar), 127.8 (2C, Ar), 127.7 (Ar), 127.6 (Ar), 102.7 (C-1, $J_{C1,H1}$ = 153.3 Hz), 101.6 (C-1'', $J_{C1'',H1''}$ = 172.3 Hz), 99.5 (C-1', $J_{C1',H1'}$ = 174.5 Hz), 81.5 (C-4''), 81.1 (C-3), 80.8 (C-4'), 80.5 (C-4), 78.5 (C-2), 76.8 (C-3'), 75.7 (ArCH$_2$), 75.3 (ArCH$_2$), 74.8 (ArCH$_2$), 74.7 (ArCH$_2$), 72.5 (C-2'), 72.2 (C-5), 71.4 (C-2'' or C-3''), 71.2 (C-2'' or C-3''), 68.6 (C-5'), 68.2 (C-5''), 57.2 (OCH$_3$), 21.1 (COCH$_3$), 18.15 (C-6, C-6' or C-6''), 18.11 (2C, C-6, C-6' or C-6''); HRMS (ESI) calcd. for $C_{49}H_{60}NaO_{14}$ $[M+Na]^+$ 895.3875 found 895.3884.



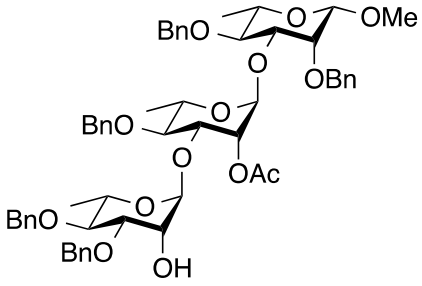
Methyl 3,4-di-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-2,4-di-*O*-benzyl-β-L-rhamnopyranoside (3.130). To a solution of **3.128** (23.0 mg, 0.0277 mmol) in toluene (10.0 mL) was added di-*n*-butyltin oxide (10.3 mg, 0.0415 mmol) and the reaction mixture was stirred at reflux for 3 h. The mixture was then cooled to room temperature before tetrabutylammonium bromide (13.4 mg, 0.0415 mmol) and benzyl bromide (7.1 mg, 4.9 μL, 0.0415 mmol) were added. After stirring for 1 h at reflux, the solution was then cooled to room temperature and concentrated under reduced pressure. The resulting residue was purified

by column chromatography (2:1, hexane–EtOAc) to give **3.130** (24.4 mg, 96%) as a colorless oil. $[\alpha]^{25}_{D}$ +1.2 (*c* 1.0, $CHCl_3$); R_f 0.67 (1:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 700 MHz) δ_H 7.46–7.42 (m, 2H, ArH), 7.39–7.27 (m, 22H, ArH), 7.21–7.16 (m, 1H, ArH), 5.11–5.08 (m, 2H, H-1', H-1''), 5.04 (d, 1H, J_{gem} = 12.8 Hz, ArCH_2), 4.88 (d, 1H, J_{gem} = 11.0 Hz, ArCH_2), 4.76 (d, 1H, J_{gem} = 11.0 Hz, ArCH_2), 4.72 (d, 1H, J_{gem} = 12.8 Hz, ArCH_2), 4.67–4.60 (m, 5H, ArCH_2), 4.55 (d, 1H, J_{gem} = 11.0 Hz, ArCH_2), 4.36 (br s, 1H, H-1), 4.02–3.99 (m, 1H, H-2''), 3.95 (dd, 1H, $J_{3'',2''}$ = 3.6 Hz, $J_{3'',4''}$ = 9.2 Hz, H-3''), 3.94-3.92 (m, 1H, H-2'), 3.85–3.78 (m, 3H, H-2, H-3', H-5'), 3.69–3.61 (m, 3H, H-3, H-4, H-5''), 3.54 (s, 3H, OCH_3), 3.49 (app t, 1H, $J_{4',3'}$ = $J_{4',5'}$ = 9.2 Hz, H-4'), 3.39 (app t, 1H, $J_{4'',3''}$ = $J_{4'',5''}$ = 9.2 Hz, H-4''), 3.34 (app dq, 1H, $J_{5,6}$ = 6.2 Hz, $J_{5,4}$ = 8.8 Hz, H-5), 2.39 (d, 1H, $J_{OH,2'}$ = 1.9 Hz, 2'-OH), 2.03 (d, 1H, $J_{OH,2''}$ = 3.0 Hz, 2''-OH),1.39 (d, 3H, $J_{6,5}$ = 6.2 Hz, H-6), 1.27 (d, 3H, $J_{6'',5''}$ = 6.2 Hz, H-6''), 1.19 (d, 3H, $J_{6',5'}$ = 6.2 Hz, H-6'); ^{13}C NMR ($CDCl_3$, 175 MHz) δ_C 138.8 (Ar), 138.5 (Ar), 138.3 (Ar), 138.1 (Ar), 138.0 (Ar), 128.72 (2C, Ar), 128.70 (2C, Ar), 128.61 (2C, Ar), 128.56 (2C, Ar), 128.4 (2C, Ar), 128.2 (2C, Ar), 128.1 (2C, Ar), 128.04 (Ar), 128.0 (Ar), 127.97 (2C,Ar), 127.89 (2C, Ar), 127.84 (Ar), 127.7 (2C, Ar), 127.6 (Ar), 102.7 (C-1, $J_{C1,H1}$ = 153.5 Hz), 101.6 (C-1', $J_{C1',H1'}$ = 171.8 Hz), 101.0 (C-1'', $J_{C1'',H1''}$ = 171.8 Hz), 81.0 (C-4), 80.6 (C-3), 80.3 (C-4''), 79.90 (C-4'), 79.89 (C-3''), 79.5 (C-3'), 78.4 (C-2), 75.7 (Ar*C*H_2), 75.6 (Ar*C*H_2), 75.2 (Ar*C*H_2), 74.6 (Ar*C*H_2), 72.3 (Ar*C*H_2), 72.1 (C-5), 71.3 (C-2''), 69.0 (C-2'), 68.5 (C-5'), 68.2 (C-5''), 57.3 (OCH_3), 18.12 (C-6'), 18.08 (C-6), 17.98 (C-6''); HRMS (ESI) calcd. for $C_{54}H_{64}NaO_{13}$ $[M+Na]^+$ 943.4239; found 943.4228.



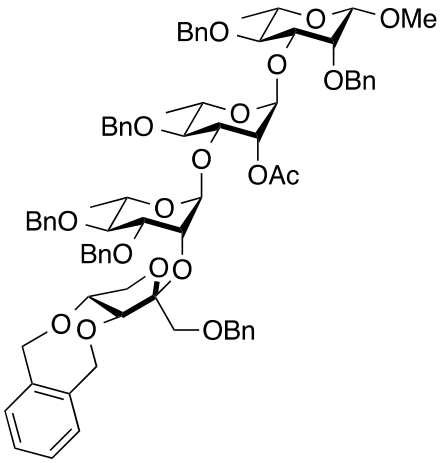
Methyl 1-*O*-benzyl-3,4-*O*-xylylidene-β-D-xylulofuranosyl-(2→2)-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-[1-*O*-benzyl-3,4-*O*-xylylidene-β-D-xylulofuranosyl-(2→2)]-4-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-2,4-di-*O*-benzyl-β-L-rhamnopyranoside (3.131β). A mixture of **3.70** (7.0 mg, 0.0155 mmol), **3.140** (16.1 mg, 0.0129 mmol) and 4 Å molecular sieves in CH_2Cl_2 (0.43 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –78 ^oC and then *N*-iodosuccinimide (4.2 mg, 0.0186 mmol) and silver triflate (0.8 mg, 3.1 μmol) were added. After stirring for 1 h at – 78 ºC, triethylamine was added. The reaction was warmed to room temperature and then a small amount of water was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The solution was then dried over $MgSO_4$, filtered and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatography (4:1, hexane–EtOAc) to give **3.131β** (11.7 mg, 58%) as a colorless oil. $[\alpha]^{25}_D$ +22.0 (*c* 1.1, $CHCl_3$); R_f 0.32 (2:1, hexane–EtOAc); ^1H NMR ($CDCl_3$, 700 MHz) δ_H 7.46–7.41 (m, 2H, ArH), 7.36–7.10 (m, 37H, ArH), 7.07–7.05 (m, 2H, ArH), 6.94–6.91 (m, 2H, ArH), 5.15 (br s, 1H), 5.09 (d, 1H, J_{gem} 11.7 Hz, ArCH_2), 5.01 (br s, 1H), 4.91 (d, 1H, J_{gem} = 11.7 Hz, ArCH_2), 4.87 (d, 1H, J_{gem} = 11.7 Hz, ArCH_2), 4.81–4.69 (m, 7H, ArCH_2), 4.63–4.55 (m, 5H), 4.47–4.31 (m, 9H), 4.21–4.10 (m, 7H), 3.91–3.82 (m, 3H),

3.74–3.70 (m, 1H), 3.63–3.47 (m, 14H), 3.31–3.26 (m, 1H), 1.28 (d, 3H, J = 6.7 Hz), 1.13 (d, 3H, J = 6.7 Hz), 1.04 (d, 3H, J = 6.7 Hz); ^{13}C NMR ($CDCl_3$, 175 MHz) δ_C 139.2, 138.9, 138.6, 138.5, 138.4, 137.0, 136.9, 136.8, 131.62, 131.60, 131.3, 131.1, 129.3, 129.2, 128.7, 128.6, 128.5, 128.4, 128.3, 128.15, 128.07, 128.0, 127.9, 127.7, 127.68, 127.58 ,127.5, 127.46, 127.43, 127.4, 127.3, 107.2, 107.1, 102.9, 101.8, 100.8, 82.1, 80.5, 80.1, 80.0, 79.1, 79.06, 75.6, 74.6, 74.5, 73.4, 73.3, 73.0, 72.8, 721, 70.4, 70.1, 69.5, 69.46, 69.43, 69.2, 68.9, 57.3, 18.7, 18.2, 18.1; HRMS (ESI) calcd. for $C_{94}H_{104}NaO_{21}$ $[M+Na]^+$ 1591.6962; found 1591.6966.



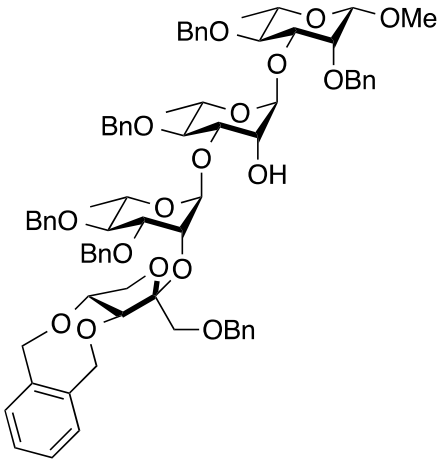
Methyl 3,4-di-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-acetyl-4-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-2,4-di-*O*-benzyl-β-L-rhamnopyranoside (3.132). To a solution of the **3.129** (18.0 mg, 0.0206 mmol) in toluene (5.0 mL) was added di-*n*-butyltin oxide (7.7 mg, 0.0309 mmol) and the reaction mixture was stirred at reflux for 3 h. The mixture was then cooled to room temperature before tetrabutylammonium bromide (10.0 mg, 0.0309 mmol) and benzyl bromide (5.3 mg, 3.7 μL, 0.0309 mmol) were added. After stirring for 1 h at reflux, the reaction mixture was moved to room temperature and concentrated under reduced pressure. The resulting residue was purified by column chromatography (4:1, hexane–EtOAc) to give **3.132** (16.0 mg, 81%) as a colorless oil. $[\alpha]^{25}_D$ –8.6 (*c* 0.6, $CHCl_3$); R_f 0.51 (2:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.44–7.41 (m, 2H, ArH), 7.39–7.24 (m, 22H, ArH), 7.20–7.15 (m, 1H, ArH), 5.30 (dd, 1H, $J_{2',1'}$ = 1.9 Hz, $J_{2',3'}$ = 3.3 Hz, H-2'), 5.07–5.03 (m, 2H, H-1', ArCH_2), 5.00

(d, 1H, $J_{1'',2''}$ = 1.6 Hz, H-1''), 4.93 (d, 1H, J_{gem} = 11.0 Hz, ArCH_2), 4.84 (d, 1H, J_{gem} = 11.0 Hz, ArCH_2), 4.71–4.52 (m, 7H, ArCH_2), 4.32 (br s, 1H, H-1), 4.08 (dd, 1H, $J_{3',2'}$ = 3.3 Hz, $J_{3',4'}$ = 9.3 Hz, H-3'), 3.91–3.89 (m, 1H, H-2''), 3.78 (d, 1H, $J_{2,1}$ = 2.4 Hz, H-2), 3.76–3.59 (m, 5H, H-3, H-4, H-5', H-3'', H-5''), 3.51 (s, 3H, OCH_3), 3.43 (app t, 1H, $J_{4'',3''} = J_{4'',5''}$ = 9.3 Hz, H-4''), 3.37 (app t, 1H, $J_{4',3'} = J_{4',5'}$ = 9.3 Hz, H-4'), 3.34 (m, 1H, H-5), 2.32 (d, 1H, $J_{OH,2''}$ = 2.2 Hz, 2''-OH), 2.07 (s, 3H, COCH_3), 1.31 (d, 3H, $J_{6,5}$ = 6.2 Hz, H-6), 1.20 (d, 3H, $J_{6'',5''}$ = 6.2 Hz, H-6''), 1.18 (d, 3H, $J_{6',5'}$ = 6.2 Hz, H-6'); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 170.0 (C=O), 138.9 (Ar), 138.6 (Ar), 138.5 (Ar), 138.3 (Ar), 138.2 (Ar), 128.72 (2C, Ar), 128.69 (2C, Ar), 128.59 (2C, Ar), 128.56 (2C, Ar), 128.54 (2C, Ar), 128.4 (2C, Ar), 128.2 (2C, Ar), 128.1 (Ar), 127.95 (Ar), 127.93 (2C,Ar), 127.87 (2C, Ar), 127.8 (Ar), 127.62 (2C, Ar), 127.57 (Ar), 102.7 (C-1, $J_{C1,H1}$ = 153.5 Hz), 101.4 (C-1'', $J_{C1'',H1''}$ = 171.8 Hz), 99.3 (C-1', $J_{C1',H1'}$ = 171.8 Hz), 81.1 (C-3), 80.5 (C-4), 80.4 (C-4'), 80.0 (C-4''), 79.9 (C-3''), 78.5 (C-2), 77.4 (C-3'), 75.7 (ArCH$_2$), 75.4 (ArCH$_2$), 75.1 (ArCH$_2$), 74.7 (ArCH$_2$), 72.5 (C-2'), 72.20 (ArCH$_2$), 72.18 (C-5), 69.2 (C-2''), 68.5 (C-5' or C-5''), 68.4 (C-5' or C-5''), 57.3 (OCH_3), 21.2 (COCH$_3$), 18.1 (2C, C-6, C-6' or C-6''), 18.0 (C-6, C-6' or C-6''); HRMS (ESI) calcd. for $C_{56}H_{66}NaO_{14}$ $[M+Na]^+$ 985.4345 found 985.4350.



Methyl 2-*O*-benzyl-3,4-*O*-xylylidene-β-D-xylulofuranosyl-(2→2)-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-acetyl-4-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-2,4-di-*O*-benzyl-β-L-rhamnopyranoside (3.133β). A mixture of **3.70** (30.6 mg, 0.068 mmol), **3.132** (60.1 mg, 0.0624 mmol), and 4Å molecular sieves in CH_2Cl_2 (2.0 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –78 °C and *N*-iodosuccinimide (18.4 mg, 0.0817 mmol) and silver triflate (1.8 mg, 6.8 μmol) were added. After stirring for 3 h at –78 °C, triethylamine was added. The reaction was warmed to room temperature and then a small amount of water was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The solution was then dried over $MgSO_4$, filtered and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatography (2:1, hexane–EtOAc) to give **3.133α** (21.0 mg, 26%) and **3.133β** (50.7 mg, 63%) both as colorless oils. Data for **3.133β:** $[\alpha]^{25}_D$ +3.9 (*c* 0.2, $CHCl_3$); R_f 0.13 (2:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.44–7.41 (m, 2H, ArH), 7.40–7.37 (m, 2H, ArH), 7.36–7.20 (m, 27H, ArH), 7.14–7.10 (m, 1H, ArH), 7.08–7.05 (m, 2H, ArH), 5.30 (dd, 1H, $J_{2',1'}$ = 1.9 Hz, $J_{2',3'}$ = 3.3 Hz, H-2'), 5.08–5.02 (m, 2H, H-1', ArCH_2), 4.99–4.91 (m, 3H, H-1'', ArCH_2), 4.87–4.45 (m, 11H, ArCH_2), 4.39–4.30 (m, 3H, H-1, H-4'''', ArCH_2), 4.23–4.17 (m, 2H, H-3'''', ArCH_2),

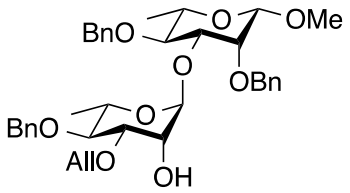
4.14–4.10 (m, 1H, H-3'), 4.08–4.06 (m, 1H, H-2''), 3.97–3.91 (m, 1H, H-5a''''), 3.79 (d, 1H, $J_{2,1}$ = 2.4 Hz, H-2), 3.76–3.59 (m, 5H, H-4, H-5', H-3'', H-4'', H-5''), 3.55–3.46 (m, 5H, OCH_3, H-1a'''', H-5b''''), 3.43 (d, 1H, J_{gem} = 11.0 Hz, H-1b''''), 3.36 (app t, 1H, $J_{4',3'} = J_{4',5'}$ = 9.3 Hz, H-4'), 3.33–3.26 (m, 1H, H-5), 2.06 (s, 3H, COCH_3), 1.31 (d, 3H, $J_{6,5}$ = 6.2 Hz, H-6), 1.16 (d, 3H, $J_{6',5'}$ = 6.2 Hz, H-6'), 1.14 (d, 3H, $J_{6'',5''}$ = 6.2 Hz, H-6''); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 170.1 (C=O), 139.0 (Ar), 138.9 (Ar), 138.7 (Ar), 138.6 (Ar), 138.5 (Ar), 138.3 (Ar), 136.9 (Ar), 136.7 (Ar), 131.6 (Ar), 131.2 (Ar), 129.4 (Ar), 129.3 (Ar), 128.8 (Ar), 128.6 (Ar), 128.5 (Ar), 128.43 (Ar), 128.37 (Ar), 128.1 (Ar), 128.0 (Ar), 127.76 (Ar), 127.75 (Ar), 127.64 (Ar), 127.62 (Ar), 127.60 (Ar), 127.57 (Ar), 127.52 (Ar), 127.48 (Ar), 107.3 (C-2''''), 102.8 (C-1, $J_{C1,H1}$ = 153.1 Hz), 101.7 (C-1'', $J_{C1'',H1''}$ = 172.0 Hz), 99.5 (C-1', $J_{C1',H1'}$ = 173.5 Hz), 82.0 (C-3''''), 81.4, 80.6, 80.3, 80.2, 80.0, 78.7, 78.4, 75.8, 75.3, 75.0, 74.8, 74.5, 73.3, 72.8, 72.6, 72.2, 70.5, 70.1, 69.5, 69.4, 69.3, 68.9, 68.5, 57.3 (OCH_3), 21.2 (COOCH_3), 18.2, 18.13, 18.10; HRMS (ESI) calcd. for $C_{76}H_{86}NaO_{18}$ $[M+Na]^+$ 1309.5706 found 1309.5707.



Methyl 2-*O*-benzyl-3,4-*O*-xylylidene-α-D-xylulofuranosyl-(2→2)-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-2,4-di-*O*-benzyl-β-L-rhamnopyranoside (3.134). To a solution of the **3.133β** (50.7 mg, 0.039 mmol) in CH_3OH (2.0

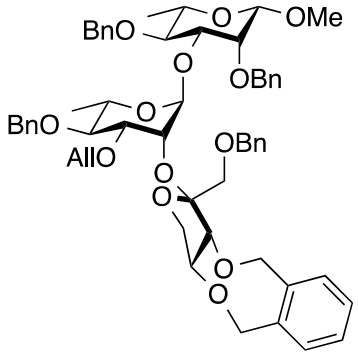
mL) was added sodium methoxide (0.16 mg, 3.9 μmol) and the reaction mixture was stirred at room temperature. After stirring for 24 h, the reaction mixture was neutralized by the addition of Amberlite IR-120 H^+ resin. The solution was filtered and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatography (2:1, hexane–EtOAc) to give **3.134** (45.6 mg, 93%) as a colorless oil. $[\alpha]^{25}_D$ +11.4 (*c* 1.0, $CHCl_3$); R_f 0.41 (1:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.45–7.41 (m, 2H, ArH), 7.37–7.22 (m, 28H, ArH), 7.20–7.16 (m, 1H, ArH), 7.15–7.10 (m, 1H, ArH), 7.09–7.07 (m, 2H, ArH), 5.09 (d, 1H, $J_{1',2'}$ = 1.3 Hz, H-1'), 5.06–4.98 (m, 3H, H-1'', ArCH_2), 4.88 (d, 1H, J_{gem} = 11.0 Hz, ArCH_2), 4.83–4.67 (m, 6H, ArCH_2), 4.65–4.58 (m, 3H, ArCH_2), 4.55 (d, 1H, J_{gem} = 11.0 Hz, ArCH_2), 4.46 (d, 1H, J_{gem} = 11.0 Hz, ArCH_2), 4.42–4.36 (m, 2H, H-4_{Xul}, ArCH_2), 4.35 (s, 1H, H-1), 4.26–4.19 (m, 2H, H-3_{Xul}, ArCH_2), 4.13–4.10 (m, 1H, H-2''), 4.04–3.96 (m, 3H, H-2', H-3', H-$5a_{Xul}$), 3.80 (d, 1H, $J_{2,1}$ = 2.7 Hz, H-2), 3.76 (dd, 1H, $J_{3'',2''}$ = 2.7 Hz, $J_{3'',4''}$ = 9.2 Hz, H-3''), 3.72–3.65 (m, 3H, H-3, H-5', H-5''), 3.62 (app t, 1H, $J_{4,3} = J_{4,5}$ = 9.2 Hz, H-4), 3.58–3.50 (m, 6H, OCH_3, H-4'', H-$1a_{Xul}$, H-$5b_{Xul}$), 3.46 (d, 1H, J_{gem} = 11.2 Hz, H-$1b_{Xul}$), 3.38–3.29 (m, 2H, H-4', H-5), 1.37 (d, 3H, $J_{6,5}$ = 6.2 Hz, H-6), 1.18 (d, 3H, $J_{6',5'}$ = 6.2 Hz, H-6'), 1.15 (d, 3H, $J_{6'',5''}$ = 6.2 Hz, H-6''); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.9 (Ar), 138.64 (Ar), 138.55 (Ar), 138.53 (Ar), 138.4 (Ar), 138.1 (Ar), 136.9 (Ar), 136.7 (Ar), 131.7 (Ar), 131.2 (Ar), 129.4 (Ar), 129.3 (Ar), 129.3 (Ar), 128.7 (Ar), 128.6 (Ar), 128.5 (Ar), 128.43 (Ar), 128.37 (Ar), 128.26 (Ar), 128.15 (Ar), 128.09 (Ar), 127.88 (Ar), 127.85 (Ar), 127.77 (Ar), 127.73 (Ar), 127.61 (Ar), 127.58 (Ar), 127.54 (Ar), 107.3 (C-2_{Xul}), 102.8 (C-1, $J_{C1,H1}$ = 152.7 Hz), 101.7 (C-1'', $J_{C1'',H1''}$ = 171.0 Hz), 101.6 (C-1', $J_{C1',H1'}$ = 172.5 Hz), 82.1 (C-3_{Xul}), 81.0, 80.9, 80.3, 80.02, 80.00, 78.6, 78.4, 75.8, 75.3, 75.1, 74.5, 73.3, 73.3, 72.8, 72.2, 71.6, 70.5, 70.1, 69.52, 69.50, 69.41, 68.9, 68.3, 57.3

(OCH_3), 18.4, 18.1, 18.0; HRMS (ESI) calcd. for $C_{74}H_{84}NaO_{17}$ $[M+Na]^+$ 1267.5601 found 1267.5608.



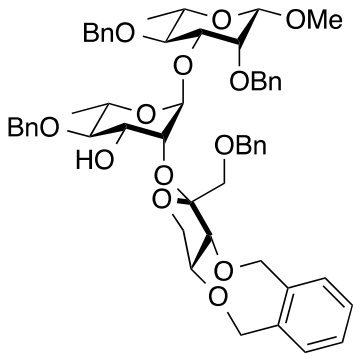
Methyl 3-*O*-allyl-4-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-2,4-di-*O*-benzyl-β-L-rhamnopyranoside (3.135). To a solution of the **3.125** (158 mg, 0.266 mmol) in toluene (30.0 mL) was added di-*n*-butyltin oxide (99 mg, 0.399 mmol) and the mixture was heated at reflux for 3 h. The mixture was then cooled to room temperature before tetrabutylammonium bromide (128 mg, 0.399 mmol) and allyl bromide (38.5 mg, 34.5 μL, 0.399 mmol) were added. After stirring for 2 h at reflux, the reaction mixture was concentrated and the resulting residue was purified by column chromatography (4:1, hexane–EtOAc) to give **3.135** (103 mg, 77%) as a colorless oil. $[\alpha]^{25}_D$ +20.2 (*c* 1.0, $CHCl_3$); R_f 0.36 (2:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.47–7.43 (m, 2H, ArH), 7.39–7.27 (m, 12H, ArH), 7.22–7.18 (m, 1H, ArH), 5.92 (ddt, 1H, *J* = 5.7, 10.5, 17.1 Hz, OCH_2CH=CH_2), 5.28 (dq, 1H, *J* = 1.7, 17.1 Hz, OCH_2CH=CH_2), 5.19–5.15 (m, 2H, OCH_2CH=CH_2, H-1'), 5.02 (d, 1H, J_{gem} = 12.4 Hz, ArCH_2), 4.86 (d, 1H, J_{gem} = 11.4 Hz, ArCH_2), 4.78 (d, 1H, J_{gem} = 10.9 Hz, ArCH_2), 4.74 (d, 1H, J_{gem} = 12.4 Hz, ArCH_2), 4.65 (d, 1H, J_{gem} = 10.9 Hz, ArCH_2), 4.61 (d, 1H, J_{gem} = 11.4 Hz, ArCH_2), 4.36 (br s, 1H, H-1), 4.14 (ddt, 1H *J* = 1.7, 5.7, 12.8 Hz, OCH_2CH=CH_2), 4.09 (ddt, 1H, *J* = 1.7, 5.7, 12.8 Hz, OCH_2CH=CH_2), 4.01–3.99 (m, 1H, H-2'), 3.82 (d, 1H, $J_{2,3}$ = 2.7 Hz, H-2), 3.74–3.67 (m, 3H, H-3, H-3', H-5'), 3.64 (app t, 1H, $J_{4,3} = J_{4,5}$ = 9.6 Hz, H-4), 3.53 (s, 3H, OCH_3), 3.40 (app t, 1H, $J_{4',3'} = J_{4',5'}$ = 9.1 Hz, H-4'), 3.35 (app dq, $J_{5,6}$ = 6.1 Hz, $J_{5,4}$ = 9.6 Hz, H-5), 2.40 (d, 1H, $J_{OH,\,2'}$ = 1.5 Hz, 2'-OH),

1.40 (d, 3H, $J_{6,5}$ = 6.1 Hz, H-6), 1.22 (d, 3H, $J_{6',5'}$ = 6.4 Hz, H-6'); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.8 (Ar), 138.7 (Ar), 138.0 (Ar), 134.6 ($OCH_2CH{=}CH_2$), 128.5 (2C, Ar), 128.3 (2C, Ar), 128.1 (2C, Ar), 128.0 (2C, Ar), 127.9 (Ar), 127.8 (2C, Ar), 127.7 (Ar), 127.5 (Ar), 127.3 (Ar), 117.3 ($OCH_2CH{=}CH_2$), 102.6 (C-1, $J_{C1,H1}$ = 154.0 Hz), 101.1 (C-1', $J_{C1',H1'}$ = 172.2 Hz), 81.0 (C-4), 80.0 (C-3), 79.8 (C-3'), 79.4 (C-4'), 78.1 (C-5'), 75.5 ($ArCH_2$), 75.0 ($ArCH_2$), 74.4 ($ArCH_2$), 72.0 (C-5), 71.0 ($OCH_2CH{=}CH_2$), 69.1 (C-2'), 68.0 (C-2), 57.1 (OCH_3), 17.9 (C-6), 17.84 (C-6'); HRMS (ESI) calcd. for $C_{37}H_{46}NaO_9$ $[M+Na]^+$ 657.3034; found 657.3034.



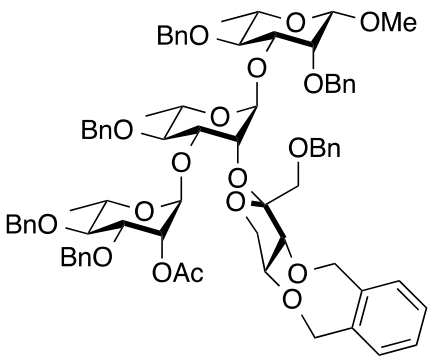
Methyl 1-*O*-benzyl-3,4-*O*-xylylidene-β-D-xylulofuranosyl-(2→2)-3-*O*-allyl-4-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-2,4-di-*O*-benzyl-β-L-rhamnopyranoside (3.136β). A mixture of **3.70** (32.2 mg, 0.072 mmol), **3.135** (38.0 mg, 0.060 mmol), and 4Å molecular sieves in CH_2Cl_2 (2.0 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –78 °C and *N*-iodosuccinimide (19.4 mg, 0.0864 mmol) and silver triflate (1.9 mg, 7.2 μmol) were added. After stirring for 1 h at –78 °C, triethylamine was added. The reaction was warmed to room temperature and then a small amount of water was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The solution was then dried over $MgSO_4$, filtered and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatography (4:1, hexane–EtOAc) to give **3.136α** (15.3 mg, 26%) and **3.136β** (30.6

mg, 52%) both as colorless oils. $[\alpha]^{25}_{D}$ +45.6 (*c* 0.9, $CHCl_3$) for **3.136α**; $[\alpha]^{25}_{D}$ +14.1 (*c* 0.4, $CHCl_3$) for **3.136β**; R_f 0.55 (2:1, hexane–EtOAc) for **3.136α**; R_f 0.30 (2:1, hexane–EtOAc) for **3.136β**; Data for **3.136β**: ^{1}H NMR ($CDCl_3$, 700 MHz) δ_H 7.44–7.41 (m, 2H, ArH), 7.38–7.23 (m, 19H, ArH), 7.20–7.16 (m, 3H, ArH), 5.77–5.73 (m, 1H, OCH_2CH=CH_2), 5.17 (dq, 1H, *J* = 17.3, 1.7 Hz, OCH_2CH=CH_2), 5.06–5.00 (m, 3H, OCH_2CH=CH_2, 2 x ArCH_2), 4.96 (br s, 1H, H-1'), 4.88–4.81 (m, 3H, ArCH_2), 4.79 (d, 1H, J_{gem} = 12.9 Hz, ArCH_2), 4.76 (d, 1H, J_{gem} = 12.9 Hz, ArCH_2), 4.66 (d, 1H, J_{gem} = 12.0 Hz, ArCH_2), 4.57 (d, 1H, J_{gem} = 11.5 Hz, ArCH_2), 4.53 (d, 1H, J_{gem} = 11.5 Hz, ArCH_2), 4.51 (d, 1H, J_{gem} = 12.5 Hz, ArCH_2), 4.41–4.37 (m, 2H, ArCH_2, H-4''), 4.31 (s, 1H, H-1), 4.25 (d, 1H, $J_{3'',4''}$ = 6.4 Hz, H-3''), 4.11 (app t, 1H, $J_{2',1'} = J_{2',3'}$ = 2.4 Hz, H-2'), 4.01–3.92 (m, 3H, H-5''a, 2 x OCH_2CH=CH_2), 3.79 (d, 1H, $J_{2,3}$ = 2.8 Hz, H-2), 3.69 (dq, 1H, $J_{5',4'}$ = 9.3 Hz, $J_{5',6'}$ = 6.4 Hz, H-5'), 3.66 (dd, 1H, $J_{3',2'}$ = 2.4 Hz, $J_{3',4'}$ = 9.3 Hz, H-3'), 3.63 (dd, 1H, $J_{3,2}$ = 2.8 Hz, $J_{3,4}$ = 9.7 Hz, H-3), 3.58–3.50 (m, 4H, H-4, H-1''a, H-1''b, H-5''b), 3.49 (s, 3H, OCH_3), 3.45 (app t, $J_{4',3'} = J_{4',5'}$ = 9.3 Hz, H-4'), 3.30 (app dq, $J_{5,6}$ = 6.2 Hz, $J_{5,4}$ = 9.1 Hz, H-5), 1.27 (d, 3H, $J_{6,5}$ = 6.2 Hz, H-6), 1.18 (d, 3H, $J_{6',5'}$ = 6.4 Hz, H-6'); ^{13}C NMR ($CDCl_3$, 175 MHz) δ_C 139.1 (Ar), 138.8 (Ar), 138.30 (Ar), 138.26 (Ar), 136.7 (Ar), 136.1 (Ar), 134.9 (OCH_2CH=CH_2), 131.5 (Ar), 131.0 (Ar), 129.2 (Ar), 129.1 (Ar), 128.4 (2C, Ar), 128.3 (2C, Ar), 128.2 (2C, Ar), 128.1 (2C, Ar), 127.8 (2C, Ar), 127.72 (2C, Ar), 127.71 (Ar), 127.6 (2C, Ar), 127.54 (2C, Ar), 127.50 (Ar), 127.3 (Ar), 127.2 (Ar), 116.7 (OCH_2CH=CH_2), 107.1 (C-2''), 102.6 (C-1, $J_{C1,H1}$ = 154.6 Hz), 101.6 (C-1', $J_{C1,H1}$ = 173.6 Hz), 82.0 (C-3''), 80.9 (C-3), 80.5 (C-4), 80.1 (C-4'), 79.7 (C-4''), 78.5 (C-2), 78.2 (C-3'), 75.3 (ArCH_2), 74.6 (ArCH_2), 74.5 (ArCH_2), 73.3 (ArCH_2), 72.0 (C-5), 71.7 (OCH_2CH=CH_2), 70.4 (C-5''), 69.9 (C-2'), 69.5 (ArCH_2), 69.3 (ArCH_2), 68.9 (C-5'), 68.5 (C-1''), 57.1 (OCH_3), 18.1 (C-6), 17.9 (C-6'); HRMS (ESI) calcd. for $C_{57}H_{66}NaO_{13}$ $[M+Na]^+$ 981.4396; found 981.4385.



Methyl 1-*O*-benzyl-3,4-*O*-xylylidene-β-D-xylulofuranosyl-(2→2)-4-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-2,4-di-*O*-benzyl-β-L-rhamnopyranoside (3.137). To a solution of **3.136β** (30.6 mg, 0.0319 mmol) in THF (1.0 mL), degassed under vaccum, and stirred under an Ar atmosphere, (1,5-cyclooctadiene) bis-(methyldiphenylphosphine)iridium I hexafluorophosphate catalyst (1.3 mg, 1.6 μmol) was added, followed by further degassing of the mixture. The suspension was stirred for 30 min at 0 ºC, and the catalyst was then activated with hydrogen. At this point, the solution became nearly colorless. The excess of hydrogen gas was removed by exchange of Ar gas. The reaction mixture was then stirred for 24 h at room temperature under an Ar atmosphere. The solvent was then evaporated, and the residue was dissolved in acetone–water (9:1, 2.0 mL). To the solution was then added HgO (10.4 mg, 0.0479 mmol) and $HgCl_2$ (13.0 mg, 0.0479 mmol). After stirring for 24 h at room temperature, the solvent was evaporated and the residue was dissolved in EtOAc and washed with 10% KI solution, satd aq $Na_2S_2O_3$, and then water. The organic layer was then dried over $MgSO_4$, filtered and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatography (4:1, hexane–EtOAc) to give **3.137** (23.5 mg, 80%) as a colorless oil. $[\alpha]^{25}_D$ +15.5 (*c* 1.5, $CHCl_3$); R_f 0.30 (2:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.45–7.39 (m, 4H, ArH), 7.35–7.24 (m, 17H, ArH), 7.21–7.17 (m, 3H, ArH), 5.10 (d, 1H, $J_{1',2'}$ = 1.2 Hz, H-1'), 5.04 (d, 1H, J_{gem} = 11.7 Hz, ArCH_2), 4.96 (d, 1H, J_{gem} = 13.2 Hz, ArCH_2), 4.93 (d, 1H, J_{gem} = 11.7 Hz, ArCH_2), 4.83 (d,

1H, J_{gem} = 11.4 Hz, ArCH_2), 4.78 (d, 1H, J_{gem} = 12.3 Hz, ArCH_2), 4.75 (d, 1H, J_{gem} = 12.3 Hz, ArCH_2), 4.69 (d, 1H, J_{gem} = 11.4 Hz, ArCH_2), 4.68 (d, 1H, J_{gem} = 13.2 Hz, ArCH_2), 4.61 (d, 1H, J_{gem} = 11.4 Hz, ArCH_2), 4.55 (d, 1H, J_{gem} = 11.4 Hz, ArCH_2), 4.47 (d, 1H, J_{gem} = 12.4 Hz, ArCH_2), 4.40 (d, 1H, J_{gem} = 12.4 Hz, ArCH_2), 4.32 (s, 1H, H-1), 4.28 (app dt, $J_{4'',3''} = J_{4'',5''b}$ = 5.3 Hz, $J_{4'',5''a}$ = 8.0 Hz, H-4''), 4.10 (dd, 1H, $J_{5''a,4''}$ = 8.0 Hz, J_{gem} = 9.6 Hz, H-5''), 4.04 (dd, 1H, $J_{2',1'}$ = 1.2 Hz, $J_{2',3'}$ = 3.3 Hz, H-2'), 4.00–3.97 (m, 1H, H-3'), 3.97 (d, 1H, $J_{3'',4''}$ = 5.3 Hz, H-3''), 3.85 (d, 1H, $J_{2,3}$ = 2.6 Hz, H-2), 3.75 (dq, 1H, $J_{5',4'}$ = 9.4 Hz, $J_{5',6'}$ = 6.1 Hz, H-5'), 3.63 (dd, 1H, $J_{3,2}$ = 2.6 Hz, $J_{3,4}$ = 9.5 Hz, H-3), 3.58 (dd, 1H, $J_{4,3}$ = 9.5 Hz, $J_{4,5}$ = 8.8 Hz, H-4), 3.57 (d, 1H, J_{gem} = 10.9 Hz, H-1''a), 3.51 (s, 3H, OCH_3), 3.53–3.47 (m, 1H, H-5''), 3.34 (d, 1H, J_{gem} = 10.9 Hz, H-1''b), 3.31 (app dq, $J_{5,6}$ = 6.4 Hz, $J_{5,4}$ = 8.8 Hz, H-5), 3.25 (app t, 1H, $J_{4',3'} = J_{4',5'}$ = 9.3 Hz, H-4'), 1.32 (d, 3H, $J_{6,5}$ = 6.4 Hz, H-6), 1.17 (d, 3H, $J_{6',5'}$ = 6.1 Hz, H-6'); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 139.2 (Ar), 138.8 (Ar), 138.5 (Ar), 137.6 (Ar), 136.8 (Ar), 135.9 (Ar), 131.6 (Ar), 131.3 (Ar), 129.5 (Ar), 128.41 (2C, Ar), 128.39 (2C, Ar), 128.15 (2C, Ar), 128.11 (2C, Ar), 127.8 (2C, Ar), 127.7 (2C, Ar), 127.62 (2C, Ar), 127.61 (2C, Ar), 127.57 (2C, Ar), 127.3 (Ar), 127.2 (Ar), 106.5 (C-2''), 102.6 (C-1, $J_{C1,H1}$ = 152.9 Hz), 101.4 (C-1', $J_{C1',H1'}$ = 173.9 Hz), 84.3 (C-3''), 81.8 (C-4'), 81.7 (C-4), 80.9 (C-4''), 80.3 (C-3), 78.3 (C-2), 75.2 (Ar*C*H$_2$), 74.4 (Ar*C*H$_2$), 74.2 (Ar*C*H$_2$), 73.33 (C-2'), 73.26 (Ar*C*H$_2$), 72.1 (C-5), 71.0 (C-3'), 70.4 (C-5''), 69.7 (C-1''), 69.5 (Ar*C*H$_2$), 69.0 (Ar*C*H$_2$), 67.8 (C-5'), 57.1 (OCH_3), 18.1 (C-6), 17.9 (C-6'); HRMS (ESI) calcd. for $C_{54}H_{62}NaO_{13}$ $[M+Na]^+$ 941.4083; found 941.4080.



Methyl 2-*O*-acetyl-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-[1-*O*-benzyl-3,4-*O*-xylylidene-β-D-xylulofuranosyl-(2→2)]-4-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-2,4-di-*O*-benzyl-β-L-rhamnopyranoside (3.139). A mixture of **3.137** (8.8 mg, 0.0179 mmol), **3.138** (13.7 mg, 0.0149 mmol), and 4Å molecular sieves in CH_2Cl_2 (1.0 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to 0 ºC and *N*-iodosuccinimide (4.8 mg, 0.0215 mmol) and silver triflate (0.9 mg, 3.6 μmol) were added. After stirring for 2 h at 0 ºC, triethylamine was added. The reaction was warmed to room temperature and then a small amount of water was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The solution was then dried over $MgSO_4$, filtered and the filtrate concentrated under reduced pressure. The resulting residue was purified by column chromatography (4:1, hexane–EtOAc) to give **3.139** (17.5 mg, 91%) as a colorless oil. $[\alpha]^{25}_D$ +25.0 (*c* 1.3, $CHCl_3$); R_f 0.36 (2:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 700 MHz) δ_H 7.47–7.44 (m, 3H, ArH), 7.38–7.15 (m, 29H, ArH), 6.98–6.94 (m, 2H, ArH), 5.51 (br s, 1H), 5.15–5.07 (m, 3H), 4.96 (d, 1H, J_{gem} = 13.0 Hz, ArCH_2), 4.97 (d, 1H, J_{gem} = 11.1 Hz, ArCH_2), 4.87 (d, 1H, J_{gem} = 11.1 Hz, ArCH_2), 4.84 (d, 1H, J_{gem} = 11.1 Hz, ArCH_2), 4.77–4.72 (m, 3H, ArCH_2), 4.66–4.54 (m, 5H, ArCH_2), 4.41–4.32 (m, 4H), 4.20–4.11 (m, 5H), 4.02–3.94 (m, 2H), 3.86–3.84 (m, 1H), 3.75–3.71 (m 1H), 3.64–3.55 (m, 5H) 3.53–3.50 (m, 4H, OCH_3), 3.40 (app t, 1H, *J* = 9.2 Hz), 3.33–3.28 (m, 1H), 2.06 (s, 3H, CH_3CO), 1.28 (d, 3H, $J_{6,5}$ = 6.1 Hz), 1.18 (d, 3H, *J* = 6.1 Hz), 1.12 (d, 3H, *J* = 6.1 Hz); ^{13}C

NMR ($CDCl_3$, 175 MHz) δ_C 170.3 (C=O), 139.0 (Ar), 138.9 (Ar), 138.49 (Ar), 138.44 (Ar), 138.34 (Ar), 138.25 (Ar), 136.9 (Ar), 136.8 (Ar), 131.6 (Ar), 131.3 (Ar), 129.4 (Ar), 129.2 (Ar), 128.6 (Ar), 128.5 (Ar), 128.4 (Ar), 128.36 (Ar), 128.3 (Ar), 128.2 (Ar), 128.0 (Ar), 127.9 (Ar), 127.84 (Ar), 127.79 (Ar), 127.7 (Ar), 127.6 (Ar), 127.6 (Ar), 127.4 (Ar), 127.33 (Ar), 107.1, 102.8, 101.6, 99.3, 82.8, 82.2, 80.6, 80.5, 80.1, 80.0, 78.8, 78.4, 75.7, 75.6, 75.5, 74.7, 74.4, 73.4, 72.5, 72.2, 71.9, 70.4, 69.4, 69.3, 69.2, 69.1, 68.8, 68.5, 57.3, 21.2 (CH_3CO), 18.5, 18.2, 18.1; HRMS (ESI) calcd. for $C_{76}H_{86}NaO_{18}$ $[M+Na]^+$ 1309.5706; found 1309.5706.

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Chapter 4

Improvement of the β-Stereoselectivity in Xylulofuranosylation Reactions via the Use of a 1,4-*O*-siloxane-bridged Xylulose Thioglycoside Donor

4.1 Background

4.1.1 Overview of stereoselective β-xylulofuranosylation

β-D-Xylulofuranose (β-D-Xul*f*) residues have been identified in several different micro-organisms[1–3]. However, before my work in this area (Chapter 3), there were no reports of chemical approaches to synthesize oligosaccharides containing these residues. As described in Chapter 3, the use of conformationally-restricted xylulofuranose (Xul*f*) donors **3.70** and **3.71** successfully provided modest to good β-selectivity (**Figure 4.1a**) with various glycosyl acceptors. The reaction was particularly good using acceptors **3.84** and **3.85** (**Figure 4.1b**), which lead to linkages present in oligosaccharides found in nature. Compared to the results with Xul*f* donors **3.104** and **3.105** (**Figure 4.1b**), which do not have a xylylene group at the O-3 and O-4 positions, **3.70** and **3.71** provided improved β-selectivity. It is believed this is because the xylylene group conformationally-restricts the ring leading to a single electrophilic intermediate that undergoes "inside attack" by the alcohol. Moreover, neighboring group participation from an acyl group on O-1 was observed to increase β-selectivity. It was proposed that the α-spiro intermediate **3.103** forms in preference to the β-spiro intermediate **3.101** due to the anomeric effect and steric effects (**Figure 4.1c**); therefore, the formation of β-D-Xul*f* linkages is further enhanced.

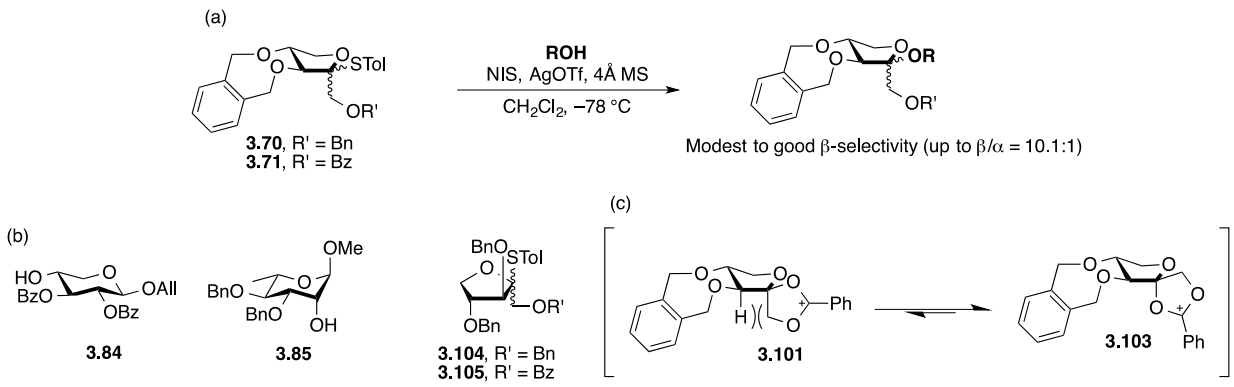


Figure 4.1. (a) Stereoselectivity results of glycosylations with conformationally-restricted Xul*f* donors **3.70** and **3.71**. (b) Structures of acceptors **3.84** and **3.85** and donors **3.104** and **3.105**. (c) Plausible intermediates produced by neighboring group participation of an O-1 acyl group.

Although, β-selectivity was observed with donors **3.70** and **3.71**, we still encountered problems while making the pentasaccharide repeating unit (**3.116**) of *Yersinia enterocolitica* O:5/O:5,27 LPS. For instance, the separation of both diastereomers from each xylulofuranosylation step was needed. When I attempted to add both residues at the same time, the four diastereomeric products could not be separated. Therefore, further improvements are needed. Our approach to improve the β-selectivity in xylulofuranosylation reactions is described in this Chapter.

4.1.2 Idea for improving the stereoselectivity of xylulofuranosylation

Fructose, a six-carbon ketose, has a similar structure to xylulose except that it has an additional hydroxymethyl group at C-5 (**Figure 4.2a**). In natural glycoconjugates, fructose is found almost exclusively in the furanose form (Fru*f*) and as the β-glycoside. Thus, previous studies of fructofuranosylation can provide hints for increasing β-selectivity in xylulofuranosylation. In 2000, Oscarson and coworkers[4] developed a novel siloxane-bridged Fru*f* donor (**4.1**) that fur-

nished exclusive β-selectivity with a variety of glycosyl acceptors (**Figure 4.2b**). The exclusive β-fructofuranosylation was proposed to arise from the bulkiness of siloxane group, which prevents the attack of the glycosyl acceptor from the bottom face, which led to the formation of β-Fru*f* linkages (**Figure 4.2c**). Therefore, I thought that donor **4.2**, which has a siloxane group bridging O-1 and O-4 in Xul*f*, might have improved β-selectivity (**Figure 4.2d**).

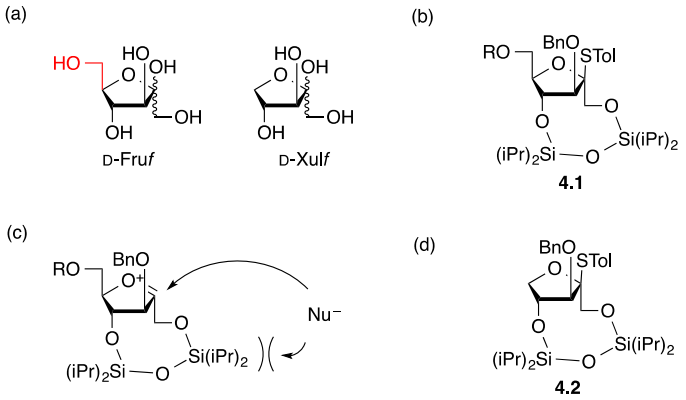


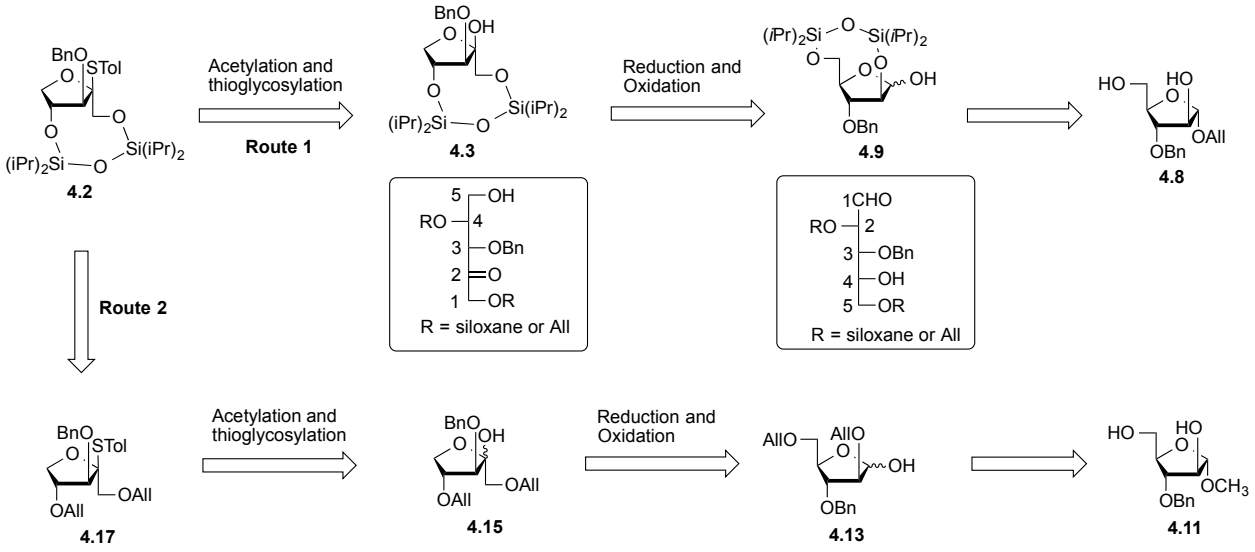
Figure 4.2. (a) Structures of D-Fru*f* and D-Xul*f*. (b) Structure of siloxane-bridged Fru*f* donor **4.1** developed by Oscarson and coworkers. (c) Steric hindrance from the bottom face of the ring in the electrophilic intermediate derived from **4.1**. (d) Structure of siloxane-bridged Xul*f* donor **4.2**.

4.1.3 Research objective and retrosynthesis

In the work described in this Chapter, my goal was to extend the β-selective fructofuranosylation methodology using a siloxane-bridged donor to β-xylulofuranosylation. Two challenges had to be overcome. The first challenge was to synthesize β-Xul*f* donor **4.2** and the second was to characterize the anomeric configuration of the Xul*f* moieties in the products.

With regard to the first challenge, similar to our strategy in Chapter 3, I proposed that **4.2** could be synthesized from arabinose. Two possible routes were designed (**Scheme 4.1**). I envi-

sioned that the siloxane group could be introduced either at an early stage (Route 1) or a late stage (Route 2). The stability of siloxane group is a concern in the early-stage route because of the use of acidic and basic conditions after its introduction. Problems with the late stage route are its slightly longer length as well as the selectivity of the thioglycosylation (a good yield of the β-anomer is required). In addition, this route requires temporary protecting groups at O-1 and O-4, will be removed at a late stage, allowing subsequent installation of the siloxane group.



Scheme 4.1. Retrosynthesis of siloxane-bridged Xul*f* donor **4.2** via two different routes.

As for the second challenge, from our results in Chapter 3, the anomeric configuration of the Xul*f* residues was determined by the chemical shift of the anomeric carbon, accompanied by 2D ^{1}H–^{1}H TROESY data and one X-ray crystal structure. However, anomalous chemical shifts of the anomeric carbon in siloxane-bridged Fru*f* glycosides (i.e., **4.4**) have been reported (**Figure 4.3**)[4]. I anticipated that I might see C-2 chemical shifts outside the normal range in glycosides obtained using siloxane-bridged Xul*f* donor **4.2**. Thus, one more step to remove the siloxane group might be necessary for determining the anomeric configuration using the C-2 chemical shift value.

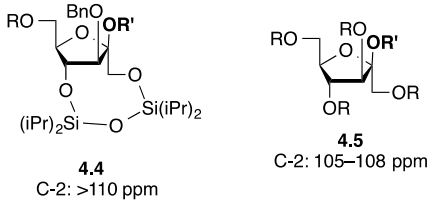


Figure 4.3. C-2 chemical shifts of siloxane-bridged Fru*f* glycosides (**4.4**) and those lacking this cyclic protecting group (**4.5**)[4].

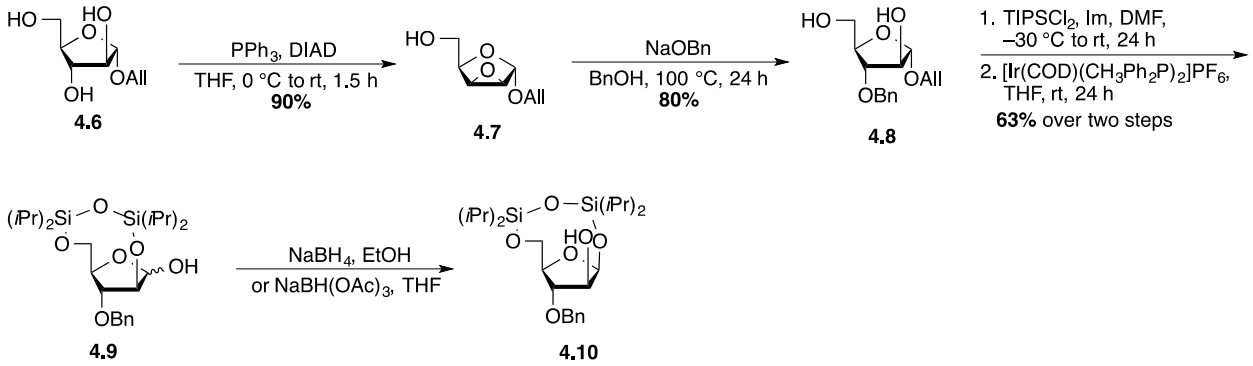
In this Chapter, I will describe my work on constructing the siloxane-bridged donor **4.2** and its use in: (1) improving the stereoselectivity of β-xylulofuranosylation and (2) the synthesis of Xul*f*-containing glycans.

4.2 Results and Discussion

4.2.1 Synthesis of siloxane-bridged Xul*f* donor 4.2

The synthesis of **4.2** was initially attempted via Route 1 – installation of the siloxane group at an early stage – to reduce the number of steps (**Scheme 4.2**). Therefore, allyl arabino-furanoside (**4.6**) was synthesized following the reported procedure[5]. The allyl glycoside was used, instead of the more easily obtained methyl glycoside[6], as I was worried that the siloxane would not survive the acidic conditions needed to cleave the aglycone as needed later in the route. Treatment of **4.6** with triphenylphosphine and diisopropyl azodicarboxylate (DIAD) provided 2,3-anhydrosugar **4.7** in 90% yield. The epoxide was then opened by the treatment of sodium benzyloxide in benzyl alcohol to obtain **4.8** in 80% yield. Installation of siloxane group at the O-2 and O-5 positions and the removal of allyl group were performed to afford **4.9** in 63% yield over two steps. The reduction of hemicacetal **4.9** was attempted by treatment with sodium boro-hydride; however, only the silyl migration product **4.10** was obtained. The silyl migration prod-

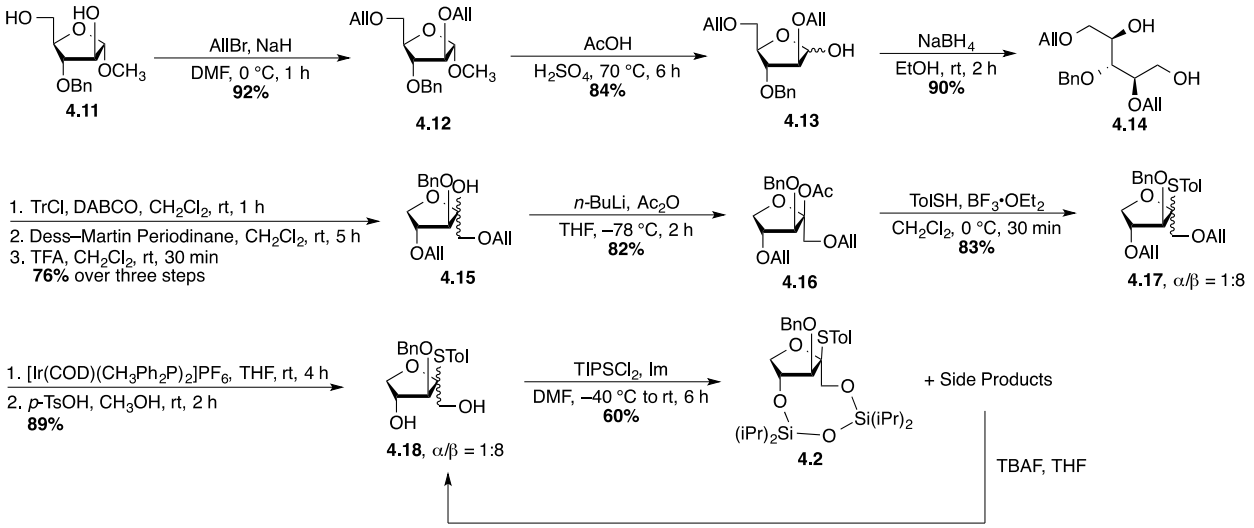
uct **4.10** was confirmed by the correlation of H-2 and the C-2 hydroxyl group hydrogen using a 2D ^{1}H–^{1}H COSY experiment. A weaker reducing agent, sodium triacetoxyborohydride, was also used but the silyl migration product **4.10** was also observed as the only product.



Scheme 4.2. Original attempt to synthesize **4.2** via early-stage introduction of the siloxane group.

Due to our inability to reduce **4.9** without migration of the siloxane and also the anticipated siloxane lability in later reaction stages at the route, I shifted my attention to Route 2 – late stage siloxane introduction (**Scheme 4.3**). This approach required that temporary protecting groups be installed early in the sequence. We chose allyl ethers for this purpose. Starting with **4.11**[7] treatment with allyl bromide and sodium hydride gave a 92% yield of methyl glycoside **4.12**. Hydrolysis of **4.12** under acidic conditions afforded hemiacetal **4.13** in 84% yield; this compound was reduced with sodium borohydride to provide, in 90% yield, diol **4.14**. The conversion of diol **4.14** into xylulose derivative **4.15** was executed in three straightforward steps: tritylation of the primary alcohol, oxidation of the secondary alcohol and trityl group deprotection to give the product in 76% overall yield. Using *n*-BuLi and acetic anhydride, the xylulosyl acetate **4.16** was obtained in good (82%) yield. Subsequent thioglycosylation gave an inseparable α/β mixture of Xul*f* donor **4.17** in good yield and stereoselectivity (83%, α/β = 1:8). The stereo-

chemistry of **4.17β** was determined by the correlation of two the H-1's with H-3 in the 1D NOESY spectrum, which was absent in **4.17α**. This stereoselectivity was important as only the β-glycoside can undergo reaction with the siloxane reagent to give the desired product. The allyl groups of **4.17** were then removed in good yield (83%) to afford **4.18**, again as an inseparable α/β mixture. The siloxane group was installed on **4.18** to obtain the target donor **4.2** in 60% yield. Although **4.2** was only obtained in modest yield, the side products could be converted back to starting material **4.18** by the treatment with TBAF.

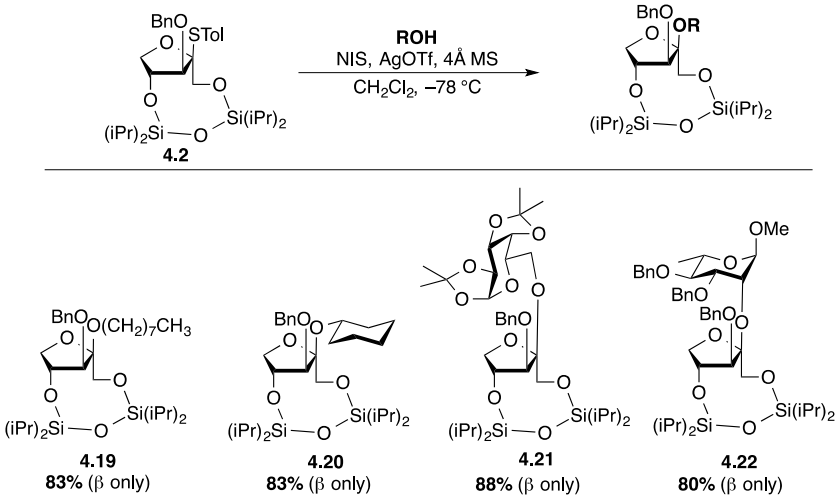


Scheme 4.3. Synthesis of xylulose thioglycoside **4.2**.

4.2.2 Stereoselectivity of xylulofuranosylation using 4.2 and characterization of anomeric configuration of xylulofuranoside products

With the desired Xul*f* donor **4.2** in hand, the stereoselectivity of xylulofuranosylation was investigated with four different acceptors (**3.78**, **3.80**, **3.82** and **3.85**, **Scheme 4.4**). These same compounds were also investigated with the 3,4-*O*-xylylene-protected Xul*f* donors **3.70** and **3.71**. Therefore, a comparison of the selectivity could be made. Whereas glycosylations with **3.70** and

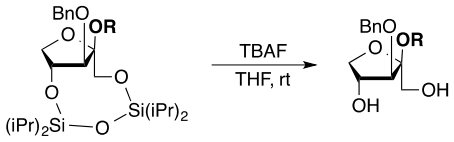
3.71 had moderate to good β-selectivity, with **4.2** only the β-Xul*f* glycosides **4.19**–**4.22** were obtained. Thus, as I hypothesized, the trend reported by Oscarson and coworkers for Fru*f* thioglycosides are the same for Xul*f* thioglycosides.



Scheme 4.4. Stereoselectivity of glycosylation reactions with Xul*f* donor **4.2**.

Characterization of the anomeric configuration of the 1,4-*O*-siloxane-protected Xul*f* glycosides **4.19**–**4.22** was, as expected, a challenge. According to my observations of Xul*f* C-2 chemical shifts in Chapter 3 (**Section 3.2.3**), higher field (105–108 ppm) C-2 resonances were assigned as β-Xul*f* and signals for C-2 at lower field (108–110 ppm) were assigned as α-Xul*f*. However, the C-2 chemical shifts of all of the siloxane-protected Xul*f* glycosides **4.19**–**4.22** were in the range of 108–110 ppm (**Table 4.1**). This would suggest that the compounds are α-Xul*f* glycosides, contrary to our expectation. However, because I was mindful of the anomalous C-2 chemical shifts reported for 1,4-*O*-siloxane-protected Fru*f* glycosides (**4.4**, **Figure 4.3**)[4], I assumed that the siloxane group also distorts the Xul*f* furanose ring to give unusual ^{13}C chemical shifts. This was confirmed by treatment of **4.19**–**4.22** with TBAF to remove the siloxane group. The products after removal of this cyclic protecting group (**4.23**–**4.26**) had ^{13}C chemical shifts in

the normal range (105–108 ppm) thus confirming the anomeric configuration to be β (**Table 4.1**). Furthermore, the 2D ^{1}H–^{1}H TROESY spectra of **4.23–4.26** were also obtained and they all had correlations between H-1 and H-3, which also indicates the β-configuration.



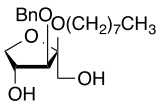
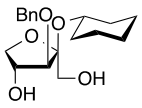
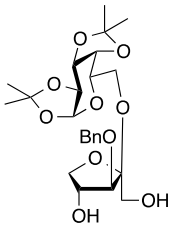
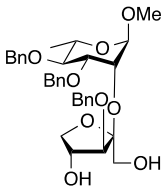
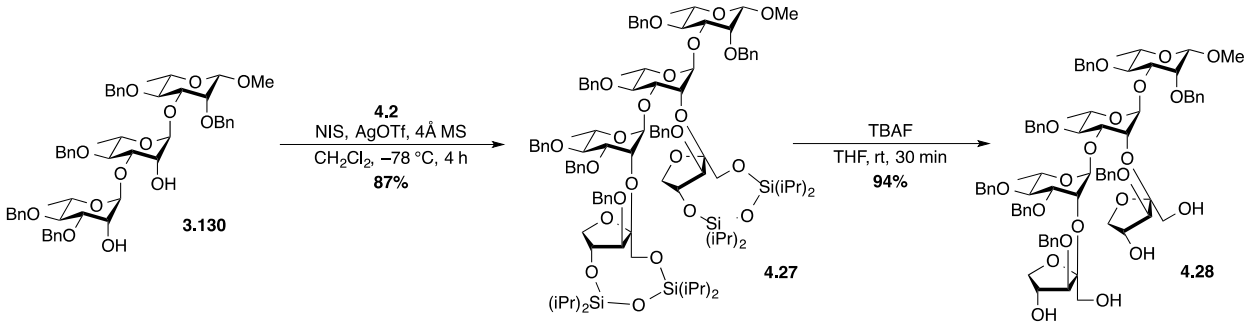
Siloxane-bridged Xul*f*	**4.19** C-2: 108.8 ppm	**4.20** C-2: 109.2 ppm	**4.21** C-2: 108.7 ppm	**4.22** C-2: 109.5 ppm
1,4-diol Xul*f*				
	4.23 C-2: 105.6 ppm	**4.24** C-2: 105.9 ppm	**4.25** C-2: 106.3 ppm	**4.26** C-2: 107.5 ppm

Table 4.1. C-2 chemical shifts of siloxane-protected (**4.19–4.22)** and deprotected (**4.23–4.26**) Xul*f* glycosides

4.2.3 Application of the methodology to the synthesis of Xul*f*-containing glycans

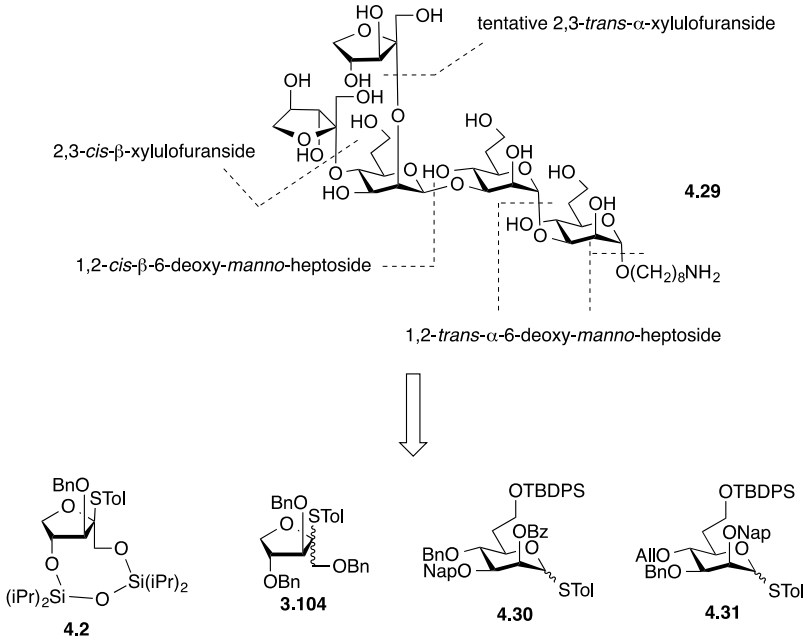
This methodology was first applied to the synthesis of the pentasaccharide repeating unit (**3.116**) of *Y. enterocolitica* O:5/O:5,27[1] LPS. As discussed in **Section 3.2.4**, in my previous synthesis of this compound, the two Xul*f* motifs had to be installed separately because the mixture of four diastereomers formed when they were added simultaneously was impossible to separate. Even then, the separation of the two diastereomers was also difficult when the Xul*f* motifs were installed one after the other. This issue was solved by using donor **4.2** (**Scheme 4.5**). Glycosylation of trisaccharide acceptor **3.130** with **4.2** provided only the ββ diastereomer of pentasaccha-

ride **4.27** in high (87%) yield. To confirm the anomeric configurations of both Xul*f* residues in **4.27**, the C-2 chemical shifts were obtained (109.1 and 108.8 ppm); both were outside the range of normal β-Xul*f* residues. Therefore, the siloxane group was removed by the treatment of TBAF. The C-2 of the Xul*f* residues of **4.28** were observed at 107.1 and 107.3 ppm, confirming the β-Xul*f* configurations.



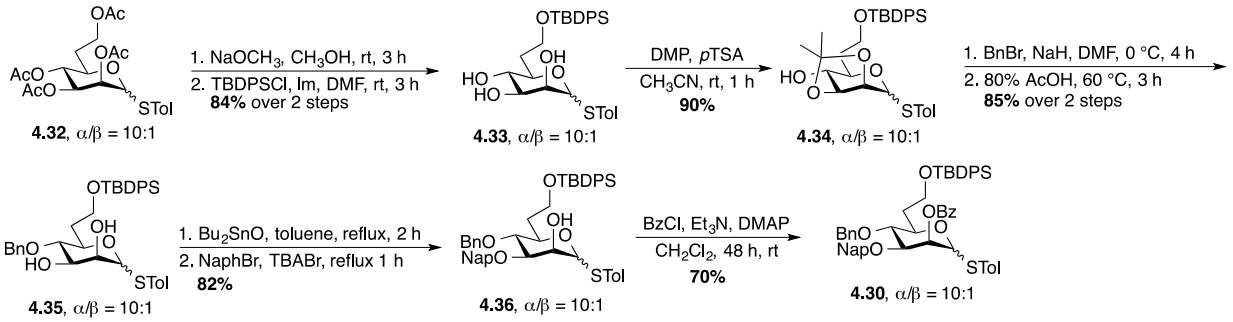
Scheme 4.5. Application of siloxane-bridged Xul*f* donor **4.2** to synthesize **4.28**.

I then turned my attention to a more complex target: the repeating unit of the *Campylobacter jejuni* RM1221 capsular polysaccharide (**4.29**, **Scheme 4.6**)[3]. This pentasaccharide contains one 6-deoxy-β-D-*manno*-heptopyranoside linkage, two 6-deoxy-D-*manno*-heptopyranoside linkages, one α-Xul*f* linkage and one β-Xul*f* linkage The major challenges in synthesizing this pentasaccharide are: (1) the formation of the β-Xul*f* linkage; (2) the preparation of 6-deoxy-D-*manno*-heptose; and (3) the formation of 6-deoxy-β-D-*manno*-heptopyranoside linkage. I envisioned the Xul*f* donor **4.2** could be applied to solve the first challenge. The preparation of thioglycoside derivatives of 6-deoxy-*manno*-heptose has been reported[8], and could be used to prepare the two substrates: **4.30** and **4.31**. Compound **4.31** could be used to generate the 6-deoxy-β-D-*manno*-heptopyranoside linkage via intramolecular aglycone delivery (IAD) and **4.30** could be used to introduce the 6-deoxy-α-D-*manno*-heptopyranoside linkage.



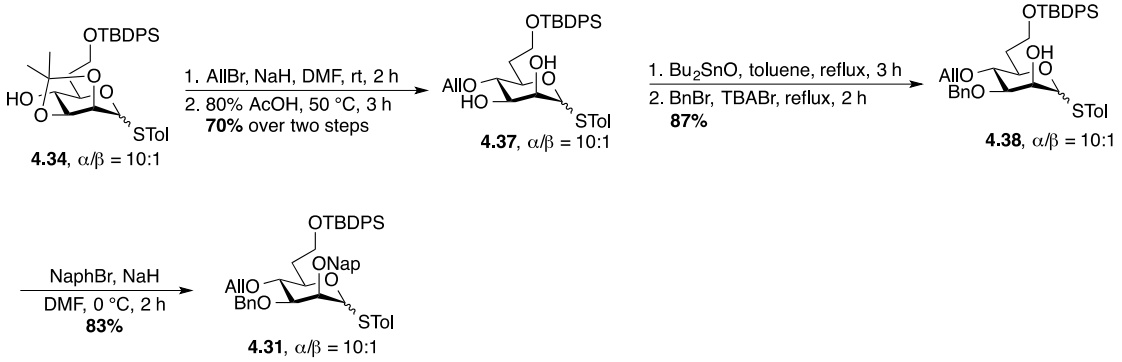
Scheme 4.6. Retrosynthesis of pentasaccharide **4.29**.

The synthesis of **3.104** and **4.2** has been described above, in **Sections 3.2.2** and **4.2.1**, respectively. The synthesis of **4.30** and **4.31** is shown in **Scheme 4.7** and started from the peracetylated 6-deoxy-D-*manno*-heptose thioglycoside **4.32**[8]. Treatment of **4.32** with a catalytic amount of sodium methoxide in methanol, followed by silylation of the primary alcohol, afforded **4.33** in 84% yield over the two steps. The 2,3-*cis*-diol was then protected with an isopropylidene ketal to provide a 90% yield of **4.34**. Benzylation of O-4 and hydrolysis of the ketal led to **4.35**, which was obtained in 85% yield over two steps. Regioselective naphthylation of the C-3 hydroxyl group was performed via an organotin intermediate to give **4.36**. Finally, the C-2 hydroxyl group in **4.36** was benzoylated to afford the thioglycoside **4.30** in 57% overall yield from **4.35**. This compound will be used as the donor for the formation of the α-D-*manno*-heptopyranoside linkages.



Scheme 4.7. Synthesis of thioglycoside donor **4.30**.

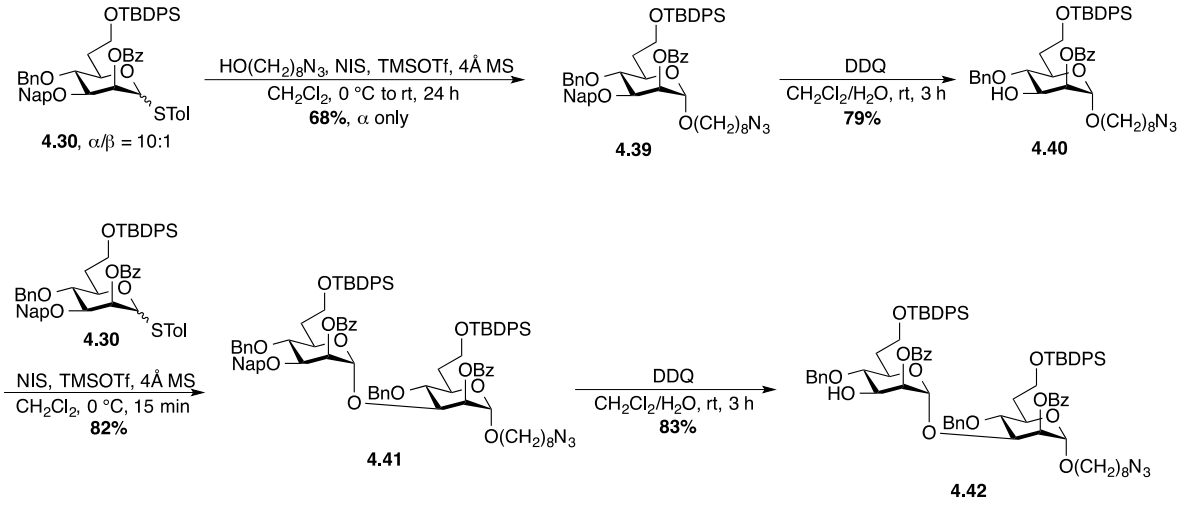
The synthesis of thioglycoside donor **4.31** was performed from 2,3-*O*-isopropylidene derivative **4.34** (**Scheme 4.8**). The C-4 hydroxyl group of **4.34** was allylated and, after removal of the isopropylidene ketal by acid hydrolysis, diol **4.37** was obtained in 70% yield over the two steps. Regioselective benzylation of the C-3 hydroxyl group (to give **4.38**) and the naphthylation of the C-2 hydroxyl group gave, in 72% yield over the two steps, **4.31**, which will serve as the donor for the introduction of the β-D-*manno*-heptopyranoside linkages.



Scheme 4.8. Synthesis of thioglycoside donor **4.31**.

With the four monosaccharide thioglycosides (**3.104**, **4.2**, **4.30** and **4.31**) in hand, I first synthesized disaccharide **4.42** (**Scheme 4.9**). This was done via the glycosylation of 8-

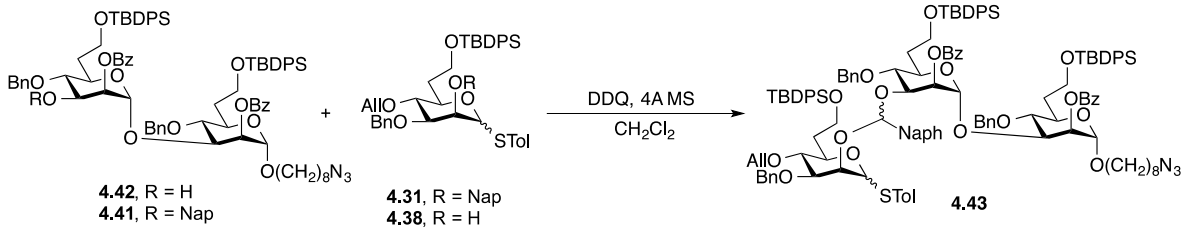
azidooctanol with **4.30** in the presence of NIS and TMSOTf to give only the α-glycoside **4.39** in 68% yield ($^1J_{C1,H1}$ = 171.5 Hz). The naphthylmethyl group in **4.39** was then deprotected with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) to afford acceptor **4.40** in 79% yield. Subsequent reaction of thioglycoside donor **4.30** and acceptor **4.40**, promoted by NIS and TMSOTf, generated and 82% yield of the α-linked disaccharide **4.41** ($^1J_{C1,H1}$ = 172.1 Hz and $^1J_{C1',H1'}$ = 173.5 Hz). Removal of the naphthylmethyl group in **4.41** with DDQ afforded disaccharide acceptor **4.42** in 83% yield.



Scheme 4.9. Synthesis of disaccharide acceptor **4.42**.

Having synthesized acceptor **4.42** and monosaccharide donor **4.31**, I proceeded to a key step – the formation of the β-D-*manno*-heptopyranoside linkage via IAD[9]. In the first step, the 2-*O*-naphthyl-thioglycoside donor **4.31** and the disaccharide acceptor **4.42** were tethered via a single electron transfer process to give a mixed acetal **4.43**. In an initial attempt, 1.0 equivalent of the acceptor **4.42** and 1.2 equivalents of the donor **4.31** were treated with DDQ (**Table 4.2**, entry 1). The desired mixed acetal **4.43** was obtained in 60% yield, but unreacted **4.42** was also recovered, together with the **4.38**, the product arising from loss of the napthylmethyl group from the

donor. I then increased the equivalents of donor **4.31** from 1.2 to 2.0 (**Table 4.2**, entry 2), and obtained a 77% yield of mixed acetal **4.43**. I also investigated the IAD strategy by interchanging the coupling partners (**Table 4.2**, entry 3). This was done by reacting the 3'-*O*-naphthylmethyl disaccharide **4.41** and thioglycoside **4.38**, which has a free hydroxyl group at C-2. I attempted this, as if successful, it would reduce the number of steps needed to make both the donor and acceptor. However, less amount of mixed acetal **4.43** and more of side products **4.38** and **4.42** were observed on TLC when using this approach and it was therefore abandoned.

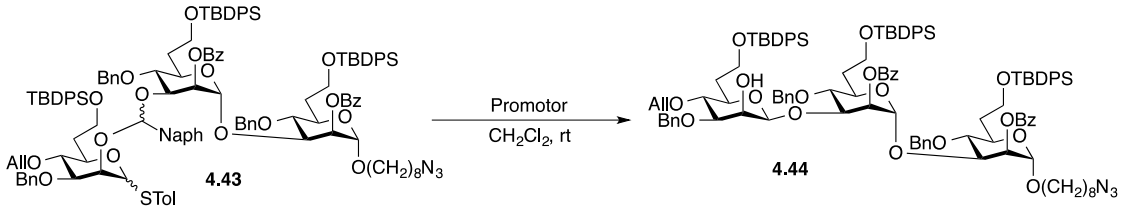


Entry	Acceptor (Equiv.)	Donor (Equiv.)	Yield of **4.43** (%)
1	**4.42** (1.0)	**4.31** (1.2)	~60
2	**4.42** (1.0)	**4.31** (2.0)	~77
3	**4.41** (1.0)	**4.38** (2.0)	–

Table 4.2. Attempts to make mix acetal **4.43** via the IAD strategy.

In the second step of IAD, the mixed acetal is converted to the glycoside. This was attempted first by treating **4.43** with the methyl trifluoromethanesulfonate and 2,6-di-*tert*-butyl-4-methylpyridine (MeOTf–DTBMP) promoter system. Under these conditions, the reaction went very slowly. The reaction was stopped after 24 hours, but only a small amount of the desired product **4.44** was obtained (**Table 4.3**, entry 1). Due to the slow reaction with MeOTf–DTBMP, the coupling reaction was attempted by treatment with dimethyl(methylthio)sulfonium trifluoromethanesulfonate (DMTST) (**Table 4.3**, entry 2). However, under these conditions I obtained a large amount of disaccharide **4.42** and monosaccharide **4.38**, and again a very small amount of

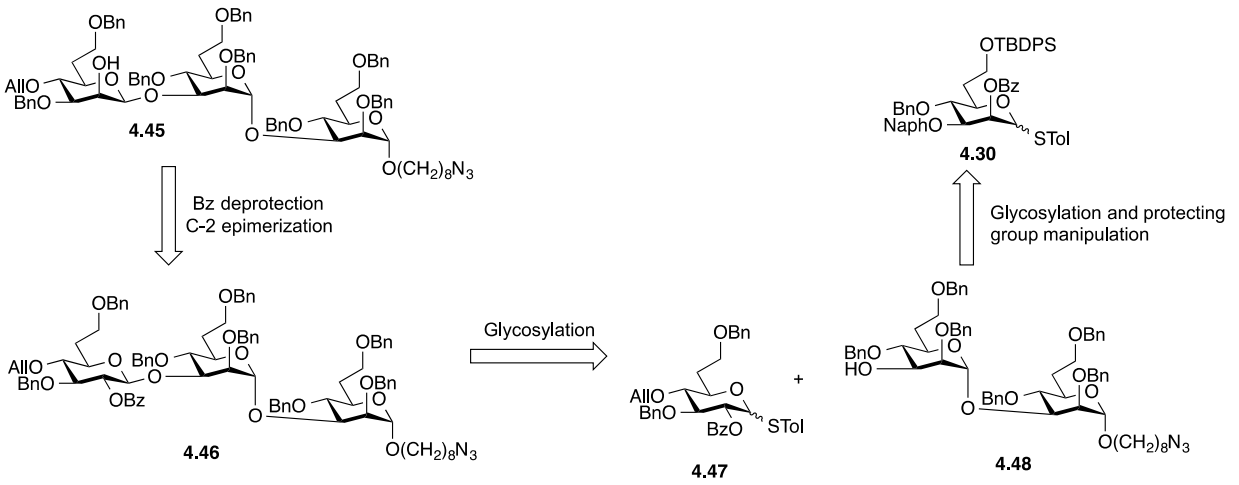
the desired product **4.44**. Thus, the mixed acetal **4.43** was treated with a higher amount of the MeOTf–DTBMP promotor to increase the reaction rate (**Table 4.3**, entry 3). Faster production of desired product **4.44** was observed by TLC, but the reaction did not go to completion, even when the reaction was left for four days. Under these conditions, the **4.44** ($^1J_{C1,H1}$ = 172.1 Hz and $^1J_{C1',H1'}$ = 172.8 Hz, $^1J_{C1,H1}$ = 156.4 Hz) was obtained only in 28% yield from **4.42**.



Entry	Promotor (Equiv.)	reaction time (h)	Yield of **4.44** from **4.42**
1	MeOTf–DTBMP (3.0)	24	3%
2	DMTST (3.0)	12	5%
3	MeOTf–DTBMP (10.0)	96	28%

Table 4.3. Attempts to synthesize trisaccharide **4.44** from **4.43**.

Although the desired trisaccharide **4.44** was synthesized by the IAD strategy, the low yield and long reaction time limited our approach to make pentasaccharide **4.29**. In addition, because of the time constraints of my Ph.D., I could not proceed further with the small amount of the synthesized trisaccharide. Recently, a gold-catalyzed glycosylation was used in the formation of the 1,2-*cis*-β-heptopyranoside linkage in the synthesis of the same trisaccharide[10], but only modest stereoselectivity was reported (β:α = 5:1 to 2.8:1). Therefore, the use of other methodology to introduce these residues is necessary. One possibility is an oxidation–reduction strategy (**Scheme 4.10**). A 6-deoxy-β-D-*gluco*-heptopyranoside could be installed via neighboring group participation of an ester group at C-2. Deprotection of this ester and C-2 inversion would then provide the 6-deoxy-β-D-*manno*-heptopyranoside.



Scheme 4.10. Retrosynthetic design of trisaccharide **4.45** using an oxidation–reduction strategy to introduce the 6-deoxy-β-D-*manno*-heptopyranoside.

4.3 Conclusion

A siloxane-protected thioglycoside donor (**4.2**) was synthesized to investigate its ability to introduce Xul*f* residues stereoselectively into oligosaccharides. I found that **4.2** exclusively produced β-Xul*f* glycosides with four different acceptors (**3.78**, **3.80**, **3.82** and **3.85**). The selectivity presumably arises by the siloxane blocking the attack of the nucleophile (the acceptor alcohol) from the bottom face of electrophilic intermediate formed upon activation of the donor. A similar system has been exploited in the synthesis of β-Fru*f* glycosides[4].

As was observed for β-Fru*f* glycosides[4], the C-2 chemical shifts in the siloxane-protected β-Xul*f* glycosides **4.19**–**4.22** were anomalous. Therefore, the determination of the anomeric configuration could only be done after removal of this protecting group to give **4.23**–**4.26**. In these partially-deprotected compounds, C-2 chemical shifts in the range of 105–108 ppm confirmed

the β-stereochemistry. The 2D ^{1}H–^{1}H TROESY data of **4.23**–**4.26** also supported the β-stereochemistry.

Thioglycoside **4.2** was successfully used in the synthesis of a protected derivative (**4.27**) of the pentasaccharide repeating unit of *Y. enterocolitica* O:5/O:5,27 LPS. Trisaccharide diol acceptor **3.130**, which generated four inseparable pentasaccharide isomers in the coupling reaction with thioglycoside donor **3.70** (Chapter 3), was coupled with **4.2** to generate exclusively **4.27**. We also attempted to synthesize the pentasaccharide repeating unit from *C. jejuni* RM1221. However, I was unable to do so given problems in the synthesis of a key intermediate, trisaccharide **4.44**, which contains a 6-deoxy-β-D-*manno*-heptopyranoside linkage.

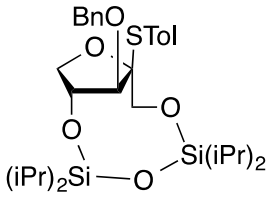
4.4 Experimental data

4.4.1 General experimental methods

Reactions were carried out in oven-dried glassware. 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 oxide catalyst under nitrogen. Unless stated otherwise, all reactions were carried out at room temperature under a positive pressure of argon and were monitored by TLC on silica gel 60 F_{254} (0.25 mm, E. Merck). Spots were detected under UV light or by charring with 10% H_2SO_4, in EtOH. Unless otherwise indicated, all column chromatography was performed on silica gel 60 (40–60 μm). The ratio between silica gel and crude product ranged from 100 to 50:1 (w/w). Optical rotations were measured at 22 ± 2 °C at the sodium D line (589 nm) and are in units of deg·mL(dm·g)$^{-1}$. ^{1}H NMR spectra were recorded at 500 or 700 MHz, and chemical shifts are referenced to $CHCl_3$ (7.26 ppm, $CDCl_3$). ^{13}C NMR spectra were recorded at 125 or 175 MHz, and ^{13}C chemical shifts were referenced to internal $CDCl_3$ (77.23 ppm, $CDCl_3$). In the processing of

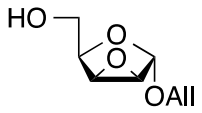
reaction mixtures, solutions of organic solvents were washed with equal amounts of aqueous solutions. Organic solutions were concentrated under vacuum at < 40 ºC (bath). Electrospray mass spectra were recorded on samples suspended in mixtures of THF with CH_3OH and added NaCl.

4.4.2 Experimental details for new compounds

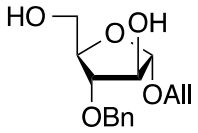


***p*-Tolyl 3-*O*-benzyl-1,4-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-2-thio-β-D-xylulofuranoside (4.2).** To a solution of **4.18** (530 mg, 1.53 mmol) in DMF (15.3 mL) was added imidazole (312 mg, 4.59 mmol) at room temperature and then the mixture was cooled to –40 °C. 1,3-Dichloro-1,1,3,3-tetraisopropyldisiloxane was then added dropwise. The reaction mixture was stirred at –40 °C for 1 h, and then warmed to room temperature and stirred for 5 h. Excess 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane was quenched by the addition of CH_3OH, before the solution was diluted with EtOAc and washed with water. The organic layer was dried over $MgSO_4$, filtered and the filtrate was concentrated. The resulting residue was purified by column chromatography (20:1, hexane–EtOAc) to give **4.2** (480 mg, 60%) as a colorless oil; $[\alpha]^{25}_D$ –54.1 (*c* 0.6, $CHCl_3$); R_f 0.47 (10:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.49–7.41 (m, 4H, ArH), 7.38–7.33 (m, 2H, ArH), 7.32–7.27 (m, 1H, ArH), 7.12–7.08 (m, 2H, ArH), 4.81 (d, 1H, J_{gem} = 11.9 Hz, ArCH_2), 4.70 (d, 1H, J_{gem} = 11.9 Hz, ArCH_2), 4.55 (d, 1H, $J_{4,5a}$ = 4.0 Hz, H-4), 4.50 (dd, 1H, $J_{5a,4}$ = 4.0 Hz, J_{gem} = 10.0 Hz, H-5a), 4.44 (br s, 1H, H-3), 3.95 (d, 1H, J_{gem} = 10.0 Hz, H-5b), 3.86 (d, 1H, J_{gem} = 12.1 Hz, H-1a), 3.71 (d, 1H, J_{gem} = 12.1 Hz, H-1b), 2.34 (s, 3H, ArCH_3), 1.07–0.75 (m, 28H, Si(*i*Pr)$_2$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.7 (Ar), 137.8 (Ar), 136.9 (2C, Ar), 129.4 (2C, Ar), 128.6 (2C, Ar), 128.0 (Ar), 127.9 (2C, Ar),

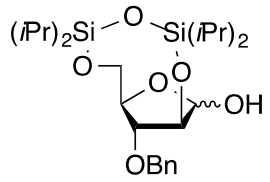
127.7 (Ar), 99.9 (C-2), 87.2 (C-3), 79.2 (C-4), 74.7 (Ar*C*H_2), 73.6 (C-5), 65.3 (C-1), 21.4 (Ar*C*H_3), 17.73 (($C$$H_3$)$_2$CHSi), 17.72 (($C$$H_3$)$_2$CHSi), 17.66 (($C$$H_3$)$_2$CHSi), 17.62 (($C$$H_3$)$_2$CHSi), 17.59 (($C$$H_3$)$_2$CHSi), 17.57 (($C$$H_3$)$_2$CHSi), 17.46 (($C$$H_3$)$_2$CHSi), 17.37 (($C$$H_3$)$_2$CHSi), 14.1 (($CH_3$)$_2$*C*HSi), 13.9 (($CH_3$)$_2$*C*HSi), 13.7 (($CH_3$)$_2$*C*HSi), 13.4 (($CH_3$)$_2$*C*HSi); HRMS (ESI) calcd. for $C_{31}H_{48}NaO_5SSi_2$ $[M+Na]^+$ 611.2653 found 611.2658.



Allyl 2,3-anhydro-α-D-lyxofuranoside (4.7). To a solution of **4.6** (1.18 g, 6.20 mmol) in tetrahydrofuran (30 mL) was added triphenylphosphine (1.95 g, 7.44 mmol) at room temperature, and then the mixture was cooled to 0 °C. Diisopropylazodicarboxylate (1.50 g, 1.46 mL, 7.44 mmol) was added dropwise over 5 min. After complete addition of the reagent, the reaction mixture was warmed to room temperature. After stirring for 1.5 h at room temperature, the reaction mixture was concentrated and the residue was purified by column chromatography (4:1, hexane–EtOAc) to give **4.7** (960 mg, 90%) as a colorless oil. $[\alpha]^{25}_D$ +69.4 (*c* 1.4, $CHCl_3$); R_f 0.32 (3:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 5.89 (dddd, 1H, *J* = 17.0, 10.4, 6.1, 5.4 Hz, OCH_2C*H*=CH_2), 5.29 (dq, 1H, *J* = 17.0, 1.7 Hz, OCH_2CH=C*H*$_2$), 5.20 (dq, 1H, *J* = 10.4, 1.2 Hz, OCH_2CH=C*H*$_2$), 5.11 (s, 1H, H-1), 4.24 (ddt, 1H, *J* = 12.7, 5.4, 1.2 Hz, OC*H*$_2$CH=CH_2), 4.14 (m, 1H, H-4), 4.03 (ddt, 1H, *J* = 12.7, 6.1, 1.2 Hz, OC*H*$_2$CH=CH_2), 3.86 (m, 2H, H-5a, H-5b), 3.75 (dd, 1H, $J_{2,1}$ = 0.5 Hz, $J_{2,3}$ = 2.9 Hz, H-2), 3.68 (d, 1H, $J_{3,2}$ = 2.9 Hz, H-3), 2.22 (t, 1H, *J* = 5.6 Hz, OH); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 133.7 (OCH_2CH=CH_2), 117.9 (OCH_2CH=*C*H$_2$), 100.4 (C-1), 76.2 (C-4), 69.0 (O*C*H$_2$CH=CH_2), 61.8 (C-5), 55.9 (C-3), 54.2 (C-2); HRMS (ESI) calcd. for $C_8H_{12}NaO_4$ $[M+Na]^+$ 195.0628 found 195.0631.

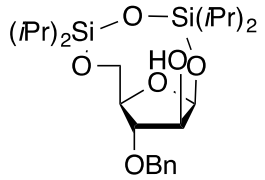


Allyl 3-*O*-benzyl-α-D-arabinofuranoside (4.8). To a solution of **4.7** (550 mg, 3.19 mmol) in benzyl alcohol (4 mL) was added 1M sodium benzyloxide in benzyl alcohol (4.79 mL, 4.79 mmol) at room temperature, and then the mixture was heated to 100 °C. After stirring at 100 °C for 24 h, the reaction mixture was cooled to room temperature and 1N HCl was added. The solution was diluted with CH_2Cl_2 and the organic layer was washed with water. The organic layer was dried over $MgSO_4$ and then filtered, concentrated. The residue was then purified by column chromatography (4:1, hexane–EtOAc) to give **4.8** (715 mg, 80%) as a colorless oil. $[\alpha]^{25}_D$ +105.8 (*c* 1.7, $CHCl_3$); R_f 0.26 (3:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 700 MHz) δ_H 7.36–7.31 (m, 4H, ArH), 7.30–7.27 (m, 1H, ArH), 5.95–5.87 (m, 1H, OCH_2CH=CH_2), 5.33–5.27 (m, 1H, OCH_2CH=CH_2), 5.21–5.17 (m, 1H, OCH_2CH=CH_2), 5.01 (br s, 1H, H-1), 4.70 (d, 1H, J_{gem} = 12.3 Hz, ArCH_2), 4.55 (d, 1H, J_{gem} = 12.3 Hz, ArCH_2), 4.24–4.18 (m, 3H, H-3, H-4, OCH_2CH=CH_2), 4.03–3.98 (m, 1H, OCH_2CH=CH_2), 3.85 (dd, 1H, $J_{2,1}$ = 1.2 Hz, $J_{2,3}$ = 4.3 Hz, H-2), 3.81 (dd, 1H, $J_{5a,4}$ = 2.6 Hz, J_{gem} = 11.9 Hz, H-5a), 3.58 (dd, 1H, $J_{5b,4}$ = 2.9 Hz, J_{gem} = 11.9 Hz, H-5b), 3.43 (br s, 1H, OH) 2.84 (br s, 1H, OH); ^{13}C NMR ($CDCl_3$, 175 MHz) δ_C 137.8 (Ar), 134.2 (OCH_2CH=CH_2), 128.5 (2C, Ar), 127.9 (Ar), 127.8 (2C, Ar), 117.9 (OCH_2CH=CH_2), 107.9 (C-1), 85.0 (C-2), 83.7 (C-4), 79.0 (C-3), 72.2 (ArCH_2), 68.1 (OCH_2CH=CH_2), 62.0 (C-5); HRMS (ESI) calcd. for $C_{15}H_{20}NaO_5$ $[M+Na]^+$ 303.1203 found 303.1207.



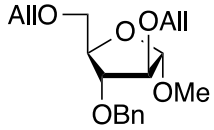
3-*O*-benzyl-2,5-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-α/β-D-arabinofuranose (4.9). To a solution of **4.8** (180 mg, 0.642 mmol) in DMF (6.4 mL) was added imidazole (174 mg, 2.57 mmol) and 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane (267 mL, 0.835 mmol) at –30 °C. The mixture was stirred at –30 °C for 2 h and then warmed to room temperature. After stirring at room temperature for 24 h, excess 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane was quenched by addition of CH_3OH, before the solution was diluted with EtOAc and washed with water. The organic layer was dried over $MgSO_4$, filtered and the filtrate was concentrated. To a solution of residue in THF (6.4 mL), degassed under vacuum, and stirred under an Ar atmosphere, (1,5-cyclooctadiene) bis-(methyldiphenylphosphine)iridium I hexafluorophosphate catalyst (16.3 mg, 0.019 mmol) was added, followed by further degassing of the mixture. The suspension was stirred for 30 min at 0 ºC, and the catalyst was then activated with hydrogen. At this point, the solution became nearly colorless. The excess hydrogen gas was removed by exchange with Ar gas. The reaction mixture was then stirred for 24 h at room temperature under an Ar atmosphere. The solvent was then evaporated, and the residue was dissolved in acetone–water (9:1, 10.0 mL). The solution was then added HgO (208 mg, 0.963 mmol) and $HgCl_2$ (261 mg, 0.963 mmol). After stirring for 24 h at room temperature, the solvent was evaporated and the residue was diluted with EtOAc and washed with 10% KI solution, satd. aq. $Na_2S_2O_3$, and water. The organic layer was then dried over $MgSO_4$, filtered and the filtrate was concentrated. The residue was then purified by column chromatography (4:1, hexane–EtOAc) to give **4.9** (211 mg, 63%, minor:major = 1:1.2) as a colorless oil; R_f 0.33 (4:1, hexane–EtOAc); **Minor**: ^{1}H NMR ($CDCl_3$, 700 MHz) δ_H

7.37–7.27 (m, 5H, ArH), 5.62 (dd, 1H, $J_{1,2}$ = 3.3 Hz, $J_{1,OH}$ = 12.2 Hz, H-1), 4.71–4.62 (m, 1H, ArCH_2), 4.51 (d, 1H, J_{gem} = 12.3 Hz, ArCH_2), 4.37 (br s, 1H, H-3), 4.28 (dd, 1H, $J_{4,5a}$ = 6.8 Hz, $J_{4,5b}$ = 10.6 Hz, H-4), 4.24 (d, 1H, $J_{2,1}$ = 3.3 Hz, H-2), 4.11 (d, 1H, $J_{OH,1}$ = 12.2 Hz, OH), 4.01 (dd, 1H, $J_{5a,4}$ = 6.8 Hz, J_{gem} = 10.6 Hz, H-5a), 3.72 (app t, 1H, $J_{5b,4}$ = J_{gem} = 10.6 Hz, H-5b), 1.22–0.72 (m, 28H, Si(*i*Pr)$_2$); ^{13}C NMR ($CDCl_3$, 175 MHz) δ_C 137.5 (Ar), 128.7 (2C, Ar), 128.1 (Ar), 127.7 (2C, Ar), 100.3 (C-1), 81.4 (C-3), 81.0 (C-4), 75.2 (C-2), 71.4 (Ar*C*H$_2$), 63.1 (C-5), 17.7–17.2 (8C, Si(CH*C*H$_3$)$_2$), 13.83 (Si(*C*HCH$_3$)$_2$), 13.7 (Si(*C*HCH$_3$)$_2$), 13.4 (Si(*C*HCH$_3$)$_2$), 12.76 (Si(*C*HCH$_3$)$_2$); **Major**: ^{1}H NMR ($CDCl_3$, 700 MHz) δ_H 7.37–7.27 (m, 5H, ArH), 5.26 (d, 1H, $J_{1,OH}$ = 12.2 Hz, H-1), 4.71–4.62 (m, 2H, H-4, ArCH_2), 4.55 (d, 1H, J_{gem} = 12.3 Hz, ArCH_2), 4.39 (br s, 1H, H-3), 4.33 (br s, 1H, H-2), 3.97 (dd, 1H, $J_{5a,4}$ = 7.1 Hz, J_{gem} = 10.8 Hz, H-5), 3.74 (app t, 1H, $J_{5b,a}$ = J_{gem} = 10.8 Hz, H-5b), 3.49 (d, 1H, $J_{OH,1}$ = 12.2 Hz, OH), 1.22–0.72 (m, 28H, Si(*i*Pr)$_2$); ^{13}C NMR ($CDCl_3$, 175 MHz) δ_C 137.2 (Ar), 128.8 (2C, Ar), 128.3 (Ar), 127.8 (2C, Ar), 105.5 (C-1), 83.6 (C-4), 81.4 (C-2), 80.3 (C-3), 71.9 (Ar*C*H$_2$), 62.7 (C-5), 17.7–17.2 (8C, Si(CH*C*H$_3$)$_2$), 13.77 (Si(*C*HCH$_3$)$_2$), 13.6 (Si(*C*HCH$_3$)$_2$), 13.5 (Si(*C*HCH$_3$)$_2$), 12.84 (Si(*C*HCH$_3$)$_2$); HRMS (ESI) calcd. for $C_{24}H_{42}NaO_6Si_2$ $[M+H]^+$ 505.2412 found 505.2410.



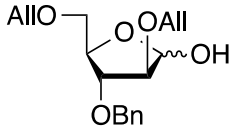
3-*O*-benzyl-1,5-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-β-D-arabinofuranose (4.10). To a solution of **4.9** (42.8 mg, 0.10 mmol) in EtOH (5.0 mL) was added sodium borohydride (7.5 mg, 0.2 mmol) at room temperature. After stirring at room temperature for 5 min, 1N HCl was added. The mixture was diluted with EtOAc and the organic layer was washed with water and satd. aq. $NaHCO_3$. The organic layer was dried over $MgSO_4$, filtered and the filtrate was concen-

trated. The residue was then purified by column chromatography (15:1, hexane–EtOAc) to give **4.10** (34.0 mg, 79%) as a colorless oil. R_f 0.39 (9:1, hexane–EtOAc); $[\alpha]^{25}_D$ –17.8 (*c* 0.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.39–7.32 (m, 4H, ArH), 7.30–7.27 (m, 1H, ArH), 5.51 (d, 1H, $J_{1,2}$ = 4.8 Hz, H-1), 4.83 (d, 1H, J_{gem} = 11.8 Hz, ArC*H*$_2$), 4.65 (d, 1H, J_{gem} = 11.8 Hz, ArC*H*$_2$), 4.24 (ddd, 1H, $J_{2,1}$ = 4.8 Hz, $J_{2,3}$ = 6.3 Hz, $J_{2,OH}$ = 9.9 Hz, H-2), 4.04 (app t, 1H, $J_{3,2}$ = $J_{3,4}$ = 6.3 Hz, H-3), 3.98–3.92 (m, 2H, H-4, H-5a), 3.83 (dd, 1H, $J_{5b,4}$ = 4.4 Hz, J_{gem} = 12.0 Hz, H-5b), 2.75 (d, 1H, $J_{OH,2}$ = 9.9 Hz, 2-OH), 1.30–0.85 (m, 28H, SiC*H*(C*H*$_3$)$_2$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.2 (Ar), 128.6 (2C, Ar), 127.93 (2C, Ar), 127.90 (Ar), 96.9 (C-1), 82.7 (C-3), 82.1 (C-4), 79.0 (C-2), 72.3 (Ar*C*H$_2$), 63.5 (C-5), 17.67 (2C, SiCH(*C*H$_3$)$_2$), 17.63 (SiCH(*C*H$_3$)$_2$), 17.55 (SiCH(*C*H$_3$)$_2$), 17.51 (2C, SiCH(*C*H$_3$)$_2$), 17.47 (SiCH(*C*H$_3$)$_2$), 17.46 (SiCH(*C*H$_3$)$_2$), 13.5 (Si*C*H(CH$_3$)$_2$), 13.26 (Si*C*H(CH$_3$)$_2$), 13.24 (Si*C*H(CH$_3$)$_2$), 12.7 (Si*C*H(CH$_3$)$_2$); HRMS (ESI) calcd. for $C_{24}H_{42}NaO_6Si_2$ $[M+Na]^+$ 505.2412 found 505.2409.



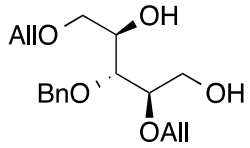
Methyl 2,5-di-*O*-allyl-3-*O*-benzyl-α-D-arabinofuranoside (4.12). To a solution of **4.11**[7] (200 mg, 0.787 mmol) in DMF (15.7 mL) was added allyl bromide (163 μL, 1.89 mmol) and sodium hydride (94 mL, 2.36 mmol) at 0 °C. After stirring at 0 °C for 1 h, CH_3OH was added. The mixture was then diluted with EtOAc and the organic layer was washed with water. The organic layer was dried over $MgSO_4$, filtered and the filtrate was concentrated. The residue was then purified by column chromatography (8:1, hexane–EtOAc) to give **4.12** (242 mg, 92%) as a colorless oil. $[\alpha]^{25}_D$ +66.3 (*c* 1.0, $CHCl_3$); R_f 0.27 (4:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.36–7.26 (m, 5H, ArH), 5.93–5.83 (m, 2H, OCH_2CH=CH_2), 5.31–5.23 (m, 2H, OCH_2CH=C*H*$_2$), 5.22–5.15 (m, 2H, OCH_2CH=C*H*$_2$), 4.91 (br s, 1H, H-1), 4.66 (d, 1H, J_{gem} = 12.1 Hz, ArC*H*$_2$),

4.59 (d, 1H, J_{gem} = 12.1 Hz, ArCH_2), 4.19 (ddd, 1H, $J_{4,3}$ = 6.4 Hz, $J_{4,5a}$ = 4.0 Hz, $J_{4,5b}$ = 5.6 Hz, H-4), 4.02–3.99 (m, 3H, OCH_2CH=CH_2), 3.96–3.93 (m, 2H, H-2, OCH_2CH=CH_2), 3.83 (d, 1H, $J_{3,2}$ = 2.4 Hz, $J_{3,4}$ = 6.4 Hz, H-3), 3.58 (dd, 1H, $J_{5a,4}$ = 4.0 Hz, J_{gen} = 10.6 Hz, H-5a), 3.55 (dd, 1H, $J_{5b,4}$ = 5.6 Hz, J_{gem} = 10.6 Hz, H-5b), 3.40 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.0 (Ar), 134.7 (OCH_2CH=CH_2), 134.2 (OCH_2CH=CH_2), 128.4 (2C, Ar), 128.0 (2C, Ar), 127.8 (Ar), 117.5 (OCH_2CH=CH_2), 117.2 (OCH_2CH=CH_2), 107.4 (C-1), 88.2 (C-2), 83.6 (C-3), 80.9 (C-4), 72.5 (ArCH_2), 72.3 (OCH_2CH=CH_2), 70.9 (OCH_2CH=CH_2), 70.1 (C-5), 55.0 (OCH_3); HRMS (ESI) calcd. for $C_{19}H_{26}NaO_5$ $[M+Na]^+$ 357.1672 found 356.1668.



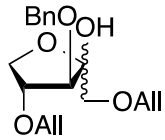
2,5-Di-*O*-allyl-3-*O*-benzyl-α/β-D-arabinofuranose (4.13). To a solution of **4.12** (120 mg, 0.359 mmol) in AcOH (4.0 mL) was added sulfuric acid (1.0 mL) at room temperature, and the solution was heated to 70 °C. After stirring at 70 °C for 6 h, the solution was cooled to room temperature and the mixture was diluted with EtOAc, before the organic layer was washed with water and satd. aq. $NaHCO_3$. The organic layer was dried over $MgSO_4$, filtered and the filtrate was concentrated. The residue was then purified by column chromatography (4:1, hexane–EtOAc) to give **4.13** (96 mg, 84%, α:β = 1.2:1) as a colorless oil. R_f 0.10 (4:1, hexane–EtOAc); **4.13α**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.38–7.27 (m, 5H, ArH), 5.98–5.81 (m, 2H, OCH_2CH=CH_2), 5.34 (br s, 1H, H-1), 5.33–5.15 (m, 4H, OCH_2CH=CH_2), 4.70–4.55 (m, 2H, ArCH_2), 4.43 (app dt, 1H, $J_{4,3}$ = 3.9 Hz, $J_{4,5a}$ = $J_{4,5b}$ = 6.1 Hz, H-4), 4.16–3.95 (m, 4H, OCH_2CH=CH_2), 3.94 (d, 1H, $J_{2,3}$ = 1.8 Hz, H-2), 3.89 (dd, 1H, $J_{3,2}$ = 1.8 Hz, $J_{3,4}$ = 3.9 Hz, H-3), 3.57–3.44 (m, 2H, H-5a, H-5b); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 137.5 (Ar), 134.7 (OCH_2CH=CH_2), 134.11 (OCH_2CH=CH_2), 128.6 (2C, Ar), 128.1 (Ar), 128.0 (2C, Ar), 117.7 (OCH_2CH=CH_2), 117.3 (OCH_2CH=CH_2), 101.2 (C-

1), 86.7 (C-2), 83.1 (C-3), 82.0 (C-4), 72.5 (O*C*H_2CH=CH_2), 72.2 ((Ar*C*H_2), 70.9 (O*C*H_2CH=CH_2), 70.4 (C-5); **4.13β**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.38–7.27 (m, 5H, ArH), 5.98–5.81 (m, 2H, OCH$_2$C*H*=CH_2), 5.33–5.15 (m, 5H, H-1, OCH$_2$CH=C*H$_2$*), 4.70–4.55 (m, 2H, ArC*H$_2$*), 4.16–3.95 (m, 7H, H-2, H-3, H-4, OC*H$_2$*CH=CH_2), 3.57–3.44 (m, 2H, H-5a, H-5b); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.05 (Ar), 134.22 (OCH$_2$*C*H=CH_2), 134.16 (OCH$_2$*C*H=CH_2), 128.6 (2C, Ar), 128.1 (Ar), 128.0 (2C, Ar), 118.07 (OCH$_2$CH=*C*H_2), 117.9 (OCH$_2$CH=*C*H_2), 96.2 (C-1), 84.4 (C-2), 82.0 (C-3), 80.6 (C-4), 72.6 (O*C*H_2CH=CH_2), 72.2 (Ar*C*H_2), 71.5 (O*C*H_2CH=CH_2), 70.7 (C-5); HRMS (ESI) calcd. for $C_{18}H_{24}NaO_5$ $[M+Na]^+$ 343.1516 found 343.1513.



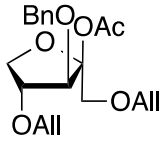
1,4-Di-*O*-allyl-3-*O*-benzyl-L-arabitol (4.14). To a solution of **4.13** (330 mg, 1.03 mmol) in EtOH (5.0 mL) was added sodium borohydride (77.9 mg, 2.06 mmol) at room temperature. After stirring at room temperature for 2 h, 1N HCl was added. The mixture was diluted with EtOAc and the organic layer was washed with water and satd. aq. $NaHCO_3$. The organic layer was dried over $MgSO_4$, filtered and the filtrate was concentrated. The residue was then purified by column chromatography (4:1, hexane–EtOAc) to give **4.14** (300 mg, 90%) as a colorless oil. $[\alpha]^{25}_D$ +2.6 (*c* 1.0, $CHCl_3$); R_f 0.44 (1:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.37–7.26 (m, 5H, ArH), 5.96–5.86 (m, 2H, OCH$_2$C*H*=CH_2), 5.31–5.22 (m, 2H, OCH$_2$CH=C*H$_2$*), 5.21–5.15 (m, 2H, OCH$_2$CH=C*H$_2$*), 4.65 (s, 2H, ArC*H$_2$*), 4.17–4.09 (m, 2H, OC*H$_2$*CH=CH_2), 4.06–3.95 (m, 3H, H-2, OC*H$_2$*CH=CH_2), 3.81–3.72 (m, 2H, H-5), 3.71–3.66 (m, 2H, H-3, H-4), 3.64 (dd, 1H, $J_{1a,2}$ = 3.6 Hz, J_{gem} = 9.8 Hz, H-1a), 3.59 (dd, 1H, $J_{1b,2}$ = 5.4 Hz, J_{gem} = 9.8 Hz, H-1b), 2.68 (br s, 2H, O*H*); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.1 (Ar), 134.8 (OCH$_2$*C*H=CH_2), 134.6

($OCH_2CH=CH_2$), 128.6 (2C, Ar), 128.4 (2C, Ar), 128.1 (Ar), 117.8 ($OCH_2CH=CH_2$), 117.5 ($OCH_2CH=CH_2$), 79.7 (C-3), 78.4 (C-4), 74.0 ($ArCH_2$), 72.5 ($OCH_2CH=CH_2$), 72.1 ($OCH_2CH=CH_2$), 71.2 (C-1), 70.7 (C-2), 61.7 (C-5); HRMS (ESI) calcd. for $C_{18}H_{26}NaO_5$ $[M+Na]^+$ 345.1672 found 345.1672.



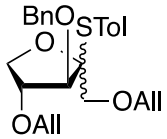
1,4-Di-*O*-allyl-3-*O*-benzyl-α/β-D-xylulofuranose (4.15). To a solution of **4.14** (300 mg, 0.93 mmol) in CH_2Cl_2 (10.0 mL) was added trityl chloride (311 mg, 1.11 mmol) and 1,4-diazabicyclo[2.2.2]octane (157 mg, 1.40 mmol) at room temperature. After stirring at room temperature for 1 h, excess trityl chloride was quenched by the addition of CH_3OH. The mixture was concentrated and dried *in vacuo* overnight. To a solution of the residue in CH_2Cl_2 (10.0 mL) was added Dess–Martin Periodinane (592 mg, 1.40 mmol) at room temperature. After stirring at room temperature for 5 h, satd. aq. $NaHCO_3$ was added. The organic layer was washed with water and dried over $MgSO_4$, filtered and the filtrate was concentrated. To a solution of the residue in CH_2Cl_2 (10.0 mL) was added trifluoroacetic acid (85 μL, 1.11 mmol) at room temperature. After stirring at room temperature for 30 min, Triethylamine was added. The mixture was concentrated and then the residue was purified by column chromatography (8:1, hexane–EtOAc) to give **4.15** (226 mg, 76%) as a colorless oil. $[\alpha]^{25}_D$ –48.5 (*c* 1.0, $CHCl_3$); R_f 0.27 (4:1, hexane–EtOAc); **4.15α**: ^1H NMR ($CDCl_3$, 700 MHz) δ_H 7.39–7.27 (m, 5H, ArH), 5.97–5.81 (m, 2H, $OCH_2CH=CH_2$), 5.31–5.16 (m, 4H, $OCH_2CH=CH_2$), 4.67 (d, 1H, J_{gem} = 12.3 Hz, $ArCH_2$), 4.65 (d, 1H, J_{gem} = 12.3 Hz, $ArCH_2$), 4.20–3.98 (m, 7H, H-3, H-4, H-5a, H-5b, $OCH_2CH=CH_2$), 3.97–3.93 (m, 1H, $OCH_2CH=CH_2$), 3.90 (br s, 1H, 2-OH) 3.72 (d, 1H, J_{gem} = 10.2 Hz, H-1a), 3.62 (d,

1H, J_{gem} = 10.2 Hz, H-1b); ^{13}C NMR ($CDCl_3$, 175 MHz) δ_H 137.9 (Ar), 134.7 ($OCH_2CH{=}CH_2$), 134.0 ($OCH_2CH{=}CH_2$), 128.7 (2C, Ar), 128.4 (2C, Ar), 128.1 (Ar), 118.0 ($OCH_2CH{=}CH_2$), 117.6 ($OCH_2CH{=}CH_2$), 105.7 (C-2), 85.2 (C-3 or C-4), 81.9 (C-3 or C-4), 73.0 ($OCH_2CH{=}CH_2$), 72.7 ($ArCH_2$), 71.5 (C-5), 71.0 ($OCH_2CH{=}CH_2$), 70.8 (C-1); **4.15β**: ^{1}H NMR ($CDCl_3$, 700 MHz) δ_H 7.39–7.27 (m, 5H, ArH), 5.97–5.81 (m, 2H, $OCH_2CH{=}CH_2$), 5.31–5.16 (m, 4H, $OCH_2CH{=}CH_2$), 4.75 (d, 1H, J_{gem} = 11.4 Hz, $ArCH_2$), 4.70 (d, 1H, J_{gem} = 11.4 Hz, $ArCH_2$), 4.20–3.98 (m, 5H, H-3, H-4, H-5a, $OCH_2CH{=}CH_2$, 2-OH), 3.97–3.93 (m, 2H, $OCH_2CH{=}CH_2$), 3.77 (dd, 1H, $J_{5b,4}$ = 3.0 Hz, J_{gem} = 9.8 Hz, H-5b), 3.54 (d, 1H, J_{gem} = 10.4 Hz, H-1a), 3.49 (d, 1H, J_{gem} = 10.4 Hz, H-1b); ^{13}C NMR ($CDCl_3$, 175 MHz) δ_C 137.4 (Ar), 134.7 ($OCH_2CH{=}CH_2$), 134.4 ($OCH_2CH{=}CH_2$), 128.8 (2C, Ar), 128.4 (2C, Ar), 128.0 (Ar), 117.6 ($OCH_2CH{=}CH_2$), 117.5 ($OCH_2CH{=}CH_2$), 103.1 (C-2), 83.3 (C-3 or C-4), 82.7 (C-3 or C-4), 73.3 ($ArCH_2$), 72.8 ($OCH_2CH{=}CH_2$), 72.5 (C-1), 70.7 ($OCH_2CH{=}CH_2$), 69.5 (C-5); HRMS (ESI) calcd. for $C_{18}H_{24}NaO_5$ $[M+Na]^+$ 343.1516 found 343.1516.



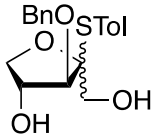
2-*O*-acetyl-1,4-di-*O*-allyl-3-*O*-benzyl-β-D-xylulofuranose (4.16). To a solution of **4.15** (900 mg, 2.81 mmol) in CH_2Cl_2 (15.0 mL) was added acetic anhydride (318 μL, 3.37 mmol) and *n*-butyllithium (1.35 mL, 3.37 mmol) at –78 °C. After stirring at –78 °C for 2 h, the mixture was warmed to room temperature, and 1N HCl was added. The mixture was diluted with EtOAc and the organic layer was washed with water and satd. aq. $NaHCO_3$. The organic layer was dried over $MgSO_4$, filtered and the filtrate was concentrated. The residue was then purified by column chromatography (4:1, hexane–EtOAc) to give **4.16** (834 mg, 82%) as a colorless oil. $[\alpha]^{25}_D$ –48.5

(*c* 1.0, $CHCl_3$); R_f 0.33 (8:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 700 MHz) δ_H 7.37–7.27 (m, 5H, ArH), 5.91–5.82 (m, 2H, OCH_2CH=CH_2), 5.29–5.22 (m, 2H, OCH_2CH=CH_2), 5.20–5.15 (m, 2H, OCH_2CH=CH_2), 4.72 (d, 1H, J_{gem} = 11.9 Hz, $ArCH_2$), 4.63 (d, 1H, J_{gem} = 11.9 Hz, $ArCH_2$), 4.38–4.31 (m, 2H, H-4, H-5a), 4.25 (d, 1H, $J_{3,4}$ = 4.6 Hz, H-3), 4.10–4.01 (m, 2H, OCH_2CH=CH_2), 3.99–3.91 (m, 2H, OCH_2CH=CH_2), 3.84–3.80 (m, 2H, H-1a, H-5b), 3.75 (d, 1H, J_{gem} = 10.7 Hz, H-1b), 2.04 (s, 3H, $COCH_3$); ^{13}C NMR ($CDCl_3$, 175 MHz) δ_C 169.5 (C=O), 138.1 (Ar), 134.62 (OCH_2CH=CH_2), 134.58 (OCH_2CH=CH_2), 128.5 (2C, Ar), 128.1 (2C, Ar), 128.0 (Ar), 117.51 (OCH_2CH=CH_2), 117.50 (OCH_2CH=CH_2), 108.5 (C-2), 84.9 (C-3), 83.2 (C-4), 73.2 ($ArCH_2$), 72.9 (OCH_2CH=CH_2), 72.1 (C-5), 71.4 (C-1), 71.1 (OCH_2CH=CH_2), 22.2 ($COCH_3$); HRMS (ESI) calcd. for $C_{20}H_{26}NaO_6S$ $[M+Na]^+$ 385.1622 found 385.1621.



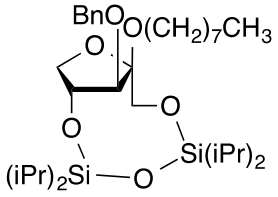
***p*-Tolyl 1,4-di-*O*-allyl-3-*O*-benzyl-2-thio-α/β-D-xylulofuranoside (4.17).** To a solution of **4.16** (550 mg, 1.52 mmol) in CH_2Cl_2 (15.0 mL) was added thiocresol (208 mg, 1.67 mmol) and boron trifluoride etherate (225 μL, 1.82 mmol) at 0 °C. After stirring at 0 °C for 30 min, triethylamine was added. The mixture was concentrated and the residue was then purified by column chromatography (4:1, hexane–EtOAc) to give **4.17** (540 mg, 83%, α/β = 1:8, inseparable) as a colorless oil; R_f 0.37 (8:1, hexane–EtOAc); **4.17β**: ^{1}H NMR ($CDCl_3$, 700 MHz) δ_H 7.46–7.40 (m, 4H, ArH), 7.39–7.35 (m, 2H, ArH), 7.32–7.29 (m, 1H, ArH), 7.13–7.08 (m, 2H, ArH), 5.90–5.76 (m, 2H, OCH_2CH=CH_2), 5.28–5.16 (m, 3H, OCH_2CH=CH_2), 5.14–5.10 (m, 1H, OCH_2CH=CH_2), 4.86 (d, 1H, J_{gem} = 12.1 Hz, $ArCH_2$), 4.69 (d, 1H, J_{gem} = 12.1 Hz, $ArCH_2$), 4.44–4.40 (m, 2H, H-3, H-5a), 4.32–4.29 (m, 1H, H-4), 4.02–3.90 (m, 2H, OCH_2CH=CH_2), 3.89 (dd, 1H, $J_{5b,4}$ =3.0 Hz,

J_{gem} = 9.4 Hz, H-5b), 3.87–3.83 (m, 1H, OCH_2CH=CH_2), 3.59 (d, 1H, J_{gem} = 11.7 Hz, H-1a), 3.38 (d, 1H, J_{gem} = 11.7 Hz, H-1b), 2.34 (s, 3H, ArCH_3); ^{13}C NMR ($CDCl_3$, 175 MHz) δ_C 138.7 (Ar), 138.1 (Ar), 136.6 (2C, Ar), 134.8 (OCH$_2$*C*H=CH$_2$), 134.6 (OCH$_2$*C*H=CH$_2$), 129.5 (2C, Ar), 128.5 (2C, Ar), 128.3 (2C, Ar), 127.9 (Ar), 127.4 (Ar), 117.5 (OCH$_2$CH=*C*H$_2$), 117.2 (OCH$_2$CH=*C*H$_2$), 98.2 (C-2), 86.9 (C-3), 84.2 (C-4), 73.1 (Ar*C*H$_2$), 72.6 (O*C*H$_2$CH=CH$_2$), 71.9 (C-1), 70.8 (O*C*H$_2$CH=CH$_2$), 69.7 (C-5), 21.4 (Ar*C*H$_3$); HRMS (ESI) calcd. for $C_{25}H_{30}NaO_4S$ $[M+Na]^+$ 449.1757 found 449.1753.



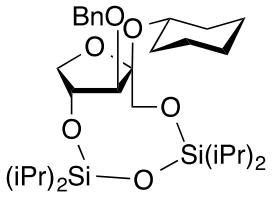
***p*-Tolyl 3-*O*-benzyl-2-thio-α/β-D-xylulofuranoside (4.18).** To a solution of **4.17** (730 mg, 1.71 mmol) in THF (17.1 mL), degassed under vacuum, and stirred under an Ar atmosphere, (1,5-cyclooctadiene) bis-(methyldiphenylphosphine)iridium(I) hexafluorophosphate catalyst (72 mg, 86 μmol) was added, followed by further degassing of the mixture. The suspension was stirred for 30 min at 0 ºC, and the catalyst was then activated with hydrogen. At this point, the solution became nearly colorless. The excess hydrogen gas was removed by exchange with Ar gas. The reaction mixture was then stirred for 4 h at room temperature under an Ar atmosphere. The solvent was then evaporated, and the residue was dissolved in CH_3OH (17.1 mL). To the solution was then added *p*-toluenesulfonic acid (29.5 mg, 0.171 mmol). After stirring for 2 h at room temperature, triethylamine was added, and the mixture was concentrated. The resulting residue was purified by column chromatography (2:1, hexane–EtOAc) to give **4.18** (530 mg, 89%, α/β = 1:8, inseparable) as a colorless oil; R_f 0.31 (1:1, hexane–EtOAc); **4.18β**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.46–7.29 (m, 7H, ArH), 7.14–7.09 (m, 2H, ArH), 4.81 (d, 1H, J_{gem} = 11.9 Hz, ArCH_2),

4.69 (d, 1H, J_{gem} = 11.9 Hz, ArCH_2), 4.45–4.37 (m, 2H, H-4, H-5a), 4.19 (d, 1H, J = 1.6 Hz, H-3), 3.86–3.81 (m, 1H, H-5b), 3.64 (d, 1H, J_{gem} = 11.8 Hz, H-1a), 3.52 (d, 1H, J_{gem} = 11.8 Hz, H-1b), 2.75 (br s, 1H, OH), 2.34 (s, 3H, ArCH_3), 2.28 (br s, 1H, OH); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 139.1 (Ar), 137.8 (Ar), 136.7 (2C, Ar), 129.6 (2C, Ar), 128.7 (2C, Ar), 128.2 (Ar), 128.0 (2C, Ar), 127.0 (Ar), 98.4 (C-2), 88.4 (C-3), 76.7 (C-4), 73.7 (ArCH$_2$), 72.6 (C-5), 65.5 (C-1), 21.4 (ArCH$_3$); HRMS (ESI) calcd. for $C_{19}H_{22}NaO_4S$ $[M+Na]^+$ 369.1131 found 369.1130.



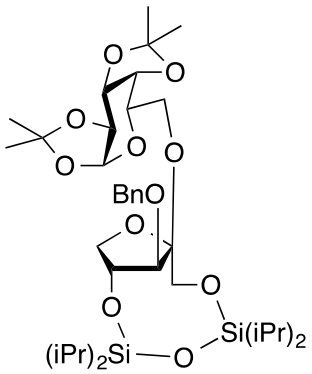
Octyl 3-*O*-benzyl-1,4-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-β-D-xylulofuranoside (4.19). To a solution of **4.2** (19.4 mg, 0.0330 mmol) and **3.80** (5.2 mg, 0.0400 mmol) in CH_2Cl_2 (1.3 mL) was added 4Å MS at room temperature. After stirring for 30 min at room temperature, the reaction was cooled to –78 °C. To the mixture was added *N*-iodosuccinimide (8.9 mg, 0.0400 mmol) and silver triflate (1.7 mg, 0.0066 mmol) at –78 °C. After stirring at –78 °C for 4 h, triethylamine was added. The reaction was warmed to room temperature and then a small amount of H_2O was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The mixture was dried over $MgSO_4$ and then filtered and concentrated. The resulting residue was purified by column chromatography (50:1, hexane–EtOAc) to give **4.19** (16.2 mg, 83%, β only) as a colorless oil; $[\alpha]^{25}_D$ –30.8 (*c* 0.4, $CHCl_3$); R_f 0.47 (10:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.40–7.26 (m, 5H, ArH), 4.86 (d, 1H, J_{gem} = 12.1 Hz, ArCH_2), 4.59 (d, 1H, J_{gem} = 12.1 Hz, ArCH_2), 4.46 (d, 1H, $J_{4,5a}$ = 4.1 Hz, H-4), 4.29 (dd, 1H, $J_{5a,4}$ = 4.1 Hz, J_{gem} = 9.6 Hz, H-5a), 4.26 (br s, 1H, H-3), 4.00 (d, 1H, J_{gem} = 12.0 Hz, H-1a), 3.95 (d, 1H, J_{gem} = 12.0 Hz, H-1b), 3.83

(d, 1H, J_{gem} = 9.6 Hz, H-5b), 3.67 (t, 2H, J = 6.6 Hz, octyl OCH_2), 1.66–1.55 (m, 2H, octyl CH_2), 1.41–1.20 (m, 10H, octyl CH_2), 1.10–0.71 (m, 31H, SiCH(CH_3)$_2$, octyl CH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.7 (Ar), 128.4 (2C, Ar), 127.9 (2C, Ar), 127.8 (Ar), 108.8 (C-2), 83.3 (C-3), 78.8 (C-4), 75.1 (C-5), 73.2 (ArCH$_2$), 64.2 (C-1), 63.1 (octyl OCH$_2$), 32.1 (octyl CH$_2$), 30.7 (octyl CH$_2$), 29.6 (octyl CH$_2$), 29.5 (octyl CH$_2$), 26.4 (octyl CH$_2$), 22.9 (octyl CH$_2$), 17.70 ((CH$_3$)$_2$CHSi), 17.59 (3C, SiCH(CH$_3$)$_2$), 17.57 (2C, SiCH(CH$_3$)$_2$), 17.52 (SiCH(CH$_3$)$_2$), 17.41 (SiCH(CH$_3$)$_2$), 14.3 (SiCH(CH$_3$)$_2$), 13.8 (2C, SiCH(CH$_3$)$_2$), 13.6 (SiCH(CH$_3$)$_2$), 13.2 (octyl CH$_3$); HRMS (ESI) calcd. for $C_{32}H_{58}NaO_6Si_2$ $[M+Na]^+$ 617.3664 found 617.3663.



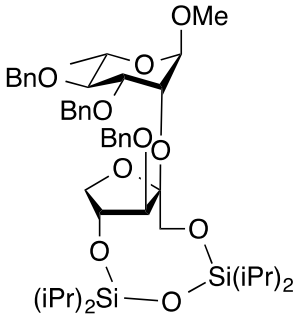
Cyclohexyl 3-*O*-benzyl-1,4-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-β-D-xylulofuranoside (4.20). To a solution of **4.2** (7.2 mg, 0.012 mmol) and **3.78** (1.5 mg, 0.015 mmol) in CH_2Cl_2 (0.50 mL) was added 4Å MS at room temperature. After stirring at room temperature for 30 min, the reaction mixture was cooled to –78 °C. To the mixture was added *N*-iodosuccinimide (3.3 mg, 0.015 mmol) and silver triflate (0.6 mg, 0.0024 mmol) at –78 °C. After stirring at –78 °C for 4 h, triethylamine was added. The reaction was warmed to room temperature and then a small amount of H_2O was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The mixture was dried over $MgSO_4$ and then filtered and concentrated. The resulting residue was purified by column chromatography (10:1, hexane–EtOAc) to give **4.20** (5.7 mg, 83%, β only) as a colorless oil; $[\alpha]^{25}_D$ –23.9 (*c* 0.10, $CHCl_3$); R_f 0.36 (10:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.38–7.29 (m, 4H, ArH), 7.28–7.26 (m, 1H, ArH), 4.88

(d, 1H, J_{gem} = 12.0 Hz, ArCH_2), 4.58 (d, 1H, J_{gem} = 12.0 Hz, ArCH_2), 4.44 (d, 1H, $J_{4,5a}$ = 4.2 Hz, H-4), 4.30 (dd, 1H, $J_{5a,4}$ = 4.2 Hz, J_{gem} = 9.8 Hz, H-5a), 4.22 (br s, 1H, H-3), 4.02 (d, 1H, J_{gem} = 12.1 Hz, H-1a), 3.90 (d, 1H, J_{gem} = 12.1 Hz, H-1b), 3.85–3.77 (m, 2H, H-5b, cyclohexyl OC*H*) 1.90–1.79 (m, 2H, cyclohexyl CH_2) 1.76–1.67 (m, 2H, cyclohexyl CH_2), 1.51–1.23 (m, 6H, cyclohexyl CH_2), 1.07–0.75 (m, 28H, SiC*H*(CH_3)$_2$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.8 (Ar), 128.4 (2C, Ar), 128.0 (2C, Ar), 127.7 (Ar), 109.2 (C-2), 83.5 (C-3), 78.9 (C-4), 75.0 (C-5), 73.3 (Ar*C*H$_2$), 71.6 (cyclohexyl O*C*H), 64.5 (C-1), 34.8 (cyclohexyl *C*H$_2$), 34.7 (cyclohexyl *C*H$_2$), 25.9 (cyclohexyl *C*H$_2$), 24.66 (cyclohexyl *C*H$_2$), 24.62 (cyclohexyl *C*H$_2$), 17.7 (SiCH(*C*H$_3$)$_2$), 17.64 (SiCH(*C*H$_3$)$_2$), 17.62 (2C, SiCH(*C*H$_3$)$_2$), 17.59 (2C, SiCH(*C*H$_3$)$_2$), 17.54 (SiCH(*C*H$_3$)$_2$), 17.4 (SiCH(*C*H$_3$)$_2$), 13.8 (2C, Si*C*H(CH$_3$)$_2$), 13.6 (Si*C*H(CH$_3$)$_2$), 13.3 (Si*C*H(CH$_3$)$_2$); HRMS (ESI) calcd. for $C_{30}H_{52}NaO_6Si_2$ $[M+Na]^+$ 587.3195 found 587.3195.



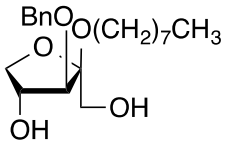
3-*O*-benzyl-1,4-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-β-D-xylulofuranosyl-(2→6)-1,2,3,4-di-*O*-isopropylidene-α-D-galactopyranose (4.21). To a solution of **4.2** (15.6 mg, 0.027 mmol) and **3.82** (8.3 mg, 0.032 mmol) in CH_2Cl_2 (1.1 mL) was added 4Å MS at room temperature. After stirring for 30 min at room temperature, the reaction mixture was cooled to –78 °C. To the mixture was added *N*-iodosuccinimide (7.1 mg, 0.032 mmol) and silver triflate (1.4 mg, 0.0050 mmol) at –78 °C. After stirring at –78 °C for 3 h, triethylamine was added. The reaction

was warmed to room temperature and then a small amount of H_2O was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The mixture was dried over $MgSO_4$ and then filtered and concentrated. The resulting residue was purified by column chromatography (20:1, hexane–EtOAc) to give **4.21** (16.8 mg, 88%, β only) as a colorless oil; $[\alpha]^{25}_D$ –77.2 (*c* 0.2, $CHCl_3$); R_f 0.65 (4:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.39–7.35 (m, 2H, ArH), 7.34–7.29 (m, 2H, ArH), 7.28–7.23 (m, 1H, ArH), 5.53 (d, 1H, $J_{1,2}$ = 5.0 Hz, H-1_{Gal}), 4.86 (d, 1H, J_{gem} = 12.0 Hz, ArCH_2), 4.61–4.54 (m, 2H, ArCH_2, H-3_{Gal}), 4.47 (d, 1H, $J_{4,5}$ = 4.1 Hz, H-4_{Xul}), 4.32–4.25 (m, 4H, H-2_{Gal}, H-4_{Gal}, H-3_{Xul}, H-$5a_{Xul}$), 4.05–4.00 (m, 2H, H-5_{Gal}, H-$1a_{Xul}$), 3.95–3.80 (m, 4H, H-$6a_{Gal}$, H-$6b_{Gal}$, H-$1b_{Xul}$, H-$5b_{Xul}$), 1.50 (s, 3H, (CH_3)$_2$C), 1.44 (s, 3H, (CH_3)$_2$C), 1.32 (s, 6H, (CH_3)$_2$C), 1.14–0.78 (m, 28H, SiCH(CH_3)$_2$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.7 (Ar), 128.4 (2C, Ar), 128.0 (2C, Ar), 127.7 (Ar), 109.3 ((CH$_3$)$_2$*C*), 108.74 ((CH$_3$)$_2$*C*), 108.69 (C-2_{Xul}), 96.6 (C-1_{Gal}), 83.8 (C-3_{Xul}), 79.1 (C-4_{Xul}), 75.0 (C-5_{Xul}), 73.1 (Ar*C*H$_2$), 71.2 (C-2_{Gal}), 71.0 (C-4_{Gal}), 70.9 (C-3_{Gal}), 67.6 (C-5_{Gal}), 65.1 (C-1_{Xul}), 62.0 (C-6_{Gal}), 26.3 ((*C*H$_3$)$_2$C), 26.2 ((*C*H$_3$)$_2$C), 25.3 ((*C*H$_3$)$_2$C), 24.6 ((*C*H$_3$)$_2$C), 17.69 (SiCH(*C*H$_3$)$_2$), 17.63–17.54 (5C, SiCH(*C*H$_3$)$_2$), 17.53 (SiCH(*C*H$_3$)$_2$), 17.4 (SiCH(*C*H$_3$)$_2$), 13.9 (Si*C*H(CH$_3$)$_2$), 13.8 (Si*C*H(CH$_3$)$_2$), 13.5 (Si*C*H(CH$_3$)$_2$), 13.3 (Si*C*H(CH$_3$)$_2$); HRMS (ESI) calcd. for $C_{36}H_{60}NaO_{11}Si_2$ $[M+Na]^+$ 747.3566 found 747.3562.

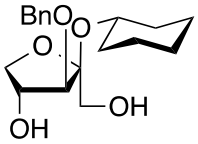


Methyl 3-*O*-benzyl-1,4-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-β-D-xylulofuranosyl-(2→2)-3,4-di-*O*-benzyl-α-L-rhamnopyranoside (4.22). To a solution of **4.2** (11.0 mg, 0.019 mmol) and **3.85** (8.0 mg, 0.022 mmol) in CH_2Cl_2 (0.75 mL) was added 4Å MS at room tempera-

ture. After stirring at room temperature for 30 min, the reaction mixture was cooled to –78 °C. To the mixture was added *N*-iodosuccinimide (5.1 mg, 0.022 mmol) and silver triflate (1.0 mg, 0.0037 mmol) at –78 °C. After stirring at –78 °C for 4 h, triethylamine was added. The reaction was warmed to room temperature and then a small amount of H_2O was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The mixture was dried over $MgSO_4$ and then filtered and concentrated. The resulting residue was purified by column chromatography (10:1, hexane–EtOAc) to give **4.22** (10.2 mg, 80%, β only) as a colorless oil; $[\alpha]^{25}_D$ –13.7 (*c* 0.2, $CHCl_3$); R_f 0.12 (4:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.39–7.35 (m, 4H, ArH), 7.33–7.17 (m, 11H, ArH), 5.06 (d, 1H, J_{gem} = 12.4 Hz, ArC*H*$_2$), 4.81 (d, 1H, J_{gem} = 11.7 Hz, ArC*H*$_2$), 4.78 (d, 1H, J_{gem} = 1.8 Hz, H-1$_{Rha}$), 4.70 (d, 1H, J_{gem} = 10.9 Hz, ArC*H*$_2$), 4.63 (d, 1H, J_{gem} = 11.7 Hz, ArC*H*$_2$), 4.58 (d, 1H, J_{gem} = 12.4 Hz, ArC*H*$_2$), 4.47 (d, 1H, $J_{4,5}$ = 3.7 Hz, H-4$_{Xul}$), 4.35–4.28 (m, 4H, H-2$_{Rha}$, H-3$_{Xul}$, H-5a$_{Xul}$, ArC*H*$_2$), 4.03 (s, 2H, H-1a$_{Xul}$, H-1b$_{Xul}$), 3.86–3.81 (m, 2H, H-3$_{Rha}$, H-5b$_{Xul}$), 3.63 (dq, 1H, $J_{5,4}$ = 9.4 Hz, $J_{5,6}$ = 6.1 Hz, H-5$_{Rha}$), 3.66 (app t, 1H, $J_{4,3}$ = $J_{4,5}$ = 9.4 Hz, H-4$_{Rha}$), 3.30 (s, 3H, OCH_3), 1.24 (d, 1H, $J_{6,5}$ = 6.1 Hz, H-6$_{Rha}$), 1.08–0.80 (m, 28H, SiC*H*(C*H*$_3$)$_2$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 139.2 (Ar), 139.1 (Ar), 138.9 (Ar), 128.3 (2C, Ar), 128.39 (4C, Ar), 128.2 (2C, Ar), 127.8 (Ar), 127.6 (2C, Ar), 127.5 (3C, Ar), 127.4 (Ar), 109.5 (C-2$_{Xul}$), 100.6 (C-1$_{Rha}$), 83.7 (C-3$_{Xul}$), 80.3 (C-4$_{Rha}$), 79.2 (C-4$_{Xul}$), 79.1 (C-3$_{Rha}$), 75.3 (C-5$_{Xul}$), 75.2 (Ar*C*H$_2$), 72.9 (Ar*C*H$_2$), 71.9 (Ar*C*H$_2$), 69.8 (C-2$_{Rha}$), 67.9 (C-5$_{Rha}$), 64.2 (C-1$_{Xul}$), 54.8 (O*C*H$_3$), 18.2 (C-6$_{Rha}$), 17.68 (SiCH(*C*H$_3$)$_2$), 17.64 (SiCH(*C*H$_3$)$_2$), 17.61 (SiCH(*C*H$_3$)$_2$), 17.57 (SiCH(*C*H$_3$)$_2$), 17.56 (SiCH(*C*H$_3$)$_2$), 17.55 (2C, SiCH(*C*H$_3$)$_2$), 17.40 (SiCH(*C*H$_3$)$_2$), 13.8 (Si*C*H(CH$_3$)$_2$), 13.7 (Si*C*H(CH$_3$)$_2$), 13.6 (Si*C*H(CH$_3$)$_2$), 13.3 (Si*C*H(CH$_3$)$_2$); HRMS (ESI) calcd. for $C_{45}H_{66}NaO_{10}Si_2$ $[M+Na]^+$ 845.4087 found 845.4077.

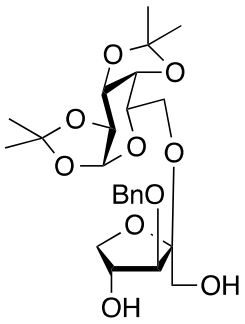


Octyl 3-*O*-benzyl-β-D-xylulofuranoside (4.23). To a solution of **4.19** (12.5 mg, 0.0210 mmol) in THF (2.0 mL) was added 1M tetra-*n*-butylammonium fluoride (63 μL, 0.063 mmol) at room temperature. After stirring at room temperature for 30 min, the reaction mixture was concentrated. The resulting residue was purified by column chromatography (2:1, hexane–EtOAc) to give **4.23** (6.8 mg, 92%, β only) as a colorless oil; $[\alpha]^{25}_{D}$ –52.1 (*c* 0.3, $CHCl_3$); R_f 0.13 (2:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.42–7.34 (m, 4H, ArH), 7.33–7.29 (m, 1H, ArH), 4.86 (d, 1H, J_{gem} = 12.2 Hz, ArCH_2), 4.62 (d, 1H, J_{gem} = 12.2 Hz, ArCH_2), 4.50–4.45 (m, 1H, H-4), 4.15 (dd, 1H, $J_{5a,4}$ = 6.5 Hz, J_{gem} = 9.4 Hz, H-5a), 3.98 (d, 1H, $J_{3,4}$ = 5.1 Hz, H-3), 3.73–3.60 (m, 4H, H-1a, H-1b, H-5b, octyl OCH_2), 3.52 (app dt, 1H, *J* = 6.6, 9.0 Hz, octyl OCH_2), 1.97 (br s, 1H, OH), 1.84 (br s, 1H, OH), 1.61–1.51 (m, 2H, octyl CH_2), 1.36–1.20 (m, 10H, octyl CH_2), 0.88 (t, 3H, *J* = 7.1 Hz, octyl CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.6 (Ar), 128.8 (2C, Ar), 128.20 (Ar), 128.17 (2C, Ar), 105.6 (C-2), 86.6 (C-3), 76.2 (C-4), 73.3 (C-5), 71.7 (ArCH_2), 63.8 (C-1), 62.5 (octyl OCH_2), 32.1 (octyl CH_2), 30.5 (octyl CH_2), 29.6 (octyl CH_2), 29.5 (octyl CH_2), 26.4 (octyl CH_2), 22.9 (octyl CH_2), 14.3 (octyl CH_3); HRMS (ESI) calcd. for $C_{20}H_{32}NaO_5$ $[M+Na]^+$ 375.2142 found 375.2141.



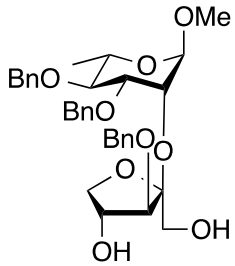
Cyclohexyl 3-*O*-benzyl-β-D-xylulofuranoside (4.24). To a solution of **4.20** (5.7 mg, 0.010 mmol) in THF (1.0 mL) was added 1M tetra-*n*-butylammonium fluoride (30 μL, 0.030 mmol) at

room temperature. After stirring at room temperature for 30 min, the reaction mixture was concentrated. The resulting residue was purified by column chromatography (10:1, hexane–EtOAc) to give **4.24** (3.0 mg, 94%, β only) as a colorless oil; $[\alpha]^{25}_{D}$ –15.7 (*c* 0.1, $CHCl_3$); R_f 0.32 (1:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.43–7.34 (m, 4H, ArH), 7.33–7.28 (m, 1H, ArH), 4.86 (d, 1H, J_{gem} = 12.4 Hz, ArC*H*$_2$), 4.62 (d, 1H, J_{gem} = 12.4 Hz, ArC*H*$_2$), 4.51–4.46 (m, 1H, H-4), 4.16 (dd, 1H, $J_{5a,4}$ = 6.6 Hz, J_{gem} = 9.5 Hz, H-5a), 3.95 (d, 1H, $J_{3,4}$ = 5.4 Hz, H-3), 3.76–3.63 (m, 3H, H-1a, H-5b, cyclohexyl OC*H*), 3.60 (dd, 1H, J_{gem} = 11.4 Hz, $J_{1b,OH}$ = 7.3 Hz, H-1b), 1.89 (d, 1H, $J_{OH,4}$ = 5.0 Hz, 4-OH) 1.83–1.70 (m, 5H, cyclohexyl C*H*$_2$, 1-OH) 1.54–1.49 (m, 1H, cyclohexyl C*H*$_2$), 1.44–1.34 (m, 2H, cyclohexyl C*H*$_2$), 1.32–1.11 (m, 3H, cyclohexyl C*H*$_2$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.7 (Ar), 128.8 (2C, Ar), 128.3 (2C, Ar), 128.2 (Ar), 105.9 (C-2), 86.4 (C-3), 76.0 (C-4), 73.3 (Ar*C*H$_2$), 71.5 (C-5), 71.1 (cyclohexyl O*C*H), 63.7 (C-1), 35.0 (cyclohexyl *C*H$_2$), 34.6 (cyclohexyl *C*H$_2$), 25.7 (cyclohexyl *C*H$_2$), 24.89 (cyclohexyl *C*H$_2$), 24.88 (cyclohexyl *C*H$_2$); HRMS (ESI) calcd. for $C_{18}H_{26}NaO_5$ $[M+Na]^+$ 345.1672 found 345.1672.



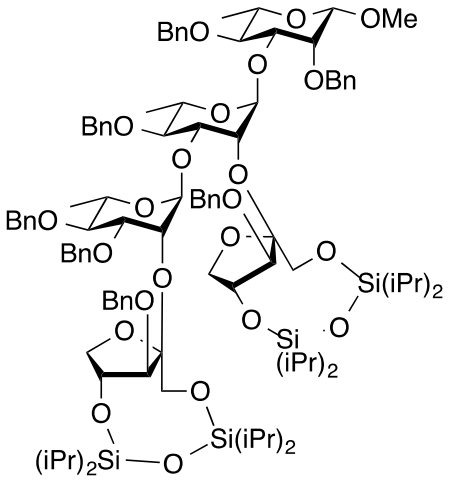
3-*O*-benzyl-β-D-xylulofuranosyl-(2→6)-1,2,3,4-di-*O*-isopropylidene-α-D-galactopyranose (4.25). To a solution of **4.21** (12.4 mg, 0.017 mmol) in THF (1.0 mL) was added 1M tetra-*n*-butylammonium fluoride (51.3 μL, 0.051 mmol) at room temperature. After stirring at room temperature for 30 min, the reaction mixture was concentrated. The resulting residue was puri-

fied by column chromatography (1:1, hexane–EtOAc) to give **4.25** (7.8 mg, 95%, β only) as a colorless oil; $[\alpha]^{25}_{D}$ –136.6 (*c* 0.2, $CHCl_3$); R_f 0.15 (1:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.42–7.38 (m, 2H, ArH), 7.36–7.31 (m, 2H, ArH), 7.28–7.26 (m, 1H, ArH), 5.55 (d, 1H, $J_{1,2}$ = 4.9 Hz, H-1_{Gal}), 4.89 (d, 1H, J_{gem} = 12.0 Hz, ArCH_2), 4.63–4.55 (m, 2H, ArCH_2, H-3_{Gal}), 4.44–4.40 (m, 1H, H-4_{Xul}), 4.33 (dd, 1H, $J_{2,1}$ = 4.9 Hz, $J_{2,3}$ = 2.4 Hz, H-2_{Gal}), 4.22 (dd, 1H, $J_{4,3}$ = 7.9 Hz, $J_{4,5}$ = 1.7 Hz, H-4_{Gal}), 4.15 (dd, 1H, $J_{5a,4}$ = 5.6 Hz, J_{gem} = 9.6 Hz, H-$5a_{Xul}$), 4.06 (ddd, 1H, $J_{5,4}$ = 1.7 Hz, $J_{5,6a}$ = 8.0 Hz, $J_{5,6b}$ = 3.4 Hz, H-5_{Gal}), 3.94–3.84 (m, 3H, H-$6a_{Gal}$, H-$1a_{Xul}$, H-3_{Xul}), 3.74 (dd, 1H, $J_{6b,5}$ = 3.4 Hz, J_{gem} = 11.8 Hz, H-$6b_{Gal}$), 3.68 (dd, 1H, $J_{5b,4}$ = 3.4 Hz, J_{gem} = 9.6 Hz, H-$5b_{Xul}$), 3.46 (dd, 1H, $J_{1b,OH}$ = 7.3 Hz, J_{gem} = 12.2 Hz, H-$1b_{Xul}$), 3.04 (br s, 1H, 1-OH), 1.92 (br s, 1H, 4-OH), 1.48 (s, 3H, (CH_3)$_2$C), 1.44 (s, 3H, (CH_3)$_2$C), 1.33 (s, 6H, (CH_3)$_2$C); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.7 (Ar), 128.6 (2C, Ar), 128.2 (2C, Ar), 127.9 (Ar), 109.7 ((CH$_3$)$_2$*C*), 109.2 ((CH$_3$)$_2$*C*), 106.3 (C-2_{Xul}), 96.5 (C-1_{Gal}), 88.4 (C-3_{Xul}), 77.3 (C-4_{Xul}), 73.2 (Ar*C*H$_2$), 71.6 (C-5_{Xul}), 71.5 (C-4_{Gal}), 70.89 (C-2_{Gal}), 70.87 (C-3_{Gal}), 68.3 (C-5_{Gal}), 62.9 (C-1_{Xul}), 61.6 (C-6_{Gal}), 26.22 ((*C*H$_3$)$_2$C), 26.21 ((*C*H$_3$)$_2$C), 25.2 ((*C*H$_3$)$_2$C), 24.6 ((*C*H$_3$)$_2$C); HRMS (ESI) calcd. for $C_{24}H_{34}NaO_{10}$ $[M+Na]^+$ 505.2044 found 505.2043.



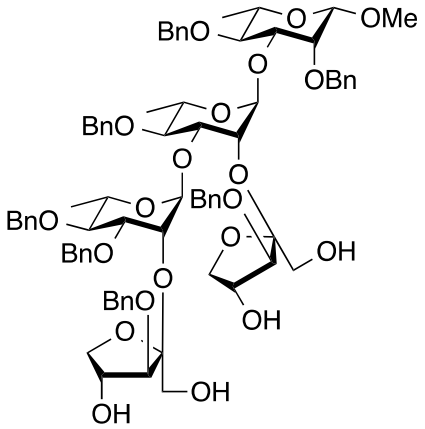
Methyl 3-*O*-benzyl-β-D-xylulofuranosyl-(2→2)-3,4-di-*O*-benzyl-α-L-rhamnopyranoside (4.26). To a solution of **4.22** (10.2 mg, 0.012 mmol) in THF (1.0 mL) was added 1M tetra-*n*-butylammonium fluoride (37.2 μL, 0.037 mmol) at room temperature. After stirring at room

temperature for 30 min, the reaction mixture was concentrated. The resulting residue was purified by column chromatography (4:1, hexane–EtOAc) to give **4.26** (6.5 mg, 90%) as a colorless oil; $[\alpha]^{25}_{D}$ –20.8 (*c* 0.2, $CHCl_3$); R_f 0.33 (2:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.46–7.42 (m, 2H, ArH), 7.36–7.19 (m, 13H, ArH), 5.00 (d, 1H, J_{gem} = 12.2 Hz, ArCH_2), 4.82 (d, 1H, J_{gem} = 11.3 Hz, ArCH_2), 4.73 (d, 1H, J_{gem} = 11.3 Hz, ArCH_2), 4.67 (d, 1H, J_{gem} = 11.3 Hz, ArCH_2), 4.58 (d, 1H, J_{gem} = 12.2 Hz, ArCH_2), 4.50 (d, 1H, J_{gem} = 1.8 Hz, H-1_{Rha}), 4.44–4.38 (m, 2H, H-4_{Xul}, ArCH_2), 4.20 (dd, 1H, $J_{OH,1a}$ = 1.7 Hz, $J_{OH,1b}$ = 11.7 Hz, 1-OH_{Xul}), 4.11 (dd, 1H, $J_{5a,4}$ = 4.4 Hz, J_{gem} = 9.6 Hz, H-$5a_{Xul}$), 4.06 (dd, 1H, $J_{2,1}$ = 1.8 Hz, $J_{2,3}$ = 3.1 Hz, H-2_{Rha}), 3.94 (d, 1H, $J_{3,4}$ = 2.7 Hz, H-3_{Xul}), 3.88 (dd, 1H, $J_{3,2}$ = 3.1 Hz, $J_{3,4}$ = 9.6 Hz, H-3_{Rha}), 3.77 (dd, 1H, $J_{1a,OH}$ = 1.7 Hz, J_{gem} = 12.9 Hz, H-$1a_{Xul}$), 3.71 (dd, 1H, $J_{5b,4}$ = 2.6 Hz, J_{gem} = 9.6 Hz, H-$5b_{Xul}$), 3.64 (dq, 1H, $J_{5,4}$ = 9.6 Hz, $J_{5,6}$ = 6.1 Hz, H-5_{Rha}), 3.48 (app t, 1H, $J_{4,3}$ = $J_{4,5}$ = 9.6 Hz, H-4_{Rha}), 3.37–3.28 (m, 4H, H-$1b_{Xul}$, OCH_3), 1.87 (br s, 1H, 4-OH_{Xul}), 1.23 (d, 1H, $J_{6,5}$ = 6.2 Hz, H-6_{Rha}); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 139.1 (Ar), 138.4 (Ar), 137.2 (Ar), 128.79 (2C, Ar), 128.73 (2C, Ar), 128.60 (2C, Ar), 128.52 (2C, Ar), 128.49 (Ar), 128.0 (2C, Ar), 127.9 (Ar), 127.7 (2C, Ar), 127.6 (Ar), 107.5 (C-2_{Xul}), 100.9 (C-1_{Rha}), 88.2 (C-3_{Xul}), 81.4 (C-4_{Rha}), 79.1 (C-3_{Rha}), 77.4 (C-4_{Xul}), 75.4 (Ar*C*H_2), 75.0 (Ar*C*H_2), 73.0 (Ar*C*H_2), 71.9 (C-5_{Xul}), 70.3 (C-2_{Rha}), 68.1 (C-5_{Rha}), 62.5 (C-1_{Xul}), 54.8 (O*C*H_3), 17.9 (C-6_{Rha}); HRMS (ESI) calcd. for $C_{33}H_{40}NaO_9$ $[M+Na]^+$ 603.2565 found 603.2568.



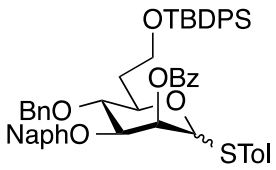
Methyl 3-*O*-benzyl-1,4-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-β-D-xylulofuranosyl-(2→2)-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-[3-*O*-benzyl-1,4-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-β-D-xylulofuranosyl-(2→2)]-4-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-2,4-di-*O*-benzyl-β-L-rhamnopyranoside (4.27). To a solution of **4.2** (11.0 mg, 0.019 mmol) and **3.130** (7.2 mg, 0.0078 mmol) in CH_2Cl_2 (0.50 mL) was added 4Å MS at room temperature. After stirring at room temperature for 30 min, the reaction mixture was cooled to –78 °C. To the mixture was added *N*-iodosuccinimide (10.0 mg, 0.045 mmol) and silver triflate (1.0 mg, 0.0037 mmol) at –78 °C. After stirring at –78 °C for 4 h, triethylamine was added. The reaction was warmed to room temperature and then a small amount of H_2O was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The mixture was dried over $MgSO_4$ and then filtered and concentrated. The resulting residue was purified by column chromatography (20:1, hexane–EtOAc) to give **4.27** (12.5 mg, 87%, β,β only) as a colorless oil; $[\alpha]^{25}_D$ –24.0 (*c* 0.6, $CHCl_3$); R_f 0.36 (10:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.53–7.49 (m, 2H, ArH), 7.40–7.08 (m, 33H, ArH), 5.31 (br s, 1H, H-1'), 5.17 (d, 1H, $J_{1'',2''}$ = 1.2 Hz, H-1''), 5.10 (d, 1H, J_{gem} = 12.5 Hz, ArCH_2), 5.00 (d, 1H, J_{gem} = 12.5 Hz, ArCH_2), 4.96 (d, 1H, J_{gem} = 11.5 Hz, ArCH_2), 4.90 (d, 1H, J_{gem} = 12.3 Hz, ArCH_2), 4.76 (d, 1H, J_{gem} = 12.3 Hz,

ArCH_2), 4.72–4.62 (m, 3H, ArCH_2), 4.61–4.49 (m, 4H, ArCH_2), 4.42 (d, 1H, J = 4.0 Hz), 4.35–4.26 (m, 7H), 4.21 (br s, 1H), 4.18 (d, 1H, J_{gem} = 12.3 Hz, ArCH_2), 4.14–4.07 (m, 2H), 4.04 (d, 1H, J =11.8 Hz), 3.98–3.87 (m, 2H), 3.89 (d, 1H, J =12.3 Hz), 3.86–3.79 (m, 3H), 3.72–3.60 (m, 4H), 3.55–3.47 (m, 5H), 3.30–3.20 (m, 2H), 1.21 (d, 3H, J = 6.2 Hz), 1.16 (d, 3H, J = 6.4 Hz), 1.05–0.71 (m, 59H, SiCH(CH_3)$_2$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 139.3 (Ar), 139.20 (Ar), 139.19 (Ar), 139.15 (Ar), 139.12 (Ar), 139.10 (Ar), 138.5 (Ar), 128.5 (Ar), 128.44 (Ar), 128.42 (Ar), 128.34 (Ar), 128.33 (Ar), 128.2 (Ar), 128.15 (Ar), 127.8 (Ar), 127.5 (Ar), 127.44 (Ar), 127.41 (Ar), 127.3 (Ar), 127.1 (Ar), 126.9 (Ar), 109.1 (C-2), 108.8 (C-2), 102.8 (C-1, $J_{C1,H1}$ = 153.7 Hz), 102.2 (C-1', $J_{C1',H1'}$ = 175.7 Hz), 101.5 (C-1'', $J_{C1'',H1''}$ = 176.3 Hz), 84.5, 83.9, 82.3, 81.4, 80.6, 80.2, 79.55, 79.45, 79.42, 78.9, 75.5, 75.0, 74.90, 74.87, 74.78, 74.4, 74.3, 73.1, 72.7, 72.5, 72.4, 72.1, 70.4, 69.3, 69.0, 66.0, 64.3, 57.3 (O*C*H$_3$), 18.3, 18.0, 17.9, 17.8, 17.69, 17.67, 17.65, 17.64, 17.6, 17.56, 17.55, 17.5, 17.4, 13.86, 13.76, 13.71, 13.6, 13.5, 13.46, 13.45, 13.3; HRMS (ESI) calcd. for $C_{102}H_{148}NO_{23}Si_4$ $[M+NH_4]^+$ 1866.9514 found 1866.9517.



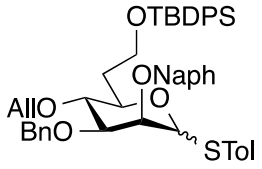
Methyl 3-*O*-benzyl-β-D-xylulofuranosyl-(2→2)-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-[3-*O*-benzyl-β-D-xylulofuranosyl-(2→2)]-4-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-2,4-di-*O*-benzyl-β-L-rhamnopyranoside (4.28). To a solution of **4.27** (5.8 mg, 0.00314 mmol)

in THF (1.0 mL) was added 1M tetra-*n*-butylammonium fluoride (9.4 μL, 0.00941 mmol) at room temperature. After stirring at room temperature for 30 min, the reaction mixture was concentrated. The resulting residue was purified by column chromatography (1:1, hexane–EtOAc) to give **4.28** (4.0 mg, 94%) as a colorless oil; $[\alpha]^{25}_{D}$ –27.5 (*c* 0.2, $CHCl_3$); R_f 0.20 (1:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.53–7.49 (m, 2H, ArH), 7.46–7.11 (m, 31H, ArH), 7.06–7.02 (m, 2H, ArH), 5.17–5.12 (m, 2H, H-1', ArCH_2), 4.99 (br s, 1H, H-1''), 4.97–4.87 (m, 3H, ArCH_2), 4.79–4.73 (m, 2H, ArCH_2), 4.71–4.54 (m, 5H, ArCH_2), 4.51–4.45 (m, 2H), 4.37–4.28 (m, 4H), 4.22–4.15 (m, 3H), 4.12–4.05 (m, 2H), 3.95–3.88 (m, 2H), 3.84–3.80 (m, 2H), 3.74–3.58 (m, 6H), 3.58–3.43 (m, 7H), 3.40 (dd, 1H, *J* = 3.1, 9.6 Hz), 3.33 (dq, 1H, *J* = 6.2, 8.6 Hz), 3.28–3.17 (m, 2H), 2.80 (dd, 1H, *J* = 2.8, 9.8 Hz), 1.89 (br s, 1H, OH), 1.31 (d, 3H, *J* = 6.2 Hz), 1.16 (d, 3H, *J* = 6.4 Hz), 1.03 (d, 3H, *J* = 6.3 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 139.3 (Ar), 139.20 (Ar), 138.85 (Ar), 138.79 (Ar), 138.5 (Ar), 138.4 (Ar), 137.3 (Ar), 128.7 (Ar), 128.63 (Ar), 128.60 (Ar), 128.49 (Ar), 128.48 (Ar), 128.33 (Ar), 128.29 (Ar), 127.84 (Ar), 127.82 (Ar), 127.76 (Ar), 127.6 (Ar), 127.34 (Ar), 127.30 (Ar), 127.2 (Ar), 126.6 (Ar), 107.3 (C-2), 107.1 (C-2), 102.8 (C-1, $J_{C1,H1}$ = 153.3 Hz), 102.4 (C-1'', $J_{C1'',H1''}$ = 176.8 Hz), 101.1 (C-1', $J_{C1',H1'}$ = 176.3 Hz), 87.9, 87.6, 82.4, 82.0, 80.9, 80.4, 79.4, 79.3, 76.7, 75.5, 75.1, 75.0, 74.6, 74.3, 73.2, 73.1, 72.9, 72.2, 72.1, 72.0, 72.4, 71.5, 70.1, 69.6, 69.2, 63.3, 62.4, 57.4 (O*C*H_3), 18.06, 18.01, 17.7; HRMS (ESI) calcd. for $C_{78}H_{92}NaO_{21}$ $[M+Na]^+$ 1387.6023 found 1387.6027.



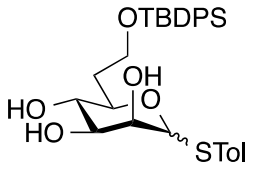
***p*-Tolyl 2-*O*-benzoyl-4-*O*-benzyl-7-*O*-*tert*-butyldiphenylsilyl-3-*O*-(2-naphthyl)-1-thio-α/β-D-*manno*-heptopyranoside (4.30).** To a solution of **4.36** (1.7 g, 2.21 mmol) in CH_2Cl_2 (25 mL)

was added triethylamine (459 μL, 3.31 mmol), benzoyl chloride (308 μL, 2.65 mmol) and 4-dimethylaminopyridine (27 mg, 0.221 mmol) at room temperature. After stirring at room temperature for 48 h, excess benzoyl chloride was quenched by the addition of CH_3OH. The mixture was concentrated and the resulting residue was purified by column chromatography (20:1, hexane–EtOAc) to give **4.30** (1.34 g, 70%, α/β 10:1) as a white foam; R_f 0.62 (4:1, hexane–EtOAc); Data for **4.30α**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 8.12–8.04 (m, 2H, ArH), 7.84–7.74 (m, 3H, ArH), 7.89–7.77 (m, 4H, ArH), 7.72–7.64 (m, 5H, ArH), 7.63–7.56 (m, 1H, ArH), 7.50–7.30 (m, 14H, ArH), 7.00–6.95 (m, 2H, ArH), 5.93 (dd, 1H, $J_{2,1}$ = 1.8 Hz, $J_{2,3}$ = 2.9 Hz, H-2), 5.49 (d, 1H, $J_{1,2}$ = 1.8 Hz, H-1), 5.00 (d, 1H, J_{gem} = 11.7 Hz, ArCH_2), 4.97 (d, 1H, J_{gem} = 11.7 Hz, ArCH_2), 4.78 (d, 1H, J_{gem} = 11.7 Hz, ArCH_2), 4.68 (d, 1H, J_{gem} = 11.7 Hz, ArCH_2), 4.45 (app dt, 1H, $J_{5,4}$ = $J_{5,6b}$ = 9.7 Hz, $J_{5,6a}$ = 1.9 Hz, H-5), 4.14 (dd, 1H, $J_{3,2}$ = 2.9 Hz, $J_{3,4}$ = 9.7 Hz, H-3), 3.87–3.75 (m, 2H, H-7a, H-7b), 3.72 (app t, 1H, $J_{4,3}$ = $J_{4,5}$ = 9.7 Hz, H-4), 2.29 (s, 3H, ArCH_3), 2.35–2.24 (m, 1H, H-6a), 1.87–1.75 (m, 1H, H-6b), 1.08 (s, 9H, Si(CCH_3)$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 165.9 (C=O), 138.6 (Ar), 138.1 (Ar), 135.8 (2C, Ar), 135.7 (2C, Ar), 135.4 (Ar), 134.3 (Ar), 134.2 (Ar), 133.45 (Ar), 133.42 (Ar), 133.2 (Ar), 132.9 (2C, Ar), 130.1 (Ar), 130.1 (2C, Ar), 130.0 (2C, Ar), 129.70 (2C, Ar), 129.63 (2C, Ar), 128.53 (2C, Ar), 128.3 (Ar), 128.1 (Ar), 128.0 (2C, Ar), 127.82 (Ar), 127.79 (3C, Ar), 127.77 (2C, Ar), 127.1 (Ar), 126.3 (Ar), 126.1 (Ar), 126.0 (Ar), 86.7 (C-1, $J_{C1,H1}$ = 169.0 Hz), 78.95 (C-3 or C-4), 78.86 (C-3 or C-4), 75.4 (ArCH$_2$), 71.9 (ArCH$_2$), 71.1 (C-2), 69.5 (C-5), 60.6 (C-7), 35.3 (C-6), 27.1 (SiC(CH$_3$)$_3$), 21.3 (ArCH$_3$), 19.4 (SiC(CH$_3$)$_3$); HRMS (ESI) calcd. for $C_{55}H_{56}NaO_6SSi$ $[M+Na]^+$ 895.3459 found 895.3458.



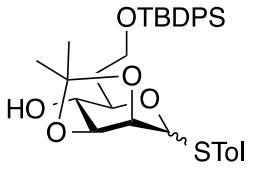
***p*-Tolyl 4-*O*-allyl-3-*O*-benzyl-7-*O*-*tert*-butyldiphenylsilyl-2-*O*-(2-naphthyl)-1-thio-α/β-D-*manno*-heptopyranoside (4.31).** To a solution of **4.38** (1.0 g, 1.45 mmol) in DMF (20 mL) was added 2-(bromomethyl)naphthalene (397 mg, 1.8 mmol) and sodium hydride (90 mg, 2.24 mmol) at 0 °C. After stirring at 0 °C for 2 h, CH_3OH was added. The mixture was diluted with EtOAc and then washed with water. The organic layer was dried over $MgSO_4$, filtered and the filtrate was concentrated. The resulting residue was purified by column chromatography (20:1, hexane–EtOAc) to give **4.31** (1.0 g, 83%, α/β 10:1) as a colorless oil; R_f 0.37 (10:1, hexane–EtOAc); Data for **4.31α**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.85–7.80 (m, 1H, ArH), 7.77–7.72 (m, 2H, ArH), 7.70–7.66 (m, 4H, ArH), 7.50–7.45 (m, 3H, ArH), 7.43–7.40 (m, 2H, ArH), 7.39–7.30 (m, 10H, ArH), 7.23–7.18 (m, 2H, ArH), 6.92–6.87 (m, 2H, ArH), 5.99–5.90 (m, 1H, OCH_2CH=CH_2), 5.41 (d, 1H, $J_{1,2}$ = 1.6 Hz, H-1), 5.33–5.27 (m, 1H, OCH_2CH=CH_2), 5.20–5.16 (m, 1H, OCH_2CH=CH_2), 4.86 (d, 1H, J_{gem} = 13.0 Hz, $ArCH_2$), 4.79 (d, 1H, J_{gem} = 13.0 Hz, $ArCH_2$), 4.65 (d, 1H, J_{gem} = 11.8 Hz, $ArCH_2$), 4.58 (d, 1H, J_{gem} = 11.8 Hz, $ArCH_2$), 4.46–4.41 (m, 1H, OCH_2CH=CH_2), 4.23 (app dt, 1H, $J_{5,4}$ = $J_{5,6b}$ = 9.6 Hz, $J_{5,6a}$ = 2.3 Hz, H-5), 4.15–4.10 (m, 1H, OCH_2CH=CH_2), 4.02 (dd, 1H, $J_{2,1}$ = 1.6 Hz, $J_{2,3}$ = 3.1 Hz, H-2), 3.833–3.73 (m, 3H, H-3, H-7a, H-7b), 3.63 (app t, 1H, $J_{4,3}$ = $J_{4,5}$ = 9.6 Hz, H-4), 2.26 (s, 3H, $ArCH_3$), 2.24–2.17 (m, 1H, H-6a), 1.85–1.76 (m, 1H, H-6b), 1.05 (s, 9H, $Si(CCH_3)_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.6 (Ar), 137.6 (Ar), 135.82 (2C, Ar), 135.76 (2C, Ar), 135.6 (OCH_2CH=CH_2), 135.3 (Ar), 134.4 (Ar), 134.3 (Ar), 133.4 (Ar), 133.2 (Ar), 132.4 (2C, Ar), 130.8 (Ar), 129.9 (2C, Ar), 129.66 (Ar), 129.63 (Ar), 128.6 (2C, Ar), 128.4 (Ar), 128.1 (2C, Ar), 127.90 (2C, Ar), 127.89 (Ar), 127.79

(2C, Ar), 127.76 (2C, Ar), 127.0 (Ar), 126.3 (Ar), 126.2 (Ar), 126.1 (Ar), 116.7 ($OCH_2CH{=}\mathit{C}H_2$), 86.5 (C-1, $J_{C1,H1}$ = 167.9 Hz), 80.4 (C-3), 79.2 (C-4), 76.6 (C-2), 74.2 ($O\mathit{C}H_2CH{=}CH_2$), 72.45 ($ArCH_2$), 72.44 ($ArCH_2$), 69.8 (C-5), 60.7 (C-7), 35.1 (C-6), 27.1 ($SiC(CH_3)_3$), 21.3 ($ArCH_3$), 19.4 ($SiC(CH_3)_3$); HRMS (ESI) calcd. for $C_{51}H_{56}NaO_5SSi$ $[M+Na]^+$ 831.3510 found 831.3519.



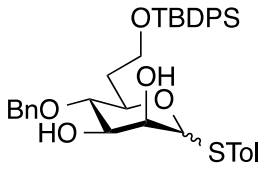
***p*-Tolyl 7-*O*-*tert*-butyldiphenylsilyl-1-thio-α/β-D-*manno*-heptopyranoside (4.33).** To a solution of **4.32** (5.0 g, 10.7 mmol) in CH_3OH–CH_2Cl_2 (4:1, 100 mL) was added sodium methoxide (42.7 mg, 1.07 mmol) at room temperature. After stirring at room temperature for 3 h, the reaction mixture was neutralized by the addition of Amberlite IR-120 H^+ resin. The mixture was filtered and the filtrate was concentrated. To a solution of the residue in DMF (100 mL) was added imidazole (1.1 g, 16.0 mmol) and *tert*-butyl(chloro)diphenylsilane (3.3 mL, 12.8 mmol) at room temperature. After stirring at room temperature for 3 h, excess *tert*-butyl(chloro)diphenylsilane was quenched by addition of excess amount of CH_3OH. The mixture was diluted with EtOAc and washed with water. The organic layer was dried over $MgSO_4$, filtered and the filtrate was concentrated. The resulting residue was purified by column chromatography (1:1, hexane–EtOAc) to give **4.33** (4.8 g, 84%, α/β 10:1) as a white foam; R_f 0.40 (1:2, hexane–EtOAc); Data for **4.33α**: ^{1}H NMR ($CDCl_3$, 700 MHz) δ_H 7.69–7.63 (m, 4H, ArH), 7.46–7.34 (m, 6H, ArH), 7.31–7.28 (m, 2H, ArH), 7.01–6.97 (m, 2H, ArH), 5.43 (br s, 1H, H-1), 4.23 (d, 1H, $J_{2,3}$ = 2.5 Hz, H-2), 4.19 (app dt, 1H, $J_{5,4}$ = 9.4 Hz, $J_{5,6a}$ = $J_{5,6b}$ = 5.5 Hz, H-5), 3.89–3.83 (m, 2H, H-3, OH), 3.83–3.75 (m, 2H, H-7a, H-7b), 3.73 (app t, 1H, $J_{4,3}$ = $J_{4,5}$ = 9.4 Hz, H-4), 3.12 (br s, 1H, OH), 2.86 (br s, 1H, OH), 2.27 (s, 3H, $ArCH_3$), 2.07–2.01 (m, 1H, H-6a), 1.87–1.80 (m, 1H, H-6b),

1.05 (s, 9H, Si(CCH_3)$_3$); ^{13}C NMR ($CDCl_3$, 175 MHz) δ_C 137.7 (Ar), 135.79 (2C, Ar), 135.71 (2C, Ar), 133.3 (Ar), 133.1 (Ar), 132.2 (2C, Ar), 130.4 (Ar), 130.08 (Ar), 130.0 (Ar), 129.96 (2C, Ar), 129.92 (Ar), 128.0 (3C, Ar), 88.1 (C-1, $J_{C1,H1}$ = 168.8 Hz), 72.3 (C-3 or C-4), 72.25 (C-3 or C-4), 72.1 (C-2), 71.3 (C-5), 61.2 (C-7), 35.8 (C-6), 27.0 (SiC(CH$_3$)$_3$), 21.3 (ArCH$_3$), 19.3 (SiC(CH$_3$)$_3$); HRMS (ESI) calcd. for $C_{30}H_{38}NaO_5SSi$ $[M+Na]^+$ 561.2101 found 561.2099.



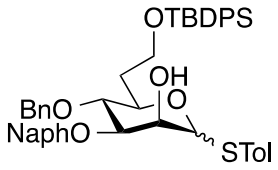
***p*-Tolyl 7-*O*-*tert*-butyldiphenylsilyl-2,3-*O*-isopropylidene-1-thio-α/β-D-*manno*-heptopyranoside (4.34).** To a solution of **4.33** (4.8 g, 8.9 mmol) in CH_3CN (90 mL) was added 2,2-dimethoxypropane (1.3 mL, 10.7 mmol) and *p*-toluenesulfonic acid (153 mg, 0.89 mmol) at room temperature. After stirring at room temperature for 1 h, triethylamine was added. The mixture was concentrated and the resulting residue was purified by column chromatography (4:1, hexane–EtOAc) to give **4.34** (4.66 g, 90%, α/β 10:1) as a white foam; R_f 0.25 (4:1, hexane–EtOAc); Data for **4.34α**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.68–7.61 (m, 4H, ArH), 7.47–7.35 (m, 6H, ArH), 7.33–7.28 (m, 2H, ArH), 7.01–6.96 (m, 2H, ArH), 5.71 (br s, 1H, H-1), 4.36 (d, 1H, $J_{2,3}$ = 5.5 Hz, H-2), 4.17 (dd, 1H, $J_{3,2}$ = 5.5 Hz, $J_{3,4}$ = 7.7 Hz, H-3), 4.14–4.07 (m, 1H, H-5), 3.77–3.61 (m, 3H, H-4, H-7a, H-7b), 3.25 (br s, 1H, 4-OH), 2.26 (s, 3H, ArCH_3), 2.00–1.90 (m, 1H, H-6a), 1.86–1.77 (m, 1H, H-6b), 1.56 (s, 3H, C(CH_3)$_2$), 1.39 (s, 3H, C(CH_3)$_2$), 1.05 (s, 9H, Si(CCH_3)$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 137.8 (Ar), 135.76 (2C, Ar), 135.71 (2C, Ar), 133.42 (Ar), 133.36 (Ar), 132.4 (2C, Ar), 129.96 (2C, Ar), 129.93 (3C, Ar), 129.76 (Ar), 127.92 (3C, Ar), 109.8 (C(CH$_3$)$_2$), 84.4 (C-1, $J_{C1,H1}$ = 168.5 Hz), 78.2 (C-3), 76.5 (C-2), 73.5 (C-4), 69.0

(C-5), 60.7 (C-7), 34.9 (C-6), 28.4 (C(CH_3)$_2$), 27.0 (SiC(CH_3)$_3$), 26.6 (C(CH_3)$_2$), 21.3 (ArCH_3), 19.2 (SiC(CH$_3$)$_3$); HRMS (ESI) calcd. for $C_{33}H_{42}NaO_5SSi$ $[M+Na]^+$ 601.2414 found 601.2416.



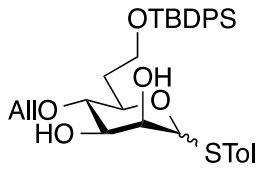
***p*-Tolyl 4-*O*-benzyl-7-*O*-*tert*-butyldiphenylsilyl-1-thio-α/β-D-*manno*-heptopyranoside (4.35)**. To a solution of **4.34** (3.0 g, 5.19 mmol) in DMF (50 mL) was added benzyl bromide (0.74 mL, 6.22 mmol) and sodium hydride (311 mg, 7.78 mmol) at 0 °C. After stirring at 0 °C for 4 h, CH_3OH was added. The mixture was diluted with EtOAc and washed with water. The organic layer was dried over $MgSO_4$, filtered and the filtrate was concentrated. The residue was then dissolved in 80% AcOH (50 mL) and the mixture was heated to 60 °C. After stirring at 60 °C for 3 h, the reaction mixture was cooled to room temperature and then co-evaporated with toluene. The resulting residue was purified by column chromatography (2:1, hexane–EtOAc) to give **4.35** (2.77 g, 85%, α/β 10:1) as a white foam; R_f 0.42 (1:1, hexane–EtOAc); Data for **4.35α**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.69–7.62 (m, 4H, ArH), 7.46–7.29 (m, 13H, ArH), 6.96–6.92 (m, 2H, ArH), 5.38 (d, 1H, $J_{1,2}$ = 1.7 Hz, H-1), 4.76–4.70 (m, 2H, ArCH_2), 4.35 (app dt, 1H, $J_{5,4}$ = $J_{5,6b}$ = 9.0 Hz, $J_{5,6a}$ = 2.0 Hz, H-5), 4.19 (dd, 1H, $J_{2,1}$ = 1.7 Hz, $J_{2,3}$ = 3.4 Hz, H-2), 3.96 (dd, 1H, $J_{3,2}$ = 3.4 Hz, $J_{3,4}$ = 9.0 Hz, H-3), 3.79–3.69 (m, 2H, H-7a, H-7b), 3.48 (app t, 1H, $J_{4,3}$ = $J_{4,5}$ = 9.0 Hz, H-4), 2.27 (s, 3H, ArCH_3), 2.22–2.13 (m, 1H, H-6a), 1.83–1.71 (m, 1H, H-6b), 1.05 (s, 9H, Si(CCH_3)$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_H 138.4 (Ar), 137.7 (Ar), 135.78 (2C, Ar), 135.74 (2C, Ar), 134.3 (Ar), 134.1 (Ar), 132.4 (2C, Ar), 130.3 (Ar), 129.9 (2C, Ar), 129.72 (Ar), 129.69 (Ar), 128.8 (2C, Ar), 128.2 (Ar), 128.0 (2C, Ar), 127.78 (2C, Ar), 127.77 (2C, Ar), 87.9 (C-1, $J_{C1,H1}$ = 167.3 Hz), 80.5 (C-4), 74.9 (ArCH$_2$), 72.6 (C-2), 72.1 (C-3), 69.0 (C-5), 60.5 (C-7), 35.0

(C-6), 27.1 (SiC(CH_3)$_3$), 21.3 (ArCH_3), 19.4 (SiC(CH$_3$)$_3$); HRMS (ESI) calcd. for $C_{37}H_{44}NaO_5SSi$ $[M+Na]^+$ 651.2571 found 651.2572.



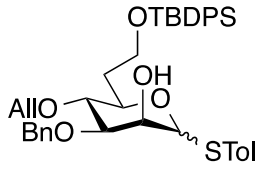
***p*-Tolyl 4-*O*-benzyl-7-*O*-*tert*-butyldiphenylsilyl-3-*O*-(2-naphthyl)-1-thio-α/β-D-manno-heptopyranoside (4.36).** To a solution of **4.35** (2.0 g, 3.18 mmol) in toluene (60 mL) was added di-*n*-butyltin oxide (1.2 g, 4.77 mmol) at room temperature, and the reaction mixture was heated to reflux. After stirring at reflux for 2 h, the mixture was cooled to room temperature before 2-naphthyl bromide (1.04 g, 4.77 mmol) and tetra-*n*-butylammonium bromide (1.5 g, 4.77 mmol) were added. The mixture was then heated to reflux. After stirring at reflux for 1 h, the reaction mixture was cooled to room temperature and concentrated. The resulting residue was purified by column chromatography (4:1, hexane–EtOAc) to give **4.36** (2.0 g, 82%, α/β 10:1) as a white foam; R_f 0.17 (4:1, hexane–EtOAc); Data for **4.36α**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.89–7.77 (m, 4H, ArH), 7.69–7.63 (m, 4H, ArH), 7.54–7.28 (m, 16H, ArH), 6.96–6.90 (m, 2H, ArH), 5.47 (d, 1H, $J_{1,2}$ = 1.4 Hz, H-1), 4.95 (d, 1H, J_{gem} = 11.4 Hz, ArCH_2), 4.90 (d, 1H, J_{gem} = 11.4 Hz, ArCH_2), 4.87 (d, 1H, J_{gem} = 11.4 Hz, ArCH_2), 4.67 (d, 1H, J_{gem} = 11.4 Hz, ArCH_2), 4.35 (app dt, 1H, $J_{5,4}$ = $J_{5,6b}$ = 9.7 Hz, $J_{5,6a}$ = 2.1 Hz, H-5), 4.33–4.30 (m, 1H, H-2), 3.98 (dd, 1H, $J_{3,2}$ = 3.4 Hz, $J_{3,4}$ = 9.7 Hz, H-3), 3.79–3.68 (m, 2H, H-7a, H-7b), 3.63 (app t, 1H, $J_{4,3}$ = $J_{4,5}$ = 9.7 Hz, H-4), 2.71 (d, 1H, $J_{OH,2}$ = 1.8 Hz, 2-OH), 2.27 (s, 3H, ArCH_3), 2.24–2.16 (m, 1H, H-6a), 1.80–1.69 (m, 1H, H-6b), 1.05 (s, 9H, SiC(CH_3)$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.6 (Ar), 137.7 (Ar), 135.78 (2C, Ar), 135.74 (2C, Ar), 135.3 (Ar), 134.4 (Ar), 134.2 (Ar), 133.5 (Ar), 133.3 (Ar), 132.4 (2C, Ar), 130.2 (Ar), 129.9 (2C, Ar), 129.67 (Ar), 129.65 (Ar), 128.63 (Ar), 128.58 (2C,

Ar), 128.2 (Ar), 127.91 (2C, Ar), 127.84 (Ar), 127.83 (Ar), 127.76 (2C, Ar), 127.74 (2C, Ar), 127.0 (Ar), 126.5 (Ar), 126.3 (Ar), 126.0 (Ar), 87.5 (C-1, $J_{C1,H1}$ = 168.0 Hz), 80.6 (C-3), 78.9 (C-4), 75.4 (Ar*C*H_2), 72.5 (Ar*C*H_2), 70.1 (C-2), 69.2 (C-5), 60.5 (C-7), 35.0 (C-6), 27.1 (SiC(*C*H_3)$_3$), 21.3 (Ar*C*H_3), 19.4 (Si*C*(CH$_3$)$_3$); HRMS (ESI) calcd. for $C_{48}H_{52}NaO_5SSi$ $[M+Na]^+$ 791.3197 found 791.3204.



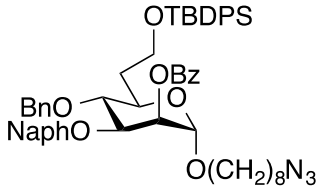
***p*-Tolyl 4-*O*-allyl-7-*O*-*tert*-butyldiphenylsilyl-1-thio-α/β-D-*manno*-heptopyranoside (4.37).** To a solution of **4.35** (1.66 g, 2.87 mmol) in DMF (28 mL) was added allyl bromide (298 μL, 3.44 mmol) and sodium hydride (172 mg, 4.30 mmol) at 0 °C. After stirring at 0 °C for 2 h, CH_3OH was added. The mixture was diluted with EtOAc and then washed with water. The organic layer was dried over $MgSO_4$, filtered and the filtrate was concentrated. The residue was then dissolved in 80% AcOH (28 mL) and heated to 50 °C. After stirring at 50 °C for 3 h, the reaction mixture was cooled to room temperature and the mixture was co-evaporated with toluene. The resulting residue was purified by column chromatography (2:1, hexane–EtOAc) to give **4.37** (1.15 g, 70%, α/β 10:1) as a white foam; R_f 0.12 (2:1, hexane–EtOAc); Data for **4.37α**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.68–7.62 (m, 4H, ArH), 7.44–7.28 (m, 8H, ArH), 6.96–6.92 (m, 2H, ArH), 5.98–5.88 (m, 1H, OCH_2CH=CH_2), 5.36 (d, 1H, $J_{1,2}$ = 1.5 Hz, H-1), 5.34–5.29 (m, 1H, OCH_2CH=CH_2), 5.24–5.20 (m, 1H, OCH_2CH=CH_2), 4.28 (app dt, 1H, $J_{5,4}$ = $J_{5,6b}$ = 9.8 Hz, $J_{5,6a}$ = 2.4 Hz, H-5), 4.24–4.14 (m, 3H, H-2, OCH_2CH=CH_2), 3.95–3.89 (m, 1H, H-3), 3.77–3.67 (m, 2H, H-7a, H-7b), 3.35 (app t, 1H, $J_{4,3}$ = $J_{4,5}$ = 9.8 Hz, H-4), 2.54–2.46 (m, 2H, OH), 2.26 (s, 3H, ArCH_3), 2.15–2.06 (m, 1H, H-6a), 1.78–1.69 (m, 1H, H-6b), 1.03 (s, 9H, Si(CCH_3)$_3$); ^{13}C NMR

($CDCl_3$, 125 MHz) δ_C 137.7 (Ar), 135.81 (2C, Ar), 135.76 (2C, Ar), 134.9 ($OCH_2CH=CH_2$), 134.3 (Ar), 134.2 (Ar), 132.4 (2C, Ar), 130.3 (Ar), 129.9 (2C, Ar), 129.74 (Ar), 129.71 (Ar), 128.81 (2C, Ar), 128.79 (2C, Ar), 117.5 ($OCH_2CH=CH_2$), 87.9 (C-1, $J_{C1,H1}$ = 167.9 Hz), 80.4 (C-4), 73.8 ($OCH_2CH=CH_2$), 72.6 (C-3), 72.1 (C-2), 69.1 (C-5), 60.6 (C-7), 34.9 (C-6), 27.1 ($SiC(CH_3)_3$), 21.3 ($ArCH_3$), 19.4 ($SiC(CH_3)_3$); HRMS (ESI) calcd. for $C_{33}H_{42}NaO_5SSi$ $[M+Na]^+$ 601.2414 found 601.2410.



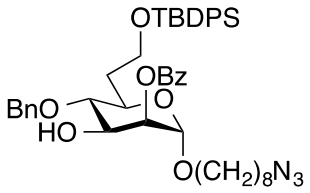
***p*-Tolyl 4-*O*-allyl-3-*O*-benzyl-7-*O*-*tert*-butyldiphenylsilyl-1-thio-α/β-D-*manno*-heptopyranoside (4.38).** To a solution of **4.37** (1.0 g, 2.87 mmol) in toluene (60 mL) was added di-*n*-butyltin oxide (1.07 g, 4.3 mmol) at room temperature and the reaction mixture was heated to reflux. After stirring at reflux for 3 h, the mixture was cooled to room temperature before benzyl bromide (511 μL, 4.3 mmol) and tetra-*n*-butylammonium bromide (1.39 g, 4.3 mmol) were added. The mixture was then heated to reflux. After stirring at reflux for 2 h, the reaction mixture was cooled to room temperature and concentrated. The resulting residue was purified by column chromatography (10:1, hexane–EtOAc) to give **4.38** (1.0 g, 87%, α/β 10:1) as a white foam; R_f 0.33 (4:1, hexane–EtOAc); Data for **4.38α**: ^1H NMR ($CDCl_3$, 700 MHz) δ_H 7.68–7.63 (m, 4H, ArH), 7.44–7.40 (m, 2H, ArH), 7.39–7.31 (m, 9H, ArH), 7.31–7.28 (m, 2H, ArH), 6.95–6.92 (m, 2H, ArH), 5.96–5.89 (m, 1H, $OCH_2CH=CH_2$), 5.42 (d, 1H, $J_{1,2}$ = 1.2 Hz, H-1), 5.31–5.27 (m, 1H, $OCH_2CH=CH_2$), 5.20–5.17 (m, 1H, $OCH_2CH=CH_2$), 4.73 (d, 1H, J_{gem} = 11.5 Hz, $ArCH_2$), 4.69 (d, 1H, J_{gem} = 11.5 Hz, $ArCH_2$), 4.36–4.33 (m, 1H, $OCH_2CH=CH_2$), 4.25 (app dt, 1H, $J_{5,4} = J_{5,6b}$ = 9.6 Hz, $J_{5,6a}$ = 2.2 Hz, H-5), 4.23–4.21 (m, 1H, H-2), 4.12–4.09 (m, 1H, $OCH_2CH=CH_2$), 3.80

(dd, 1H, $J_{3,2}$ = 3.2 Hz, $J_{3,4}$ = 9.0 Hz, H-3), 3.74–3.67 (m, 2H, H-7a, H-7b), 3.43 (app t, 1H, $J_{4,3}$ = $J_{4,5}$ = 9.6 Hz, H-4), 2.61 (d, 1H, $J_{OH,2}$ = 2.0 Hz, 2-OH), 2.26 (s, 3H, ArCH_3), 2.15–2.11 (m, 1H, H-6a), 1.76–1.69 (m, 1H, H-6b), 1.03 (s, 9H, SiC(CH_3)$_3$); ^{13}C NMR ($CDCl_3$, 175 MHz) δ_C 137.9 (Ar), 137.6 (Ar), 135.82 (2C, Ar), 135.75 (2C, Ar), 135.1 ($OCH_2CH{=}CH_2$), 134.4 (Ar), 134.2 (Ar), 132.4 (2C, Ar), 130.3 (Ar), 129.9 (2C, Ar), 129.69 (Ar), 129.66 (Ar), 128.8 (2C, Ar), 128.3 (Ar), 128.1 (2C, Ar), 127.77 (2C, Ar), 127.76 (2C, Ar), 116.9 ($OCH_2CH{=}CH_2$), 87.4 (C-1, $J_{C1,H1}$ = 167.9 Hz), 80.4 (C-3), 78.7 (C-4), 74.2 ($OCH_2CH{=}CH_2$), 72.5 (ArCH_2), 70.1 (C-2), 69.2 (C-5), 60.6 (C-7), 34.9 (C-6), 27.1 (SiC(CH_3)$_3$), 21.3 (ArCH_3), 19.4 (SiC(CH_3)$_3$); HRMS (ESI) calcd. for $C_{40}H_{48}NaO_5SSi$ $[M+Na]^+$ 691.2884 found 691.2880.



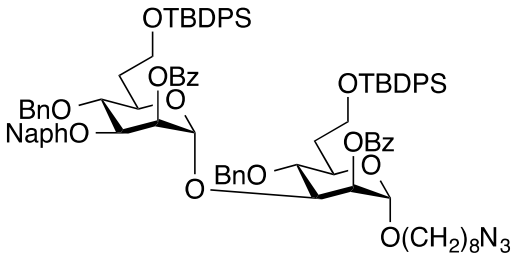
8-Azidooctyl 2-*O*-benzoyl-4-*O*-benzyl-7-*O*-*tert*-butyldiphenylsilyl-3-*O*-(2-naphthyl)-α-D-*manno*-heptopyranoside (4.39). To a solution of **4.30** (700 mg, 0.802 mmol) and 8-azidooctanol (164 mg, 0.96 mmol) in CH_2Cl_2 (16 mL) was added 4 Å MS at room temperature. After stirring at room temperature for 30 min, the mixture was then cooled to 0 °C before *N*-iodosuccinimide (220 mg, 0.96 mmol) and trimethylsilyl trifluoromethanesulfonate (14 μL, 0.080 mmol) were added. The mixture was gradually warmed to room temperature. After stirring at room temperature for 24 h, triethylamine was added. A small amount of H_2O was added, followed by solid $Na_2S_2O_3{\cdot}5H_2O$ until the solution was colorless. The mixture was dried over $MgSO_4$ and then filtered and concentrated. The resulting residue was purified by column chromatography (20:1, hexane–EtOAc) to give **4.39** (500 mg, 68%, α only) as a colorless syrup;

$[\alpha]^{25}_{D}$ –15.8 (*c* 0.1, $CHCl_3$); R_f 0.43 (10:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 8.10–8.06 (m, 2H, ArH), 7.84–7.74 (m, 3H, ArH), 7.80–7.65 (m, 7H, ArH), 7.64–7.56 (m, 2H, ArH), 7.48–7.27 (m, 13H, ArH), 5.64 (dd, 1H, $J_{2,1}$ = 1.8 Hz, $J_{2,3}$ = 3.2 Hz, H-2), 4.96–4.91 (m, 2H, ArC*H*$_2$), 4.85 (d, 1H, $J_{1,2}$ = 1.8 Hz, H-1), 4.73 (d, 1H, J_{gem} = 11.6 Hz, ArC*H*$_2$), 4.62 (d, 1H, J_{gem} = 11.0 Hz, ArC*H*$_2$), 4.14 (dd, 1H, $J_{3,2}$ = 3.2 Hz, $J_{3,4}$ = 9.5 Hz, H-3), 3.97–3.87 (m, 2H, H-5, H-7a), 3.84 (ddd, 1H, $J_{7b,6a}$ = 7.3 Hz, $J_{7b,6b}$ = 4.1 Hz, J_{gem} = 10.4 Hz, H-7b), 3.66 (app dt, 1H, *J* = 6.6, 9.5 Hz, OC*H*$_2$), 3.62 (app t, 1H, $J_{4,3}$ = $J_{4,5}$ = 9.5 Hz, H-4), 3.35 (app dt, 1H, *J* = 6.6, 9.5 Hz, octyl OC*H*$_2$), 3.23 (app t, 1H, *J* = 7.0 Hz, C*H*$_2$N$_3$), 2.31–2.22 (m, 1H, H-6a), 1.79–1.70 (m, 1H, H-6b), 1.62–1.47 (m, 4H, octyl C*H*$_2$), 1.38–1.20 (m, 8H, octyl C*H*$_2$), 1.06 (s, 9H, SiC(C*H*$_3$)$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 166.1 (C=O), 138.7 (Ar), 138.1 (Ar), 135.84 (Ar), 135.76 (2C, Ar), 135.70 (2C, Ar), 134.3 (Ar), 134.1 (Ar), 133.45 (Ar), 133.36 (Ar), 133.1 (Ar), 130.3 (Ar), 130.1 (2C, Ar), 129.74 (2C, Ar), 129.72 (2C, Ar), 128.6 (2C, Ar), 128.5 (2C, Ar), 128.2 (Ar), 128.1 (2C, Ar), 127.8 (4C, Ar), 126.8 (Ar), 126.2 (Ar), 126.1 (Ar), 125.9 (Ar), 97.6 (C-1, $J_{C1,H1}$ = 171.5 Hz), 78.8 (C-4), 78.7 (C-3), 75.4 (Ar*C*H$_2$), 71.8 (Ar*C*H$_2$), 69.7 (C-2), 68.1 (C-5), 67.9 (octyl O*C*H$_2$), 60.6 (C-7), 51.7 (*C*H$_2$N$_3$), 35.4 (C-6), 29.54 (octyl *C*H$_2$), 29.49 (octyl *C*H$_2$), 29.2 (octyl *C*H$_2$), 29.0 (octyl *C*H$_2$), 27.1 (SiC(*C*H$_3$)$_3$), 26.9 (octyl *C*H$_2$), 26.2 (octyl *C*H$_2$), 19.4 (Si*C*(CH$_3$)$_3$); HRMS (ESI) calcd. for $C_{56}H_{65}N_3NaO_7Si$ $[M+Na]^+$ 942.4484 found 942.4479.



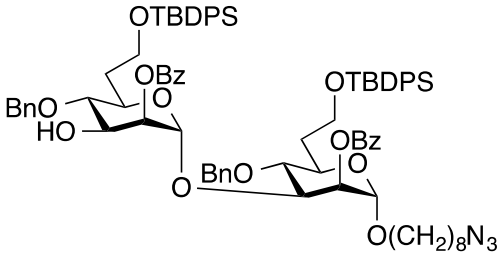
8-Azidooctyl 2-*O*-benzoyl-4-*O*-benzyl-7-*O*-*tert*-butyldiphenylsilyl-α-D-*manno*-heptopyranoside (4.40). To a solution of **4.39** (135 mg, 0.15 mmol) in a mixture of CH_2Cl_2–

H_2O (5.0 mL, 10:1) was added 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (40 mg, 0.18 mmol) at room temperature. After stirring at room temperature for 3 h, satd. aq. $NaHCO_3$ was added. The mixture was diluted with CH_2Cl_2 and washed with satd. aq. $NaHCO_3$. The organic layer was dried over $MgSO_4$, filtered and the filtrate was concentrated. The resulting residue was purified by column chromatography (10:1, hexane–EtOAc) to give **4.40** (90 mg, 79%) as a colorless oil; $[\alpha]^{25}_D$ –0.7 (*c* 0.3, $CHCl_3$); R_f 0.36 (4:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 8.06–8.00 (m, 2H, ArH), 7.69–7.64 (m, 4H, ArH), 7.61–7.56 (m, 7H, ArH), 7.48–7.28 (m, 13H, ArH), 5.33 (dd, 1H, $J_{2,1}$ = 1.6 Hz, $J_{2,3}$ = 3.5 Hz, H-2), 4.84–4.81 (m, 2H, H-1, ArC*H*$_2$), 4.70 (d, 1H, J_{gem} = 11.1 Hz, ArC*H*$_2$), 4.62 (d, 1H, J_{gem} = 11.0 Hz, ArC*H*$_2$), 4.26 (ddd, 1H, $J_{3,2}$ = 3.5 Hz, $J_{3,4}$ = 9.1 Hz, $J_{3,OH}$ = 5.2 Hz, H-3), 3.96–3.80 (m, 3H, H-5, H-7a, H-7b), 3.66 (app dt, 1H, *J* = 6.6, 9.5 Hz, octyl OC*H*$_2$), 3.62 (app t, 1H, $J_{4,3}$ = $J_{4,5}$ = 9.1 Hz, H-4), 3.34 (app dt, 1H, *J* = 6.6, 9.5 Hz, octyl OC*H*$_2$), 3.23 (app t, 1H, *J* = 7.0 Hz, C*H*$_2$N$_3$), 2.27–2.20 (m, 1H, H-6a), 2.09 (d, 1H, $J_{OH,3}$ = 5.2 Hz, 3-OH), 1.78–1.70 (m, 1H, H-6b), 1.61–1.48 (m, 4H, octyl C*H*$_2$), 1.37–1.22 (m, 8H, octyl C*H*$_2$), 1.06 (s, 9H, SiC(C*H*$_3$)$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 166.5 (C=O), 138.5 (Ar), 135.77 (2C, Ar), 135.71 (2C, Ar), 134.2 (Ar), 134.1 (Ar), 133.5 (Ar), 130.05 (2C, Ar), 129.99 (Ar), 129.78 (Ar), 129.76 (Ar), 128.72 (2C, Ar), 128.65 (2C, Ar), 128.10 (2C, Ar), 128.07 (Ar), 127.8 (4C, Ar), 97.3 (C-1, $J_{C1,H1}$ = 171.7 Hz), 80.5 (C-4), 75.1 (Ar*C*H$_2$), 73.6 (C-2), 70.9 (C-3), 67.9 (octyl O*C*H$_2$), 67.8 (C-5), 60.5 (C-7), 51.7 (*C*H$_2$N$_3$), 35.3 (C-6), 29.55 (octyl *C*H$_2$), 29.49 (octyl *C*H$_2$), 29.2 (octyl *C*H$_2$), 29.0 (octyl *C*H$_2$), 27.1 (SiC(*C*H$_3$)$_3$), 26.8 (octyl *C*H$_2$), 26.2 (octyl *C*H$_2$), 19.4 (Si*C*(CH$_3$)$_3$); HRMS (ESI) calcd. for $C_{45}H_{57}N_3NaO_7Si$ $[M+Na]^+$ 802.3858 found 802.3849.



8-azidooctyl (2-*O*-benzoyl-4-*O*-benzyl-7-*O*-*tert*-butyldiphenylsilyl-3-*O*-(2-naphthyl)-α-D-*manno*-heptopyranosyl)-(1→3)-2-*O*-benzoyl-4-*O*-benzyl-7-*O*-*tert*-butyldiphenylsilyl-α-D-*manno*-heptopyranoside (4.41). To a solution of **4.30** (322 mg, 0.37 mmol) and **4.40** (240 mg, 0.31 mmol) in CH_2Cl_2 (13.0 mL) was added 4Å MS at room temperature. After stirring for 30 min at room temperature. The reaction mixture was cooled to 0 °C, and *N*-iodosuccinimide (100 mg, 0.44 mmol) and trimethylsilyl trifluoromethanesulfonate (13.4 μL, 0.074 mmol) were then added. After stirring at 0 °C for 15 min, triethylamine was added. The reaction was warmed to room temperature and then a small amount of H_2O was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The mixture was dried over $MgSO_4$ and then filtered and concentrated. The resulting residue was purified by column chromatography (20:1, hexane–EtOAc) to give **4.41** (280 mg, 82%) as a colorless oil; $[\alpha]^{25}_D$ –18.3 (*c* 0.6, $CHCl_3$); R_f 0.43 (4:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 8.01–7.96 (m, 4H, ArH), 7.76–7.48 (m, 14H, ArH), 7.41–7.21 (m, 28H, ArH), 7.13–7.09 (m, 2H, ArH), 5.60 (dd, 1H, $J_{2',1'}$ = 2.1 Hz, $J_{2',3'}$ = 2.8 Hz, H-2'), 5.31 (dd, 1H, $J_{2,1}$ = 1.9 Hz, $J_{2,3}$ = 3.2 Hz, H-2), 5.17 (d, 1H, $J_{1',2'}$ = 2.1 Hz, H-1'), 4.79–4.75 (m, 3H, H-1, ArCH_2), 4.69 (d, 1H, J_{gem} = 11.6 Hz, ArCH_2), 4.53 (d, 1H, J_{gem} = 10.9 Hz, ArCH_2), 4.48–4.44 (m, 2H, ArCH_2), 4.25 (dd, 1H, $J_{3,2}$ = 3.2 Hz, $J_{3,4}$ = 9.4 Hz, H-3), 3.96 (dd, 1H, $J_{3',2'}$ = 2.8 Hz, $J_{3',4'}$ = 9.3 Hz, H-3'), 3.92–3.72 (m, 6H, H-5, H-7a, H-7b, H-5', H-7'a, H-7'b), 3.63–3.51 (m, 3H, H-4, H-4', octyl OCH_2), 3.26 (app dt, 1H, *J* = 6.7, 9.5 Hz, octyl OCH_2), 3.19 (app t, 3H, *J* = 7.0 Hz, CH_2N_3), 2.21–2.12 (m, 1H, H-6a), 2.10–2.03 (m, 1H, H-6'a), 1.93–1.82

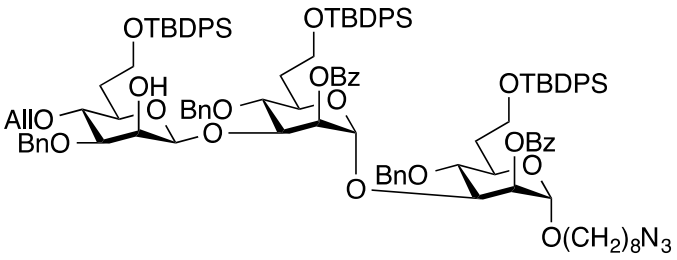
(m, 1H, H-6'b), 1.71–1.63 (m, 1H, H-6b), 1.55–1.49 (m, 2H, octyl CH_2), 1.46–1.39 (m, 2H, octyl CH_2), 1.32–1.14 (m, 8H, octyl CH_2), 1.05 (s, 9H, Si(CCH_3)$_3$), 1.04 (s, 9H, SiC(CH_3)$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 165.74 (C=O), 165.73 (C=O), 138.8 (Ar), 138.0 (Ar), 135.8 (Ar), 135.74 (Ar), 135.7 (Ar), 135.67 (Ar), 134.4 (Ar), 134.2 (Ar), 134.0 (Ar), 133.4 (Ar), 133.3 (Ar), 133.0 (Ar), 130.2 (Ar), 130.1 (Ar), 130.02 (Ar), 129.97 (Ar), 129.8 (Ar), 129.7 (Ar), 129.61 (Ar), 129.6 (Ar), 128.64 (Ar), 128.60 (Ar), 128.57 (Ar), 128.3 (Ar), 128.2 (Ar), 128.06 (Ar), 128.05 (Ar), 128.0 (Ar), 127.80 ((Ar), 127.77 (Ar), 127.74 (Ar), 127.72(Ar), 127.5 (Ar), 126.6 (Ar), 126.1 (Ar), 126.0 (Ar), 125.9 (Ar), 99.4 (C-1', $J_{C1',H1'}$ = 173.5 Hz), 97.0 (C-1, $J_{C1,H1}$ = 172.1 Hz), 79.6 (2C, C-4, C-4'), 78.2 (C-3'), 76.9 (C-3), 75.5 (ArCH$_2$), 74.4 (ArCH$_2$), 73.0 (C-2), 71.7 (ArCH$_2$), 69.9 (C-2'), 69.7 (C-5 or C-5'), 68.1 (C-5 or C-5'), 67.9 (octyl OCH$_2$), 60.8 (C-7 or C-7'), 60.5 (C-7 or C-7'), 51.7 (CH$_2$N$_3$), 35.2 (C-6), 35.1 (C-6'), 29.5 (octyl CH$_2$), 29.4 (octyl CH$_2$), 29.3 (octyl CH$_2$), 29.0 (octyl CH$_2$), 27.15 (SiC(CH$_3$)$_3$), 27.07 (SiC(CH$_3$)$_3$), 26.9 (octyl CH$_2$), 26.1 (octyl CH$_2$), 19.46 (SiC(CH$_3$)$_3$), 19.42 (SiC(CH$_3$)$_3$); HRMS (ESI) calcd. for $C_{93}H_{109}N_3NaO_{13}Si_2$ $[M+Na]^+$ 1550.7078 found 1550.7112.



8-Azidooctyl (2-*O*-benzoyl-4-*O*-benzyl-7-*O*-*tert*-butyldiphenylsilyl-α-D-*manno*-heptopyranosyl)-(1→3)-2-*O*-benzoyl-4-*O*-benzyl-7-*O*-*tert*-butyldiphenylsilyl-α-D-*manno*-heptopyranoside (4.42). To a solution of **4.41** (60 mg, 0.039 mmol) in a mixture of CH_2Cl_2–H_2O (3.0 mL, 10:1) was added 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (10.7 mg, 0.047 mmol) at room temperature. After stirring at room temperature for 3 h, satd. aq. $NaHCO_3$ was added and

then the mixture was diluted with CH_2Cl_2. The organic layer was washed with satd. aq. $NaHCO_3$ and the organic layer was dried over $MgSO_4$, filtered and the filtrate was concentrated. The resulting residue was purified by column chromatography (4:1, hexane–EtOAc) to give **4.42** (45 mg, 83%) as a colorless oil; $[\alpha]^{25}_D$ –3.4 (*c* 0.5, $CHCl_3$); R_f 0.25 (4:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 8.05–8.00 (m, 2H, ArH), 7.95–7.91 (m, 2H, ArH), 7.70–7.62 (m, 8H, ArH), 7.61–6.54 (m, 2H, ArH), 7.47–7.21 (m, 26H, ArH), 7.13–7.09 (m, 2H, ArH), 5.36 (dd, 1H, $J_{2',1'}$ = 1.7 Hz, $J_{2',3'}$ = 3.2 Hz, H-2'), 5.30 (dd, 1H, $J_{2,1}$ = 1.8 Hz, $J_{2,3}$ = 3.2 Hz, H-2), 5.17 (d, 1H, $J_{1',2'}$ = 1.7 Hz, H-1'), 4.86 (d, 1H, J_{gem} = 10.9 Hz, ArC*H*$_2$), 4.75 (d, 1H, $J_{1,2}$ = 1.8 Hz, H-1), 4.63 (d, 1H, J_{gem} = 11.9 Hz, ArC*H*$_2$), 4.62 (d, 1H, J_{gem} = 11.4 Hz, ArC*H*$_2$), 4.57 (d, 1H, J_{gem} = 11.4 Hz, ArC*H*$_2$), 4.24 (dd, 1H, $J_{3,2}$ = 3.2 Hz, $J_{3,4}$ = 9.3 Hz, H-3), 4.07 (ddd, 1H, $J_{3',2'}$ = 3.2 Hz, $J_{3',4'}$ = 9.2 Hz, $J_{3',OH}$ = 4.5 Hz, H-3'), 4.00–3.75 (m, 6H, H-5, H-7a, H-7b, H-5', H-7'a, H-7'b), 3.63 (app t, $J_{4,3} = J_{4,5}$ = 9.3 Hz, H-4), 3.56–3.50 (m, 2H, H-4', octyl OC*H*$_2$), 3.25 (app dt, 1H, *J* = 6.7, 9.5 Hz, octyl OC*H*$_2$), 3.19 (app t, 3H, *J* = 7.0 Hz, C*H*$_2$N$_3$), 2.21–2.13 (m, 1H, H-6a), 2.12–2.06 (m, 1H, H-6'a), 2.00 (d, 1H, $J_{OH,3'}$ = 4.5 Hz, 3'-OH), 1.93–1.84 (m, 1H, H-6'b), 1.72–1.63 (m, 1H, H-6b), 1.55–1.49 (m, 2H, octyl C*H*$_2$), 1.46–1.36 (m, 2H, octyl C*H*$_2$), 1.33–1.12 (m, 8H, octyl C*H*$_2$), 1.06 (s, 9H, SiC(C*H*$_3$)$_3$), 1.04 (s, 9H, SiC(C*H*$_3$)$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 166.1 (C=O), 165.7 (C=O), 138.5 (Ar), 138.1 (Ar), 135.8 (Ar), 135.74 (Ar), 135.67 (Ar), 134.4 (Ar), 134.2 (Ar), 134.0 (Ar), 133.44 (Ar), 133.40 (Ar), 130.1 (Ar), 130.01 (Ar), 130.00 (Ar), 129.83 (Ar), 129.76 (Ar), 129.73 (Ar), 129.66 (Ar), 129.64 (Ar), 128.7 (Ar), 128.6 (Ar), 128.3 (Ar), 128.2 (Ar), 127.93 (Ar), 127.88 (Ar), 127.80 (Ar), 127.77 (Ar), 127.75 (Ar), 99.3 (C-1', $J_{C1',H1'}$ = 173.2 Hz), 97.0 (C-1, $J_{C1,H1}$ = 172.1 Hz), 79.8 (C-4), 79.0 (C-4'), 76.5 (C-3), 75.6 (Ar*C*H$_2$), 73.7 (Ar*C*H$_2$), 73.2 (C-2'), 73.0 (C-2), 70.0 (C-3'), 69.4 (C-5 or C-5'), 68.2 (C-5 or C-5'), 67.9 (octyl O*C*H$_2$), 60.9 (C-7 or C-7'), 60.5 (C-7 or C-7'), 51.6 (*C*H$_2$N$_3$), 35.2 (C-6), 35.0 (C-6'), 29.5 (octyl

*C*H$_2$), 29.4 (octyl *C*H$_2$), 29.2 (octyl *C*H$_2$), 29.0 (octyl *C*H$_2$), 27.15 (SiC(*C*H$_3$)$_3$), 27.08 (SiC(*C*H$_3$)$_3$), 26.9 (octyl *C*H$_2$), 26.1 (octyl *C*H$_2$), 19.47 (Si*C*(CH$_3$)$_3$), 19.43 (Si*C*(CH$_3$)$_3$); HRMS (ESI) calcd. for $C_{82}H_{97}N_3NaO_{13}Si_2$ $[M+Na]^+$ 1410.6452 found 1410.6464.



8-Azidooctyl (4-*O*-Allyl-3-*O*-benzyl-7-*O*-*tert*-butyldiphenylsilyl-β-D-*manno*-heptopyranosyl)-(1→3)-(2-*O*-benzoyl-4-*O*-benzyl-7-*O*-*tert*-butyldiphenylsilyl-α-D-*manno*-heptopyranosyl)-(1→3)-2-*O*-benzoyl-4-*O*-benzyl-7-*O*-*tert*-butyldiphenylsilyl-α-D-*manno*-heptopyranoside (4.44). To a solution of **4.31** (23.3 mg, 0.0288 mmol) and **4.42** (20 mg, 0.0144 mmol) in CH_2Cl_2 (1.0 mL) was added 4Å MS at room temperature. After stirring for 30 min, 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (7.9 mg, 0.0346 mmol) was added. After stirring at room temperature for 2 h, satd. aq. $NaHCO_3$ was added and then the mixture was diluted with EtOAc. The organic layer was washed with satd. aq. $NaHCO_3$ and the organic layer was dried over $MgSO_4$. The mixture was then filtered and the filtrate was concentrated. The resulting residue was purified by column chromatography (20:1 to 10:1, hexane–EtOAc) to give a diastereomeric mixture of **4.43** (~77%) as a colorless oil. To a solution of **4.43** (31.6 mg, 0.011 mmol) in CH_2Cl_2 was added 4Å MS at room temperature. After stirring for 30 min, methyl trifluoromethanesulfonate (11.7 μL, 0.11 mmol) and 2,6-di-*tert*-butyl-4-methylpyridine (20.7 mg, 0.11 mmol) were added. After stirring at room temperature for 4 days, triethylamine was added and the mixture was concentrated. The mixture was purified by column chromatography (20:1 to

10:1, hexane–EtOAc) to give **4.44** (7.8 mg, 28% from **4.42**) as a colorless oil; R_f 0.22 (4:1, hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 8.00–7.97 (m, 2H, ArH), 7.93–7.89 (m, 2H, ArH), 7.55–7.55 (m, 15H, ArH), 7.40–7.07 (m, 37H, ArH), 5.81–5.71 (m, 1H, OCH_2CH=CH_2), 5.44 (dd, 1H, $J_{2',1'}$ = 2.3 Hz, $J_{2',3'}$ = 3.1 Hz, H-2'), 5.31 (dd, 1H, $J_{2,1}$ = 2.0 Hz, $J_{2,3}$ = 3.2 Hz, H-2), 5.17–5.05 (m, 3H, H-1', OCH_2CH=CH_2), 4.80 (d, 1H, $J_{1,2}$ = 2.0 Hz, H-1), 4.71 (d, 1H, J_{gem} = 11.0 Hz, ArCH_2), 4.64 (d, 1H, J_{gem} = 11.0 Hz, ArCH_2), 4.57 (d, 1H, J_{gem} = 11.4 Hz, ArCH_2), 4.49–4.44 (m, 2H, ArCH_2), 4.36 (d, 1H, J_{gem} = 11.0 Hz, ArCH_2), 4.28 (br s, 1H, H-1''), 4.26–4.18 (m, 3H), 3.90–3.48 (m, 15H), 3.30–3.16 (m, 4H), 2.20–2.08 (m, 1H), 2.03–1.60 (m, 5H), 1.46–1.39 (m, 4H, octyl CH_2), 1.24–1.14 (m, 8H, octyl CH_2), 1.04 (s, 9H, Si(CCH_3)$_3$), 1.03 (s, 9H, SiC(CH_3)$_3$), 1.00 (s, 9H, SiC(CH_3)$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 165.9 (C=O), 165.7 (C=O), 138.5 (Ar), 138.3 (Ar), 137.9 (Ar), 135.77 (Ar), 135.73 (Ar), 135.71 (Ar), 137.66 (Ar), 135.3 (OCH_2CH=CH_2), 134.41 (Ar), 134.38 (Ar), 134.27 (Ar), 134.21 (Ar), 134.0 (Ar), 133.5 (Ar), 133.4 (Ar), 130.0 (Ar), 129.99 (Ar), 129.91 (Ar), 129.75 (Ar), 129.72 (Ar), 129.62 (Ar), 128.70 (Ar), 128.67 (Ar), 128.66 (Ar), 128.5 (Ar), 128.3 (Ar), 128.03 (Ar), 127.95 (Ar), 127.86 (Ar), 127.80 (Ar), 127.76 (Ar), 127.73 (Ar), 127.48 (Ar), 116.4 (OCH_2CH=CH_2), 99.5 (C-1', $J_{C1',H1'}$ = 172.8 Hz), 98.0 (C-1'', $J_{C1'',H1''}$ = 156.4 Hz), 96.9 (C-1, $J_{C1,H1}$ = 172.1 Hz), 81.4, 79.4, 77.7, 76.6, 75.5, 75.4, 73.9, 73.6, 72.8, 72.5, 71.1, 70.3, 69.7, 68.3, 68.1, 68.0, 60.9, 60.7, 60.5, 51.6 (CH_2N_3), 35.3, 35.2, 35.1, 29.4 (2 x octyl CH_2), 29.2 (octyl CH_2), 29.0 (octyl CH_2), 27.1 (2 x SiC(CH_3)$_3$), 27.0 (SiC(CH_3)$_3$), 26.8 (octyl CH_2), 26.1 (octyl CH_2), 19.44 (SiC(CH_3)$_3$), 19.41 (SiC(CH_3)$_3$), 19.38 (SiC(CH_3)$_3$); HRMS (ESI) calcd. for $C_{115}H_{141}N_4O_{18}Si_3$ $[M+NH_4]^+$ 1949.9543 found 1949.9558.

4.5 References

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Chapter 5

Investigation of Stereoselective Fructofuranosylation with Conformationally-Restricted Donors

5.1 Background

5.1.1 Overview of stereoselective fructofuranosylation and hypothesis

Fructose (Fru) is a 2-ketohexose that is found nearly exclusively in the furanose ring form in nature. Fructofuranoside (Fru*f*) residues are present in natural compounds such as sucrose and fructosans, as well as in bacterial polysaccharides (**Figure 5.1a**)[1,2]. Apart from a few exceptions, Fru*f* in natural saccharides are all β-linked. When it comes to the synthesis of β-Fru*f* glycosides, only two major methodologies, both developed by Oscarson and co-workers[3,4], are available. The concepts behind these two methodologies were discussed in Chapters 3 and 4. One is the IAD methodology using a Fru*f* donor with a *p*-methoxybenzyl group on O-2 (**3.1**, **Figure 5.1b)**. The other is the use of the siloxane-bridged Fru*f* donor **4.1**, which affords exclusively β-Fru*f* glycosides.

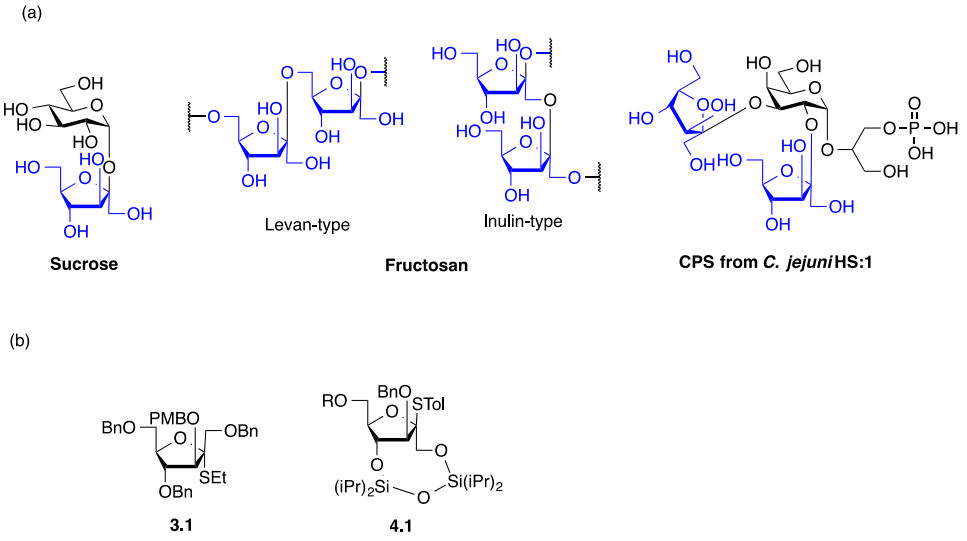


Figure 5.1. (a) Structures of sucrose, fructosan and the repeating unit of the capsular polysaccharide from *C. jejuni* HS:1; (b) Fru*f* donors developed by Oscarson and co-workers for exclusive β-fructofuranosylation

As mentioned in **Section 3.1.2.4**, although conformationally-restricted donors have been successfully investigated for the synthesis of 1,2-*cis*-aldofuranosides[5–9] (**Figure 5.2a**), no studies had been reported in which conformationally-restricted donors had been used in ketofuranosylation. This methodology was first developed by me for 2,3-*cis*-xylulofuranosylation (Chapter 3). In that work, modest to good β-selectivity using xylylene-protected Xul*f* donor **3.70** and **3.71** (**Figure 5.2b**) was observed. In this Chapter, I tested the same methodology on another ketofuranose, Fru*f*, by studying the glycosylation stereoselectivity using xylylene-protected donors **5.1** and **5.2** (**Figure 5.2c**).

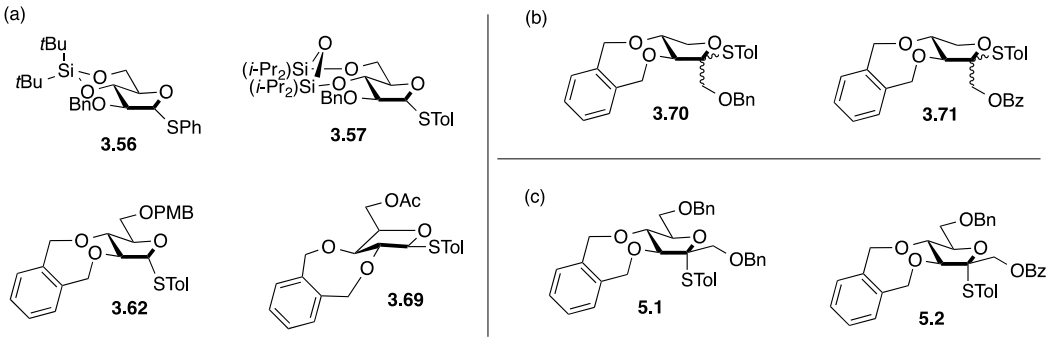
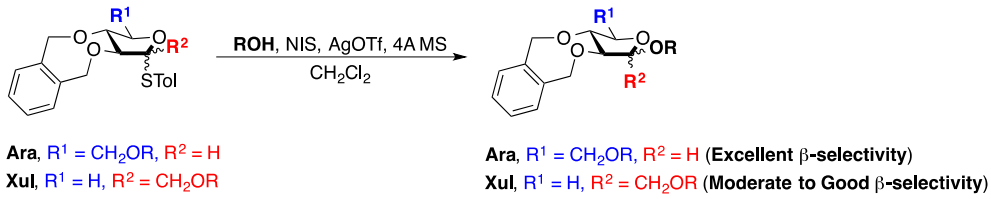


Figure 5.2. (a) Conformationally-restricted donors **3.56**, **3.57**, **3.62** and **3.69** for the stereoselective synthesis of 1,2-*cis*-aldofuranosides; (b) Conformationally-restricted Xul*f* donors **3.70** and **3.71** for 2,3-*cis*-xylulofuranosylation; (c) Xylylene-protected Fru*f* donors **5.1** and **5.2** to be explored for 2,3-*cis*-fructofuranosylation.

Comparing the results of arabinofuranosylation[8] and xylulofuranosylation (Chapter 3) using xylylene-protected donors, decreased β-selectivity was observed in the latter case (**Scheme 5.1**). The structural difference between Ara*f* and Xul*f* is the position of the hydroxymethyl group. This group is at C-4 in Ara*f* and C-1 in Xul*f*. I hypothesized that the electrophilic intermediate produced from the Ara*f* donor would be more conformationally-rigid than the same species pro-

duced from the Xul*f* donor because the CH_2OR group at the C-4 on furan ring prefers the pseudo-equatorial position. This would lead to a single intermediate that would result better β-selectivity via "inside attack" (**Figure 5.3a**). Therefore, I further hypothesized that the extra CH_2OR group in xylylene-protected Fru*f* would, compared to the Xul*f* derivative, be more β-selective (**Figure 5.3b**).



Scheme 5.1. Comparison of the stereoselectivity in the formation of Ara*f* and Xul*f* glycosides using xylylene-protected donors.

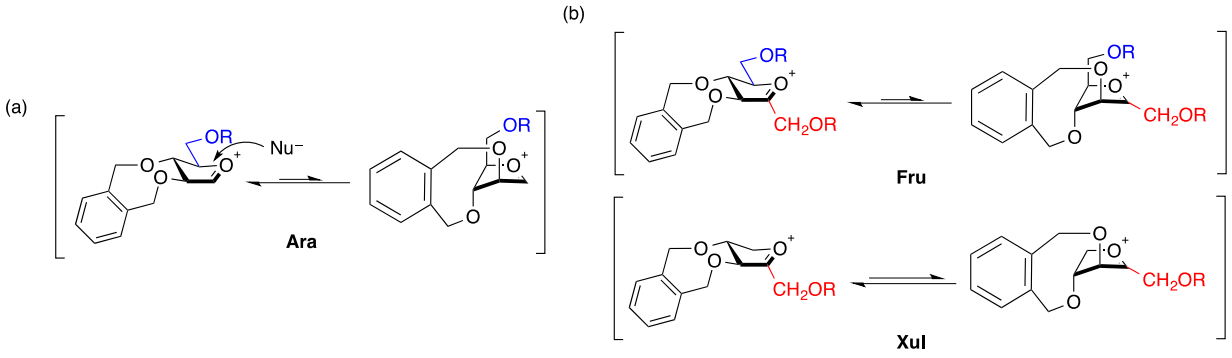
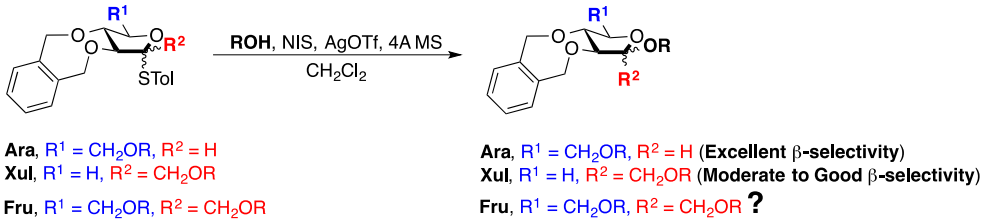


Figure 5.3. (a) Plausible intermediates of the xylylene-protected arabinofuranosyl oxacarbenium ion; (b) Plausible intermediates of the xylylene-protected fructofuranosyl and xylulofuranosyl oxacarbenium ions.

5.1.2 Research objectives

In this chapter, I describe my work on synthesizing xylylene-protected Fru*f* donors **5.1** and **5.2** and studying their stereoselectivity in fructofuranosylation reactions. This is the first study on the use of conformationally-restricted Fru*f* donors in glycosylation reactions. It should be noted, however, that donor **4.1** (**Figure 5.1b**) would be expected to be conformationally rigidified, although its design did not take this feature into account. This study will also allow the influence of the two hydroxylmethyl groups on the stereoselectivity to be further probed (**Scheme 5.2**).



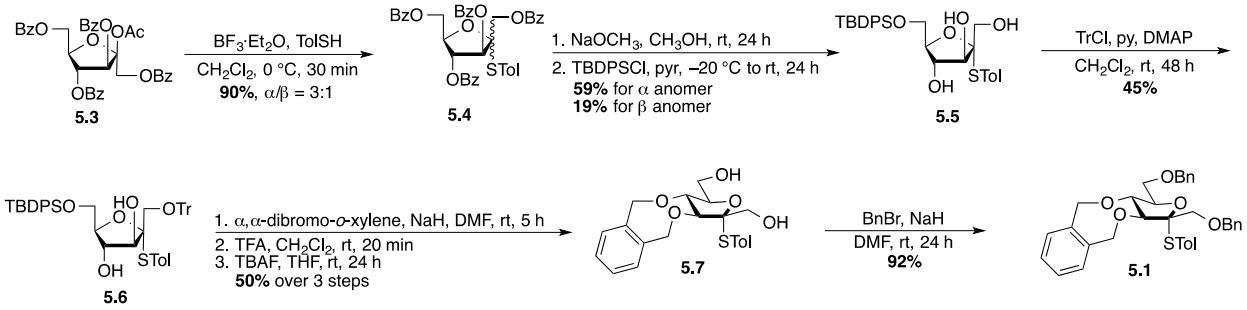
Scheme 5.2. Stereoselectivity results using conformationally-restricted donors in arabinofuranosylation and xylulofuranosylation reactions and extension to fructofuranosylation.

5.2 Results and Discussion

5.2.1 Synthesis of xylylene-protected Fru*f* thioglycoside donor 5.1 and 5.2, and stereoselectivity study of frucofuranosylation

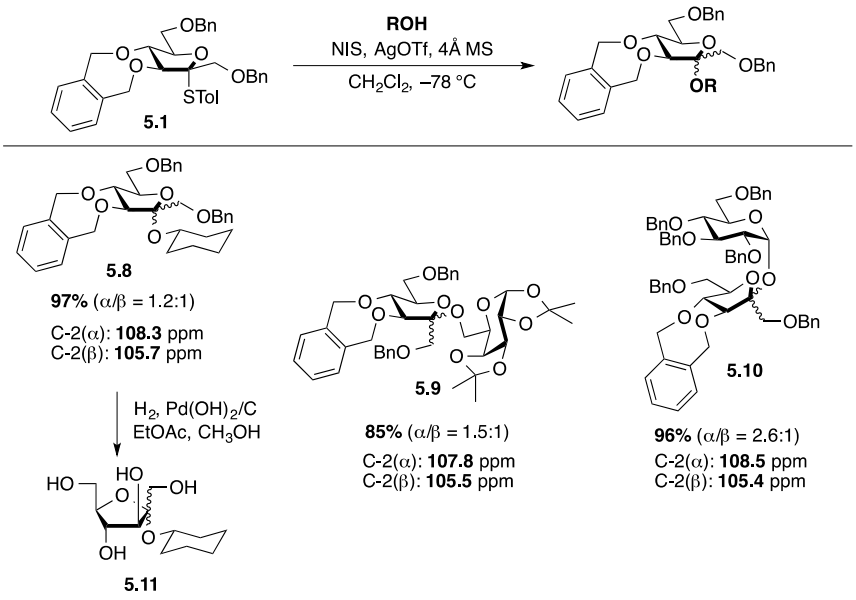
The synthesis of xylylene-protected Fru*f* donor **5.1** began from **5.3**[10] (**Scheme 5.3**). Thioglycosylation of **5.3** was performed using *p*-toluenethiol and boron trifluoride etherate to give **5.4** in 90% yield as a 3:1 α:β ratio. This compound was then de-*O*-acylated to remove all benzoyl groups and the C-6 hydroxyl group in the product was protected as a TBDPS ether. The two

anomers of **5.5** could be separated at this step. The combined yield of the both anomers over the two steps was 78%. Tritylation of **5.5α** was performed to give a 45% yield of **5.6**. Incorporation of the xylylene group was achieved upon treatment with α,α'-dibromo-*o*-xylene and NaH, and subsequent removal of the TBDPS and trityl group gave **5.7** in 50% yield from **5.6** over the three steps. Finally, benzylation of the diol **5.7** was performed to afford **5.1** in 92% yield.



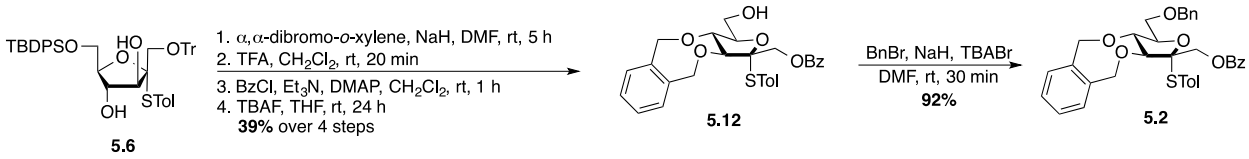
Scheme 5.3. Synthesis of xylylene-protected Fru*f* thioglycoside donor **5.1**.

The stereoselectivity of fructofuranosylation using **5.1** was tested using the NIS–AgOTf promotor system. The Fru*f* donor **5.1** was initially studied with three different acceptors (**Scheme 5.4**). To my surprise, the reactions proceed with either no selectivity (i.e., 1:1, α:β mixture of glycosides) or were α selective. The anomeric configuration of fructofuranosides **5.8**–**5.10** was determined from the chemical shifts of the C-2 resonances in ^{13}C NMR spectrum. C-2 signals more downfield (106–109 ppm) were assigned as α-Fru*f* glycosides and the C-2 resonance more upfield (103–106 ppm) were assigned as β-Fru*f* glycosides. To avoid false-characterization arising from the cyclic protecting group, the xylylene group of **5.8** was also removed to confirm the anomeric configuration. The C-2 of the corresponding product (**5.11**) was observed at 109.3 ppm for α-Fru*f* and 105.7 ppm for β-Fru*f*.



Scheme 5.4. Stereoselectivity of fructofuranosylation using xylylene-protected donor **5.1**.

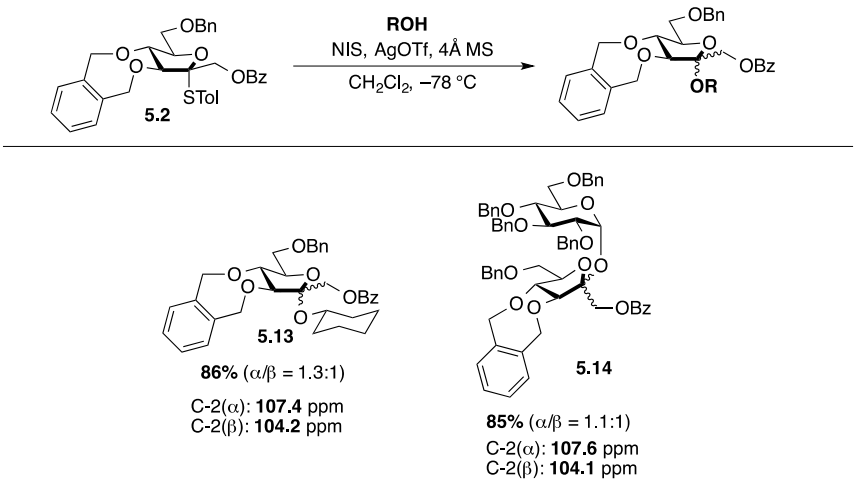
As mentioned in **Section 3.2.2**, the installation of a benzoyl group on O-1 in the xylylene-protected donors increased the β-stereoselectivity. Therefore, 1-*O*-Bz Fru*f* donor **5.2** was also synthesized (**Scheme 5.5**). Starting from **5.6**, Fru*f* derivative **5.12**, with a free C-6 hydroxyl group was obtained in 39% yield over four steps. After which, the benzyl group was installed on O-6 to give a 92% yield of **5.2**.



Scheme 5.5. Synthesis of Fru*f* donor **5.2**

Using donor **5.2**, the stereoselectivity of fructofuranosylation was studied with two acceptors (**Scheme 5.6**). The glycosylation was performed under the same conditions as above. Again, I was surprised to find the reactions were either unselective or slightly α selective in both

cases. However, there was a slight improvement in the β-selectivity observed in the case of **5.14** compared to **5.10**.



Scheme 5.6. Stereoselectivity of fructofuranosylation using xylylene-protected Fru*f* donor **5.2**.

5.2.2 Further investigation of stereoselective fructofuranosylation with conformationally-restricted Fru*f* donors 5.15 and 5.16

Due to the unexpected stereoselectivity in the glycosylations with **5.1** and **5.2**, two other conformationally-restricted Fru*f* donors, **5.15** and **5.16**, were synthesized to study their stereoselectivity (**Figure 5.4**). Donors **5.15** and **5.16**, differ from **5.1** and **5.2** in that the conformationally-restricting xylylene group at O-3 and O-4, has been replaced with a silyl acetal or siloxane spanning O-4 and O-6. This allowed me to probe if the poor selectivity arose from the xylylene group.

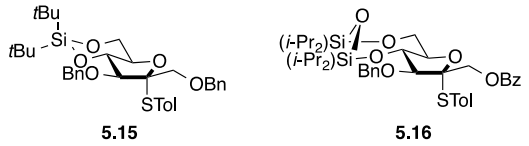
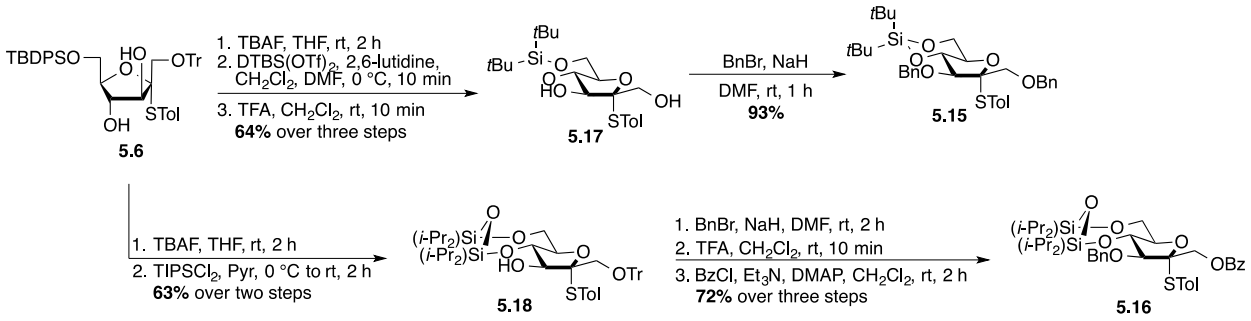


Figure 5.4. Conformationally-restricted Fru*f* donors **5.15** and **5.16**.

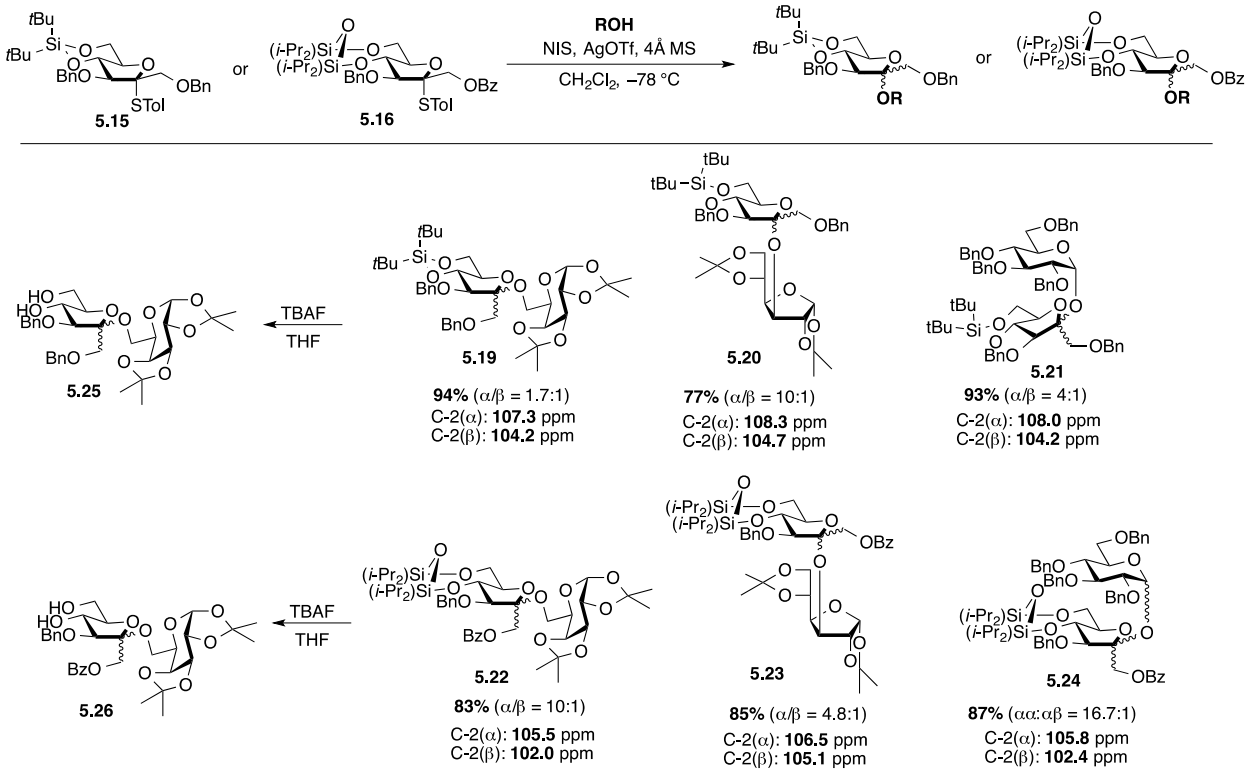
To synthesize **5.15** (**Scheme 5.7**), the TBDPS group of **5.6** was removed in presence of TBAF, followed by the installation of DTBS group and removal of trityl group to give **5.17** in 64% yield over the three steps. Benzylation of **5.17** was executed under standard conditions to provide a 93% yield of **5.15**. Donor **5.16** was also synthesized starting from **5.6** (**Scheme 5.7)**, by TBDPS group removal in the presence of TBAF, followed by installation of the siloxane group at the O-4 and O-6 positions to afford, over the reaction sequence, a 63% yield of **5.18**. The C-3 hydroxyl group of **5.18** was benzylated, the trityl group was removed under acidic conditions and finally the C-1 hydroxyl group was benzoylated under standard conditions to provide a 72% yield of siloxane-protected Fru*f* donor **5.16**.



Scheme 5.7. Synthesis of conformationally-restricted Fru*f* donors **5.15** and **5.16**.

The stereoselectivity of fructofuranosylation with **5.15** and **5.16** was studied with three sugar-based acceptors (**Scheme 5.8**). Unfortunately, the α-glycoside (**5.19**–**5.24**) was obtained as the major product in all six cases. Like the glycosylations discussed above, the anomeric configuration of **5.19**–**5.24** was determined by the chemical shifts of the C-2 resonances in the ^{13}C NMR spectra. To confirm the assignments, in two cases (**5.19** and **5.22**) the DTBS or siloxane group was removed also to give **5.25** and **5.26**. The C-2 of **5.25** was observed at 109.0 ppm for

α-Fru*f* and 104.0 ppm for β-Fru*f*. The C-2 of **5.26** was observed at 108.1 ppm for α-Fru*f* and 102.8 ppm for β-Fru*f*.



Scheme 5.8. Fructofuranosylation using donors **5.15** and **5.16**.

5.2.3 Discussion of the unexpected stereoselectivity results

The results described in **Sections 5.2.1** and **5.2.2** are totally contrary to my original hypothesis that the C-5 hydroxymethyl group in the electrophilic intermediate generated from a conformationally-restricted Fru*f* donor would lead to better β-selectivity in fructofuranosylation compared to the xylulofuranosylation. In contrast, I observed that for all four donors (**5.1**, **5.2**, **5.15** and **5.16**) the glycosylations showed either no selectivity (1:1 α:β) or they were α-selective.

The plausible causes of this undesired stereoselectivity compared to the results seen with arabinofuranosylation and xylulofuranosylation, is discussed below.

A fused bicyclic species such as **5.27** should be an appropriately constrained analogue to exist as a single oxacarbenium ion (**Figure 5.5a**). Nucleophilic attack on the anomeric carbon by the glycosyl acceptor via "inside attack" [11,12] would give the β-furanoside. The oxacarbenium intermediates for the xylylene-protected Ara*f*, Xul*f* and Fru*f* ring systems and Newman projections down the C-1–C-2 bond (Ara*f*) or C-2–C-3 bond (Xul*f* and Fru*f*) are shown in **Figure 5.5b**. As shown in the Newman projections, nucleophilic attack should take place from the top face of the furan ring due to the steric hindrance of H-2 (aldose) or H-3 (ketose), leading to the formation of the *cis*-furanoside.

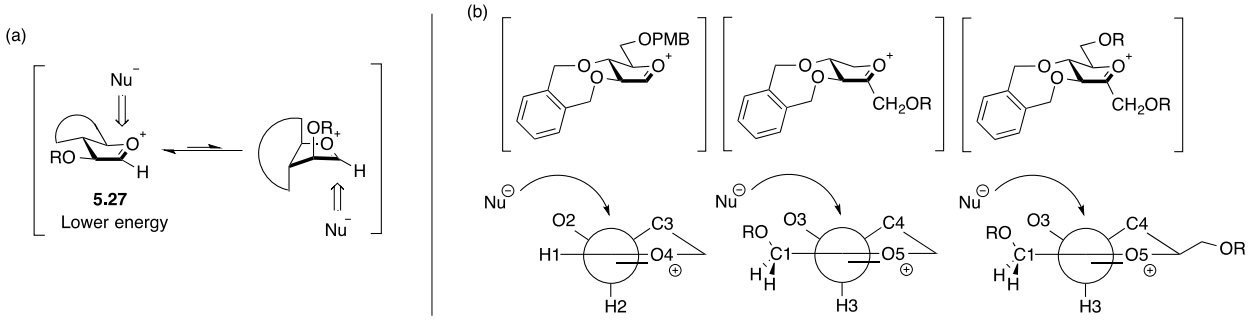


Figure 5.5. (a) Proposed conformational equilibrium in oxacarbenium ion **5.27**; (b) Intermediates and Newman projections of xylylene-protected Ara*f*, Xul*f* and Fru*f* ring systems.

Based on the results described above and in Chapter 3, the CH_2OR group at the anomeric carbon of the Xul*f* and Fru*f* intermediates influences the stereoselectivity. Using the Felkin–Ahn model, the Newman projections of ketofuranoses down the C-1–C-2 bond (shown in **Figure 5.6)** indicate that the O-1 is more preferred to be above the furanose ring because of the repulsion of O-1 and H-3 (**Figure 5.6**). Nucleophilic attack from this conformer would be expected to take

place from the bottom face of furan ring to give the α-ketofuranoside. Thus, the observed decreased β-selectivity in xylulofuranosylation and fructofuranosylation could be explained via the competition between these two phenomena (inside attack and bottom face attack).

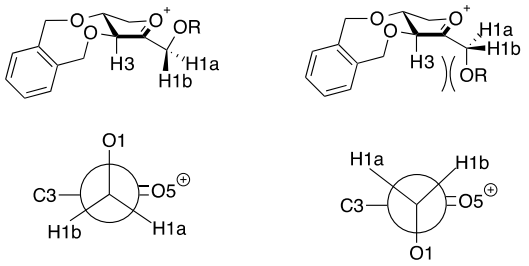


Figure 5.6. (a) Plausible Newman projections down the C-1–C-2 bond and repulsion of O-1 and H-3.

The lesser influence of the $-CH_2OR$ group at C-4 in aldofuranoses was discussed by Woerpel and co-workers[13]. This substituent was shown not to strongly bias the conformational equilibrium, nor is it involved in destabilizing interactions in the transition state for nucleophilic attack. The rotation of the C-4–C-5 bond significantly influences the stability of the aldofuranosyl ring[14]. According to calculations of Ara*f* oxacarbenium ions by Codée and coworkers[15], the ^3E envelope conformation is the most stable, and the most stable of the three C-5–O-5 rotamers is *gg* followed by *gt* and then *tg* (**Figure 5.7a**). The conformation of both the Xul*f* and Fru*f* is restricted to the ^3E envelope conformation via the cyclic protecting group. I hypothesize that, like the C-4 substituent in the Ara*f* ring system, the $-CH_2OR$ at C-5 in the Fru*f* oxacarbenium prefers to adopt the *gg* rotamer (**Figure 5.7b**). In trying to rationalize the differences in selectivity I considered two things. First, the reactions leading to Xul*f* glycosides **3.70**, **3.81** and **3.85** are slightly more β-selective compared to the reactions giving Fru*f* glycosides **5.8**, **5.9** and **5.13** (**Figure 5.7c**). Second, higher α-selectivity is seen in reactions with the DTBS-protected or siloxane-protected Fru*f* donors **5.15** and **5.16** compared to the xylylene-protected Fru*f* donors **5.1**

and **5.2** (**Figure 5.7d**). In xylylene-protected Fru*f* donors **5.1** and **5.2**, the O-6 of *gg* conformer stabilizes the oxacarbenium ion via through-space interactions. On the other hand, in the DTBS-protected or siloxane-protected Fru*f* donors **5.15** and **5.16**, the C-5–C-6 bond necessarily adopts the *gt* conformation (**Figure 5.7e**) and thus such stabilization of the oxacarbenium ion is not possible. As a result, it would be expected that the C-1–O-1 bond plays a greater role in stabilizing the oxacarbenium ion intermediate produced from **5.15** and **5.16**. Using the Felkin–Anh model presented above, this would lead to fixing of the C-1–O-1 bond on the top face of the ring (compard to **5.1** and **5.2**) in turn enhancing α-selectivity.

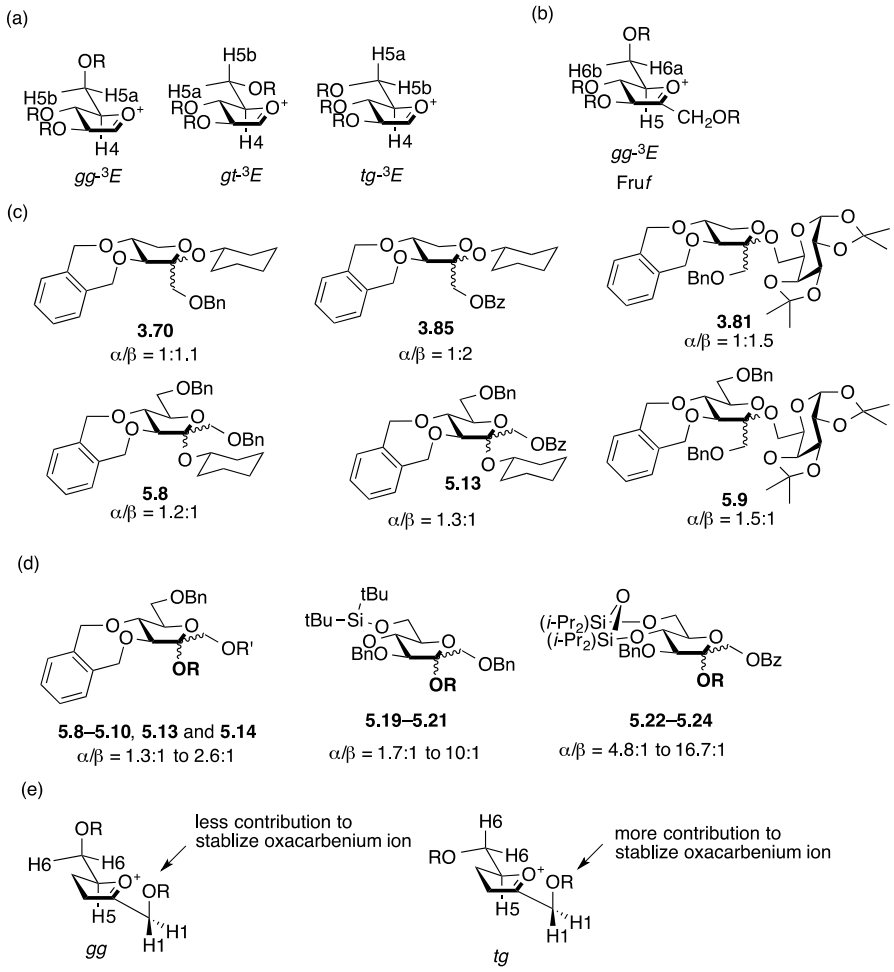


Figure 5.7. (a) The three C-5–O-5 rotamers of Ara*f* oxacarbenium ions; (b) The plausible C-6–O-6 conformer of Fru*f* oxacarbenium ion; (c) Comparison of selectivity in reactions leading to Xul*f* glycosides (**3.70**, **3.81** and **3.85**) and the corresponding Fru*f* glycosides (**5.8**, **5.9** and **5.13**) using xylylene-protected donors; (d) Comparisons of selectivity in fructofuranosylation using three different conformationally-restricted donors; (e) Comparison of the oxacarbenium ions with different conformers at O-6.

To investigate the influence of these hydroxymethyl groups on the glycosylation stereoselectivity, it will be necessary to carry out computational investigations on oxacarbenium ions **5.28**–**5.32** (**Figure 5.8**). Such studies are on-going.

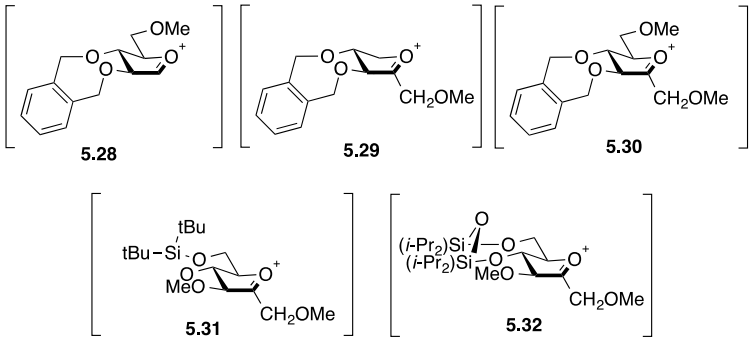


Figure 5.8. Oxacarbenium ions **5.28**–**5.32** for computational studies.

5.3 Conclusion

Xylylene-protected Fru*f* donors **5.1** and **5.2**, DTBS-protected Fru*f* donor **5.15** and siloxane-protected Fru*f* donor **5.16** were prepared to study their stereoselectivity in fructofuranosylation reactions. My original hypothesis was that the $-CH_2OR$ group at C-5 of the Fru*f* donors would further stabilize the ^3E envelope conformation and lead to better β-selectivity compared to the related Xul*f* donors. However, when studied, none of the Fru*f* donors provided the desired β-glycoside with high selectivity. Instead, the reactions were either unselective or α-selective.

These findings are in contrast to the high β-selectivity observed using conformationally-restricted donors in two different aldofuranosides (Ara*f* and Xyl*f*)[5–9]. However, the results in this Chapter and those discussed in Chapter 3 for xylulofuranosylation suggest that the stereoselectivity 'rules' seen in aldofuranoses do not hold for ketofuranosides and that frings substituted with two hydroxylmethyl groups provide a particular challenge in stereoselective glycosylations.

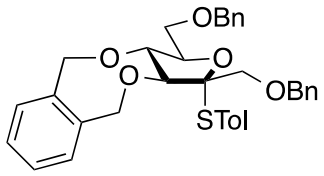
From my results, it could be that rotation about the C-1–O1 bond might be a major factor that influences the stereoselectivity of the reaction. To probe this, computational studies of five intermediates **5.28**–**5.32** are in progress.

5.4 Experimental data

5.4.1 General experimental methods

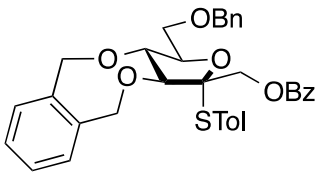
Reactions were carried out in oven-dried glassware. All reagents used were purchased from commercial sources and were used without further purification unless noted. Solvents used in reactions were purified by successive passage through columns of alumina and copper oxide catalyst under nitrogen. Unless stated otherwise, all reactions were carried out at room temperature under a positive pressure of argon and were monitored by TLC on silica gel 60 F_{254} (0.25 mm, E. Merck). Spots were detected under UV light or by charring with 10% H_2SO_4, in EtOH. Unless otherwise indicated, all column chromatography was performed on silica gel 60 (40–60 μm). The ratio between silica gel and crude product ranged from 100 to 50:1 (w/w). Optical rotations were measured at 22 ± 2 °C at the sodium D line (589 nm) and are in units of deg·mL(dm·g)$^{-1}$. ^{1}H NMR spectra were recorded at 500, 600 or 700 MHz, and chemical shifts are referenced to $CHCl_3$ (7.26 ppm, $CDCl_3$). ^{13}C NMR spectra were recorded at 125, 150 or 175 MHz, and ^{13}C chemical shifts were referenced to internal $CDCl_3$ (77.23 ppm, $CDCl_3$). In the processing of reaction mixtures, solutions of organic solvents were washed with equal amounts of aqueous solutions. Organic solutions were concentrated under vacuum at < 40 ºC (bath). Electrospray mass spectra were recorded on samples suspended in mixtures of THF with CH_3OH and added NaCl.

5.4.2 Experimental details for new compounds



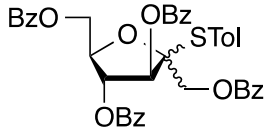
***p*-Tolyl 1,6-di-*O*-benzyl-2-thio-3,4-*O*-xylylene-α-D-fructofuranoside (5.1).** To a solution of **5.7** (23.8 mg, 0.0611 mmol) in DMF (1.0 mL) was added benzyl bromide (23.0 mg, 15.9 μL, 0.135 mmol) and sodium hydride (6.1 mg, 0.153 mmol) at 0 °C. After stirring for 24 h, CH_3OH was added. Dilution of the mixture with EtOAc provided a solution that was washed with water. The organic layer was dried with $MgSO_4$, filtered and the filtrate was concentrated. The residue was purified by column chromatography (15:1, hexane–EtOAc) to give **5.1** (32 mg, 92%) as a colorless oil. $[\alpha]^{25}_D$ +104.1 (*c* 1.0, $CHCl_3$); TLC (9:1, hexane–EtOAc) R_f 0.32; ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.43–7.20 (m, 16H, ArH), 7.06–7.00 (m, 2H, ArH), 4.97 (d, 1H, J_{gem} = 12.6 Hz, ArC*H*$_2$), 4.86 (d, 1H, J_{gem} = 12.6 Hz, ArC*H*$_2$), 4.78 (d, 1H, J_{gem} = 12.6 Hz, ArC*H*$_2$), 4.77 (d, 1H, J_{gem} = 12.6 Hz, ArC*H*$_2$), 4.56 (d, 1H, J_{gem} = 12.2 Hz, ArC*H*$_2$), 4.54 (d, 1H, J_{gem} = 12.2 Hz, ArC*H*$_2$), 4.51 (d, 1H, J_{gem} = 12.2 Hz, ArC*H*$_2$), 4.48 (d, 1H, J_{gem} = 12.2 Hz, ArC*H*$_2$), 4.26 (ddd, 1H, $J_{5,4}$ = 8.4 Hz, $J_{5,6a}$ = 2.8 Hz, $J_{5,6b}$ = 5.9 Hz, H-5), 4.10–4.03 (m, 2H, H-3, H-4), 3.70 (dd, 1H, $J_{6a,5}$ = 2.8 Hz, J_{gem} = 11.1 Hz, H-6a), 3.62 (dd, 1H, $J_{6b,5}$ = 5.9 Hz, J_{gem} = 11.1 Hz, H-6b), 3.58 (d, 1H, J_{gem} = 10.8 Hz, H-1a), 3.53 (d, 1H, J_{gem} = 10.8 Hz, H-1b), 2.33 (s, 3H, ArC*H*$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.7 (Ar), 138.66 (Ar), 138.5 (Ar), 136.4 (2C, Ar), 136.15 (2C, Ar), 136.07 (Ar), 131.6 (Ar), 131.3 (Ar), 129.41 (Ar), 129.37 (Ar), 129.35 (2C, Ar), 128.3 (2C, Ar), 128.1 (2C, Ar), 127.6 (2C, Ar), 127.5 (2C, Ar), 127.4 (Ar), 127.2 (Ar), 96.1 (C-2), 86.8 (C-3), 81.8 (C-4), 78.8 (C-5), 73.3 (Ar*C*H$_2$), 73.1 (Ar*C*H$_2$), 70.6 (C-1), 70.1 (Ar*C*H$_2$), 69.7 (C-6), 69.1

(Ar*C*H$_2$), 21.3 (Ar*C*H$_3$); HRMS (ESI) calcd. for $C_{35}H_{36}NaO_5S$ $[M+Na]^+$ 591.2176 found 591.2178.



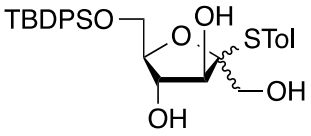
***p*-Tolyl 1-*O*-benzoyl-6-*O*-benzyl-2-thio-3,4-*O*-xylylene-α-D-fructofuranoside (5.2).** To a solution of **5.12** (67.0 mg, 0.140 mmol) in DMF (2.0 mL) was added tetra-*n*-butylammonium bromide (13.5 mg, 0.0420 mmol), benzyl bromide (17.9 μL, 0.154 mmol) and sodium hydride (6.7 mg, 0.168 mmol) at room temperature. After stirring for 30 min, CH_3OH was added. Dilution of the mixture with EtOAc provided a solution that was washed with water. The organic layer was dried over $MgSO_4$ and the mixture was filtered and the filtrate was concentrated. The residue was purified by column chromatography (15:1, hexane–EtOAc) to give **5.2** (75.0 mg, 92%) as a colorless oil. $[\alpha]^{25}_D$ +109.3 (*c* 1.0, $CHCl_3$); TLC (9:1, hexane–EtOAc) R_f 0.29; ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.90–7.86 (m, 2H, ArH), 7.49–7.40 (m, 3H, ArH), 7.37–7.22 (m, 10H, ArH), 7.17–7.13 (m, 1H, ArH), 7.05 (d, 2H, J = 8.1 Hz, ArH), 4.92 (d, 1H, J_{gem} = 12.7 Hz, ArC*H*$_2$), 4.80 (d, 1H, J_{gem} = 12.7 Hz, ArC*H*$_2$), 4.73 (d, 1H, J_{gem} = 12.7 Hz, ArC*H*$_2$), 4.69 (d, 1H, J_{gem} = 12.7 Hz, ArC*H*$_2$), 4.59 (d, 1H, J_{gem} = 11.7 Hz, ArC*H*$_2$), 4.54 (d, 1H, J_{gem} = 12.5 Hz, H-1a), 4.47 (d, 1H, J_{gem} = 12.5 Hz, H-1b), 4.32 (ddd, 1H, $J_{5,4}$ = 8.7 Hz, $J_{5,6a}$ = 2.2 Hz, $J_{5,6b}$ = 5.0 Hz, H-5), 4.28 (d, 1H, J_{gem} = 11.7 Hz, ArC*H*$_2$), 4.14 (d, 1H, $J_{3,4}$ = 6.1 Hz, H-3), 4.08 (dd, 1H, $J_{4,3}$ = 6.1 Hz, $J_{4,5}$ = 8.7 Hz, H-4), 3.76 (dd, 1H, $J_{6a,5}$ = 2.2 Hz, J_{gem} = 11.0 Hz, H-6a), 3.61 (dd, 1H, $J_{6b,5}$ = 5.0 Hz, J_{gem} = 11.0 Hz, H-6b), 2.32 (s, 3H, ArC*H*$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 166.1 (C=O), 139.4 (Ar), 138.5 (Ar), 136.3 (2C, Ar), 136.0 (Ar), 132.7 (Ar), 131.8 (Ar), 131.3 (Ar), 130.6 (Ar), 129.84 (2C, Ar), 129.76 (2C, Ar), 129.71 (2C, Ar), 129.6 (Ar), 128.5 (2C, Ar), 128.3 (2C, Ar),

127.71 (2C, Ar), 127.66 (Ar), 127.2 (Ar), 94.4 (C-2), 88.3 (C-3), 80.8 (C-4), 78.4 (C-5), 73.3 (Ar*C*H_2), 70.0 (Ar*C*H_2), 69.0 (Ar*C*H_2), 68.5 (C-6), 65.0 (C-1), 21.4 (Ar*C*H_3); HRMS (ESI) calcd. for $C_{35}H_{34}NaO_6S$ $[M+Na]^+$ 605.1968 found 605.1969.



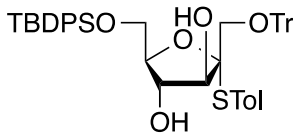
***p*-Tolyl 1,3,4,6-tetra-*O*-benzoyl-2-thio-α/β-D-fructofuranoside (5.4).** To a solution of the **5.3**[10] (634 mg, 1.00 mmol) and thiocresol (149 mg, 1.20 mmol) in CH_2Cl_2 (10.0 mL) was added boron trifluoride diethyl etherate (161 μL, 185 mg, 1.30 mmol) at 0 °C. After stirring for 30 min, the reaction mixture was added satd. aq. $NaHCO_3$ and then diluted with EtOAc. The organic layer was then washed with brine and water. The organic layers were dried over $MgSO_4$ and then filtered. The filtrate was concentrated and the resulting residue was purified by column chromatography (4:1, hexane–EtOAc) to give an α/β mixture of **5.4** (634 mg, 90%, α:β = 3:1) as a colorless oil. TLC (4:1, hexane–EtOAc) R_f 0.26; **5.4α**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 8.16–8.12 (m, 2H, ArH), 8.04–8.00 (m, 2H, ArH), 7.97–7.94 (m, 2H, ArH), 7.90–7.86 (m, 2H, ArH), 7.64–7.24 (m, 14H, ArH), 7.11 (d, 2H, J = 7.4 Hz, ArH), 6.02 (d, 1H, $J_{3,4}$ = 2.9 Hz, H-3), 5.74 (dd, 1H, $J_{4,3}$ = 2.9 Hz, $J_{4,5}$ = 6.7 Hz, 1H, H-4), 5.01 (ddd, 1H, $J_{5,4}$ = 6.7 Hz, $J_{5,6a}$ = 3.4 Hz, $J_{5,6b}$ = 5.6 Hz, H-5), 4.86 (dd, 1H, $J_{6a,5}$ = 3.4 Hz, J_{gem} = 12.1 Hz, H-6a), 4.73 (dd, 1H, $J_{6b,5}$ = 5.6 Hz, J_{gem} = 12.1 Hz, H-6b), 4.50–4.47 (m, 2H, H-1), 2.33 (s, 3H, ArC*H*$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 166.2 (C=O), 165.82 (C=O), 165.77 (C=O), 165.1 (C=O), 140.05 (Ar), 136.7 (Ar), 133.82 (Ar), 133.6 (Ar), 133.3 (Ar), 130.5–128.4 (Ar), 125.5 (Ar), 95.1 (C-2), 82.1 (C-3), 79.6 (C-5), 78.8 (C-4), 63.6 (C-6), 63.2 (C-1), 21.5 (Ar*C*H_3); **5.4β**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 8.18–8.15 (m, 4H, ArH), 8.07–8.02 (m, 4H, ArH), 7.65–7.23 (m, 14H, ArH), 7.08 (d, 2H, J = 7.3 Hz, ArH), 6.39 (d,

1H, $J_{3,4}$ = 6.1 Hz, H-3), 6.14 (app t, 1H, $J_{4,3} = J_{4,5}$ = 6.1 Hz, H-4), 4.94 (m, 2H, H-6), 4.74–4.70 (m, 1H, H-5), 4.57–4.45 (m, 2H, H-1), 2.31 (s, 3H, ArC*H*$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 166.4 (C=O), 165.82 (C=O), 165.77 (C=O), 165.3 (C=O), 139.8 (Ar), 136.7 (Ar), 133.9 (Ar), 133.8 (Ar), 133.3 (Ar), 133.27 (Ar), 130.5–128.5 (Ar), 125.1 (Ar), 94.9 (C-2), 80.4 (C-5), 78.4 (C-3), 78.1 (C-4), 66.1 (C-1), 64.7 (C-6), 21.4 (Ar*C*H$_3$); HRMS (ESI) calcd. for $C_{41}H_{34}NaO_9S$ $[M+H]^+$ 725.1816 found 725.1811.

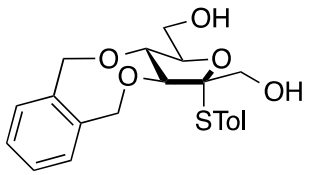


***p*-Tolyl 6-*O*-*tert*-butyldiphenylsilyl-2-thio-α/β-D-fructofuranoside (5.5).** To a solution of **5.4** (634 mg, 0.9 mmol) in a mixture of CH_3OH–CH_2Cl_2 (10.0 mL, 9:1) was added catalytic amount of $NaOCH_3$ (3.6 mg, 0.09 mmol) at room temperature. After stirring for 24 h, the solution was neutralized by addition of Amberlite IR-120 H^+ resin. The mixture was filtered, the filtrate was concentrated, and the resulting residue was dried *in vacuo* overnight. To a solution of the residue in pyridine (10.0 mL) was added TBDPSCl (229 μL, 242 mg, 0.880 mmol) at –20 °C. The reaction was warmed to room temperature and stirred overnight. After stirring for 24 h, excess TBDPSCl was quenched by the addition of CH_3OH. The mixture was then diluted with CH_2Cl_2 and washed with 1N HCl, satd. aq. $NaHCO_3$, water and brine. The organic layer was then dried over $MgSO_4$ and filtered. The filtrate was concentrated and the resulting residue was purified by column chromatography (2:1, hexane–EtOAc) to give **5.5α** (76.9 mg, 20%) as a colorless oil and **5.5β** (231 mg, 60%) as a colorless oil. Data for **5.5α**: $[\alpha]^{25}_D$ +123.0 (*c* 1.0, $CHCl_3$); TLC (1:1, hexane–EtOAc) R_f 0.29; ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.69–7.63 (m, 4H, ArH), 7.48–7.34 (m, 8H, ArH), 7.12 (d, 2H, *J* = 8.1 Hz, ArH), 4.23 (ddd, 1H, $J_{4,3}$ = 3.7 Hz, $J_{4,5}$ = 5.8 Hz, $J_{4,OH}$ = 7.7

Hz, H-4), 4.18 (dt, 1H, $J_{5,4}$ = 5.8 Hz, $J_{5,6a}$ = $J_{5,6b}$ = 3.2 Hz, H-5), 4.15 (dd, 1H, $J_{3,4}$ = 3.7 Hz, $J_{3,OH}$ = 9.0 Hz, H-3), 3.92 (dd, 1H, $J_{6a,5}$ = 3.2 Hz, J_{gem} = 11.4 Hz, H-6a), 3.81 (dd, 1H, $J_{6b,5}$ = 3.2 Hz, J_{gem} = 11.4 Hz, H-6b), 3.72 (dd, 1H, J_{gem} = 12.1 Hz, $J_{1a,OH}$ = 7.8 Hz, H-1a), 3.69 (dd, 1H, J_{gem} = 12.1 Hz, $J_{1b,OH}$ = 6.1 Hz, H-1b), 3.61 (d, 1H, $J_{OH,3}$ = 9.0 Hz, 3-OH), 2.69 (d, 1H, $J_{OH,4}$ = 7.7 Hz, 4-OH), 2.40 (dd, 1H, $J_{OH,1a}$ = 7.8 Hz, $J_{OH,1b}$ = 6.1 Hz, 1-OH), 2.35 (s, 3H, ArCH_3), 1.06 (s, 9H, SiC(CH_3)$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 139.4 (Ar), 136.1 (2C, Ar), 135.7 (2C, Ar), 135.6 (2C, Ar), 132.6 (Ar), 132.5 (Ar), 130.1 (Ar), 130.0 (Ar), 129.7 (2C, Ar), 127.90 (2C, Ar), 127.88 (2C, Ar), 126.1 (Ar), 96.7 (C-2), 83.9 (C-3), 83.1 (C-5), 79.0 (C-4), 63.6 (C-1), 63.5 (C-6), 26.8 (SiC(CH$_3$)$_3$), 21.3 (ArCH$_3$), 19.3 (SiC(CH$_3$)$_3$); HRMS (ESI) calcd. for $C_{29}H_{36}NaO_5SSi$ $[M+Na]^+$ 547.1945 found 547.1941. Data for **5.5β**: $[\alpha]^{25}_D$ –112.6 (*c* 1.0, $CHCl_3$); TLC (1:1, hexane–EtOAc) R_f 0.14; ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.78–7.74 (m, 2H, ArH), 7.73–7.70 (m, 2H, ArH), 7.47 (d, 2H, *J* = 8.3 Hz, ArH), 7.44–7.34 (m, 6H, ArH), 7.04 (d, 2H, *J* = 8.3 Hz, ArH), 4.52–4.44 (m, 2H, H-3, H-4), 4.30 (br s, 1H, OH), 4.07–4.01 (m, 1H, H-5), 3.95 (dd, 1H, $J_{6a,5}$ = 4.4 Hz, J_{gem} = 11.0 Hz, H-6a), 3.91 (dd, 1H, $J_{6b,5}$ = 4.8 Hz, J_{gem} = 11.0 Hz, H-6b), 3.61 (d, 1H, J_{gem} = 12.1 Hz, H-1a), 3.56 (br s, 1H, OH), 3.53 (d, 1H, J_{gem} = 12.1 Hz, H-1b), 2.75 (br s, 1H, 1-OH), 2.31 (s, 3H, ArCH_3), 1.10 (s, 9H, SiC(CH_3)$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.7 (Ar), 136.2 (2C, Ar), 135.68 (2C, Ar), 135.67 (2C, Ar), 132.91 (Ar), 132.84 (Ar), 129.93 (Ar), 129.89 (Ar), 129.5 (2C, Ar), 127.88 (2C, Ar), 127.86 (2C, Ar), 126.3 (Ar), 97.4 (C-2), 83.9 (C-5), 79.7 (C-3), 77.6 (C-4), 64.9 (C-1), 64.8 (C-6), 26.9 (SiC(CH$_3$)$_3$), 21.2 (ArCH$_3$), 19.3 (SiC(CH$_3$)$_3$); HRMS (ESI) calcd. for $C_{29}H_{36}NaO_5SSi$ $[M+Na]^+$ 547.1945 found 547.1946.

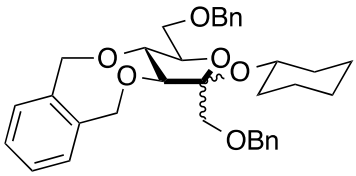


***p*-Tolyl 6-*O*-*tert*-butyldiphenylsilyl-1-*O*-trityl-2-thio-α-D-fructofuranoside (5.6).** To a solution of **5.5α** (210 mg, 0.400 mmol) in CH_2Cl_2 (4.0 mL) was added pyridine (64.4 μL, 0.800 mmol), TrCl (134 mg, 0.480 mmol) and DMAP (4.9 mg, 0.0400 mmol) at room temperature. After stirring for 24 h, CH_3OH was added. The mixture was then diluted with EtOAc and washed with 1N HCl, satd. aq. $NaHCO_3$, water and brine. The organic layer was then dried over $MgSO_4$ and then filtered. The filtrate was concentrated and the resulting residue was purified by column chromatography (4:1, hexane–EtOAc) to give **5.6** (137 mg, 45%) as a colorless foam. $[\alpha]^{25}_D$ +60.9 (*c* 1.0, $CHCl_3$); TLC (4:1, hexane–EtOAc) R_f0.20; ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.67–7.60 (m, 4H, ArH), 7.49-7.39 (m, 8H, ArH), 7.37–7.29 (m, 4H, ArH), 7.28–7.21 (m, 9H, ArH), 7.12–7.08 (m, 2H, ArH), 6.96–6.91 (m, 2H, ArH), 4.27–4.21 (m, 3H, H-3, H-4, H-5), 3.85–3.74 (m, 3H, H-6a, 3-OH, 4-OH), 3.49 (d, 1H, J_{gem} = 9.5 Hz, H-1a), 3.34–3.28 (m, 2H, H-1b, H-6b), 2.30 (s, 3H, ArC*H*$_3$), 1.03 (s, 9H, SiC(C*H*$_3$)$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 143.3 (Ar), 138.8 (Ar), 135.64 (Ar), 135.60 (Ar), 132.46 (Ar), 132.34 (Ar), 129.96 (Ar), 129.88 (Ar), 129.4 (Ar), 128.8 (Ar), 127.85 (Ar), 127.79 (Ar), 127.0 (Ar), 126.3 (Ar), 98.1 (C-2), 87.3 (*C*Ph$_3$), 85.7 (C-3), 82.7 (C-5), 80.0 (C-4), 64.3 (C-6), 63.5 (C-1), 26.8 (SiC(*C*H$_3$)$_3$) 21.3 (Ar*C*H$_3$), 19.3 (Si*C*(CH$_3$)$_3$); HRMS (ESI) calcd. for $C_{48}H_{50}NaO_5SSi$ $[M+Na]^+$ 789.3040 found 789.3035.



***p*-Tolyl 3,4-*O*-xylylene-2-thio-α-D-fructofuranoside (5.7).** To a solution of **5.6** (400 mg, 0.521 mmol) in DMF (5.2 mL) was added NaH (52.1 mg, 1.30 mol) and α,α'-dibromo-*o*-xylylene (151 mg, 0.574 mmol) at 0 ºC. After stirring at 0 °C for 2 h, CH_3OH was added. The mixture was diluted with EtOAc and washed with H_2O. The organic layer was dried over $MgSO_4$, and the mixture was filtered. The filtrate was concentrated and the resulting residue was dried *in vacuo* overnight. To a solution of the residue in CH_2Cl_2 was added TFA (59 μL, 0.780 mmol) at room temperature. After stirring for 20 min, the reaction was neutralized by the addition of satd. aq. $NaHCO_3$. Dilution of the mixture with CH_2Cl_2 provided a solution that was washed with water and brine. The organic layer was dried over $MgSO_4$, filtered and the filtrate was concentrated. The residue was dried *in vacuo* overnight. To a solution of the residue in THF (5.2 mL) was added 1M tetra-*n*-butylammonium fluoride (0.780 mL, 0.780 mmol) at room temperature. After stirring for 24 h, the reaction mixture was concentrated and the residue was purified by column chromatography (2:1, hexane–EtOAc) to give **5.7** (101 mg, 50% over three steps) as a colorless oil. $[\alpha]^{25}_D$ +197.9 (*c* 1.0, $CHCl_3$); TLC (2:1, hexane–EtOAc) R_f 0.17; ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.44–7.40 (m, 2H, ArH), 7.37–7.30 (m, 4H, ArH), 7.08–7.04 (m, 2H, ArH), 5.03 (d, 1H, J_{gem} = 12.5 Hz, ArCH_2), 4.84 (d, 1H, J_{gem} = 12.5 Hz, ArCH_2), 4.80 (d, 1H, J_{gem} = 12.5 Hz, ArCH_2), 4.77 (d, 1H, J_{gem} = 12.5 Hz, ArCH_2), 4.24–4.16 (m, 2H, H-4, H-5), 4.09 (d, 1H, $J_{3,4}$ = 5.1 Hz, H-3), 3.92 (dd, 1H, $J_{6a,5}$ = 2.6 Hz, J_{gem} = 12.5 Hz, H-6a), 3.76 (d, 1H, J_{gem} = 12.0 Hz, H-1a), 3.70 (dd, 1H, $J_{6b,5}$ = 2.9 Hz, J_{gem} = 12.5 Hz, H-6b), 3.51 (d, 1H, J_{gem} = 12.0 Hz, H-1b), 2.32 (s, 3H, ArCH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_H 139.2 (Ar), 136.5 (Ar), 136.2 (2C, Ar), 134.6 (Ar),

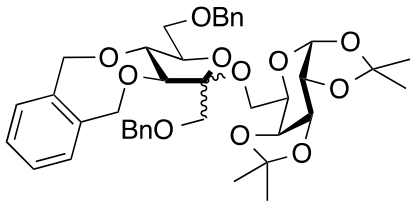
131.8 (Ar), 131.6 (Ar), 130.1 (Ar), 129.8 (Ar), 129.5 (2C, Ar), 126.9 (Ar), 95.9 (C-2), 88.3 (C-3), 81.4 (C-4), 79.6 (C-5), 70.2 (Ar*C*H_2), 68.6 (Ar*C*H_2), 65.0 (C-6), 61.0 (C-1), 21.3 (Ar*C*H_3); HRMS (ESI) calcd. for $C_{21}H_{24}NaO_5S$ $[M+Na]^+$ 411.1237 found 411.1238.



Cyclohexyl 1,6-di-*O*-benzyl-3,4-*O*-xylylene-α-D-fructofuranoside (5.8α) and **Cyclohexyl 1,6-di-*O*-benzyl-3,4-*O*-xylylene-β-D-fructofuranoside (5.8β).** A mixture of **5.1** (16.1 mg, 0.0283 mmol), cyclohexanol (3.4 mg, 0.0340 mmol) and 4Å molecular sieves in CH_2Cl_2 (1.1 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –78 °C before *N*-iodosuccinimide (7.6 mg, 0.0340 mmol) and silver triflate (1.5 mg, 5.7 μmol) were added. The reaction mixture was slowly warmed to –60 °C. After stirring at –60 °C for 2 h, triethylamine was added to the reaction mixture. The reaction was warmed to room temperature and then a small amount of H_2O was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The mixture was dried over $MgSO_4$ and then filtered and the filtrate was concentrated. The resulting residue was purified by column chromatography (10:1 to 5:1, hexane–EtOAc) to give **5.8α** (8.0 mg, 52%) as a colorless oil and **5.8β** (7.0 mg, 45%) as a colorless oil. Data for **5.8α**: $[\alpha]^{25}_D$ +58.7 (*c* 0.6, $CHCl_3$); TLC (5:1, hexane–EtOAc) R_f 0.38; ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.40–7.33 (m, 3H, ArH), 7.32–7.21 (m, 11H, ArH), 4.91 (d, 1H, J_{gem} = 12.7 Hz, Ar*C*H_2), 4.88 (d, 1H, J_{gem} = 12.7 Hz, Ar*C*H_2), 4.78 (d, 1H, J_{gem} = 12.7 Hz, Ar*C*H_2), 4.72 (d, 1H, J_{gem} = 12.7 Hz, Ar*C*H_2), 4.50 (d, 1H, J_{gem} = 12.0 Hz, Ar*C*H_2), 4.54–4.47 (m, 3H, ArC*H*$_2$), 4.13 (ddd, 1H, $J_{5,4}$ = 8.8 Hz, $J_{5,6a}$ = 2.6 Hz, $J_{5,6b}$ = 6.0 Hz, H-5), 4.11 (d, 1H, $J_{3,4}$ = 5.5 Hz, 1H, H-3), 3.85 (dd, 1H, $J_{4,3}$ = 5.5 Hz, $J_{4,5}$ = 8.8 Hz, H-4), 3.73–3.65 (m, 1H, cyclohexyl OC*H*), 3.61 (d, 1H,

J_{gem} = 10.5 Hz, H-1a), 3.60 (dd, 1H, $J_{6a,5}$ = 2.6 Hz, J_{gem} = 11.2 Hz, H-6a), 3.53 (dd, 1H, $J_{6b,5}$ = 6.0 Hz, J_{gem} = 11.2 Hz, 1H, H-6b), 3.51 (d, 1H, J_{gem} = 10.5 Hz, H-1b), 1.89–1.76 (m, 2H, cyclohexyl CH_2), 1.73–1.62 (m, 2H, cyclohexyl CH_2), 1.52–1.44 (m, 1H, cyclohexyl CH_2), 1.35–1.07 (m, 5H, cyclohexyl CH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.8 (Ar), 138.6 (Ar), 136.9 (Ar), 136.3 (Ar), 131.9 (Ar), 131.5 (Ar), 129.64 (Ar), 129.57 (Ar), 128.5 (2C, Ar), 128.3 (2C, Ar), 128.0 (2C, Ar), 127.7 (2C, Ar), 127.6 (Ar), 127.5 (Ar), 108.5 (C-2), 88.3 (C-3), 82.1 (C-4), 78.5 (C-5), 73.5 (ArCH$_2$), 73.3 (cyclohexyl OCH), 71.2 (C-6), 70.1 (ArCH$_2$), 70.0 (ArCH$_2$), 69.3 (ArCH$_2$), 68.8 (C-1), 35.2 (cyclohexyl CH$_2$), 34.4 (cyclohexyl CH$_2$), 25.8 (cyclohexyl CH$_2$), 25.0 (cyclohexyl CH$_2$), 24.9 (cyclohexyl CH$_2$); HRMS (ESI) calcd. for $C_{34}H_{40}NaO_6$ $[M+Na]^+$ 567.2717 found 567.2709. Data for **5.8β**: $[\alpha]^{25}_D$ +0.6 (*c* 0.7, $CHCl_3$); TLC (5:1, hexane–EtOAc) R_f 0.31; ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.38–7.25 (m, 12H, ArH), 7.23–7.19 (m, 2H, ArH), 5.07 (d, 1H, J_{gem} = 13.5 Hz, ArCH_2), 4.93 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.81 (d, 1H, J_{gem} = 13.5 Hz, ArCH_2), 4.80 (d, 1H, J_{gem} = 12.7 Hz, ArCH_2), 4.60–4.54 (m, 3H, ArCH_2), 4.46 (d, 1H, J_{gem} = 12.3 Hz, ArCH_2), 4.27 (d, 1H, $J_{3,4}$ = 7.6 Hz H-3), 4.14 (app t, $J_{4,3}$ = $J_{4,5}$ = 7.6 Hz, H-4), 3.96 (ddd, $J_{5,4}$ = 7.6 Hz, $J_{5,6a}$ = 3.4 Hz, $J_{5,6b}$ = 6.6 Hz, 1H, H-5), 3.66–3.53 (m, 4H, H-1a, H-6a, H-6b, cyclohexyl OCH), 3.45(d, 1H, J_{gem} = 10.1 Hz, H-1b) 1.90–1.81 (m, 1H, cyclohexyl CH_2), 1.80–1.73 (m, 3H, cyclohexyl CH_2), 1.69–1.60 (m, 1H, cyclohexyl CH_2), 1.50–1.43 (m, 1H, cylcohexyl CH_2), 1.35–1.06 (m, 5H, cyclohexyl CH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.41 (Ar), 138.39 (Ar), 136.9 (Ar), 136.8 (Ar), 132.0 (Ar), 130.7 (Ar), 129.2 (Ar), 129.1 (Ar), 128.52 (2C, Ar), 128.49 (2C, Ar), 127.9 (2C, Ar), 127.8 (2C, Ar), 127.74 (Ar), 127.69 (Ar), 105.9 (C-2), 82.2 (C-3), 81.9 (C-4), 78.8 (C-5), 73.52 (ArCH$_2$), 73.47 (ArCH$_2$), 71.9 (cyclohexyl OCH), 71.8 (C-1), 71.5 (C-6), 70.5 (ArCH$_2$), 70.0 (ArCH$_2$), 35.4 (cyclohexyl CH$_2$), 34.2 (cyclohexyl CH$_2$), 25.7

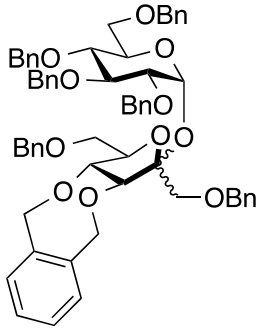
(cyclohexyl *C*H_2), 25.2 (cyclohexyl *C*H_2), 25.0 (cyclohexyl *C*H_2); HRMS (ESI) calcd. for $C_{34}H_{40}NaO_6$ $[M+Na]^+$ 567.2717 found 567.2712.



1,6-Di-*O*-benzyl-3,4-*O*-xylylene-α-D-fructofuranosyl-(2→6)-1,2,4,5-di-*O*-isopropylidene-α-D-galactopyranose (5.9α) and **1,6-di-*O*-benzyl-3,4-*O*-xylylene-β-D-fructofuranosyl-(2→6)-1,2,4,5-di-*O*-isopropylidene-α-D-galactopyranose (5.9β).** A mixture of **5.1** (22.4 mg, 0.0394 mmol), **3.73** (12.3 mg, 0.0473 mmol) and 4Å molecular sieves in CH_2Cl_2 (1.58 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –78 °C before *N*-iodosuccinimide (10.6 mg, 0.0473 mmol) and silver triflate (2.0 mg, 7.9 μmol) were added. After stirring at –78 °C for 1 h, triethylamine was added to the reaction mixture. The reaction was warmed to room temperature and then a small amount of H_2O was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The mixture was dried over $MgSO_4$ and then filtered and the filtrate was concentrated. The resulting residue was purified by column chromatography (4:1 to 2:1, hexane–EtOAc) to give **5.9α** (14.2 mg, 51%) as a colorless oil and **5.9β** (9.4 mg, 34%) as a colorless oil. Data for **5.9α**: $[\alpha]^{25}_D$ +11.5 (*c* 0.9, $CHCl_3$); TLC (2:1, hexane–EtOAc) R_f 0.42; ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.40–7.22 (m, 14H, ArH), 5.48 (d, 1H, $J_{1,2}$ = 5.0 Hz, H-1_{Gal}), 4.89 (d, 1H, J_{gem} = 12.6 Hz, ArCH_2), 4.88 (d, 1H, J_{gem} = 12.6 Hz, ArCH_2), 4.75 (d, 1H, J_{gem} = 12.6 Hz, ArCH_2), 4.73 (d, 1H, J_{gem} = 12.6 Hz, ArCH_2), 4.59–4.46 (m, 5H, H-3_{Gal}, ArCH_2), 4.25 (dd, 1H, $J_{2,1}$ = 5.0 Hz, $J_{2,3}$ = 2.4 Hz, H-2_{Gal}), 4.21 (dd, 1H, $J_{4,3}$ = 1.7, $J_{4,5}$ = 7.9 Hz, H-4_{Gal}), 4.18 (d, 1H, $J_{3,4}$= 5.4 Hz, H-3_{Fru}), 4.12 (ddd, 1H, $J_{5,4}$ = 8.1 Hz, $J_{5,6a}$ = 2.5 Hz, $J_{5,6b}$ =

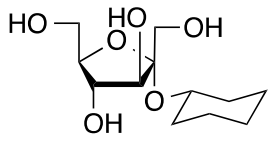
5.4 Hz, H-5_{Fru}), 3.93–3.87 (m, 2H, H-5_{Gal}, H-4_{Fru}) 3.77 (dd, 1H, $J_{6a,5}$ = 6.2 Hz, J_{gem} = 10.1 Hz, H-$6a_{Gal}$), 3.72 (dd, 1H, $J_{6b,5}$ = 6.4 Hz, J_{gem} = 10.1 Hz, H-$6b_{Gal}$), 3.64–3.51 (m, 4H, H-$1a_{Fru}$, H-$1b_{Fru}$, H-$6a_{Fru}$, H-$6b_{Fru}$), 1.48 (s, 3H, C(CH_3)$_2$), 1.39 (s, 3H, C(CH_3)$_2$), 1.30 (s, 3H, C(CH_3)$_2$), 1.29 (s, 3H, C(CH_3)$_2$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.9 (Ar), 138.6 (Ar), 136.7 (Ar), 136.3 (Ar), 131.9 (Ar), 131.6 (Ar), 129. 7 (Ar), 129.6 (Ar), 128.4 (2C, Ar), 128.3 (2C, Ar), 127.9 (2C, Ar), 127.8 (2C, Ar), 127.6 (Ar), 127.5 (Ar), 109.3 (*C*$(CH_3)_2$), 108.7 (*C*$(CH_3)_2$), 108.0 (C-2_{Fru}), 96.5 (C-1_{Gal}), 87.4 (C-3_{Fru}), 82.0 (C-4_{Fru}), 78.7 (C-5_{Fru}), 73.6 (Ar*C*H_2), 73.3 (Ar*C*H_2), 71.3 (C-4_{Gal}), 70.9 (C-2_{Gal}), 70.8 (C-3_{Gal}), 70.0 (Ar*C*H_2), 69.5 (Ar*C*H_2), 69.1 (C-1_{Fru} or C-6_{Fru}), 68.7 (C-1_{Fru} or C-6_{Fru}), 67.5 (C-5_{Gal}), 61.1 (C-6_{Gal}), 26.3 (C(*C*H_3)$_2$), 26.2 (C(*C*H_3)$_2$), 25.2 (C(*C*H_3)$_2$), 24.7 (C(*C*H_3)$_2$); HRMS (ESI) calcd. for $C_{40}H_{48}NaO_{11}$ $[M+Na]^+$ 727.3089 found 727.3086. Data for **5.9β**: $[\alpha]^{25}_D$ –26.5 (*c* 0.4, $CHCl_3$); TLC (2:1, hexane–EtOAc) R_f 0.25; ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.38–7.33 (m, 2H, ArH), 7.32–7.25 (m, 10H, ArH), 7.23–7.20 (m, 2H, ArH), 5.49 (d, 1H, $J_{1,2}$ = 5.1 Hz, H-1_{Gal}), 5.02 (d, 1H, J_{gem} = 13.2 Hz, ArCH_2), 4.85–4.78 (m, 3H, ArCH_2), 4.61–4.54 (m, 3H, ArCH_2), 4.52 (dd, 1H, $J_{3,2}$ = 2.3 Hz, $J_{3,4}$ = 8.0 Hz, H-3_{Gal}), 4.50 (d, 1H, J_{gem} = 13.2 Hz, ArCH_2), 4.28 (d, 1H, $J_{3,4}$ = 7.3 Hz, H-3_{Fru}), 4.25 (dd, 1H, $J_{2,1}$ = 5.1 Hz, $J_{3,2}$ = 2.3 Hz, H-2_{Gal}), 4.18 (dd, 1H, $J_{4,3}$ = 8.0 Hz, $J_{4,5}$ = 1.7 Hz, H-4_{Gal}), 4.14 (app t, 1H, $J_{4,3}$ = $J_{4,5}$ = 7.3 Hz, H-4_{Fru}), 4.03 (ddd, 1H, $J_{5,4}$ = 7.3 Hz, $J_{5,6a}$ = 4.0 Hz, $J_{5,6b}$ = 6.5 Hz, H-5_{Fru}), 3.94–3.90 (m, 1H, H-5_{Gal}), 3.76 (dd, 1H, $J_{6a,5}$ = 7.3 Hz, J_{gem} = 10.1 Hz, H-$6a_{Gal}$), 3.70–3.61 (m, 3H, H-$6b_{Gal}$, H-$6a_{Fru}$, H-$6b_{Fru}$), 3.56 (d, 1H, J_{gem} = 10.4 Hz, H-$1a_{Fru}$), 3.50 (d, 1H, J_{gem} = 10.4 Hz, H-$1b_{Fru}$), 1.50 (s, 3H, C(CH_3)$_2$), 1.40 (s, 3H, C(CH_3)$_2$), 1.31 (s, 3H, C(CH_3)$_2$), 1.29 (s, 3H, C(CH_3)$_2$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.6 (Ar), 138.4 (Ar), 136.9 (Ar), 136.7 (Ar), 131.6 (Ar), 131.3 (Ar), 129.3 (Ar), 129.2 (Ar), 128.53 (2C, Ar), 128.50 (2C, Ar), 127.9 (2C, Ar), 127.8 (2C, Ar), 127.7 (Ar), 127.6 (Ar), 109.1 (*C*$(CH_3)_2$), 108.6 (*C*$(CH_3)_2$), 105.7 (C-2_{Fru}), 96.4 (C-1_{Gal}), 82.3 (C-3_{Fru}), 82.1 (C-4_{Fru}),

79.7 (C-5_{Fru}), 73.6 (Ar*C*H_2), 73.3 (Ar*C*H_2), 71.5 (C-6_{Fru}), 71.1 (C-2_{Gal}), 71.0 (C-3_{Gal}), 70.8 (C-4_{Gal}), 70.5 (C-1_{Fru}), 70.1 (Ar*C*H_2), 69.9 (Ar*C*H_2), 67.1 (C-5_{Gal}), 61.2 (C-6_{Gal}), 26.4 (C(*C*H_3)$_2$), 26.3 (C(*C*H_3)$_2$), 25.2 (C(*C*H_3)$_2$), 24.7 (C(*C*H_3)$_2$); HRMS (ESI) calcd. for $C_{40}H_{48}NaO_{11}$ $[M+Na]^+$ 727.3089 found 727.3087.

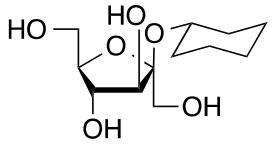


1,6-Di-*O*-benzyl-3,4-*O*-xylylene-α-D-fructofuranosyl-(2→1)-2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside (5.10α) and **1,6-di-*O*-benzyl-3,4-*O*-xylylene-β-D-fructofuranosyl-(2→1)-2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside (5.10β).** A mixture of **5.1** (21.5 mg, 0.0378 mmol), 2,3,4,6-tetra-*O*-benzyl glucopyranose (24.5 mg, 0.0454 mmol) and 4Å molecular sieves in CH_2Cl_2 (1.5 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –78 °C before *N*-iodosuccinimide (10.5 mg, 0.0454 mmol) and silver triflate (2.0 mg, 7.6 μmol) were added. After stirring –78 °C for 30 min, triethylamine was added to the reaction mixture. The reaction was warmed to room temperature and then a small amount of H_2O was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The mixture was dried over $MgSO_4$ and then filtered and the filtrate was concentrated. The resulting residue was purified by column chromatography (6:1, hexane–EtOAc) to give an α/β mixture of **5.10** (35.7 mg, 96%, α/β = 2.6:1) as a colorless oil. TLC (4:1, hexane–EtOAc) R_f 0.47; Data for **5.10α**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.46–7.07 (m, 34H, ArH), 5.51 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-1_{Glc}),

4.98 (d, 1H, J_{gem} = 11.6 Hz, ArCH_2), 4.94–4.36 (m, 15H, ArCH_2), 4.33 (ddd, 1H, $J_{5,4}$ = 8.6 Hz, $J_{5,6a}$ = 2.4 Hz, $J_{5,6b}$ = 5.9 Hz, H-5_{Fru}), 4.26 (d, 1H, $J_{3,4}$ = 5.7 Hz, H-3_{Fru}), 4.07–3.93 (m, 3H, H-3_{Glc}, H-5_{Glc}, H-4_{Fru}), 3.76–3.43 (m, 8H, H-2_{Glc}, H-4_{Glc}, H-$6a_{Glc}$, H-$6b_{Glc}$, H-$1a_{Fru}$, H-$1b_{Fru}$, H-$6a_{Fru}$, H-$6b_{Fru}$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 139.3 (Ar), 139.2 (Ar), 138.58 (Ar), 138.55 (Ar), 138.50 (Ar), 138.2 (Ar), 136.8 (Ar), 136.3 (Ar), 132.0 (Ar), 131.5 (Ar), 129.8 (Ar), 129.6 (Ar), 128.6–127.2 (Ar), 108.6 (C-2_{Fru}), 90.3 (C-1_{Glc}), 88.6 (C-3_{Fru}), 81.9 (C-3_{Glc} or C-4_{Fru}), 81.6 (C-3_{Glc} or C-4_{Fru}), 79.5 (C-2_{Glc}), 78.6 (C-5_{Fru}), 77.9 (C-4_{Glc}), 75.6 (ArCH$_2$), 75.3 (ArCH$_2$), 73.62 (ArCH$_2$), 73.56 (ArCH$_2$), 73.4 (ArCH$_2$), 72.3 (ArCH$_2$), 70.9 (C-5_{Glc}), 70.2 (ArCH$_2$), 69.7 (C-1_{Fru}), 69.5 (C-6_{Fru}), 69.3 (ArCH$_2$), 68.5 (C-6_{Glc}); Data for **5.10β**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.46–7.07 (m, 34H, ArH), 5.71 (d, 1H, J_{gem} = 3.9 Hz, H-1_{Glc}), 4.94–4.36 (m, 17H, H-3_{Fru}, ArCH_2), 4.24 (app t, 1H, $J_{4,3}$ = $J_{4,5}$ = 7.2 Hz, H-4_{Fru}), 4.10 (app dt, 1H, $J_{5,4}$ = $J_{5,6a}$ = 7.2 Hz, $J_{5,6b}$ = 4.0 Hz, H-5_{Fru}), 4.07–3.91 (m, 2H, H-3_{Glc}, H-5_{Glc}), 3.83 (dd, 1H, $J_{6a,5}$ = 7.2 Hz, J_{gem} = 11.1 Hz, H-$6a_{Fru}$), 3.76–3.43 (m, 6H, H-2_{Glc}, H-4_{Glc}, H-$6a_{Glc}$, H-$6b_{Glc}$, H-$1a_{Fru}$, H-$6b_{Fru}$), 3.29 (d, 1H, J_{gem} = 11.1 Hz, H-$1b_{Fru}$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.8 (Ar), 138.6 (Ar), 138.4 (Ar), 138.36 (Ar), 137.0 (Ar), 136.7 (Ar), 129.1 (Ar), 129.0 (Ar), 128.6–127.5 (Ar), 105.6 (C-2_{Fru}), 89.5 (C-1_{Glc}), 82.1 (C-3_{Glc}), 81.7 (C-3_{Fru}), 80.9 (C-4_{Fru}), 80.4 (C-5_{Fru}), 80.0 (C-2_{Glc}), 77.9 (C-4_{Glc}), 75.7 (ArCH$_2$), 75.1 (ArCH$_2$), 73.55 (ArCH$_2$), 73.5 (ArCH$_2$), 73.4 (ArCH$_2$), 72.4 (ArCH$_2$), 71.7 (C-6_{Fru}), 70.9 (C-6_{Glc}), 70.7 (ArCH$_2$), 70.5 (ArCH$_2$), 70.2 (C-5_{Glc}), 68.8 (C-1_{Fru}); HRMS (ESI) calcd. for $C_{62}H_{68}NO_{11}$ $[M+NH_4]^+$ 1002.4787 found 1002.4788.

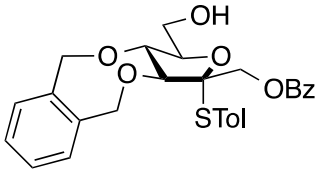


Cyclohexyl α-D-fructofuranoside (5.11α). To a solution of **5.8α** (8.0 mg, 14.7 μmol) in EtOAc–CH_3OH (1:1, 1.0 mL) was added $Pd(OH)_2/C$ (10 mg) at room temperature. The reaction mixture was stirred under an H_2 atmosphere by exchange of three cycles of vacuum/H_2. After stirring for 30 min, the reaction mixture was filtered and the filtrate was concentrated. The resulting residue was purified by column chromatography (9:1, EtOAc–CH_3OH) to give **5.11α** (4.3 mg, 89%) as a colorless oil. $[\alpha]^{25}_D$ +59.5 (*c* 0.2, CH_3OH); TLC (9:1, EtOAc–CH_3OH) R_f 0.41; ^1H NMR ($CDCl_3$, 500 MHz) δ_H 4.04 (d, 1H, $J_{3,4}$ = 5.1 Hz, H-3), 3.93–3.86 (m, 2H, H-4, H-5), 3.80–3.73 (m, 2H, H-6a, cyclohexyl OC*H*), 3.68 (d, 1H, J_{gem} = 11.7 Hz, H-1a), 3.63 (dd, 1H, $J_{6b,5}$ = 4.2 Hz, J_{gem} = 11.7 Hz, H-6b), 3.60 (d, 1H, J_{gem} = 11.7 Hz, H-1b), 1.90–1.80 (m, 2H, cyclohexyl CH_2), 1.76–1.68 (m, 2H, cyclohexyl CH_2), 1.57–1.50 (m, 1H, cyclohexyl CH_2), 1.39–1.20 (m, 5H, cyclohexyl CH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 109.3 (C-2), 84.2 (C-3), 83.7 (C-5), 78.1 (C-4), 71.8 (cyclohexyl O*C*H), 62.8 (C-6), 62.6 (C-1), 35.9 (cyclohexyl *C*H_2), 35.7 (cyclohexyl *C*H_2), 26.7 (cyclohexyl *C*H_2), 25.6 (2C, cyclohexyl *C*H_2); HRMS (ESI) calcd. for $C_{12}H_{22}NaO_6$ $[M+Na]^+$ 285.1309 found 285.1314.



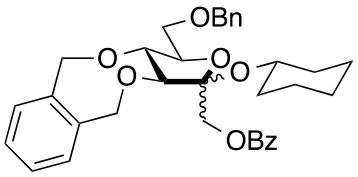
Cyclohexyl β-D-fructofuranoside (5.11β). To a solution of **5.8β** (7.0 mg, 12.9 μmol) in EtOAc–CH_3OH (1:1, 1.0 mL) was added $Pd(OH)_2/C$ (10 mg) at room temperature. The reaction mixture was stirred under an H_2 atmosphere by exchange of three cycles of vacuum/H_2. After stirring for

30 min, the reaction mixture was filtered and the filtrate was concentrated. The resulting residue was purified by column chromatography (9:1, EtOAc–CH_3OH) to give **5.11β** (3.2 mg, 87%) as a colorless oil. $[\alpha]^{25}_D$ –27.4 (*c* 0.3, CH_3OH); TLC (9:1, EtOAc–CH_3OH) R_f 0.35; ^1H NMR ($CDCl_3$, 500 MHz) δ_H 4.08 (d, 1H, $J_{3,4}$ = 7.9 Hz, H-3), 3.87 (app t, 1H, $J_{4,3}$ = $J_{4,5}$ = 7.9 Hz, H-4), 3.84–3.80 (m, 1H, cyclohexyl OC*H*)), 3.76–3.71 (m, 2H, H-5, H-6a), 3.67–3.60 (m, 2H, H-1a, H-6a), 3.49 (d, 1H, J_{gem} = 11.8 Hz, H-1b), 1.80–1.67 (m, 3H, cyclohexyl CH_2), 1.57–1.50 (m, 1H, cyclohexyl CH_2), 1.38–1.23 (m, 6H, cyclohexyl CH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 105.6 (C-2), 83.1 (C-5), 77.8 (C-3), 77.2 (C-4), 71.5 (cyclohexyl O*C*H), 65.1 (C-6), 62.6 (C-1), 36.1 (cyclohexyl *C*H_2), 35.8 (cyclohexyl *C*H_2), 26.7 (cyclohexyl *C*H_2), 25.7 (cyclohexyl *C*H_2), 25.6 (cyclohexyl *C*H_2); HRMS (ESI) calcd. for $C_{12}H_{22}NaO_6$ $[M+Na]^+$ 285.1309 found 285.1311.



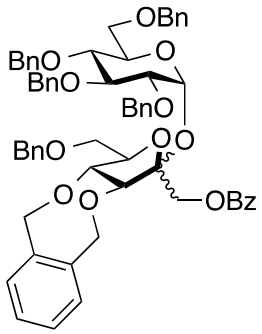
***p*-Tolyl 1-*O*-benzoyl-2-thio-3,4-*O*-xylylene-α-D-fructofuranoside (5.12).** To a solution of **5.6** (39.5 mg, 0.0516 mmol) in DMF (1.0 mL) was added NaH (3.1 mg, 0.0774 mol) and α,α'-dibromo-o-xylylene (14.6 mg, 0.0619 mmol) at 0 ºC. After stirring at 0 °C for 2 h, CH_3OH was added. The mixture was diluted with EtOAc and washed with H_2O. The organic layer was dried over $MgSO_4$ and the mixture was filtered. The filtrate was concentrated and the resulting reisude was dried *in vacuo* overnight. To a solution of the residue in CH_2Cl_2 (1.0 mL) was added TFA (5.7 μL, 0.0773 mmol) at room temperature. After stirring for 20 min, the reaction was neutralized by addition of satd. aq. $NaHCO_3$. Dilution of the mixture with CH_2Cl_2 provided a solution that was washed with water and brine. The organic layer was dried over $MgSO_4$, filtered and the

filtrate was concentrated. The resulting residue was dried *in vacuo* overnight. To a solution of the residue in CH_2Cl_2 (1.0 mL) was added Et_3N (10.7 μL, 0.0773 mol), BzCl (7.2 μL, 0.0619 mmol) and DMAP (1.2 mg, 0.0103 mmol) at room temperature. After stirring for 30 min, excess BzCl was quenched by the addition of CH_3OH and the solution was then concentrated. The resulting residue dried *in vacuo* overnight. To a solution of the residue in THF (1.0 mL) was added 1M TBAF (77.3 μL, 0.0773 mmol) at room temperature. After 48 h, the reaction mixture was concentrated and the residue was purified by column chromatography (4:1, hexane–EtOAc) to give **5.12** (9.9 mg, 39% over three steps) as a colorless oil. $[\alpha]^{25}_D$ +112.7 (*c* 1.0, $CHCl_3$); TLC (4:1, hexane–EtOAc) R_f 0.27; ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.90–7.85 (m, 2H, ArH), 7.54–7.49 (m, 1H, ArH), 7.41–7.33 (m, 5H, ArH), 7.31–7.26 (m, 2H, ArH), 7.22–7.18 (m, 1H, ArH), 7.10–7.05 (m, 2H, ArH), 4.89 (d, 1H, J_{gem} = 12.6 Hz, ArC*H*$_2$), 4.87 (d, 1H, J_{gem} = 12.6 Hz, ArC*H*$_2$), 4.79 (d, 1H, J_{gem} = 12.6 Hz, ArC*H*$_2$), 4.70 (d, 1H, J_{gem} = 12.6 Hz, ArC*H*$_2$), 4.66 (d, 1H, J_{gem} = 11.8 Hz, H-1a), 4.25 (dd, 1H, $J_{4,3}$ = 6.2 Hz, $J_{4,5}$ = 8.6 Hz, H-4), 4.22 (d, 1H, J_{gem} = 11.8 Hz, H-1b), 4.15 (d, 1H, $J_{3,4}$ = 6.2 Hz, H-3), 4.10 (app dt, 1H, $J_{5,4}$ = 8.6 Hz, $J_{5,6a}$ = $J_{5,6b}$ = 2.5 Hz, H-5), 3.87 (dd, 1H, $J_{6a,5}$ = 2.5 Hz, J_{gem} = 12.4 Hz, H-6a), 3.66 (dd, 1H, $J_{6b,5}$ = 2.5 Hz, J_{gem} = 12.4 Hz, H-6b), 2.34 (s, 3H, ArC*H*$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_H 166.2 (C=O), 139.4 (Ar), 136.2 (2C, Ar), 136.1 (Ar), 135.7 (Ar), 132.8 (Ar), 131.6 (Ar), 131.2 (Ar), 130.2 (Ar), 129.65 (2C, Ar), 129.60 (2C, Ar), 129.54 (Ar), 129.52 (Ar), 128.3 (2C, Ar), 126.8 (Ar), 94.2 (C-2), 87.8 (C-3), 79.9 (C-4), 79.4 (C-5), 70.0 (Ar*C*H$_2$), 68.7 (Ar*C*H$_2$), 65.6 (C-1), 60.8 (C-6), 21.3 (Ar*C*H$_3$); HRMS (ESI) calcd. for $C_{28}H_{28}NaO_6S$ $[M+Na]^+$ 515.1499 found 515.1498.



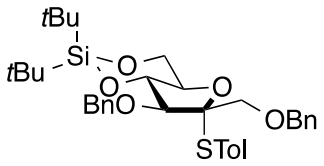
Cyclohexyl 1-*O*-benzoyl-6-*O*-benzyl-3,4-*O*-xylylene-α-D-fructofuranoside (5.13α) and **Cyclohexyl 1-*O*-benzoyl-6-*O*-benzyl-3,4-*O*-xylylene-β-D-fructofuranoside (5.13β).** A mixture of **5.2** (24.5 mg, 0.0420 mmol), cyclohexanol (5.1 mg, 0.050 mmol) and 4Å molecular sieves in CH_2Cl_2 (1.7 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –78 °C before *N*-iodosuccinimide (11.4 mg, 0.050 mmol) and silver triflate (2.2 mg, 8.4 μmol) were added. The reaction mixture was slowly warmed to –40 °C. After stirring for 5 h, triethylamine was added to the reaction mixture. The reaction was warmed to room temperature and then a small amount of H_2O was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The mixture was dried over $MgSO_4$ and then filtered and the filtrate was concentrated. The resulting residue was purified by column chromatography (10:1 to 4:1, hexane–EtOAc) to give **5.13α** (11.4 mg, 49%) as a colorless oil and **5.13β** (8.8 mg, 38%) as a colorless oil. Data for **5.13α**: $[\alpha]^{25}_D$ +67.2 (*c* 0.9, $CHCl_3$); TLC (4:1, hexane–EtOAc) R_f 0.41; ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.98–7.92 (m, 2H, ArH), 7.53–7.47 (m, 1H, ArH), 7.38–7.26 (m, 8H, ArH), 7.24–7.18 (m, 3H, ArH), 4.91 (d, 1H, J_{gem} = 12.6 Hz, Ar*CH*$_2$), 4.81 (d, 1H, J_{gem} = 12.6 Hz, Ar*CH*$_2$), 4.72 (d, 1H, J_{gem} = 12.6 Hz, Ar*CH*$_2$), 4.70 (d, 1H, J_{gem} = 12.6 Hz, Ar*CH*$_2$), 4.52 (d, 1H, J_{gem} = 12.6 Hz, Ar*CH*$_2$), 4.47 (d, 1H, J_{gem} = 12.6 Hz, Ar*CH*$_2$), 4.46 (d, 1H, J_{gem} = 11.3 Hz, H-1a), 4.43 (d, 1H, J_{gem} = 11.3 Hz, H-1b), 4.15 (ddd, 1H, $J_{5,4}$ = 9.1 Hz, $J_{5,6a}$ = 2.3 Hz, $J_{5,6b}$ = 5.0 Hz, H-5), 4.13 (d, 1H, $J_{3,4}$ = 5.8 Hz, H-3), 3.97 (dd, 1H, $J_{4,3}$ = 5.8 Hz, $J_{4,5}$ = 9.1 Hz, H-4), 3.84–3.76 (m, 1H, cyclohexyl OC*H*), 3.66 (dd, 1H, $J_{6a,5}$ = 2.3 Hz, J_{gem} = 11.3 Hz, H-6a), 3.53 (dd, 1H, $J_{6b,5}$ = 5.0 Hz, J_{gem} = 11.3 Hz, H-6b), 1.87–1.64 (m, 2H, cyclohexyl C*H*$_2$), 1.53–1.47 (m, 3H, cy-

clohexyl CH_2), 1.37–1.09 (m, 5H, cyclohexyl CH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 166.3 (C=O), 138.5 (Ar), 136.6 (Ar), 136.1 (Ar), 132.8 (Ar), 131.9 (Ar), 131.4 (Ar), 130.7 (Ar), 129.9 (2C, Ar), 129.7 (Ar), 129.5 (Ar), 128.50 (2C, Ar), 128.43 (2C, Ar), 127.70 (2C, Ar), 127.66 (Ar), 107.7 (C-2), 89.1 (C-3), 81.4 (C-4), 78.9 (C-5), 73.3 (ArCH_2), 71.5 (cyclohexyl OCH), 70.1 (ArCH_2), 69.1 (C-6), 68.8 (ArCH_2), 62.5 (C-1), 35.3 (cyclohexyl CH_2), 34.6 (cyclohexyl CH_2), 25.7 (cyclohexyl CH_2), 24.84 (cyclohexyl CH_2), 24.82 (cyclohexyl CH_2); HRMS (ESI) calcd. for $C_{34}H_{38}NaO_7$ $[M+Na]^+$ 581.2510 found 581.2516. Data for **5.13β**: $[\alpha]^{25}_D$ –5.3 (*c* 0.9, $CHCl_3$); TLC (4:1, hexane–EtOAc) R_f 0.35; ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.98–7.92 (m, 2H, ArH), 7.58–7.53 (m, 1H, ArH), 7.43–7.39 (m, 2H, ArH), 7.35–7.26 (m, 8H, ArH), 7.18–7.14 (m, 1H, ArH), 5.11 (d, 1H, J_{gem} = 12.9 Hz, ArCH_2), 4.93 (d, 1H, J_{gem} = 12.9 Hz, ArCH_2), 4.81–4.76 (m, 2H, ArCH_2), 4.57 (s, 2H, ArCH_2), 4.40 (d, 1H, J_{gem} = 11.8 Hz, H-1a), 4.31 (d, 1H, J_{gem} = 11.8 Hz, H-1b), 4.21–4.16 (m, 2H, H-3, H-4), 4.03–3.97 (m, 1H, H-5), 3.76–3.69 (m, 1H, cyclohexyl OCH), 3.64 (dd, 1H, $J_{6a,5}$ = 3.0 Hz, J_{gem} = 10.3 Hz, H-6a), 3.59 (dd, 1H, $J_{6b,5}$ = 6.6 Hz, J_{gem} = 10.3 Hz, H-6b), 1.90–1.80 (m, 2H, cyclohexyl CH_2), 1.71–1.64 (m, 2H, cyclohexyl CH_2), 1.52–1.45 (m, 1H, cyclohexyl CH_2), 1.44–1.05 (m, 5H, cyclohexyl CH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 166.1 (C=O), 138.2 (Ar), 136.8 (Ar), 136.4 (Ar), 133.2 (Ar), 131.9 (Ar), 130.8 (Ar), 130.1 (Ar), 129.9 (2C, Ar), 129.3 (Ar), 129.2 (Ar), 128.58 (2C, Ar), 128.56 (2C, Ar), 127.97 (2C, Ar), 127.83 (Ar), 104.3 (C-2), 82.7 (C-3), 81.9 (C-4), 79.3 (C-5), 73.5 (ArCH_2), 71.9 (cyclohexyl OCH), 71.5 (C-6), 70.7 (ArCH_2), 70.1 (ArCH_2), 65.2 (C-1), 35.1 (cyclohexyl CH_2), 34.2 (cyclohexyl CH_2), 25.7 (cyclohexyl CH_2), 25.2 (cyclohexyl CH_2), 25.0 (cyclohexyl CH_2); HRMS (ESI) calcd. for $C_{34}H_{38}NaO_7$ $[M+Na]^+$ 581.2510 found 581.2508.



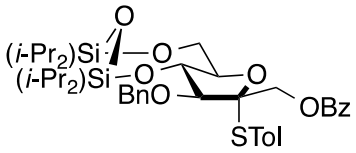
1-*O*-benzoyl-6-*O*-benzyl-3,4-*O*-xylylene-α-D-fructofuranosyl-(2→1)-2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside (5.14α) and **1-*O*-benzoyl-6-*O*-benzyl-3,4-*O*-xylylene-β-D-fructofuranosyl-(2→1)-2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside (5.14β).** A mixture of **5.2** (13.1 mg, 0.0225 mmol), 2,3,4,6-tetra-*O*-benzyl glucopyranose (14.6 mg, 0.0270 mmol) and 4Å molecular sieves in CH_2Cl_2 (0.9 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –78 °C before *N*-iodosuccinimide (6.0 mg, 0.0270 mmol) and silver triflate (1.2 mg, 4.5 μmol) were added. After stirring at –78 °C for 30 min, triethylamine was added to the reaction mixture. The reaction was warmed to room temperature and then a small amount of H_2O was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The mixture was dried over $MgSO_4$ and then filtered and the filtrate was concentrated. The resulting residue was purified by column chromatography (6:1, hexane–EtOAc) to give an α/β mixture of **5.14** (19.2 mg, 85%, α/β = 1.1:1) as a colorless oil. TLC (4:1, hexane–EtOAc) R_f 0.35; Data for **5.14α**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.98–7.90 (m, 2H, ArH), 7.57–7.07 (m, 32H, ArH), 5.56 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-1_{Glc}), 5.02–4.24 (m, 18H, H-$1a_{Fru}$, H-$1b_{Fru}$, H-3_{Fru}, H-5_{Fru}, ArCH_2), 4.05–3.96 (m, 2H, H-3_{Glc}, H-4_{Fru}), 3.75–3.69 (m, 1H, H-4_{Glc}), 3.67–3.50 (m, 4H, H-2_{Glc}, H-5_{Glc}, H-$6a_{Glc}$, H-$6a_{Fru}$), 3.46 (dd, 1H, $J_{6b,5}$ = 4.8 Hz, J_{gem} = 11.5 Hz, H-$6b_{Fru}$), 3.40 (dd, 1H, $J_{6b,5}$ = 1.6 Hz, J_{gem} = 10.8 Hz, H-$6b_{Glc}$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 166.0 (C=O), 139.2–127.4 (multi C, Ar), 107.8 (C-2_{Fru}), 90.6 (C-1_{Glc}), 88.9 (C-3_{Fru}), 82.0 (C-3_{Glc}), 80.7 (C-

4_{Fru}), 79.3 (C-2_{Glc}), 78.8 (C-5_{Fru}), 77.7 (C-4_{Glc}), 75.9–72.5 (5C, Ar*C*H_2), 71.2 (C-5_{Glc}), 70.1 (Ar*C*H_2), 68.8 (Ar*C*H_2), 68.4 (C-6_{Glc}), 69.3 (C-6_{Fru}), 64.5 (C-1_{Fru}); Data for **5.14β**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.46–7.07 (m, 34H, ArH), 5.71 (d, 1H, J_{gem} = 3.9 Hz, H-1_{Glc}), 4.94–4.36 (m, 17H, H-3_{Fru}, ArC*H*$_2$), 4.24 (app t, 1H, $J_{4,3} = J_{4,5}$ = 7.2 Hz, H-4_{Fru}), 4.10 (app dt, 1H, $J_{5,4} = J_{5,6a}$ = 7.2 Hz, $J_{5,6b}$ = 4.0 Hz, H-5_{Fru}), 4.07–3.91 (m, 2H, H-3_{Glc}, H-5_{Glc}), 3.83 (dd, 1H, $J_{6a,5}$ = 7.2 Hz, J_{gem} = 11.1 Hz, H-$6a_{Fru}$), 3.76–3.43 (m, 6H, H-2_{Glc}, H-4_{Glc}, H-$6a_{Glc}$, H-$6b_{Glc}$, H-$1a_{Fru}$, H-4_{Fru}), 3.29 (d, 1H, J_{gem} = 11.1 Hz, H-$1b_{Fru}$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.8–127.5 (multi C, Ar), 105.6 (C-2_{Fru}), 89.5 (C-1_{Glc}), 82.2 (C-3_{Fru}), 81.8 (C-3_{Fru}), 80.9 (C-4_{Fru}), 80.7 (C-5_{Fru}), 79.7 (C-2_{Glc}), 77.9 (C-4_{Glc}), 75.9–72.5 (5C, Ar*C*H_2), 71.5 (C-6_{Fru}), 71.0 (C-5_{Glc}), 70.3 (Ar*C*H_2), 70.25 (Ar*C*H_2), 68.7 (C-6_{Glc}), 63.2 (C-1_{Fru}); HRMS (ESI) calcd. for $C_{62}H_{66}NO_{12}$ $[M+NH_4]^+$ 1016.4580 found 1016.4581.



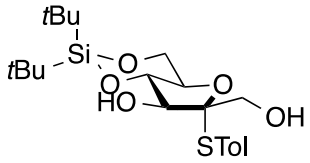
***p*-Tolyl 1,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-2-thio-α-D-fructofuranoside (5.15).** To a solution of **5.17** (70.0 mg, 0.164 mmol) in DMF (2.0 mL) was added benzyl bromide (23.4 μL, 0.197 mmol) and NaH (10.0 mg, 0.246 mmol) at room temperature. After stirring for 1 h, CH_3OH was added. The mixture was diluted with EtOAc and washed with water. The organic layer was dried over $MgSO_4$, and then the mixture was filtered and the filtrate was concentrated. The residue was purified by column chromatography (6:1, hexane–EtOAc) to give **5.15** (92.5 mg, 93%) as a colorless oil. $[\alpha]^{25}_D$ +61.6 (*c* 0.1, $CHCl_3$); TLC (6:1, hexane–EtOAc) R_f 0.20; ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.40–7.22 (m, 12H, ArH), 7.06 (d, 2H, *J* = 8.1 Hz, ArH), 4.84 (d, 1H J_{gem} = 12.4 Hz, ArC*H*$_2$), 4.80 (d, 1H J_{gem} = 12.4 Hz, ArC*H*$_2$), 4.51 (d, 1H J_{gem} = 12.4 Hz, ArC*H*$_2$),

4.46 (d, 1H J_{gem} = 12.4 Hz, ArCH_2), 4.30–4.23 (m, 2H, H-4, H-6a), 4.00 (d, 1H, $J_{3,4}$ = 7.9 Hz, H-3), 3.89 (dd, 1H, $J_{6b,5}$ = 9.3 Hz, J_{gem} = 10.5 Hz, H-6b), 3.69–3.61 (m, 2H, H-1a, H-5), 3.51 (d, 1H, J_{gem} = 10.9 Hz, H-1b), 2.32 (s, 3H, ArCH_3), 1.00 (s, 9H, SiC(CH_3)$_3$), 0.91 (s, 9H, SiC(CH_3)$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 139.3 (Ar), 138.6 (Ar), 138.4 (Ar), 136.6 (2C, Ar), 129.6 (2C, Ar), 128.6 (Ar), 128.4 (2C, Ar), 128.3 (2C, Ar), 128.0 (2C, Ar), 127.7 (2C, Ar), 127.5 (Ar), 127.4 (Ar), 95.1 (C-2), 87.1 (C-3), 80.2 (C-4), 73.7 (ArCH$_2$), 72.8 (C-5), 72.5 (ArCH$_2$), 71.4 (C-1), 67.6 (C-6), 27.6 (SiC(CH$_3$)$_3$), 27.2 (SiC(CH$_3$)$_3$), 22.8 (SiC(CH$_3$)$_3$), 21.4 (ArCH$_3$), 20.2 (SiC(CH$_3$)$_3$); HRMS (ESI) calcd. for $C_{35}H_{46}NaO_5SSi$ $[M+Na]^+$ 629.2727 found 629.2727.



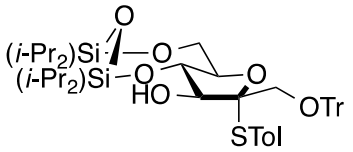
***p*-Tolyl 1-*O*-benzoyl-3-*O*-benzyl-4,6-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-2-thio-α-D-fructofuranoside (5.16).** To a solution of **5.18** (280 mg, 0.363 mmol) in DMF (3.6 mL), was added benzyl bromide (51.8 μL, 0.436 mmol) at room temperature. After stirring for 1 h, CH_3OH was added. The solution was diluted with CH_2Cl_2 and washed with satd. aq. $NaHCO_3$ and water. The organic layer was dried over $MgSO_4$ and then the mixture was filtered. The filtrate was concentrated and the resulting residue was dried *in vacuo* overnight. To a solution of the residue in CH_2Cl_2 (3.6 mL) was added TFA (41.7 μL, 0.545 mmol) at room temperature. After stirring for 10 min, the reaction was neutralized by satd. aq. $NaHCO_3$ and diluted with CH_2Cl_2. The organic layer was dried over $MgSO_4$ and then the mixture was filtered, The filtrate was concentrated and the resulting residue was dried *in vacuo* overnight. To a solution of the residue in CH_2Cl_2 (3.6 mL) was added Et_3N (60.3 μL, 0.436 mmol), BzCl (46.6 μL, 0.400 mmol) and DMAP (4.4 mg, 0.0363 mmol) at room temperature. After stirring for 2 h, excess BzCl was

quenched by addition of CH_3OH and diluted with EtOAc, washed with water. The organic layer was dried over $MgSO_4$, filtered and concentrated. The residue was purified by column chromatography (20:1, hexane–EtOAc) to give **5.16** (189 mg, 72%) as a colorless oil. TLC (20:1, hexane–EtOAc) R_f 0.31; $[\alpha]^{25}_D$ –25.7 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 700 MHz) δ_H 8.00–7.97 (m, 2H, ArH), 7.54–7.50 (m, 1H, ArH), 7.43 (d, 2H, *J* = 8.1 Hz, ArH), 7.38–7.34 (m, 2H, ArH), 7.28–7.19 (m, 5H, ArH), 7.08 (d, 2H, *J* = 8.1 Hz, ArH), 4.78 (d, 1H, J_{gem} = 12.4 Hz, ArCH_2), 4.74 (d, 1H, J_{gem} = 12.4 Hz, ArCH_2), 4.41–4.34 (m, 3H, H-1a, H-1b, H-4), 4.12 (d, 1H, $J_{3,4}$ = 7.0 Hz, H-3), 4.05–3.99 (m, 2H, H-5, H-6a), 3.93–3.88 (m, 1H, H-6b), 2.31 (s, 3H, ArCH_3), 1.10–0.82 (m, 28H, SiCH(CH_3)$_2$); ^{13}C NMR ($CDCl_3$, 175 MHz) δ_C 166.0 (C=O), 139.4 (Ar), 137.8 (Ar), 136.2 (2C, Ar), 132.9 (Ar), 130.5 (Ar), 129.82 (2C, Ar), 129.77 (2C, Ar), 128.39 (2C, Ar), 129.36 (2C, Ar), 127.74 (2C, Ar), 127.70 (Ar), 127.2 (Ar), 92.4 (C-2), 90.7 (C-3), 78.6 (C-5), 77.6 (C-4), 73.9 (ArCH$_2$), 64.9 (C-1), 62.5 (C-6), 21.4 (ArCH$_3$), 17.7 (SiCH(*C*H$_3$)$_2$), 17.53 (SiCH(*C*H$_3$)$_2$), 17.48 (2C, SiCH(*C*H$_3$)$_2$), 17.26 (SiCH(*C*H$_3$)$_2$), 17.24 (SiCH(*C*H$_3$)$_2$), 17.20 (2C, SiCH(*C*H$_3$)$_2$), 13.53 (Si*C*H(CH$_3$)$_2$), 13.27 (Si*C*H(CH$_3$)$_2$), 13.24 (Si*C*H(CH$_3$)$_2$), 12.9 (Si*C*H(CH$_3$)$_2$); HRMS (ESI) calcd. for $C_{39}H_{54}NaO_7SSi_2$ $[M+Na]^+$ 745.3021 found 745.3009.



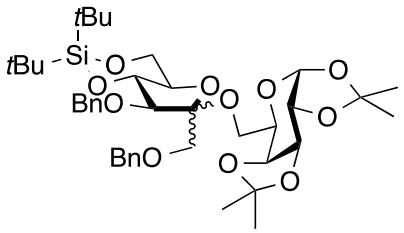
***p*-Tolyl 4,6-*O*-di-*tert*-butylsilylene-2-thio-α-D-fructofuranoside (5.17).** To a solution of **5.6** (197 mg, 0.257 mmol) in THF (2.5 mL), was added 1M TBAF (0.385 mL, 0.385 mmol) at room temperature. After stirring for 2 h, the reaction mixture was the filtrate was concentrated. The residue was diluted with EtOAc and washed with satd. aq. $NaHCO_3$. The organic layer was dried over $MgSO_4$, and then the mixture was filtered and the filtrate was concentrated. To a solution of

the residue in pyridine (5.5 mL) was added DTBS(OTf)$_2$ (97 μL, 0.302 mmol) at 0 °C. After stirring for 2 h, the reaction mixture was diluted with EtOAc, washed with 1N HCl and satd. aq. $NaHCO_3$. The organic layer was dried over $MgSO_4$, and the mixture was filtered and the filtrate was concentrated. The resulting residue was purified by column chromatography (8:1, hexane–EtOAc) to give 1-O-tritylated product, which is labile in $CDCl_3$. Therefore, to a solution of the residue in CH_2Cl_2 (1.8 mL) was added TFA (14.8 μL, 0.194 mmol) at room temperature. After stirring for 10 min, satd. aq. $NaHCO_3$ was added. The mixture was diluted with EtOAc, and washed with water and brine. The organic layer was dried over $MgSO_4$ and then filtered and the filtrate was concentrated. The resulting residue was purified by column chromatography (4:1, hexane–EtOAc) to give **5.17** (70.0 mg, 64% over three steps) as a colorless oil. $[\alpha]^{25}_D$ +114.3 (*c* 0.4, $CHCl_3$); TLC (2:1, hexane–EtOAc) R_f 0.50; ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.42 (d, 2H, *J* = 8.1 Hz, ArH), 7.12 (d, 2H, *J* = 8.1 Hz, ArH), 4.40–4.32 (m, 1H, H-6a), 4.15–4.11 (m, 1H, H-3), 3.99–3.92 (m, 3H, H-4, H-5, H-6b), 3.75 (d, 1H, J_{gem} = 12.1 Hz, H-1a), 3.55 (d, 1H, J_{gem} = 12.1 Hz, H-1b), 2.33 (s, 3H, ArC*H*$_3$), 1.06 (s, 9H, SiC(C*H*$_3$)$_3$), 1.01 (s, 9H, SiC(C*H*$_3$)$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 139.6 (Ar), 136.2 (2C, Ar), 129.8 (2C, Ar), 126.8 (Ar), 95.3 (C-2), 83.6 (C-3), 83.0 (C-5), 72.0 (C-4), 67.3 (C-6), 64.7 (C-1), 27.6 (SiC(*C*H$_3$)$_3$), 27.3 (SiC(*C*H$_3$)$_3$), 22.9 (Si*C*(CH$_3$)$_3$), 21.4 (Ar*C*H$_3$), 20.3 (Si*C*(CH$_3$)$_3$); HRMS (ESI) calcd. for $C_{21}H_{34}NaO_5SSi$ $[M+Na]^+$ 449.1788 found 449.1790.



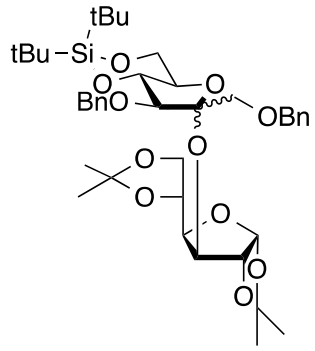
***p*-Tolyl 4,6-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-1-*O*-trityl-2-thio-α-D-fructofuranoside (5.18).** To a solution of **5.6** (441 mg, 0.578 mmol) in THF (6.0 mL), was added 1M TBAF (0.865 mL, 0.865 mmol) at room temperature. After stirring for 2 h, the reaction mixture was the filtrate was concentrated. The resulting residue was diluted with EtOAc and washed with satd. aq. $NaHCO_3$. The organic layer was dried over $MgSO_4$, and then the mixture was filtered. The filtrate was concentrated and the resulting residue was dried *in vacuo*. To a solution of the residue in pyridine (5.5 mL) was added $TIPSCl_2$ (193 μL, 0.603 mmol) at 0 °C. After stirring for 2 h, the reaction mixture was diluted with EtOAc, washed with 1N HCl and satd. aq. $NaHCO_3$. The organic layer was dried over $MgSO_4$, filtered and the filtrate was concentrated. The resulting residue was purified by column chromatography (15:1, hexane–EtOAc) to give **5.18** (280 mg, 63%) as a colorless oil. TLC (9:1, hexane–EtOAc) R_f 0.69; ^{1}H NMR ($CDCl_3$, 600 MHz) δ_H 7.41–7.36 (m, 6H, ArH), 7.29–7.20 (m, 11H, ArH), 7.00 (d, 2H, J = 8.1 Hz, ArH), 4.33 (dd, 1H, $J_{4,3}$ = 6.7 Hz, $J_{4,5}$ = 8.7 Hz, H-4), 4.23 (dd, 1H, $J_{3,4}$ = 6.7 Hz, $J_{3,OH}$ = 9.2 Hz, H-3), 4.14–4.07 (m, 2H, H-6a, H-6b), 3.96 (app dt, 1H, $J_{5,4}$ = 8.7 Hz, $J_{5,6a}$ = $J_{5,6b}$ = 3.8 Hz, H-5), 3.51 (d, 1H, $J_{OH,3}$ = 9.2 Hz, OH), 3.36 (d, 1H, J_{gem} = 10.3 Hz, H-1a), 3.33 (d, 1H, J_{gem} = 10.3 Hz, H-1b), 2.32 (s, 3H, ArCH_3), 1.21–0.89 (m, 28H, SiCH(CH_3)$_2$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ_C 143.7 (Ar), 138.5 (Ar), 135.3 (Ar), 129.5 (Ar), 128.8 (Ar), 128.0 (Ar), 128.0 (Ar), 127.4 (Ar), 93.8 (C-2), 88.2 (CPh$_3$), 85.6 (C-3), 79.0 (C-4), 78.9 (C-5), 67.2 (C-1), 62.0 (C-6), 21.4 (ArCH$_3$), 17.8 (SiCH(CH$_3$)$_2$), 17.64 (SiCH(CH$_3$)$_2$), 17.60 (SiCH(CH$_3$)$_2$), 17.57 (SiCH(CH$_3$)$_2$), 17.36 (SiCH(CH$_3$)$_2$), 17.33 (SiCH(CH$_3$)$_2$), 17.28 (SiCH(CH$_3$)$_2$), 17.25 (SiCH(CH$_3$)$_2$), 13.6

(Si*C*H(CH$_3$)$_2$), 13.4 (Si*C*H(CH$_3$)$_2$), 13.3 (Si*C*H(CH$_3$)$_2$), 12.8 (Si*C*H(CH$_3$)$_2$); HRMS (ESI) calcd. for $C_{44}H_{58}NaO_6SSi_2$ $[M+Na]^+$ 793.3385 found 793.3384.



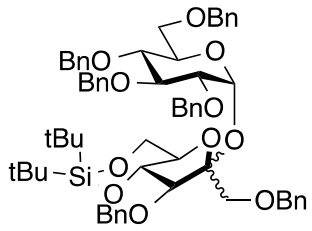
1,3-Di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-fructofuranosyl-(2→6)-1,2,4,5-di-*O*-isopropylidene-α-D-galactopyranose (5.19α) and **1,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-β-D-fructofuranosyl-(2→6)-1,2,4,5-di-*O*-isopropylidene-α-D-galactopyranose (5.19β).** A mixture of **5.15** (20.0 mg, 0.0330 mmol), **3.73** (10.3 mg, 0.0395 mmol) and 4Å molecular sieves in CH_2Cl_2 (1.3 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –78 °C before *N*-iodosuccinimide (8.9 mg, 0.050 mmol) and silver triflate (1.7 mg, 6.6 μmol) were added. The reaction mixture was slowly warmed to –40 °C. After stirring at –40 °C for 5 h, triethylamine was added to the reaction mixture. The reaction was warmed to room temperature and then a small amount of H_2O was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The mixture was dried over $MgSO_4$ and then filtered. The filtrate was concentrated and the resulting residue was purified by column chromatography (8:1 to 4:1, hexane–EtOAc) to give an α/β mixture of **5.19** (23.1 mg, 94%, α/β = 1.7:1) as a colorless oil. TLC (4:1, hexane–EtOAc) R_f 0.36; Data for **5.19α**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.40–7.22 (m, 10H, ArH), 5.50 (d, 1H, $J_{1,2}$ = 4.9 Hz, H-1$_{Gal}$), 4.82–4.73 (m, 2H, ArC*H*$_2$), 4.60–4.52 (m, 3H, H-3$_{Gal}$, ArC*H*$_2$), 4.36–4.26 (m, 2H, H-2$_{Gal}$, H-6a$_{Fru}$), 4.24 (d, 1H, $J_{4,3}$ = 1.7 Hz, $J_{4,5}$ = 8.0 Hz, H-4$_{Gal}$), 4.16–4.10 (m, 1H, H-4$_{Fru}$), 4.08 (d, 1H, $J_{3,4}$ = 7.8 Hz, H-3$_{Fru}$), 4.01–3.86 (m, 3H, H-5$_{Gal}$, H-5$_{Fru}$, H-6b$_{Fru}$), 3.80–3.69 (m, 2H, H-6a$_{Gal}$, H-6b$_{Gal}$), 3.63 (d, 1H, J_{gem} = 10.9 Hz, H-

1a$_{Fru}$), 3.59 (d, 1H, J_{gem} = 10.9 Hz, H-1b$_{Fru}$), 1.51 (s, 3H, C(C*H*$_3$)$_2$), 1.42 (s, 3H, C(C*H*$_3$)$_2$), 1.32 (s, 6H, C(C*H*$_3$)$_2$), 1.03 (s, 9H, SiC(C*H*$_3$)$_3$), 1.00 (s, 9H, SiC(C*H*$_3$)$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.6 (Ar), 138.3 (Ar), 128.2 (2C, Ar), 128.17 (2C, Ar), 127.6 (2C, Ar), 127.55 (Ar), 127.36 (2C, Ar), 127.30 (Ar), 109.1 (*C*(CH$_3$)$_2$), 108.5 (*C*(CH$_3$)$_2$), 107.3 (C-2$_{Fru}$), 96.4 (C-1$_{Gal}$), 88.4 (C-3$_{Fru}$), 81.0 (C-4$_{Fru}$), 73.6 (Ar*C*H$_2$), 72.5 (C-5$_{Fru}$), 72.3 (Ar*C*H$_2$), 71.1 (C-2$_{Gal}$ or C-4$_{Gal}$), 70.73 (C-2$_{Gal}$ or C-4$_{Gal}$), 70.66 (C-3$_{Gal}$), 68.0 (C-1$_{Fru}$), 67.7 (C-6$_{Fru}$), 67.3 (C-5$_{Gal}$), 61.5 (C-6$_{Gal}$), 27.5 (SiC(*C*H$_3$)$_3$), 27.1(SiC(*C*H$_3$)$_3$), 26.1 (C(*C*H$_3$)$_2$), 26.0 (C(*C*H$_3$)$_2$), 25.0 (C(*C*H$_3$)$_2$), 24.5 (C(*C*H$_3$)$_2$), 22.6 (Si*C*(CH$_3$)$_3$), 20.1 (Si*C*(CH$_3$)$_3$). Data for **5.19β**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.40–7.22 (m, 10H, ArH), 5.50 (d, 1H, $J_{1,2}$ = 4.9 Hz, H-1$_{Gal}$), 4.82–4.73 (m, 2H, ArH), 4.64–4.53 (m, 2H, H-3$_{Gal}$, ArC*H*$_2$), 4.47 (d, 1H, J_{gem} = 12.1 Hz, ArC*H*$_2$), 4.36–4.25 (m, 4H, H-2$_{Gal}$, H-4$_{Gal}$, H-4$_{Fru}$, H-6a$_{Fru}$), 4.20 (d, 1H, $J_{3,4}$ = 8.2 Hz, H-3$_{Fru}$), 4.01–3.86 (m, 2H, H-5$_{Gal}$, H-6b$_{Fru}$), 3.81–3.69 (m, 2H, H-6a$_{Gal}$, H-5$_{Fru}$), 3.68–3.65 (m, 1H, H-6b$_{Gal}$), 3.54 (s, 2H, H-1a$_{Fru}$, H-1b$_{Fru}$), 1.50 (s, 3H, C(C*H*$_3$)$_2$), 1.39 (s, 3H, C(C*H*$_3$)$_2$), 1.32 (s, 3H, C(C*H*$_3$)$_2$), 1.31 (s, 3H, C(C*H*$_3$)$_2$), 1.07 (s, 9H, SiC(C*H*$_3$)$_3$), 0.97 (s, 9H, SiC(C*H*$_3$)$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.5 (Ar), 138.0 (Ar), 128.3 (2C, Ar), 128.1 (2C, Ar), 127.7 (2C, Ar), 127.6 (2C, Ar), 127.4 (2C, Ar), 109.0 (*C*(CH$_3$)$_2$), 108.5 (*C*(CH$_3$)$_2$), 104.2 (C-2$_{Fru}$), 96.3 (C-1$_{Gal}$), 81.7 (C-3$_{Fru}$), 80.4 (C-4$_{Fru}$), 73.6 (Ar*C*H$_2$), 73.1 (C-5$_{Fru}$), 72.6 (C-1$_{Fru}$), 71.8 (Ar*C*H$_2$), 70.8 (C-2$_{Gal}$), 70.68 (C-3$_{Gal}$), 70.6 (C-4$_{Gal}$), 69.1 (C-6$_{Fru}$), 67.9 (C-5$_{Gal}$), 61.4 (C-6$_{Gal}$), 27.5 (SiC(*C*H$_3$)$_3$), 27.1 (SiC(*C*H$_3$)$_3$), 26.1 (C(*C*H$_3$)$_2$), 26.0 (C(*C*H$_3$)$_2$), 25.0 (C(*C*H$_3$)$_2$), 24.5 (C(*C*H$_3$)$_2$), 22.6 (Si*C*(CH$_3$)$_3$), 20.1 (Si*C*(CH$_3$)$_3$); HRMS (ESI) calcd. for $C_{40}H_{62}NO_{11}Si$ $[M+NH_4]^+$ 760.4087 found 760.4082.



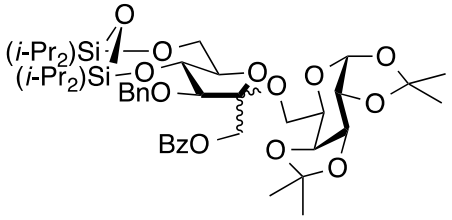
1,3-Di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-fructofuranosyl-(2→6)-1,2,4,6-di-*O*-isopropylidene-α-D-glucofuranose (5.20α) and **1,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-β-D-fructofuranosyl-(2→6)-1,2,4,6-di-*O*-isopropylidene-α-D-glucofuranose (5.20β).** A mixture of **5.16** (16.1 mg, 0.0265 mmol), **3.74** (8.3 mg, 0.0318 mmol) and 4Å molecular sieves in CH_2Cl_2 (1.1 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –78 °C and then *N*-iodosuccinimide (7.3 mg, 0.0318 mmol) and silver triflate (1.4 mg, 5.3 μmol) were added. The reaction mixture was slowly warmed to –40 °C. After stirring –40 °C for 4 h, triethylamine was added to the reaction mixture. The reaction was warmed to room temperature and then a small amount of H_2O was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The mixture was dried over $MgSO_4$ and then filtered. The filtrate was concentrated and the resulting residue was purified by column chromatography (8:1 to 4:1, hexane–EtOAc) to give an α/β mixture of **5.20** (15.2 mg, 77%, α/β = 10:1) as colorless oil. TLC (4:1, hexane–EtOAc) R_f 0.33; Data for **5.20α**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.39–7.25 (m, 10H, ArH), 5.85 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-1$_{Glc}$), 4.77 (s, 2H, ArC*H*$_2$), 4.58–4.50 (m, 3H, H-2$_{Glc}$, ArC*H*$_2$), 4.41 (d, 1H, J = 3.4 Hz, H-3$_{Glc}$), 4.34 (dd, 1H, $J_{6a,5}$ = 5.4 Hz, J_{gem} = 9.8 Hz, H-6a$_{Fru}$), 4.29–4.15 (m, 3H, H-4$_{Glc}$, H-5$_{Glc}$, H-4$_{Fru}$), 4.04–3.95 (m, 3H, H-6a$_{Glc}$, H-6b$_{Glc,}$ H-3$_{Fru}$), 3.92 (dd, 1H, $J_{6b,5}$ = 9.3 Hz, J_{gem} = 9.8 Hz, H-6b$_{Fru}$), 3.83 (ddd, 1H, $J_{5,4}$ = $J_{5,6b}$ = 9.3 Hz, $J_{5,6a}$ = 5.4 Hz, H-5$_{Fru}$), 3.69 (d, 1H, J_{gem} = 11.2 Hz, H-1a$_{Fru}$), 3.65 (d, 1H, J_{gem} = 11.2 Hz, H-1b$_{Fru}$), 1.49

(s, 3H, C(CH_3)$_2$), 1.36 (s, 3H, C(CH_3)$_2$), 1.30 (s, 3H, C(CH_3)$_2$), 1.26 (s, 3H, C(CH_3)$_2$), 1.04 (s, 9H, SiC(CH_3)$_3$), 1.00 (s, 9H, SiC(CH_3)$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.4 (Ar), 138.3 (Ar), 128.48 (2C, Ar), 128.47 (2C, Ar), 127.8 (2C, Ar), 127.75 (Ar), 127.72 (Ar), 127.62 (2C, Ar), 112.1 (*C*(CH$_3$)$_2$), 109.0 (*C*(CH$_3$)$_2$), 108.3 (C-2$_{Fru}$), 105.3 (C-1$_{Glc}$), 89.0 (C-3$_{Fru}$), 84.7 (C-2$_{Glc}$), 80.9 (C-4$_{Fru}$), 80.4 (C-4$_{Glc}$), 76.9 (C-3$_{Glc}$), 73.9 (Ar*C*H$_2$), 73.1 (C-5$_{Fru}$), 73.0 (C-5$_{Glc}$), 72.4 (Ar*C*H$_2$), 69.1 (C-1$_{Fru}$), 67.8 (C-6$_{Fru}$), 67.0 (C-6$_{Glc}$), 27.7 (SiC(*C*H$_3$)$_3$), 27.3 (SiC(*C*H$_3$)$_3$), 27.1 ((C(*C*H$_3$)$_2$)), 26.9 (C(*C*H$_3$)$_2$), 26.7 (C(*C*H$_3$)$_2$), 25.5 (C(*C*H$_3$)$_2$), 22.8 (Si*C*(CH$_3$)$_3$), 20.3 (Si*C*(CH$_3$)$_3$); HRMS (ESI) calcd. for $C_{40}H_{62}NO_{11}Si$ $[M+NH_4]^+$ 760.4087 found 760.4083.



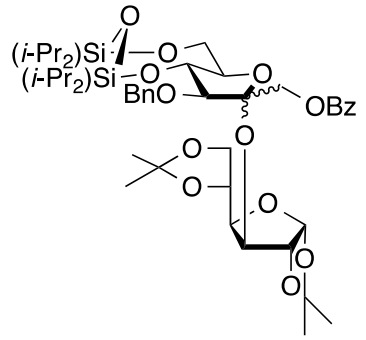
1,3-Di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-fructofuranosyl-(2→1)-2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside (5.21α) and **1,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-β-D-fructofuranosyl-(2→1)-2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside (5.21β).** A mixture of **5.15** (19.6 mg, 0.0324 mmol), 2,3,4,6-tetra-*O*-benzyl glucopyranose (21.1 mg, 0.0390 mmol) and 4Å molecular sieves in CH_2Cl_2 (1.3 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –78 °C before *N*-iodosuccinimide (8.7 mg, 0.0389 mmol) and silver triflate (1.7 mg, 6.5 μmol) were added. The reaction was slowly warmed to –40 °C. After stirring at –40 °C for 5 h, triethylamine was added to the reaction mixture. The reaction was warmed to room temperature and then a small amount of H_2O was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The mixture was dried over $MgSO_4$ and then filtered and the filtrate was concentrated. The resulting residue was purified by

column chromatography (8:1 to 4:1, hexane–EtOAc) to give an α/β mixture of **5.21** (30.7 mg, 93%, α/β = 4:1) as a colorless oil. TLC (4:1, hexane–EtOAc) R_f 0.39; Data for **5.21α**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.40–7.09 (m, 30H, ArH), 5.51 (d, 1H, $J_{1,2}$ = 3.5 Hz, H-1_{Glc}), 5.02–4.38 (m, 12H, ArCH_2), 4.25 (dd, 1H, $J_{4,3}$ = 7.8 Hz, $J_{4,5}$ = 9.3 Hz, H-4_{Fru}), 4.18 (dd, 1H, $J_{6a,5}$ = 5.0 Hz, J_{gem} = 8.8 Hz, H-$6a_{Fru}$), 4.10 (d, 1H, $J_{3,4}$ = 7.8 Hz, H-3_{Fru}), 4.02–3.87 (m, 4H, H-3_{Glc}, H-4_{Glc}, H-5_{Fru}, H-$6b_{Fru}$), 3.82–3.41 (m, 6H, H-2_{Glc}, H-5_{Glc}, H-$6a_{Glc}$, H-$6b_{Glc}$, H-$1a_{Fru}$, H-$1b_{Fru}$), 1.03 (s, 9H, SiC(CH_3)$_3$), 0.93 (s, 9H, SiC(CH_3)$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 139.3–127.3 (multi C, Ar), 107.8 (C-2_{Fru}), 90.8 (C-1_{Glc}), 89.5 (C-3_{Fru}), 81.9 (C-3_{Glc}), 80.9 (C-4_{Fru}), 79.8 (C-2_{Glc}), 77.8 (C-5_{Glc}), 75.7 (C-5_{Fru}), 75.3 (ArCH_2), 73.8 (ArCH_2), 73.6 (ArCH_2), 72.7 (ArCH_2), 72.6 (ArCH_2), 72.5 (ArCH_2), 72.4 (C-3_{Glc}), 71.2 (C-4_{Glc}), 69.9 (C-1_{Fru}), 68.7 (C-6_{Glc}), 67.7 (C-6_{Fru}), 27.6 (SiC(CH_3)$_3$), 27.3 (SiC(CH_3)$_3$), 22.8 (SiC(CH_3)$_3$), 20.2 (SiC(CH_3)$_3$); HRMS (ESI) calcd. for $C_{62}H_{74}NaO_{11}Si$ $[M+Na]^+$ 1045.4893 found 1045.4885.



1-*O*-benzoyl-3-*O*-benzyl-4,6-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-α-D-fructofuranosyl-(2→6)-1,2,4,5-di-*O*-isopropylidene-α-D-galactopyranose (5.22α) and **1-*O*-benzoyl-3-*O*-benzyl-4,6-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-β-D-fructofuranosyl-(2→6)-1,2,4,5-di-*O*-isopropylidene-α-D-galactopyranose (5.22β).** A mixture of **5.16** (16.5 mg, 0.0228 mmol), **3.73** (7.1 mg, 0.0274 mmol) and 4Å molecular sieves in CH_2Cl_2 (0.9 mL) was stirred under an Ar atmosphere at room temperature for 15 min. The mixture was then cooled to –78 °C and then *N*-iodosuccinimide (6.1 mg, 0.0274 mmol) and silver triflate (1.2 mg, 4.6 μmol)

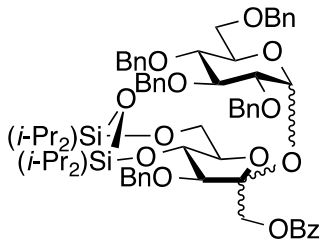
were added. The reaction mixture was slowly warmed to –40 °C. After stirring at –40 °C for 3 h, triethylamine was added to the reaction mixture. The reaction was warmed to room temperature and then a small amount of H_2O was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The mixture was dried over $MgSO_4$ and then filtered. The filtrate was concentrated and the resulting residue was purified by column chromatography (20:1 to 5:1, hexane–EtOAc) to give an α/β mixture of **5.22** (16.2 mg, 83%, α/β = 10:1) as a colorless oil. TLC (5:1, hexane–EtOAc) R_f 0.27; Data for **5.22α**: ^{1}H NMR ($CDCl_3$, 700 MHz) δ_H 8.04–7.99 (m, 2H, ArH), 7.55–7.50 (m, 1H, ArH), 7.40–7.35 (m, 2H, ArH), 7.25–7.15 (m, 5H, ArH), 5.50 (d, 1H, $J_{1,2}$ = 5.0 Hz, H-1_{Gal}), 4.72 (d, 1H, J_{gem} = 12.5 Hz, ArH), 4.70 (d, 1H, J_{gem} = 12.5 Hz, ArH), 4.55 (dd, 1H, $J_{3,2}$ = 7.8 Hz, $J_{3,4}$ = 1.8 Hz, H-3_{Gal}), 4.51 (d, 1H, J_{gem} = 11.9 Hz, H-$1a_{Fru}$), 4.46 (d, 1H, J_{gem} = 11.9 Hz, H-$1b_{Fru}$), 4.33 (m, 1H, H-4_{Fru}), 4.30–4.26 (m, 2H, H-2_{Gal}, H-4_{Gal}), 4.17 (d, 1H, $J_{3,4}$ = 6.0 Hz, H-3_{Fru}), 4.01–3.73 (m, 6H, H-5_{Gal}, H-$6a_{Gal}$, H-$6b_{Gal}$, H-5_{Fru}, H-$6a_{Fru}$, H-$6b_{Fru}$), 1.51 (s, 3H, C(CH_3)$_2$), 1.36 (s, 3H, C(CH_3)$_2$), 1.32 (s, 3H, C(CH_3)$_2$), 1.18 (s, 3H, C(CH_3)$_2$), 1.11–0.90 (m, 28H, SiCH(CH_3)$_2$); ^{13}C NMR ($CDCl_3$, 175 MHz) δ_C 166.0 (C=O), 138.1 (Ar), 133.0 (Ar), 130.5 (Ar), 129.9 (2C, Ar), 128.43 (2C, Ar), 128.35 (2C, Ar), 127.65 (2C, Ar), 127.61 (Ar), 109.4 (C(CH$_3$)$_2$), 108.7 (C(CH$_3$)$_2$), 105.7 (C-2_{Fru}), 96.5 (C-1_{Gal}), 89.6 (C-3_{Fru}), 81.1 (C-5_{Fru}), 77.8 (C-4_{Fru}), 73.0 (ArCH$_2$), 71.1 (C-2_{Gal} or C-4_{Gal}), 70.9 (C-2_{Gal} or C-4_{Gal}), 70.8 (C-3_{Gal}), 67.1 (C-5_{Gal}), 63.3 (C-6_{Fru}), 62.0 (C-1_{Fru}), 60.7 (C-6_{Gal}), 26.3 (C(CH$_3$)$_2$), 26.1 (C(CH$_3$)$_2$), 25.2 (C(CH$_3$)$_2$), 24.6 (C(CH$_3$)$_2$), 17.7 (SiCH(CH$_3$)$_2$), 17.5 (3C, SiCH(CH$_3$)$_2$), 17.4 (2C, SiCH(CH$_3$)$_2$), 17.30 (SiCH(CH$_3$)$_2$), 17.26 (SiCH(CH$_3$)$_2$), 13.7 (SiCH(CH$_3$)$_2$), 13.4 (SiCH(CH$_3$)$_2$), 13.2 (SiCH(CH$_3$)$_2$), 12.9 (SiCH(CH$_3$)$_2$); HRMS (ESI) calcd. for $C_{44}H_{66}NaO_{13}Si_2$ $[M+Na]^+$ 881.3934 found 881.3938.



1-*O*-benzoyl-3-*O*-benzyl-4,6-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-α-D-fructofuranosyl-(2→3)-1,2,5,6-di-*O*-isopropylidene-α-D-glucopyranose (5.23α) and **1-*O*-benzoyl-3-*O*-benzyl-4,6-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-β-D-fructofuranosyl-(2→3)-1,2,5,6-di-*O*-isopropylidene-α-D-glucopyranose (5.23β).** A mixture of **5.16** (23.4 mg, 0.0324 mmol), **3.74** (10.1 mg, 0.0389 mmol) and 4Å molecular sieves in CH_2Cl_2 (1.3 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –78 °C before *N*-iodosuccinimide (8.7 mg, 0.0389 mmol) and silver triflate (1.7 mg, 6.5 μmol) were added. The reaction mixture was slowly warmed to –40 °C. After stirring at –40 °C for 3 h, triethylamine was added to the reaction mixture. The reaction was warmed to room temperature and then a small amount of H_2O was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The mixture was dried over $MgSO_4$ and then filtered. The filtrate was concentrated and the resulting residue was purified by column chromatography (20:1 to 5:1, hexane–EtOAc) to give an α/β mixture of **5.23** (23.5 mg, 85%, α/β = 4.8:1) as a colorless oil. TLC (5:1, hexane–EtOAc) R_f 0.27; Data for **5.23α**: ^{1}H NMR ($CDCl_3$, 700 MHz) δ_H 8.04–8.01 (m, 2H, ArH), 7.56–7.52 (m, 1H, ArH), 7.41–7.37 (m, 2H, ArH), 7.26–7.19 (m, 5H, ArH), 5.86 (d, 1H, $J_{1,2}$ = 3.5 Hz, H-1_{Glc}), 4.77–4.66 (m, 2H, ArCH_2), 4.65 (d, 1H, $J_{2,1}$ = 3.5 Hz, H-2_{Glc}), 4.61 (d, 1H, J_{gem} = 12.1 Hz, H-$1a_{Fru}$), 4.51 (d, 1H, $J_{3,4}$ = 3.1 Hz, H-3_{Glc}), 4.47 (d, 1H, J_{gem} = 12.1 Hz, H-$1b_{Fru}$), 4.36 (app t, 1H, $J_{4,3} = J_{4,5}$ = 7.2 Hz, H-4_{Fru}), 4.28 (app dt, 1H, $J_{5,6a} = J_{5,6b}$ = 5.6 Hz, $J_{5,4}$ = 8.2 Hz,

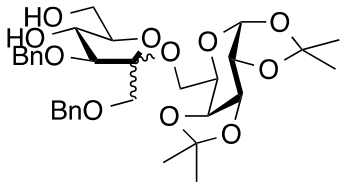
H-5$_{Glc}$), 4.14 (d, 1H, $J_{3,4}$ = 7.2 Hz, H-3$_{Fru}$), 4.10 (dd, 1H, $J_{4,3}$ = 3.1 Hz, $J_{4,5}$ = 8.2 Hz, H-4$_{Glc}$), 4.04 (dd, 1H, $J_{6a,5}$ = 5.6 Hz, J_{gem} = 8.6 Hz, H-6a$_{Glc}$), 4.01 (dd, 1H, $J_{6a,5}$ = 2.9 Hz, J_{gem} = 12.0 Hz, H-6a$_{Fru}$), 3.99 (dd, 1H, $J_{6b,5}$ = 5.6 Hz, J_{gem} = 8.6 Hz, H-6b$_{Glc}$), 3.93 (app dt, 1H, $J_{5,4}$ = $J_{5,6b}$ = 7.2 Hz, $J_{5,6a}$ = 2.9 Hz, H-5$_{Fru}$), 3.78 (dd, 1H, $J_{6b,5}$ = 7.2 Hz, J_{gem} = 12.0 Hz, H-6b$_{Fru}$), 1.49 (s, 3H, C(CH_3)$_2$), 1.37 (s, 3H, C(CH_3)$_2$), 1.30 (s, 3H, C(CH_3)$_2$), 1.20 (s, 3H, C(CH_3)$_2$), 1.09–0.80 (m, 28H, SiCH(CH_3)$_2$); ^{13}C NMR ($CDCl_3$, 175 MHz) δ_C 166.0 (C=O), 137.7 (Ar), 133.1 (Ar), 130.4 (Ar), 129.9 (2C, Ar), 128.5 (2C, Ar), 128.4 (2C, Ar), 127.8 (Ar), 127.7 (2C, Ar), 112.1 (C(CH$_3$)$_2$), 109.3 (C(CH$_3$)$_2$), 106.5 (C-2$_{Fru}$), 105.4 (C-1$_{Glc}$), 90.9 (C-3$_{Fru}$), 84.7 (C-2$_{Glc}$), 81.2 (C-5$_{Fru}$), 81.0 (C-4$_{Glc}$), 77.9 (C-4$_{Fru}$), 76.3 (C-3$_{Glc}$), 73.2 (ArCH$_2$), 72.5 (C-5$_{Glc}$), 67.7 (C-6$_{Glc}$), 63.8 (C-6$_{Fru}$), 62.7 (C-1$_{Fru}$), 27.14 (C(CH$_3$)$_2$), 27.08 (C(CH$_3$)$_2$), 26.6 (C(CH$_3$)$_2$), 25.4 (C(CH$_3$)$_2$), 17.7 (SiCH(CH$_3$)$_2$), 17.6 (SiCH(CH$_3$)$_2$), 17.53 (SiCH(CH$_3$)$_2$), 17.47 (SiCH(CH$_3$)$_2$), 17.33 (SiCH(CH$_3$)$_2$), 17.31 (SiCH(CH$_3$)$_2$), 17.29 (SiCH(CH$_3$)$_2$), 17.27 (SiCH(CH$_3$)$_2$), 13.5 (SiCH(CH$_3$)$_2$), 13.3 (SiCH(CH$_3$)$_2$), 13.2 (SiCH(CH$_3$)$_2$), 12.9 (SiCH(CH$_3$)$_2$); Data for **5.23β**: ^{1}H NMR ($CDCl_3$, 700 MHz) δ_H 8.04–8.01 (m, 2H, ArH), 7.56–7.52 (m, 1H, ArH), 7.41–7.37 (m, 2H, ArH), 7.26–7.19 (m, 5H, ArH), 5.76 (d, 1H, $J_{1,2}$ = 3.5 Hz, H-1$_{Glc}$), 4.77–4.66 (m, 2H, ArCH_2), 4.56 (d, 1H, $J_{2,1}$ = 3.5 Hz, H-2$_{Glc}$), 4.48–4.46 (m, 1H, H-1a$_{Fru}$), 4.44 (d, 1H, J_{gem} = 12.1 Hz, H-1b$_{Fru}$), 4.37–4.26 (m, 2H), 4.19 (d, 1H, J = 4.1 Hz), 4.16 (d, 1H, $J_{3,4}$ = 6.9 Hz, H-3$_{Fru}$), 4.06–3.70 (m, 6H), 1.46 (s, 3H, C(CH_3)$_2$), 1.33 (s, 6H, C(CH_3)$_2$), 1.32 (s, 3H, C(CH_3)$_2$), 1.09–0.80 (m, 28H, SiCH(CH_3)$_2$); ^{13}C NMR ($CDCl_3$, 175 MHz) δ_C 166.1 (C=O), 138.1 (Ar), 133.1 (Ar), 130.4 (Ar), 129.9 (2C, Ar), 128.5 (2C, Ar), 128.3 (2C, Ar), 127.7 (2C, Ar), 127.6 (Ar), 112.3 (C(CH$_3$)$_2$), 106.6 (C-1$_{Glc}$), 105.1 (C-2$_{Fru}$), 100.9 (C(CH$_3$)$_2$) 89.8, 84.2, 81.0, 79.7, 77.7, 75.1, 73.3, 71.6, 67.7, 63.0, 62.8, 27.4 (C(CH$_3$)$_2$), 27.2 (C(CH$_3$)$_2$), 26.7 (C(CH$_3$)$_2$), 25.5 (C(CH$_3$)$_2$), 17.7–17.2 (8C, SiCH(CH$_3$)$_2$), 13.7 (SiCH(CH$_3$)$_2$), 13.3 (SiCH(CH$_3$)$_2$), 13.1

(Si*C*H(CH$_3$)$_2$), 12.9 (Si*C*H(CH$_3$)$_2$); HRMS (ESI) calcd. for $C_{44}H_{66}NaO_{13}Si_2$ $[M+Na]^+$ 881.3934 found 881.3936.



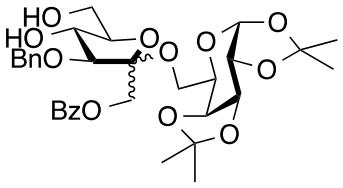
1-*O*-benzoyl-3-*O*-benzyl-4,6-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-α-D-fructofuranosyl-(2→1)-2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside (5.24α) and **1-*O*-benzoyl-3-*O*-benzyl-4,6-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-β-D-fructofuranosyl-(2→1)-2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside (5.24β)**. A mixture of **5.16** (23.2 mg, 0.0321 mmol), 2,3,4,6-tetra-*O*-benzyl glucopyranose (20.8 mg, 0.0385 mmol) and 4Å molecular sieves in CH_2Cl_2 (1.3 mL) was stirred under an Ar atmosphere at room temperature for 30 min. The mixture was then cooled to –78 °C before *N*-iodosuccinimide (8.7 mg, 0.0389 mmol) and silver triflate (1.7 mg, 6.5 μmol) were added. The remperature was slowly warmed to –40 °C. After stirring at –40 °C for 4 h, triethylamine was added to the reaction mixture. The reaction was warmed to room temperature and then a small amount of H_2O was added, followed by solid $Na_2S_2O_3 \cdot 5H_2O$ until the solution was colorless. The mixture was dried over $MgSO_4$ and then filtered. The filtrate was concentrated and the resulting residue was purified by column chromatography (8:1 to 4:1, hexane–EtOAc) to give an α/β mixture of **5.24** (31.8 mg, 87%, α/β = 16.7:1) as a colorless oil. TLC (10:1, hexane–EtOAc) R_f 0.21; Data for **5.24α**: ^{1}H NMR ($CDCl_3$, 700 MHz) δ_H 7.98–7.95 (m, 2H, ArH), 7.55–7.51 (m, 1H, ArH), 7.38–7.10 (m, 27H, ArH), 5.56 (d, 1H, $J_{1,2}$ = 3.8 Hz, H-1$_{Glc}$), 5.00 (d, 1H, J_{gem} = 11.0 Hz, ArC*H*$_2$), 4.85 (d, 1H, 1H, J_{gem} = 11.0 Hz, ArC*H*$_2$), 4.85 (d, 1H, 1H, J_{gem} = 11.4 Hz, ArC*H*$_2$), 4.75–4.68 (m, 4H, ArC*H*$_2$), 4.61 (d, 1H, J_{gem} = 12.4 Hz,

H-1a$_{Fru}$), 4.54 (d, 1H, J_{gem} = 12.0 Hz, ArCH_2), 4.47 (d, 1H, J_{gem} = 11.4 Hz, ArCH_2), 4.41 (d, 1H, J_{gem} = 12.4 Hz, H-1a$_{Fru}$), 4.31 (dd, 1H, $J_{4,3}$ = 6.8 Hz, $J_{4,5}$ = 8.4 Hz, H-4$_{Fru}$), 4.28 (d, 1H, J_{gem} = 12.0 Hz, ArCH_2), 4.23 (d, 1H, $J_{3,4}$ = 6.8 Hz, H-3$_{Fru}$), 4.01–3.94 (m, 2H, H-3$_{Glc}$, H-5$_{Fru}$), 3.88–3.86 (m, 1H, H-5$_{Glc}$), 3.74–3.69 (m, 3H, H-4$_{Glc}$, H-6a$_{Fru}$, H-6b$_{Fru}$), 3.58 (dd, 1H, $J_{2,1}$ = 3.8 Hz, $J_{2,3}$ = 9.6 Hz, H-2$_{Glc}$), 3.55 (dd, 1H, $J_{6a,5}$ = 2.6 Hz, J_{gem} = 10.7 Hz, H-6a$_{Glc}$), 3.29 (dd, 1H, $J_{6b,5}$ = 1.2 Hz, J_{gem} = 10.7 Hz, H-6a$_{Glc}$), 1.08–0.86 (m, 28H, SiCH(CH_3)$_2$)); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 165.9 (C=O), 139.1 (Ar), 138.6 (Ar), 138.4 (Ar), 138.0 (Ar), 137.9 (Ar), 132.9 (Ar), 130.4 (Ar), 129.8 (Ar), 128.6 (Ar), 128.54 (Ar), 128.51 (Ar), 128.48 (Ar), 128.41 (Ar), 128.38 (Ar), 128.2 (Ar), 128.1 (Ar), 128.0 (Ar), 127.9 (Ar), 127.8 (Ar), 127.74 (Ar), 127.70 (Ar), 127.68 (Ar), 127.65 (Ar), 127.60 (Ar), 127.58 (Ar), 105.8 (C-2$_{Fru}$), 91.3 (C-3$_{Fru}$), 90.7 (C-1$_{Glc}$), 82.0 (C-3$_{Glc}$), 79.7 (C-2$_{Glc}$), 79.3 (C-5$_{Fru}$), 77.7 (C-4$_{Glc}$), 76.9 (C-4$_{Fru}$), 75.8 (ArCH$_2$), 75.3 (ArCH$_2$), 73.9 (ArCH$_2$), 73.7 (ArCH$_2$), 72.9 (ArCH$_2$), 71.5 (C-5$_{Glc}$), 68.4 (C-6$_{Glc}$), 63.6 (C-1$_{Fru}$), 61.8 (C-6$_{Fru}$), 17.7 (SiCH(CH$_3$)$_2$), 17.53 (2C, SiCH(CH$_3$)$_2$), 17.51 (SiCH(CH$_3$)$_2$), 17.34 (SiCH(CH$_3$)$_2$), 17.27 (SiCH(CH$_3$)$_2$), 17.23 (SiCH(CH$_3$)$_2$), 17.17 (SiCH(CH$_3$)$_2$), 13.6 (SiCH(CH$_3$)$_2$), 13.24 (SiCH(CH$_3$)$_2$), 13.20 (SiCH(CH$_3$)$_2$), 12.8 (SiCH(CH$_3$)$_2$); HRMS (ESI) calcd. for $C_{66}H_{82}NaO_{13}Si_2$ $[M+Na]^+$ 1161.5186 found 1161.5199.



1,3-Di-*O*-benzyl-α-D-fructofuranosyl-(2→6)-1,2,4,5-di-*O*-isopropylidene-α-D-galactopyranose (5.25). To a solution of an α/β mixture of **5.19** (18.7 mg, 0.0252 mmol) in THF (1.0 mL) was added 1M TBAF (100 μL, 0.100 mmol) at room temperature. After stirring for 1 h,

the reaction mixture was concentrated. The residue was purified by column chromatography (1:1 to 1:2, hexane–EtOAc) to give an α/β mixture of **5.25** (13.4 mg, 99%, α/β = 1.7:1) as colorless oil. TLC (1:1, hexane–EtOAc) R_f 0.17; Data for **5.25α**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.38–7.23 (m, 10H, ArH), 5.55 (d, 1H, $J_{1,2}$ = 5.1 Hz, H-1_{Gal}), 4.69 (d, 1H, J_{gem} = 11.6 Hz, ArCH_2), 4.62–4.50 (m, 4H, H-3_{Gal}, ArCH_2), 4.35–4.28 (m, 2H, H-2_{Gal}, H-5_{Fru}), 4.19-4.11 (m, 2H, H-4_{Gal}, H-3_{Fru}), 3.99–3.92 (m, 2H, H-5_{Gal}, H-4_{Fru}), 3.83–3.55 (m, 6H, H-$6a_{Gal}$, H-$6b_{Gal}$, H-$1a_{Fru}$, H-$1b_{Fru}$, H-$6a_{Fru}$, H-6_{Fru}), 1.51 (s, 3H, C(CH_3)$_2$), 1.44 (s, 3H, C(CH_3)$_2$), 1.32 (s, 3H, C(CH_3)$_2$), 1.31 (s, 3H, C(CH_3)$_2$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 137.8 (Ar), 137.4 (Ar), 128.7–127.9 (multi C, Ar), 109.9 (*C*(CH$_3$)$_2$), 109.1 (*C*(CH$_3$)$_2$), 109.0 (C-2_{Fru}), 96.5 (C-1_{Gal}), 88.0 (C-5_{Fru}), 86.0 (C-4_{Fru}), 76.1 (C-3_{Fru}), 74.0 (Ar*C*H$_2$), 72.2 (Ar*C*H$_2$), 71.5 (C-1_{Fru}), 71.1 (C-4_{Gal}), 70.7 (2C, C-3_{Gal}, C-2_{Gal}), 67.9 (C-5_{Gal}), 65.9 (C-1_{Fru}), 63.1 (C-6_{Gal}), 60.4 (C-6_{Fru}), 26.21 (C(*C*H$_3$)$_2$), 26.20 (C(*C*H$_3$)$_2$), 25.0 (C(*C*H$_3$)$_2$), 24.6 (C(*C*H$_3$)$_2$); Data for **5.25β**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 7.38–7.23 (m, 10H, ArH), 5.51 (d, 1H, $J_{1,2}$ = 5.1 Hz, H-1_{Gal}), 4.78 (d, 1H, J_{gem} = 11.6 Hz, ArCH_2), 4.62–4.50 (m, 4H, H-3_{Gal}, ArCH_2), 4.46–4.40 (m, 1H), 4.35–4.28 (m, 2H), 4.19-4.11 (m, 1H), 3.99–3.92 (m, 3H), 3.83–3.55 (m, 5H), 1.54 (s, 3H, C(CH_3)$_2$), 1.43 (s, 3H, C(CH_3)$_2$), 1.34 (s, 3H, C(CH_3)$_2$), 1.33 (s, 3H, C(CH_3)$_2$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 138.7 (Ar), 137.7 (Ar), 128.7–127.9 (multi C, Ar), 109.6 (*C*(CH$_3$)$_2$), 108.8 (*C*(CH$_3$)$_2$), 104.0 (C-2_{Fru}), 96.6 (C-1_{Gal}), 85.4, 81.8, 74.0, 73.9, 72.9, 71.4, 70.8, 70.7, 67.8, 66.7, 61.1, 60.7, 26.3 (C(*C*H$_3$)$_2$), 26.1 (C(*C*H$_3$)$_2$), 25.1 (C(*C*H$_3$)$_2$), 24.4 (C(*C*H$_3$)$_2$); HRMS (ESI) calcd. for $C_{32}H_{42}NaO_{11}$ $[M+Na]^+$ 625.2619 found 625.2611.



1-*O*-benzoyl-3-*O*-benzyl-α-D-fructofuranosyl-(2→6)-1,2,4,5-di-*O*-isopropylidene-α-D-galactopyranose (5.26α) and 1-*O*-benzoyl-3-*O*-benzyl-β-D-fructofuranosyl-(2→6)-1,2,4,5-di-*O*-isopropylidene-α-D-galactopyranose (5.26β). To a solution of an α/β mixture of **5.22** (16.2 mg, 0.0189 mmol) in THF (1.0 mL) was added 1M TBAF (28.4 μL, 0.0284 mmol) at room temperature. After stirring for 30 min, reaction mixture was concentrated. The resulting residue was purified by column chromatography (5:1 to 2:1, hexane–EtOAc) to give a α/β mixture of **5.26** (10.2 mg, 88%, α/β = 10:1) as a colorless oil. TLC (1:1, hexane–EtOAc) R_f 0.20; Data for **5.26α**: ^{1}H NMR ($CDCl_3$, 700 MHz) δ_H 7.96–7.92 (m, 2H, ArH), 7.59–7.55 (m, 1H, ArH), 7.44–7.40 (m, 2H, ArH), 7.33–7.29 (m, 2H, ArH), 7.26–7.21 (m, 3H, ArH), 5.53 (d, 1H, $J_{1,2}$ = 5.1 Hz, H-1_{Gal}), 4.80 (d, 1H, J_{gem} = 11.6 Hz,H-$1a_{Fru}$), 4.75 (d, 1H, J_{gem} = 12.0 Hz, ArCH_2), 4.59–4.55 (m, 2H, ArCH_2, H-3_{Gal}), 4.39–4.36 (m, 2H, H-$1b_{Fru}$, H-5_{Fru}), 4.30 (dd, 1H, $J_{2,1}$ = 5.1 Hz, $J_{2,3}$ = 2.5 Hz, H-2_{Gal}), 4.21 (br s, 1H, H-4_{Fru}), 4.15 (m, 1H, H-4_{Gal}), 4.01–3.96 (m, 2H, H-$6a_{Gal}$, H-3_{Fru}), 3.89–3.81 (m, 2H, H-5_{Gal}, H-$6a_{Fru}$), 3.78 (dd, 1H, $J_{6b,5}$ = 4.4 Hz, J_{gem} = 12.0 Hz, H-$6b_{Fru}$), 3.63 (dd, 1H, $J_{6b,5}$ = 2.1 Hz, J_{gem} = 10.2 Hz, H-$6b_{Gal}$), 1.44 (s, 3H, C(CH_3)$_2$), 1.43 (s, 3H, C(CH_3)$_2$), 1.29 (s, 6H, C(CH_3)$_2$); ^{13}C NMR ($CDCl_3$, 175 MHz) δ_C 165.9 (C=O), 137.1 (Ar), 133.3 (Ar), 130.1 (Ar), 129.9 (2C, Ar), 128.7 (2C, Ar), 128.6 (2C, Ar), 128.3 (2C, Ar), 128.2 (Ar), 109.9 (*C*(CH$_3$)$_2$), 109.1 (*C*(CH$_3$)$_2$), 108.1 (C-2_{Fru}), 96.4 (C-1_{Gal}), 88.7 (C-5_{Fru}), 86.0 (C-4_{Fru}), 75.6 (C-3_{Fru}), 72.0 (Ar*C*H$_2$), 71.3 (C-4_{Gal}), 71.0 (C-2_{Gal}), 70.8 (C-3_{Gal}), 67.8 (C-5_{Gal}), 63.1 (C-6_{Fru}), 60.5 (C-6_{Gal}), 59.9 (C-1_{Fru}), 26.20 (C(*C*H$_3$)$_2$), 26.17 (C(*C*H$_3$)$_2$), 25.0 (C(*C*H$_3$)$_2$), 24.6 (C(*C*H$_3$)$_2$); HRMS (ESI) calcd. for $C_{32}H_{40}NaO_{12}$ $[M+Na]^+$ 639.2412 found 639.2416.

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Chapter 6

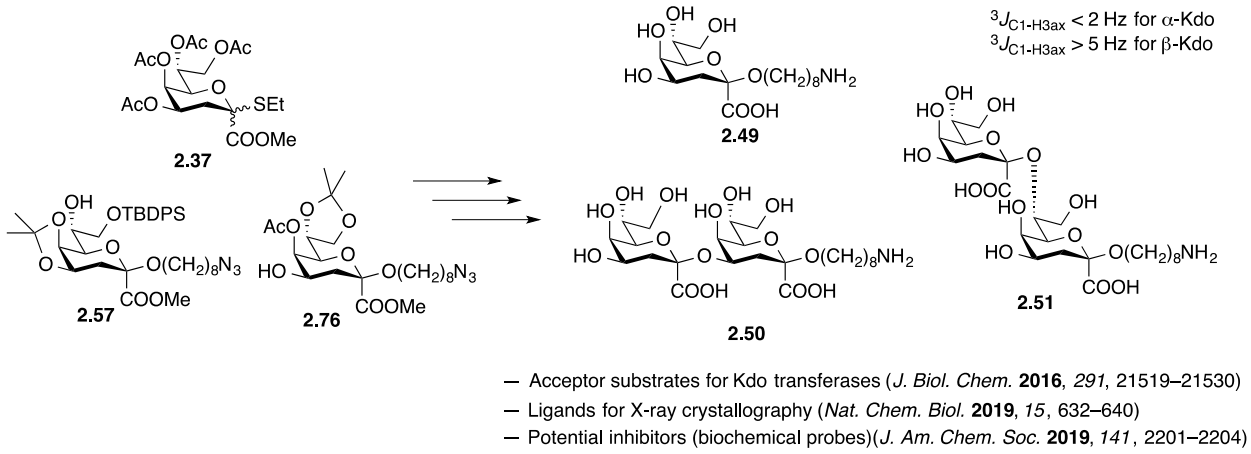
Summary and Future Work

6.1 Summary and future work

In my thesis research, I have investigated the chemistry of three ketose sugars. This thesis includes the synthesis of β-Kdo-containing oligosaccharides (Chapter 2), methodology development for stereoselective β-xylulofuranosylation and its application to the synthesis of β-Xul*f*-containing glycans (Chapter 3 and 4), and use of conformationally-restricted donors to furnish β-fructofuranosides (Chapter 5). Also included is a discussion of the influence the side chains in arabinofuranosylation[1], xylulofuranosylation, and fructofuranosylation using conformationally-restricted donors (Chapter 5).

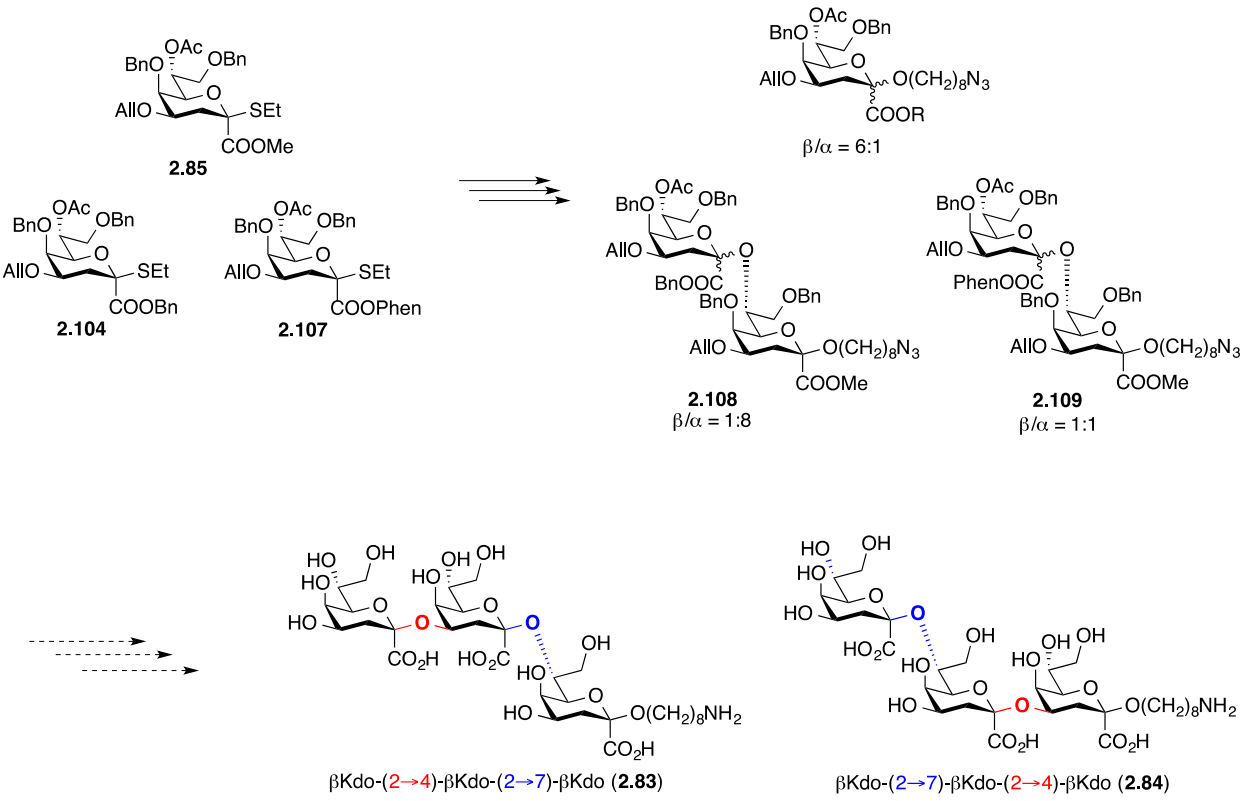
6.1.1 Synthesis of β-Kdo fragments for biological studies

In Chapter 2, I described the synthesis of three Kdo-containing glycans, **2.49**–**2.51,** which were obtained from peracetylated Kdo thioglycoside **2.37** and two Kdo glycosyl acceptors, **2.57** and **2.76** (**Scheme 6.1**) or 8-azidooctanol. Monosaccharide **2.49** was obtained exclusively as the β-glycoside via glycosylation of **2.37** with 8-azidooctanol using the IBr–AgOTf promotor system followed by deprotection. Disaccharides **2.50** and **2.51** were synthesized from glycosylation of **2.76** or **2.57** with **2.37**, followed by global deprotection. Although the stereoselectivity was poor to moderate in the synthesis of the disaccharides, the desired β anomers could be purified by column chromatography. The anomeric configuration of all Kdo glycosides was characterized using proton-coupled ^{13}C NMR experiments. The target molecules were also attached to different tags at the reducing end to provide molecules for biosynthetic studies[2,3] and in the development of assays to screen for potential inhibitors of the Kdo glycosyltransferase KpsC[4].



Scheme 6.1. Summary of the synthetic work in Chapter 2.

The synthesis of trisaccharides **2.83** and **2.84** (**Scheme 6.2**) was attempted via the use of orthogonally-protected donors **2.85**, **2.104** and **2.107**. The design of orthogonally-protected donors was done to reduce the number of steps after every glycosylation when accessing oligosaccharides larger than a disaccharide. However, the stereoselectivity of the glycosylations and the isolation of the diastereomers produced in the reactions were issues using this approach. A β:α anomer ratio of 6:1 was observed in the glycosylation of 8-azidooctanol with **2.85** or **2.104**. However, the stereoselectivity of the reaction for the formation of β-(2→7)-linked disaccharides **2.108** and **2.109** was unsatisfying (a 1:8 β:α ratio for **2.108** and a 1:1 β:α ratio for **2.109**). Currently, achieving β-selectivity in Kdo glycosylations is a big issue to overcome. New approaches to β-selective Kdo glycosylations should therefore be further investigated to achieve more consistent and better stereoselectivity.

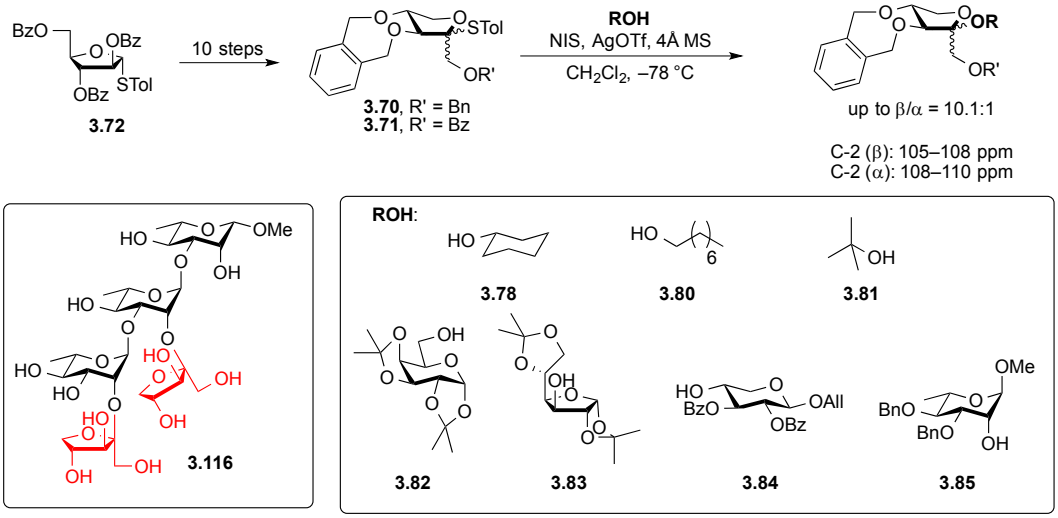


Scheme 6.2. Summary of the attempts to synthesize Kdo-trisaccharides using orthogonally-protected donors in Chapter 2.

6.1.2 Methodology development for the selectivity of 2,3-*cis*-β-xylulofuranosylation

In Chapter 3, I described a stereoselectivity study of xylulofuranosylation using conformationally-locked xylulose donors **3.70** and **3.71** (**Scheme 6.3**). The donors were designed based on the concept that restricting the conformation of the electrophilic intermediate produced upon thioglycoside activation would result in preferential *cis*-glycoside formation. The three major achievements are: (1) Donors **3.70** and **3.71** were successfully synthesized in ten steps from D-arabinose derivative **3.72**; (2) Moderate to good β selectivity in the xylulofuranosylation was observed with a variety of acceptors using donors containing a xylylene group at the O-3,O-4 posi-

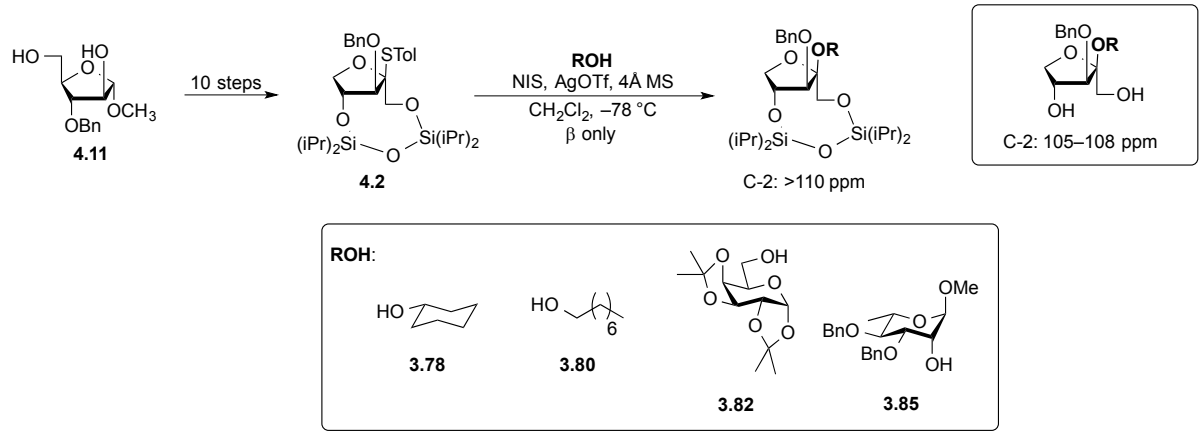
tions and a benzoyl group at O-1; (3) Characterization of the anomeric configuration of all xylulofuranosides was achieved by the chemical shift of C-2, accompanied with 2D ^{1}H–^{1}H TROESY experiments and one X-ray structure. Finally, thioglycoside donor **3.70** was successfully applied to the synthesis of the pentasaccharide **3.116** repeating unit of *Y. enterocolitica* O:5/O:5,27 LPS[5].



Scheme 6.3. Summary of the xylulofuranosylation stereoselectivity study reported in Chapter 3.

In Chapter 4, I improved the β-selectivity of xylulofuranosylation using siloxane-protected xylulose donor **4.2** (**Scheme 6.4**). The donor was designed based on the concept that hindering the nucleophile approach to the electrophilic intermediate from the α-face of furanose ring would favor *cis*-glycoside formation. The three major achievements are: (1) The siloxane-protected xylulose donor **4.2** was synthesized in ten steps from known compound D-arabinose derivative **4.11**; (2) The stereoselectivity was studied using four different acceptors and exclusively β-selective xylulofuranosylation was accomplished; (3) The anomeric characterization of siloxane-protected xylulofuranosides was achieved by detecting the C2 chemical shift of desi-

lylated xylulofuranosides and their 2D ^{1}H–^{1}H TROESY spectra, where the normal C-2 chemical shift appears at higher field (105–108 ppm) was assigned as β-xylulofuranosides.



Scheme 6.4. Summary of the xylulofuranosylation stereoselectivity study reported in Chapter 4.

The siloxane-protected thioglycoside donor **4.2** was successfully applied to the synthesis of protected pentasaccharide of *Y. enterocolitica* O:5/O:5,27 LPS[5]. However, I suffered at the glycosylation step with low yield and extremely long reaction time in making the desired trisaccharide acceptor when I tried to approach the synthesis of the pentasaccharide repeating unit from *C. jejuni* RM1221 CPS[6]. Therefore, the introduction of the heptoside both with high yield should be improved in the future due to the low yield and long reaction time of the IAD strategy. In addition, the siloxane-protected thioglycoside donor **4.2** can be further utilized for making more complicated β-Xul*f*-containing glycans[6,7]. Because the current route to donor **4.2** is tedious, developing a shorter route to this compound should also be a topic for future investigation.

6.1.3 Stereoselectivity study of 2,3-*cis*-β-fructofuranosylation using conformationally-restricted donors

In Chapter 5, our initial objective was to extend the methodology of using conformationally-restricted donors to obtain β-fructofuranosides. However, using donors **5.1**, **5.2**, **5.15** and **5.16** resulted in either no selectivity or α-selective fructofuranosylation. The influence of side chains on stereoselectivity was discussed via the results of arabinofuranosylation[8], xylulofuranosylation (Chapter 3) and fructofuranosylation (Chapter 5). Based on these results, the stereoselectivity appears to be influenced significantly by the $–CH_2OR$ group at the anomeric carbon of ketofuranoses but lesser to extend by the $–CH_2OR$ group at C-5 of the ketofuranose ring. From my results, the conformation of C1–O1 bond might be a major factor that influences the stereoselectivity. Therefore, computational studies of intermediates **5.28**–**5.32** should be completed to better understand their conformation. Such studies could lead to more selective donors for the formation of β-fructofuranosides and β-xylulofuranosides (**Figure 6.1**).

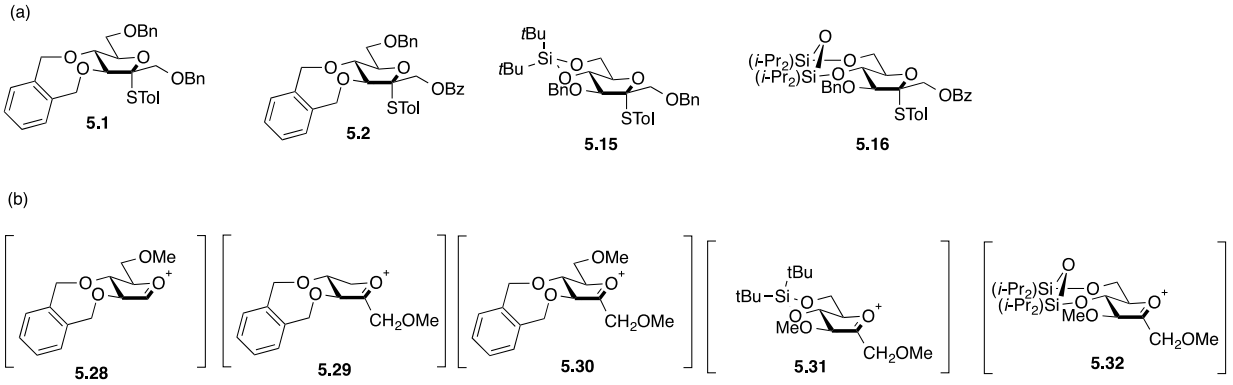


Figure 6.1. (a) Four conformationally-restricted donors **5.1**, **5.2**, **5.15**, **5.16** used in Chapter 5. (b) Five intermediates proposed for computational studies.

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Appendix

X-ray crystallographic data for 3.115β

XCL Code: TLL1701 **Date:** 17 March 2017

Compound: {1-(Cyclohexyloxy)-1,3,3a,9a-tetrahydrofuro[3,4-*b*][1,4]benzodioxin-1-yl}-methanol

Formula: $C_{19}H_{26}O_5$

Supervisor: T. L. Lowary **Crystallographer:** R. McDonald

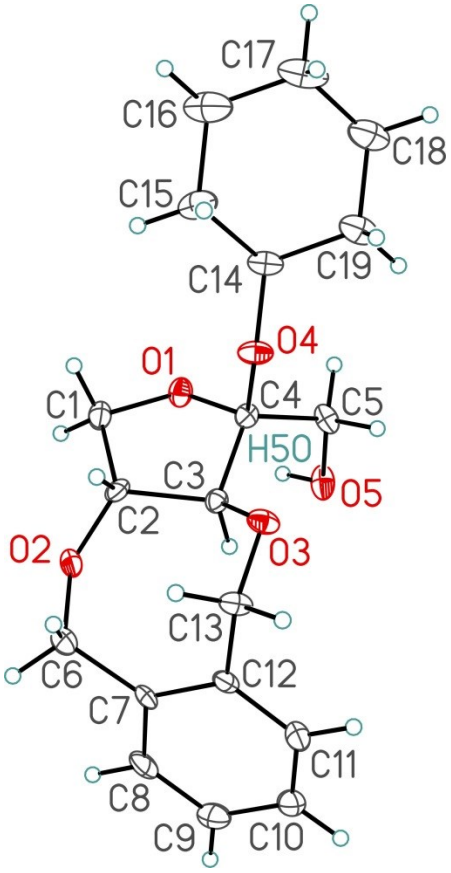

Figure Legend: Perspective view of the {1-(cyclohexyloxy)-1,3,3a,9a-tetrahydrofuro[3,4-*b*]-[1,4]benzodioxin-1-yl}methanol molecule showing the atom labelling scheme. Non-hydrogen atoms are represented by Gaussian ellipsoids at the 30% probability level. Hydrogen atoms are shown with arbitrarily small thermal parameters.

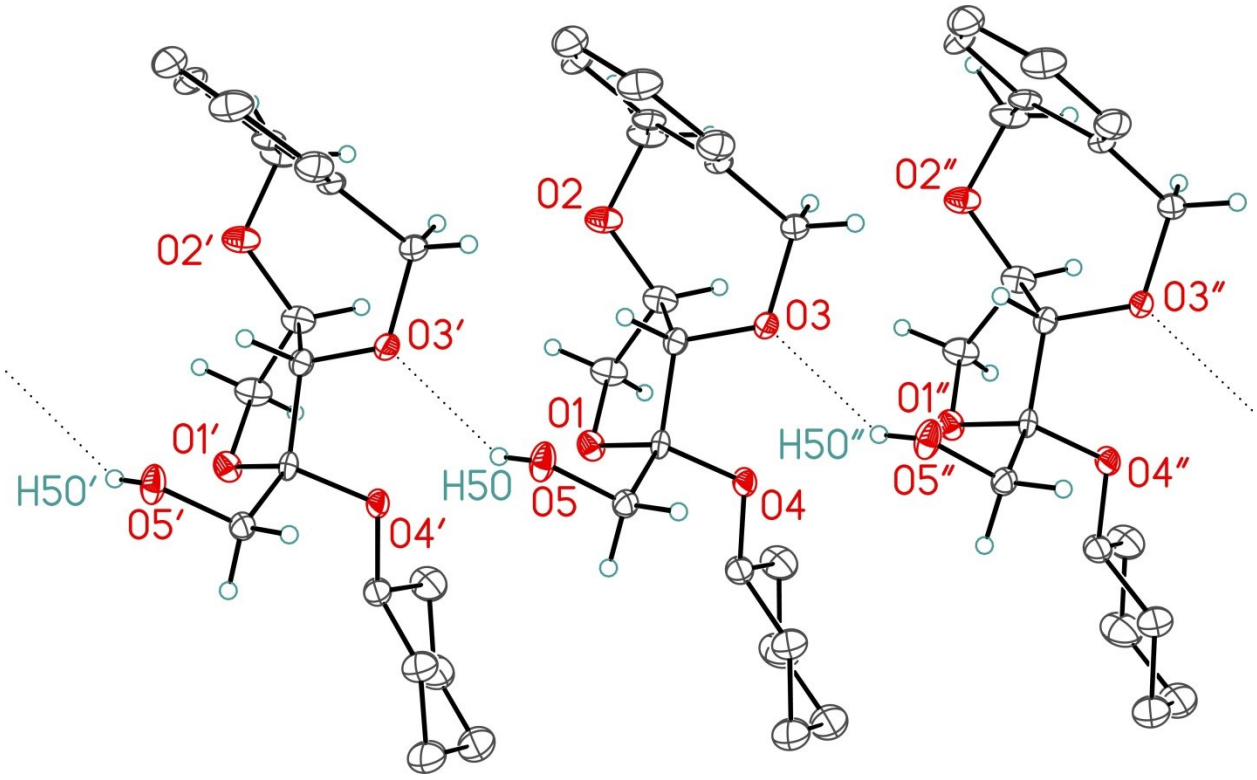

Figure Legend: Illustration of hydrogen-bonded interactions (dotted lines) between adjacent molecules in the crystal lattice. Primed atoms are related to unprimed ones via the crystallographic translational symmetry operation (x–1, y, z). Double-primed atoms are related to unprimed ones via the crystallographic translational symmetry operation (x+1, y, z). The chain propagates in a direction parallel to the crystal unit cell's a axis.

Table 1. Crystallographic Experimental Details

A. Crystal Data	
formula	$C_{19}H_{26}O_5$
formula weight	334.40
crystal dimensions (mm)	0.60 × 0.10 × 0.04
crystal system	monoclinic
space group	$P2_1$ (No. 4)
unit cell parameters[a]	
a (Å)	5.3125 (2)
b (Å)	12.3867 (5)
c (Å)	13.7161 (6)
β (deg)	90.529 (3)
V (Å^3)	902.54 (6)
Z	2
ρ_{calcd} (g cm^{-3})	1.230
μ (mm^{-1})	0.719
B. Data Collection and Refinement Conditions	
diffractometer	Bruker D8/APEX II CCD[b]
radiation (λ [Å])	Cu Kα (1.54178) (microfocus source)
temperature (°C)	–100
scan type	ω and ϕ scans (1.0°) (5-10 s exposures)
data collection 2θ limit (deg)	136.90
total data collected	5417 ($-6 \le h \le 6$, $-14 \le k \le 14$, $-15 \le l \le 13$)
independent reflections	3190 (R_{int} = 0.0916)
number of observed reflections (*NO*)	2371 [$F_o^2 \ge 2\sigma(F_o^2)$]
structure solution method	intrinsic phasing (*SHELXT-2014*[c])
refinement method	full-matrix least-squares on F^2 (*SHELXL–2014*[d])
absorption correction method	Gaussian integration (face-indexed)
range of transmission factors	1.0000–0.6245
data/restraints/parameters	3190 / 0 / 218
Flack absolute structure parameter[e]	0.0(4)
goodness-of-fit (*S*)[f] [all data]	1.009
final *R* indices[g]	
R_1 [$F_o^2 \ge 2\sigma(F_o^2)$]	0.0828
wR_2 [all data]	0.2221
largest difference peak and hole	0.357 and –0.415 e Å^{-3}

[a]Obtained from least-squares refinement of 3968 reflections with 6.44° < 2θ < 136.32°.

[b]Programs for diffractometer operation, data collection, data reduction and absorption correction were those supplied by Bruker.

(continued)

Table 1. Crystallographic Experimental Details (continued)

[c]Schneider, T. R.; Sheldrick, G. M. *Acta Crystallogr.* **2002**, *D58*, 1772-1779.

[d]Sheldrick, G. M. *Acta Crystallogr.* **2015**, *C71*, 3–8.

[e]Flack, H. D. *Acta Crystallogr.* **1983**, *A39*, 876–881; Flack, H. D.; Bernardinelli, G. *Acta Crystallogr.* **1999**, *A55*, 908–915; Flack, H. D.; Bernardinelli, G. *J. Appl. Cryst.* **2000**, *33*, 1143–1148. The Flack parameter will refine to a value near zero if the structure is in the correct configuration and will refine to a value near one for the inverted configuration. In this case the relatively large standard uncertainty indicates that the structural data alone should not be used to confirm absolute stereochemistry, but should be used in conjunction with the established stereochemistry of the precursor compound.

[f]$S = [\Sigma w(F_o^2 - F_c^2)^2/(n - p)]^{1/2}$ (n = number of data; p = number of parameters varied; $w = [\sigma^2(F_o^2) + (0.1292P)^2]^{-1}$ where $P = [\mathrm{Max}(F_o^2, 0) + 2F_c^2]/3$).

[g]$R_1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$; $wR_2 = [\Sigma w(F_o^2 - F_c^2)^2/\Sigma w(F_o^4)]^{1/2}$.

Table 2. Atomic Coordinates and Equivalent Isotropic Displacement Parameters

Atom	*x*	*y*	*z*	U_{eq}, Å^2
O1	-0.2665(8)	0.0698(4)	0.2292(3)	0.0291(11)*
O2	-0.1909(9)	0.2280(4)	0.4231(3)	0.0338(11)*
O3	0.2065(7)	0.0117(4)	0.4057(3)	0.0288(11)*
O4	0.1429(7)	0.0008(4)	0.2154(3)	0.0298(11)*
O5	-0.4057(8)	-0.1192(4)	0.3362(4)	0.0348(12)*
C1	-0.1989(14)	0.1792(6)	0.2559(5)	0.0348(16)*
C2	-0.0483(13)	0.1715(6)	0.3505(5)	0.0289(14)*
C3	-0.0281(10)	0.0499(5)	0.3692(4)	0.0220(12)*
C4	-0.0844(9)	-0.0002(5)	0.2713(4)	0.0211(13)*
C5	-0.1958(11)	-0.1122(6)	0.2729(5)	0.0285(14)*
C6	-0.0605(15)	0.2487(6)	0.5139(5)	0.0382(17)*
C7	-0.0665(12)	0.1521(5)	0.5814(5)	0.0264(14)*
C8	-0.2482(13)	0.1508(6)	0.6540(5)	0.0343(17)*
C9	-0.2701(13)	0.0653(7)	0.7169(5)	0.0378(16)*
C10	-0.1091(15)	-0.0218(7)	0.7088(5)	0.0390(17)*
C11	0.0748(13)	-0.0211(6)	0.6374(5)	0.0342(16)*
C12	0.0988(10)	0.0635(6)	0.5734(4)	0.0239(13)*
C13	0.2953(11)	0.0587(6)	0.4954(4)	0.0297(15)*
C14	0.1208(12)	-0.0218(7)	0.1135(5)	0.0338(16)*
C15	0.2527(15)	0.0667(8)	0.0568(6)	0.047(2)*
C16	0.2488(18)	0.0449(10)	-0.0528(7)	0.063(3)*
C17	0.3602(18)	-0.0659(10)	-0.0752(7)	0.063(3)*
C18	0.2290(16)	-0.1541(9)	-0.0178(6)	0.054(2)*
C19	0.2310(15)	-0.1315(8)	0.0893(6)	0.047(2)*

Anisotropically-refined atoms are marked with an asterisk (*). The form of the anisotropic displacement parameter is: $\exp[-2\pi^2(h^2a^{*2}U_{11} + k^2b^{*2}U_{22} + l^2c^{*2}U_{33} + 2klb^*c^*U_{23} + 2hla^*c^*U_{13} + 2hka^*b^*U_{12})]$.

Table 3. Selected Interatomic Distances (Å)

Atom1	Atom2	Distance	Atom1	Atom2	Distance
O1	C1	1.449(9)	C7	C8	1.393(9)
O1	C4	1.418(7)	C7	C12	1.410(9)
O2	C2	1.439(8)	C8	C9	1.373(11)
O2	C6	1.442(9)	C9	C10	1.382(12)
O3	C3	1.420(6)	C10	C11	1.390(10)
O3	C13	1.437(7)	C11	C12	1.374(10)
O4	C4	1.437(6)	C12	C13	1.503(8)
O4	C14	1.429(8)	C14	C15	1.519(10)
O5	C5	1.422(7)	C14	C19	1.517(12)
C1	C2	1.521(9)	C15	C16	1.527(11)
C2	C3	1.531(9)	C16	C17	1.528(16)
C3	C4	1.507(8)	C17	C18	1.519(14)
C4	C5	1.509(9)	C18	C19	1.496(11)
C6	C7	1.513(10)			

Table 4. Selected Interatomic Angles (deg)

Atom1	Atom2	Atom3	Angle	Atom1	Atom2	Atom3	Angle
C1	O1	C4	107.6(5)	C6	C7	C8	117.7(6)
C2	O2	C6	115.6(5)	C6	C7	C12	123.5(6)
C3	O3	C13	116.6(5)	C8	C7	C12	118.9(6)
C4	O4	C14	117.3(4)	C7	C8	C9	121.4(7)
O1	C1	C2	106.5(5)	C8	C9	C10	119.7(6)
O2	C2	C1	106.5(6)	C9	C10	C11	119.5(7)
O2	C2	C3	113.6(5)	C10	C11	C12	121.6(7)
C1	C2	C3	103.9(5)	C7	C12	C11	118.9(6)
O3	C3	C2	116.5(5)	C7	C12	C13	121.5(6)
O3	C3	C4	110.1(5)	C11	C12	C13	119.6(6)
C2	C3	C4	104.1(5)	O3	C13	C12	113.6(5)
O1	C4	O4	110.6(5)	O4	C14	C15	109.0(6)
O1	C4	C3	103.9(5)	O4	C14	C19	111.1(6)
O1	C4	C5	107.6(5)	C15	C14	C19	110.7(6)
O4	C4	C3	108.1(4)	C14	C15	C16	112.0(8)
O4	C4	C5	110.3(5)	C15	C16	C17	110.8(9)
C3	C4	C5	116.1(5)	C16	C17	C18	111.2(7)
O5	C5	C4	112.0(5)	C17	C18	C19	112.0(8)
O2	C6	C7	112.0(6)	C14	C19	C18	112.5(8)

Table 5. Hydrogen-Bonded Interactions

D–H···A	D–H (Å)	H···A (Å)	D···A (Å)	∠D–H···A (deg)
O5–H5O···O3[a]	0.84	2.20	2.796(6)	128.4

[a]At $x-1, y, z$.

Table 6. Torsional Angles (deg)

Atom1	Atom2	Atom3	Atom4	Angle
C4	O1	C1	C2	-25.7(7)
C1	O1	C4	O4	-77.9(6)
C1	O1	C4	C3	37.9(6)
C1	O1	C4	C5	161.5(5)
C6	O2	C2	C1	-168.5(6)
C6	O2	C2	C3	77.8(7)
C2	O2	C6	C7	-82.5(7)
C13	O3	C3	C2	57.2(7)
C13	O3	C3	C4	175.4(5)
C3	O3	C13	C12	47.4(8)
C14	O4	C4	O1	-54.0(7)
C14	O4	C4	C3	-167.1(6)
C14	O4	C4	C5	64.9(7)
C4	O4	C14	C15	128.6(6)
C4	O4	C14	C19	-109.1(7)
O1	C1	C2	O2	-117.1(6)
O1	C1	C2	C3	3.0(7)
O2	C2	C3	O3	-104.5(6)
O2	C2	C3	C4	134.1(5)
C1	C2	C3	O3	140.3(5)
C1	C2	C3	C4	18.8(6)
O3	C3	C4	O1	-160.3(5)
O3	C3	C4	O4	-42.8(7)
O3	C3	C4	C5	81.8(6)
C2	C3	C4	O1	-34.7(6)
C2	C3	C4	O4	82.8(6)
C2	C3	C4	C5	-152.6(5)
O1	C4	C5	O5	-65.7(7)
O4	C4	C5	O5	173.6(5)
C3	C4	C5	O5	50.2(7)
O2	C6	C7	C8	-97.8(7)
O2	C6	C7	C12	81.4(8)
C6	C7	C8	C9	178.6(7)
C12	C7	C8	C9	-0.6(10)
C6	C7	C12	C11	-178.9(6)
C6	C7	C12	C13	-0.4(9)
C8	C7	C12	C11	0.2(9)
C8	C7	C12	C13	178.7(6)
C7	C8	C9	C10	0.2(11)
C8	C9	C10	C11	0.6(11)
C9	C10	C11	C12	-0.9(11)
C10	C11	C12	C7	0.5(10)
C10	C11	C12	C13	-178.0(7)
C7	C12	C13	O3	-87.9(8)
C11	C12	C13	O3	90.5(7)
O4	C14	C15	C16	177.0(7)
C19	C14	C15	C16	54.5(9)
O4	C14	C19	C18	-175.6(6)
C15	C14	C19	C18	-54.3(8)
C14	C15	C16	C17	-55.0(10)
C15	C16	C17	C18	54.3(10)
C16	C17	C18	C19	-54.5(11)
C17	C18	C19	C14	54.7(9)

Table 7. Anisotropic Displacement Parameters (U_{ij}, Å^2)

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O1	0.0271(19)	0.025(3)	0.035(3)	0.0027(19)	-0.0051(17)	0.0019(19)
O2	0.051(3)	0.019(3)	0.031(3)	-0.0036(19)	-0.005(2)	0.004(2)
O3	0.0209(18)	0.042(3)	0.024(3)	-0.0067(18)	-0.0004(15)	0.0072(19)
O4	0.0186(18)	0.048(3)	0.022(3)	-0.002(2)	0.0043(15)	-0.005(2)
O5	0.022(2)	0.024(3)	0.059(3)	0.004(2)	0.011(2)	-0.002(2)
C1	0.052(4)	0.021(4)	0.032(4)	0.002(3)	-0.005(3)	-0.001(3)
C2	0.044(3)	0.023(4)	0.020(4)	0.007(2)	0.001(3)	-0.008(3)
C3	0.021(2)	0.022(4)	0.024(3)	0.002(2)	0.002(2)	0.002(2)
C4	0.013(2)	0.025(4)	0.025(3)	0.003(2)	0.002(2)	0.004(2)
C5	0.022(3)	0.025(4)	0.039(4)	-0.008(3)	0.002(2)	0.000(3)
C6	0.058(4)	0.026(4)	0.031(4)	-0.007(3)	-0.006(3)	-0.003(3)
C7	0.038(3)	0.018(4)	0.023(4)	-0.010(2)	-0.002(2)	-0.001(3)
C8	0.035(3)	0.035(5)	0.034(4)	-0.015(3)	0.004(3)	0.011(3)
C9	0.039(3)	0.046(5)	0.028(4)	-0.005(3)	0.007(3)	-0.004(3)
C10	0.060(4)	0.029(4)	0.028(4)	-0.001(3)	0.007(3)	-0.005(4)
C11	0.044(4)	0.024(4)	0.034(4)	-0.005(3)	-0.003(3)	0.004(3)
C12	0.026(3)	0.026(4)	0.019(3)	-0.007(2)	0.000(2)	0.003(3)
C13	0.027(3)	0.043(5)	0.020(3)	-0.005(3)	0.000(2)	0.002(3)
C14	0.028(3)	0.051(5)	0.023(4)	-0.005(3)	0.002(2)	-0.003(3)
C15	0.053(4)	0.058(6)	0.031(4)	0.006(4)	0.002(3)	-0.010(4)
C16	0.064(5)	0.088(9)	0.037(5)	-0.008(5)	0.008(4)	-0.022(6)
C17	0.054(5)	0.097(9)	0.038(6)	-0.017(5)	0.012(4)	-0.004(5)
C18	0.054(5)	0.071(8)	0.037(5)	-0.015(4)	0.001(3)	0.006(5)
C19	0.045(4)	0.060(6)	0.035(5)	-0.013(4)	0.002(3)	0.003(4)

The form of the anisotropic displacement parameter is:
$\exp[-2\pi^2(h^2a^{*2}U_{11} + k^2b^{*2}U_{22} + l^2c^{*2}U_{33} + 2klb^*c^*U_{23} + 2hla^*c^*U_{13} + 2hka^*b^*U_{12})]$

Table 8. Derived Atomic Coordinates and Displacement Parameters for Hydrogen Atoms

Atom	*x*	*y*	*z*	U_{eq}, Å^2
H5O	-0.5180	-0.0759	0.3174	0.052
H1A	-0.3520	0.2235	0.2654	0.042
H1B	-0.0964	0.2129	0.2042	0.042
H2	0.1223	0.2045	0.3430	0.035
H3	-0.1633	0.0283	0.4155	0.026
H5A	-0.2495	-0.1325	0.2061	0.034
H5B	-0.0653	-0.1642	0.2946	0.034
H6A	-0.1393	0.3112	0.5467	0.046
H6B	0.1168	0.2677	0.5002	0.046
H8	-0.3592	0.2105	0.6601	0.041
H9	-0.3955	0.0659	0.7659	0.045
H10	-0.1240	-0.0817	0.7516	0.047
H11	0.1867	-0.0807	0.6326	0.041
H13A	0.3558	0.1328	0.4822	0.036
H13B	0.4403	0.0161	0.5199	0.036
H14	-0.0617	-0.0218	0.0949	0.041
H15A	0.4294	0.0723	0.0797	0.057
H15B	0.1689	0.1366	0.0698	0.057
H16A	0.3471	0.1014	-0.0865	0.076
H16B	0.0733	0.0482	-0.0775	0.076
H17A	0.3426	-0.0809	-0.1458	0.076
H17B	0.5420	-0.0659	-0.0586	0.076
H18A	0.0526	-0.1605	-0.0410	0.065
H18B	0.3139	-0.2239	-0.0300	0.065
H19A	0.4065	-0.1349	0.1140	0.056
H19B	0.1332	-0.1881	0.1230	0.056