Synthesis of Highly Branched Chlorella Virus *N*-glycans

by

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Abstract

Chloroviruses are large, dsDNA-containing viruses that live in terrestrial waters. Like many viruses, they produce *N*-linked glycoproteins. However, the glycan structures on chlorovirus *N*-linked glycoproteins differ from all others identified to date. Chloroviruses, also differ from other viruses, in that they do not use host biosynthetic machinery to make their *N*-linked glycans; they do so using the carbohydrate-processing enzymes they produce. The structures of these unusual glycans were reported in 2013 by De Castro and coworkers at the University of Napoli in Italy. These complex molecules feature a core 'hyper-branched' fucose residue in which every hydroxyl group is glycosylated. Methods for the chemical synthesis of chlorovirus *N*-glycans would provide molecules for biological and biochemical studies leading to an increased understanding of their function and assembly.

This thesis will focus on developing synthetic approaches to access chlorovirus *N*-glycans and, in turn, provide new insights for the synthesis of the highly branched oligosaccharides. In Chapter 2, I describe the development of a synthetic approach to assemble these complex structures. The synthesis of the *N*-glycan isolated from ATCV-1, which contains the simplest structural motif of all chloroviruses, was accomplished using a "counter-clockwise" assembly sequence.

In Chapter 3, I detail the extension of this "counter-clockwise" assembly approach to two of the most complex chlorovirus *N*-glycans among those characterized. The synthesis of the nonasaccharide *N*-glycan from virus PBCV-1 was successful. However, the synthesis of the NY-2A$_1$ *N*-glycan, also a nonasaccharide, was not, due to the failure in introducing a tetrasaccharide unit onto the 'hyper-branched' fucose moiety. Based on this work, I conclude that the developed "counter-clockwise" assembly approach is applicable for the synthesis of most chlorovirus *N*-glycans reported to date, except NY-2A$_1$.

In Chapter 4, I report my work to synthesize various probes for understanding the biosynthesis of the PBCV-1 *N*-glycan. This involved the synthesis of molecules that are expected to be substrates for two glycosyltransferases (A064R and A075L).

Preface

Chapter 2 – Part of this chapter was published:

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Professor Lowary and I wrote the paper together. I was the only experimentalist on this work.

Chapter 3 and 4 – The work described in these chapters was done solely by me and have not been published.

Dedicated to

My Wife Ms. Yi Xie

and My Family!

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List of Abbreviations

$[\alpha]_D$	specific rotation (sodium D Line)
Å	Angstrom
Ac	acetyl
Ac_2O	acetic anhydride
AgOTf	silver trifluromethanesulfonate
All	allyl
AllBr	allyl bromide
app	apparent
Ar	aromatic
Asn	asparagine
ATCV-1	*Acanthocystis turfacea* chlorella virus 1
BDA	benzaldehyde dimethyl acetal
Bn	benzyl
BnBr	benzyl bromide
br s	broad singlet (NMR spectra)
Bz	benzoyl
BzCl	benzoyl chloride
CAN	ceric ammonium nitrate
Cbz	benzyloxycarbonyl
ClAc	chloroacetyl

CH_3OTf	trifluoromethanesulfonate
COSY	correlation spectroscopy
CSA	camphorsulfonic acid
C.neoformans	*Cryptococcus neoformans*
C. variabilis	*Chlorella variabilis*
d	doublet (NMR spectra)
DAST	diethylaminosulfur trifluoride
DCM	dichloromethane
ddd	doublet of doublet of doublet (NMR spectra)
DMAP	4-(dimethylamino)pyridine
DMF	dimethylformamide
DMP	dimethoxypropane
DNA	deoxyribonucleic acid
dq	doublet of quartet (NMR spectra)
dsDNA	double straned DNA
dt	doublet of triplet (NMR spectra)
DTBS	di-*tert*-butylsilyl
$DTBS(OTf)_2$	di-*tert*-butylsilyl bis(trifloromethanesulfonate)
E. coli	*Escherichia coli*
EDC·HCl	*N*-(3-dimethylaminopropyl)-*N*'-ethylcarbodiimide hydrochloride

ER	endoplasmic reticulum
ESI	electrospray ionization
Et_2O	diethyl ether
Et_3SiH	triethylsilane
EtOAc	ethyl acetate
EtOH	ethanol
Fuc	fucose
Gal	galactose
GC-MS	gas chromatography-mass spectrometry
Glc	glucose
GlcNAc	*N*-acetylglucosamine
HAD	hydrogen-bond-mediated aglycone delivery
HATU	1-[bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxide hexafluorophosphate
HMBC	heteronuclear multiple bond correlation
HRMS	high-resolution mass spectrometry
HSQC	heteronuclear single quantum coherence
Hz	hertz
$[Ir(COD)(CH_3Ph_2P)_2]PF_6$	(1,5-cyclooctadiene)bis (methyldiphenylphosphine)iridium (I) hexafluorophosphate

*i*Pr	isopropyl
LAH	lithium aluminum hydride
Lev	levulinoyl
LevOH	levulinic acid
m	multiplet (NMR spectra)
MALDI	matrix-assisted laser desorption/ionization
Man	mannose
Me	methyl
Me_3P	trimethylphosphine
NBS	*N*-bromosuccinimide
n-Bu_2SnO	di-*n*-butyltin oxide
NIS	*N*-iodosuccinimide
NMR	nuclear magnetic resonance
Nu	nucleophile
PBCV-1	*Paramecium bursaria* chlorella virus 1
Pico	picoloyl
PG	protecting group
Ph	phenyl
$PhC(OCH_3)_3$	trimethyl orthobenzoate
PMB	*p*-methoxybenzyl
PMP	*p*-methoxphenyl

PPh_3	triphenylphosphine
ppm	parts per million
PTFACl	2,2,2-trifluoro-*N*-phenylacetimidoyl chloride
p-TsOH	*para*-toluenesulfonic acid
py	pyridine
q	quartet (NMR spectra)
R_f	retention factor
RG II	rhamnogalacturonan II
Rha	rhamnose
RNA	ribonucleic acid
s	singlet (NMR spectra)
Ser	serine
TBAB	tetrabutylammonium bromide
TBAI	tetrabutylammonium iodide
TBS	*tert*-butyldimethylsilyl
TBSCl	*tert*-butyldimethylsilyl chloride
TBSOTf	*tert*-butyldimethylsilyl trifluoromethanesulfonate
t-Bu	*tert*-butyl
TEA	triethylamine
TFA	trifluoroacetic acid
TfOH	trifluoromethanesulfonic acid

THF	tetrahydrofuran
Thr	threonine
TLC	thin layer chromatography
TMS	trimethylsilyl
$TMSN_3$	azidotrimethylsilane
TMSOTf	trimethylsilyl trifluoromethanesulfonate
Tol	*p*-tolyl
$(TolS)_2$	*p*-tolyl disulfide
Tr	trityl
Ts	toluenesulfonyl
UDP	uridine diphosphate
Xyl	xylose
$ZrCp_2Cl_2$	bis(cyclopentadienyl)zirconium(IV) dichloride

Chapter 1

Introduction

1.1 Viruses

Viruses are widespread members of the biosphere[1,2] and can infect organisms from all three super kingdoms of life (bacteria, archaea and eukarya). Figure 1-1 shows a generic representation of a virus's structure,[3] which contains a genomic nucleic acid, typically a single type (either RNA or DNA), surrounded by a protein coat called a capsid. The capsid protects the viral genome from the environment and allows the virus to attach to specific receptors on the host cell. The genome and protective protein coat together form the nucleocapsid, which may have an icosahedral, helical or complex symmetry. The nucleocapsid is the simplest structure of a fully assembled virus (also known as a virion); however, some viruses are also enclosed by an outer envelope made of a lipid bilayer. In addition, many viruses also produce glycoprotein spikes on their outer envelopes.

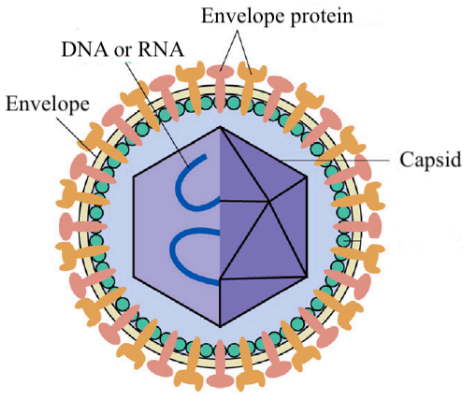


Figure 1-1: Generic representation of a virus's structure. Reprinted with permission from Elsevier: Molecular Virology of Human Pathogenic Viruses, Academic Press: New York, USA, **2017**; pp. 21–29.

The presence of viral surface glycoproteins is necessary for the recognition of the host via binding to the cell surface.[4] These glycoproteins can also facilitate the delivery of viral genetic material into host cells.[4] Moreover, these surface glycoproteins prevent attacks on the virus from the host immune system and the glycans on them influence their folding, stability and bioactivity.[5,6]

Typically, viral infections are highly specific for their hosts. This specificity results from the requirement that the virus hijacks the biosynthetic machinery of the host cell to replicate.[5,6] However, exceptions to this common belief are starting to emerge from viruses that are referred to as giant viruses. The genomes of these viruses encode many of their own enzymes and hence do not fully rely on host biosynthetic pathways for replication. Particularly important for my thesis is that giant viruses can produce their own carbohydrate-processing enzymes.

1.2 Chloroviruses

Giant viruses are defined as those that have large particle sizes and have genomes larger than 300 kilobase pairs.[7] They can encode many proteins not normally found in typical viruses such as HIV, Ebola or coronavirus.[8]

Chloroviruses, a member of the *Phycodnaviridae* family, belong to the giant virus group. They are dsDNA-containing viruses with an icosahedral shape that are found in freshwater sources. Their usual host is *Chlorella*-like green algae (Figure 1-2).[9–11]

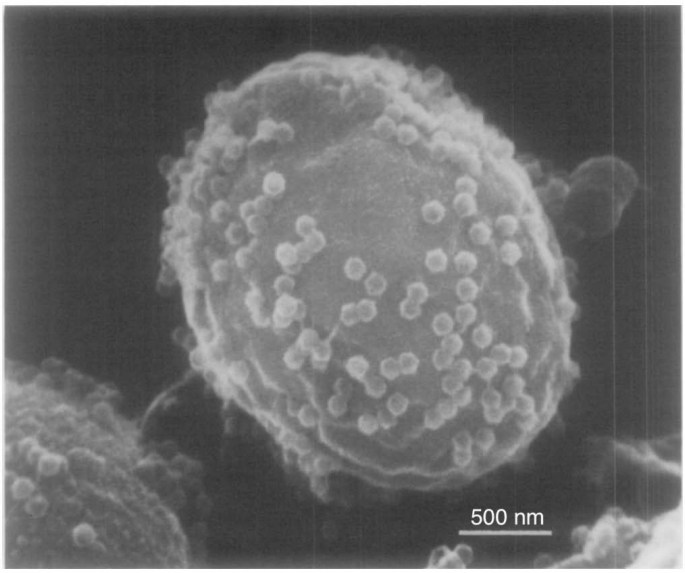


Figure 1-2: A scanning electron micrograph showing viral particles of chlorovirus attached to its algal host. Reprinted with permission from Elsevier: *Virology* **1984***, 138,* 341–346.

The algal hosts of chloroviruses are commonly found in nature to exist in symbiosis with protists, eukaryotic organisms different from animals, plants or fungi.[13] Examples of protists relevant to chlorovirus host are *Paramecium bursaria*, *Hydra viridis* or *Acanthocytis turfacea*.[11] For instance, in the protozoan *P. bursaria*, the algae live within the protist cell and provide it with nutrients via photosynthesis. In turn, the protozoan protects the algae. Figure 1-3 shows *P. bursaria* and its symbiont chlorella algae cells. Interestingly, during this symbiotic relationship, the algae are resistant to chlorovirus infection until there is a disruption of the relationship between it and the protist.

Figure 1-3: *Paramecium bursaria* and its symbiont chlorella algal cells. Reprinted with permission from The British Society for Plant Pathology: *Mol. Plant Pathol.* **2005**, *6*, 213–224.

Chloroviruses are classified into four groups based on their host specificity: 1) NC64A viruses infect *Chlorella variabilis* NC64A; 2) OSy viruses are specific for *Chlorella variabilis* Syngen 2–3; 3) Pbi viruses infect *Chlorella Pbi*; and 4) SAG viruses infect *Chlorella heliazae* 3.83.[11,15] The genomes of 43 chloroviruses infecting these four different hosts have been sequenced, assembled and annotated.[16–21] Some of these viruses encode genes thought to be involved in manipulating carbohydrates including enzymes involved in: 1) sugar nucleotide synthesis; 2) polysaccharide biosynthesis; and 3) the synthesis of glycans attached to viral capsid proteins.[11,22] In addition, it is believed that the glycosylation of viral proteins occurs independently of the algal endoplasmic reticulum (ER) and Golgi apparatus.[22]

All these characteristics make the chloroviruses unusual microorganisms. Because the *P. bursaria* chlorella virus 1 (PBCV-1) is the most studied, it will be used to describe the chlorovirus infection cycle.

1.3 *Paramecium bursaria* chlorella virus 1

PBCV-1 was initially isolated in 1982 by Van Etten and co-workers.[23] It is a large icosahedral virus that replicates in *Chlorella variabilis*, an algae[22,24] that is normally a symbiont with *P. bursaria*. PBCV-1 has a structure consisting of a dsDNA genome, surrounded by a protein core, a lipid bilayer membrane, and an outer icosahedral capsid shell (Figure 1-4B).[10,25–27]

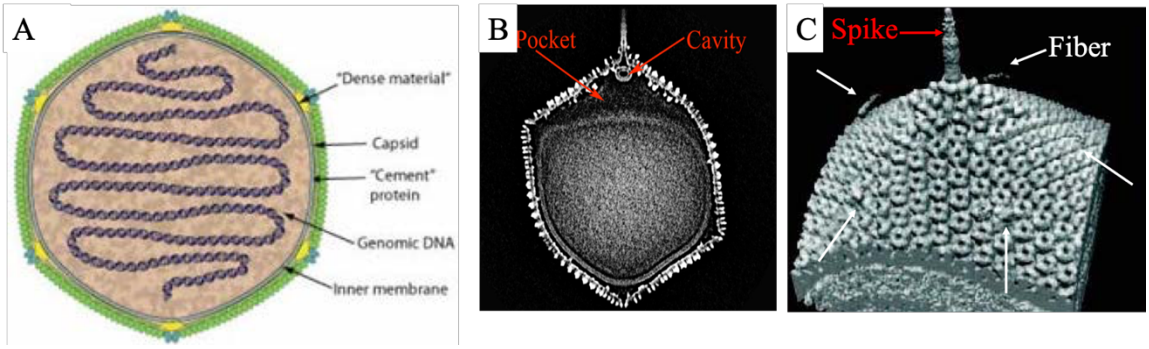


Figure 1-4: A) Schematic structure of the PBCV-1 virion; B) electron micrograph of PBCV-1; C) surface view of the PBCV-1 spike structure and fibers. Image A and C: reprinted with permission from Elsevier: *Trends Plant Sci.* **2012**, *17*, 1–8; image B: reprinted with permission from PNAS: *Proc. Natl. Acad. Sci. U.S.A.* **2011**, *108*, 14837–14842.

One of the PBCV-1 vertices has a bacteriophage-like spike structure that extends outward and a few external fibers that protrude from some of the capsid proteins (Figure 1-4C).[9,27] It is believed that PBCV-1 attaches specifically to *C. variabilis* using this spike structure and the external fibers.

1.3.1 The PBCV-1 life cycle

There are six steps needed for PBCV-1 replication: attachment, penetration, uncoating, replication, assembly, and release. The viral spike protein appears to provide the first contact with the algal cell wall. In micrographs showing the initial binding of the virus to algal cells, the orientation of the spike is always facing towards the cell wall (Figure 1-5A).[9,28] Figure 1-5B shows that the virus is also attached to the cell wall by hair-like fibers,[9,28] suggesting that the fibers probably aid in holding the virus onto the cell wall.

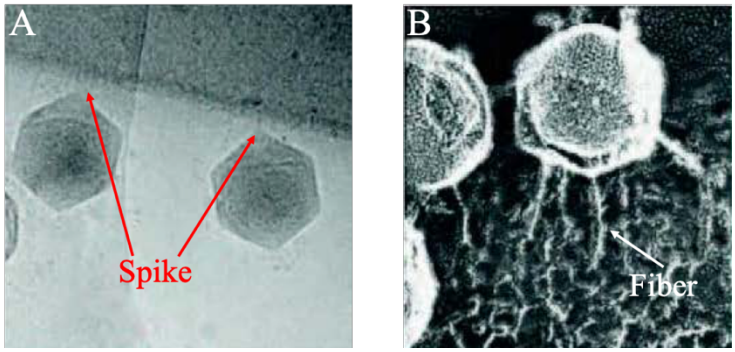


Figure 1-5: A) Initial attachment of PBCV-1 to *C. variabilis*, reprinted with permission from PNAS: *Proc. Natl. Acad. Sci. U.S.A.* **2011**, *108*, 14837–14842; B) PBCV-1 attached to the cell wall. Reprinted with permission from American Society for Microbiology: *Microbiol. Rev.* **1991**, *55*, 586–620.

After the attachment of PBCV-1 to the algae, the degradation of the algal cell wall occurs immediately at the binding site using a viral enzyme that is likely stored in the cavity of the spike (Figure 1-4B).[10,28,12] When the cell wall is degraded, the inner membrane in the virus fuses with the algal membrane, producing a tunnel through which viral DNA and some viral proteins are ejected into the cytoplasm of the algae. This process leads to an empty viral capsid being attached to the cell surface (Figure 1-6).

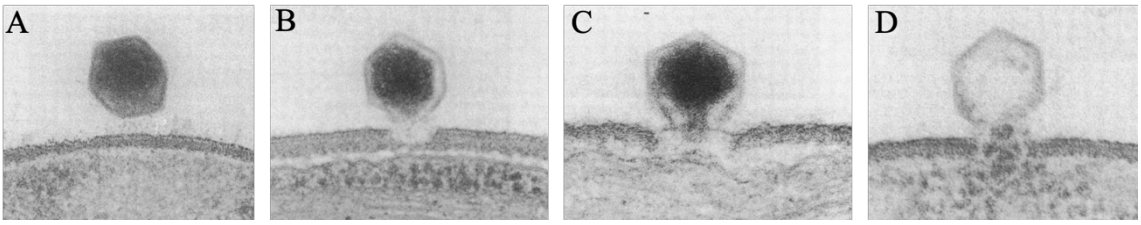


Figure 1-6: Infection of *C. variabilis* by PBCV-1. A) Viral particle in close proximity to the algae; B) Attachment of PBCV-1 onto the cell wall; C) Digestion of the cell wall; D) Delivery of the viral DNA and proteins. Reprinted with permission from Elsevier: *Virology* **1984**, *138*, 341–346.

Chloroviruses do not appear to produce an RNA polymerase[29] and thus they cannot transcribe their DNA into RNA. Therefore, once it is present in the algal cytoplasm, the PBCV-1 DNA genome is thought to move to the host nucleus where it can be transcribed into RNA and also be replicated. Newly produced viral DNA and RNA are released into the cytoplasm where formation of the virus capsid occurs. The DNA is next packaged into the virus capsid, and the PBCV-1 progeny viruses are released by cell lysis.[24,30,31]

A schematic diagram of the PBCV-1 replication cycle is shown in Figure 1-7.[9] Although extensively studied, many steps remain unclear. With regard to my thesis, which focuses on chlorovirus *N*-linked glycans, it is important to note that the glycosylation of viral proteins occurs independently of the ER and Golgi apparatus.[11] This is different in comparison to other viruses. Identifying the glycan structure of the major capsid protein could potentially help in understanding its function during the life cycle of the virus and its biosynthetic pathway.

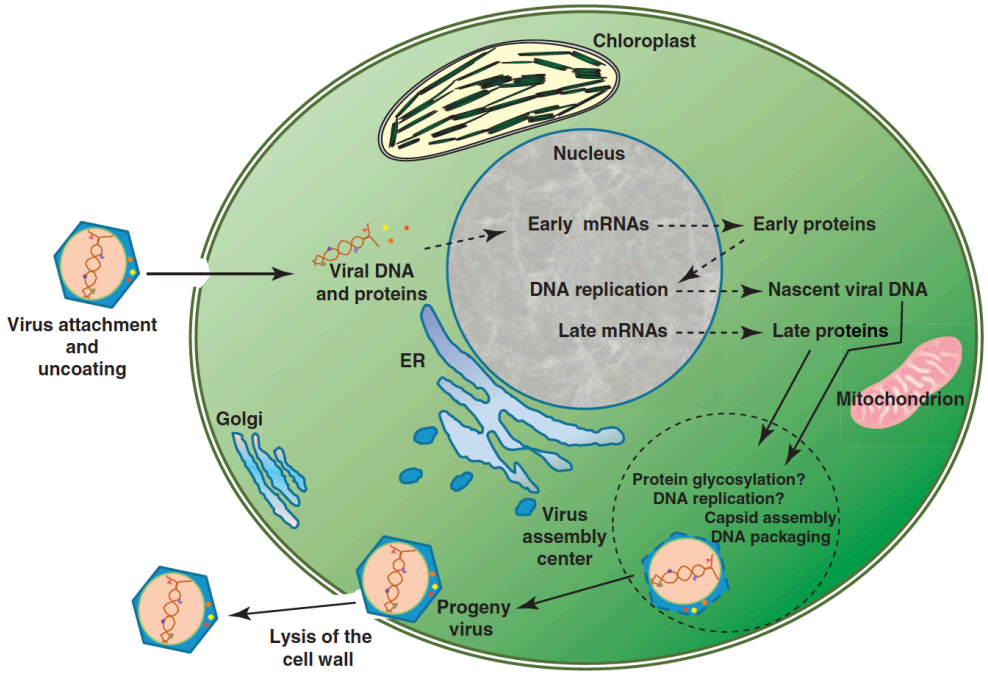


Figure 1-7: Proposed replication cycle of PBCV-1. (→) Known events; (⇢) hypothesized events. Reprinted with permission from Elsevier: *Trends Plant Sci.* **2012**, *17*, 1–8.

1.3.2 *N*-Glycan structure on PBCV-1 major capsid protein

N-Glycosylation of proteins is widespread and is found in organisms including bacteria, viruses, plants, archaea, and mammals.[32–36] Many viruses have structural proteins that are glycosylated.[22] Viral surface glycoproteins are also essential for promoting the recognition of host cells and can help the virus to avoid the immune system of the host. In addition, the presence of *N*-linked glycans is crucial for protein folding, stability, and bioactivity.

Viruses usually hijack host glycosyltransferases and glycosidases, located in the ER and Golgi apparatus, to make their *N*-glycans.[22] As a result, the structure of the glycans on virus glycoproteins are host-specific and they resemble those produced by the host. The only way to modify the glycan structure is to grow the virus in a different host or to mutate the genes of the viral protein to change the glycosylation site.

In contrast, chloroviruses produce enzymes to glycosylate proteins, including their major capsid protein (Vp54).[11] In other words, the glycosylation pattern of the major capsid protein is virus-specific, not host-specific. Because of this, the prediction was that the glycan structure on the PBCV-1 major capsid protein would be different from all other organisms. In 2013, De Castro and co-workers reported the structures of the PBCV-1 Vp54 *N*-glycans using a combination of gas chromatography-mass spectrometry (GC-MS), NMR spectroscopy, and MALDI mass spectrometry techniques.[37] The glycan structure contains 8–10 monosaccharide residues connected in a highly branched manner. In particular, they contain a fully-substituted fucose residue, referred to as ‘hyper-branched’ (Figure 1-8). A total of four glycoforms are present, which arise from the two monosaccharides that are

found non-stoichiometrically: L-arabinofuranose and D-mannose. The major species is a nonasaccharide containing D-mannose but lacking L-arabinofuranose.

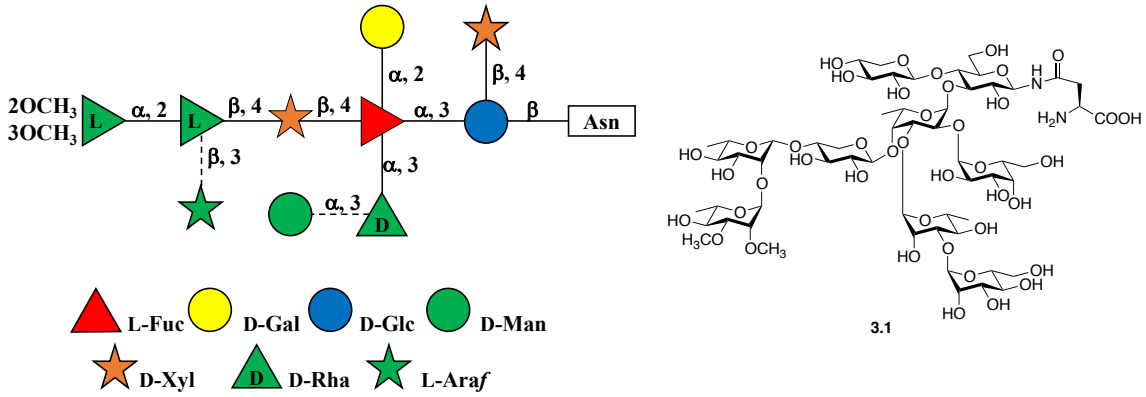


Figure 1-8: Structure of *N*-glycans of the major capsid protein Vp54 from chlorovirus PBCV-1 in both pictorial and line-bond form. Dashed lines represent nonstoichiometric residues.

The PBCV-1 *N*-glycan has a number of interesting features in addition to the highly branched structure and 'hyper-branched' fucose residue. First, it does not resemble any other *N*-linked glycan reported to date (although other chloroviruses produce analogous structures as detailed below). Second, the carbohydrate residue linked to the protein is *β*-glucose, not *β*-*N*-acetylglucosamine, which is present in all *N*-linked glycoproteins produced by viruses that infect mammals. Finally, the Asn-residues that are glycoslyated are not found in the Asn-X-(Thr/Ser) sequon,[37] which is required for eukaryotic and prokaryotic *N*-glycosylation.

1.3.3 *N*-Linked glycans from chloroviruses share a common core structure

De Castro and co-workers later determined[38–40] the structures of *N*-glycans for the capsid proteins of all four chlorovirus types. These are shown in Figure 1-9 and are grouped based on their host specificity.

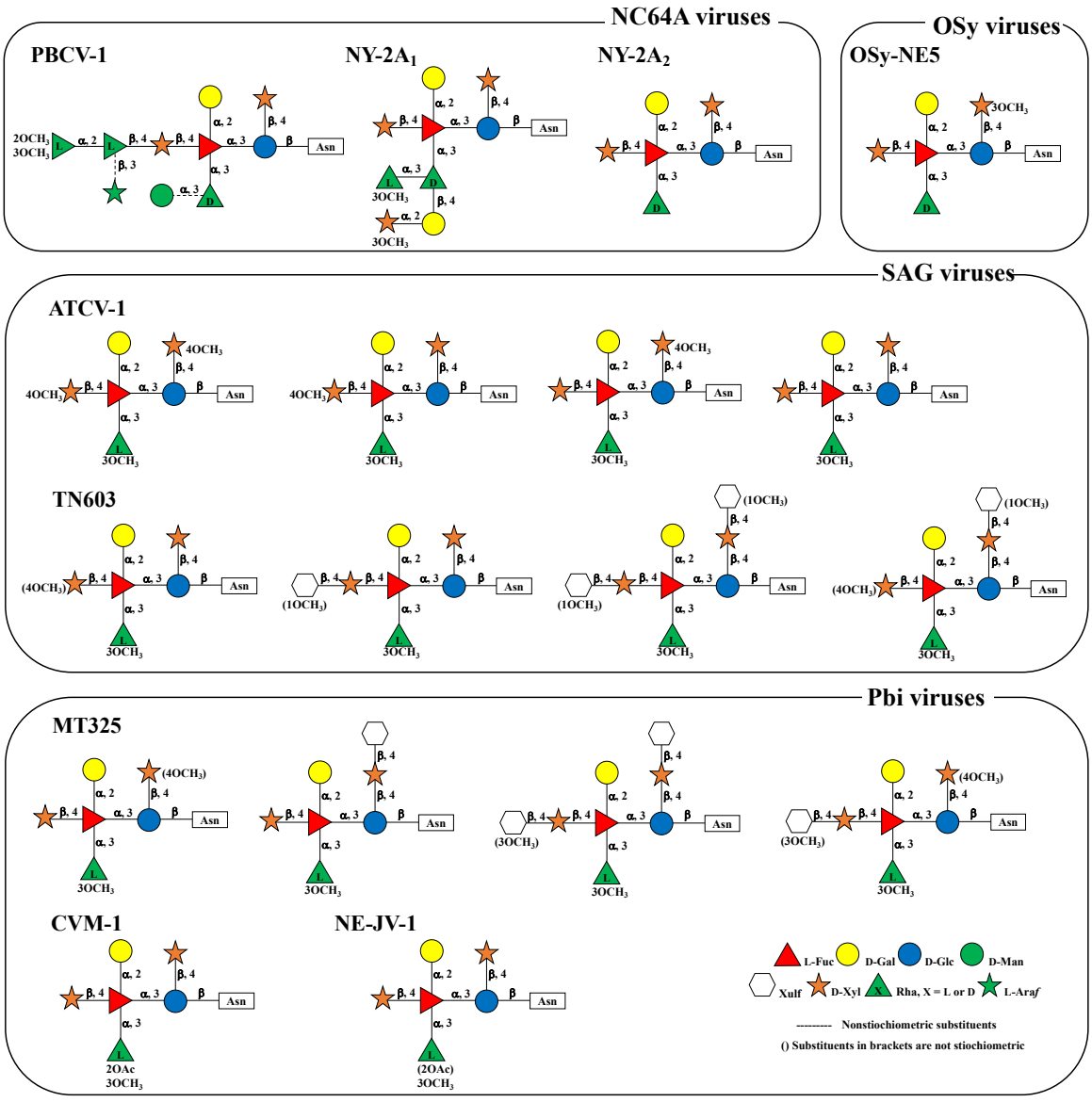


Figure 1-9: Structures of capsid protein *N*-glycans from all four chlorovirus types; monosaccharides are in the pyranose form unless otherwise indicated.[38–40]

As displayed in Figure 1-10, the core structure of all of chlorovirus *N*-glycans consists of a pentasaccharide with a β-glucose linked asparagine (Asn) residue, a 'hyper-branched' α-fucose residue, two β-xylose residues (one proximal and one distal), and an α-galactose. This conserved core is shown in the red box. In all of the structures, the O-3 position of the fucose moiety is linked to a rhamnose. This residue is semi-conserved because the configuration (D- or L-) differs depending on the virus. More complex structures (Figure 1-10) are produced by elaboration of this core motif through the addition of additional sugar residues, including the rare pentulose xylulose, and/or capping with methyl groups.

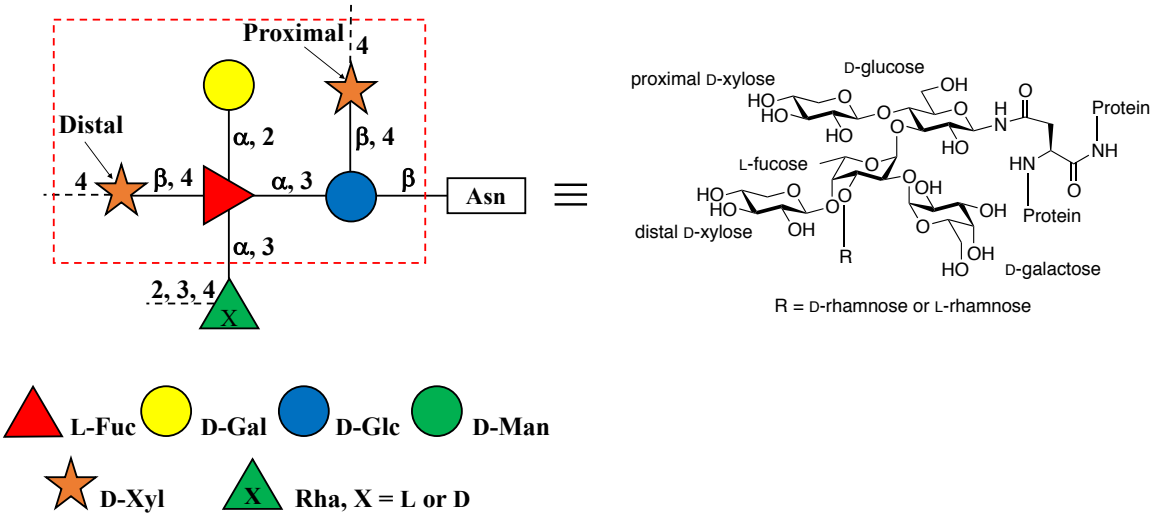


Figure 1-10: Conserved pentasaccharide core of chlorovirus *N*-glycans in both pictorial and line-bond form.

If one considers the complexity of the branching pattern on the 'hyper-branched' fucose residue, some pattern emerge. First, the O-4 of the fucose unit is usually attached to a monosaccharide, and in some cases to a disaccharide. The only exception is the PBCV-1

N-glycan, which contains either a tri- or tetrasaccharide at this position. Second, in the majority of the structures, the C-3 hydroxyl group of the fucose is linked to a monosaccharide, with two exceptions: PBCV-1 and NY-2A$_1$, which contain a disaccharide and tetrasaccharide, respectively, at this position. Finally, the O-2 of the fucose is glycosylated with a single α-galactose residue in all of the chloroviruses *N*-glycans. Thus, of all of the chlorovirus *N*-glycan structures that have been identified, the PBCV-1 and NY-2A$_1$ strains produce the two most structurally complex derivatives.

1.3.4 Chlorovirus PBCV-1 encoded glycosyltransferases

The discovery of these *N*-glycans has prompted interest in understanding how their biosynthesis occurs, including identifying and characterizing the proteins involved. By comparison of the gene sequence of known glycosyltransferases with the PBCV-1 genome, Van Etten and co-workers postulated that the organism produces six putative glycosyltransferases: A064R (638 amino acids), A111/114R (860 aa), A219/222/226R (677 aa), A473L (517 aa), A546L (396 aa), and A075L (280 aa).[11,22,41] The genes that encode these enzymes are scattered throughout the viral genome and, based on their sequence, most are predicted to be soluble. Thus, a hypothesis is that the glycosylation process occurs in the host cytoplasm and that the six enzymes are responsible for the assembly of either most, if not all, of the nine (or ten) monosaccharides present in the major capsid protein glycan.

According to the genetic and glycan structural evidence from 21 antigenic variants of PBCV-1, the proteins produced from genes *a064r*, *a075l*, *a071r* and *a111/114r* have been predicted.[42] The gene *a064r* is proposed to encode a 639-amino acid protein with three domains: Domain 1 is a *β*-L-rhamnosyltransferase, Domain 2 is an *α*-L-rhamnosyltransferase and Domain 3 is a methyltransferase (Figure 1-11). The *a071r gene* has been proposed to encode a glycosyltransferase that attaches the rhamnose unit onto the fucose.[42] Both *a075l* and *a111/114r* are conserved among all 43 chloroviruses characterized to date.[11,42] This observation suggests that the proteins produced from these genes are involved in the assembly of the core glycan structure. It was suggested that gene *a075l* encodes a *β*-xylosyltransferase and gene *a111/114r* encodes a protein that contains at least three domains to assemble the tetrasaccharide core as shown in the red box in Figure 1-11.

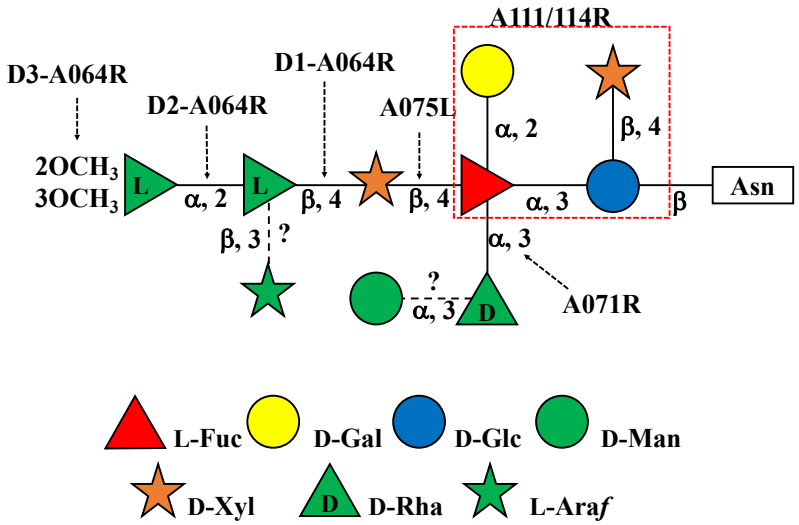


Figure 1-11: PBCV-1 *N*-glycan structure with the predicted glycosyltransferases involved in glycosidic bond formation.

1.3.5 Summary

In conclusion, PBCV-1 produces a capsid protein with an unusual *N*-glycan. Eight different chloroviruses, representing the four chlorovirus groups, produce related structures and all share a common pentasaccharide core structure containing a 'hyper-branched' fucose unit that is glycosylated at the three hydroxyl groups. PBCV-1 encodes its own glycosyltransferases, which have been suggested to function not in the ER or the Golgi of the host, but rather in the cytoplasm. The functions of four glycosyltransferases encoded by PBCV-1 have been proposed, but not demonstrated. The next challenge is to confirm these predictions, which requires access to potential substrates for the enzyme. Typically, it is difficult to isolate pure compounds from natural complex glycan mixtures. Moreover, the quantities obtained from natural sources are often too limited for biochemical experiments. Thus, the chemical synthesis of these *N*-glycans is essential. Such heavily branched carbohydrate residues are rare in nature and have thus not been the subject of significant synthetic investigations. The next section will describe strategies to access these unusual carbohydrates.

1.4 Synthesis of 'hyper-branched' oligosaccharides

In developing a route to chlorovirus *N*-glycans, I envisioned that the primary challenge would be the preparation of the 'hyper-branched' fucose residue. Thus, in this section, I will review some known synthetic methodologies to access the heavily branched carbohydrate molecules (**1.1**–**1.4**, Figure 1-12).

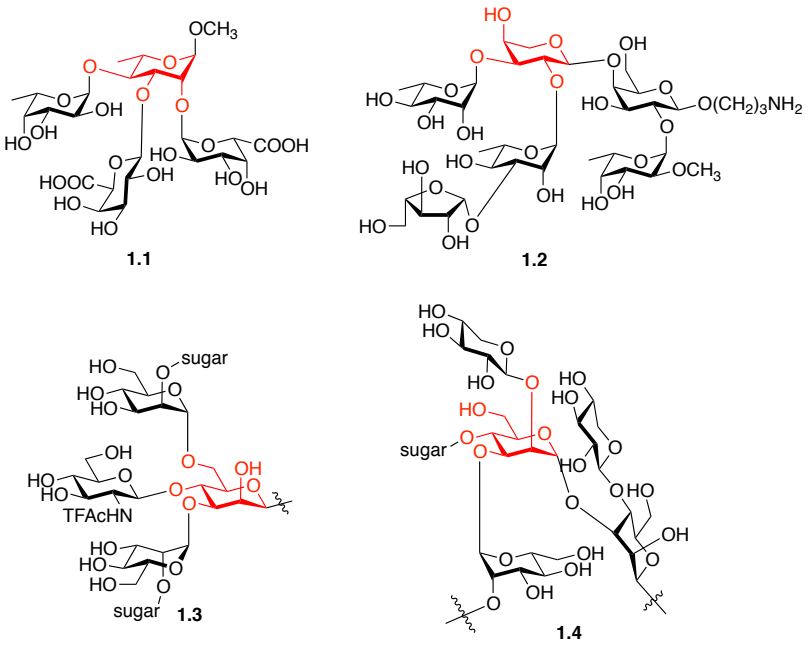
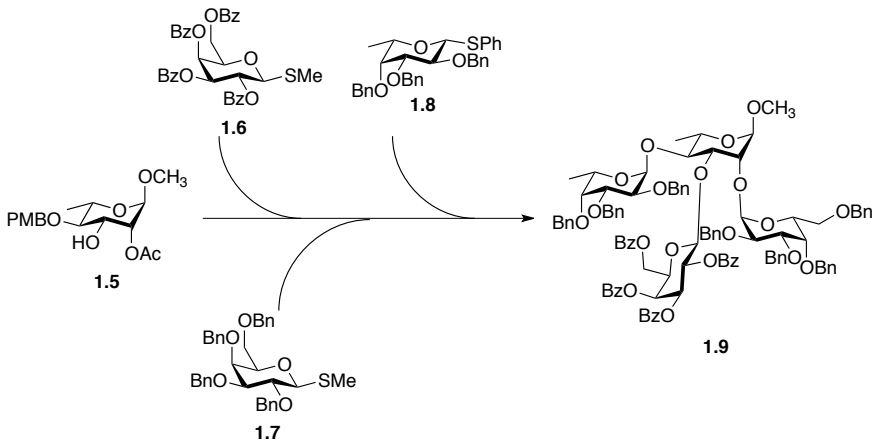


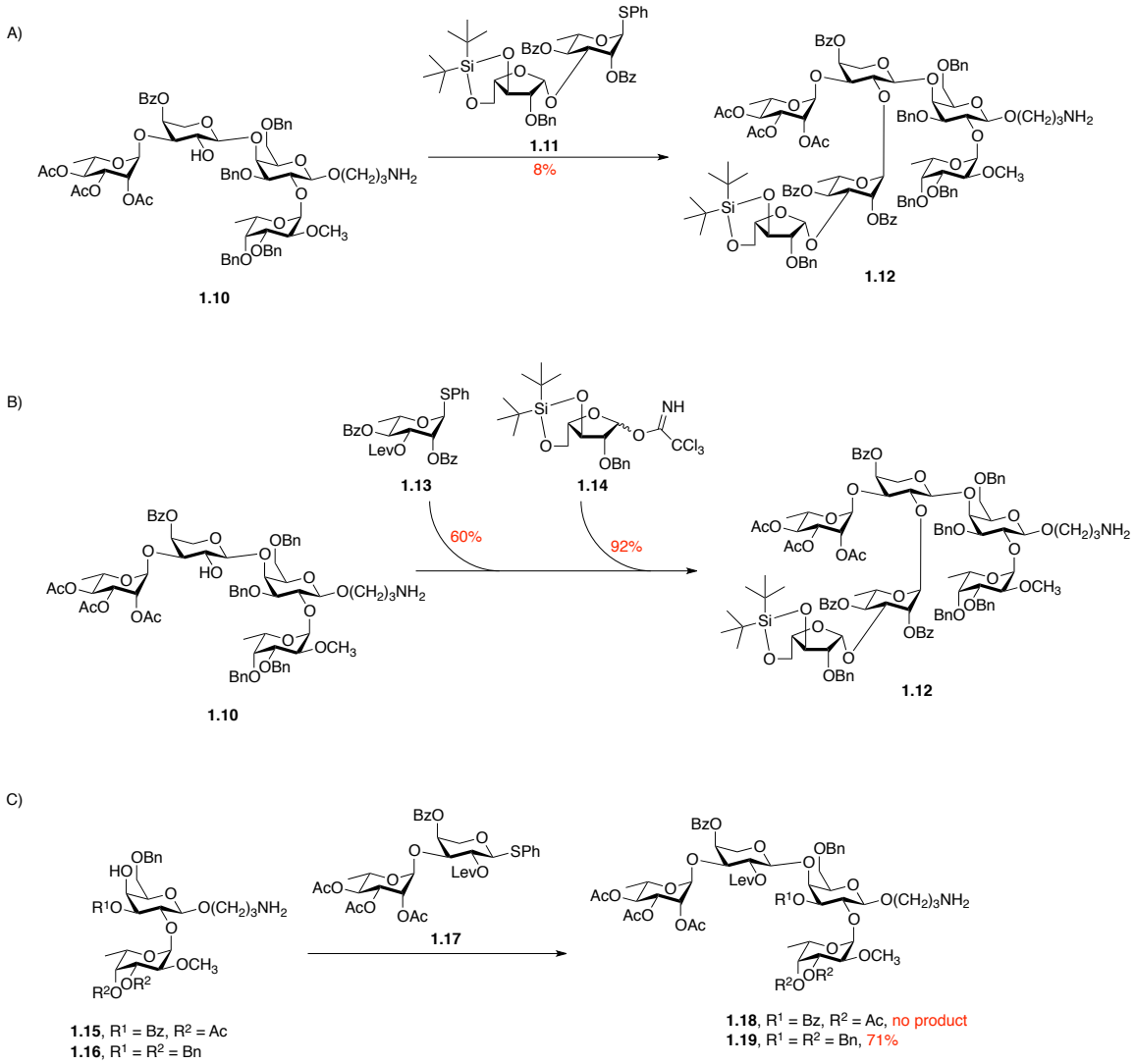
Figure 1-12: Structures of highly branched carbohydrate residues **1.1**–**1.4**, which have been previously synthesized.

Rhamnogalacturonan II (RG II) is a highly complex plant polysaccharide that is composed of four structurally different oligosaccharides referred as side chains A–D. One of these, side chain A, contains a rhamnose residue in which every hydroxyl group is glycosylated. In 2005, Field and co-workers synthesized the tetrasaccharide fragment **1.1** of the RG II side chain A (Figure 1-12).[43] The glycosylation sequence involved the addition of monosaccharides (**1.6**–**1.8**) first to the C-3 hydroxyl group on acceptor **1.5**, followed by the C-2 hydroxyl group and finally the C-4 hydroxyl group (Scheme 1-1). The sequence was designed mainly to simplify and reduce the number of protecting group manipulations.



Scheme 1-1: Synthesis of tetrasaccharide **1.9** related to side chain A of RG II.

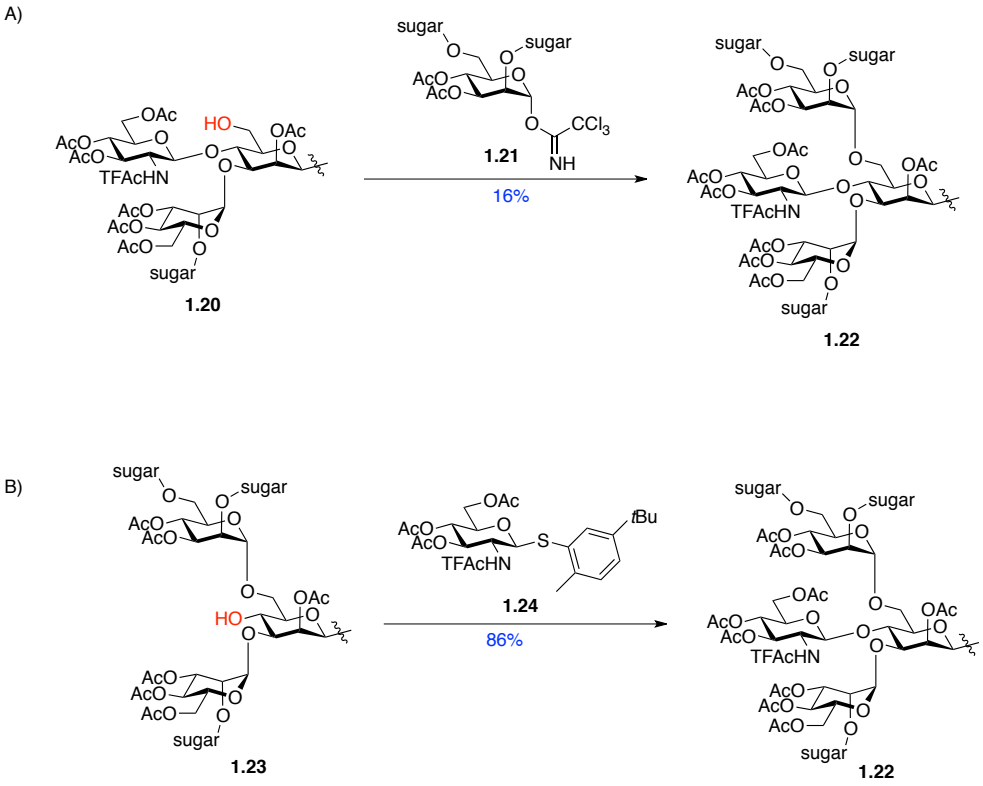
In addition, Boons and co-workers prepared hexasaccharide **1.2**, which was derived from RG II side chain B (Figure 1-12).[44] This is a good example to show that the addition sequence can influence the reaction outcome. The incorporation of a disaccharide moiety **1.11** on the C-2 hydroxyl group of tetrasaccharide **1.10** gave only an 8% yield (Scheme 1-2A) of the hexasaccharide product. In contrast, a stepwise addition of monosaccharides (**1.13** and **1.14**) to this position was more efficient (Scheme 1-2B). Moreover, this example shows that the reactivity of a glycosyl acceptor can be tuned through the choice of protecting groups (Scheme 1-2C). The incorporation of disaccharide donor **1.17** onto C-4 hydroxyl group of galactose disaccharide acceptor **1.15** containing all ester groups was unsuccessful. However, after replacing them with benzyl ethers (**1.16**), the reaction gave the desired product **1.19** in 71% yield.



Scheme 1-2: A) Synthesis of **1.12** through a 4+2 glycosylation; B) Synthesis of **1.12** through a stepwise addition of monosaccharides; C) Synthesis of tetrasaccharide **1.19** showing the effect of protecting groups on the acceptor.

The synthesis of two other heavily branched oligosaccharides (**1.3** and **1.4**, Figure 1-12) also presented some unexpected results during late stage glycosylations. As shown in the synthesis of oligosaccharide **1.22** (Scheme 1-3), the addition of the *N*-trifluoroacetyl-

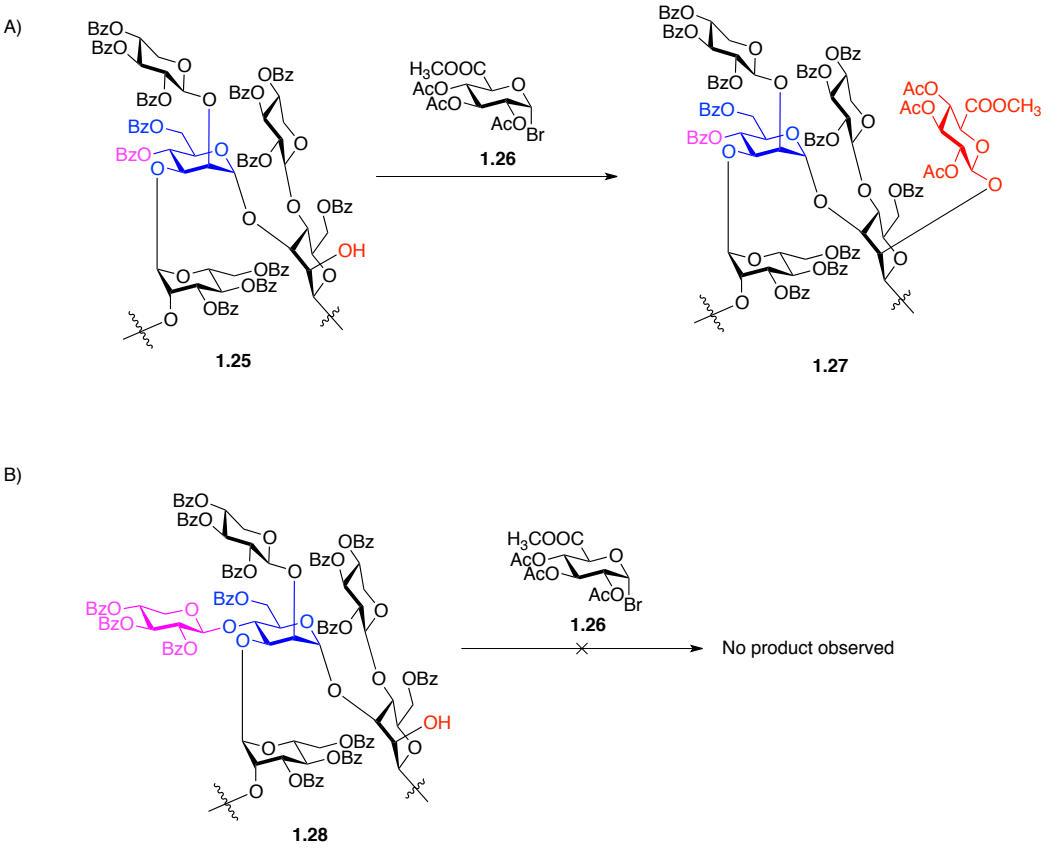
glucosamine residue prior to the construction of the α-(1→6)-mannosidic linkage provided the desired compound in only 16% yield (Scheme 1-3A).[45] However, if the addition sequence was performed in the opposite manner, the yield increased to 86% (Scheme 1-3B).[46,47] This result reveals that the glycosylation sequence for highly branched bisected *N*-glycans strongly impacts the reaction outcome.



Scheme 1-3: Synthesis of highly branched oligosaccharide **1.22** through A) final reaction with **1.21**; B) final reaction with **1.24**.

In addition, Kong and co-workers observed that a change in the substitution of an oligosaccharide, not even on the sugar residue undergoing glycosylation, can significantly affect the coupling reaction. For instance, as shown in Scheme 1-4, the attempted synthesis

of the 2,3,4-trisubstituted mannose residue in **1.27** from the *Cryptococcus neoformans* serotype C capsular polysaccharide indicated that the substitution on the C-4 position of the blue mannose residue (Bz vs. a xylose residue, shown in magenta) affects the reactivity of the C-2 hydroxyl group one residue away (shown in red).[48,49] The hypothesis was that the xylose moiety (**1.28**) changed the acceptor conformation, in turn increasing the steric hindrance around the reacting hydroxyl group. Similar effects have also been observed by Oscarson and co-workers in the stereoselectivity of glycosylation in similar systems.[50]



Scheme 1-4: The effect of xylose residue on the glycosylation of donor **1.26**.

The examples above show that the structural complexity and diversity of heavily branched oligosaccharide leads to synthetic challenges in their preparation. However, they also provide some insight into how the synthesis of chlorovirus *N*-glycans could be achieved. For example, the selection of protecting groups will not only influence glycosylation reactivity, but also the stereoselectivity and deprotection efficiency and this should be considered together during the design of building blocks. In addition, the fully substituted fucose residue requires protecting groups for each hydroxyl group, which must be compatible with each other and be tolerant under various reaction conditions. Moreover, steric congestion around the fucose hydroxyl groups will increase as the molecule is assembled and this will lead to a decrease in reactivity for the corresponding acceptor. As a result, I expect that a specific glycosylation sequence will be crucial for the assembly of chlorovirus *N*-glycans.

1.5 Overview of thesis research

The overall goal of my thesis research is to develop an approach for the chemical synthesis of chlorovirus *N*-glycans and apply it to a series of target molecules. The first part of this thesis will focus on the development of a versatile strategy to access these structures; I anticipate these studies will also provide insights into the synthesis of highly congested oligosaccharides in general. The second part of this thesis will focus on developing probes to help unravel the pathways involved in chlorovirus *N*-glycan

biosynthesis. Eventually, the results of these studies will allow comparison between chemical and biochemical synthesis of these complex carbohydrates.

1.5.1 Research objective 1 – Development of a chemical approach to synthesize chlorovirus *N*-glycans

The structure of chlorovirus *N*-glycans is species specific and they all share a common pentasaccharide consisting of D-glucose, L-fucose, D-galactose and two D-xylose moieties (Figure 1-10).[38] The addition of either a D-rhamnose or L-rhamnose forms a hexasaccharide core that is semi-conserved. Given their highly branched structure, I hypothesized that the construction of these targets would require a certain assembly sequence. This research objective contains two aims: 1) development of a synthetic approach to the simplest of these compounds, and 2) investigation of its feasibility on more complex chlorovirus *N*-glycans.

Aim 1. The first aim is developing a synthetic route to chlorovirus *N*-glycans. In Chapter 2, I describe my work on the synthesis of the *N*-glycan isolated from *Acanthocystis turfacea* chlorella virus 1 (ATCV-1, Figure 1-14). This hexasaccharide structure is the simplest of all chlorovirus *N*-glycans.

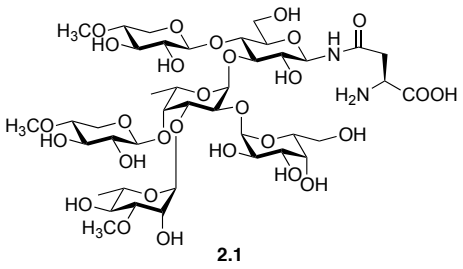


Figure 1-13: Chlorovirus *N*-glycan **2.1** from strain ATCV-1.

Aim 2. The second aim is to apply the route developed in Chapter 2 to the preparation of more complex *N*-glycan targets. In Chapter 3, I will describe my work towards the synthesis of the PBCV-1 *N*-glycan and the NY-2A$_1$ *N*-glycan (Figure 1-15). Both of these structures are nonasaccharides, and are the most complex of the chlorovirus *N*-glycans reported to date. I believe that if the synthesis of these two complex glycans is possible using my approach, it will be a reliable method to make any chlorovirus *N*-glycan.

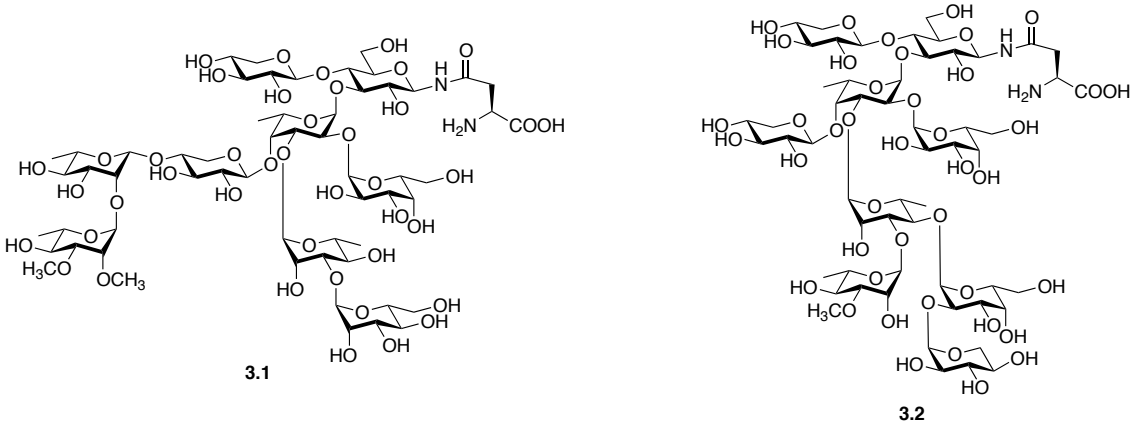


Figure 1-14: Structure of *N*-glycan from virus PBCV-1 (**3.1**) and from virus NY-2A$_1$ (**3.2**).

1.5.2 Research objective 2 – Synthesis of PBCV-1 N-glycan biosynthetic probes

In Chapter 4, I will describe my work to synthesize various probes for understanding the biosynthesis of the PBCV-1 *N*-glycan, with a focus on two glycosyltransferases (A064R and A075L) for which functions have been proposed. Four oligosaccharides were designed as probes for the A064R glycosyltransferase and another four as probes for the A075L glycosyltransferase. Biochemical assays using these compounds are being performed by our collaborator, Dr. Cristina De Castro, at the University of Napoli in Italy.

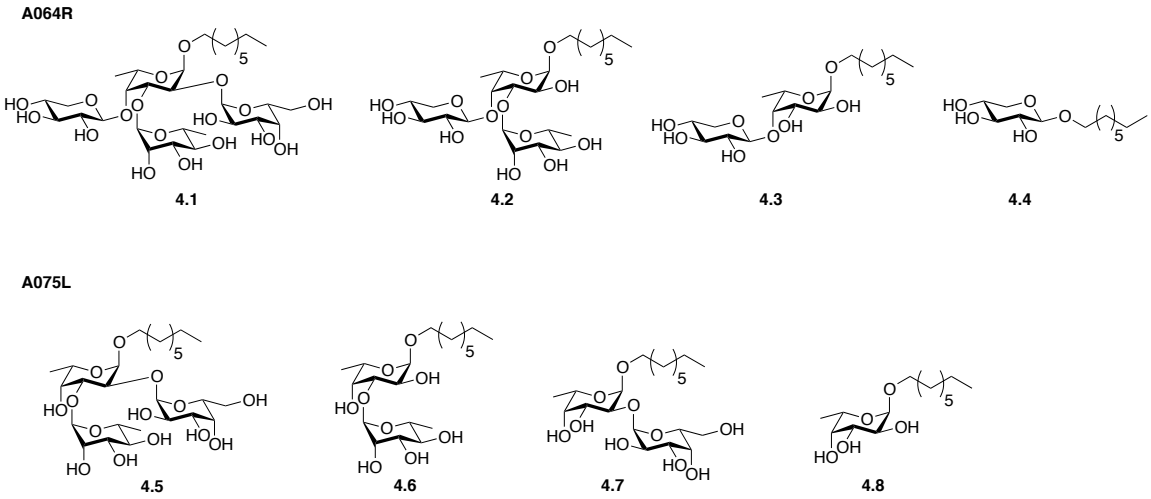


Figure 1-15: Structure of the synthetic probes **4.1**–**4.8** inspired from PBCV-1 *N*-glycan.

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Chapter 2

Synthesis of the Highly Branched Hexasaccharide Core of Chlorella Virus *N*-linked Glycans

A portion of this Chapter has been published:

Lin, S.; Lowary, T. L. *Chem. Eur. J.* **2018**, *24*, 16992–16996.

2.1 Background

Chloroviruses are large icosahedral viruses found in freshwater sources.[1–3] They are part of the family *Phycodnaviridae*, which infect algae.[1–3] Recently, the DNA of the *Acanthocystis turfacea* chlorella virus 1 (ATCV-1) was isolated from the throat swabs of healthy human adults participating in a study involving measurements of cognitive functioning.[1] This discovery was the first report of a human infection by a chlorovirus. Cognitive tests were performed on 92 individuals and the results indicated that the presence of ATCV-1 might affect memory and spatial awareness. With this finding in mind, a series of behaviour tests were performed on mice. The studies revealed that ATCV-1 could potentially decrease performance in recognition memory and cognitive assessments. The presence of the virus DNA could also change gene expression in the brain, possibly leading to disruption of pathways involved in learning and memory. These changes in gene expression could also impact the immune response in the brain due to infection by the virus. Later, Petro and co-workers[5] also confirmed that the ATCV-1 infection could lead to brain inflammation resulting in damage. In 2016, De Castro and co-workers[6] characterized the structure of *N*-linked oligosaccharides present in chlorovirus ATCV-1. The structure of this *N*-linked glycan is a mixture of four different compounds **2.1**–**2.4** (Figure 2-1), sharing the same oligosaccharide scaffold and methylated in a non-stoichiometric fashion at the C-4 hydroxyl group of both xylose moieties. In the discussion below, the xylose attached to the glucose is referred to as proximal and whereas the xylose attached to the fucose is referred to as distal.

As discussed in Chapter 1, the structure of chlorella virus *N*-linked glycans is species-specific, but the core region is conserved in the *N*-glycans of all the chloroviruses studied to date.[6–8] Compound **2.1** is one of the simplest structures reported; it consists of six neutral monosaccharide residues: D-glucose, L-fucose, 4-OMe-D-xylose (two units), 3-OMe-L-rhamnose and D-galactose, organized in a highly branched fashion. This chapter describes the first chemical synthesis of chlorella virus *N*-linked glycans, using **2.1** as a target.

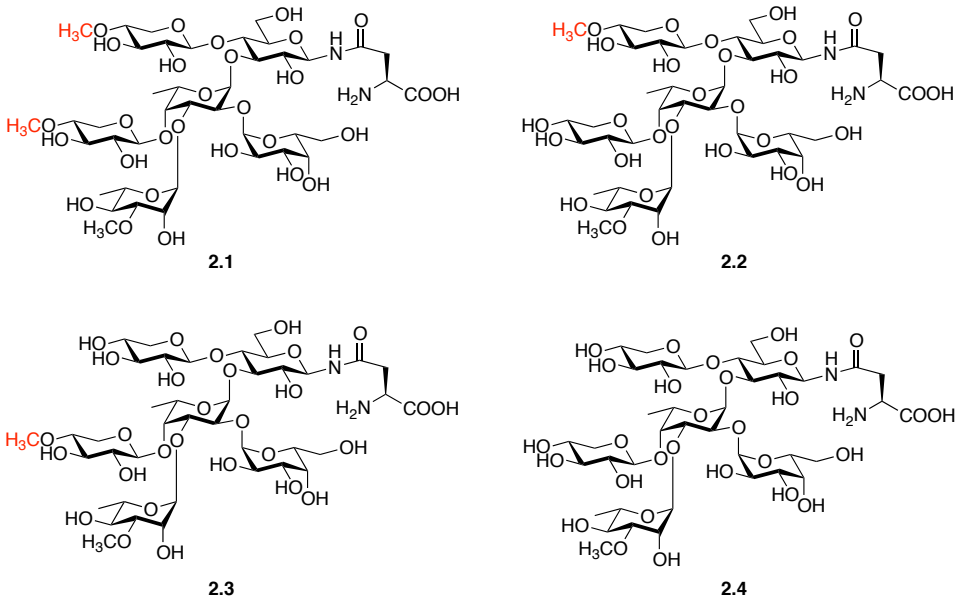


Figure 2-1: Structure of *N*-glycans **2.1**–**2.4** from ATCV-1.

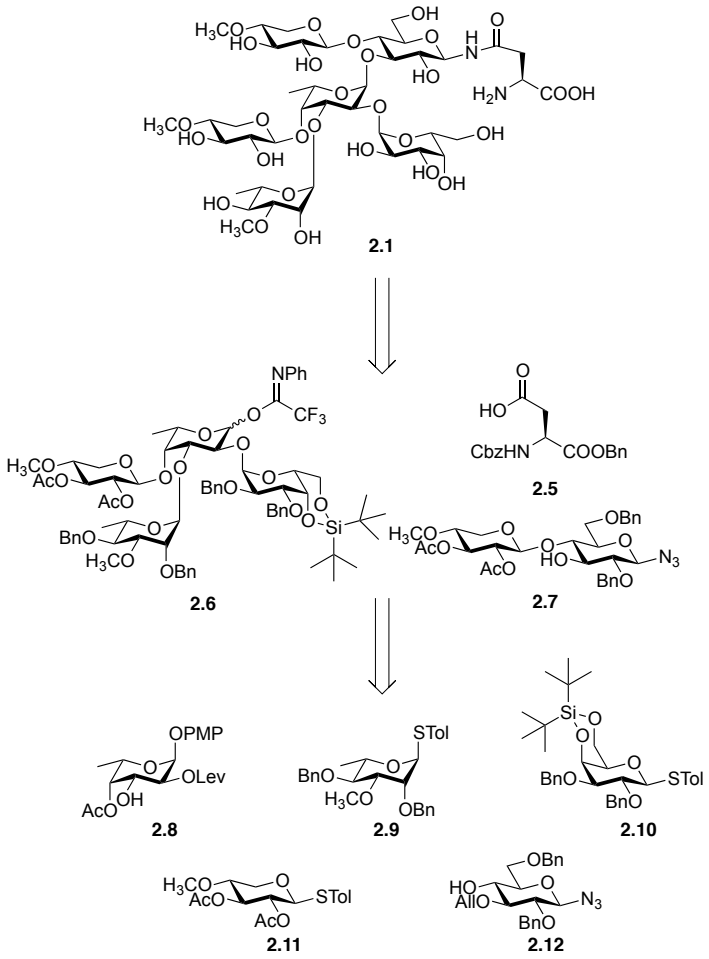
2.2 Results and discussions

2.2.1 Attempts to synthesize the ATCV-1 hexasaccharide through a convergent 4+2 approach

In developing a route to hexasaccharide **2.1**, I envisioned that the primary challenge would be the preparation of the 'hyper-branched' fucose residue in which every hydroxyl

group is glycosylated. The synthesis of a similar 'hyper-branched' rhamnose residue had been successful as described in Chapter 1 (Figure 1-12).[9] Thus, the first approach I studied was a convergent 4+2 strategy (Scheme 2-1), involving the preparation of a tetrasaccharide donor **2.6** and a disaccharide acceptor **2.7**. This approach had less number of steps required for manipulating protecting groups.

Protecting groups can have significant influence on the reactivity of glycosyl donors and acceptors. They can also affect the stereoselectivity of glycosylation and deprotection efficiency. Thus, there were some basic principles I used to design the building blocks: 1) thioglycoside donors were used because of their stability to a wide range of conditions for protecting group manipulations as well as glycosylations;[10] thioglycosides can also be activated under various conditions, including extremely mild conditions;[11] 2) building blocks with orthogonal protecting groups should be achieved in the least number of synthetic steps; 3) esters were only used to induce stereoselective glycosylation or as a temporarily protecting group, otherwise ethers were chosen to improve reactivity; 4) the introduction of an anomeric azido group, instead of an amide, on the glucose moiety could prevent the formation of glycosyl imidate by-products during the glycosylations. More detailed reasons for why I chose different protecting groups will be discussed later.



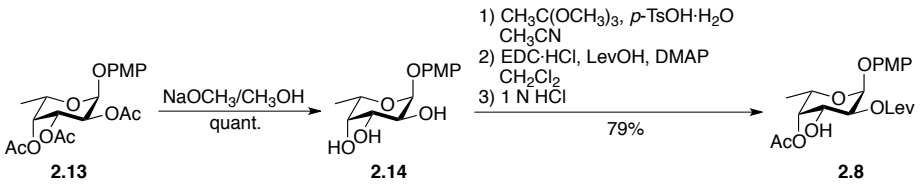
Scheme 2-1: Retrosynthetic analysis of hexasaccharide **2.1** through a 4+2 convergent strategy.

With these plans in mind, the tetrasaccharide donor **2.6** could be synthesized from four different monosaccharides **2.8**–**2.11**. The disaccharide acceptor **2.7** could be obtained by a glycosylation of the glucose acceptor **2.12** and xylose donor **2.11**. In total, five different carbohydrate building blocks (**2.8**–**2.12**) are needed.

One advantage for the design of these building blocks was that even if this approach was shown to be unsuccessful, the majority of them could still be used in other assembly strategies. But, if the 4+2 glycosylation were successful, this would provide a hexasaccharide that could be further elaborated via azide reduction, coupling with the commercially- available protected amino acid **2.5**, and global deprotection to afford the desired target **2.1**.

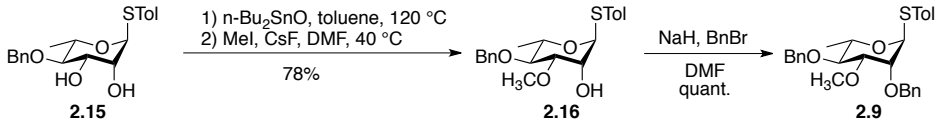
2.2.1.1 Synthesis of building blocks 2.8–2.12

The synthesis of **2.8** (Scheme 2-2) started from PMP glycoside **2.13**, which was prepared from L-fucose in two steps as reported in the literature.[12] Subsequent Zemplén deacetylation was performed to generate the desired triol **2.14** in quantitative yield. Reaction of **2.14** with trimethyl orthoacetate and *p*-toluenesulfonic acid gave the 3,4-*O*-orthoester intermediate. The C-2 hydroxyl group was then directly protected as a levulinate ester and subsequent regioselective opening of the orthoester under acidic conditions provided the desired acceptor **2.8** in 79% yield. The use of the PMP glycoside, as opposed to a thioglycoside, was to avoid aglycon transfer[11] during the construction of tetrasaccharide **2.6**. The 4-methoxyphenyl group could be converted to the corresponding acetimidate donor at a late stage. A levulinate ester was used on O-2 as it could be removed selectively in the presence of the 4-O acetyl group.



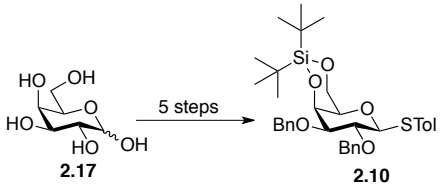
Scheme 2-2: Synthesis of fucose acceptor **2.8**.

The synthesis of rhamnose donor **2.9** (Scheme 2-3) began with compound **2.15**, which was prepared from L-rhamnose in six steps as reported by Mukhopadhyay and co-workers.[13] The selective methylation was done in two steps. First, the dibutylstannylene acetal was formed by reacting diol **2.15** with dibutyltin oxide at reflux with a Dean–Stark apparatus. After concentration, methyl iodide and cesium fluoride in DMF were added at 40 °C to afford the desired O-3 regioiosmer **2.16** in 78% yield. The structure was confirmed by the correlation between H-3 and methyl group in the HMBC spectrum. The hydroxyl group was then benzylated to give the rhamnose donor **2.9** in quantitative yield. Although an ester group on C-2 hydroxyl group was absent, the formation of a α-glycosidic linkage was expected to be predominant because of the anomeric effect.[14]



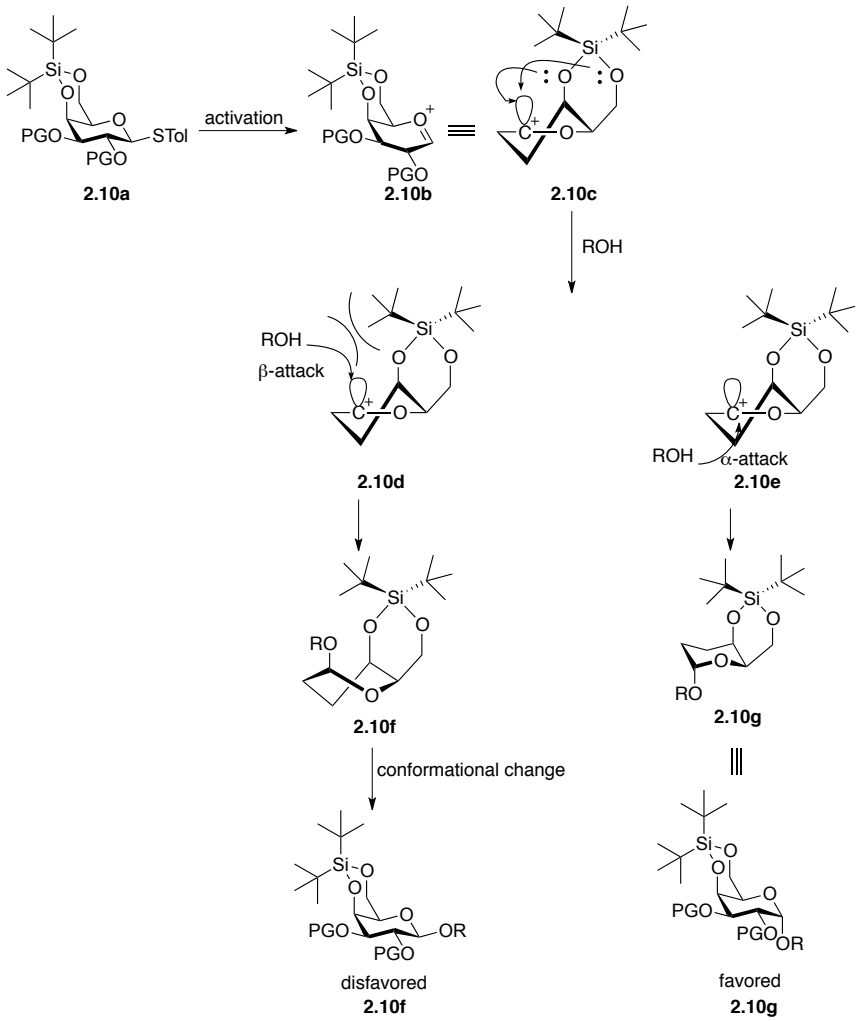
Scheme 2-3: Synthesis of rhamnose donor **2.9**.

Galactose donor **2.10** was obtained from D-galactose (**2.17**) over five steps according to a procedure reported in the literature.[15] The di-*tert*-butylsilylene (DTBS) group was chosen to promote α-selectivity during the glycosylation reaction as explained in the next paragraph (Scheme 2-5).[16]



Scheme 2-4: Synthesis of galactose donor **2.10**.

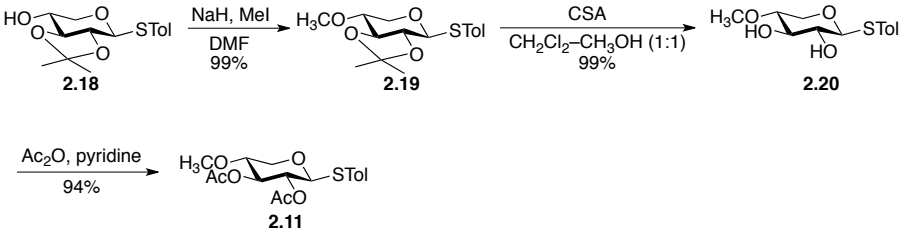
Upon activation of the thioglycoside, the lone pair electrons on O-4 and O-6 (**2.10c**) are proposed to donate electron density into the empty *p*-orbital of the anomeric carbon, which results in the stabilization of the oxocarbenium intermediate. The incoming nucleophile could attack from either the β-face (**2.10d**) or the α-face (**2.10e**). However, due to the presence of the bulky *tert*-butyl groups, nucleophilic attack from the β-face is blocked. Moreover, the attack via the β-face would proceed through a twist-boat-like conformer, which would need to undergo a conformational change to afford the β-product **2.10f**. On the other hand, α-face attack would proceed through a chair-like conformer **2.10g**.[16] Hence, nucleophilic attack occurs predominantly via the pathway leading to the α-galactosidic linkage.



Scheme 2-5: Proposed mechanism of DTBS-directed α-galactosylation.[16]

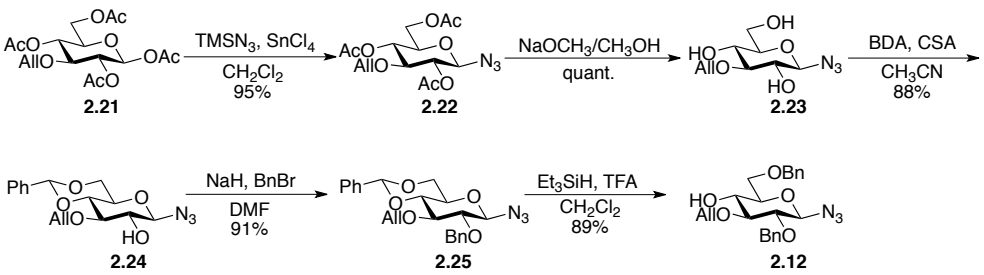
The preparation of xylose donor **2.11** (Scheme 2-6) started with acetonide **2.18**, which was synthesized from D-xylose in five steps as previously reported.[17] The free hydroxyl group was methylated to afford **2.19** in 99% yield. Subsequent removal of the isopropylidene ketal was performed using camphorsulfonic acid in a dichloromethane–methanol (1:1) solution to give diol **2.20** in 99% yield. Acetylation of the diol with acetic anhydride in pyridine afforded the xylose donor **2.11** in 94% yield. Acetate protecting

groups were selected for three reasons: 1) no purification was required following installation; 2) they could be used as a directing group for β-glycosylation; 3) they could be easily deprotected later.



Scheme 2-6: Synthesis of xylose donor **2.11**.

The synthesis of acceptor **2.12** was achieved starting with compound **2.21** (Scheme 2-7), which was prepared from D-glucose over five steps as reported in the literature.[18] Compound **2.21** was first treated with azidotrimethylsilane and tin(IV) chloride to generate the desired glycosyl azide **2.22** in 95% yield. Subsequent deprotection of the acetyl groups upon treatment with sodium methoxide gave **2.23** in quantitative yield. The C-4 and C-6 hydroxyl groups were protected as a benzylidene acetal to provide **2.24** in 88% yield and the benzylation of **2.24** generated **2.25** in 91% yield. Finally, the regioselective opening of the benzylidene acetal was performed to afford the desired glucose acceptor **2.12** in 89% yield. The allyl ether was used as a temporary protecting group as it is compatible with the benzyl ether and azido groups, and it was stable during the manipulation of protecting groups and glycosylations.



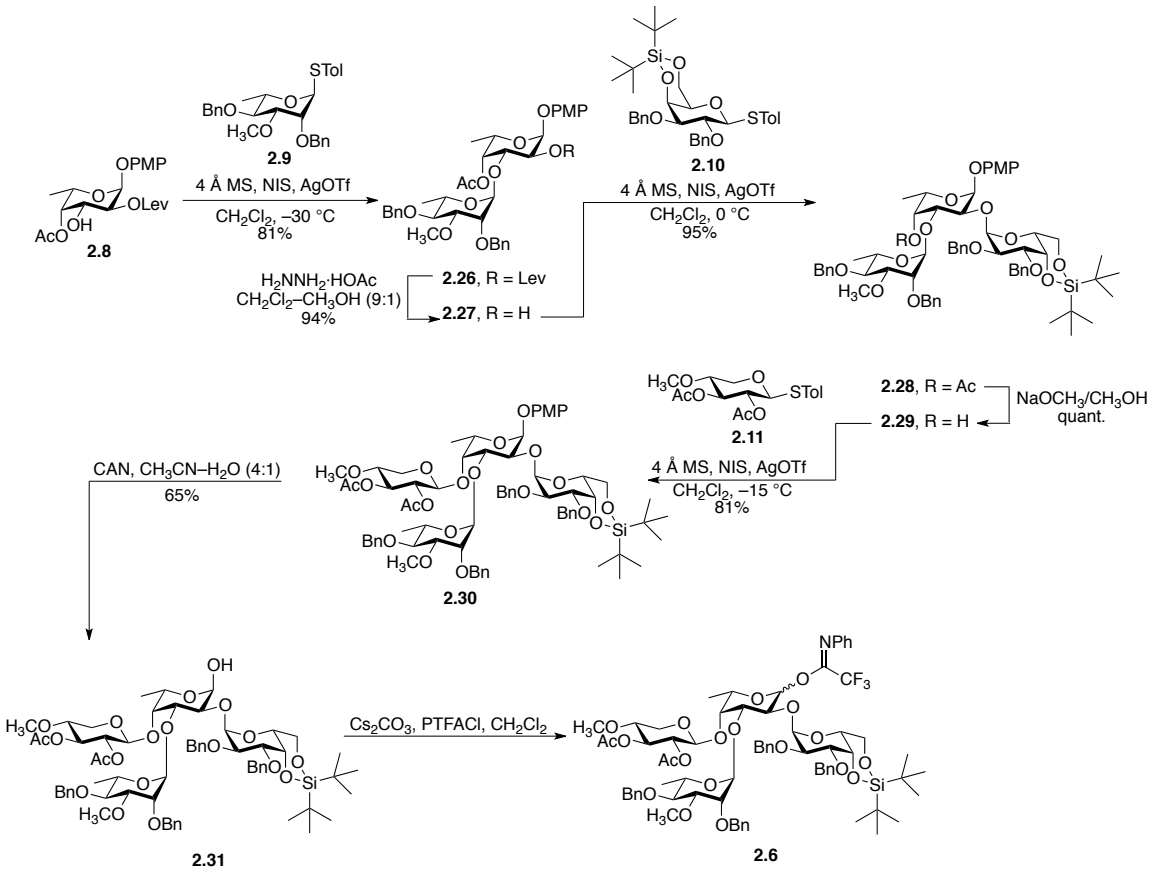
Scheme 2-7: Synthesis of glucose acceptor **2.12**.

2.2.1.2 Synthesis of tetrasaccharide donor 2.6 and disaccharide acceptor 2.7

With all the necessary building blocks constructed, the tetrasaccharide donor **2.6** and disaccharide **2.7** were assembled. The synthesis of tetrasaccharide **2.6** (Scheme 2-8) started with the glycosylation of glycosyl acceptor **2.8** with donor **2.9**; disaccharide **2.26** was generated in 81% yield with exclusive α-selectivity. The α-selectivity was confirmed by the coupling constant between Rha-H-1 and Rha-C-1 ($^1J_{C\text{-}H}$ = 171.9 Hz) in the ^{1}H coupled HSQC spectrum. The stereoselectivity was proposed to be driven by the anomeric effect. Subsequent chemoselective removal of the levulinoyl group with hydrazine acetate, followed by glycosylation with **2.10** gave trisaccharide **2.28** in 89% yield over the two steps and with an excellent α-selectivity. The di-*tert*-butylsilylene group induced high α-selectivity as expected,[16] and the stereochemistry was confirmed by the coupling constant between Gal-H-1 and Gal-C-1 ($^1J_{C\text{-}H}$ = 169.3 Hz) in the ^{1}H coupled HSQC spectrum. The acetate group was then deprotected under Zemplén conditions to give alcohol **2.29** in quantitative yield. The glycosylation of acceptor **2.29** and xylose donor **2.11** was performed and tetrasaccharide **2.30**, containing a highly branched fucose residue, was obtained in 81%

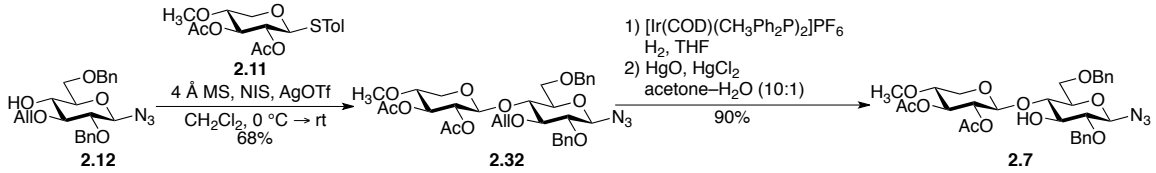
yield. The β-selectivity was promoted by neighbouring group participation of the C-2 acetoxy group; the stereochemistry was confirmed by the coupling constant between Xyl-H-1 and Xyl-H-2 ($^3J_{H1\text{-}H2}$ = 6.8 Hz). The successful synthesis of tetrasaccharide **2.30** indicated that the construction of a 'hyper-branched' fucose residue containing a small functional group (a PMP group) at the reducing end was not a problem.

The removal of the 4-methoxyphenyl group was accomplished using ceric ammonium nitrate to afford the corresponding hemiacetal **2.31** in 65% yield. Conversion of **2.31** to the acetimidate donor **2.6** was achieved by treatment with 2,2,2-trifluoro-*N*-phenylacetimidoyl chloride and cesium carbonate.



Scheme 2-8: Synthesis of tetrasaccharide donor **2.6**.

With tetrasaccharide donor **2.6** in hand, I prepared disaccharide **2.7** as illustrated in Scheme 2-9. An NIS/AgOTf-promoted glycosylation of glucose acceptor **2.12** with xylose donor **2.11** resulted in the expected disaccharide **2.32** with exclusive β-selectivity. The β-stereochemistry was supported by the coupling constant of Xyl-H-1 to Xyl-H-2 ($^3J_{H1\text{-}H2}$ = 7.8 Hz). The product was then subjected to cleavage of the allyl ether to afford alcohol **2.7** in 61% yield over two steps.

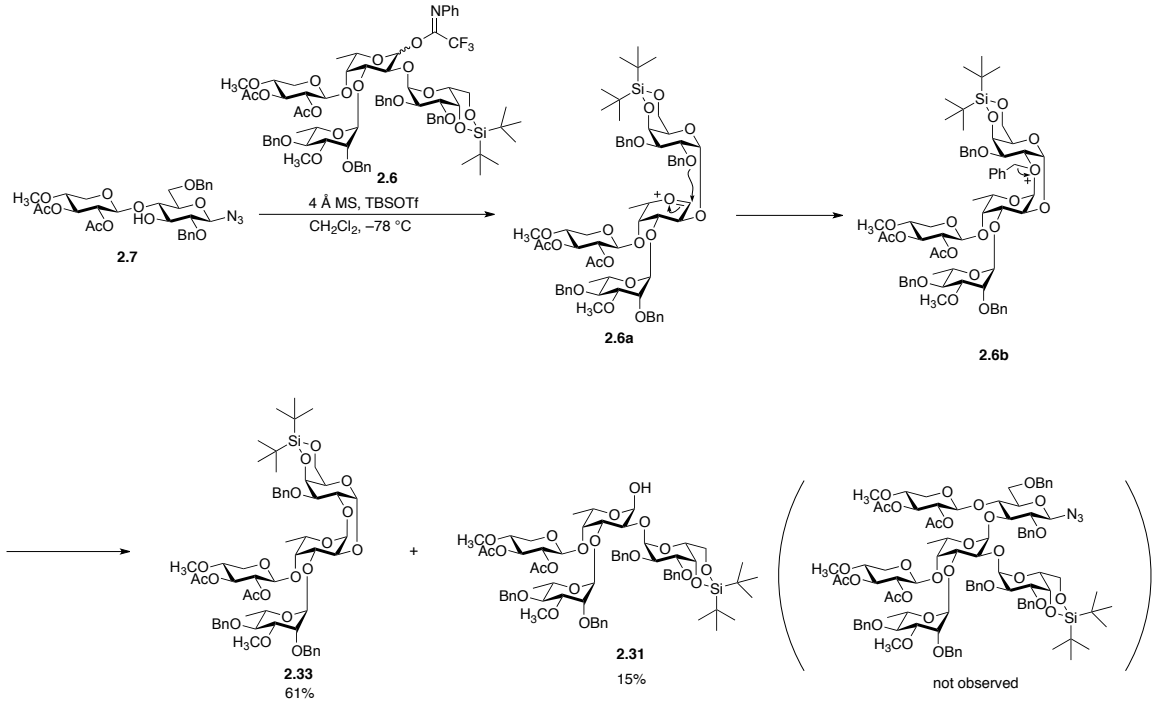


Scheme 2-9: Synthesis of disaccharide acceptor **2.7**.

2.2.1.3 Attempted synthesis of hexasaccharide

My first glycosylation attempt was to couple donor **2.6** with acceptor **2.7** (Scheme 2-10). Activation of the *N*-phenyl-trifluoroacetimidate donor **2.6** was achieved using TBSOTf at –78 °C, but the desired hexasaccharide was not formed. Unexpectedly, product **2.33**, containing a fused tricyclic ring system, was obtained in 61% yield, together with a 15% yield of the hydrolyzed imidate donor **2.31**. The structure of **2.33** was suggested by the coupling constant of Fuc-H-1 to Fuc-H-2 ($^3J_{H1\text{-}H2}$ = 3.6 Hz), and the correlation between Fuc-H-1 and Gal-C-2 in the HMBC spectrum. The high-resolution mass spectrum was also consistent with this structure. I postulated that the failure of the 4+2 glycosylation was due

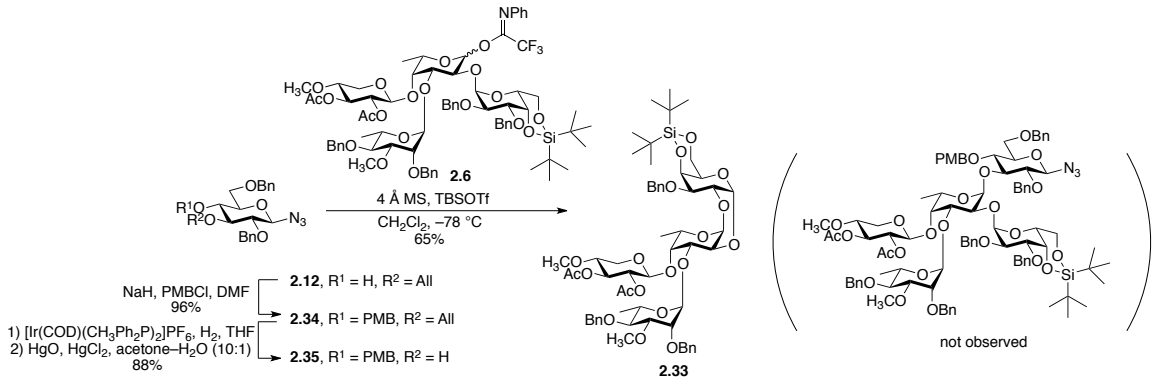
to the high reactivity of the imidate donor and steric congestion near the free hydroxyl group in **2.7**. Thus, upon activation of the imidate, O-2 of the galactose residue acted as a nucleophile to attack the oxocarbenium ion leading to an oxonium ion intermediate that, upon subsequent loss of a benzyl cation gave compound **2.33**.[19–22]



Scheme 2-10: Attempted synthesis of hexasaccharide moiety using a convergent 4+2 approach and the proposed mechanism for the formation of **2.33**.

After this result, I also explored a 4+1 glycosylation between donor **2.6** and a suitably protected glucose derivative (**2.35**, Scheme 2-11), which was prepared from **2.12** through protection of the C-4 hydroxyl group as a 4-methyoxybenzyl ether group and deprotection of allyl ether in 84% overall yield. My thinking was that replacing the large proximal xylose residue with a smaller PMB group would lead to the desired glycosylation product.

However, the reaction was still unsuccessful and compound **2.33** was again formed as the major product, this time in 65% yield. In addition, an inverse glycosylation[23,24] between donor **2.6** and acceptor **2.7** was tried by premixing **2.7** with the activator, prior to the slow addition of **2.6**. This method was attempted to minimize decomposition of the donor but, unfortunately, **2.33** was again the dominant product. The glycosylation of **2.7** or **2.35** with a trisaccharide donor (lacking a xylose moiety) was explored next (a 3+1 or 3+2 glycosylation), but cyclized products analogous to **2.33** were observed. These results suggest that the absence of a galactose moiety on the fucose is crucial for the assembly of the Fuc-(1→3)-Glc linkage. In other words, the galactose has to be introduced after the formation of the Fuc-(1→3)-Glc linkage.

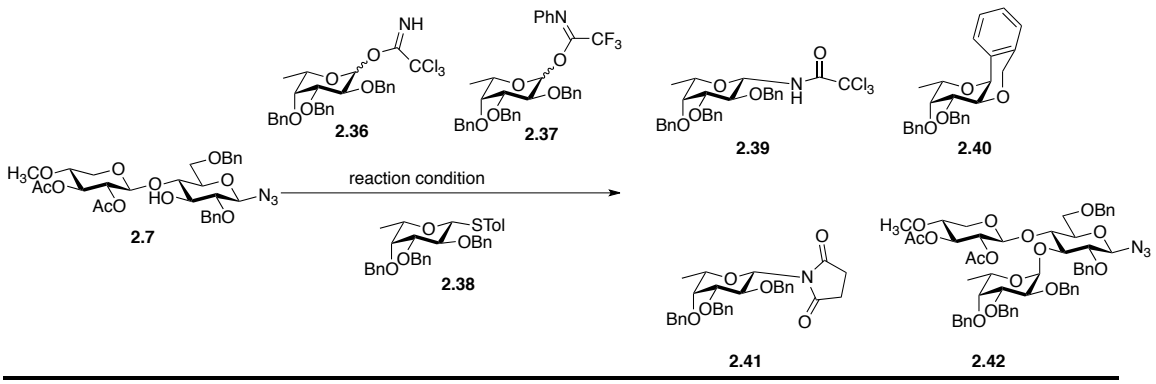


Scheme 2-11: Attempted 4+1 glycosylation.

2.2.1.4 Investigations of the conditions for the assembly of Fuc-(1→3)-Glc linkage

The failure of a convergent strategy prompted me to investigate conditions to assemble the Fuc-(1→3)-Glc linkage. As a result, donors **2.36**,[25] **2.37**,[26] and **2.38**[27] (Table 2-1) were prepared respectively using literature procedures. These species differ in the nature of the activatable group at the anomeric centre and include two different acetimidates (**2.36** and **2.37**) and a thioglycoside (**2.38**).

Table 2-1: Model reaction for the construction of Fuc-(1→3)-Glc linkage.



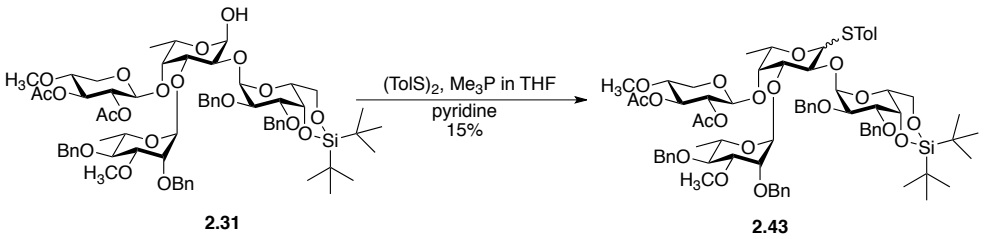
Donor	Activators	Solvent	T (°C)	Products (Yield)
2.36	TfOH	CH_2Cl_2	–78	**2.39** (53%)
2.37	TfOH	CH_2Cl_2	–78	**2.40** (60%)
2.38	NIS/AgOTf	CH_2Cl_2	–50 to rt	**2.41** (26%) and **2.42** (30%)
2.38	CH_3OTf	Et_2O	rt	**2.42** (74%)

The glycosylation reactions were performed using disaccharide acceptor **2.7**. The first attempt was to glycosylate **2.7** with trichloroacetimidate donor **2.36** under TBSOTf

activation at –78 °C. No desired product **2.42** was observed, and glycosyl amide **2.39**, a well-known by-product of reactions of trichloroacetimidate donors with unreactive alcohols,[28] was obtained in 53% yield. The *N*-phenyl-trifluoroacetimidate donor **2.37** was synthesized and designed to avoid the formation of the rearranged glycosyl amide product **2.39**.[29] Although no glycosyl amide product was formed, the cyclized by-product **2.40** was generated in 60% yield. I then turned my attention to the thioglycoside donor **2.38** using NIS/AgOTf as the promotor, and compounds **2.41**[30] and **2.42** were obtained in an approximate 1:1 ratio, in 26% and 30% yields, respectively. Therefore, while the described compound could be obtained, it was in only in low yield. All these examples indicate that the C-3 hydroxyl group in **2.7** is unreactive. Thus, upon activation of the donor, it will either undergo an intramolecular reaction to generate **2.40** or react with other reagents present in the reaction system to form **2.39**/**2.41**. After this analysis, I postulated that the activation process has to be milder so that the reactivity of the activation process could be matched with the reactivity of acceptor **2.7**. As a result, a CH_3OTf-promoted glycosylation[30–31] was performed at room temperature, and the desired trisaccharide **2.42** was obtained in 74% yield. This result suggested that thioglycosides were a suitable donor for construction of the Fuc-(1→3)-Glc linkage using CH_3OTf as the activator.

With this result in mind, the attempted transformation of hemiacetal **2.31** to the corresponding thioglycoside **2.43** was implemented (Scheme 2-12). Treatment of **2.31** with trimethylphosphine and *p*-tolyl disulfide[32] for three days gave the desired thioglycoside **2.43** as an anomeric mixture, albeit, in 15% yield. The unreacted starting material was

recovered. The presence of this compound was confirmed by high resolution mass spectrometry (HR-MS). Due to the low yield of this transformation at late stage of the synthesis, I abandoned this route.

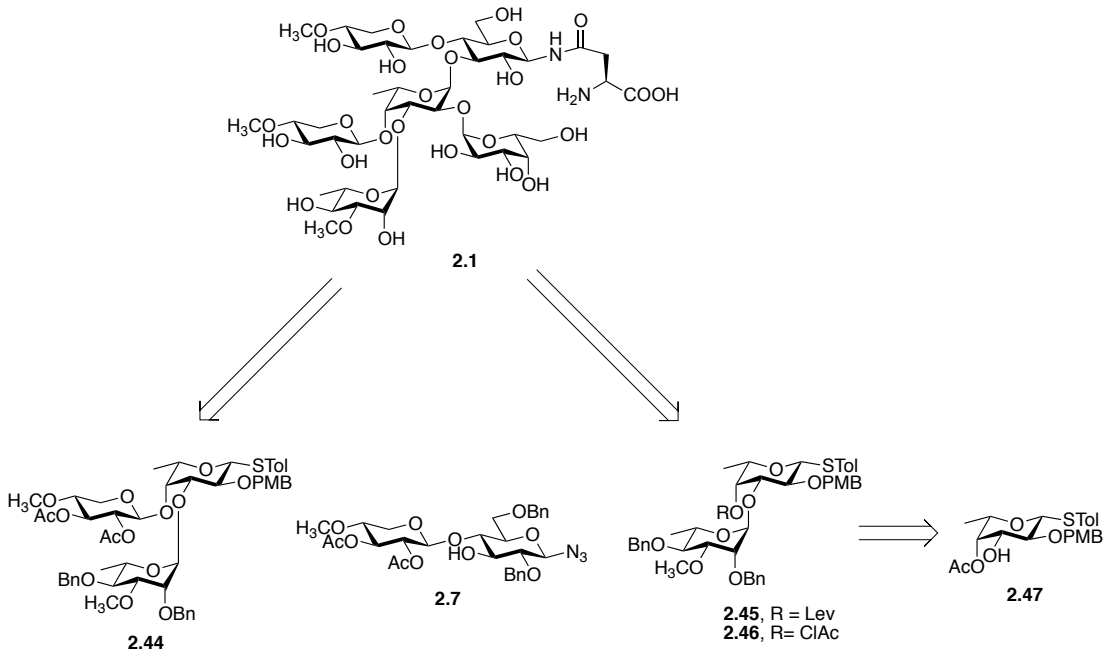


2.31 **2.43**

Scheme 2-12: Attempted conversion of hemiacetal **2.31** to thioglycoside **2.43**.

2.2.1.5 Summary

In summary, a convergent approach for the synthesis of the ATCV-1 *N*-linked hexasaccharide was attempted. The failure of this approach indicated that: 1) the C-3 hydroxyl group on the acceptor **2.7** and **2.35** have poor reactivity, presumably due to steric congestion; thus, a relatively less reactive thioglycoside donor with a milder activation (CH_3OTf) was better suited for the construction of the Fuc-(1→3)-Glc linkage to avoid various by-products; 2) the galactose moiety should be installed after the construction of Fuc-(1→3)-Glc linkage to avoid the formation of tricyclic by-product such as **2.33**. Therefore, I decided to try a 3+2 or 2+2 glycosylation strategy with a thiofucoside donor, which I hypothesized would be a reasonable solution to this problem (Scheme 2-13).



Scheme 2-13: Retrosynthetic analysis of hexasaccharide **2.1** through a 3+2 or 2+2 convergent strategy.

2.2.2 Synthesis of hexasaccharide through a 3+2 or 2+2 approach

To test the above hypothesis, I focused first on a 3+2 approach. This approach required the synthesis of trisaccharide **2.44**, which could be coupled with disaccharide **2.7**. However, my initial attempts to synthesize **2.44** from available building blocks resulted in an extremely low yield of the product. In addition, the glycosylation of **2.7** with **2.44** gave an anomeric mixture in an approximately 1:1 ratio. As a result, I abandoned this approach.

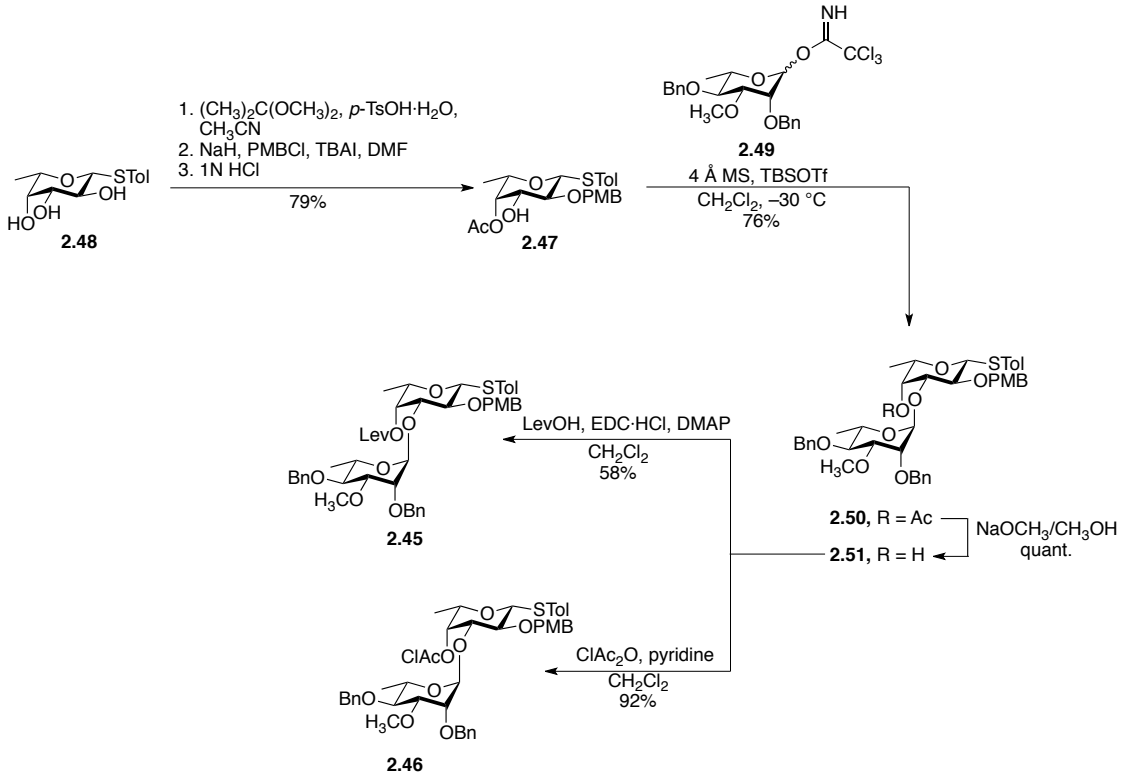
I then turned to the 2+2 approach, which required a disaccharide donor. From literature reports,[24,33,34] I learned that the presence of an ester group on the C-4 hydroxyl group of the fucose donor can help to induce high α-selectivity during glycosylation reactions. An

acetate ester would be the normal choice. However, the presence of acetyl groups in disaccharide acceptor **2.7** led me to choose other acyl protecting groups for the C-4 hydroxyl group of the fucose as this would need to be selectively cleaved. I proposed to exchange the acetyl group with either a levulinoyl group or a chloroacetyl group to compare the reaction efficiency of these two different protecting groups. Thus, I envisioned that **2.45** and **2.46** could be good donor candidates for the assembly of hexasaccharide **2.1**. In addition, both of them can be prepared from the same building block.

2.2.2.1 Synthesis of disaccharide donor 2.45 and 2.46

With this plan in mind, the synthesis of the disaccharide donors started (Scheme 2-14) from triol **2.48**, which was prepared from L-fucose in three steps as reported in the literature.[35] Reaction of **2.48** with trimethyl orthoacetate and *p*-toluenesulfonic acid gave the 3,4-*O*-orthoester intermediate. This reaction was followed by the addition of 4-methoxybenzyl chloride in the presence of sodium hydride and tetra-*n*-butylammonium iodide and a subsequent regioselective opening of the orthoester under acidic conditions to give the desired acceptor **2.47** in 79% yield. A TBSOTf-promoted glycosylation was then performed between acceptor **2.47** and donor **2.49** to obtain the disaccharide **2.50** in 76% yield with excellent α-selectivity. The stereochemistry was confirmed by the coupling constant between the Fuc-H-1 and Fuc-C-1 ($^1J_{C\text{-}H}$ = 171.9 Hz) in the ^{1}H coupled HSQC spectrum. Subsequent removal of the acetyl group under the Zemplén conditions gave **2.51** in quantitative yield. The C-4 hydroxyl group of **2.51** was then protected as either a

levulinate ester or chloroacetate ester to provide **2.45** or **2.46**, in 58% or 92% yields, respectively. I believe that the low yield for the installation of the levulinoyl group is probably due to steric congestion around the C-4 hydroxyl group as a chloroacetyl group is relatively smaller than a levulinoyl group.

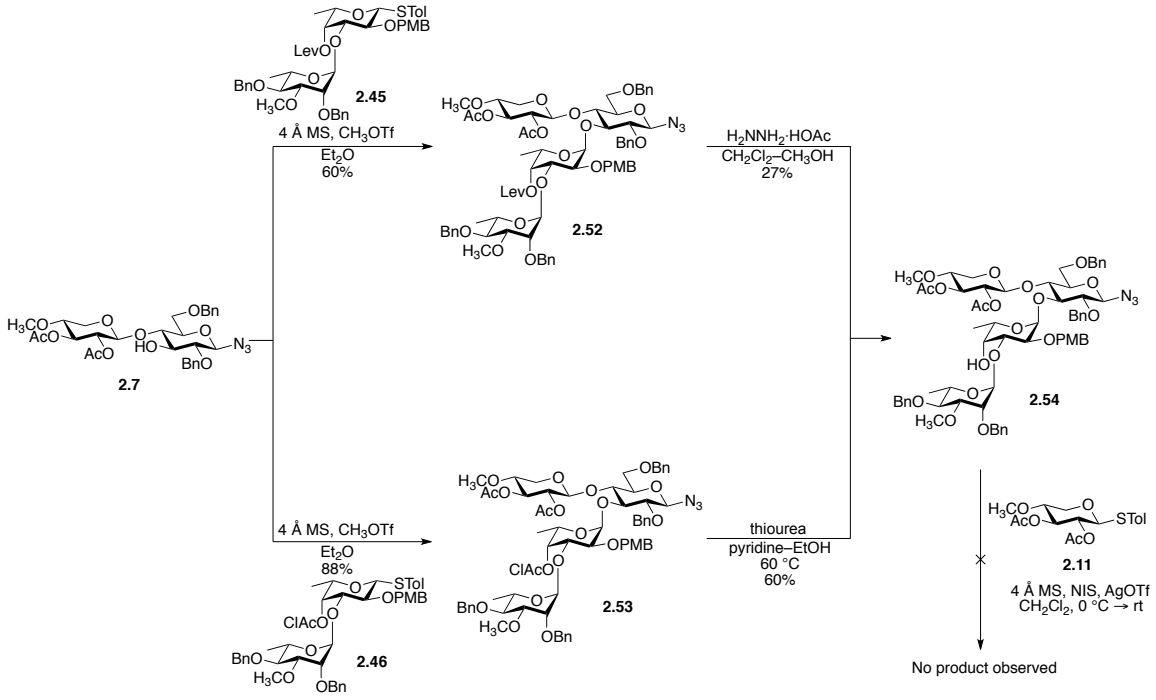


Scheme 2-14: Synthesis of disaccharide donor **2.45** and **2.46**.

2.2.2.2 Influence of the rhamnose unit for the introduction of the distal xylose residue

With disaccharide donors **2.45** and **2.46** in hand, the 2+2 glycosylations (Scheme 2-15) were performed with acceptor **2.7**. Based on the results discussed in Section 2.2.1.4, a CH_3OTf-activated glycosylation was performed to provide tetrasaccharides **2.52** and **2.53**

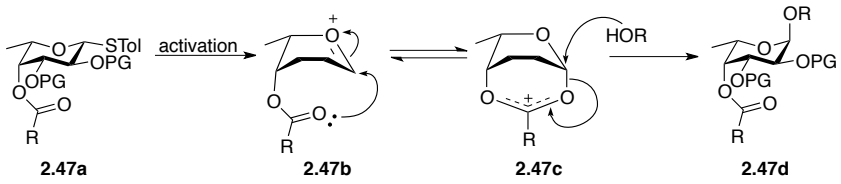
in excellent α-selectivity, in 60% and 88% yield respectively. The α-selectivity was deduced by the coupling constant between Fuc-H-1 and Fuc-C-1 ($^1J_{C\text{-}H}$ = 175.2 Hz for **2.52** and 175.3 Hz for **2.53**) in the ^{1}H coupled HSQC spectrum.



Scheme 2-15: Synthesis of tetrasaccharides **2.52** and **2.53** and attempted incorporation of a distal xylose residue onto tetrasaccharide **2.54**.

As shown in Scheme 2-16, the high α-selectivity could be explained by remote participation of the ester group on O-4 of fucose derivative **2.47a**. The levulinoyl group in **2.52** was then removed chemoselectively with hydrazine acetate to give tetrasaccharide acceptor **2.54** in 27% yield. Alternatively, the chloroacetyl group on **2.53** was removed using thiourea at 60 °C to afford **2.54** in 60% yield. Overall, these findings suggested that the chloroacetyl group is a better protecting group than the levulinoyl group, with respect

to the reaction yields for protection, glycosylation and deprotection on fucose. The low to modest yields of the deprotection, and the low yields in installing the levulinate group, however, also point to the sterically congested nature near the C-4 center of the fucose residue in these molecules.



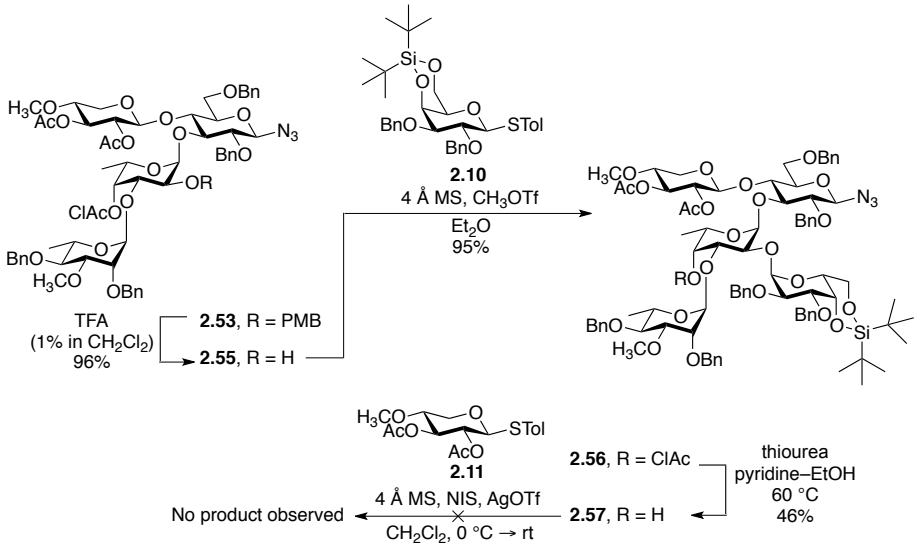
Scheme 2-16: Plausible mechanism for α-fucosidation via remote participation.

Having the tetrasaccharide acceptor **2.54** in hand, the hexasaccharide could be obtained by adding the xylose residue followed by the galactose residue or vice versa. I attempted the first of these approaches first. However, the incorporation of xylose residue **2.11** onto tetrasaccharide **2.54** was unsuccessful under either NIS/AgOTf or CH_3OTf conditions (Scheme 2-15). The failure of the reaction was probably due to the steric congestion at the C-4 hydroxyl group next to the rhamnose moiety.

With this in mind, I then envisioned that the introduction of the galactose on the fucose moiety might potentially change the conformation of the pentasaccharide, which could then result in an increase of reactivity of the C-4 hydroxyl group. Accordingly, as shown in Scheme 2-17, tetrasaccharide **2.53** was treated with 1% TFA in dichloromethane to remove the 4-methoxybenzyl group to obtain **2.55** in 96% yield. An initial attempt to glycosylate **2.55** with **2.10** under the activation of NIS and AgOTf resulted in a complex mixture of

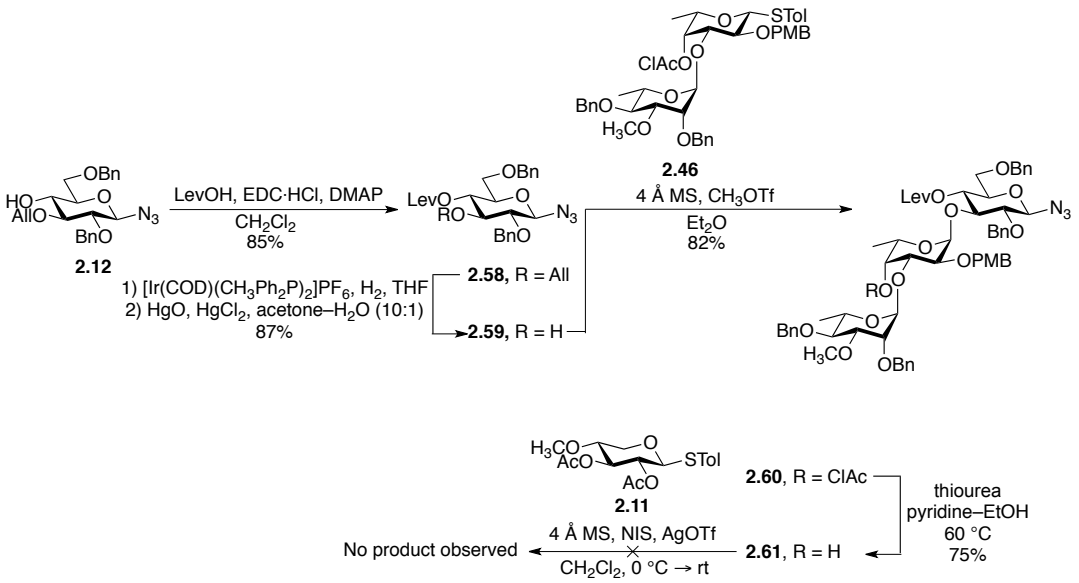
products. However, CH_3OTf-promoted glycosylation gave the desired pentasaccharide **2.56** in 95% yield with exclusive α-selectivity. The stereochemistry was again confirmed by the coupling constant of Gal-C-1 to Gal-H-1 ($^1J_{C\text{-}H}$ = 167.1 Hz) in the ^1H coupled HSQC spectrum. This result further supported that with an unreactive acceptor, CH_3OTf-activation could slowly activate the donor without converting it to undesired by-products. Thus, CH_3OTf was used as the activator for the incorporation of the galactose residue throughout the synthesis.

With pentasaccharide **2.56** in hand, subsequent deprotection of the chloroacetyl group was attempted using thiourea in 1:1 pyridine–ethanol at 60 °C to give acceptor **2.57** in 46% yield. I then investigated both NIS/AgOTf and CH_3OTf-promoted glycosylations of acceptor **2.57** using donor **2.11**. However, no desired product was obtained under either conditions and only acceptor **2.57** was recovered.



Scheme 2-17: Successful synthesis of pentasaccharide **2.56** and attempted incorporation of the distal xylose residue on pentasaccharide **2.57**.

Given the difficulties encountered in the addition of the distal xylose on tetrasaccharide **2.54** and pentasaccharide **2.57**, I wanted to investigate any long-range influence of the proximal xylose on the glycosylation used to introduce the distal xylose residue. Thus, I decided to try the incorporation of a xylose residue onto trisaccharide **2.61** (Scheme 2-18). To access **2.61**, glycosyl azide **2.12** was first treated with levulinic acid in the presence of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride and 4-(dimethylamino)pyridine to provide **2.58** in 85% yield. Subsequent removal of the allyl ether group using $[Ir(COD)(CH_3Ph_2P)_2]PF_6$ and cleavage of the resulting vinyl ether generated the desired acceptor **2.59** in 87% yield. Conversion of **2.59** into trisaccharide **2.60** was achieved using a CH_3OTf-promoted glycosylation with donor **2.46**. The reaction proceeded in 82% yield with an excellent α-selectivity. The stereochemistry was induced by the coupling constant between Fuc-H-1 and Fuc-C-1 ($^1J_{C\text{-}H}$ = 170.8 Hz) in the ^1H coupled HSQC spectrum. The chloroacetyl group was then removed using thiourea to afford acceptor **2.61** in 75% yield. The installation of a xylose residue was investigated by reaction with **2.11** but, unfortunately, no desired product was observed and only the acceptor **2.61** was recovered.



Scheme 2-18: Attempted incorporation of the distal xylose residue on trisaccharide **2.61** via reaction with **2.11**.

2.2.2.3 Summary

A convergent 2+2 glycosylation approach was explored, and the conclusions are summarized below. First, the 2+2 glycosylation generated the desired tetrasaccharide using CH_3OTf as an activator and gave an excellent α-selectivity. Second, the addition of the distal xylose residue onto the C-4 hydroxyl group of the fucose of these oligosaccharides was unsuccessful. This is presumably due to: 1) the rhamnose moiety next to the fucose C-4 hydroxyl group, which creates steric hindrance in the glycosylation and 2) the size of the aglycone on fucose (i.e., PMP vs sugar), which impacts the glycosylation sequence of monosaccharides to this 'hyper-branched' residue. It appears that the latter is particularly important as the synthesis of tetrasaccharide **2.30** (aglycone = PMP, Scheme 2-8), which

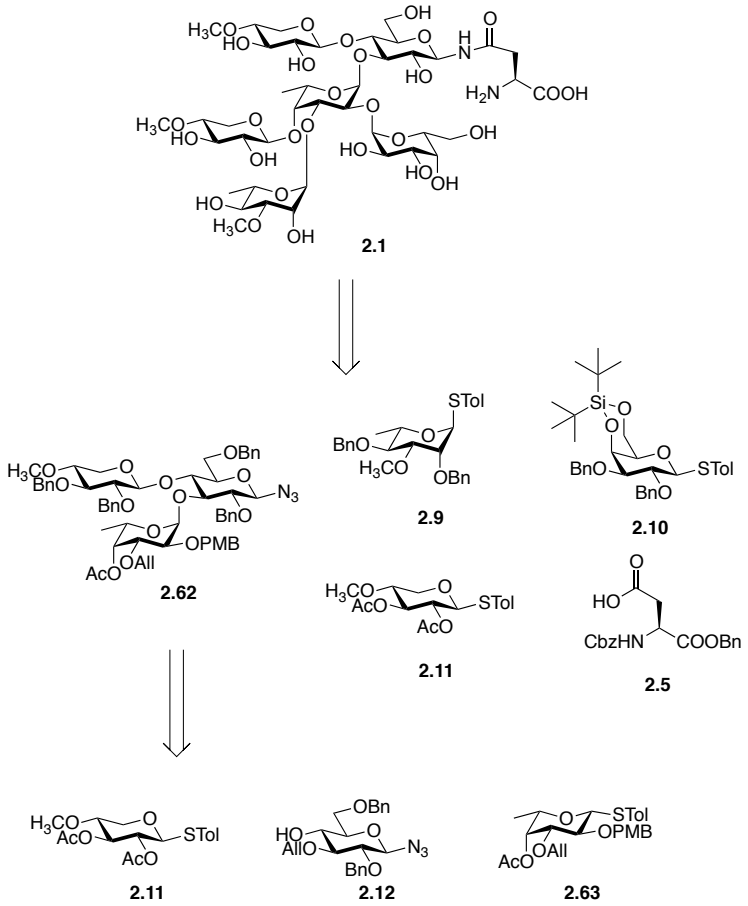
involved the addition of the xylose after the rhamnose, was successful. Finally, the overall yield of the reactions using a chloroacetyl protecting group on the fucose was higher than with the levulinoyl group, but the yield for removing the chloroacetyl group decreased as the size of the molecule increased.

2.2.3 Synthesis of hexasaccharide through a linear approach

With all the failures encountered, I came to the following conclusions: 1) the synthesis of trisaccharide **2.42**, which contains the glucose, fucose and proximal xylose, can be achieved (Table 2-1); 2) the proximal xylose should be assembled prior to the fucose as the C-4 hydroxyl group is less reactive than the C-3 hydroxyl group (Scheme 2-18);[36] 3) ester groups on the C-4 hydroxyl group of the fucose donor can help induce α-selectivity (Scheme 2-15); 4) the C-4 hydroxyl group on the fucose has low reactivity and accessibility, especially with a rhamnose moiety on the C-3 hydroxyl group (Schemes 2-15, 2-17 and 2-18); 5) the galactose moiety should be installed after the formation of the Fuc-(1→3)-Glc bond to avoid the formation of the tricyclic by-product **2.33** (Scheme 2-10).

With these results in mind, I decided to investigate a linear approach, in which the trisaccharide **2.62** (Scheme 2-19), containing a fucose residue with three orthogonal protecting groups, should be first synthesized first from **2.11**, **2.12** and **2.63**. In addition, as mentioned in Section 2.2.2.2, the deprotection of either levulinoyl group or chloroacetyl group led to low yields. As I would like to avoid loss of materials at a late stage of the synthesis, I decided to replace the acetyl groups on disaccharide **2.32** with benzyl groups

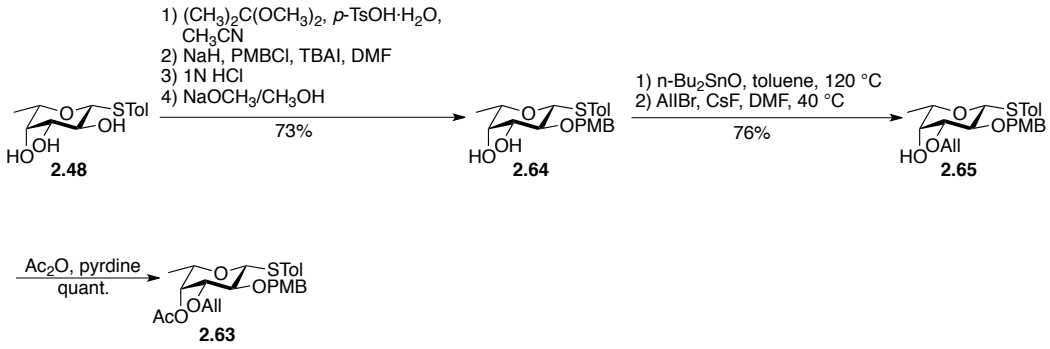
prior to the installation of the fucose moiety. This strategy could also help increasing the reactivity of the trisaccharide acceptor as all the protecting groups will be ether groups instead of electron-withdrawing ester groups. From **2.62**, the elaboration to the target **2.1** could be achieved by sequential addition of the monosaccharide residues via donors **2.9**–**2.11**. The xylose moiety (donor **2.11**) would be added first due to the low reactivity of the C-4 axial hydroxyl group. The next step would be addition of the rhamnose via donor **2.9** and then the galactose using **2.10**. After the assembly of the hexasaccharide, glycosyl azide reduction, coupling with protected aspartic acid derivative **2.5**, and finally deprotection would provide the target **2.1**.



Scheme 2-19: Retrosynthetic analysis of hexasaccharide **2.1** through a linear approach.

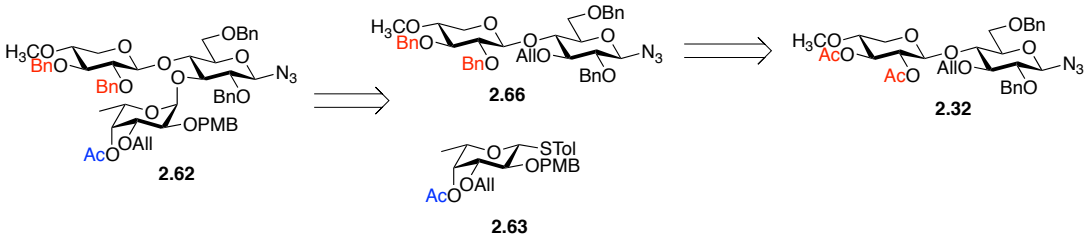
2.2.3.1 Synthesis of a protected derivative of hexasaccharide 2.1

The synthesis started with the preparation of the fucose building block **2.63**, containing three orthogonal protecting groups (Scheme 2-20). Compound **2.64**, which has a 4-methoxybenzyl ether on the C-2 hydroxyl group and the C-3 and C-4 hydroxyl groups unprotected, was first prepared from triol **2.48** over four steps in a one-pot synthesis. Reaction of **2.48** with trimethyl orthoacetate and *p*-toluenesulfonic acid gave the 3,4-*O*-orthoester intermediate. This reaction was followed by the addition of 4-methoxybenzyl chloride in the presence of sodium hydride and tetra-*n*-butylammonium iodide and a subsequent regioselective opening of the orthoester and deacetylation to give the desired acceptor **2.64** in 73% yield. Regioselective allylation of the C-3 hydroxyl group in diol **2.64** was achieved by treatment with dibutyltin oxide in toluene at reflux, followed by the addition of allyl bromide and cesium fluoride at 40 °C. This reaction provided compound **2.65** with two orthogonal protecting groups (an allyl ether and a 4-methoxybenzyl ether) in 76% yield. Finally, the C-4 hydroxyl group was protected with an acetyl group to provide building block **2.63** in quantitative yield. As described above, an acetyl group on the C-4 hydroxyl group was chosen instead of a levulinoyl group or a chloroacetyl group because the removal of the acetyl group gives a much higher yield.



Scheme 2-20: Synthesis of building block **2.63**.

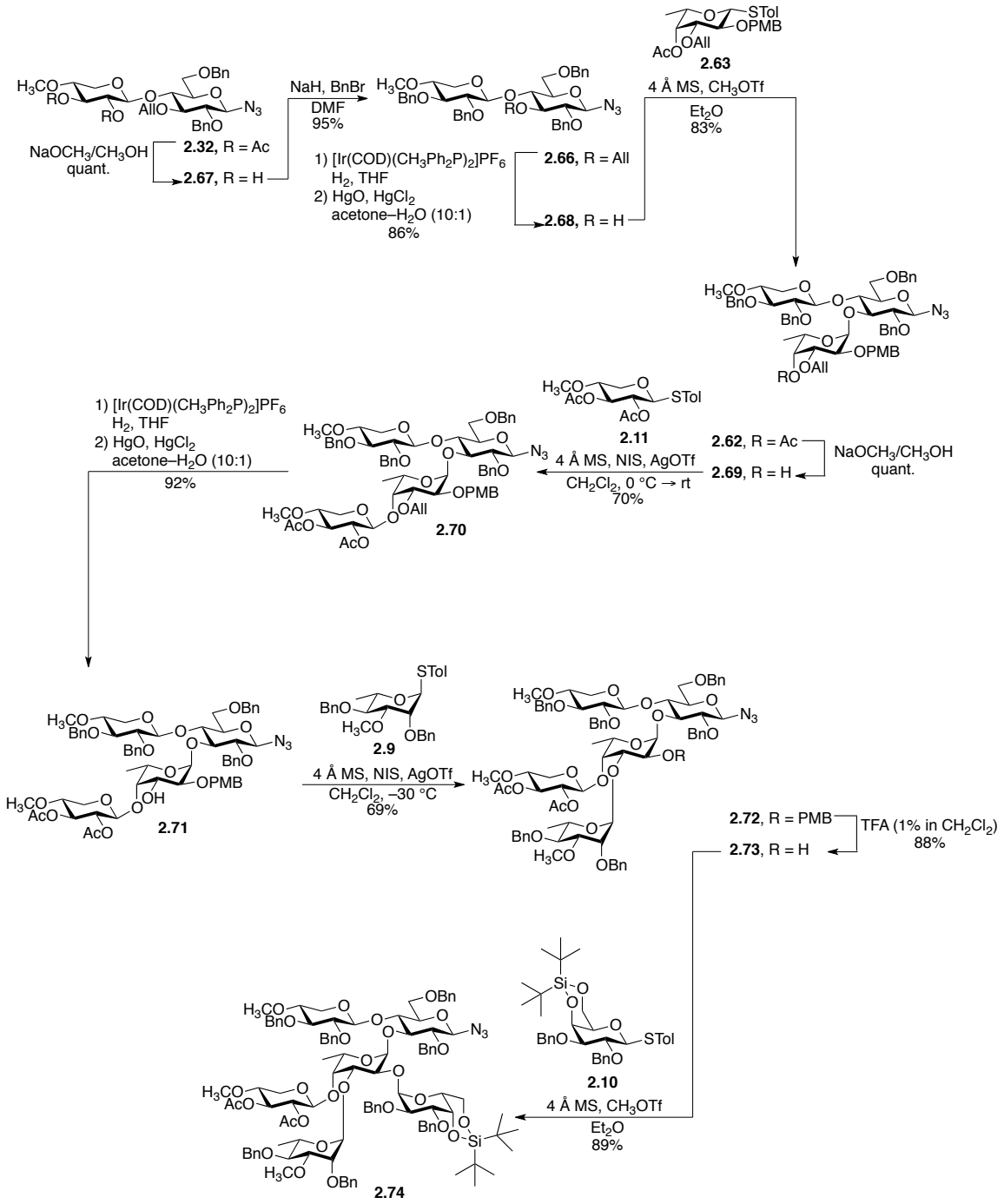
The fucose donor **2.63** contains an acetyl group. After its coupling with a disaccharide containing the glucose and proximal xylose, this acetate (shown in blue) will need to be deprotected selectively for the first glycosylation reaction to produce the 'hyper-branched' structure. For this reason, it was necessary to convert all of the acetyl groups (shown in red) on disaccharide **2.32** to a different protecting group (Scheme 2-21).



Scheme 2-21: Conversion of acetate groups to benzyl groups.

As a result, deacetylation of **2.32** using Zemplén conditions generated diol **2.67** in quantitative yield (Scheme 2-22). Subsequent benzylation of the free hydroxyl groups, followed by treatment with (1,5-cyclooctadiene)bis(methyldiphenylphosphine)iridium (I)

hexafluorophosphate catalyst, which isomerized the double bond, and cleavage of the resulting vinyl ether with aqueous mercuric salts generated the desired disaccharide acceptor **2.68** in 86% yield over two steps.



Scheme 2-22: Synthesis of hexasaccharide **2.74**.

Having completed this protecting group exchange and generated a glycosyl acceptor, conversion of **2.68** into trisaccharide **2.62** was achieved by a CH_3OTf-promoted glycosylation with donor **2.63**. This reaction proceeded in 83% yield and with an excellent α-selectivity. The stereochemistry was confirmed by coupling constant between Fuc-H-1 and Fuc-C-1 ($^1J_{C\text{-}H}$ = 174.1 Hz) in the ^1H coupled HSQC spectrum.

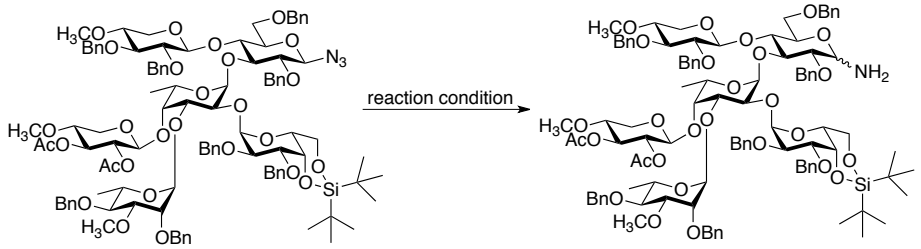
Having a robust route to trisaccharide **2.62** in place and based on my previous experiences, I planned to install the xylose before the rhamnose. Thus, the acetyl group in **2.62** was first removed under Zemplén conditions and the resulting alcohol **2.69** was glycosylated by a NIS/AgOTf-promoted reaction with xylose donor **2.11** to give the desired β-product **2.70** in 70% yield over two steps; 5% of the α-product was also isolated. The stereochemistry was determined by coupling constant of Xyl-C-1 to Xyl-H-1 ($^1J_{C\text{-}H}$ = 165.2 Hz for the β-glycoside and 174.6 Hz for the α-glycoside) in the ^1H coupled HSQC spectrum. Moving on from **2.70**, the allyl ether was deprotected to provide the desired tetrasaccharide acceptor **2.71** in 92% yield. This compound was further glycosylated with rhamnose donor **2.9** using NIS/AgOTf conditions at –30 °C to generate the desired pentasaccharide **2.72** in 69% yield with α-configuration. In addition, 8% of the β-glycoside was isolated. The stereochemistry was determined by the coupling constant between Rha-H-1 and Rha-C-1 ($^1J_{C\text{-}H}$ = 167.6 Hz for the α-glycoside and 163.6 Hz for the β-glycoside) in the ^1H coupled HSQC spectrum. Treatment of **2.72** with 1% TFA in dichloromethane resulted in the removal of the 4-methoxybenzyl group in 88% yield generating pentasaccharide **2.73**, bearing a single hydroxyl group. Glycosylation of this acceptor with

galactose donor **2.10** gave the desired hexasaccharide **2.74** with exclusive α-selectivity[16] in 89% yield. The stereochemistry was again confirmed by the coupling constant of Gal-C-1 to Gal-H-1 ($^1J_{C\text{-}H}$ = 170.6 Hz) in the ^{1}H coupled HSQC spectrum. The success of this "counter-clockwise" approach to introduce substituents onto the fucose residue can be rationalized by the need to glycosylate the least reactive (axial) alcohol first,[36] followed by the C-3 hydroxyl group and finally the C-2 position. Adding the last two carbohydrate residues onto **2.70** in the opposite order could be expected to fail, because glycosylation of O-2 and deprotection of the allyl group would provide an alcohol very sterically hindered by two carbohydrate residues at the C-3 position.

2.2.3.2 Reduction of glycosyl azide, amidation and global deprotection leading to 2.1

The final key step in the synthesis of hexasaccharide **2.1** was the introduction of the protected amino acid **2.5**. Reduction of the glycosyl azide **2.74** to the amine was investigated first. A standard method for azide reduction is catalytic hydrogenation (e.g., H_2, Pd–C). It is known that benzyl ether groups can also be removed under these conditions, unless a catalyst poison is added.[9] I anticipated the resulting deprotected compound would be difficult to handle and purify and my initial thought was to reduce the glycosyl azide chemoselectively using a Staudinger reaction[37–41] or with propanedithiol.[42–45] Those reactions are common approaches that are applied on carbohydrate derivatives.

Table 2-2: Investigation of the reduction of glycosyl azide **2.74**.

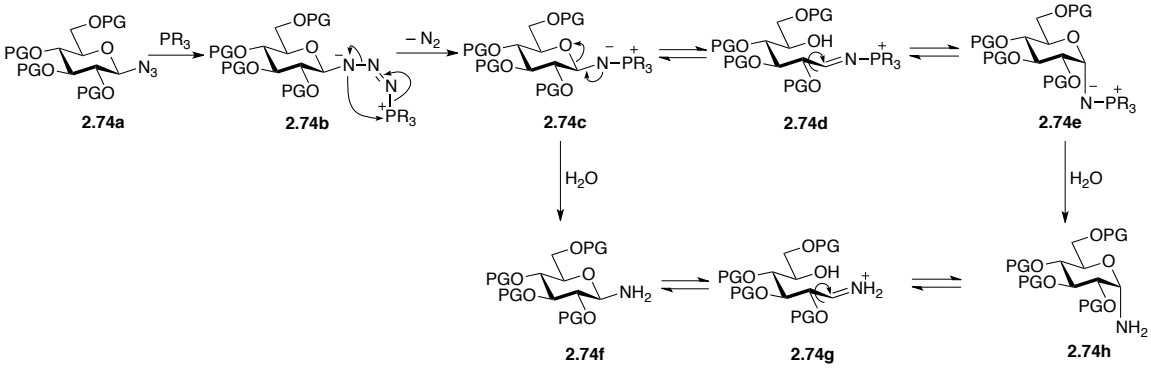


2.74 **2.75**

Entry	Reagent	Additives	Solvent	T (°C)	Result (β:α)
1	PMe_3 in THF	None	THF–H_2O (2:1)	rt	~ 1:1
2	Propanedithiol, TEA	None	Pyridine–H_2O (4:1)	rt	~ 1:1
3	H_2, Pd/C	None	Pyridine	rt	~ 2:1
4	H_2, Pd/C	None	Pyridine	0 °C	~ 2:1
5	H_2, Pd/C	1.1 eq Et_3N	THF	rt	~ 10:1

Thus, the reduction of **2.74** was initially performed by treatment with trimethylphosphine (Table 2-2, entry 1). However, this reaction resulted in the formation of an anomeric mixture of glycosyl amine **2.75** in an approximate 1:1 ratio. This result could be rationalized by anomerization of the glycosyl iminophosphorane intermediate **2.74d** (Scheme 2-23) during the reduction process.[46–52] Alternatively, the glycosyl amine could mutarotate (**2.74g**). A similar degree of anomerization was also observed upon treatment with 1,3-propanedithiol (entry 2). Because there is no iminophosphorane

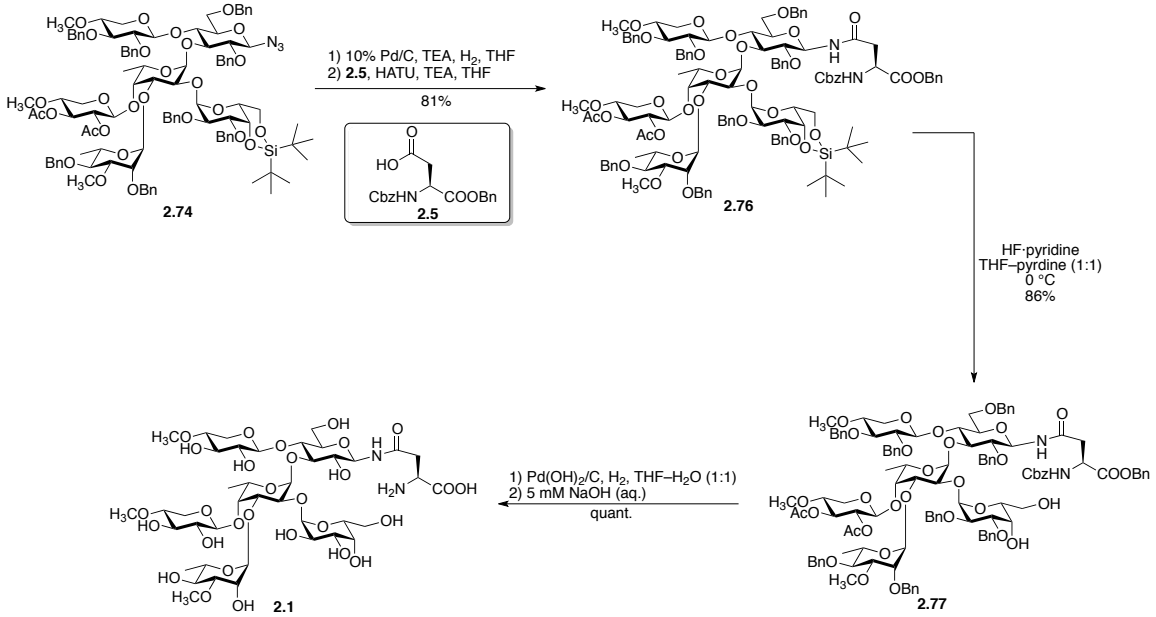
intermediate in the reduction with 1,3-propanedithiol, the anomerization must occur on the product glycosyl amine.



Scheme 2-23: Anomerization during the Staudinger reaction via a glycosyl iminophosphorane intermediate **2.74d** or mutatoration of the glycosyl amine product.

In searching for a solution, I found a report by Sajiki describing that the addition of a nitrogen-containing base during palladium-catalyzed hydrogenations could inhibit benzyl ether hydrogenolysis during glycosyl azide reduction.[53] With this in mind, my first attempt for the reduction of glycosyl azide **2.74** was accomplished in pyridine at room temperature (Table 2-2, entry 3). The desired glycosyl amine **2.75** was obtained in quantitative yield with all of the benzyl groups intact. Although this method did work, an anomeric mixture of glycosyl amines was observed in a β:α ratio of 2:1. Lowering the temperature to 0 °C did not improve the ratio (Table 2-2, entry 4). As a result, I decided to decrease the amount of base in the reaction mixture, and chose to do the reaction in the presence of a stoichiometric amount of triethylamine. These conditions (Table 2-2, entry 5) gave **2.75** in an approximate 10:1 β:α ratio.

The resulting glycosyl amine (β:α = 10:1) was then coupled with amino acid **2.5**, which had been pre-activated with HATU (Scheme 2-24). The fully protected hexasaccharide **2.76** with a β-glycosyl amide linkage was obtained in 81% yield over two steps from the glycosyl azide. To accomplish the deprotection of **2.76**, the di-*tert*-butylsilylene group was first cleaved using HF·pyridine at 0 °C to furnish the diol **2.77** in 86% yield. Debenzylation was then done using 20% palladium hydroxide on carbon in THF–H_2O (1:1). The use of methanol instead of water resulted in the methylation of the amino group through reductive amination of trace amounts of formaldehyde present in solution.[54,55] Finally, the acetyl groups were removed with 5 mM aqueous NaOH to generate the desired glycan **2.1** in quantitative yield over two steps. Overall, hexasaccharide **2.1** was successfully synthesized using a linear synthesis starting from **2.12** in 16 steps and in 13% overall yield.



Scheme 2-24: Synthesis of **2.1** from **2.74** via reduction, amidation and global deprotection.

2.2.3.3 Comparison between the ^{1}H NMR spectrum of 2.1 and the natural product

A comparison of the ^{1}H NMR spectrum of **2.1** with that reported for the natural product was made (Figure 2-2). The red trace is the anomeric region of the ^{1}H NMR spectrum obtained from synthetic **2.1** in D_2O measured at 700 MHz and 300 K. The blue trace is the anomeric region of the ^{1}H NMR spectrum obtained on the naturally-isolated glycan in D_2O measured at 600 MHz and 310 K. The latter trace was generated from a free-induction decay (FID) file provided by Professor Cristina De Castro at the University of Naples. Based on the comparison of the chemical shift of the anomeric protons, I am confident that the structure of my chemically synthesized glycan **2.1** agrees with the natural product.

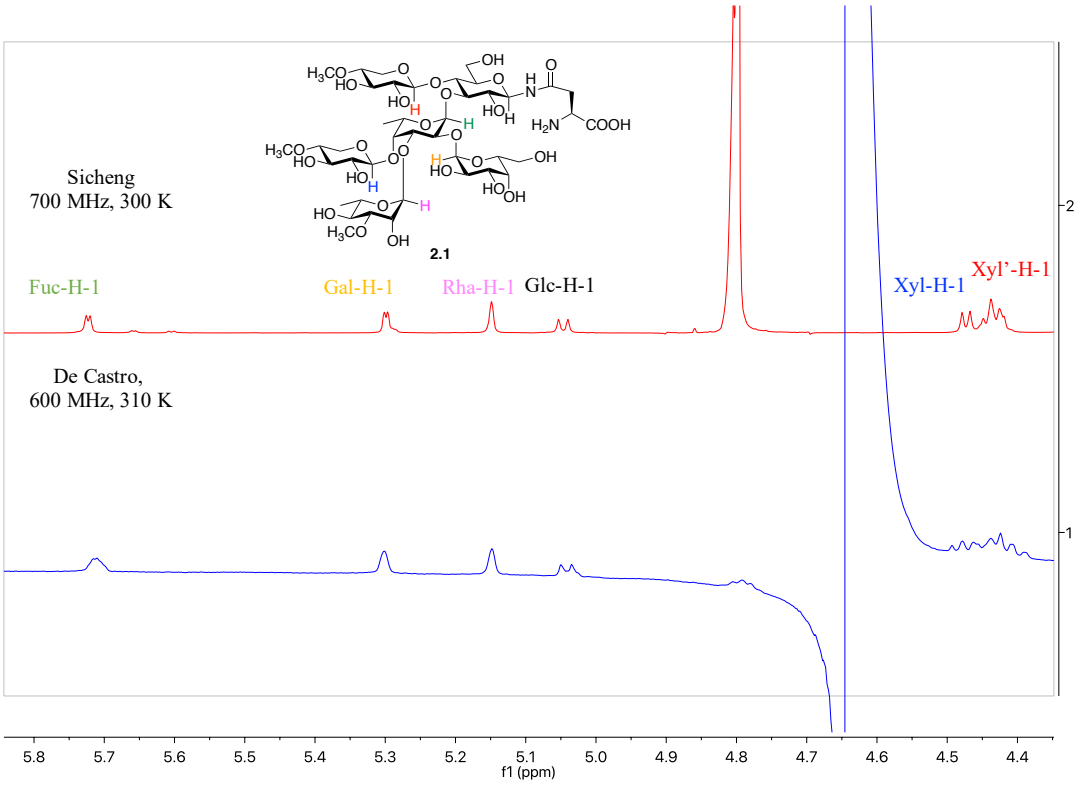
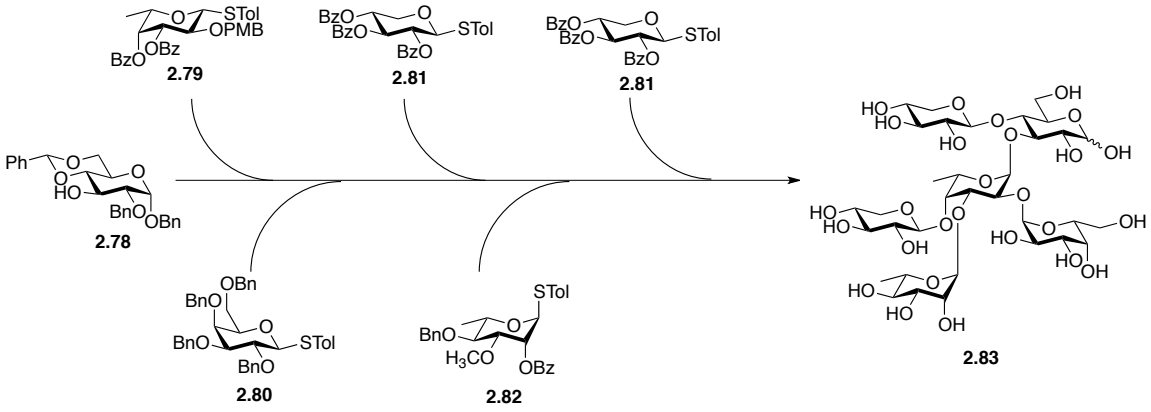


Figure 2-2: Comparison of anomeric region between the ^{1}H NMR of **2.1** and the natural product.

2.3 Conclusion

In conclusion, the work described in this chapter described the first synthesis of chlorella virus *N*-linked glycans, which are characterized by an unprecedented structure containing a glucosyl-asparagine residue and a fucose residue in which all three of the hydroxyl groups are glycosylated. Attempts to achieve the hexasaccharide motif using a convergent 4+2 approach failed; instead, a tricyclic by-product **2.33** was obtained. I postulated that this approach failed because of the high reactivity of the donor **2.6** and steric hindrance of the hydroxyl group at the C-3 position in acceptor **2.7**. Alternatively, 2+3 and 2+2 glycosylation approaches were attempted, but due to low yields and low selectivity, these approaches were abandoned. These results led me to implement a linear approach, which was successful. The route involved first the synthesis of a trisaccharide (**2.62**) with a fucose residue containing three orthogonal protecting groups. Then, the distal xylose was added to the least reactive C-4 hydroxyl group on the fucose followed by the introduction of the rhamnose and galactose to the C-3 and the C-2 hydroxyl groups, respectively. A key feature for the success of this approach was the "counter-clockwise" introduction of the carbohydrate residues onto the fucose moiety. Based on this result, we proposed that this would be a general approach to access any chlorovirus *N*-glycans.[56] In that regard, the synthesis of additional, more complex, derivatives of these structurally intriguing molecules will be discussed in next chapters to explore the feasibility of this "counter-clockwise" assembly approach.

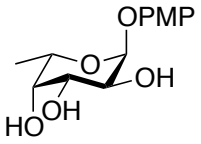
Interestingly, shortly after we published our synthesis of **2.1**,[56] another assembly strategy for the synthesis of the ATCV-1 *N*-glycan was reported by Ye and co-workers (Scheme 2-25).[57] They developed an approach in which a similar hexasaccharide **2.83** (but lacking the amino acid moiety) could be prepared by the introduction of the fucose moiety **2.79** onto the glucose **2.78** first, followed by galactose **2.80**, distal xylose **2.81** and rhamnose **2.82**. The proximal xylose **2.81** was then installed at the end of the synthesis. As detailed above, I did not explore this sequence of additions of monosaccharides, although the early formation of the Fuc-(1→3)-Glc linkage is a feature of both my, and Ye and coworkers, approach.



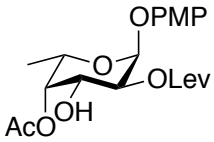
Scheme 2-25: Assembly sequence for the synthesis of hexasaccharide **2.83** (Ye's approach).[57]

2.4 Experimental section

General Methods: All reagents were purchased from commercial sources and were used without further purification unless noted. Reaction solvents were purified by successive passage through columns of alumina and copper under argon. Unless stated otherwise, all reactions were performed at room temperature and under a positive pressure of argon and were monitored by TLC on Silica Gel G-25 F254 (0.25 mm). Visualization of the reaction components was achieved using UV fluorescence (254 nm) and/or by charring with acidified anisaldehyde solution in ethanol, acetic acid and sulfuric acid. Organic solvents were evaporated under reduced pressure, and the products were purified by column chromatography on silica gel (230−400 mesh). Optical rotations were measured in a microcell (1 cm, 1 mL) at ambient temperature and are in units of degrees·mL/(g·dm). ^{1}H NMR spectra were recorded at 400 MHz, 500 MHz, 600 MHz, or 700 MHz and chemical shifts are referenced to residual $CHCl_3$ (7.26 ppm, $CDCl_3$) or CHD_2OD (3.30 ppm, CD_3OD). ^{13}C NMR spectra were recorded at 125 MHz and chemical shifts are referenced to $CDCl_3$ (77.0 ppm) or CD_3OD (49.3 ppm). Reported splitting patterns are abbreviated as s = singlet, d = doublet, t = triplet, m = multiplet, br = broad, app = apparent. Assignments of NMR spectra were based on two-dimensional experiments (^{1}H−^{1}H COSY, HSQC, and HMBC). High-resolution ESI-MS spectra (time-of-flight analyzer) were recorded on samples suspended in THF or CH_3OH and with added NaCl.

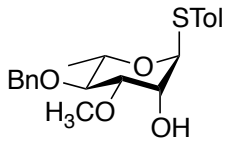


4-Methoxyphenyl α-L-fucopyranoside (2.14): To a stirred solution of 4-methoxyphenyl 2,3,4-tri-*O*-acetyl-α-L-fucopyranoside **2.13**[12] (5.50 g, 13.9 mmol) in CH_3OH (100 mL) was added a solution of $NaOCH_3$ in CH_3OH (10 mL, 0.5 M). The reaction mixture was stirred for 1 h at room temperature, then neutralized by addition of Amberlite® IR-120 (H^+) cation exchange resin, filtered and the filtrate was concentrated to afford **2.14** (3.75 g, quant.) as a white solid. R_f 0.33 (9:1 CH_2Cl_2–CH_3OH); $[\alpha]_D$ –215 (*c* 0.38, CH_3OH); ^1H NMR (500 MHz; CD_3OD): δ 7.05–7.02 (m, 2H, Ar), 6.85–6.81 (m, 2H, Ar), 5.30 (d, 1H, J = 3.7 Hz, H-1), 4.09 (qd, J = 6.6, 0.8 Hz, 1H), 3.92 (dd, 1H, J = 10.2, 3.3 Hz, H-3), 3.86 (dd, 1H, J = 10.2, 3.7 Hz, H-2), 3.74 (s, 3H, PhOC$\underline{H}_3$), 3.72 (dd, 1H, J = 3.2, 0.8 Hz, H-4), 1.19 (d, 3H, J = 6.6 Hz, H-6); ^{13}C NMR (125 MHz; CD_3OD): δ 156.5 (Ar), 152.8 (Ar), 119.4 (Ar), 115.5 (Ar), 100.5 (C-1), 73.6 (C-4), 71.6 (C-3), 69.9 (C-2), 68.3 (C-5), 56.1 (PhO$\underline{C}H_3$), 16.6 (C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{13}H_{18}NaO_6$: 293.0996; Found 293.0999.



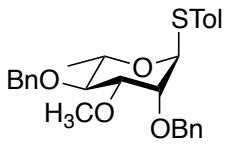
4-Methoxyphenyl 4-*O*-acetyl-2-*O*-levulinoyl-α-L-fucopyranoside (2.8): To a stirred solution of **2.14** (1.13 g, 4.18 mmol) in dry CH_3CN (20 mL) was added trimethyl orthoacetate (0.80 mL, 6.27 mmol) and *p*-toluenesulfonic acid monohydrate (79.9 mg, 0.42 mmol) at 0 °C. The reaction mixture was stirred for 1 h under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was

concentrated. The crude reaction mixture was then dissolved in dry CH_2Cl_2 (40 mL), then EDC·HCl (2.01 g. 10.5 mmol), levulinic acid (1.22 g, 10.5 mmol) and 4-(dimethylamino)pyridine (51.0 mg, 0.42 mmol) successively. The reaction mixture was stirred for 1h at room temperature, then treated with 1N HCl (40 mL). After stirring for 0.5 h, the aqueous layer was extracted with CH_2Cl_2 (40 mL × 3), and the combined organic layers were washed with saturated $NaHCO_3$ (aq.), dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (1:1 hexane–EtOAc) to afford **2.8** (1.36 g, 79%) as a viscous oil. R_f 0.14 (1:1 hexane–EtOAc); $[\alpha]_D$ –155 (*c* 0.71, $CHCl_3$); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.02–6.99 (m, 2H, Ar), 6.87–6.83 (m, 2H, Ar), 5.54 (d, 1H, J = 3.7 Hz, H-1), 5.35 (dd, 1H, J = 3.6, 1.2 Hz, H-4), 5.16 (dd, 1H, J = 10.4, 3.7 Hz, H-2), 4.44 (ddd, 1H, J = 10.4, 4.8, 3.8 Hz, H-3), 4.28 (qd, 1H, J = 6.5, 0.8 Hz, H-5), 3.79 (s, 3H, PhOC$\underline{H}_3$), 2.81–2.78 (m, 2H, $COCH_2C\underline{H}_2COCH_3$), 2.73–2.60 (m, 2H, $COC\underline{H}_2CH_2COCH_3$), 2.47 (d, 1H, J = 5.1 Hz, 3-OH), 2.22 (s, 3H, $COC\underline{H}_3$), 2.18 (s, 3H, $COCH_2CH_2COC\underline{H}_3$), 1.17 (d, 3H, J = 6.6 Hz, H-6); ^{13}C NMR (125 MHz; $CDCl_3$): δ 206.8 (C=O), 172.9 (C=O), 171.2 (C=O), 155.3 (Ar), 150.8 (Ar), 118.1 (Ar), 114.7 (Ar), 96.2 (C-1), 73.3 (C-4), 71.4 (C-2), 67.1 (C-3), 65.7 (C-5), 55.7 (PhO$\underline{C}H_3$), 38.1 ($COCH_2\underline{C}H_2COCH_3$), 29.8 ($COCH_2CH_2CO\underline{C}H_3$), 28.1 ($CO\underline{C}H_2CH_2COCH_3$), 20.8 ($CO\underline{C}H_3$), 16.2 (C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{20}H_{26}NaO_9$: 433.1469; Found 433.1465.



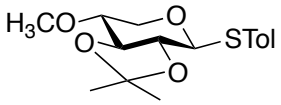
***p*-Tolyl 4-*O*-benzyl-3-*O*-methyl-1-thio-α-L-rhamnopyranoside (2.16):** To a stirred solution of *p*-tolyl 4-*O*-benzyl-1-thio-α-L-rhamnopyranoside **2.15**[13] (2.03 g, 5.63 mmol) in dry toluene (56 mL) was added dibutyltin oxide (1.68 g, 6.76 mmol) at room temperature. The reaction mixture was heated at reflux overnight at 120 °C under an Ar atmosphere. The reaction mixture was cooled to room temperature, concentrated and dried under high vacuum for 5 h. To a solution of the tin acetal in dry DMF (28 mL) was added cesium fluoride (1.28 g, 8.45 mmol) and methyl iodide (3.50 mL, 56.3 mmol) successively at room temperature. The reaction mixture was stirred overnight at 40 °C under an Ar atmosphere, then diluted with EtOAc (200 mL) and washed with brine. The aqueous layer was extracted with EtOAc (50 mL × 3), and combined organic layers were dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (3:1 hexane–EtOAc) to afford **2.16** (1.64 g, 78%) as a viscous oil. R_f 0.34 (2:1 hexane–EtOAc); $[\alpha]_D$ –253 (*c* 0.39, $CHCl_3$); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.40–7.30 (m, 7H, Ar), 7.14–7.13 (m, 2H, Ar), 5.49 (d, 1H, J = 1.5 Hz, H-1), 4.88 (d, 1H, J = 11.1 Hz, PhC$\underline{H}_2$), 4.66 (d, 1H, J = 11.1 Hz, PhC$\underline{H}_2$), 4.32 (dt, 1H, J = 3.4, 1.8 Hz, H-2), 4.22 (dq, 1H, J = 9.4, 6.1 Hz, H-5), 3.60 (dd, 1H, J = 9.0, 3.3 Hz, H-3), 3.54 (s, 3H, OCH_3), 3.45 (t, 1H, J = 9.3 Hz, H-4), 2.58 (d, 1H, J = 2.2 Hz, 2-OH), 2.35 (s, 3H, ArC$\underline{H}_3$), 1.32 (d, 3H, J = 6.2 Hz, H-6); ^{13}C NMR (125 MHz; $CDCl_3$): δ 138.4 (Ar), 137.6 (Ar), 132.1 (Ar), 130.3 (Ar), 129.8 (Ar), 128.4 (Ar), 128.0 (Ar), 127.8 (Ar), 87.5 (C-1), 82.0 (C-3), 80.1 (C-4), 75.3 (Ph$\underline{C}H_2$),

69.4 (C-2), 68.5 (C-5), 57.5 (O<u>C</u>H$_3$), 21.1 (Ar<u>C</u>H$_3$), 17.8 (C-6); HRMS (ESI) Calc. for [M + Na]$^+$ $C_{21}H_{26}NaO_4S$: 397.1444; Found 397.1552.

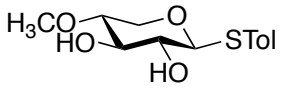


***p*-Tolyl 2,4-di-*O*-benzyl-3-*O*-methyl-1-thio-α-L-rhamnopyranoside (2.9):** To a stirred solution of **2.16** (1.95 g, 5.21 mmol) in dry DMF (12 mL) was added sodium hydride (0.52 g, 13 mmol, 60% dispersion in mineral oil) in one portion at 0 °C. After stirring for 30 min, benzyl bromide (0.93 mL, 7.8 mmol) was added dropwise, and the reaction mixture was warmed to room temperature and stirred overnight under an Ar atmosphere. Then, CH_3OH was added at 0 °C and the solution was concentrated. The crude residue was diluted with CH_2Cl_2 (200 mL), washed with saturated $NaHCO_3$ (aq.), dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (12:1 hexane–EtOAc) to afford **2.9** (2.42 g, quant.) as a viscous oil. R_f 0.34 (8:1 hexane–EtOAc); $[\alpha]_D$ –93 (*c* 0.39, $CHCl_3$); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.40–7.29 (m, 12H, Ar), 7.13–7.11 (m, 2H, Ar), 5.47 (d, 1H, *J* = 1.4 Hz, H-1), 4.96 (d, 1H, *J* = 11.0 Hz, PhC<u>H</u>$_2$), 4.75 (d, 1H, *J* = 12.4 Hz, PhC<u>H</u>$_2$), 4.69 (d, 1H, *J* = 12.4 Hz, PhC<u>H</u>$_2$), 4.66 (d, 1H, *J* = 11.0 Hz, PhC<u>H</u>$_2$), 4.17 (dq, 1H, *J* = 8.7, 6.1 Hz, H-5), 4.06 (dd, 1H, *J* = 2.7, 1.8 Hz, H-2), 3.61 (t, 1H, *J* = 9.4 Hz, H-4), 3.58 (dd, 1H, *J* = 9.4, 3.2 Hz, H-3), 3.44 (s, 3H, OC<u>H</u>$_3$), 2.35 (s, 3H, ArC<u>H</u>$_3$), 1.36 (d, 3H, *J* = 6.2 Hz, H-6); ^{13}C NMR (125 MHz; $CDCl_3$): δ 138.8 (Ar), 137.9 (Ar), 137.5 (Ar), 131.9 (Ar), 130.9 (Ar), 129.8 (Ar), 128.4 (2 × Ar), 128.0 (Ar), 127.9 (Ar), 127.8 (Ar), 127.6 (Ar), 86.1 (C-1), 82.1 (C-3), 80.6 (C-4), 75.7 (C-2), 75.3 (Ph<u>C</u>H$_2$),

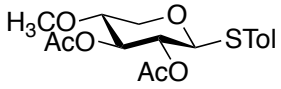
72.1 (Ph<u>C</u>H$_2$), 69.1 (C-5), 57.5 (O<u>C</u>H$_3$), 21.1 (Ar<u>C</u>H$_3$), 17.9 (C-6); HRMS (ESI) Calc. for [M + Na]$^+$ $C_{28}H_{32}NaO_4S$: 487.1914; Found 487.1913.



***p*-Tolyl 2,3-*O*-isopropylidene-4-*O*-methyl-1-thio-β-D-xylopyranoside (2.19):** To a stirred solution of *p*-tolyl 2,3-*O*-isopropylidene-1-thio-β-D-xylopyranoside **2.18**[17] (1.40 g, 4.72 mmol) in dry DMF (15mL) was added sodium hydride (0.38 g, 9.5 mmol, 60% dispersion in mineral oil) in one portion at 0 °C. After stirring for 30 min, methyl iodide (1.46 mL, 23.6 mmol) was added dropwise, and the reaction mixture was warmed to room temperature and stirred for 2 h under an Ar atmosphere. Then, CH_3OH was added at 0 °C and the solution was concentrated. The crude residue was diluted with CH_2Cl_2 (150 mL), washed with saturated $NaHCO_3$ (aq.), dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (3:1 hexane–EtOAc) to afford **2.19** (1.44 g, 99%) as a white solid. R_f 0.31 (4:1 hexane–EtOAc); $[\alpha]_D$ –48 (*c* 2.1, $CHCl_3$); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.50–7.47 (m, 2H, Ar), 7.16–7.13 (m, 2H, Ar), 4.74 (d, 1H, J = 9.5 Hz, H-1), 4.20 (dd, 1H, J = 11.8, 4.5 Hz, H-5a), 3.57–3.53 (m, 2H, H-3, H-4), 3.47 (s, 3H, OC<u>H</u>$_3$), 3.25–3.20 (m, 2H, H-2, H-5b), 2.36 (s, 3H, ArCH$_3$), 1.50 (s, 3H, C(C<u>H</u>$_3$)$_2$), 1.46 (s, 3H, C(C<u>H</u>$_3$)$_2$); ^{13}C NMR (125 MHz; $CDCl_3$): δ 138.4 (Ar), 133.6 (Ar), 129.6 (Ar), 127.9 (Ar), 111.2 (<u>C</u>(CH$_3$)$_2$), 85.5 (C-1), 82.1 (C-3), 77.5 (C-4), 75.3 (C-2), 68.0 (C-5), 58.0 (O<u>C</u>H$_3$), 26.8 (C(<u>C</u>H$_3$)$_2$), 26.6 (C(<u>C</u>H$_3$)$_2$), 21.2 (Ar<u>C</u>H$_3$); HRMS (ESI) Calc. for [M + Na]$^+$ $C_{16}H_{22}NaO_4S$: 333.1131; Found 333.1138.

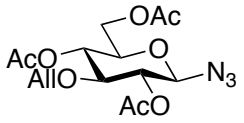


***p*-Tolyl 4-*O*-methyl-1-thio-β-D-xylopyranoside (2.20):** To a stirred solution of **2.19** (1.44 g, 4.64 mmol) in CH_2Cl_2–CH_3OH (15 mL, 1:1) was added camphorsulfonic acid (1.08 g, 4.64 mmol) at room temperature. The reaction mixture was stirred overnight at room temperature. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (1:1 hexane–EtOAc) to afford **2.20** (1.24 g, 99%) as a viscous oil. R_f 0.13 (1:1 hexane–EtOAc); $[\alpha]_D$ –73.8 (*c* 2.8, $CHCl_3$); ^{1}H NMR (400 MHz; $CDCl_3$): δ 7.44–7.41 (m, 2H, Ar), 7.13–7.11 (m, 2H, Ar), 4.47 (d, 1H, J = 9.0 Hz, H-1), 4.22–4.15 (m, 1H, H-5a), 3.62–3.57 (m, 1H, H-3), 3.46 (s, 3H, OC$\underline{H}_3$), 3.36 (t, 1H, J = 8.7 Hz, H-2), 3.28–3.19 (m, 2H, H-4, H-5b), 3.17 (br s, 1H, 3-OH), 3.00 (br s, 1H, 2-OH), 2.34 (s, 3H, ArCH_3); ^{13}C NMR (125 MHz; $CDCl_3$): δ 138.5 (Ar), 133.4 (Ar), 129.8 (Ar), 127.9 (Ar), 88.8 (C-1), 78.6 (C-4), 76.3 (C-3), 71.8 (C-2), 66.5 (C-5), 58.5 (O$\underline{C}H_3$), 21.2 (Ar$\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{13}H_{18}NaO_4S$: 293.0818; Found 293.0817.



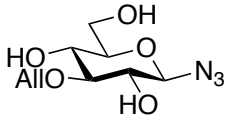
***p*-Tolyl 2,3-di-*O*-acetyl-4-*O*-methyl-1-thio-β-D-xylopyranoside (2.11):** To a stirred solution of **2.20** (1.33 g, 4.64 mmol) in pyridine (10 mL) was added acetic anhydride (5 mL) dropwise at room temperature. The reaction mixture was stirred for 2 h at room temperature, then the solvent was evaporated. The crude residue was diluted with CH_2Cl_2 (150 mL) and washed with 1N HCl and saturated $NaHCO_3$ (aq.). The organic layer was

dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (4:1 hexane–EtOAc) to afford **2.11** (1.55 g, 94%) as a white solid. R_f 0.24 (4:1 hexane–EtOAc); $[\alpha]_D$ –54.4 (*c* 0.77, $CHCl_3$); ^1H NMR (500 MHz; $CDCl_3$): δ 7.40–7.38 (m, 2H, Ar), 7.15–7.14 (m, 2H, Ar), 5.10 (t, 1H, J = 8.6 Hz, H-3), 4.88 (t, 1H, J = 8.9 Hz, H-2), 4.66 (d, 1H, J = 9.1 Hz, H-1), 4.24 (dd, 1H, J = 11.5, 4.8 Hz, H-5a), 3.45–3.39 (m, 4H, H-4, OC$\underline{H}_3$), 3.32 (dd, 1H, J = 11.5, 9.6 Hz, H-5b), 2.36 (s, 3H, ArC$\underline{H}_3$), 2.10 (s, 3H, COC$\underline{H}_3$), 2.08 (s, 3H, COC$\underline{H}_3$); ^{13}C NMR (125 MHz; $CDCl_3$): δ 170.1 (C=O), 169.6 (C=O), 138.5 (Ar), 133.3 (Ar), 129.8 (Ar), 128.4 (Ar), 86.7 (C-1), 76.7 (C-4), 74.5 (C-3), 70.3 (C-2), 66.7 (C-5), 58.7 (O$\underline{C}H_3$), 21.2 (Ar$\underline{C}H_3$), 20.9 (2 × CO$\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{17}H_{22}NaO_6S$: 377.1029; Found 377.1028.



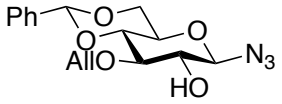
2,4,6-Tri-*O*-acetyl-3-*O*-allyl-β-D-glucopyranosyl azide (2.22): To a stirred solution of 1,2,4,6-tetra-*O*-acetyl-3-*O*-allyl-β-D-glucopyranose **2.21**[18] (15.3 g, 39.4 mmol) in dry CH_2Cl_2 (150 mL) was added azidotrimethylsilane (5.73 mL, 43.3 mmol) and tin(IV) chloride (4.67 mL, 39.4 mmol) successively at room temperature. The reaction mixture was stirred for 1.5 h at room temperature under an Ar atmosphere, then washed with saturated $NaHCO_3$ (aq.) and brine. The aqueous layer was extracted with CH_2Cl_2 (100 mL × 3), and the combined organic layers were dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (2:1 hexane–EtOAc) to afford **2.22** (13.9 g, 95%) as a clear viscous oil. R_f 0.35 (2:1 hexane–EtOAc); $[\alpha]_D$ –415

(*c* 0.52, $CHCl_3$); ^1H NMR (400 MHz; $CDCl_3$): δ 5.77 (ddt, 1H, *J* = 17.2, 10.4, 5.6 Hz, $OCH_2C\underline{H}=CH_2$), 5.21 (dq, 1H, *J* = 17.2, 1.6 Hz, $OCH_2CH=C\underline{H}_2$), 5.15 (dq, 1H, *J* = 10.4, 1.4 Hz, $OCH_2CH=C\underline{H}_2$), 5.07 (dd, 1H, *J* = 9.9, 9.4 Hz, H-4), 4.96 (dd, 1H, *J* = 9.4, 8.9 Hz, H-2), 4.49 (d, 1H, *J* = 8.8 Hz, H-1), 4.22 (dd, 1H, *J* = 12.4, 5.0 Hz, H-6a), 4.16 (dd, 1H, *J* = 12.4, 2.6 Hz, H-6b), 4.10 (ddt, *J* = 12.8, 5.5, 1.6 Hz, $OC\underline{H}_2CH=CH_2$), 4.06 (ddt, *J* = 12.8, 5.6, 1.4 Hz, $OC\underline{H}_2CH=CH_2$), 3.68 (ddd, 1H, *J* = 10.0, 5.0, 2.6 Hz, H-5), 3.60 (app t, 1H,, *J* = 9.4 Hz, H-3), 2.13 (s, 3H, $COC\underline{H}_3$), 2.10 (s, 3H, $COC\underline{H}_3$), 2.09 (s, 3H, $COC\underline{H}_3$); ^{13}C NMR (125 MHz; $CDCl_3$): δ 170.7 (C=O), 169.2 (C=O), 169.1 (C=O), 134.0 ($OCH_2\underline{C}H=CH_2$), 117.2 ($OCH_2CH=\underline{C}H_2$), 88.1 (C-1), 79.7 (C-3), 74.4 (C-5), 73.2 ($O\underline{C}H_2CH=CH_2$), 71.9 (C-2), 69.2 (C-4), 62.1 (C-6), 20.8 (3 × $CO\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{15}H_{21}N_3NaO_8$: 394.1221; Found 394.1220.



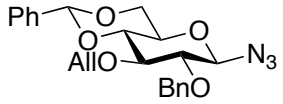
3-*O*-Allyl-β-D-glucopyranosyl azide (2.23): To a stirred solution of **2.22** (13.9 g, 37.3 mmol) in CH_3OH (100 mL) was added a solution of $NaOCH_3$ in CH_3OH (10 mL, 0.5 M). The reaction mixture was stirred for 2 h at room temperature, then neutralized by addition of Amberlite® IR-120 (H^+) cation exchange resin, filtered and the filtrate was concentrated to afford **2.23** (9.15 g, quant.) as a syrup. R_f 0.11 (1:1 hexane–EtOAc); $[\alpha]_D$ –261 (*c* 0.55, CH_3OH); ^1H NMR (500 MHz; CD_3OD): δ 5.99 (ddt, 1H, *J* = 17.3, 10.4, 5.8 Hz, $OCH_2C\underline{H}=CH_2$), 5.27 (dq, 1H, *J* = 17.3, 1.8 Hz, $OCH_2CH=C\underline{H}_2$), 5.11 (dq, 1H, *J* = 10.4, 1.6 Hz, $OCH_2CH=C\underline{H}_2$), 4.48 (d, 1H, *J* = 8.4 Hz, H-1), 4.36 (ddt, 1H, *J* = 12.5, 5.8, 1.6 Hz,

OC<u>H</u>$_2$CH=CH$_2$), 4.33 (ddt, 1H, J = 12.2, 5.8, 1.5 Hz, OC<u>H</u>$_2$CH=CH$_2$), 3.86 (dd, 1H, J = 12.0, 1.8 Hz, H-6a), 3.67 (dd, 1H, J = 12.0, 5.3 Hz, H-6b), 3.39–3.33 (m, 2H, H-4, H-5), 3.25–3.19 (m, 2H, H-3, H-2); ^{13}C NMR (125 MHz; CD_3OD): δ 136.9 (OCH$_2$<u>C</u>H=CH$_2$), 116.7 (OCH$_2$CH=<u>C</u>H$_2$), 92.1 (C-1), 85.9 (C-3), 80.1 (C-5), 75.2 (O<u>C</u>H$_2$CH=CH$_2$), 74.8 (C-2), 70.9 (C-4), 62.5 (C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_9H_{15}N_3NaO_5$: 268.0904; Found 268.0903.



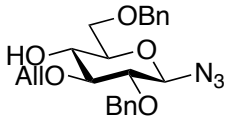
3-*O*-Allyl-4,6-*O*-benzylidene-β-D-glucopyranosyl azide (2.24): To a stirred solution of **2.23** (9.15 g, 37.3 mmol)) in dry CH_3CN (150 mL) were added benzaldehyde dimethyl acetal (16.8 mL, 112 mmol) and camphorsulfonic acid (2.60 g, 11.2 mmol) successively. The reaction mixture was stirred overnight at room temperature under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (4:1 hexane–EtOAc) to afford **2.24** (10.9 g, 88%) as a white solid. R_f 0.29 (4:1 hexane–EtOAc); $[\alpha]_D$ –420 (*c* 0.45, $CHCl_3$); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.51–7.48 (m, 2H, Ar), 7.42–7.38 (m, 3H, Ar), 5.96 (ddt, 1H, J = 17.2, 10.3, 5.4 Hz, OCH$_2$C<u>H</u>=CH$_2$), 5.58 (s, 1H, PhC<u>H</u>), 5.32 (dq, 1H, J = 17.2, 1.5 Hz, OCH$_2$CH=C<u>H</u>$_2$), 5.23 (dq, 1H, J = 10.3, 1.3 Hz, OCH$_2$CH=C<u>H</u>$_2$), 4.69 (d, 1H, J = 8.6 Hz, OCH$_2$C<u>H</u>=CH$_2$), 4.48 (ddt, 1H, J = 12.7, 5.4, 1.3 Hz, OC<u>H</u>$_2$CH=CH$_2$), 4.40 (dd, 1H, J = 10.5, 4.9 Hz, H-6a), 4.26 (ddt, 1H, J = 12.7, 6.2, 1.0 Hz, OC<u>H</u>$_2$CH=CH$_2$), 3.81 (t, 1H, J = 10.3 Hz, H-6b), 3.67 (t, 1H, J = 9.2 Hz, H-4), 3.61 (t, 1H,

J = 8.9 Hz, H-3), 3.56 (td, 1H, J = 9.6, 4.8 Hz, H-5), 3.48 (t, 1H, J = 8.6 Hz, H-2), 2.59 (br s, 1H, 2-OH); ^{13}C NMR (125 MHz; $CDCl_3$): δ 137.0 (Ar), 134.5 ($OCH_2\underline{C}H=CH_2$), 129.1 (Ar), 128.3 (Ar), 126.0 (Ar), 117.7 ($OCH_2CH=\underline{C}H_2$), 101.3 (Ph$\underline{C}$H), 90.5 (C-1), 81.1 (C-4), 80.3 (C-3), 73.7 ($O\underline{C}H_2CH=CH_2$), 73.7 (C-2), 68.5 (C-5), 68.4 (C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{16}H_{19}N_3NaO_5$: 356.1217; Found 356.1222.



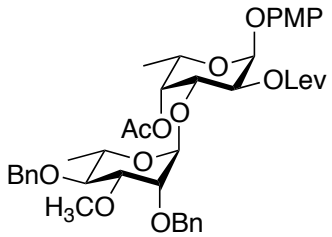
3-*O*-Allyl-2-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranosyl azide (2.25): To a stirred solution of **2.24** (10.9 g, 32.8 mmol) in dry DMF (30 mL) was added sodium hydride (2.98 g, 74.6 mmol, 60% dispersion in mineral oil) in one portion at 0 °C. After stirring for 30 min, benzyl bromide (8.86 mL, 74.6 mmol) was added dropwise and the reaction mixture was warmed to room temperature and stirred overnight under an Ar atmosphere. Then, CH_3OH was added at 0 °C and the mixture was concentrated. The crude residue was diluted with CH_2Cl_2 (200 mL), washed with saturated $NaHCO_3$ (aq.), dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (12:1 hexane–EtOAc) to afford **2.25** (12.7 g, 91%) as a white solid. R_f 0.67 (4:1 hexane–EtOAc); $[\alpha]_D$ –27.2 (*c* 1.4, $CHCl_3$); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.51–7.49 (m, 2H, Ar), 7.43–7.32 (m, 8H, Ar), 5.97 (ddt, 1H, J = 17.2, 10.4, 5.8 Hz, $OCH_2C\underline{H}=CH_2$), 5.57 (s, 1H, Ph$\underline{C}$H), 5.32 (dq, 1H, J = 17.2, 1.6 Hz, $OCH_2CH=C\underline{H}_2$), 5.20 (dq, J = 10.4, 1.5 Hz, $OCH_2CH=C\underline{H}_2$), 4.87 (d, 1H, J = 10.7 Hz, Ph$C\underline{H}_2$), 4.86 (d, 1H, J = 10.7 Hz, Ph$C\underline{H}_2$), 4.73 (d, 1H, J = 8.5 Hz, H-1), 4.44 (ddt, 1H, J = 12.6, 5.6, 1.3 Hz, $OC\underline{H}_2CH=CH_2$), 4.40 (dd,

1H, J = 10.5, 5.0 Hz, H-6a), 4.28 (ddt, 1H, J = 12.5, 5.8, 1.3 Hz, OC<u>H</u>$_2$CH=CH$_2$), 3.79 (t, 1H, J = 10.2 Hz, H-6b), 3.70 (t, 1H, J = 8.9 Hz, H-3), 3.65 (t, 1H, J = 9.2 Hz, H-4), 3.51 (td, 1H, J = 9.5, 4.9 Hz, H-5), 3.37 (t, 1H, J = 8.5 Hz, H-2); ^{13}C NMR (125 MHz; $CDCl_3$): δ 137.7 (Ar), 137.1 (Ar), 134.9 (OCH$_2$<u>C</u>H=CH$_2$), 129.0 (Ar), 128.5 (Ar), 128.3 (Ar), 128.0 (Ar), 126.0 (Ar), 117.1 (OCH$_2$CH=<u>C</u>H$_2$), 101.2 (Ph<u>C</u>H), 90.7 (C-1), 81.3 (C-2), 81.2 (C-4), 81.0 (C-3), 75.7 (Ph<u>C</u>H$_2$), 74.1 (O<u>C</u>H$_2$CH=CH$_2$), 68.5 (C-6), 68.2 (C-5); HRMS (ESI) Calc. for [M + Na]$^+$ $C_{23}H_{25}N_3NaO_5$: 446.1686; Found 446.1679.



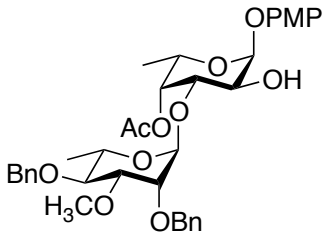
3-*O*-Allyl-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (2.12): To a stirred solution of **2.25** (8.94 g, 21.1 mmol) in dry CH_2Cl_2 (100 mL) was added triethylsilane (16.9 mL, 106 mmol) and trifluoroacetic acid (8.11 mL, 106 mmol) successively at room temperature. The reaction mixture was stirred for 2 h at 0 °C and then poured into saturated $NaHCO_3$ (aq.). The aqueous layer was extracted with CH_2Cl_2 (100 mL × 3), and the combined organic layers were dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (4:1 hexane–EtOAc) to afford **2.12** (8.02 g, 89%) as a viscous oil. R_f 0.26 (4:1 hexane–EtOAc); $[\alpha]_D$ –33.5 (*c* 2.2, $CHCl_3$); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.41–7.31 (m, 10H, Ar), 5.96 (ddt, 1H, J = 17.2, 10.4, 5.6 Hz, OCH$_2$C<u>H</u>=CH$_2$), 5.31 (dq, 1H, J = 17.2, 1.5 Hz, OCH$_2$CH=C<u>H</u>$_2$), 5.21 (dq, 1H, J = 10.4, 1.2 Hz, OCH$_2$CH=C<u>H</u>$_2$), 4.87 (d, 1H, J = 10.8 Hz, PhC<u>H</u>$_2$), 4.77 (d, 1H, J = 10.7 Hz, PhC<u>H</u>$_2$), 4.65 (d, 1H, J = 12.1 Hz, PhC<u>H</u>$_2$), 4.63 (d, 1H, J = 8.6 Hz, H-1), 4.61 (d, 1H, J = 12.1 Hz,

PhC$\underline{H}_2$), 4.40 (ddt, 1H, J = 12.6, 5.5, 1.5 Hz, OC$\underline{H}_2$CH=CH$_2$), 4.29 (ddt, 1H, J = 12.6, 6.0, 1.5 Hz, OC$\underline{H}_2$CH=CH$_2$), 3.80 (dd, 1H, J = 10.7, 4.3 Hz, H-6a), 3.77 (dd, 1H, J = 10.3, 4.5 Hz, H-6b), 3.64 (td, 1H, J = 9.2, 2.1 Hz, H-4), 3.55 (dt, 1H, J = 9.4, 4.6 Hz, H-5), 3.39 (t, 1H, J = 9.0 Hz, H-3), 3.30 (t, 1H, J = 8.8 Hz, H-2), 2.72 (d, 1H, J = 2.4 Hz, 4-OH); ^{13}C NMR (125 MHz; $CDCl_3$): δ 137.7 (2 × Ar), 134.9 (OCH$_2\underline{C}$H=CH$_2$), 128.5 (2 × Ar), 128.2 (Ar), 128.0 (Ar), 127.9 (Ar), 127.8 (Ar), 117.3 (OCH$_2$CH=$\underline{C}$H$_2$), 90.2 (C-1), 84.1 (C-3), 81.2 (C-2), 76.2 (C-4), 75.1 (Ph$\underline{C}$H$_2$), 74.3 (O$\underline{C}$H$_2$CH=CH$_2$), 73.8 (Ph$\underline{C}$H$_2$), 71.3 (C-5), 69.8 (C-6); HRMS (ESI) Calc. for $[M + NH_4]^+$ $C_{23}H_{31}N_4O_5$: 443.2289; Found 443.2287.



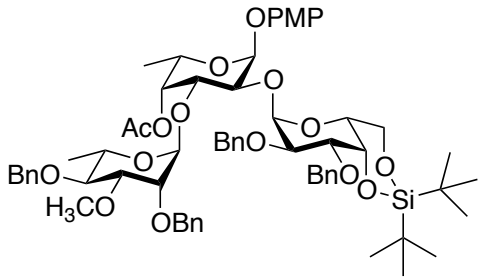
4-Methoxyphenyl 2,4-di-*O*-benzyl-3-*O*-methyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-2-*O*-levulinoyl-α-L-fucopyranoside (2.26): To a stirred solution of acceptor **2.8** (424 mg, 1.03 mmol) and donor **2.9** (576 mg, 1.24 mmol) in dry CH_2Cl_2 (15 mL) was added molecular sieves (1.5 g, 4Å, powder). After stirring for 30 min at room temperature, the reaction mixture was cooled to –30 °C, and then *N*-iodosuccinimide (349 mg, 1.55 mmol) and silver trifluoromethanesulfonate (54 mg, 0.21 mmol) were added successively. The resulting solution was stirred for 1 h at –30 °C under an Ar atmosphere. Excess triethylamine was added to quench the acid and the mixture was filtered and the filtrate was washed with saturated $Na_2S_2O_3$ (aq.) and saturated $NaHCO_3$ (aq.). The aqueous layer was extracted with CH_2Cl_2 (50 mL × 3), and the combined organic extracts were dried over

Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (3:1 hexane–EtOAc) to afford **2.26** (629 mg, 81%) as a syrup. R_f 0.36 (2:1 hexane–EtOAc); $[\alpha]_D$ –117 (*c* 3.3, $CHCl_3$); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.48–7.46 (m, 2H, Ar), 7.39–7.23 (m, 8H, Ar), 6.98–6.95 (m, 2H, Ar), 6.85–6.82 (m, 2H, Ar), 5.51 (d, 1H, J = 3.7 Hz, Fuc-H-1), 5.35 (d, 1H, J = 2.6 Hz, Fuc-H-4), 5.16 (dd, 1H, J = 10.6, 3.7 Hz, Fuc-H-2), 5.14 (d, 1H, J = 1.7 Hz, Rha-H-1), 4.92 (d, 1H, J = 11.1 Hz, PhC$\underline{H}_2$), 4.78 (d, 1H, J = 12.5 Hz, PhC$\underline{H}_2$), 4.68 (d, 1H, J = 12.5 Hz, PhC$\underline{H}_2$), 4.62 (d, 1H, J = 11.1 Hz, PhC$\underline{H}_2$), 4.46 (dd, 1H, J = 10.6, 3.3 Hz, Fuc-H-3), 4.26 (q, 1H, J = 6.5 Hz, Fuc-H-5), 3.84 (dq, 1H, J = 9.2, 6.2 Hz, Rha-H-5), 3.77 (s, 3H, PhOC$\underline{H}_3$), 3.59 (dd, 1H, J = 3.2, 1.8 Hz, Rha-H-2), 3.51 (t, 1H, J = 9.3 Hz, Rha-H-4), 3.43 (dd, 1H, J = 9.3, 3.2 Hz, Rha-H-3), 3.30 (s, 3H, OC$\underline{H}_3$), 2.61–2.49 (m, 4H, CO(C$\underline{H}_2$)$_2$COCH$_3$), 2.16 (s, 3H, COC$\underline{H}_3$), 1.97 (s, 3H, CO(CH$_2$)$_2$COC$\underline{H}_3$), 1.38 (d, 3H, J = 6.2 Hz, Rha-H-6), 1.16 (d, 3H, J = 6.5 Hz, Fuc-H-6); ^{13}C NMR (125 MHz; $CDCl_3$): δ 206.0 (C=O), 172.3 (C=O), 170.8 (C=O), 155.3 (Ar), 150.7 (Ar), 139.2 (Ar), 138.4 (Ar), 128.2 (Ar), 128.1 (Ar), 127.6 (2 × Ar), 127.4 (Ar), 118.2 (Ar), 114.7 (Ar), 96.2 (Fuc-C-1), 93.6 (Rha-C-1, $^1J_{C\text{-}H}$ = 171.9 Hz), 81.4 (Rha-C-3), 80.1 (Rha-C-4), 75.0 (Ph$\underline{C}$H$_2$), 73.3 (Rha-C-2), 72.1 (Ph$\underline{C}$H$_2$), 69.4 (Fuc-C-4), 68.9 (Fuc-C-2), 68.2 (Fuc-C-3), 68.0 (Rha-C-5), 65.2 (Fuc-C-5), 57.3 (O$\underline{C}$H$_3$), 55.7 (PhO$\underline{C}$H$_3$), 37.6 (COCH$_2\underline{C}$H$_2$COCH$_3$), 29.5 (COCH$_2$CH$_2$CO$\underline{C}$H$_3$), 27.9 (CO$\underline{C}$H$_2$CH$_2$COCH$_3$), 20.8 (CO$\underline{C}$H$_3$), 18.1 (Rha-C-6), 16.1 (Fuc-C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{41}H_{50}NaO_{13}$: 773.3144; Found 773.3144.



4-Methoxyphenyl 2,4-di-*O*-benzyl-3-*O*-methyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-α-L-fucopyranoside (2.27): To a stirred solution of **2.26** (629 mg, 0.838 mmol) in CH_2Cl_2–CH_3OH (10 mL, 9:1) was added hydrazine acetate (155 mg, 1.68 mmol) at room temperature. After stirring for 2 h at room temperature, the reaction mixture was concentrated and the crude residue was purified by flash chromatography (3:1 hexane–EtOAc) to afford **2.27** (516 mg, 94%) as a white foam. R_f 0.36 (2:1 hexane–EtOAc); $[\alpha]_D$ –145 (*c* 2.5, $CHCl_3$); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.50–7.48 (m, 2H, Ar), 7.40–7.28 (m, 8H, Ar), 7.04–7.01 (m, 2H, Ar), 6.88–6.84 (m, 2H, Ar), 5.50 (d, 1H, J = 3.9 Hz, Fuc-H-1), 5.33 (dd, 1H, J = 3.3, 0.9 Hz, Fuc-H-4), 5.10 (d, 1H, J = 1.7 Hz, Rha-H-1), 4.95 (d, 1H, J = 11.1 Hz, PhC$\underline{H}_2$), 4.79 (d, 1H, J = 12.4 Hz, PhC$\underline{H}_2$), 4.75 (d, 1H, J = 12.4 Hz, PhC$\underline{H}_2$), 4.65 (d, 1H, J = 11.1 Hz, PhC$\underline{H}_2$), 4.22 (qd, 1H, J = 6.8, 0.9 Hz, Fuc-H-5), 4.14 (dd, 1H, J = 10.1, 3.4 Hz, Fuc-H-3), 4.01–3.94 (m, 2H, Rha-H-5, Fuc-H-2), 3.80 (s, 3H, PhOC$\underline{H}_3$), 3.72 (t, 1H, J = 2.0 Hz, Rha-H-2), 3.58–3.57 (m, 2H, Rha-H-3, Rha-H-4), 3.38 (s, 3H, OC$\underline{H}_3$), 2.38 (d, 1H, J = 8.5 Hz, 2-OH), 2.17 (s, 3H, COC$\underline{H}_3$), 1.37 (d, 3H, J = 6.2 Hz, Rha-H-6), 1.17 (d, 3H, J = 6.5 Hz, Fuc-H-6); ^{13}C NMR (125 MHz; $CDCl_3$): δ 170.6 (C=O), 155.3 (Ar), 150.6 (Ar), 138.9 (Ar), 138.5 (Ar), 128.3 (Ar), 128.2 (Ar), 128.0 (Ar), 127.9 (Ar), 127.5 (Ar), 118.1 (Ar), 114.7 (Ar), 98.5 (Fuc-C-1), 95.5 (Rha-C-1), 81.4 (Rha-C-3), 80.1 (Rha-C-4), 75.1 (Ph$\underline{C}H_2$), 74.4 (Rha-C-2), 74.0 (Fuc-C-3), 72.5 (Ph$\underline{C}H_2$), 70.0 (Fuc-

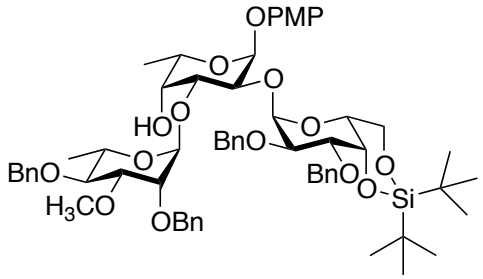
C-4), 68.5 (Rha-C-5), 67.6 (Fuc-C-2), 65.4 (Fuc-C-5), 57.4 (O<u>C</u>H$_3$), 55.7 (PhO<u>C</u>H$_3$), 20.8 (CO<u>C</u>H$_3$), 18.1 (Rha-C-6), 16.1 (Fuc-C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{36}H_{44}NaO_{11}$: 675.2776; Found 675.2780.



4-Methoxyphenyl 2,4-di-*O*-benzyl-3-*O*-methyl-α-L-rhamnopyranosyl-(1→3)-[2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranosyl-(1→2)]-4-*O*-acetyl-α-L-fucopyranoside (2.28): To a stirred solution of acceptor **2.27** (102 mg, 156 μmol) and *p*-tolyl 2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranoside **2.10**[15] (114 mg, 187 μmol) in dry CH_2Cl_2 (5.0 mL) was added molecular sieves (500 mg, 4Å, powder). After stirring for 30 min at room temperature, the reaction mixture was cooled to –10 °C, and then *N*-iodosuccinimide (70.1 mg, 312 μmol) and silver trifluoromethanesulfonate (8.0 mg, 31 μmol) were added successively. The resulting solution was stirred for 1 h at 0 °C under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was washed with saturated $Na_2S_2O_3$ (aq.) and saturated $NaHCO_3$ (aq.). The aqueous layer was extracted with CH_2Cl_2 (20 mL × 3) and the combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (7:1 hexane–EtOAc) to afford **2.28** (168 mg, 95%) as a syrup. R_f 0.26 (7:1 hexane–EtOAc); $[\alpha]_D$ –50.7 (*c* 3.0,

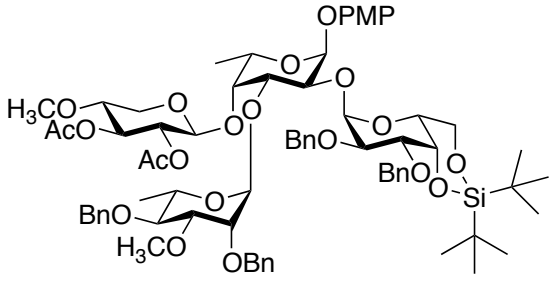
$CHCl_3$); ^1H NMR (700 MHz; $CDCl_3$): δ 7.49–7.48 (m, 2H, Ar), 7.36–7.20 (m, 15H, Ar), 7.14–7.13 (m, 3H, Ar), 6.90–6.87 (m, 2H, Ar), 6.79–6.76 (m, 2H, Ar), 5.71 (d, 1H, J = 3.5 Hz, Fuc-H-1), 5.38 (d, 1H, J = 2.4 Hz, Fuc-H-4), 5.15 (d, 1H, J = 1.1 Hz, Rha-H-1), 4.91 (d, 1H, J = 13.2 Hz, PhC$\underline{H}_2$), 4.89 (d, 1H, J = 11.4 Hz, PhC$\underline{H}_2$), 4.81 (d, 1H, J = 12.6 Hz, PhC$\underline{H}_2$), 4.71 (d, 1H, J = 12.6 Hz, PhC$\underline{H}_2$), 4.67 (d, 1H, J = 3.8 Hz, Gal-H-1), 4.64 (d, 1H, J = 11.4 Hz, PhC$\underline{H}_2$), 4.60 (d, 1H, J = 12.2 Hz, PhC$\underline{H}_2$), 4.55 (d, J = 13.2 Hz, PhC$\underline{H}_2$), 4.54 (d, 1H, J = 12.2 Hz, PhC$\underline{H}_2$), 4.49–4.45 (m, 2H, Fuc-H-3, Rha-H-5), 4.26 (d, 1H, J = 2.8 Hz, Gal-H-4), 4.07 (q, 1H, J = 6.8 Hz, Fuc-H-5), 3.86 (dd, 1H, J = 10.4, 3.5 Hz, Fuc-H-2), 3.80 (dd, 1H, J = 10.1, 3.8 Hz, Gal-H-2), 3.75 (s, 3H, PhOC$\underline{H}_3$), 3.72 (dd, 1H, J = 9.5, 3.3 Hz, Rha-H-3), 3.68 (dd, 1H, J = 10.1, 3.0 Hz, Gal-H-3), 3.65 (dd, 1H, J = 3.3, 1.5 Hz, Rha-H-2), 3.58 (br s, 1H, Gal-H-5), 3.55 (t, 1H, J = 9.5 Hz, Rha-H-4), 3.44 (dd, 1H, J = 12.8, 2.0 Hz, Gal-H-6a), 3.10 (dd, 1H, J = 12.8, 1.4 Hz, Gal-H-6b), 3.05 (s, 3H, OC$\underline{H}_3$), 2.22 (s, 3H, COC$\underline{H}_3$), 1.40 (d, 3H, J = 6.2 Hz, Rha-H-6), 1.09 (d, 3H, J = 6.5 Hz, Fuc-H-6), 0.92 (s, 9H, C(C$\underline{H}_3$)$_3$), 0.84 (s, 9H, C(C$\underline{H}_3$)$_3$); ^{13}C NMR (125 MHz; $CDCl_3$): δ 170.6 (C=O), 154.6 (Ar), 150.3 (Ar), 139.8 (Ar), 139.6 (Ar), 139.3 (Ar), 138.8 (Ar), 128.2 (Ar), 128.1 (3 × Ar), 128.0 (2 × Ar), 127.8 (Ar), 127.4 (Ar), 127.3 (Ar), 127.2 (Ar), 127.1 (Ar), 116.2 (Ar), 114.8 (Ar), 101.9 (Gal-C-1, $^1J_{C\text{-}H}$ = 169.3 Hz), 96.4 (Fuc-C-1), 94.1 (Rha-C-1), 81.3 (Rha-C-3), 80.3 (Rha-C-4), 78.4 (Gal-C-3), 77.4 (Fuc-C-2), 75.2 (Ph$\underline{C}H_2$), 74.7 (Rha-C-2), 74.0 (Gal-C-2), 73.1 (Ph$\underline{C}H_2$), 72.1 (Ph$\underline{C}H_2$), 71.9 (Ph$\underline{C}H_2$), 71.7 (Gal-C-4), 69.6 (Fuc-C-4), 69.0 (Fuc-C-3), 68.0 (Rha-C-5), 67.9 (Gal-C-5), 66.8 (Gal-C-6), 64.8 (Fuc-C-5), 57.1 (O$\underline{C}H_3$), 55.6 (PhO$\underline{C}H_3$), 27.5 (C($\underline{C}H_3$)$_3$), 27.2 (C($\underline{C}H_3$)$_3$), 23.3 ($\underline{C}$(CH$_3$)$_3$), 20.8 (CO$\underline{C}H_3$),

20.6 (C(CH$_3$)$_3$), 18.1 (Rha-C-6), 16.2 (Fuc-C-6); HRMS (ESI) Calc. for [M + Na]$^+$ $C_{64}H_{82}NaO_{16}Si$: 1157.5264; Found 1157.5266.



4-Methoxyphenyl 2,4-di-*O*-benzyl-3-*O*-methyl-α-L-rhamnopyranosyl-(1→3)-[2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranosyl-(1→2)]-α-L-fucopyranoside (2.29): To a stirred solution of **2.28** (136 mg, 120 μmol) in CH_3OH (4.0 mL) was added a solution of $NaOCH_3$ in CH_3OH (0.4 mL, 0.5 M). The reaction mixture was stirred for 7 h at room temperature, then neutralized by the addition of Amberlite® IR-120 (H^+) cation exchange resin. The solution was filtered and the filtrate was concentrated to afford **2.29** (131 mg, quant.) as a syrup. R_f 0.14 (4:1 hexane–EtOAc); $[\alpha]_D$ –785 (*c* 0.45, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.42–7.41 (m, 2H, Ar), 7.38–7.35 (m, 2H, Ar), 7.32–7.21 (m, 13H, Ar), 7.16–7.14 (m, 3H, Ar), 6.88–6.86 (m, 2H, Ar), 6.77–6.75 (m, 2H, Ar), 5.64 (d, 1H, *J* = 3.6 Hz, Fuc-H-1), 4.89 (d, 1H, *J* = 11.5 Hz, PhC$\underline{H}_2$), 4.88 (d, 1H, *J* = 12.3 Hz, PhC$\underline{H}_2$), 4.86 (d, 1H, *J* = 13.3 Hz, PhC$\underline{H}_2$), 4.84 (d, 1H, *J* = 1.5 Hz, Rha-H-1), 4.66–4.57 (m, 6H, Gal-H-1, 5 × PhC$\underline{H}_2$), 4.47 (dq, 1H, *J* = 9.5, 6.2 Hz, Rha-H-5), 4.28 (d, 1H, *J* = 2.9 Hz, Gal-H-4), 4.27 (dd, 1H, *J* = 10.1, 3.1 Hz, Fuc-H-3), 3.88 (qd, 1H, *J* = 6.8, 0.7 Hz, Fuc-H-5), 3.83–3.81 (m, 2H, Rha-H-2, Fuc-H-2), 3.80 (dd, 1H, *J* = 10.2, 3.8 Hz, Gal-H-2), 3.76 (dd, 1H, *J* = 9.3, 3.4 Hz, Rha-H-'), 3.75 (s, 3H, PhOC$\underline{H}_3$),

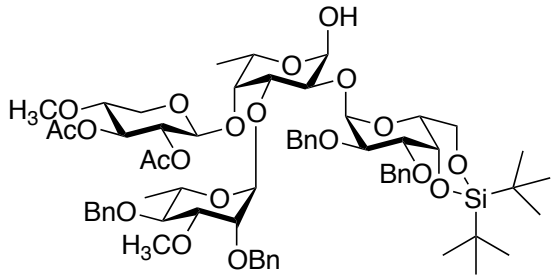
3.70 (dd, 1H, J = 10.1, 3.0 Hz, Gal-H-3), 3.64 (d, 1H, J = 2.2 Hz, Fuc-H-4), 3.58 (br s, 1H, Gal-H-5), 3.54 (t, 1H, J = 9.3 Hz, Rha-H-4), 3.42 (dd, 1H, J = 12.8, 2.1 Hz, Gal-H-6a), 3.29 (s, 3H, OC$\underline{H}_3$), 3.09 (dd, 1H, J = 12.8, 1.5 Hz, Gal-H-6b), 2.05 (br s, 1H, 4-OH), 1.37 (d, 3H, J = 6.2 Hz, Rha-H-6), 1.20 (d, 1H, J = 6.6 Hz, Fuc-H-6), 0.91 (s, 9H, C(C$\underline{H}_3$)$_3$), 0.81 (s, 9H, C(C$\underline{H}_3$)$_3$); ^{13}C NMR (125 MHz; $CDCl_3$): δ 154.5 (Ar), 150.4 (Ar), 139.6 (Ar), 139.5 (Ar), 139.0 (Ar), 138.3 (Ar), 128.5 (Ar), 128.3 (Ar), 128.2 (Ar), 128.2 (Ar), 128.1 (Ar), 128.0 (Ar), 127.9 (Ar), 127.8 (Ar), 127.4 (Ar), 127.3 (2 × Ar), 127.2 (Ar), 116.2 (Ar), 114.7 (Ar), 101.9 (Gal-C-1), 96.3 (Fuc-C-1), 81.5 (Rha-C-1), 80.5 (Rha-C-4), 78.4 (Gal-C-3), 76.8 (Fuc-C-2), 75.6 (Rha-C-2), 75.1 (Ph$\underline{C}H_2$), 73.6 (Ph$\underline{C}H_2$), 73.4 (Gal-C-2), 72.9 (Ph$\underline{C}H_2$), 71.6 (Ph$\underline{C}H_2$), 71.5 (Gal-C-4), 71.3 (Fuc-C-3), 68.1 (Rha-C-5), 68.0 (Fuc-C-4), 67.9 (Gal-C-5), 66.8 (Gal-C-6), 65.5 (Fuc-C-5), 57.9 (O$\underline{C}H_3$), 55.6 (PhO$\underline{C}H_3$), 27.5 (C($\underline{C}H_3$)$_3$), 27.2 (C($\underline{C}H_3$)$_3$), 23.3 ($\underline{C}$(CH$_3$)$_3$), 20.6 ($\underline{C}$(CH$_3$)$_3$), 18.1 (Rha-C-6), 16.3 (Fuc-C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{62}H_{80}NaO_{15}Si$: 1115.5159; Found 1115.5173.



4-Methoxyphenyl 2,3-di-*O*-acetyl-4-*O*-methyl-β-D-xylopyranosyl-(1→4)-[2,4-di-*O*-benzyl-3-*O*-methyl-α-L-rhamnopyranosyl-(1→3)]-[2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranosyl-(1→2)]-α-L-fucopyranoside (2.30): To a stirred solution of acceptor **2.29** (104 mg, 95.3 μmol) and donor **2.11** (42.5 mg, 114 μmol) in dry

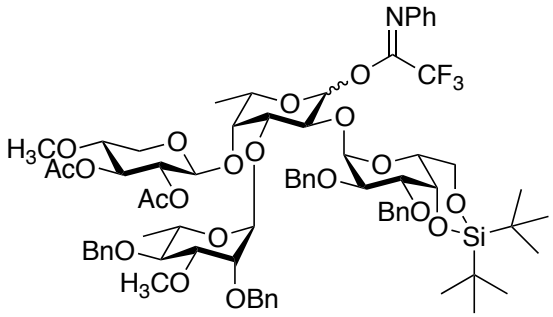
CH_2Cl_2 (5.0 mL) was added molecular sieves (500 mg, 4Å, powder). After stirring for 30 min at room temperature, the reaction mixture was cooled to –15 °C and then *N*-iodosuccinimide (32.2 mg, 143 μmol) and silver trifluoromethanesulfonate (4.9 mg, 19 μmol) were added successively. The resulting solution was stirred for 1 h at –15 °C under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was washed with saturated $Na_2S_2O_3$ (aq.) and saturated $NaHCO_3$ (aq.). The aqueous layer was extracted with CH_2Cl_2 (20 mL × 3) and the combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (3:1 hexane–EtOAc) to afford **2.30** (102 mg, 81%) as a syrup. R_f 0.36 (2:1 hexane–EtOAc); $[\alpha]_D$ –70.1 (*c* 1.1, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.43–7.42 (m, 2H, Ar), 7.38–7.34 (m, 4H, Ar), 7.30–7.23 (m, 11H, Ar), 7.15–7.13 (m, 3H, Ar), 6.85–6.83 (m, 2H, Ar), 6.76–6.73 (m, 2H, Ar), 5.60 (d, 1H, J = 3.5 Hz, Fuc-H-1), 5.11 (d, 1H, J = 1.2 Hz, Rha-H-1), 5.07 (t, 1H, J = 8.5 Hz, Xyl-H-3), 5.03 (dd, 1H, J = 8.9, 6.9 Hz, Xyl-H-2), 4.89 (d, 1H, J = 13.2 Hz, PhC$\underline{H}_2$), 4.89 (d, 1H, J = 11.4 Hz, PhC$\underline{H}_2$), 4.83 (d, 1H, J = 12.5 Hz, PhC$\underline{H}_2$), 4.69 (d, 1H, J = 12.6 Hz, PhC$\underline{H}_2$), 4.68 (d, 1H, J = 3.7 Hz, Gal-H-1), 4.65 (d, 1H, J = 11.4 Hz, PhC$\underline{H}_2$), 4.60 (d, 1H, J = 13.2 Hz, PhC$\underline{H}_2$), 4.60 (d, 1H, J = 12.2 Hz, PhC$\underline{H}_2$), 4.53 (d, 1H, J = 12.2 Hz, PhC$\underline{H}_2$), 4.45 (d, 1H, J = 6.8 Hz, Xyl-H-1), 4.39 (dq, 1H, J = 9.5, 6.2 Hz, Rha-H-5), 4.31 (dd, 1H, J = 10.5, 3.0 Hz, Fuc-H-3), 4.24 (d, 1H, J = 2.6 Hz, Gal-H-4), 3.94 (dd, 1H, J = 3.1, 1.6 Hz, Rha-H-2), 3.93–3.86 (m, 5H, Xyl-H-5a, Fuc-H-4, Rha-H-3, Fuc-H-5, Fuc-H-2), 3.80 (dd, 1H, J = 10.2, 3.6 Hz, Gal-H-2), 3.74 (s, 3H, PhOC$\underline{H}_3$), 3.70 (dd, 1H, J = 10.1, 3.0 Hz, Gal-H-3),

3.59 (br s, 1H, Gal-H-5), 3.57 (t, 1H, J = 9.6 Hz, Rha-H-4), 3.42–3.39 (m, 2H, Xyl-H-4, Gal-H-6a), 3.34 (s, 3H, OC$\underline{H}_3$), 3.25 (s, 3H, OC$\underline{H}_3$), 3.13 (dd, 1H, J = 11.8, 9.3 Hz, Xyl-H-5b), 3.09 (dd, 1H, J = 12.7, 1.4 Hz, Gal-H-6b), 2.10 (s, 3H, COC$\underline{H}_3$), 2.07 (s, 3H, COC$\underline{H}_3$), 1.38 (d, 3H, J = 6.3 Hz, Rha-H-6), 1.17 (d, 3H, J = 6.6 Hz, Fuc-H-6), 0.91 (s, 9H, C(C$\underline{H}_3$)$_3$), 0.82 (s, 9H, C(C$\underline{H}_3$)$_3$); ^{13}C NMR (125 MHz; $CDCl_3$): δ 170.2 (C=O), 169.7 (C=O), 154.4 (Ar), 150.4 (Ar), 139.7 (Ar), 139.6 (Ar), 139.2 (Ar), 139.0 (Ar), 128.4 (Ar), 128.3 (Ar), 128.2 (Ar), 128.1 (2 × Ar), 127.8 (Ar), 127.5 (2 × Ar), 127.4 (Ar), 127.2 (2 × Ar), 127.1 (Ar), 116.2 (Ar), 114.7 (Ar), 101.9 (Xyl-C-1), 101.6 (Gal-C-1), 96.3 (Fuc-C-1), 94.1 (Rha-C-1), 81.8 (Rha-C-3), 80.6 (Rha-C-4), 78.2 (Gal-C-3), 77.0 (Fuc-C-2 & Xyl-C-4), 76.1 (Rha-C-2), 75.3 (Fuc-C-4), 75.2 (Ph$\underline{C}H_2$), 73.9 (Gal-C-2), 73.1 (Xyl-C-3), 73.0 (Ph$\underline{C}H_2$), 72.8 (Ph$\underline{C}H_2$), 71.8 (Ph$\underline{C}H_2$), 71.7 (Gal-C-4), 71.5 (Xyl-C-2), 69.5 (Fuc-C-3), 68.0 (Rha-C-5), 67.8 (Gal-C-5), 66.8 (Gal-C-6), 66.2 (Fuc-C-5), 62.9 (Xyl-C-5), 58.7 (O$\underline{C}H_3$), 57.6 (O$\underline{C}H_3$), 55.6 (PhO$\underline{C}H_3$), 27.5 (C($\underline{C}H_3$)$_3$), 27.2 (C($\underline{C}H_3$)$_3$), 23.3 ($\underline{C}$(CH$_3$)$_3$), 20.9 (2 × CO$\underline{C}H_3$), 20.6 ($\underline{C}$(CH$_3$)$_3$), 18.1 (Rha-C-6), 16.6 (Fuc-C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{72}H_{94}NaO_{21}Si$: 1345.5949; Found 1345.5961.

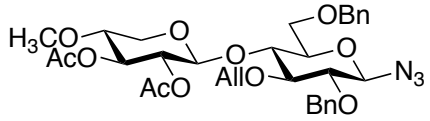


2,3-Di-*O*-acetyl-4-*O*-methyl-β-D-xylopyranosyl-(1→4)-[2,4-di-*O*-benzyl-3-*O*-methyl-α-L-rhamnopyranosyl-(1→3)]-[2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranosyl-(1→2)]-α-L-fucopyranose (2.31): To a stirred solution of **2.30** (49.6 mg, 37.5 μmol) in CH_3CN–H_2O (2.0 mL, 4:1) was added ceric(IV) ammonium nitrate (61.9 mg, 113 μmol) at 0 °C. The reaction mixture was stirred for 2 h at 0 °C. The solution was diluted with CH_2Cl_2 (25 mL) and then washed with saturated $NaHCO_3$ (aq.). The organic layer was dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (1:1 hexane–EtOAc) to afford **2.31** (29.9 mg, 65%) as a clear viscous oil. R_f 0.28 (1:1 hexane–EtOAc); $[\alpha]_D$ –32.9 (*c* 0.68, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.43–7.41 (m, 2H), 7.36–7.33 (m, 5H), 7.31–7.26 (m, 9H), 7.24–7.15 (m, 5H), 5.22 (d, 1H, *J* = 2.5 Hz, Fuc-H-1), 5.17 (d, 1H, *J* = 1.5 Hz, Rha-H-1), 5.03 (t, 1H, *J* = 8.8 Hz), 4.93 (dd, 1H, *J* = 9.1, 7.1 Hz), 4.88–4.86 (m, 2H, Gal-H-1), 4.83 (d, 1H, *J* = 12.4 Hz), 4.79 (d, 1H, *J* = 12.4 Hz), 4.71 (d, 1H, *J* = 12.4 Hz), 4.65 (d, 1H, *J* = 12.4 Hz), 4.60 (d, 1H, *J* = 11.2 Hz), 4.57 (s, 2H), 4.43 (d, 1H, *J* = 2.8 Hz), 4.41 (d, 1H, *J* = 7.1 Hz, Xyl-H-1), 4.16 (dd, 1H, *J* = 12.5, 2.0 Hz), 4.13 (dd, 1H, *J* = 8.7, 3.0 Hz), 4.09-4.01 (m, 3H), 3.93–3.87 (m, 4H), 3.83–3.80 (m, 2H), 3.76–3.72 (m, 2H), 3.53 (t, 1H, *J* = 9.4 Hz), 3.35–3.31 (m, 4H), 3.26 (s, 3H), 2.05 (s, 3H), 2.04 (s, 3H), 1.29 (d, 3H, *J* = 6.2 Hz), 1.25

(d, 3H, J = 6.8 Hz), 1.00 (s, 9H), 0.91 (s, 9H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 170.2, 169.5, 139.2, 139.1, 139.0, 138.9, 128.3 (2 × C), 128.2 (3 × C), 128.1, 127.9, 127.5 (2 × C), 127.3 (2 × C), 127.2, 101.8 (Xyl-C-1), 99.9 (Gal-C-1), 95.2 (Rha-C-1), 90.9 (Fuc-C-1), 81.7, 80.5, 77.8, 76.9, 76.4, 75.4, 75.3, 74.8, 73.6, 73.5, 73.1 (2 × C), 72.7, 71.5, 71.2, 71.1, 68.3, 68.2, 67.2, 67.0, 62.9, 58.7, 57.4, 27.6, 27.3, 23.4, 20.9, 20.80, 20.7, 18.1, 16.0; HRMS (ESI) Calc. for $[M + Na]^+$ $C_{65}H_{88}NaO_{20}Si$: 1239.5530; Found 1239.5543.

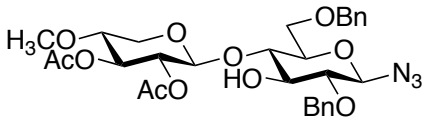


2,3-Di-*O*-acetyl-4-*O*-methyl-β-D-xylopyranosyl-(1→4)-[2,4-di-*O*-benzyl-3-*O*-methyl-α-L-rhamnopyranosyl-(1→3)]-[2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranosyl-(1→2)]-α-L-fucopyranose 1-(*N*-phenyl)-2,2,2-trifluoroacetimidate (2.6): To a solution of **2.31** (8.7 mg, 7.1 μmol) in CH_2Cl_2 (2.0 mL) was added 2,2,2-trifluoro-*N*-phenylacetimidoyl chloride (1.7 μL, 11 μmol) and cesium carbonate (4.6 mg, 14 μmol) successively. The reaction mixture was stirred overnight at room temperature. The solution was then filtered through Celite, and the filtrate was concentrated to afford **2.6**, which was used without further purification.



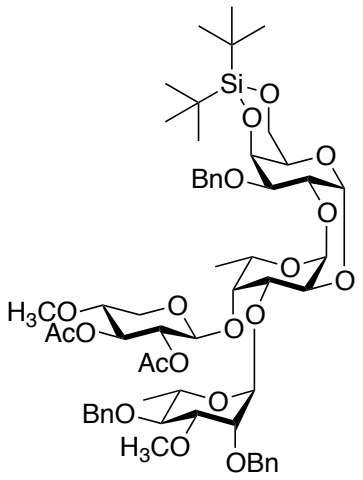
2,3-Di-*O*-acetyl-4-*O*-methyl-β-D-xylopyranosyl-(1→4)-3-*O*-allyl-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (2.32): To a stirred solution of acceptor **2.12** (616 mg, 1.45 mmol) and donor **2.11** (616 mg, 1.74 mmol) in dry CH_2Cl_2 (15 mL) was added molecular sieves (1.5 g, 4Å, powder). After stirring for 30 min at room temperature, the reaction mixture was cooled to 0 °C, and then *N*-iodosuccinimide (489 mg, 2.18 mmol) and silver trifluoromethanesulfonate (75 mg, 0.29 mmol) were added successively. The resulting solution was stirred for 1 h at room temperature under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was washed with saturated $Na_2S_2O_3$ (aq.) and saturated $NaHCO_3$ (aq.). The aqueous layer was extracted with CH_2Cl_2 (50 mL × 3) and the combined organic layer dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (3:1 hexane–EtOAc) to afford **2.32** (647 mg, 68%) as a viscous oil. R_f 0.22 (3:1 hexane–EtOAc); $[\alpha]_D$ –35.6 (*c* 1.5, $CHCl_3$); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.42–7.30 (m, 10H, Ar), 5.96 (ddt, 1H, *J* = 17.0, 10.7, 6.0 Hz, $OCH_2C\underline{H}=CH_2$), 5.27 (dq, 1H, *J* = 17.3, 1.6 Hz, $OCH_2CH=C\underline{H}_2$), 5.18 (dq, 1H, *J* = 10.5, 0.8 Hz, $OCH_2CH=C\underline{H}_2$), 4.97 (t, 1H, *J* = 9.0 Hz, Xyl-H-3), 4.83–4.78 (m, 3H, 2 × $PhC\underline{H}_2$, Xyl-H-2), 4.72 (d, 1H, *J* = 12.0 Hz, $PhC\underline{H}_2$), 4.56 (d, 1H, *J* = 8.8 Hz, Glc-H-1), 4.54 (d, 1H, *J* = 7.8 Hz, Xyl-H-1), 4.51 (d, 1H, *J* = 12.0 Hz, $PhC\underline{H}_2$), 4.39 (ddt, 1H, *J* = 11.9, 5.7, 1.4 Hz, $OC\underline{H}_2CH=CH_2$), 4.25 (ddt, 1H, *J* = 11.8, 5.9, 1.4 Hz, $OC\underline{H}_2CH=CH_2$), 4.09 (dd, 1H, *J* = 11.8, 5.2, 1.4 Hz, Xyl-H-5a),

3.89 (t, 1H, J = 9.4 Hz, Glc-H-4), 3.74–3.73 (m, 2H, Glc-H-6), 3.44-3.38 (m, 6H, Glc-H-3, Xyl-H-4, OCH_3, Glc-H-5), 3.29 (t, 1H, J = 8.9 Hz, Glc-H-2), 3.12 (dd, 1H, J = 11.7, 10.1 Hz, Xyl-H-5b), 2.07 (s, 3H, $COC\underline{H}_3$), 1.98 (s, 3H, $COC\underline{H}_3$); ^{13}C NMR (125 MHz; $CDCl_3$): δ 170.1 (C=O), 169.6 (C=O), 137.8 (Ar), 137.7 (Ar), 135.1 ($OCH_2\underline{C}H=CH_2$), 128.6 (Ar), 128.4 (Ar), 128.2 (Ar), 128.0 (Ar), 127.9 (2 × Ar), 116.9 ($OCH_2CH=\underline{C}H_2$), 100.5 (Xyl-C-1), 90.1 (Glc-C-1), 82.6 (Glc-C-3), 81.2 (Glc-C-2), 77.1 (Xyl-C-4 or Glc-C-5), 77.0 (Xyl-C-4 or Glc-C-5), 76.1 (Glc-C-4), 75.4 ($Ph\underline{C}H_2$), 74.6 ($O\underline{C}H_2CH=CH_2$), 74.0 (Xyl-C-3), 73.7 ($Ph\underline{C}H_2$), 72.2 (Xyl-C-2), 67.4 (Glc-C-6), 63.2 (Xyl-C-5), 58.8 ($O\underline{C}H_3$), 20.9 ($CO\underline{C}H_3$), 20.8 ($CO\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{33}H_{41}N_3NaO_{11}$: 678.2633; Found 678.2631.



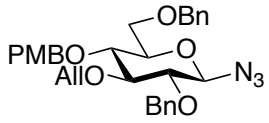
2,3-Di-*O*-acetyl-4-*O*-methyl-β-D-xylopyranosyl-(1→4)-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (2.7): To a stirred solution of **2.32** (217 mg, 331 μmol) in dry THF (6.0 mL), degassed under vacuum, and stirring under an Ar atmosphere, (1,5-cyclooctadiene)bis(methyldiphenylphosphine)iridium (I) hexafluorophosphate (16.7 mg, 19.8 μmol) was added, followed by further degassing of the reaction mixture. The suspension was stirred for 15 min at 0 °C, and the catalyst was then activated with hydrogen (2 min under a hydrogen atmosphere). The excess hydrogen was removed by three cycles of vacuum/Ar. The reaction mixture was then stirred for 2 h at room temperature under an Ar atmosphere. The solvent was then evaporated, and the residue was dissolved in acetone–

water (10:1, 6.6 mL) before HgO (100 mg, 462 μmol) and $HgCl_2$ (108 mg, 396 μmol) were added. The reaction mixture was stirred for 2 h at room temperature, the solvent was evaporated, and the residue was diluted with EtOAc (50 mL), washed with 10% KI, saturated $Na_2S_2O_3$ (aq.) and water. The aqueous layers were extracted with EtOAc (50 mL), and the combined organic layers were dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (2:1 hexane–EtOAc) to afford **2.7** (183 mg, 90%) as a syrup. R_f 0.31 (2:1 hexane–EtOAc); $[\alpha]_D$ –34.9 (*c* 1.5, $CHCl_3$); ^1H NMR (500 MHz; $CDCl_3$): δ 7.44–7.29 (m, 10H, Ar), 5.01 (t, 1H, J = 9.3 Hz, Xyl-H-3), 4.91 (d, 1H, J = 11.1 Hz, PhC$\underline{H}_2$), 4.85 (dd, 1H, J = 9.6, 7.9 Hz, Xyl-H-2), 4.83 (d, 1H, J = 11.1 Hz, PhC$\underline{H}_2$), 4.72 (d, 1H, J = 11.9 Hz, PhC$\underline{H}_2$), 4.58 (d, 1H, J = 8.6 Hz, Glc-H-1), 4.50 (d, 1H, J = 12.0 Hz, PhC$\underline{H}_2$), 4.39 (d, 1H, J = 7.9 Hz, Xyl-H-1), 4.16 (dd, 1H, J = 11.7, 5.3 Hz, Xyl-H-5a), 3.81 (s, 1H, Glc-3-OH), 3.74–3.65 (m, 4H, Glc-H-6a, Glc-H-3, Glc-H-5, Glc-H-6b), 3.49–3.43 (m, 5H, Glc-H-4, Xyl-H-4, OC$\underline{H}_3$), 3.29 (t, 1H, J = 8.6 Hz, Glc-H-2), 3.23 (dd, 1H, J = 11.7, 10.4 Hz, Xyl-H-5b), 2.08 (s, 3H, COC$\underline{H}_3$), 1.98 (s, 3H, COC$\underline{H}_3$); ^{13}C NMR (125 MHz; $CDCl_3$): δ 170.1 (C=O), 169.3 (C=O), 138.0 (Ar), 137.7 (Ar), 128.6 (Ar), 128.4 (Ar), 128.2 (Ar), 128.1 (Ar), 128.0 (Ar), 127.8 (Ar), 101.2 (Xyl-C-1), 89.7 (Glc-C-1), 80.7 (Glc-C-2), 79.2 (Glc-C-5), 76.8 (Xyl-C-4), 75.9 (Glc-C-4), 75.4 (Glc-C-3), 74.9 (Ph$\underline{C}H_2$), 74.0 (Xyl-C-3), 73.8 (Ph$\underline{C}H_2$), 71.6 (Xyl-C-2), 67.4 (Glc-C-6), 63.6 (Xyl-C-5), 59.0 (O$\underline{C}H_3$), 20.9 (CO$\underline{C}H_3$), 20.7 (CO$\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{30}H_{37}N_3NaO_{11}$: 638.2320; Found 638.2330.



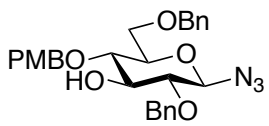
2,3-Di-*O*-acetyl-4-*O*-methyl-β-D-xylopyranosyl-(1→4)-[2,4-di-*O*-benzyl-3-*O*-methyl-α-L-rhamnopyranosyl-(1→3)]-α-L-fucopyranose 3-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranose 1,2':1':2 anhydride (**2.33**)**:** To a stirred solution of acceptor **2.7** (2.8 mg, 4.5 μmol) and donor **2.6** (7.5 mg, 5.4 μmol) in dry CH_2Cl_2 (1.0 mL) was added molecular sieves (100 mg, 4Å, powder). After stirring for 30 min at room temperature, the reaction mixture was cooled to –78 °C, and then *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.2 μL, 0.9 μmol) was added dropwise. The resulting solution was stirred at –78 °C for 1 h under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (2:1 hexane–EtOAc) to afford **2.33** (3.7 mg, 61%) as a viscous oil. R_f 0.16 (2:1 hexane–EtOAc); $[\alpha]_D$ –34.4 (*c* 0.45, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.42–7.39 (m, 4H), 7.36–7.32 (m, 8H), 7.29–7.26 (m, 3H), 5.33 (d, 1H, J = 3.6 Hz, Gal-H-1), 5.04 (d, 1H, J = 3.6 Hz, Fuc-H-1), 5.02 (t, 1H, J = 8.3 Hz), 4.91 (dd, 1H, J = 8.5, 6.6 Hz), 4.87 (d, 1H, J = 10.9 Hz), 4.84 (d, 1H, J = 1.4 Hz, Rha-H-1), 4.82 (d, 1H, J = 12.6 Hz), 4.78 (d, 1H, J = 12.4 Hz), 4.67 (d, 1H, J = 12.6 Hz), 4.65 (d, 1H, J =

12.4 Hz), 4.62 (d, 1H, J = 10.9 Hz), 4.58 (d, 1H, J = 2.7 Hz), 4.36 (dd, 1H, J = 10.5, 3.1 Hz), 4.34–4.32 (m, 2H, Xyl-H-1), 4.14–4.09 (m, 2H), 4.04–3.98 (m, 3H), 3.96 (dd, 1H, J = 10.5, 3.6 Hz), 3.88 (dd, 1H, J = 2.9, 1.9 Hz), 3.80 (dd, 1H, J = 11.9, 4.7 Hz), 3.68 (br s, 1H), 3.65–3.63 (m, 2H), 3.55 (t, 1H, J = 9.5 Hz), 3.50 (s, 3H), 3.34 (s, 3H), 3.29 (td, 1H, J = 8.3, 4.7 Hz), 3.08 (dd, 1H, J = 11.9, 8.7 Hz), 2.07 (s, 3H), 2.04 (s, 3H), 1.29 (d, 3H, J = 6.2 Hz), 1.20 (d, 3H, J = 6.6 Hz), 1.03 (s, 9H), 1.01 (s, 9H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 170.1, 169.7, 138.8, 138.7, 138.2, 128.5 (2 × C), 128.4, 128.0, 127.8, 127.7 (2 × C), 127.6, 127.5, 101.7 (Xyl-C-1), 96.2 (Rha-C-1), 88.7 (Fuc-C-1), 88.4 (Gal-C-1), 81.4, 80.6, 76.9, 76.7, 75.2, 75.1, 72.9, 72.32, 72.28, 72.0, 71.1, 70.5, 69.9, 69.6, 69.0, 68.8, 68.5, 68.0, 67.4, 62.6, 58.5, 58.1, 27.6, 27.3, 23.4, 20.9 (2 × C), 20.7, 17.9, 16.6; HRMS (ESI) Calc. for $[M + Na]^+$ $C_{58}H_{80}NaO_{19}Si$: 1131.4955; Found 1131.4959.



3-*O*-Allyl-2,6-di-*O*-benzyl-4-O-(4-methoxybenzyl)-β-D-glucopyranosyl azide (2.34): To a stirred solution of **2.12** (62.6 mg, 147 μmol) in dry DMF (3.0 mL) was added sodium hydride (11.8 mg, 294 μmol, 60% dispersion in mineral oil) in one portion at 0 °C. After stirring for 30 min, 4-methoxybenzyl chloride (30.0 μL, 221 μmol) was added dropwise, and the reaction mixture was warmed to room temperature and stirred for 2.5 h under an Ar atmosphere. Then, CH_3OH was added at 0 °C and the solution was concentrated. The crude residue was diluted with CH_2Cl_2 (25 mL), washed with saturated $NaHCO_3$ (aq.), dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was

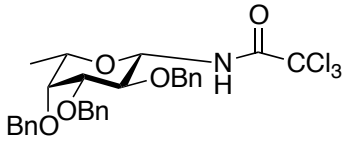
purified by flash chromatography (6:1 hexane–EtOAc) to afford **2.34** (77.1 mg, 96%) as a viscous oil. R_f 0.47 (4:1 hexane–EtOAc); $[\alpha]_D$ +2.1 (*c* 0.37, $CHCl_3$); ^1H NMR (500 MHz; $CDCl_3$): δ 7.41–7.29 (m, 10H, Ar), 7.16–7.12 (m, 2H, Ar), 6.87–6.84 (m, 2H, Ar), 5.98 (ddt, *J* =17.2, 10.5, 5.7 Hz, $OCH_2C\underline{H}=CH_2$), 5.31 (dq, *J* = 17.2, 1.7 Hz, $OCH_2CH=C\underline{H}_2$), 5.20 (dq, *J* = 10.5, 1.3 Hz, $OCH_2CH=C\underline{H}_2$), 4.87 (d, 1H, *J* = 10.7 Hz, $PhC\underline{H}_2$), 4.77 (d, 1H, *J* = 10.7 Hz, $PhC\underline{H}_2$), 4.75 (d, 1H, *J* = 10.3 Hz, $PhC\underline{H}_2$), 4.64 (d, 1H, *J* = 12.2 Hz, $PhC\underline{H}_2$), 4.59 (d, 1H, *J* = 8.7 Hz, H-1), 4.57 (d, 1H, *J* = 12.2 Hz, $PhC\underline{H}_2$) 4.49 (d, 1H, *J* = 10.3 Hz, $PhC\underline{H}_2$), 4.39 (ddt, 1H, *J* = 12.4, 5.6, 1.4 Hz, $OC\underline{H}_2CH=CH_2$), 4.33 (ddt, 1H, *J* = 12.4, 5.6, 1.4 Hz, $OC\underline{H}_2CH=CH_2$), 3.82 (s, 3H, Ar-$OC\underline{H}_3$), 3.75 (dd, 1H, *J* = 10.9, 1.9 Hz, H-6a), 3.70 (dd, 1H, *J* = 11.0, 4.4 Hz, H-6b), 3.57 (t, 1H, *J* = 9.3 Hz, H-4), 3.52–3.48 (m, 2H, H-3, H-5), 3.32 (t, 1H, *J* = 8.9 Hz, H-2); ^{13}C NMR (125 MHz; $CDCl_3$): δ 159.4 (Ar), 138.0 (Ar), 137.8 (Ar), 134.9 ($OCH_2\underline{C}H=CH_2$), 130.1 (Ar), 129.8 (Ar), 128.5 (Ar), 128.4 (Ar), 128.3 (Ar), 128.0 (Ar), 127.9 (Ar), 127.7 (Ar), 116.8 ($OCH_2CH=\underline{C}H_2$), 113.9 (Ar), 90.1 (C-1), 84.6 (C-3), 81.6 (C-2), 77.1 (C-5), 76.9 (C-4), 75.2 ($Ph\underline{C}H_2$), 74.8 ($Ph\underline{C}H_2$), 74.5 ($O\underline{C}H_2CH=CH_2$), 73.6 ($Ph\underline{C}H_2$), 68.4 (C-6), 55.3 (Ar-$O\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{31}H_{35}N_3NaO_6$: 568.2418; Found 568.2418.



2,6-Di-*O*-benzyl-4-*O*-(4-methoxybenzyl)-β-D-glucopyranosyl azide (2.35): To a stirred solution of **2.34** (73.6 mg, 135 μmol) in dry THF (3.0 mL), degassed under vacuum, and stirring under an Ar atmosphere, (1,5-

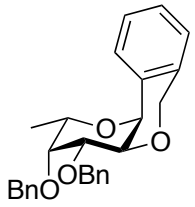
cyclooctadiene)bis(methyldiphenylphosphine)iridium (I) hexafluorophosphate (6.8 mg, 8.1 μmol) was added, followed by further degassing of the reaction mixture. The suspension was stirred for 15 min at 0 °C, and the catalyst was then activated with hydrogen (2 min under a hydrogen atmosphere). The excess hydrogen was removed by three cycles of vacuum/Ar. The reaction mixture was then stirred for 2 h at room temperature under an Ar atmosphere. The solvent was then evaporated, and the residue was dissolved in acetone–water (10:1, 5.5 mL) before HgO (40.9 mg, 189 μmol) and $HgCl_2$ (44.0 mg, 162 μmol) were added. The reaction mixture was stirred for 2 h at room temperature, then the solvent was evaporated, and the residue was diluted with EtOAc (50 mL), washed with 10% KI, saturated $Na_2S_2O_3$ (aq.) and water. The aqueous layers were extracted with EtOAc (50 mL), and the combined organic layers were dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (4:1 hexane–EtOAc) to afford **2.35** (60.2 mg, 88%) as a white solid. R_f 0.18 (4:1 hexane–EtOAc); $[\alpha]_D$ –5.2 (*c* 0.31, $CHCl_3$); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.41–7.31 (m, 10H, Ar), 7.19–7.16 (m, 2H, Ar), 6.87–6.84 (m, 2H, Ar), 4.93 (d, 1H, J = 11.2 Hz, PhC$\underline{H}_2$), 4.72 (d, 1H, J = 11.2 Hz, PhC$\underline{H}_2$), 4.71 (d, 1H, J = 10.9 Hz, PhC$\underline{H}_2$) 4.66 (d, 1H, J = 12.1 Hz, PhC$\underline{H}_2$), 4.62 (d, 1H, J = 8.6 Hz, H-1), 4.58 (d, 1H, J = 12.2 Hz, PhC$\underline{H}_2$), 4.54 (d, 1H, J = 10.9 Hz, PhC$\underline{H}_2$), 3.81 (s, 3H, Ar-OC$\underline{H}_3$), 3.79–3.69 (m, 3H, H-6a, H-6b, H-3), 3.56–3.52 (m, 2H, H-4, H-5), 3.23 (t, 1H, J = 8.9 Hz, H-2), 2.36 (d, 1H, J = 2.3 Hz, 3-OH); ^{13}C NMR (125 MHz; $CDCl_3$): δ 159.4 (Ar), 138.0 (Ar), 137.8 (Ar), 130.2 (Ar), 129.7 (Ar), 128.6 (Ar), 128.4 (Ar), 128.2 (Ar), 128.1 (Ar), 127.9 (Ar), 127.8 (Ar), 113.9 (Ar), 89.8 (C-1), 81.0 (C-2), 77.1 (C-3),

77.0 (C-4 or C-5), 76.6 (C-4 or C-5), 74.8 (Ph<u>C</u>H$_2$), 74.3 (Ph<u>C</u>H$_2$), 73.6 (Ph<u>C</u>H$_2$), 68.5 (C-6), 55.3 (Ar-O<u>C</u>H$_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{28}H_{31}N_3NaO_6$: 528.2105; Found 528.2096.



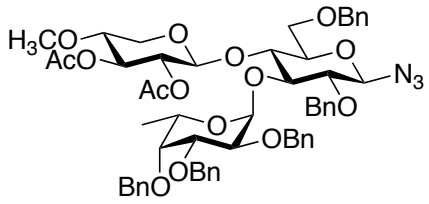
1-*N*-Trichloroacetyl-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)amine (2.39): To a stirred solution of acceptor **2.7** (28.2 mg, 45.8 μmol) and 2,3,4-tri-*O*-benzyl-1-thio-α-L-rhamnopyranosyl trichloroacetimidate **2.36**[25] (31.8 mg, 54.9 μmol) in dry CH_2Cl_2 (2.0 mL) was added molecular sieves (200 mg, 4Å, powder). After stirring for 30 min at room temperature, the reaction mixture was cooled to –78 °C, and then trifluoromethanesulfonic acid (0.4 μL, 5 μmol) was added dropwise. The resulting solution was stirred for 1 h at –78 °C under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (3:1 hexane–EtOAc) to afford **2.39** (16.7 mg, 53%) as a syrup. R_f 0.46 (3:1 hexane–EtOAc); $[\alpha]_D$ –2.7 (*c* 1.7, $CHCl_3$); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.42–7.28 (m, 15H), 7.07 (d, 1H, J = 9.2 Hz, N-H), 5.08 (t, 1H, J = 9.0 Hz, H-1), 5.01 (d, 1H, J = 11.5 Hz, PhC<u>H</u>$_2$), 4.87 (d, 1H, J = 11.1 Hz, PhC<u>H</u>$_2$), 4.79 (d, 1H, J = 11.1 Hz, PhC<u>H</u>$_2$), 4.79 (s, 2H, PhC<u>H</u>$_2$), 4.73 (d, 1H, J = 11.5 Hz, PhC<u>H</u>$_2$), 3.87 (t, 1H, J = 9.0 Hz, H-2), 3.73 (dd, 1H, J = 9.3, 2.8 Hz, H-3), 3.69–3.65 (m, 2H, H-4, H-5), 1.21 (d, 3H, J = 6.4 Hz, H-6); ^{13}C NMR (125 MHz; $CDCl_3$): δ 161.7 (C=O), 138.1 (Ar), 138.0 (Ar), 137.7 (Ar), 128.6 (3 × Ar), 128.4 (2 × Ar), 128.0 (Ar), 127.9 (Ar), 127.7 (Ar), 92.3 (<u>C</u>Cl$_3$), 83.8 (C-3), 81.0 (C-

1), 77.1 (C-2), 76.3 (C-4), 75.1 (Ph<u>C</u>H$_2$), 75.0 (Ph<u>C</u>H$_2$), 73.0 (Ph<u>C</u>H$_2$), 72.9 (C-5), 16.9 (C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{29}H_{30}Cl_3NNaO_5$: 600.1082; Found 600.1083.



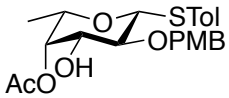
(2*S*,3*R*,4*R*,4*aR*,10*bS*)-3,4-bis(benzyloxy)-2-methyl-2,3,4,4*a*,6,10*b*-hexahydropyrano[3,2-*c*]isochromene (2.40): To a stirred solution of acceptor **2.7** (21.6 mg, 36.7 μmol) and 2,3,4-tri-*O*-benzyl-α-L-rhamnopyranose 1-(*N*-phenyl)-2,2,2-trifluoroacetimidate **2.37**[26] (26.6 mg, 44.0 μmol) in dry CH_2Cl_2 (3.0 mL) was added molecular sieves (300 mg, 4Å, powder). After stirring for 30 min at room temperature, the reaction mixture was cooled to –78 °C, and trifluoromethanesulfonic acid (0.4 μL, 4 μmol) was added dropwise. The resulting solution was stirred for 1 h at –78 °C under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (3:1 hexane–EtOAc) to afford **2.40** (11.0 mg, 60%) as a white solid. R_f 0.76 (2:1 hexane–EtOAc); $[\alpha]_D$ –47.3 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.46–7.23 (m, 13H, Ar), 7.00–6.99 (m, 1H, Ar), 4.98 (d, 1H, J = 3.9 Hz, H-1), 4.86 (d, 1H, J = 11.7 Hz, PhC<u>H</u>$_2$), 4.82 (d, 1H, J = 11.8 Hz, PhC<u>H</u>$_2$), 4.73–4.70 (m, 3H, PhC<u>H</u>$_2$), 4.68 (d, 1H, J = 11.7 Hz, PhC<u>H</u>$_2$), 4.28 (dd, 1H, J = 6.3, 4.1 Hz, H-2), 3.92–3.87 (m, 3H, H-5, H-3, H-4), 1.44 (d, 3H, J = 6.6 Hz, H-6); ^{13}C NMR (125 MHz; $CDCl_3$): δ 138.6 (Ar), 138.5 (Ar), 135.2 (Ar), 132.3 (Ar), 128.5 (Ar), 128.4 (Ar), 128.3 (Ar), 127.9 (Ar), 127.7 (2 × Ar), 127.6 (Ar), 127.0

(Ar), 123.8 (Ar), 76.7 (C-3 or C-4), 75.8 (C-3 or C-4), 73.8 (C-2), 73.5 (Ph<u>C</u>H$_2$), 72.3 (Ph<u>C</u>H$_2$), 70.4 (C-5), 65.6 (C-1), 65.2 (Ph<u>C</u>H$_2$), 15.7 (C-6); HRMS (ESI) Calc. for [M + Na]$^+$ $C_{27}H_{28}NaO_4$: 439.1880; Found 439.1882.



2,3-Di-*O*-acetyl-4-*O*-methyl-β-D-xylopyranoside-(1→4)-[2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl-(1→3)]-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (2.42): To a stirred solution of acceptor **2.7** (3.6 mg, 5.9 μmol) and *p*-tolyl 2,3,4-tri-*O*-benzyl-α-L-fucopyranoside **2.38**[27] (9.6 mg, 18 μmol) in dry Et_2O (1.0 mL) was added molecular sieves (100 mg, 4Å, powder). After stirring for 30 min at room temperature, methyl trifluoromethanesulfonate (3.3 μL, 30 μmol) was added dropwise. The resulting solution was stirred for 24 h at room temperature under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (3:1 hexane–EtOAc) to afford **2.42** (4.5 mg, 74%) as a syrup. R_f 0.50 (2:1 hexane–EtOAc); $[\alpha]_D$ –52.4 (*c* 0.36, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.41–7.23 (m, 18H, Ar), 7.17–7.10 (m, 7H, Ar), 5.57 (d, 1H, J = 3.7 Hz, Fuc-H-1), 4.96 (d, 1H, J = 11.5 Hz, PhC<u>H</u>$_2$), 4.87 (t, 1H, J = 9.5 Hz, Xyl-H-3), 4.86 (d, 1H, J = 11.2 Hz, PhC<u>H</u>$_2$), 4.82 (d, 1H, J = 11.9 Hz, PhC<u>H</u>$_2$), 4.75–4.60 (m, 7H, 6 × PhC<u>H</u>$_2$, Xyl-H-2), 4.58–4.56 (m, 2H, Glc-H-1, Fuc-H-5), 4.48 (dd, 1H, J = 8.2 Hz, Glc-H-1), 4.47 (d, 1H, J = 11.9 Hz, PhC<u>H</u>$_2$), 4.16 (dd, 1H, J = 10.2, 2.7 Hz, Fuc-H-3), 4.05

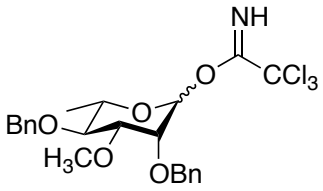
(t, 1H, J = 9.7 Hz, Glc-H-4), 4.03 (dd, 1H, J = 10.2, 3.7 Hz, Fuc-H-2), 3.90 (t, 1H, J = 9.2 Hz, Glc-H-3), 3.79 (dd, 1H, J = 11.3, 2.8 Hz, Glc-H-6a), 3.75–3.72 (m, 2H, Glc-H-6b, Xyl-H-5a), 3.67 (dd, 1H, J = 2.7, 1.3 Hz, Fuc-H-4), 3.44 (t, 1H, J = 8.8 Hz, Glc-H-2), 3.39–3.37 (m, 1H, Glc-H-5), 3.29 (s, 3H, OC$\underline{H}_3$), 3.16–3.13 (m, 1H, Xyl-H-4), 2.88 (dd, 1H, J = 11.8, 10.8 Hz, Xyl-H5b), 2.04 (s, 3H, COC$\underline{H}_3$), 1.95 (s, 3H, COC$\underline{H}_3$), 1.20 (d, 3H, J = 6.6 Hz, Fuc-H-6); ^{13}C NMR (125 MHz; $CDCl_3$): δ 170.1 (C=O), 169.0 (C=O), 139.0 (Ar), 138.9 (Ar), 138.3 (Ar), 137.8 (Ar), 137.6 (Ar), 128.6 (Ar), 128.4 (Ar), 128.2 (2 × Ar), 128.1 (2 × Ar), 128.1 (Ar), 128.0 (Ar), 127.5 (2 × Ar), 127.4 (Ar), 127.0 (Ar), 126.8 (Ar), 100.3 (Xyl-C-1), 97.2 (Fuc-C-1, $^1J_{C\text{-}H}$ = 174.8 Hz), 90.2 (Glc-C-1), 82.6 (Glc-C-2), 79.7 (Fuc-C-3), 78.9 (Fuc-C-4), 77.6 (Xyl-C-4), 77.1 (Glc-C-5), 75.4 (Fuc-C-2), 75.0 ($PhCH_2$), 74.4 (Xyl-C-3), 74.2 (Glc-C-3), 73.9 ($PhCH_2$), 73.8 ($PhCH_2$), 73.4 ($PhCH_2$), 72.8 ($PhCH_2$), 71.8 (Xyl-C-2), 67.2 (Glc-C-6), 66.3 (Fuc-C-5), 63.3 (Xyl-C-5), 58.8 (O$\underline{C}H_3$), 20.9 (CO$\underline{C}H_3$), 20.6 (CO$\underline{C}H_3$), 16.5 (Fuc-C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{57}H_{65}N_3NaO_{15}$: 1054.4308; Found 1054.4306.



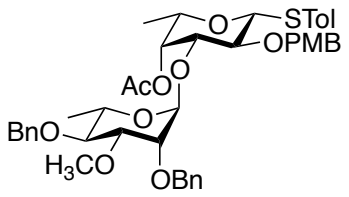
***p*-Tolyl 4-*O*-acetyl-2-*O*-(4-methoxybenzyl)-1-thio-β-L-fucopyranoside (2.47):** To a stirred solution of *p*-tolyl 1-thio-β-L-fucopyranoside **2.48**[35] (2.40 g, 8.89 mmol) in dry CH_3CN (90 mL) was added trimethyl orthoacetate (1.25 mL, 9.78 mmol) and *p*-toluenesulfonic acid monohydrate (169 mg, 0.889 mmol) successively at 0 °C. The reaction mixture was stirred for 3 h under an Ar atmosphere. Excess triethylamine was added to

quench the acid, the mixture was filtered and the filtrate was concentrated. The crude reaction mixture was then dissolved in dry DMF (24 mL), then sodium hydride (0.712 g, 17.8 mmol, 60% dispersion in mineral oil) was added in one portion at 0 °C. After stirring for 30 min, 4-methoxybenzyl chloride (1.44 mL, 10.7 mmol) and tetrabutylammonium iodide (328 mg, 0.889 mmol) were added successively, and the reaction mixture was warmed to room temperature and stirred for 1 h under an Ar atmosphere. Then, CH_3OH was added at 0 °C and the solution was concentrated. The crude residue was diluted with CH_2Cl_2 (100 mL), washed with saturated $NaHCO_3$ (aq.), dried over Na_2SO_4, filtered and the filtrate was concentrated. The reaction was then dissolved in CH_2Cl_2 (50 mL) and 1N HCl was added (50 mL). The reaction mixture was stirred for 1 h at room temperature, then the aqueous layer was extracted with CH_2Cl_2 (50 mL × 3) and combined organic layers were dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (1:1 hexane–EtOAc) to afford **2.47** (3.0 g, 79%) as a viscous oil. R_f 0.15 (2:1 hexane–EtOAc); $[\alpha]_D$ –11.2 (*c* 0.68, $CHCl_3$); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.52–7.51 (m, 2H, Ar), 7.34–7.33 (m, 2H, Ar), 7.16–7.14 (m, 2H, Ar), 6.91–6.90 (m, 2H, Ar), 5.20 (d, 1H, J = 3.4 Hz, H-4), 4.93 (d, 1H, J = 10.5 Hz, PhC$\underline{H}_2$), 4.60 (d, 1H, J = 10.6 Hz, PhC$\underline{H}_2$), 4.59 (d, 1H, J = 9.6 Hz, H-1), 3.84–3.79 (m, 4H, ArOC$\underline{H}_3$, H-3), 3.71 (q, 1H, J = 6.4 Hz, H-5), 3.58 (t, 1H, J = 9.5 Hz, H-2), 2.37 (s, 3H, ArC$\underline{H}_3$), 2.21 (d, 1H, J = 3.2 Hz, 3-OH), 2.18 (s, 3H, COC$\underline{H}_3$), 1.24 (d, 3H, J = 6.4 Hz, H-6); ^{13}C NMR (125 MHz; $CDCl_3$): δ 171.2 (C=O), 159.5 (Ar), 137.7 (Ar), 132.3 (Ar), 130.2 (Ar), 129.9 (Ar), 129.6 (Ar), 114.0 (Ar), 87.9 (C-1), 77.6 (C-2), 75.0 (Ph$\underline{C}H_2$), 73.9 (C-3), 73.2 (C-5), 72.6

(C-4), 55.3 (ArO<u>C</u>H$_3$), 21.1 (ArCH$_3$), 20.9 (CO<u>C</u>H$_3$), 16.7 (C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{23}H_{28}NaO_6S$: 455.1499; Found 455.1498.

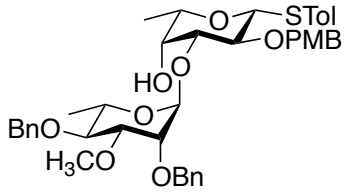


2,4-Di-*O*-benzyl-3-*O*-methyl-1-thio-α-L-rhamnopyranosyl trichloroacetimidate (2.49): To a stirred solution of **2.9** (301 mg, 0.648 mmol) in dry acetone–H_2O (11 mL, 10:1) was added and *N*-bromosuccinimide (345 mg, 1.94 mmol) at 0 °C. The reaction mixture was stirred for 2 h at room temperature, then CH_3OH was added and the solution was concentrated. The residue was then diluted with CH_2Cl_2 and washed with saturated $NaHCO_3$ (aq.). The aqueous layer was extracted with CH_2Cl_2 (50 mL × 3), and the combined organic layers were dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (2:1 hexane–EtOAc) to afford the hemiactal (227 mg, 98%). Then, to a solution of this hemiactal (191 mg, 0.533 mmol) in CH_2Cl_2 (12 mL) was added trichloroacetonitrile (1.07 mL, 10.7 mmol) and cesium carbonate (173 mg, 0.531 mmol) successively. The reaction mixture was stirred overnight at room temperature. The crude residue was then filtered through Celite, and the filtrate was concentrated to afford **2.49**, which was used without further purification.



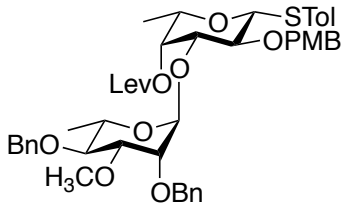
***p*-Tolyl 2,4-di-*O*-benzyl-3-*O*-methyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-2-*O*-(4-methoxybenzyl)-1-thio-β-L-fucopyranoside (2.50):** To a stirred solution of acceptor **2.47** (190 mg, 0.439 mmol) and donor **2.49** (267 mg, 0.527 mmol) in dry CH_2Cl_2 (5.0 mL) was added molecular sieves (500 mg, 4Å, powder). After stirring for 30 min at room temperature, the reaction mixture was cooled to –30 °C, and then *tert*-butyldimethylsilyl trifluoromethanesulfonate (10.0 μL, 53.0 μmol) was added dropwise. The resulting solution was stirred for 1 h at –30 °C under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (4:1 hexane–EtOAc) to afford **2.50** (258 mg, 76%) as a white foam. R_f 0.29 (4:1 hexane–EtOAc); $[\alpha]_D$ –40.6 (*c* 0.98, $CHCl_3$); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.54–7.49 (m, 4H, Ar), 7.45–7.28 (m, 10H, Ar), 7.14–7.13 (m, 2H, Ar), 6.59–6.57 (m, 2H, Ar), 5.30 (d, 1H, J = 3.1 Hz, Fuc-H-4), 5.21 (d, 1H, J = 0.2 Hz, Rha-H-1), 5.02 (d, 1H, J = 10.9 Hz, PhC$\underline{H}_2$), 4.83 (d, 1H, J = 12.7 Hz, PhC$\underline{H}_2$), 4.70 (d, 1H, J = 12.6 Hz, PhC$\underline{H}_2$), 4.64–4.59 (m, 4H, PhC$\underline{H}_2$, 2 × ArC$\underline{H}_2$, Fuc-H-1), 4.00–3.92 (m, 2H, Rha-H-5, Fuc-H-3), 3.70–3.61 (m, 6H, $ArOCH_3$, Fuc-H-5, Rha-H-2, Rha-H-3), 3.58–3.53 (m, 2H, Rha-H-4, Fuc-H-2), 3.37 (s, 3H, OCH_3), 2.36 (s, 3H, $ArCH_3$), 2.18 (s, 3H, COC$\underline{H}_3$), 1.26 (d, 3H, J = 6.4 Hz, Fuc-H-6), 1.24 (d, 3H, J = 6.1 Hz, Rha-H-6); ^{13}C NMR (125 MHz; $CDCl_3$): δ 170.7 (C=O), 159.4 (Ar), 139.3 (Ar), 138.4 (Ar), 137.6 (Ar),

132.4 (Ar), 131.0 (Ar), 130.2 (Ar), 129.6 (Ar), 128.2 (2 × Ar), 128.1 (Ar), 127.9 (Ar), 127.5 (Ar), 127.4 (Ar), 113.7 (Ar), 93.2 (Rha-C-1, $^{1}J_{C\text{-}H}$ = 170.2 Hz), 88.2 (Fuc-C-1), 81.8 (Rha-C-3), 80.7 (Rha-C-4), 75.8 (Ar<u>C</u>H$_2$), 75.5 (Fuc-C-2), 75.4 (Ph<u>C</u>H$_2$), 75.2 (Fuc-C-3), 73.5 (Rha-C-2), 72.6 (Fuc-C-5), 71.9 (Ph<u>C</u>H$_2$), 68.7 (Fuc-C-4), 67.9 (Rha-C-5), 57.6 (O<u>C</u>H$_3$), 55.3 (ArO<u>C</u>H$_3$), 21.1 (Ar<u>C</u>H$_3$), 20.9 (CO<u>C</u>H$_3$), 18.0 (Rha-C-6), 16.8 (Fuc-C-6); HRMS (ESI) Calc. for [M + Na]$^+$ $C_{44}H_{52}NaO_{10}S$: 795.3171; Found 795.3170.



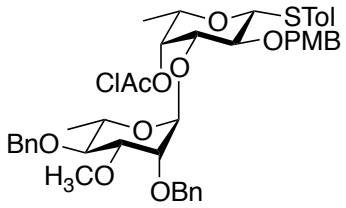
***p*-Tolyl 2,4-di-*O*-benzyl-3-*O*-methyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-(4-methoxybenzyl)-1-thio-β-L-fucopyranoside (2.51):** To a stirred solution of **2.50** (258 mg, 0.334 mmol) in CH_3OH (10 mL) was added a solution of $NaOCH_3$ in CH_3OH (1.0 mL, 0.5 M). The reaction mixture was stirred overnight at room temperature, neutralized by addition of Amberlite® IR-120 (H^+) cation exchange resin, filtered and the filtrate was concentrated to afford **2.51** (241 mg, quant.) as a white foam. R_f 0.18 (3:1 hexane–EtOAc); $[\alpha]_D$ –43.6 (*c* 0.96, $CHCl_3$); ^{1}H NMR (600 MHz; $CDCl_3$): δ 7.51–7.49 (m, 2H, Ar), 7.44–7.37 (m, 10H, Ar), 7.34–7.31 (m, 2H, Ar), 7.13–7.12 (m, 2H), 6.62–6.59 (m, 2H, Ar), 5.01 (d, 1H, *J* = 11.0 Hz, PhC<u>H</u>$_2$), 4.96 (d, 1H, *J* = 1.6 Hz, Rha-H-1), 4.85 (d, 1H, *J* = 12.3 Hz, PhC<u>H</u>$_2$), 4.72 (d, 1H, *J* = 12.2 Hz, PhC<u>H</u>$_2$), 4.65–4.61 (m, 3H, PhC<u>H</u>$_2$, 2 × ArC<u>H</u>$_2$), 4.53 (d, 1H, *J* = 9.8 Hz, Fuc-H-1), 3.97 (dq, 1H, *J* = 9.5, 6.2 Hz, Rha-H-5), 3.90 (dd, 1H, *J* = 3.1, 1.9 Hz, Rha-H-2), 3.79 (dd, 1H, *J* = 9.3, 3.1 Hz, Fuc-H-3), 3.74–3.71 (m, 2H, Fuc-H-

4, Rha-H-3), 3.69 (s, 3H, ArOC$\underline{H}_3$), 3.59–3.50 (m, 6H, Rha-H-4, Fuc-H-5, Fuc-H-2, OC$\underline{H}_3$), 2.35 (s, 3H, ArC$\underline{H}_3$), 1.36 (d, 3H, J = 6.4 Hz, Fuc-H-6), 1.28 (s, 1H, Rha-4-OH), 1.24 (d, 3H, J = 6.2 Hz, Rha-H-6); ^{13}C NMR (125 MHz; $CDCl_3$): δ 159.4 (Ar), 139.1 (Ar), 138.1 (Ar), 137.8 (Ar), 132.7 (Ar), 130.8 (Ar), 129.8 (Ar), 129.7 (Ar), 128.5 (Ar), 128.3 (Ar), 128.1 (Ar), 127.9 (Ar), 127.8 (Ar), 127.4 (Ar), 113.7 (Ar), 93.1 (Rha-C-1), 88.0 (Fuc-C-1), 82.1 (Rha-C-3), 80.7 (Rha-C-4), 77.1 (Fuc-C-3), 75.7 (Ar$\underline{C}H_2$), 75.4 (Fuc-C-2), 75.3 (Ph$\underline{C}H_2$), 74.5 (Rha-C-2), 74.0 (Fuc-C-5), 73.2 (Ph$\underline{C}H_2$), 68.1 (Rha-C-5), 67.3 (Fuc-C-4), 58.1 (O$\underline{C}H_3$), 55.3 (ArO$\underline{C}H_3$), 21.1 (Ar$\underline{C}H_3$), 18.0 (Rha-C-6), 16.8 (Fuc-C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{42}H_{50}NaO_9S$: 753.3068; Found 753.3066.



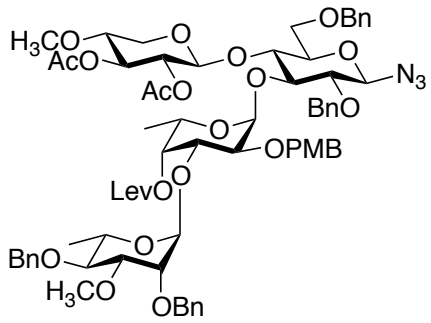
***p*-Tolyl 2,4-di-*O*-benzyl-3-*O*-methyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-levulinoyl-2-*O*-(4-methoxybenzyl)-1-thio-β-L-fucopyranoside (2.45):** To a stirred solution of **2.51** (22.2 mg, 30.4 μmol) in dry CH_2Cl_2 (2.0 mL) was added EDC·HCl (29.1 mg. 152 μmol), levulinic acid (17.6 mg, 152 μmol) and 4-(dimethylamino)pyridine (1.9 mg, 15 μmol) successively. The reaction mixture was stirred overnight at room temperature and then poured into saturated $NaHCO_3$ (aq.) and extracted with CH_2Cl_2 (15 mL × 3). The combined organic layers were dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (3:1 hexane–EtOAc) to afford **2.45** (14.6 mg, 58%) as a white foam. R_f 0.43 (2:1 hexane–EtOAc); $[\alpha]_D$ –27.1 (*c* 0.22, $CHCl_3$); ^{1}H NMR

(600 MHz; $CDCl_3$): δ 7.54–7.52 (m, 2H, Ar), 7.48–7.29 (m, 12H, Ar), 7.14–7.13 (m, 2H, Ar), 6.58–6.56 (m, 2H, Ar), 5.30 (d, 1H, J = 3.1 Hz, Fuc-H-4), 5.18 (d,1H, J = 1.4 Hz, Rha-H-1), 5.02 (d,1H, J = 10.9 Hz, PhC$\underline{H}_2$), 4.78 (d, 1H, J = 12.6 Hz, PhC$\underline{H}_2$), 4.69 (d, 1H, J = 12.6 Hz, PhC$\underline{H}_2$), 4.63–4.59 (m, 4H, PhC$\underline{H}_2$, ArC$\underline{H}_2$, Fuc-H-1), 3.98 (dq, 1H, J = 9.5, 6.1 Hz, Rha-H-5), 3.94 (dd, 1H, J = 9.4, 3.2 Hz, Fuc-H-3), 3.75 (dd, 1H, J = 3.2, 1.7 Hz, Rha-H-2), 3.69–3.65 (m, 5H, $ArOCH_3$, Fuc-H-5, Rha-H-3), 3.57–3.52 (m, 2H, Rha-H-4, Fuc-H-2), 3.48 (s, 3H, OC$\underline{H}_3$), 2.77–2.67 (m, 4H, $CO(C\underline{H}_2)_2COCH_3$), 2.36 (s, 3H, ArC$\underline{H}_3$), 2.16 (s, 3H, $CO(CH_2)_2COC\underline{H}_3$), 1.26 (d, 3H, J = 6.4 Hz, Fuc-H-6), 1.22 (d, 3H, J = 6.2 Hz, Rha-H-6); ^{13}C NMR (125 MHz; $CDCl_3$): δ 205.9 ($CO(CH_2)_2\underline{C}OCH_3$), 172.4 ($\underline{C}O(CH_2)_2COCH_3$), 159.4 (Ar), 139.3 (Ar), 138.9 (Ar), 137.6 (Ar), 132.4 (Ar), 131.0 (Ar), 130.1 (Ar), 129.6 (Ar), 128.2 (Ar), 128.1 (Ar), 127.9 (Ar), 127.7 (Ar), 127.4 (Ar), 127.3 (Ar), 113.7 (Ar), 93.3 (Rha-C-1), 88.1 (Fuc-C-1), 81.9 (Rha-C-3), 80.7 (Rha-C-4), 75.8 (Ar$\underline{C}H_2$), 75.5 (Fuc-C-2), 75.4 (Ph$\underline{C}H_2$), 75.1 (Fuc-C-3), 74.1 (Rha-C-2), 72.6 (Fuc-C-5), 72.0 ($PhCH_2$), 68.9 (Fuc-C-4), 67.9 (Rha-C-5), 57.6 (O$\underline{C}H_3$), 55.3 (ArO$\underline{C}H_3$), 37.8 ($COCH_2\underline{C}H_2COCH_3$), 29.9 ($COCH_2CH_2CO\underline{C}H_3$), 27.9 ($CO\underline{C}H_2CH_2COCH_3$), 21.1 (Ar$\underline{C}H_3$), 18.0 (Rha-C-6), 16.8 (Fuc-C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{47}H_{56}NaO_{11}S$: 851.3436; Found 851.3434.



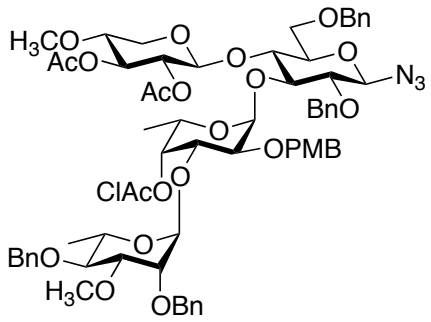
***p*-Tolyl 2,4-di-*O*-benzyl-3-*O*-methyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-chloroacetyl-2-*O*-(4-methoxybenzyl)-1-thio-β-L-fucopyranoside (2.46):** To a stirred solution of **2.51** (206 mg, 0.282 mmol) in dry CH_2Cl_2 (8.0 mL) was added chloroacetic anhydride (144 mg, 0.842 mmol), pyridine (0.14 mL, 1.7 mmol) and 4-(dimethylamino)pyridine (6.8 mg, 56 μmol) successively at 0 °C. The reaction mixture was stirred overnight at room temperature. The solution was diluted with CH_2Cl_2 (50 mL) and then washed with 1N HCl and saturated $NaHCO_3$ (aq.). The organic layer was dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (4:1 hexane–EtOAc) to afford **2.46** (208 mg, 92%) as a white foam. R_f 0.66 (2:1 hexane–EtOAc); $[\alpha]_D$ –31.1 (*c* 0.23, $CHCl_3$); ^{1}H NMR (600 MHz; $CDCl_3$): δ 7.53–7.50 (m, 4H, Ar), 7.43–7.36 (m, 8H, Ar), 7.33–7.29 (m, 2H, Ar), 7.14–7.13 (m, 2H, Ar), 6.58–6.56 (m, 2H, Ar), 5.34 (d, 1H, *J* = 3.1 Hz, Fuc-H-4), 5.18 (d, 1H, *J* = 1.4 Hz, Rha-H-1), 5.01 (d, 1H, *J* = 10.9 Hz, PhC$\underline{H}_2$), 4.82 (d, 1H, *J* = 12.5 Hz, PhC$\underline{H}_2$), 4.69 (d, 1H, *J* = 12.5 Hz, PhC$\underline{H}_2$), 4.62–4.57 (m, 4H, PhC$\underline{H}_2$, ArC$\underline{H}_2$, Fuc-H-1), 4.19–4.14 (m, 2H, COC$\underline{H}_2$Cl), 3.98–3.94 (m, 2H, Fuc-H-3, Rha-H-5), 3.72 (q, 1H, *J* = 6.5 Hz, Fuc-H-5), 3.69 (s, 3H, ArOC$\underline{H}_3$), 3.67 (dd, 1H, *J* = 3.1, 1.8 Hz, Rha-H-2), 3.59 (dd, 1H, *J* = 9.5, 3.2 Hz, Rha-H-3), 3.56–3.52 (m, 2H, Rha-H-4, Fuc-H-2), 3.33 (s, 3H, OC$\underline{H}_3$), 2.36 (s, 3H, ArC$\underline{H}_3$), 1.28 (d, 3H, *J* = 6.4 Hz, Fuc-H-6), 1.22 (d, 3H, *J* = 6.2 Hz, Rha-H-6); ^{13}C NMR (125 MHz; $CDCl_3$): δ 167.3 (C=O), 159.4 (Ar), 139.3

(Ar), 138.4 (Ar), 137.8 (Ar), 132.5 (Ar), 131.0 (Ar), 129.8 (Ar), 129.6 (Ar), 129.4 (Ar), 128.2 (3 × Ar), 127.9 (Ar), 127.5 (Ar), 127.4 (Ar), 113.7 (Ar), 93.4 (Rha-C-1), 88.1 (Fuc-C-1), 81.7 (Rha-C-3), 80.5 (Rha-C-4), 75.8 (Ar$\underline{C}H_2$), 75.5 (Ph$\underline{C}H_2$), 75.3 (Fuc-C-2), 75.1 (Fuc-C-3), 73.4 (Rha-C-2), 72.3 (Fuc-C-5), 72.09 (Ph$\underline{C}H_2$), 70.9 (Fuc-C-4), 68.1 (Rha-C-5), 57.4 (O$\underline{C}H_3$), 55.3 (ArO$\underline{C}H_3$), 40.7 (CO$\underline{C}H_2$Cl), 21.2 (Ar$\underline{C}H_3$), 18.0 (Rha-C-6), 16.9 (Fuc-C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{44}H_{51}ClNaO_{10}S$: 829.2784; Found 829.2799.



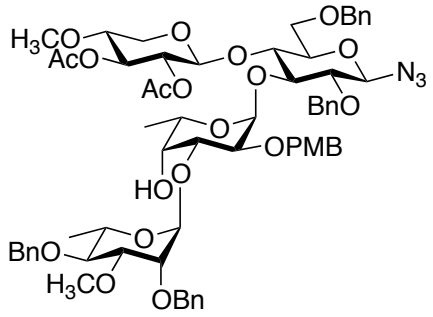
2,4-Di-*O*-benzyl-3-*O*-methyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-levulinoyl-2-*O*-(4-methoxybenzyl)-α-L-fucopyranosyl-[2,3-di-*O*-acetyl-4-*O*-methyl-β-D-xylopyranosyl-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (2.52): To a stirred solution of acceptor **2.7** (6.3 mg, 10 μmol) and donor **2.45** (17.1 mg, 20.6 μmol) in dry Et_2O (2.0 mL) was added molecular sieves (200 mg, 4Å, powder). After stirring for 30 min at room temperature, methyl trifluoromethanesulfonate (3.9 μL, 34 μmol) was added dropwise. The resulting solution was stirred for 4 h at room temperature under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (3:2 hexane–EtOAc) to afford **2.52** (8.2 mg, 60%) as a viscous oil. R_f 0.26 (2:1 hexane–EtOAc); $[\alpha]_D$ –68.1 (*c* 0.13, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.40–7.38 (m, 4H), 7.36–7.29 (m, 10H),

7.27–7.22 (m, 4H), 7.21–7.20 (m, 2H), 7.11–7.09 (m, 2H), 6.56–6.54 (m, 2H), 5.56 (d, 1H, J = 3.5 Hz, Fuc-H-1), 5.24 (d, 1H, J = 2.1 Hz), 5.08 (d, 1H, J = 1.2 Hz, Rha-H-1), 4.90 (d, 1H, J = 11.4 Hz), 4.87 (t, 1H, J = 9.5 Hz), 4.84 (d, 1H, J = 11.2 Hz), 4.76–4.73 (m, 2H), 4.69–4.64 (m, 3H), 4.60–4.51 (m, 6H, Glc-H-1), 4.48 (d, 1H, J = 12.0 Hz, 1H), 4.44-4.41 (m, 2H, Xyl-H-1), 4.03 (dq, 1H, J = 9.5, 6.0 Hz), 3.98 (t, 1H, J = 9.7 Hz), 3.84 (t, 1H, J = 9.2 Hz), 3.73-3.69 (m, 2H), 3.66–3.64 (m, 2H), 3.60 (s, 3H), 3.56 (dd, 1H, J = 9.4, 3.1 Hz), 3.49–3.45 (m, 2H), 3.40–3.35 (m, 4H), 3.27 (s, 3H), 3.18–3.14 (m, 1H), 2.89 (t, 1H, J = 11.1 Hz), 2.74–2.68 (m, 2H), 2.65–2.59 (m, 2H), 2.11 (s, 3H), 2.04 (s, 3H), 1.92 (s, 3H), 1.30 (d, 3H, J = 6.1 Hz), 1.14 (d, 3H, J = 6.6 Hz); ^{13}C NMR (125 MHz; $CDCl_3$): δ 205.9, 172.9, 170.1, 169.0, 159.1, 139.4, 139.0, 137.9, 137.5, 130.0, 129.9, 128.6, 128.4, 128.1 (2 × C), 128.0, 127.5, 127.4, 127.3, 127.2 (2 × C), 127.1, 113.6, 100.5 (Xyl-C-1), 96.5 (Fuc-C-1, $^{1}J_{C\text{-}H}$ = 175.2 Hz), 93.4 (Rha-C-1), 90.1 (Glc-C-1), 82.5, 81.5, 80.5, 77.8, 74.8, 74.6, 73.9, 73.8 (2 × C), 73.7 (2 × C), 73.4, 72.0, 71.9, 70.5, 70.4, 68.1, 67.0, 64.0, 63.1, 58.7, 57.4, 55.1, 37.8, 29.9, 29.7, 27.9, 20.9, 20.6, 18.5, 15.9; HRMS (ESI) Calc. for $[M + Na]^+$ $C_{70}H_{85}N_3NaO_{22}$: 1342.5517; Found 1342.5533.



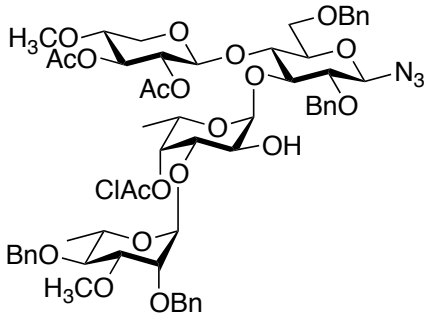
2,4-Di-*O*-benzyl-3-*O*-methyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-chloroacetyl-2-*O*-(4-methoxybenzyl)-α-L-fucopyranosyl-[2,3-di-*O*-acetyl-4-*O*-methyl-β-D-xylopyranosyl-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (2.53): To a stirred solution of acceptor **2.7** (86.1 mg, 140 μmol) and donor **2.46** (208 mg, 258 μmol) in dry Et_2O (5.0 mL) was added molecular sieves (500 mg, 4Å, powder). After stirring for 30 min at room temperature, methyl trifluoromethanesulfonate (47.0 μL, 420 μmol) was added dropwise. The resulting solution was stirred for 24 h at room temperature under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (4:1 hexane–EtOAc) to afford **2.53** (160 mg, 88%) as a syrup. R_f 0.42 (2:1 hexane–EtOAc); $[\alpha]_D$ –41.8 (*c* 0.28, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.41–7.39 (m, 4H), 7.36–7.23 (m, 14H), 7.20–7.19 (m, 2H), 7.07–7.05 (m, 2H), 6.56–6.54 (m, 2H), 5.56 (d, 1H, J = 3.5 Hz, Fuc-H-1), 5.27 (dd, J = 3.2, 1.2 Hz, 1H), 5.05 (d, 1H, J = 1.5 Hz, Rha-H-1), 4.90–4.85 (m, 3H), 4.78 (q, 1H, J = 6.9 Hz), 4.73 (t, 2H, J = 12.0 Hz), 4.68 (d, 1H, J = 12.2 Hz), 4.63 (d, 1H, J = 11.2 Hz), 4.60–4.57 (m, 3H), 4.55 (d, 1H, J = 8.7 Hz, Glc-H-1), 4.52–4.47 (m, 3H), 4.44 (d, 1H, J = 8.1 Hz, Xyl-H-1), 4.40 (d, 1H, J = 11.3 Hz), 4.11–4.07 (m, 2H), 4.04–3.97 (m, 2H), 3.84 (t, 1H, J = 9.2 Hz), 3.74–3.70 (m, 2H), 3.65–3.63 (m, 2H), 3.60 (s, 3H), 3.49–

3.46 (m, 3H), 3.37 (dt, 1H, J = 10.0, 2.1 Hz), 3.28 (s, 3H), 3.24 (s, 3H), 3.19–3.16 (m, 1H), 2.90 (t, 1H, J = 11.1 Hz), 2.05 (s, 3H), 1.93 (s, 3H), 1.29 (d, 3H, J = 6.1 Hz), 1.15 (d, 3H, J = 6.6 Hz); ^{13}C NMR (125 MHz; $CDCl_3$): δ 170.1, 169.1, 167.6, 159.1, 139.4, 138.6, 137.8, 137.4, 129.9, 129.8, 128.7, 128.4, 128.17, 128.1 (2 × C), 128.0, 127.7, 127.6, 127.5, 127.3, 127.2, 127.0, 113.6, 100.5 (Xyl-C-1), 96.3 (Fuc-C-1, $^1J_{C\text{-}H}$ = 175.3 Hz), 93.7 (Rha-C-1), 90.1 (Glc-C-1), 82.5, 81.4, 80.4, 77.8, 74.8, 74.1, 73.9, 73.7 (2 × C), 73.5, 73.2, 72.6, 72.2, 71.9, 70.4, 68.2, 67.0, 63.7, 63.1, 58.7, 57.1, 55.1, 53.4, 40.8, 20.9, 20.6, 18.5, 15.9; HRMS (ESI) Calc. for $[M + Na]^+$ $C_{67}H_{80}ClN_3NaO_{21}$: 1320.4865; Found 1320.4877.



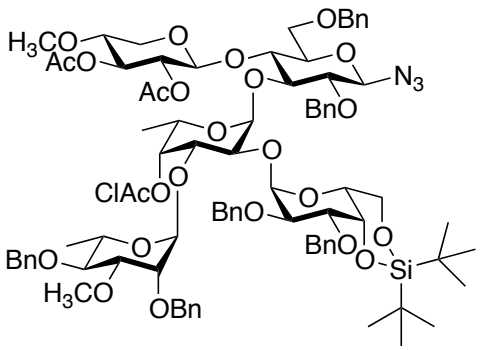
2,4-Di-*O*-benzyl-3-*O*-methyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-(4-methoxybenzyl)-α-L-fucopyranosyl-[2,3-di-*O*-acetyl-4-*O*-methyl-β-D-xylopyranosyl-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (2.54): To a stirred solution of **2.53** (23.4 mg, 18.0 μmol) in dry pyridine–EtOH (4.0 mL, 1:1) was added thiourea (4.1 mg, 54 μmol) at room temperature. The reaction mixture was stirred for 20 h at 60 °C. After cooling to room temperature, the solution was diluted with CH_2Cl_2 (40 mL) and then washed with 1N HCl and saturated $NaHCO_3$ (aq.). The organic layer was dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (1:1 hexane–EtOAc) to afford **2.54** (13.2 mg, 60%) as a syrup. R_f 0.10 (2:1 hexane–EtOAc);

$[\alpha]_D$ –75.7 (*c* 0.24, $CHCl_3$); ^1H NMR (700 MHz; $CDCl_3$): δ 7.40–7.26 (m, 18H), 7.19–7.18 (m, 2H), 7.05–7.04 (m, 2H), 6.58–6.56 (m, 2H), 5.53 (d, 1H, *J* = 3.6 Hz, Fuc-H-1), 4.89–4.83 (m, 4H), 4.73–4.72 (m, 2H, Rha-H-1), 4.61–4.55 (m, 5H, Glc-H-1), 4.51 (q, 1H, *J* = 6.9 Hz), 4.48–4.39 (m, 4H, Xyl-H-1), 4.35–4.31 (m, 2H), 4.03–3.97 (m, 2H), 3.85 (t, 1H, *J* = 9.2 Hz), 3.75–3.70 (m, 3H), 3.62 (dd, 1H, *J* = 10.1, 3.6 Hz), 3.59 (s, 3H), 3.56–3.53 (m, 2H), 3.46–3.43 (m, 5H), 3.38–3.36 (m, 1H), 3.33 (s, 3H), 3.14–3.10 (m, 1H), 2.87 (t, 1H, *J* = 11.1 Hz), 2.06 (s, 3H), 1.95 (s, 3H), 1.26 (d, 3H, *J* = 6.1 Hz), 1.24 (d, 3H, *J* = 6.8 Hz); ^{13}C NMR (125 MHz; $CDCl_3$): δ 170.1, 169.1, 159.0, 139.0, 138.2, 137.7, 137.5, 130.0, 129.8, 128.6, 128.5, 128.4, 128.2, 128.1, 128.0 (2 × C), 127.6, 127.5, 127.4, 127.0, 113.6, 100.3 (Xyl-C-1), 96.1 (Fuc-C-1), 93.7 (Rha-C-1), 90.1 (Glc-C-1), 82.6, 81.3, 80.7, 77.6, 75.5, 74.7, 74.2, 73.9, 73.7, 73.6, 73.5, 73.3, 73.1, 72.9, 72.8, 71.9, 68.4, 68.3, 67.1, 64.7, 63.2, 58.7, 58.0, 55.1, 20.9, 20.7, 18.5, 15.9; HRMS (ESI) Calc. for $[M + Na]^+$ $C_{65}H_{79}N_3NaO_{20}$: 1244.5149; Found 1244.5162.



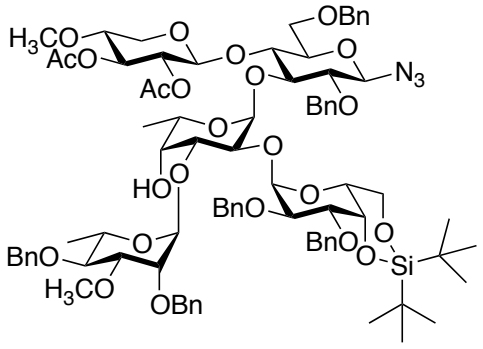
2,4-Di-*O*-benzyl-3-*O*-methyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-chloroacetyl-2-*O*-(4-methoxybenzyl)-α-L-fucopyranosyl-[2,3-di-*O*-acetyl-4-*O*-methyl-β-D-xylopyranosyl-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (2.55): To a stirred solution of **2.53** (87.6 mg, 67.5 μmol) in dry CH_2Cl_2 (5.0 mL) was added trifluoroacetic acid (50 μL)

dropwise at 0 °C. The reaction mixture was stirred for 4 h at room temperature under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (2:1 hexane–EtOAc) to afford **2.55** (76.7 mg, 96%) as a syrup. R_f 0.42 (2:1 hexane–EtOAc); $[\alpha]_D$ –65.9 (*c* 0.34, $CHCl_3$); ^1H NMR (600 MHz; $CDCl_3$): δ 7.45–7.29 (m, 20H), 5.54 (d, 1H, *J* = 3.9 Hz, Fuc-H-1), 5.27 (dd, 1H, *J* = 3.0, 0.3 Hz), 5.02 (d, 1H, *J* = 1.3 Hz, Rha-H-1), 4.94–4.87 (m, 3H), 4.79–4.68 (m, 5H), 4.63–4.60 (m, 3H), 4.53 (d, 1H, *J* = 12.0 Hz), 4.47 (d, 1H, *J* = 8.2 Hz), 4.35 (dd, 1H, *J* = 11.6, 5.4 Hz), 4.22 (dd, 1H, *J* =10.0, 3.3 Hz), 4.17–4.12 (m, 2H), 4.03 (dq, 1H, *J* = 9.2, 6.2 Hz), 3.93 (t, 1H, *J* = 9.7 Hz), 3.82 (t, 1H, *J* = 9.4 Hz), 3.77–3.73 (m, 3H), 3.72 (dd, 1H, *J* = 2.9, 1.9 Hz), 3.58 (dd, 1H, *J* = 9.5, 3.1 Hz), 3.53–3.50 (m, 2H), 3.42–3.39 (m, 2H), 3.34 (s, 3H), 3.31 (s, 3H), 3.23–3.19 (m, 1H), 2.96 (t, 1H, *J* = 11.2 Hz), 2.08 (s, 3H), 1.96 (s, 3H), 1.34 (d, 3H, *J* = 6.2 Hz), 1.17 (d, 3H, *J* = 6.6 Hz); ^{13}C NMR (175 MHz; $CDCl_3$): δ 170.1, 169.0, 167.7, 138.9, 138.5, 137.3, 137.1, 128.7, 128.5, 128.4, 128.2 (2 × C), 128.1, 128.0 (2 × C), 127.8 127.7, 127.4 (2 × C), 100.4 (Xyl-C-1), 97.5 (Fuc-C-1), 95.0 (Rha-C-1), 90.1 (Glc-C-1), 82.4, 81.3, 80.0, 77.6, 75.0, 74.9, 74.4, 74.2, 73.9, 73.8, 73.5, 72.7, 72.5 (2 × C), 71.7, 68.3, 67.5, 66.9, 64.1, 63.2, 58.8, 57.2, 40.7, 20.8, 20.6, 18.2, 15.8; HRMS (ESI) Calc. for $[M + Na]^+$ $C_{59}H_{72}ClN_3NaO_{20}$: 1200.4290; Found 1200.4308.



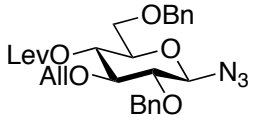
2,4-Di-*O*-benzyl-3-*O*-methyl-α-L-rhamnopyranosyl-(1→3)-[2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranosyl-(1→2)]-4-*O*-chloroacetyl-α-L-fucopyranosyl-[2,3-di-*O*-acetyl-4-*O*-methyl-β-D-xylopyranosyl-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (2.56): To a stirred solution of acceptor **2.55** (76.7 mg, 65.1 μmol) and *p*-tolyl 2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranoside **2.10**[15] (119 mg, 195 μmol) in dry Et_2O (6.0 mL) was added molecular sieves (600 mg, 4Å, powder). After stirring for 30 min at room temperature, methyl trifluoromethanesulfonate (36.8 μL, 326 μmol) was added dropwise. The resulting solution was stirred for 24 h at room temperature under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (2:1 hexane–EtOAc) to afford **2.56** (102.9 mg, 95%) as a white amorphous solid. R_f 0.46 (2:1 hexane–EtOAc); $[\alpha]_D$ –26.8 (*c* 0.40, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.44–7.32 (m, 10H), 7.28–7.24 (m, 4H), 7.22–7.18 (m, 9H), 7.16–7.12 (m, 7H), 5.62 (d, 1H, J = 3.2 Hz, Fuc-H-1), 5.29 (dd, 1H, J = 2.9, 1.2 Hz), 5.17 (d, 1H, J = 3.3 Hz, Gal-H-1), 5.14 (d, 1H, J = 1.3 Hz, Rha-H-1), 4.89 (t, 1H, J = 9.4 Hz), 4.86–4.57 (m, 13H, Glc-H-1), 4.55–4.52 (m, 2H), 4.47 (d, 1H, J = 8.1 Hz, Xyl-H-1), 4.36

(d, 1H, J = 11.8 Hz), 4.32 (d, 1H, J = 11.8 Hz), 4.20 (d, 1H, J = 2.2 Hz), 4.08–3.96 (m, 5H), 3.92–3.84 (m, 5H), 3.76–3.72 (m, 2H), 3.64 (dd, 1H, J = 3.2, 1.7 Hz), 3.58 (dd, 1H, J = 9.5, 3.2 Hz), 3.44–3.41 (m, 3H), 3.38 (dt, 1H, J = 10.1, 2.2 Hz), 3.30 (s, 3H), 3.18 (ddd, 1H, J = 10.5, 9.4, 5.2 Hz), 2.99 (s, 3H), 2.94 (t, 1H, J = 11.2 Hz), 2.06 (s, 3H), 1.93 (s, 3H), 1.16 (d, 3H, J = 6.1 Hz), 1.16 (d, 3H, J = 6.7 Hz), 0.96 (s, 9H), 0.91 (s, 9H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 170.2, 169.0, 167.8, 139.6, 139.2, 139.0, 138.4, 138.1, 137.3, 128.8, 128.4 (2 × C), 128.2 (2 × C), 128.1 (2 × C), 128.0, 127.9, 127.8, 127.5, 127.4 (2 × C), 127.2, 127.1, 126.8, 126.7, 126.4, 100.4 (Xyl-C-1), 97.0 (Gal-C-1, $^1J_{C\text{-}H}$ = 167.1 Hz), 95.5 (Fuc-C-1), 93.2 (Rha-C-1), 90.3 (Glc-C-1), 82.4, 81.3, 80.4, 77.8, 77.6, 76.6, 75.4, 75.1, 74.0, 73.9, 73.8, 73.6 (2 × C), 73.6, 72.9, 72.5 (2 × C), 72.3, 72.0, 71.9, 70.1, 69.5, 68.9, 68.1, 67.3, 67.0, 63.9, 63.2, 58.7, 56.8, 40.8, 27.7, 27.3, 23.3, 20.9, 20.6, 18.0, 15.8; HRMS (ESI) Calc. for $[M + NH_4]^+$ $C_{87}H_{114}ClN_4O_{25}Si$: 1677.7224; Found 1677.7227.



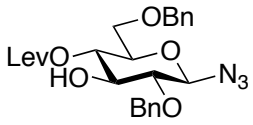
2,4-Di-*O*-benzyl-3-*O*-methyl-α-L-rhamnopyranosyl-(1→3)-[2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranosyl-(1→2)]-α-L-fucopyranosyl-[2,3-di-*O*-acetyl-4-*O*-methyl-β-D-xylopyranosyl-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (2.57): To a stirred solution of **2.56** (102 mg, 61.5 μmol) in dry pyridine–EtOH (4.0

mL, 1:1) was added thiourea (14.0 mg, 184 μmol) at room temperature. The reaction mixture was stirred for 20 h at 60 °C. After cooling to room temperature, the solution was diluted with CH_2Cl_2 (40 mL), then washed with 1N HCl and saturated $NaHCO_3$ (aq.). The organic layer was dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (2:1 hexane–EtOAc) to afford **2.57** (44.7 mg, 46%) as a white amorphous solid. R_f 0.24 (2:1 hexane–EtOAc); $[\alpha]_D$ –33.9 (*c* 0.48, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.43–7.40 (m, 4H), 7.38–7.16 (m, 23H), 7.14–7.12 (m, 1H), 7.02–7.01 (m, 2H), 5.44 (d, 1H, *J* = 3.4 Hz, Fuc-H-1), 5.33 (d, 1H, *J* = 3.7 Hz, Gal-H-1), 4.88 (t, 1H, *J* = 9.4 Hz), 4.82–4.78 (m, 4H, Rha-H-1), 4.75–4.69 (m, 3H), 4.61–4.50 (m, 8H, Glc-H-1), 4.47–4.45 (m, 3H, Xyl-H-1), 4.29 (dd, 1H, *J* = 11.6, 5.3 Hz), 4.06 (d, 1H, *J* = 2.8 Hz), 4.03 (dd, 1H, *J* = 10.1, 3.4 Hz), 3.99 (t, 1H, *J* = 9.5 Hz), 3.92–3.88 (m, 3H), 3.80 (dd, 1H, *J* = 12.4, 1.5 Hz), 3.76–3.71 (m, 4H), 3.58 (br s, 1H), 3.53 (dd, 1H, *J* = 8.7, 3.1 Hz), 3.45–3.43 (m, 1H), 3.40–3.36 (m, 2H), 3.33–3.30 (m, 7H), 3.11 (td, 1H, *J* = 9.9, 5.3 Hz), 3.06 (br s, 1H), 2.90 (t, 1H, *J* = 11.1 Hz), 2.06 (s, 3H), 1.95 (s, 3H), 1.89 (br s, 1H), 1.28 (d, 3H, *J* = 6.7 Hz), 1.02 (d, 3H, *J* = 6.1 Hz), 0.96 (s, 9H), 0.91 (s, 9H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 170.1, 169.1, 139.5, 139.1, 138.8, 138.2, 137.9, 137.4, 128.7, 128.6, 128.5, 128.3 (2 × C), 128.2 (2 × C), 128.0 (2 × C), 127.9, 127.7, 127.5, 127.4 (2 × C), 127.3, 127.2, 126.9, 125.7, 100.3, 97.3, 96.4, 93.1, 89.9, 82.3, 81.3, 80.4, 77.5, 77.1, 75.5, 74.8, 74.3, 74.2, 73.9, 73.7, 73.4, 73.3, 72.8, 72.5, 72.4, 71.9, 70.4, 70.1, 70.0, 68.7, 68.0, 67.5, 67.1, 66.8, 64.8, 63.2, 58.8, 57.8, 27.7, 27.3, 23.2, 20.9, 20.6 (2 × C), 18.2, 15.9; HRMS (ESI) Calc. for $[M + NH_4]^+$ $C_{85}H_{113}N_4O_{24}Si$: 1601.7509; Found 1601.7537.



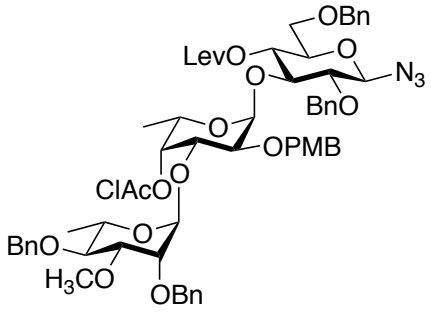
3-*O*-Allyl-2,6-di-*O*-benzyl-4-*O*-levulinoyl-β-D-glucopyranosyl azide (2.58): To a stirred solution of **2.12** (99.7 mg, 234 μmol) in dry CH_2Cl_2 (4.0 mL) was added EDC·HCl (108 mg, 561 μmol), levulinic acid (65.1 mg, 561 μmol) and 4-(dimethylamino)pyridine (2.9 mg, 23 μmol) successively. The reaction mixture was stirred overnight at room temperature and then poured into saturated $NaHCO_3$ (aq.) and extracted with CH_2Cl_2 (15 mL × 3). The combined organic layers were dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (2:1 hexane–EtOAc) to afford **2.58** (104 mg, 85%) as a white amorphous solid. R_f 0.41 (2:1 hexane–EtOAc); $[\alpha]_D$ –12.1 (*c* 0.16, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.36–7.25 (m, 10H, Ar), 5.85 (ddt, 1H, *J* = 17.2, 10.4, 5.7 Hz, $OCH_2C\underline{H}=CH_2$), 5.21 (dq, 1H, *J* = 17.2, 1.6 Hz, $OCH_2CH=C\underline{H}_2$), 5.13 (dq, 1H, *J* = 10.4, 1.4 Hz, $OCH_2CH=C\underline{H}_2$), 4.95 (t, 1H, *J* = 9.7 Hz, H-4), 4.82 (d, 1H, *J* = 10.7 Hz, $PhC\underline{H}_2$), 4.73 (d, 1H, *J* = 10.7 Hz, $PhC\underline{H}_2$), 4.60 (d, 1H, *J* = 8.6 Hz, H-1), 4.55–4.50 (m, 2H, Ar), 4.25 (ddt, 1H, *J* = 12.5, 5.6, 1.4 Hz, $OC\underline{H}_2CH=CH_2$), 4.11 (ddt, 1H, *J* = 12.5, 5.8, 1.4 Hz, $OC\underline{H}_2CH=CH_2$), 3.62 (ddd, 1H, *J* = 10.0, 5.8, 2.9 Hz, H-5), 3.58 (dd, 1H, *J* = 10.9, 2.9 Hz, H-6a), 3.53 (dd, 1H, *J* = 10.9, 5.8 Hz, H-6b), 3.49 (t, 1H, *J* = 9.3 Hz, H-3), 3.32 (t, 1H, *J* = 8.9 Hz, H-2), 2.67 (t, 2H, *J* = 6.5 Hz, $COCH_2C\underline{H}_2COCH_3$), 2.51–2.43 (m, 2H, $COC\underline{H}_2CH_2COCH_3$), 2.15 (s, 3H, $COCH_2CH_2COC\underline{H}_3$); ^{13}C NMR (175 MHz; $CDCl_3$): δ 206.1 (C=O), 171.5 (C=O), 137.8 (Ar), 137.6 (Ar), 134.6 ($OCH_2\underline{C}H=CH_2$), 128.4 (Ar), 128.3 (Ar), 128.2 (Ar), 128.0 (Ar), 127.9 (Ar), 127.6 (Ar), 117.0

($OCH_2CH=\underline{C}H_2$), 90.0 (C-1), 81.7 (C-3), 81.2 (C-2), 75.6 (C-5), 75.2 ($O\underline{C}H_2CH=CH_2$), 74.2 ($Ph\underline{C}H_2$), 73.6 ($Ph\underline{C}H_2$), 70.6 (C-4), 69.1 (C-6), 37.7 ($COCH_2\underline{C}H_2COCH_3$), 29.8 ($COCH_2CH_2CO\underline{C}H_3$), 27.9 ($CO\underline{C}H_2CH_2COCH_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{28}H_{33}N_3NaO_7$: 546.2211; Found 546.2210.



2,6-Di-*O*-benzyl-4-*O*-levulinoyl-β-D-glucopyranosyl azide (2.59): To a stirred solution of **2.58** (103 mg, 196 μmol) in dry THF (5.0 mL), degassed under vacuum, and stirring under an Ar atmosphere, (1,5-cyclooctadiene)bis(methyldiphenylphosphine)iridium (I) hexafluorophosphate catalyst (9.9 mg, 12 μmol) was added, followed by further degassing of the reaction mixture. The suspension was stirred for 15 min at 0 °C, and the catalyst was then activated with hydrogen (2 min under a hydrogen atmosphere). The excess hydrogen was removed by three cycles of vacuum/Ar. The reaction mixture was then stirred for 2 h at room temperature under an Ar atmosphere. The solvent was then evaporated, and the residue was dissolved in acetone–water (10:1, 11 mL) before HgO (59.4 mg, 274 μmol) and $HgCl_2$ (63.8 mg, 235 μmol) were added. The reaction mixture was stirred for 2 h at room temperature, then the solvent was concentrated, and the residue was diluted with EtOAc (50 mL), washed with 10% KI, saturated $Na_2S_2O_3$ (aq.) and water. The aqueous layers were extracted with EtOAc (50 mL), and the combined organic layers were dried over Na_2SO_4, filtered and the filtrate concentrated. The crude residue was purified by flash chromatography (1:1 hexane–EtOAc) to afford **2.59** (82.2 mg, 87%) as a viscous oil. R_f

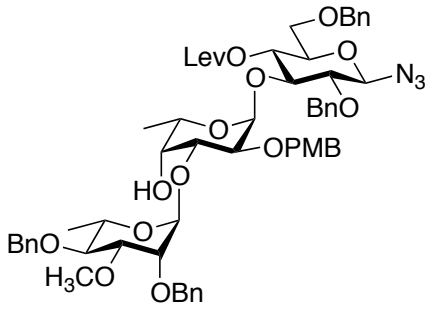
0.08 (2:1 hexane–EtOAc); $[\alpha]_D$ –3.2 (*c* 0.32, $CHCl_3$); ^1H NMR (600 MHz; $CDCl_3$): δ 7.41–7.29 (m, 10H, Ar), 4.96 (t, 1H, *J* = 9.7 Hz, H-4), 4.90 (d, 1H, *J* = 11.1 Hz, PhC$\underline{H}_2$), 4.82 (d, 1H, *J* = 11.1 Hz, PhC$\underline{H}_2$), 4.66 (d, 1H, *J* = 8.6 Hz, H-1), 4.59–4.55 (m, 2H, Ar), 3.79 (td, 1H, *J* = 9.2, 3.1 Hz, H-3), 3.68 (ddd, 1H, *J* = 10.0, 5.5, 2.6 Hz, H-5), 3.64 (dd, 1H, *J* = 11.0, 2.6 Hz, H-6a), 3.58 (dd, 1H, *J* = 11.0, 5.5 Hz, H-6b), 3.31 (t, 1H, *J* = 8.8 Hz, H-2), 2.89 (d, 1H, *J* = 3.2 Hz, 3-OH), 2.82–2.73 (m, 2H, $COCH_2C\underline{H}_2COCH_3$), 2.52 (ddd, 1H, *J* = 16.8, 7.6, 5.4 Hz, $COC\underline{H}_2CH_2COCH_3$), 2.44 (ddd, 1H, *J* = 16.8, 6.8, 5.6 Hz, $COC\underline{H}_2CH_2COCH_3$), 2.19 (s, 3H, $COCH_2CH_2COC\underline{H}_3$); ^{13}C NMR (175 MHz; $CDCl_3$): δ 207.1 (C=O), 172.2 (C=O), 137.8 (Ar), 137.7 (Ar), 128.5 (Ar), 128.3 (Ar), 128.2 (Ar), 128.1 (Ar), 127.9 (Ar), 127.7 (Ar), 89.7 (C-1), 80.7 (C-2), 75.3 (2 × C, C-5, C-3), 75.0 (Ph$\underline{C}H_2$), 73.6 (Ph$\underline{C}H_2$), 71.2 (C-4), 68.8 (C-6), 38.2 ($COCH_2\underline{C}H_2COCH_3$), 29.7 ($COCH_2CH_2CO\underline{C}H_3$), 28.0 ($CO\underline{C}H_2CH_2COCH_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{25}H_{29}N_3NaO_7$: 506.1898; Found 506.1897.



2,4-Di-*O*-benzyl-3-*O*-methyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-chloroacetyl-2-*O*-(4-methoxybenzyl)-α-L-fucopyranosyl-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (2.60): To a stirred solution of acceptor **2.59** (27.5 mg, 56.9 μmol) and donor **2.46** (76.2 mg, 94.4 μmol) in dry Et_2O (4.0 mL) was added molecular sieves (400 mg, 4Å, powder). After

stirring for 30 min at room temperature, methyl trifluoromethanesulfonate (17.4 μL, 154 μmol) was added dropwise. The resulting solution was stirred for 24 h at room temperature under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (2:1 hexane–EtOAc) to afford **2.60** (54.5 mg, 82%) as a viscous oil. R_f 0.31 (2:1 hexane–EtOAc); $[\alpha]_D$ –41.4 (*c* 0.43, $CHCl_3$); ^1H NMR (600 MHz; $CDCl_3$): δ 7.49–7.48 (m, 2H, Ar), 7.37–7.30 (m, 13H, Ar), 7.23–7.19 (m, 7H, Ar), 6.68–6.66 (m, 2H, Ar), 5.45 (d, 1H, J = 2.3 Hz, Fuc-H-4), 5.18 (d, 1H, J = 3.6 Hz, Fuc-H-1), 5.16 (d, 1H, J = 0.8 Hz, Rha-H-1), 4.97 (t, 1H, J = 9.4 Hz, Glc-H-4), 4.91 (d, 1H, J = 11.3 Hz, PhC$\underline{H}_2$), 4.88 (d, 1H, J = 10.5 Hz, PhC$\underline{H}_2$), 4.80 (d, 1H, J = 12.5 Hz, PhC$\underline{H}_2$), 4.69–4.66 (m, 2H, 2 × PhC$\underline{H}_2$), 4.64 (d, 1H, J = 8.6 Hz, Glc-H-1), 4.59–4.55 (m, 3H, 2 × PhC$\underline{H}_2$, ArC$\underline{H}_2$), 4.51 (d, 1H, J = 11.9 Hz, ArC$\underline{H}_2$), 4.45 (d, 1H, J = 11.4 Hz, Fuc-H-3), 4.24 (dd, 1H, J = 10.4, 3.1 Hz, Fuc-H-3), 4.19 (q, 1H, J = 6.6 Hz, Fuc-H-5), 4.11 (s, 2H, COC$\underline{H}_2$Cl), 3.94 (dq, 1H, J = 9.3, 6.1 Hz, Rha-H-5), 3.88 (t, 1H, J = 8.8 Hz, Glc-H-3), 3.67–3.64 (m, 5H, ArOC$\underline{H}_3$, Rha-H-2, Fuc-H-2), 3.61–3.58 (m, 2H, Glc-H-5, Glc-H-6a), 3.56–3.51 (m, 2H, Glc-H-6b, Rha-H-3), 3.46 (t, 1H, J = 9.4 Hz, Rha-H-4), 3.41 (t, 1H, J = 8.7 Hz, Glc-H-2), 3.28 (s, 3H, OC$\underline{H}_3$), 2.68 (dt, 1H, J = 18.6, 6.4 Hz, $COCH_2C\underline{H}_2COCH_3$), 2.61 (ddd, 1H, J = 18.5, 7.2, 5.8 Hz, $COCH_2C\underline{H}_2COCH_3$), 2.52–2.47 (m, 1H, $COC\underline{H}_2CH_2COCH_3$), 2.39 (ddd, 1H, J = 17.3, 7.3, 5.9 Hz, $COC\underline{H}_2CH_2COCH_3$), 2.15 (s, 3H, $COCH_2CH_2COC\underline{H}_3$), 1.11 (d, 3H, J = 6.5 Hz, Fuc-H-6), 1.09 (d, 3H, J = 6.2 Hz, Rha-H-6); ^{13}C NMR (125 MHz; $CDCl_3$): δ 206.4 (C=O), 171.7 (C=O), 167.3 (C=O), 159.2 (Ar), 139.3 (Ar), 138.6 (Ar), 137.9 (Ar), 137.7

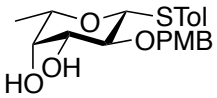
(Ar), 129.9 (Ar), 129.8 (Ar), 128.4 (Ar), 128.3 (Ar), 128.1 (2 × Ar), 128.0 (Ar), 127.9 (Ar), 127.7 (2 × Ar), 127.6 (Ar), 127.4 (Ar), 127.2 (Ar), 113.7 (Ar), 98.5 (Fuc-C-1, $^{1}J_{C\text{-}H}$ = 170.8 Hz), 93.4 (Rha-C-1), 89.9 (Glc-C-1), 81.4 (Rha-C-3), 81.2 (Glc-C-2), 81.0 (Glc-C-3), 80.4 (Rha-C-4), 75.4 (Glc-C-5), 75.2 (Ph<u>C</u>H$_2$), 74.9 (Ph<u>C</u>H$_2$), 73.9 (Rha-C-2), 73.7 (2 × C, Ph<u>C</u>H$_2$, Fuc-C-2), 73.1 (Ar<u>C</u>H$_2$), 72.2 (Fuc-C-4), 72.0 (Ph<u>C</u>H$_2$), 71.0 (Glc-C-4), 70.0 (Fuc-C-3), 69.5 (Glc-C-6), 68.0 (Rha-C-5), 65.0 (Fuc-C-5), 57.2 (O<u>C</u>H$_3$), 55.2 (ArO<u>C</u>H$_3$), 40.7 (CO<u>C</u>H$_2$Cl), 37.6 (COCH$_2$<u>C</u>H$_2$COCH$_3$), 29.8 (COCH$_2$CH$_2$CO<u>C</u>H$_3$), 27.9 (CO<u>C</u>H$_2$CH$_2$COCH$_3$), 18.2 (Rha-C-6), 15.8 (Fuc-C-6); HRMS (ESI) Calc. for $[M + NH_4]^+$ $C_{62}H_{76}ClN_4O_{17}$: 1183.4889; Found 1183.4881.



2,4-Di-*O*-benzyl-3-*O*-methyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-(4-methoxybenzyl)-α-L-fucopyranosyl-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (2.61): To a stirred solution of **2.60** (5.0 mg, 4.3 μmol) in dry pyridine–EtOH (2.0 mL, 1:1) was added thiourea (1.0 mg, 13 μmol) at room temperature. The reaction mixture was stirred for 20 h at 60 °C. After cooling to room temperature, the solution was diluted with CH_2Cl_2 (20 mL), then washed with 1N HCl and saturated $NaHCO_3$ (aq.). The organic layer was dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (1:1 hexane–EtOAc) to afford **2.61** (3.5 mg, 75%) as a viscous oil. R_f 0.21

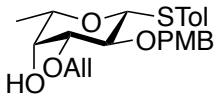
(1:1 hexane–EtOAc); $[\alpha]_D$ –38.7 (*c* 0.29, $CHCl_3$); ^1H NMR (700 MHz; $CDCl_3$): δ 7.38–7.37 (m, 2H, Ar), 7.35–7.26 (m, 13H, Ar), 7.21–7.14 (m, 7H, Ar), 6.66–6.64 (m, 2H, Ar), 5.09 (d, 1H, *J* = 3.7 Hz, Fuc-H-1), 4.91 (t, 1H, *J* = 9.4 Hz, Glc-H-4), 4.88–4.86 (m, 3H, PhC$\underline{H}_2$, Rha-H-1), 4.79 (d, 1H, *J* = 12.3 Hz, PhC$\underline{H}_2$), 4.65 (d, 1H, *J* = 12.3 Hz, PhC$\underline{H}_2$), 4.62 (d, 1H, *J* = 10.6 Hz, PhC$\underline{H}_2$), 4.60 (d, 1H, *J* = 8.6 Hz, Glc-H-1), 4.56 (d, 1H, *J* = 10.9 Hz, PhC$\underline{H}_2$), 4.54 (d, 1H, *J* = 11.4 Hz, PhC$\underline{H}_2$), 4.50 (d, 1H, *J* = 11.3 Hz, PhC$\underline{H}_2$), 4.49 (d, 1H, *J* = 11.8 Hz, PhC$\underline{H}_2$), 4.41 (d, 1H, *J* = 11.5 Hz, PhC$\underline{H}_2$), 4.04 (dd, 1H, *J* = 10.3, 3.1 Hz, Fuc-H-3), 3.97–3.92 (m, 2H, Fuc-H-5, Rha-H-5), 3.82 (t, 1H, *J* = 8.9 Hz, Glc-H-3), 3.77 (dd, 1H, *J* = 3.1, 2.1 Hz, Rha-H-2), 3.74–3.73 (m, 1H, Fuc-H-4), 3.65–3.63 (m, 4H, OC$\underline{H}_3$, Fuc-H-2), 3.59 (dd, 1H, *J* = 9.1, 3.2 Hz, RHa-H-3), 3.57–3.54 (m, 2H, Glc-H-5, Glc-H-6a), 3.53–3.50 (m, 1H, Glc-H-6b), 3.46 (d, 1H, *J* = 9.3 Hz, Rha-H-4), 3.44 (s, 3H, OC$\underline{H}_3$), 3.35 (t, 1H, *J* = 8.7 Hz, Glc-H-2), 2.67–2.57 (m, 2H, $COCH_2C\underline{H}_2COCH_3$), 2.48–2.40 (m, 2H, $COC\underline{H}_2CH_2COCH_3$), 2.13 (s, 3H, $COCH_2CH_2COC\underline{H}_3$), 1.19 (d, 3H, *J* = 6.6 Hz, Fuc-H-6), 1.05 (d, 3H, *J* = 6.2 Hz, Rha-H-6); ^{13}C NMR (125 MHz; $CDCl_3$): δ 206.3 (C=O), 171.8 (C=O), 159.2 (Ar), 139.1 (Ar), 138.1 (Ar), 138.0 (Ar), 137.7 (Ar), 130.1 (Ar), 129.7 (Ar), 128.4 (Ar), 128.3 (2 × Ar), 128.2 (Ar), 128.1 (Ar), 128.0 (Ar), 127.9 (Ar), 127.8 (Ar), 127.7 (Ar), 127.6 (Ar), 127.4 (Ar), 113.7 (Ar), 98.6 (Fuc-C-1), 93.3 (Rha-C-1), 89.8 (Glc-C-1), 81.6 (Glc-C-3), 81.5 (Rha-C-3), 81.0 (Glc-C-2), 80.6 (Rha-C-4), 75.5 (Glc-C-5), 75.3 (Ph$\underline{C}H_2$), 74.9 (Ph$\underline{C}H_2$), 73.7 (Rha-C-2), 73.6 (Fuc-C-2), 73.1 (Ph$\underline{C}H_2$), 72.8 (Ar$\underline{C}H_2$), 72.1 (Fuc-H-3), 71.0 (Glc-C-4), 69.4 (Glc-C-6), 68.2 (Fuc-C-4), 68.1 (Rha-C-5), 66.1 (Fuc-C-5), 58.0 (O$\underline{C}H_3$), 55.1 (O$\underline{C}H_3$), 37.6 ($COCH_2\underline{C}H_2COCH_3$), 29.8 ($COCH_2CH_2CO\underline{C}H_3$), 27.9

($CO\underline{C}H_2CH_2COCH_3$), 18.1 (Rha-C-6), 15.9 (Fuc-C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{60}H_{71}N_3NaO_{16}$: 1112.4727; Found 1112.4731.



***p*-Tolyl 2-*O*-(4-methoxybenzyl)-1-thio-β-L-fucopyranoside (2.64):** To a stirred solution of *p*-tolyl 1-thio-β-L-fucopyranoside **2.48**[35] (2.52 g, 9.32 mmol) in dry CH_3CN (60 mL) was added trimethyl orthoacetate (1.31 mL, 10.3 mmol) and *p*-toluenesulfonic acid monohydrate (177 mg, 0.931 mmol) successively at 0 °C. The reaction mixture was stirred for 2 h under an Ar atmosphere Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude reaction mixture was then dissolved in dry DMF (12mL), then sodium hydride (0.75 g, 19 mmol, 60% dispersion in mineral oil) was added in one portion at 0 °C. After stirring for 30 min, 4-methoxybenzyl chloride (1.51 mL, 11.2 mmol) and tetrabutylammonium iodide (344 mg, 0.931 mmol) were added successively, and the reaction mixture was warmed to room temperature and stirred for 1 h under an Ar atmosphere. Then, CH_3OH was added at 0 °C and the solution was concentrated. The crude residue was diluted with CH_2Cl_2 (100 mL), washed with saturated $NaHCO_3$ (aq.), dried over Na_2SO_4, filtered and concentrated. The reaction was then dissolved in CH_2Cl_2 (50 mL) and 1N HCl was added (50 mL). The reaction mixture was stirred for 1 h at room temperature, then the aqueous layer was extracted with CH_2Cl_2 (50 mL × 3) and combined organic layers were dried over Na_2SO_4, filtered and concentrated. To the solution of the crude residue in CH_3OH (20 mL) was added a solution

of $NaOCH_3$ in CH_3OH (2 mL, 0.5 M). The reaction mixture was stirred overnight at room temperature, then neutralized by addition of Amberlite® IR-120 (H^+) cation exchange resin, filtered and concentrated. The crude residue was purified by flash chromatography (1:1 hexane–EtOAc) to afford **2.64** (2.66 g, 73%) as a viscous oil. R_f 0.17 (1:1 hexane–EtOAc); $[\alpha]_D$ –18.0 (*c* 0.79, $CHCl_3$); ^1H NMR (500 MHz; $CDCl_3$): δ 7.51–7.49 (m, 2H, Ar), 7.35–7.33 (m, 2H, Ar), 7.16–7.14 (m, 2H, Ar), 6.92–6.91 (m, 2H, Ar), 4.92 (d, 1H, J = 10.8 Hz, PhC$\underline{H}_2$), 4.64 (d, 1H, J = 10.8 Hz, PhC$\underline{H}_2$), 4.55 (d, 1H, J = 9.7 Hz, H-1), 3.83 (s, 3H, ArOC$\underline{H}_3$), 3.75 (d, 1H, J = 3.2 Hz, H-4), 3.65–3.60 (m, 2H, H-3, H-5), 3.51 (t, 1H, J = 9.3 Hz, H-2), 2.37 (s, 3H, ArC$\underline{H}_3$), 1.36 (d, 3H, J = 6.5 Hz, H-6); ^{13}C NMR (125 MHz; $CDCl_3$): δ 159.6 (Ar), 137.7 (Ar), 132.4 (Ar), 130.2 (Ar), 130.1 (Ar), 130.0 (Ar), 129.7 (Ar), 114.1 (Ar), 87.8 (C-1), 77.7 (C-2), 75.3 (C-3), 74.9 (Ph$\underline{C}H_2$), 74.4 (C-5), 71.7 (C-4), 55.3 (ArO$\underline{C}H_3$), 21.1 ($ArCH_3$), 16.6 (C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{21}H_{26}NaO_5S$: 413.1393; Found 413.1389.

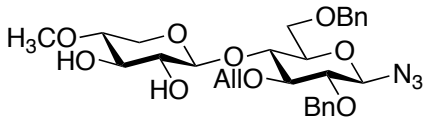


***p*-Tolyl 3-*O*-allyl-2-*O*-(4-methoxybenzyl)-1-thio-β-L-fucopyranoside (2.65):** To a stirred solution of **2.64** (2.66 g, 6.82 mmol) in dry toluene (70 mL) was added dibutyltin oxide (2.04 g, 8.18 mmol) at room temperature. The reaction mixture was heated at refluxed overnight at 120 °C under an Ar atmosphere. The reaction mixture was cooled to room temperature, concentrated and dried under high vacuum for 5 h. To a solution of the tin acetal in dry DMF (12 mL) was added cesium fluoride (1.56 g, 10.2 mmol) and allyl

bromide (1.18 mL, 13.6 mmol) successively at room temperature. The reaction mixture was stirred overnight at 60 °C under an Ar atmosphere. After cooling to room temperatre, the reaction mixture was diluted with EtOAc (200 mL) and washed with brine. The aqueous layer was extracted with EtOAc (50 mL × 3), and the combined organic layers were dried over Na_2SO_4, filtered and concentrated. The crude residue was purified by flash chromatography (2:1 hexane–EtOAc) to afford **2.65** (2.23 g, 76%) as a viscous oil. R_f 0.19 (4:1 hexane–EtOAc); $[\alpha]_D$ –0.8 (*c* 0.15, $CHCl_3$); ^{1}H NMR (600 MHz; $CDCl_3$): δ 7.51–7.49 (m, 2H, Ar), 7.39–7.36 (m, 2H, Ar), 7.13–7.12 (m, 2H, Ar), 6.91–6.89 (m, 2H, Ar), 5.96 (ddt, 1H, *J* = 17.2, 10.4, 5.7 Hz, $OCH_2C\underline{H}=CH_2$), 5.32 (dq, 1H, *J* = 17.2, 1.6 Hz, $OCH_2CH=C\underline{H}_2$), 5.22 (dq, 1H, *J* = 10.4, 1.3 Hz, $OCH_2CH=C\underline{H}_2$), 4.76 (d, 1H, *J* = 9.9 Hz, $ArC\underline{H}_2$), 4.67 (d, 1H, *J* = 9.8 Hz, $ArC\underline{H}_2$), 4.52 (d, 1H, *J* = 9.8 Hz, H-1), 4.22 (ddt, 1H, *J* = 12.7, 5.9, 1.4 Hz, $OC\underline{H}_2CH=CH_2$), 4.18 (ddt, 1H, *J* = 12.6, 5.5, 1.4 Hz, $OC\underline{H}_2CH=CH_2$), 3.82–3.81 (m, 4H, $ArOC\underline{H}_3$, H-4), 3.60 (t, 1H, *J* = 9.4 Hz, H-2), 3.56 (q, 1H, *J* = 6.5 Hz, H-5), 3.47 (dd, 1H, *J* = 9.0, 3.3 Hz, H-3), 2.35 (s, 3H, $ArC\underline{H}_3$), 2.21 (d, 1H, *J* = 2.9 Hz, 4-OH), 1.38 (d, 3H, *J* = 6.5 Hz, H-6); ^{13}C NMR (125 MHz; $CDCl_3$): δ 159.4 (Ar), 137.6 (Ar), 134.5 ($OCH_2\underline{C}H=CH_2$), 132.7 (Ar), 130.5 (Ar), 130.1 (Ar), 130.0 (Ar), 129.6 (Ar), 117.5 ($OCH_2CH=\underline{C}H_2$), 113.8 (Ar), 87.8 (C-1), 82.8 (C-3), 76.5 (C-2), 75.3 ($Ar\underline{C}H_2$), 74.2 (C-5), 71.2 ($O\underline{C}H_2CH=CH_2$), 69.6 (C-4), 55.3 ($O\underline{C}H_3$), 21.1 ($Ar\underline{C}H_3$), 16.8 (C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{24}H_{30}NaO_5S$: 453.1706; Found 453.1704.

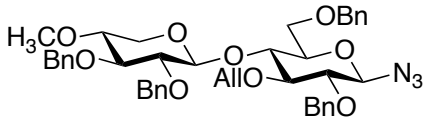
***p*-Tolyl 4-*O*-acetyl-3-*O*-allyl-2-*O*-(4-methoxybenzyl)-1-thio-β-L-fucopyranoside (2.63):** To a stirred solution of **2.65** (2.23 g, 5.18 mmol) in pyridine (10 mL) was added acetic anhydride (5.0 mL) dropwise at room temperature. The reaction mixture was stirred for 2 h at room temperature and then the solvent was evaporated. The crude residue was diluted with CH_2Cl_2 (150 mL) and washed with 1N HCl and saturated $NaHCO_3$ (aq.). The organic layer was dried over Na_2SO_4, filtered and concentrated. The crude residue was purified by flash chromatography (4:1 hexane–EtOAc) to afford **2.63** (2.46 g, quant.) as a viscous oil. R_f 0.36 (4:1 hexane–EtOAc); $[\alpha]_D$ –2.9 (*c* 0.35, $CHCl_3$); ^{1}H NMR (600 MHz; $CDCl_3$): δ 7.52–7.50 (m, 2H, Ar), 7.39–7.37 (m, 2H, Ar), 7.13–7.11 (m, 2H, Ar), 6.91–6.89 (m, 2H, Ar), 5.91 (ddt, 1H, *J* = 17.2, 10.4, 5.7 Hz, $OCH_2C\underline{H}=CH_2$), 5.32–5.28 (m, 2H, $OCH_2CH=C\underline{H}_2$, H-4), 5.19 (dq, 1H, *J* = 10.4, 1.4 Hz, $OCH_2CH=C\underline{H}_2$), 4.72 (d, 1H, *J* = 9.8 Hz, $ArC\underline{H}_2$), 4.68 (d, 1H, *J* = 9.8 Hz, $ArC\underline{H}_2$), 4.58 (d, 1H, *J* = 9.5 Hz, H-1), 4.19 (ddt, 1H, *J* = 12.5, 5.6, 1.4 Hz, $OC\underline{H}_2CH=CH_2$), 4.05 (ddt, 1H, *J* = 12.5, 5.8, 1.3 Hz, $OC\underline{H}_2CH=CH_2$), 3.83 (s, 3H, $ArOC\underline{H}_3$), 3.66 (qd, 1H, *J* = 6.4, 0.9 Hz, H-5), 3.59 (t, 1H, *J* = 9.3 Hz, H-2), 3.54 (dd, 1H, *J* = 9.1, 3.3 Hz, H-3), 2.35 (s, 3H, $ArC\underline{H}_3$), 2.19 (s, 3H, $COC\underline{H}_3$), 1.24 (d, 3H, *J* = 6.4 Hz, H-6); ^{13}C NMR (125 MHz; $CDCl_3$): δ 170.8 (C=O), 159.3 (Ar), 137.6 (Ar), 134.5 ($OCH_2\underline{C}H=CH_2$), 132.6 (Ar), 130.6 (Ar), 130.1 (Ar), 129.9 (Ar), 129.5 (Ar), 117.4 ($OCH_2CH=\underline{C}H_2$), 113.8 (Ar), 88.0 (C-1), 81.0 (C-3), 76.4 (C-2), 75.4 ($Ar\underline{C}H_2$), 72.9 (C-5),

70.9 (O<u>C</u>H$_2$CH=CH$_2$), 70.0 (C-4), 55.3 (ArO<u>C</u>H$_3$), 21.1 (Ar<u>C</u>H$_3$), 20.9 (CO<u>C</u>H$_3$), 16.8 (C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{26}H_{32}N_3O_6S$: 495.1812; Found 495.1807.



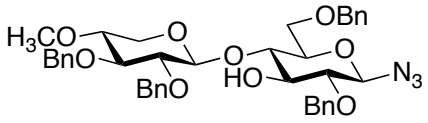
4-*O*-Methyl-β-D-xylopyranosyl-(1→4)-3-*O*-allyl-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (2.67): To a stirred solution of **2.32** (647 mg, 0.987 mmol) in CH_3OH (10 mL) was added a solution of $NaOCH_3$ in CH_3OH (2.0 mL, 0.5 M). The reaction mixture was stirred overnight at room temperature, then neutralized by addition of Amberlite® IR-120 (H^+) cation exchange resin, filtered and the filtrate was concentrated to afford **2.67** (564 mg, quant.) as a syrup. R_f 0.27 (1:2 hexane–EtOAc); $[\alpha]_D$ –18.2 (*c* 0.71, $CHCl_3$); ^{1}H NMR (600 MHz; $CDCl_3$): δ 7.40–7.31 (m, 10H, Ar), 5.96 (ddt, 1H, *J* = 17.2, 10.5, 5.6 Hz, OCH$_2$C<u>H</u>=CH$_2$), 5.28 (dq, 1H, *J* = 17.2, 1.7 Hz, OCH$_2$CH=C<u>H</u>$_2$), 5.18 (dq, 1H, *J* = 10.4, 1.5 Hz, OCH$_2$CH=C<u>H</u>$_2$), 4.84 (d, 1H, *J* = 10.6 Hz, PhC<u>H</u>$_2$), 4.76 (d, 1H, *J* = 10.6 Hz, PhC<u>H</u>$_2$), 4.69 (d, 1H, *J* = 12.1 Hz, PhC<u>H</u>$_2$), 4.60 (d, 1H, *J* = 12.1 Hz, PhC<u>H</u>$_2$), 4.59 (d, 1H, *J* = 8.6 Hz, Glc-H-1), 4.56 (d, 1H, *J* = 6.8 Hz, Xyl-H-1), 4.38–4.32 (m, 2H, OC<u>H</u>$_2$CH=CH$_2$), 4.10 (dd, 1H, *J* = 11.7, 4.5 Hz, Xyl-H-5a), 3.95–3.91 (m, 2H, Glc-H-4, Glc-H-6a), 3.78 (dd, 1H, *J* = 11.6, 2.2 Hz, Glc-H-6b), 3.54–3.47 (m, 6H, Xyl-H-3, Glc-H-5, OCH_3, Glc-H-3), 3.35–3.31 (m, 2H, Xyl-H-2, Glc-H-2), 3.28–3.25 (m, 1H, Xyl-H-4), 3.18 (dd, 1H, *J* = 11.7, 9.2 Hz, Xyl-H-5b); ^{13}C NMR (125 MHz; $CDCl_3$): δ 137.6 (Ar), 137.3 (Ar), 134.9 (OCH$_2$<u>C</u>H=CH$_2$), 128.5 (Ar), 128.3 (Ar), 128.0 (2 × Ar), 127.9 (Ar), 116.8 (OCH$_2$CH=<u>C</u>H$_2$), 103.3 (Xyl-C-1), 90.2 (Glc-C-1), 83.1 (Glc-C-3), 81.6 (Glc-C-2), 78.6

(Xyl-C-4), 76.6 (Glc-C-5), 76.3 (Glc-C-4), 75.3 (Ph<u>C</u>H$_2$), 74.4 (O<u>C</u>H$_2$CH=CH$_2$), 74.3 (Xyl-C-3), 73.7 (Ph<u>C</u>H$_2$), 73.5 (Xyl-C-2), 68.1 (Glc-C-6), 62.7 (Xyl-C-5), 58.4 (O<u>C</u>H$_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{29}H_{37}N_3NaO_9$: 594.2422; Found 594.2417.



2,3-Di-*O*-benzyl-4-*O*-methyl-β-D-xylopyranosyl-(1→4)-3-*O*-allyl-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (2.66): To a stirred solution of **2.67** (566 mg, 0.991 mmol) in dry DMF (10 mL) was added sodium hydride (158 mg, 3.96 mmol, 60% dispersion in mineral oil) in one portion at 0 °C. After stirring for 30 min, benzyl bromide (0.28 mL, 2.4 mmol) was added dropwise, and the reaction mixture was warmed to room temperature and stirred overnight under an Ar atmosphere. Then, CH_3OH was added at 0 °C and the solution was concentrated. The crude residue was diluted with CH_2Cl_2 (50 mL), washed with saturated $NaHCO_3$ (aq.), dried over Na_2SO_4, filtered and concentrated. The crude residue was purified by flash chromatography (4:1 hexane–EtOAc) to afford **2.66** (707 mg, 95%) as a syrup. R_f 0.43 (4:1 hexane–EtOAc); $[\alpha]_D$ +2.5 (*c* 0.35, $CHCl_3$); ^{1}H NMR (600 MHz; $CDCl_3$): δ 7.41–7.28 (m, 20H, Ar), 5.98 (ddt, 1H, *J* = 17.0, 10.6, 6.2 Hz, OCH$_2$C<u>H</u>=CH$_2$), 5.27 (dq, 1H, *J* = 17.2, 1.6 Hz, OCH$_2$CH=C<u>H</u>$_2$), 5.17 (dq, 1H, *J* = 10.3, 1.8 Hz, OCH$_2$C<u>H</u>=CH$_2$), 4.85 (d, 1H, *J* = 11.0 Hz, PhC<u>H</u>$_2$), 4.83–4.79 (m, 3H, 3 × PhC<u>H</u>$_2$), 4.77 (d, 1H, *J* = 11.2 Hz, PhC<u>H</u>$_2$), 4.74 (d, 1H, *J* = 11.2 Hz, PhC<u>H</u>$_2$), 4.58 (d, 1H, *J* = 8.6 Hz, Glc-H-1), 4.57 (d, 1H, *J* = 12.0 Hz, PhC<u>H</u>$_2$), 4.43 (ddt, 1H, *J* = 11.8, 5.9, 1.2 Hz, OC<u>H</u>$_2$CH=CH$_2$), 4.40 (d, 1H, *J* = 12.0 Hz, PhC<u>H</u>$_2$), 4.36 (d, 1H, *J* = 7.7 Hz, Xyl-H-1), 4.24 (ddt, 1H, *J* = 11.8, 6.1, 1.2 Hz,

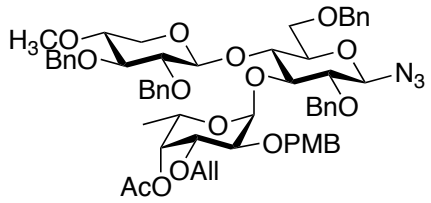
$OCH_2CH=C\underline{H}_2$), 4.01 (dd, 1H, *J* = 11.7, 5.1 Hz, Xyl-H-5a), 3.91 (t, 1H, *J* = 9.5 Hz, Glc-H-4), 3.80 (dd, 1H, *J* = 11.1, 3.8 Hz, Glc-H-6a), 3.67 (dd, 1H, *J* = 11.1, 1.6 Hz, Glc-H-6b), 3.50 (s, 3H, $OC\underline{H}_3$), 3.42 (t, 1H, *J* = 9.1 Hz, Glc-H-3), 3.40–3.33 (m, 3H, Xyl-H-3, Glc-H-5, Xyl-H-4), 3.30 (t, 1H, *J* = 8.9 Hz, Glc-H-2), 3.26 (t, 1H, *J* = 8.3 Hz, Xyl-H-2), 3.01 (dd, 1H, *J* = 11.7, 9.9 Hz, Xyl-H-5b); ^{13}C NMR (125 MHz; $CDCl_3$): δ 138.7 (Ar), 138.4 (Ar), 138.0 (2 × Ar), 135.3 ($OCH_2\underline{C}H=CH_2$), 128.4 (2 × Ar), 128.3 (2 × Ar), 128.2 (Ar), 127.9 (Ar), 127.8 (3 × Ar), 127.6 (3 × Ar), 117.0 ($OCH_2CH=\underline{C}H_2$), 103.1 (Xyl-C-1), 90.1 (Glc-C-1), 84.0 (Xyl-C-3), 82.8 (Glc-C-3), 82.1 (Xyl-C-2), 81.0 (Glc-C-2), 80.2 (Xyl-C-4), 76.8 (Glc-C-5), 76.1 (Glc-C-4), 75.4 ($Ph\underline{C}H_2$), 75.3 ($Ph\underline{C}H_2$), 75.2 ($Ph\underline{C}H_2$), 74.7 ($O\underline{C}H_2CH=CH_2$), 73.3 ($Ph\underline{C}H_2$), 67.6 (Glc-C-6), 63.4 (Xyl-C-5), 58.9 ($O\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{43}H_{49}N_3NaO_9$: 774.3361; Found 774.3357.



2,3-Di-*O*-benzyl-4-*O*-methyl-β-D-xylopyranosyl-(1→4)-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (2.68): To a stirred solution of **2.66** (622 mg, 828 μmol) in dry THF (10 mL), degassed under vacuum, and stirring under an Ar atmosphere, (1,5-cyclooctadiene)bis(methyldiphenylphosphine)iridium (I) hexafluorophosphate (42.0 mg, 49.7 μmol) was added, followed by further degassing of the reaction mixture. The suspension was stirred for 15 min at 0 °C, and the catalyst was then activated with hydrogen (2 min under a hydrogen atmosphere). The excess hydrogen was removed by three cycles of vacuum/Ar. The reaction mixture was then stirred for 2 h at room temperature under an

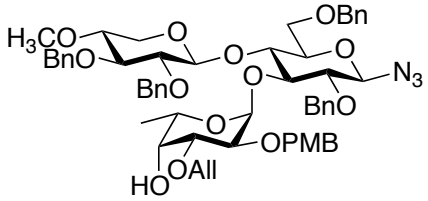
Ar atmosphere. The solvent was then evaporated, and the residue was dissolved in acetone–water (10:1, 11 mL) before HgO (251 mg, 1.16 mmol) and $HgCl_2$ (270 mg, 0.994 mmol) were added. The reaction mixture was stirred for 2 h at room temperature, then the solvent was evaporated, and the residue was diluted with EtOAc (100 mL), washed with 10% KI, saturated $Na_2S_2O_3$ (aq.) and water. The aqueous layers were extracted with EtOAc (100 mL), and the combined organic layers were dried over Na_2SO_4, filtered and concentrated. The crude residue was purified by flash chromatography (4:1 hexane–EtOAc) to afford **2.68** (507 mg, 86%) as a syrup. R_f 0.22 (4:1 hexane–EtOAc); $[\alpha]_D$ –1.9 (*c* 0.29, $CHCl_3$); ^{1}H NMR (600 MHz; $CDCl_3$): δ 7.45–7.43 (m, 2H, Ar), 7.38–7.29 (m, 16H, Ar), 7.26–7.24 (m, 2H, Ar), 4.93 (d, 1H, J = 11.0 Hz, PhC$\underline{H}_2$), 4.87 (d, 1H, J = 11.0 Hz, PhC$\underline{H}_2$), 4.85–4.80 (m, 3H, 3× PhC$\underline{H}_2$), 4.74 (d, 1H, J = 11.1 Hz, PhC$\underline{H}_2$), 4.61 (d, 1H, J = 8.6 Hz, Glc-H-1), 4.45 (d, 1H, J = 12.0 Hz, PhC$\underline{H}_2$), 4.32 (d, 1H, J = 12.0 Hz, PhC$\underline{H}_2$), 4.24 (d, 1H, J = 7.8 Hz, Xyl-H-1), 4.07 (dd, 1H, J = 11.6, 5.2 Hz, Xyl-H-5a), 4.03 (s, 1H, Glc-3-OH), 3.72 (t, 1H, J = 8.8 Hz, Glc-H-3), 3.67–3.66 (m, 2H, Glc-H-6), 3.63 (t, 1H, J = 9.3 Hz, Glc-H-4), 3.52–3.49 (m, 4H, Glc-H-5, OC$\underline{H}_3$), 3.43 (t, 1H, J = 8.9 Hz, Xyl-H-3), 3.41–3.37 (m, 1H, Xyl-H-4), 3.33-3.28 (m, 2H, Xyl-H-2, Glc-H-2), 3.13 (dd, 1H, J = 11.6, 10.3 Hz, Xyl-H-5b); ^{13}C NMR (125 MHz; $CDCl_3$): δ 138.5 (Ar), 138.1 (2 × Ar), 138.0 (Ar), 128.4 (2 × Ar), 128.1 (Ar), 127.9 (Ar), 127.8 (3 × Ar), 127.7 (3 × Ar), 103.7 (Xyl-C-1), 89.6 (Glc-C-1), 83.8 (Xyl-C-3), 81.3 (Xyl-C-2), 80.9 (Glc-C-2), 79.7 (Xyl-C-4), 79.3 (Glc-C-4), 76.2 (Glc-C-5), 75.5 (Glc-C-3, Ph$\underline{C}H_2$), 75.4 (Ph$\underline{C}H_2$), 74.9 (Ph$\underline{C}H_2$), 73.3 (Ph$\underline{C}H_2$), 67.7 (Glc-C-6),

63.6 (Xyl-C-5), 59.1 (O<u>C</u>H$_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{40}H_{45}N_3NaO_9$: 734.3048; Found 734.3044.



2,3-Di-*O*-benzyl-4-*O*-methyl-β-D-xylopyranoside-(1→4)-[4-*O*-acetyl-3-*O*-allyl-2-*O*-(4-methoxybenzyl)-α-L-fucopyranosyl-(1→3)]-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (2.62): To a stirred solution of acceptor **2.68** (650 mg, 0.913 mmol) and donor **2.63** (871 mg, 1.83 mmol) in dry Et_2O (16 mL) was added molecular sieves (1.6 g, 4Å, powder). After stirring for 30 min at room temperature, methyl trifluoromethanesulfonate (0.34 mL, 3.0 mmol) was added dropwise. The resulting solution was stirred for 4 h at room temperature under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (4:1 hexane–EtOAc) to afford **2.62** (804 mg, 83%) as a syrup. R_f 0.16 (4:1 hexane–EtOAc); $[\alpha]_D$ –29.5 (*c* 0.15, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.34–7.26 (m, 16H, Ar), 7.23–7.20 (m, 4H, Ar), 7.07–7.05 (m, 2H, Ar), 6.65–6.63 (m, 2H, Ar), 5.91 (ddt, 1H, *J* = 17.2, 10.5, 5.3 Hz, $OCH_2C\underline{H}=CH_2$), 5.52 (d, 1H, *J* = 3.6 Hz, Fuc-H-1), 5.29 (dq, 1H, *J* = 17.2, 1.7 Hz, $OCH_2CH=C\underline{H}_2$), 5.19 (d, 1H, *J* = 2.2 Hz, Fuc-H-4), 5.13 (dq, 1H, *J* = 10.5, 1.6 Hz, $OCH_2CH=C\underline{H}_2$), 4.87–4.75 (m, 5H, Fuc-H-5, 4 × $PhC\underline{H}_2$), 4.70–4.65 (m, 3H, 2 × $PhC\underline{H}_2$, $ArC\underline{H}_2$), 4.61 (d, 1H, *J* = 11.9 Hz, $PhC\underline{H}_2$), 4.58 (d, 1H, *J* = 8.6 Hz, Glc-H-1), 4.56 (d, 1H, *J* = 11.5 Hz, $PhC\underline{H}_2$), 4.39–4.36 (m, 2H, $PhC\underline{H}_2$, Xyl-H-1),

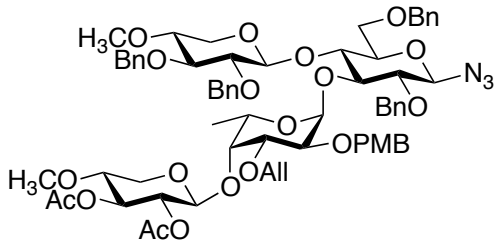
4.17 (ddt, 1H, J = 12.6, 5.3, 1.4 Hz, OC<u>H</u>$_2$CH=CH$_2$), 4.07–4.01 (m, 3H, Fuc-H-3, Glc-H-4, OC<u>H</u>$_2$CH=CH$_2$), 3.92–3.87 (m, 3H, Glc-H-6a, Xyl-H-5a, Glc-H-3), 3.74–3.70 (m, 4H, Fuc-H-2, ArOC<u>H</u>$_3$), 3.62 (dd, 1H, J = 11.3, 1.5 Hz, Glc-H-6b), 3.47 (s, 3H, OC<u>H</u>$_3$), 3.42 (t, 1H, J = 8.8 Hz, Glc-H-2), 3.37–3.35 (m, 1H, Glc-H-5), 3.29 (t, 1H, J = 9.0 Hz, Xyl-H-3), 3.21 (ddd, 1H, J = 10.5, 9.0, 5.4 Hz, Xyl-H-4), 3.03 (t, 1H, J = 8.5 Hz, Xyl-H-2), 2.89 (t, 1H, J = 11.2 Hz, Xyl-H-5b), 2.12 (s, 3H, COC<u>H</u>$_3$), 1.06 (d, 3H, J = 6.6 Hz, Fuc-H-6); ^{13}C NMR (125 MHz; CDCl$_3$): δ 170.8 (C=O), 159.1 (Ar), 138.5 (Ar) 138.1 (Ar), 137.9 (2 × Ar), 135.1 (OCH$_2$<u>C</u>H=CH$_2$), 130.3 (Ar), 129.9 (Ar), 128.5 (Ar), 128.4 (2 × Ar), 127.9, 127.8 (2 × Ar), 127.7 (3 × Ar), 127.5 (Ar), 127.1 (Ar), 116.2 (OCH$_2$CH=<u>C</u>H$_2$), 113.5 (Ar), 103.2 (Xyl-C-1), 97.6 (Fuc-C-1, $^1J_{C\text{-}H}$ = 174.1 Hz), 90.2 (Glc-C-1), 84.0 (Xyl-C-3), 82.6 (Glc-C-2), 82.3 (Xyl-C-2), 80.2 (Xyl-C-4), 77.3 (Glc-C-5), 76.4 (Fuc-C-3), 75.6 (Ph<u>C</u>H$_2$), 75.3 (Ph<u>C</u>H$_2$), 74.8 (Glc-C-4), 74.1 (Glc-C-3), 74.0 (Ph<u>C</u>H$_2$), 73.7 (Fuc-C-2), 73.4 (2 × C, Ar<u>C</u>H$_2$, Ph<u>C</u>H$_2$), 71.5 (Fuc-C-4), 70.5 (O<u>C</u>H$_2$CH=CH$_2$), 67.3 (Glc-C-6), 64.2 (Fuc-C-5), 63.5 (Xyl-C-5), 59.1 (O<u>C</u>H$_3$), 55.2 (ArO<u>C</u>H$_3$), 20.9 (CO<u>C</u>H$_3$), 16.1 (Fuc-C-6); HRMS (ESI) Calc. for [M + Na]$^+$ $C_{59}H_{69}N_3NaO_{15}$: 1082.4621; Found 108.4616.



2,3-Di-*O*-benzyl-4-*O*-methyl-β-D-xylopyranoside-(1→4)-[3-*O*-allyl-2-*O*-(4-methoxybenzyl)-α-L-fucopyranosyl-(1→3)]-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (2.69): To a stirred solution of **2.62** (768 mg, 724 μmol) in CH$_3$OH (10 mL) was

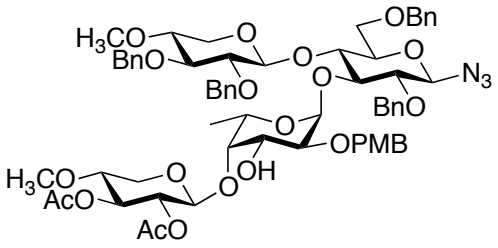
added a solution of $NaOCH_3$ in CH_3OH (2.0 mL, 0.5 M). The reaction mixture was stirred overnight at room temperature, then neutralized by addition of Amberlite® IR-120 (H^+) cation exchange resin. The solution was filtered and the filtrate was concentrated and the crude residue was purified by flash chromatography (2:1 hexane–EtOAc) to afford **2.69** (737 mg, quant.) as a syrup. R_f 0.37 (2:1 hexane–EtOAc); $[\alpha]_D$ –34.2 (*c* 0.78, $CHCl_3$); ^1H NMR (600 MHz; $CDCl_3$): δ 7.38–7.26 (m, 18H, Ar), 7.23–7.22 (m, 2H, Ar), 7.08–7.06 (m, 2H, Ar), 6.69–6.67 (m, 2H, Ar), 5.98 (ddt, 1H, *J* = 17.2, 10.6, 5.3 Hz, $OCH_2C\underline{H}=CH_2$), 5.58 (d, 1H, *J* = 3.7 Hz, Fuc-H-1), 5.32 (dq, 1H, *J* = 17.2, 1.6 Hz, $OCH_2CH=C\underline{H}_2$), 5.20 (dq, 1H, *J* = 10.4, 1.4 Hz, $OCH_2CH=C\underline{H}_2$), 4.91 (d, 1H, *J* = 11.2 Hz, $PhC\underline{H}_2$), 4.82 (s, 2H, 2 × $PhC\underline{H}_2$), 4.80–4.70 (m, 5H, Fuc-H-5, 3 × $PhC\underline{H}_2$), 4.65 (d, 1H, *J* = 11.8 Hz, $PhC\underline{H}_2$), 4.63 (d, 1H, *J* = 8.6 Hz, Glc-H-1), 4.55 (s, 2H, 2 × $ArC\underline{H}_2$), 4.41 (d, 1H, *J* = 12.0 Hz, $PhC\underline{H}_2$), 4.39 (d, 1H, *J* = 8.0 Hz, Xyl-H-1), 4.24 (ddt, 1H, *J* = 12.9, 5.1, 1.6 Hz, $OC\underline{H}_2CH=CH_2$), 4.20 (ddt, 1H, *J* = 12.9, 5.7, 1.4 Hz, $OC\underline{H}_2CH=CH_2$), 4.09 (t, 1H, *J* = 9.6 Hz, Glc-H-4), 4.01–3.96 (m, 2H, Fuc-H-3, Glc-H-3), 3.93–3.88 (m, 2H, Glc-H-6a, Xyl-H-5a), 3.78–3.77 (m, 1H, Fuc-H-4), 3.75 (dd, 1H, *J* = 9.9, 3.6 Hz, Fuc-H-2), 3.73 (s, 3H, $ArOC\underline{H}_3$), 3.65 (dd, 1H, *J* = 11.3, 1.5 Hz, Glc-H-6b), 3.48–3.45 (m, 4H, $OC\underline{H}_3$, Glc-H-2), 3.42–3.39 (m, 1H, Glc-H-5), 3.32 (t, 1H, *J* = 9.0 Hz, Xyl-H-3), 3.17 (ddd, 1H, *J* = 10.6, 8.9, 5.4 Hz, Xyl-H-4), 3.08 (t, 1H, *J* = 8.6 Hz, Xyl-H-2), 2.92 (t, 1H, *J* = 11.2 Hz, Xyl-H-5b), 1.27 (d, 3H, *J* = 6.7 Hz, Fuc-H-6); ^{13}C NMR (125 MHz; $CDCl_3$): δ 159.1 (Ar), 138.5 (Ar), 138.2 (Ar), 137.9 (2 × Ar), 135.2 ($OCH_2\underline{C}H=CH_2$), 130.2 (Ar), 129.7 (Ar), 128.5 (Ar), 128.4 (3 × Ar), 127.9 (2 × Ar), 127.7 (3 × Ar), 127.6 (Ar), 127.5 (Ar), 126.9 (Ar),

116.5 ($OCH_2CH=\underline{C}H_2$), 113.6 (Ar), 103.1 (Xyl-C-1), 97.0 (Fuc-C-1), 90.2 (Glc-C-1), 83.9 (Xyl-C-3), 82.7 (Glc-C-2), 82.4 (Xyl-C-2), 80.3 (Xyl-C-4), 78.0 (Fuc-C-3), 77.30 (Glc-C-5), 75.6 ($Ph\underline{C}H_2$), 75.3 ($Ph\underline{C}H_2$), 74.4 (Glc-C-3), 74.0 (2 × C, Glc-C-4, Fuc-C-2), 73.9 ($Ph\underline{C}H_2$), 73.4 ($Ph\underline{C}H_2$), 73.0 ($Ar\underline{C}H_2$), 71.1 ($O\underline{C}H_2CH=CH_2$), 70.7 (Fuc-C-4), 67.3 (Glc-C-6), 64.7 (Fuc-C-5), 63.5 (Xyl-C-5), 59.1 ($O\underline{C}H_3$), 55.2 ($ArO\underline{C}H_3$), 16.2 (Fuc-C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{57}H_{67}N_3NaO_{14}$: 1040.4515; Found 1040.4533.



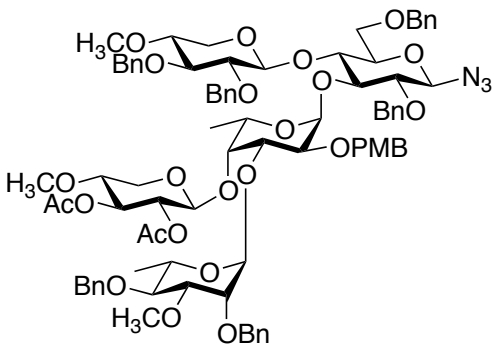
2,3-Di-*O*-acetyl-4-*O*-methyl-β-D-xylopyranosyl-(1→4)-3-*O*-allyl-2-*O*-(4-methoxybenzyl)-α-L-fucopyranosyl-(1→3)-[2,3-di-*O*-benzyl-4-*O*-methyl-β-D-xylopyranosyl-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (2.70): To a stirred solution of acceptor **2.69** (694 mg, 0.682 mmol) and donor **2.11** (799 mg, 1.36 mmol) in dry CH_2Cl_2 (16 mL) was added molecular sieves (1.6 g, 4Å, powder). After stirring for 30 min at room temperature, the reaction mixture was cooled to 0 °C, and then *N*-iodosuccinimide (368 mg, 1.64 mmol) and silver trifluoromethanesulfonate (35.0 mg, 136 μmol) were added successively. The resulting solution was stirred for 1 h at room temperature under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was washed with saturated $Na_2S_2O_3$ (aq.) and saturated $NaHCO_3$ (aq.). The aqueous layer was extracted with CH_2Cl_2 (50 mL × 3), dried

over Na_2SO_4, filtered and concentrated. The crude residue was purified by flash chromatography (2:1 hexane–EtOAc) to afford **2.70** (596 mg, 70%) as a syrup. R_f 0.20 (2:1 hexane–EtOAc); $[\alpha]_D$ –52.9 (*c* 0.15, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.34–7.23 (m, 18H), 7.17–7.16 (m, 2H), 7.11–7.09 (m, 2H), 6.66–6.64 (m, 2H), 5.97 (ddt, 1H, *J* = 17.1, 10.6, 5.3 Hz), 5.45 (d, 1H, *J* = 3.7 Hz, Fuc-H-1), 5.33 (dq, 1H, *J* = 17.2, 1.7 Hz), 5.14 (dq, 1H, *J* = 10.5, 1.5 Hz), 5.04 (t, 1H, *J* = 7.6 Hz), 4.96 (dd, 1H, *J* = 7.8, 6.0 Hz), 4.78 (s, 2H), 4.75 (d, 1H, *J* = 11.0 Hz), 4.72–4.66 (m, 4H), 4.64–4.61 (m, 2H), 4.58 (d, 1H, *J* = 5.9 Hz, Xyl-H-1), 4.54 (d, 1H, *J* = 8.6 Hz, Glc-H-1), 4.52 (d, 1H, *J* = 11.6 Hz), 4.38 (d, 1H, *J* = 11.9 Hz), 4.36 (d, 1H, *J* = 8.0 Hz, Xyl'-H-1), 4.22–4.18 (m, 2H), 4.10 (ddt, 1H, *J* = 12.7, 4.9, 1.6 Hz), 4.03 (t, 1H, *J* = 9.7 Hz), 3.98 (dd, 1H, *J* = 10.3, 2.8 Hz), 3.90–3.86 (m, 3H), 3.84 (dd, 1H, *J* = 10.3, 3.7 Hz), 3.74 (d, 1H, *J* = 2.3 Hz), 3.68 (s, 3H), 3.61 (dd, 1H, *J* = 11.3, 1.5 Hz), 3.46 (s, 3H), 3.43–3.37 (m, 5H), 3.36–3.32 (m, 2H), 3.29 (t, 1H, *J* = 9.0 Hz), 3.16 (ddd, 1H, *J* = 10.6, 8.9, 5.5 Hz), 3.03 (t, 1H, *J* = 8.6 Hz), 2.88 (t, 1H, *J* = 11.2 Hz), 2.04 (s, 3H), 1.97 (s, 3H), 1.14 (d, 3H, *J* = 6.7 Hz); ^{13}C NMR (125 MHz; $CDCl_3$): δ 170.2, 169.7, 159.0, 138.4, 138.1, 137.9 (2 × C), 135.5, 130.8, 129.7, 128.5, 128.4, 128.3, 128.1, 127.8 (2 × C), 127.7, 127.6, 127.5, 127.2, 116.1, 113.5, 103.1 (Xyl'-C-1), 101.0 (Xyl-C-1, $^1J_{C\text{-}H}$ = 165.2 Hz), 97.4 (Fuc-C-1), 90.2 (Glc-C-1), 84.0, 82.6, 82.4, 80.3, 78.7, 78.0, 77.3, 76.4, 75.8, 75.3, 74.5, 74.4, 74.1, 73.9, 73.6, 73.4, 72.0, 71.0 (2 × C), 67.3, 65.5, 63.5, 62.2, 59.0, 58.3, 55.1, 20.9 (2 × C), 16.4; HRMS (ESI) Calc. for $[M + Na]^+$ $C_{67}H_{81}N_3NaO_{20}$: 1270.5306; Found 1270.5306.



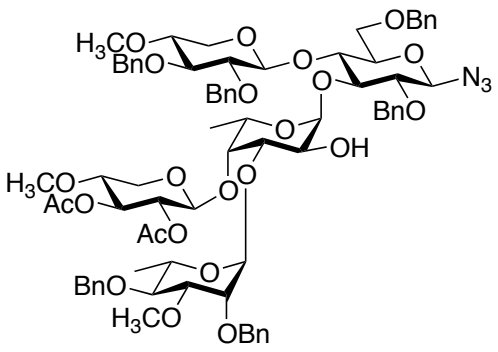
2,3-Di-*O*-acetyl-4-*O*-methyl-β-D-xylopyranosyl-(1→4)-2-*O*-(4-methoxybenzyl)-α-L-fucopyranosyl-(1→3)-[2,3-di-*O*-benzyl-4-*O*-methyl-β-D-xylopyranosyl-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (2.71): To a stirred solution of **2.70** (476 mg, 382 μmol) in dry THF (8.0 mL), degassed under vacuum, and stirring under an Ar atmosphere, (1,5-cyclooctadiene)bis(methyldiphenylphosphine)iridium (I) hexafluorophosphate (19.4 mg, 22.9 μmol) was added, followed by further degassing of the reaction mixture. The suspension was stirred for 15 min at 0 °C, and the catalyst was then activated with hydrogen (2 min under a hydrogen atmosphere). The excess hydrogen was removed by three cycles of vacuum/Ar. The reaction mixture was then stirred for 2 h at room temperature under an Ar atmosphere. The solvent was then evaporated, and the residue was dissolved in acetone–water (10:1, 7.7 mL) before HgO (116 mg, 534 μmol) and $HgCl_2$ (124 mg, 458 μmol) were added. The reaction mixture was stirred for 2 h at room temperature, then the solvent was concentrated, and the residue was diluted with EtOAc (100 mL), washed with 10% KI, saturated $Na_2S_2O_3$ (aq.) and water. The aqueous layers were extracted with EtOAc (100 mL), and the combined organic layers were dried over Na_2SO_4, filtered and concentrated. The crude residue was purified by flash chromatography (1:2 hexane–EtOAc) to afford **2.71** (424 mg, 92%) as a syrup. R_f 0.17 (1:1 hexane–EtOAc); $[\alpha]_D$ –58.5 (*c* 0.11, $CHCl_3$);

^{1}H NMR (700 MHz; $CDCl_3$): δ 7.34–7.23 (m, 18H), 7.21–7.20 (m, 2H), 7.12–7.10 (m, 2H), 6.71–6.69 (m, 2H), 5.49 (d, 1H, J = 3.7 Hz, Fuc-H-1), 5.04 (t, 1H, J = 9.3 Hz), 4.91 (dd, 1H, J = 9.5, 7.8 Hz), 4.81–4.76 (m, 4H), 4.73–4.70 (m, 2H), 4.67 (d, 1H, J = 11.1 Hz), 4.61 (d, 1H, J = 11.9 Hz), 4.57 (d, 1H, J = 8.6 Hz, Glc-H-1), 4.53 (s, 2H), 4.40 (d, 1H, J = 7.8 Hz, Xyl-H-1), 4.38 (d, 1H, J = 11.9 Hz), 4.35 (d, 1H, J = 8.1 Hz, Xyl'-H-1), 4.13–4.10 (m, 1H), 4.05 (dd, 1H, J = 11.7, 5.3 Hz), 4.02 (t, 1H, J = 9.7 Hz), 3.92 (dd, 1H, J = 11.7, 5.6 Hz), 3.89 (dd, 1H, J = 11.3, 3.0 Hz), 3.86 (t, 1H, J = 9.3 Hz), 3.72 (s, 3H), 3.61 (dd, 1H, J = 11.3, 1.6 Hz), 3.58 (d, 1H, J = 2.2 Hz), 3.51 (dd, 1H, J = 10.3, 3.7 Hz), 3.47 (s, 3H), 3.43 (ddd, 1H, J = 10.1, 9.1, 5.3 Hz), 3.40 (s, 3H), 3.39–3.35 (m, 2H), 3.27 (t, 1H, J = 9.0 Hz), 3.24 (dd, 1H, J = 11.7, 10.3 Hz), 3.20 (d, 1H, J = 10.1 Hz), 3.16 (ddd, 1H, J = 10.6, 8.9, 5.6 Hz), 3.02 (t, 1H, J = 8.6 Hz), 2.88 (t, 1H, J = 11.2 Hz), 2.05 (s, 3H), 2.01 (s, 3H), 1.10 (d, 3H, J = 6.6 Hz); ^{13}C NMR (125 MHz; $CDCl_3$): δ 170.3, 169.5, 159.0, 138.5, 138.2, 138.0, 137.9, 130.6, 129.9, 128.5, 128.4 (2 × C), 128.1, 127.8 (3 × C), 127.7, 127.6, 127.5, 127.0, 113.5, 103.2 (Xyl'-C-1), 102.6 (Xyl-C-1), 97.5 (Fuc-C-1), 90.2 (Glc-C-1), 85.0, 84.1, 82.6, 82.3, 80.2, 77.3, 76.0, 75.8, 75.2, 75.0, 74.2, 74.0 (2 × C), 73.4, 73.3, 72.0, 68.8, 67.3, 65.1, 63.8, 63.5, 59.1, 58.9, 55.2, 20.9, 20.8, 16.1; HRMS (ESI) Calc. for $[M + Na]^+$ $C_{64}H_{77}N_3NaO_{20}$: 1230.4993; Found 1230.4989.



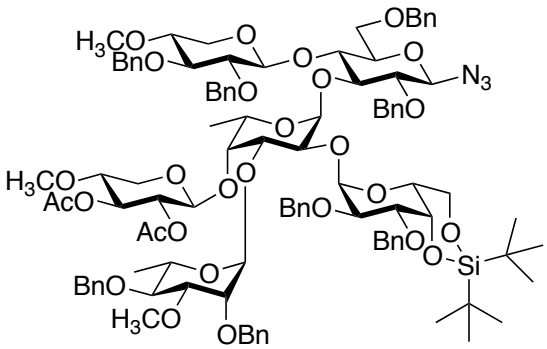
2,3-Di-*O*-acetyl-4-*O*-methyl-β-D-xylopyranosyl-(1→4)-[2,4-di-*O*-benzyl-3-*O*-methyl-α-L-rhamnopyranosyl-(1→3)]-2-*O*-(4-methoxybenzyl)-α-L-fucopyranosyl-(1→3)-[2,3-di-*O*-benzyl-4-*O*-methyl-β-D-xylopyranosyl-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (2.72): To a stirred solution of acceptor **2.71** (412 mg, 341 μmol) and donor **2.9** (317 mg, 682 μmol) in dry CH_2Cl_2 (10 mL) was added molecular sieves (1.0 g, 4Å, powder). After stirring for 30 min at room temperature, the reaction mixture was cooled to –30 °C, and then *N*-iodosuccinimide (184 mg, 818 μmol) and silver trifluoromethanesulfonate (17.5 mg, 68.2 μmol) were added successively. The resulting solution was stirred for 1 h at –30 °C under an Ar atmosphere. Excess triethylamine was added to quench the acid, the solution was filtered and the filtrate was washed with saturated $Na_2S_2O_3$ (aq.) and saturated $NaHCO_3$ (aq.). The aqueous layer was extracted with CH_2Cl_2 (50 mL × 3), dried over Na_2SO_4, filtered and concentrated. The crude residue was purified by flash chromatography (2:1 hexane–EtOAc) to afford **2.72** (362 mg, 69%) as a syrup. R_f 0.29 (2:1 hexane–EtOAc); $[\alpha]_D$ –67.7 (*c* 0.14, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.35–7.24 (m, 28H), 7.16–7.14 (m, 4H), 6.57–6.55 (m, 2H), 5.44 (d, 1H, J = 3.6 Hz, Fuc-H-1), 5.04 (t, 1H, J = 8.4 Hz), 4.99–4.97 (m, 2H, Rha-H-1), 4.89 (d, 1H, J = 11.3

Hz), 4.80–4.72 (m, 4H), 4.71 (d, 1H, J = 11.2 Hz), 4.68 (d, 1H, J = 11.3 Hz), 4.65–4.58 (m, 6H), 4.51 (d, 1H, J = 8.6 Hz, Glc-H-1), 4.45 (d, 1H, J = 6.7 Hz, Xyl-H-1), 4.42–4.37 (m, 4H), 4.30 (d, 1H, J = 7.9 Hz, Xyl'-H-1), 4.06 (dq, 1H, J = 9.6, 6.1 Hz), 3.94 (t, 1H, J = 9.6 Hz), 3.90 (t, 1H, J = 2.2 Hz), 3.86–3.82 (m, 3H), 3.74 (d, 1H, J = 2.6 Hz), 3.71 (dd, 1H, J = 10.4, 3.6 Hz), 3.66 (dd, 1H, J = 9.5, 3.0 Hz), 3.63–3.62 (m, 1H), 3.57 (s, 3H), 3.51 (t, J = 9.5 Hz, 1H), 3.45 (s, 3H), 3.42 (t, 1H, J = 8.8 Hz), 3.38 (s, 3H), 3.36–3.31 (m, 5H), 3.28 (t, 1H, J = 9.0 Hz), 3.17 (dd, 1H, J = 11.8, 9.1 Hz), 3.14–3.10 (m, 1H), 2.99 (t, 1H, J = 8.5 Hz), 2.82 (t, 1H, J = 11.0 Hz), 2.05 (s, 3H), 2.02 (s, 3H), 1.31 (d, 3H, J = 6.1 Hz), 1.15 (d, 3H, J = 6.7 Hz); ^{13}C NMR (125 MHz; $CDCl_3$): δ 170.2, 169.9, 158.9, 139.4, 138.9, 138.5, 138.2, 137.9 (2 × C), 130.5, 129.8, 128.4 (3 × C), 128.3 (2 × C), 128.2 (2 × C), 127.9, 127.8, 127.7 (2 × C), 127.5, 127.4 (2 × C), 127.3, 127.2, 126.8, 113.6, 103.2 (Xyl'-C-1), 101.4 (Xyl-C-1), 96.6 (Fuc-C-1), 93.3 (Rha-C-1, $^1J_{C\text{-}H}$ = 167.6 Hz), 90.2 (Glc-C-1), 83.9, 82.5, 82.3, 82.0, 81.0, 80.5, 75.9, 75.8, 75.7, 75.2, 74.7, 74.3, 74.1, 74.0, 73.8, 73.4, 72.7, 72.4, 71.3, 71.2, 68.0, 67.4, 65.1, 63.2, 62.7, 58.6 (2 × C), 58.0, 55.1, 20.9 (2 × C), 18.4, 16.7; HRMS (ESI) Calc. for $[M + Na]^+$ $C_{85}H_{101}N_3NaO_{24}$: 1570.6667; Found 1570.6676.



2,3-Di-*O*-acetyl-4-*O*-methyl-β-D-xylopyranosyl-(1→4)-[2,4-di-*O*-benzyl-3-*O*-methyl-α-L-rhamnopyranosyl-(1→3)]-α-L-fucopyranosyl-(1→3)-[2,3-di-*O*-benzyl-4-*O*-methyl-β-D-xylopyranosyl-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (2.73): To a stirred solution of **2.72** (362 mg, 234 μmol) in dry CH_2Cl_2 (10 mL) was added trifluoroacetic acid (100 μL) dropwise at 0 °C. The reaction mixture was stirred for 5 h at room temperature under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (3:2 hexane–EtOAc) to afford **2.73** (293 mg, 88%) as a syrup. R_f 0.50 (3:2 hexane–EtOAc); $[\alpha]_D$ –77.9 (*c* 0.58, $CHCl_3$); ^{1}H NMR (600 MHz; $CDCl_3$): δ 7.41–7.26 (m, 30H), 5.44 (d, 1H, *J* = 4.0 Hz, Fuc-H-1), 5.05 (t, 1H, *J* = 8.0 Hz), 4.96–4.92 (m, 3H, Rha-H-1), 4.86–4.75 (m, 5H), 4.73 (d, 1H, *J* = 11.2 Hz), 4.71 (d, 1H, *J* = 11.2 Hz), 4.68–4.64 (m, 3H), 4.60 (d, 1H, *J* = 8.6 Hz, Glc-H-1), 4.52 (q, 1H, *J* = 6.7 Hz), 4.47–4.44 (m, 2H, Xyl-H-1), 4.34 (d, 1H, *J* = 8.0 Hz, Xyl'-H-1), 4.24 (dd, 1H, *J* = 11.4, 5.4 Hz), 4.10–4.05 (m, 2H), 3.97 (dd, 1H, *J* = 11.9, 4.5 Hz), 3.93–3.82 (m, 5H), 3.74 (dd, 1H, *J* = 9.5, 3.1 Hz), 3.68 (d, 1H, *J* = 2.8 Hz), 3.66 (dd, 1H, *J* = 11.1, 1.4 Hz), 3.56 (t, 1H, *J* = 9.5 Hz), 3.52 (s, 3H), 3.42–3.39 (m, 5H), 3.35–3.30 (m, 5H), 3.23 (dd, 1H, *J* = 11.8,

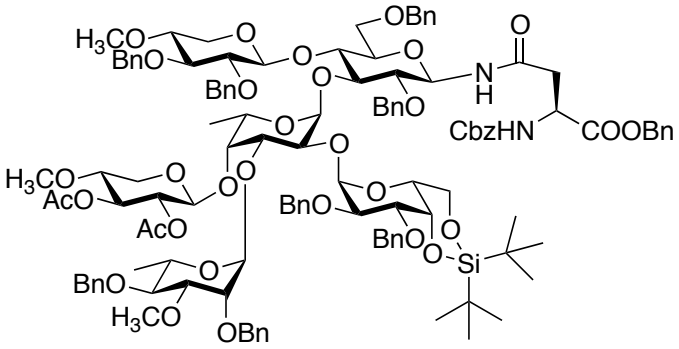
8.5 Hz), 3.14 (ddd, 1H, J = 10.4, 9.1, 5.4 Hz), 3.02 (t, 1H, J = 8.5 Hz), 2.88 (t, 1H, J = 11.1 Hz), 2.04 (s, 3H), 2.03 (s, 3H), 1.35 (d, 3H, J = 6.2 Hz), 1.16 (d, 3H, J = 6.7 Hz); ^{13}C NMR (125 MHz; $CDCl_3$): δ 170.2, 169.7, 139.0, 138.7, 138.4, 138.1, 137.8, 137.3, 128.5 (3 × C), 128.4 (2 × C), 128.3 (2 × C), 128.1, 128.0, 127.9, 127.8 (2 × C), 127.7, 127.6, 127.5, 127.4, 127.1, 103.2 (Xyl'-C-1), 101.4 (Xyl-C-1), 97.5 (Fuc-C-1), 94.9 (Rha-C-1), 90.1 (Glc-C-1), 83.8, 82.6, 82.2, 81.7, 80.6, 80.4, 77.2, 76.7, 76.5, 75.8, 75.6, 75.2, 75.0 (2 × C), 74.5, 73.9, 73.7, 73.5, 72.7, 72.1, 71.1, 68.2, 67.5, 67.3, 65.6, 63.3, 62.5, 58.8, 58.5, 58.0, 20.9 (2 × C), 18.2, 16.5; HRMS (ESI) Calc. for $[M + Na]^+$ $C_{77}H_{93}N_3NaO_{23}$: 1450.6092; Found 1450.6091.



2,3-Di-*O*-acetyl-4-*O*-methyl-β-D-xylopyranosyl-(1→4)-[2,4-di-*O*-benzyl-3-*O*-methyl-α-L-rhamnopyranosyl-(1→3)]-[2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranosyl-(1→2)]-α-L-fucopyranosyl-(1→3)-[2,3-di-*O*-benzyl-4-*O*-methyl-β-D-xylopyranosyl-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (2.74): To a stirred solution of acceptor **2.73** (293 mg, 205 μmol) and *p*-tolyl 2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranoside **2.10**[15] (249 mg, 410 μmol) in dry Et_2O (10 mL) was added molecular sieves (1.0 g, 4Å, powder). After stirring for 30 min at room temperature,

methyl trifluoromethanesulfonate (76.6 μL, 677 μmol) was added dropwise. The resulting solution was stirred for 24 h at room temperature under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (2:1 hexane–EtOAc) to afford **2.74** (350 mg, 89%) as a white foam. R_f 0.50 (2:1 hexane–EtOAc); $[\alpha]_D$ –38.5 (*c* 0.20, $CHCl_3$); ^1H NMR (700 MHz; $CDCl_3$): δ 7.35–7.18 (m, 37H), 7.14–7.12 (m, 1H), 7.08–7.07 (m, 2H), 5.43 (d, 1H, J = 3.4 Hz, Fuc-H-1), 5.29 (d, 1H, J = 3.7 Hz, Gal-H-1), 5.05 (t, 1H, J = 8.6 Hz), 4.99 (d, 1H, J = 1.3 Hz, Rha-H-1), 4.95 (dd, 1H, J = 8.9, 6.9 Hz), 4.83 (d, 1H, J = 11.3 Hz), 4.80 (d, 1H, J = 10.7 Hz), 4.77–4.73 (m, 4H), 4.71 (d, 1H, J = 11.2 Hz), 4.69 (d, 1H, J = 11.2 Hz), 4.65–4.57 (m, 6H, Glc-H-1), 4.52 (d, 1H, J = 11.3 Hz), 4.49–4.40 (m, 6H, Xyl-H-1), 4.34 (d, 1H, J = 7.9 Hz, Xyl'-H-1), 4.10–4.08 (m, 2H), 4.04 (dd,1H, J = 12.5, 1.5 Hz), 4.01 (t, 1H, J = 9.4 Hz), 3.96–3.92 (m, 2H), 3.90–3.85 (m, 4H), 3.79 (d, 1H, J = 2.6 Hz), 3.73 (dd, 1H, J = 9.9, 3.0 Hz), 3.68–3.62 (m, 3H), 3.43 (t, 1H, J = 9.5 Hz), 3.40–3.38 (m, 5H), 3.36–3.33 (m, 1H), 3.32 (s, 3H), 3.30 (t, 1H, J = 9.0 Hz), 3.21–3.17 (m, 5H), 3.12 (ddd, 1H, J = 10.5, 9.1, 5.3 Hz), 3.00 (dd, 1H, J = 8.9, 8.1 Hz), 2.86 (t, 1H, J = 11.1 Hz), 2.05 (s, 3H), 2.02 (s, 3H), 1.19 (d, 3H, J = 6.8 Hz), 1.10 (d, 3H, J = 6.2 Hz), 0.97 (s, 9H), 0.92 (s, 9H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 170.2, 169.4, 139.5, 139.3, 139.1 (2 × C), 138.5, 138.2, 138.1, 137.8, 128.5, 128.4 (3 × C), 128.2 (3 × C), 128.1, 128.0, 127.8 (3 × C), 127.7 (2 × C), 127.3 (2 × C), 127.2, 126.8 (2 × C), 126.1, 103.1 (Xyl'-C-1), 101.5 (Xyl-C-1), 97.3 (Gal-C-1, $^1J_{C\text{-}H}$ = 170.6 Hz), 96.0 (Fuc-C-1), 93.0 (Rha-C-1), 90.1 (Glc-C-1), 83.8. 82.4, 81.9, 80.7, 80.5, 77.2 (2 × C), 77.1, 76.9, 75.9, 75.7, 75.2 (2 ×

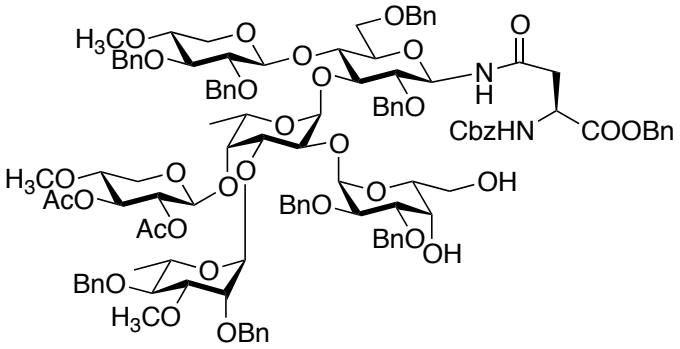
C), 75.1, 75.0, 74.0, 73.9, 73.5, 73.0, 72.8, 72.5, 72.4, 71.2, 71.1, 70.6 (2 × C), 70.0, 68.3, 67.7, 67.4, 66.9, 65.2, 63.3, 62.8, 58.7, 58.6, 57.5, 27.7, 27.4, 23.2, 20.9, 20.8, 20.7, 18.0, 16.8; HRMS (ESI) Calc. for $[M + NH_4]^+$ $C_{105}H_{135}N_4O_{28}Si$: 1927.9027; Found 1927.8990.



N^2-Benzyloxycarbonyl-N^4-{2,3-di-*O*-acetyl-4-*O*-methyl-β-D-xylopyranosyl-(1→4)-[2,4-di-*O*-benzyl-3-*O*-methyl-α-L-rhamnopyranosyl-(1→3)]- }-[2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranosyl-(1→2)]-α-L-fucopyranosyl-(1→3)-[2,3-di-*O*-benzyl-4-*O*-methyl-β-D-xylopyranosyl-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranosyl}-L-asparagine benzyl ester (2.76): To a stirred solution of **2.74** (13.5 mg, 7.06 μmol) in dry THF (1.5 mL) was added triethylamine (1.1 μL, 7.8 μmol) and 10% Pd/C (5.0 mg) successively at room temperature. After stirring for 45 min under an H_2 atmosphere (1 atm), the reaction mixture was filtered through Celite. The filtrate containing the glycosylamine was concentrated and used directly in the next step. To a stirred solution of *N*-benzyloxycarbonyl-L-aspartic acid 1-benzyl ester **4** (5.1 mg, 14 μmol) in dry THF (1.0 mL) was added HATU (6.7 mg, 18 μmol) successively at 0 °C. The reaction mixture was stirred for 1 h at 0 °C, then a solution of the glycosylamine in dry THF (1.0 mL) was added, followed by triethylamine (2.0 μL). The reaction mixture was stirred for 2 h at room

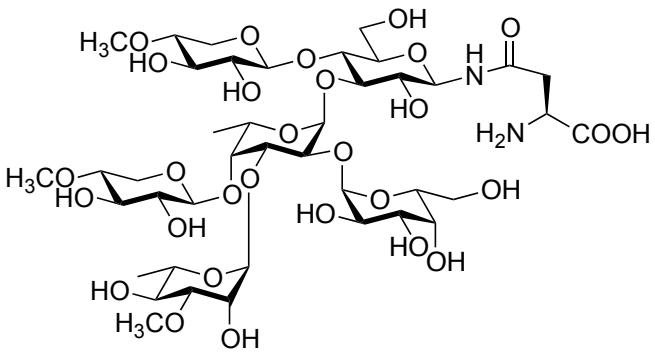
temperature under an Ar atmosphere, then diluted with CH_2Cl_2 (15 mL) and washed with brine. The aqueous layer was extracted with CH_2Cl_2 (10 mL × 3), and the combined organic extracts were dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (2:1 hexane–EtOAc) to afford **2.76** (12.7 mg, 81%) as a syrup. R_f 0.56 (3:2 hexane–EtOAc); $[\alpha]_D$ –17.9 (*c* 0.56, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.34–7.12 (m, 50H), 5.90 (d, 1H, *J* = 8.7 Hz), 5.58 (d, 1H, *J* = 8.4 Hz), 5.41 (d, 1H, *J* = 3.4 Hz, Gal-H-1), 5.38 (d, 1H, *J* = 3.3 Hz, Fuc-H-1), 5.08–4.96 (m, 8H, Glc-H-1, Rha-H-1), 4.85 (d, 1H, *J* = 11.2 Hz), 4.79–4.74 (m, 3H), 4.72–4.64 (m, 4H), 4.61–4.58 (m, 4H), 4.54–4.50 (m, 3H), 4.47 (d, 1H, *J* = 6.8 Hz, Xyl-H-1), 4.44 (d, 1H, *J* = 11.4 Hz), 4.38 (dd, 1H, *J* = 11.3, 5.3 Hz), 4.33–4.31 (m, 2H), 4.28 (d, 1H, *J* = 7.9 Hz, Xyl'-H-1), 4.23–4.18 (m, 3H), 4.13 (dd, 1H, *J* = 10.3, 3.3 Hz), 4.02 (t, 1H, *J* = 8.7 Hz), 3.98 (t, 1H, *J* = 9.3 Hz), 3.93–3.88 (m, 5H), 3.83 (dd, 1H, *J* = 10.8, 2.0 Hz), 3.80 (d, 1H, *J* = 2.2 Hz), 3.66 (dd, 1H, *J* = 9.9, 3.0 Hz), 3.61 (dd, 1H, *J* = 9.4, 3.0 Hz), 3.53 (dd, 1H, *J* = 10.6, 1.1 Hz), 3.43 (t, 1H, *J* = 9.5 Hz), 3.40–3.34 (m, 6H), 3.33 (s, 3H), 3.29–3.28 (m, 4H), 3.22–3.19 (m, 2H), 3.11 (td, 1H, *J* = 9.7, 5.3 Hz), 2.98 (t, 1H, *J* = 8.5 Hz), 2.81 (t, 1H, *J* = 11.0 Hz), 2.68 (dd, 1H, *J* = 16.5, 4.0 Hz), 2.46 (dd, 1H, *J* = 16.4, 3.8 Hz), 2.05 (s, 3H), 2.02 (s, 3H), 1.19 (d, 3H, *J* = 6.8 Hz), 1.08 (d, 3H, *J* = 6.1 Hz), 0.98 (s, 9H), 0.94 (s, 9H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 170.7, 170.2 (2 × C), 169.4, 156.1, 139.4, 139.3, 139.1, 139.0, 138.5, 138.1, 137.6, 137.5, 136.2, 135.4, 128.7, 128.5 (3 × C), 128.4, 128.3 (2 × C), 128.2 (2 × C), 128.1 (3 × C), 128.0 (2 × C), 127.9, 127.8, 127.7 (2 × C), 127.3, 127.2, 127.0 (2 × C), 126.8, 103.0 (Xyl'-C-1), 101.5 (Xyl-C-1), 96.6 (Gal-C-1), 96.4 (Fuc-C-1), 93.2 (Rha-C-1),

83.7, 82.3, 81.9, 80.7, 80.5 (2 × C), 78.3 (Glc-C-1, $^{1}J_{C\text{-}H}$ = 156.7 Hz), 77.6, 77.2, 76.9, 76.6, 75.8, 75.5, 75.2 (2 × C), 75.1, 74.8, 74.2, 74.1, 73.5, 72.8,72.7, 72.4, 71.6, 71.3, 71.2, 70.4 (2 × C), 69.9, 68.3, 67.7, 67.5, 67.3, 67.0, 65.3, 63.2, 62.7, 58.7, 58.6, 57.5, 50.5, 37.7, 27.7, 27.4, 23.3, 20.9 (2 × C), 20.7, 18.0, 16.7; HRMS (ESI) Calc. for $[M + 2Na]^{+2}$ $C_{124}H_{150}N_2Na_2O_{33}Si$: 1134.4837; Found 1134.4870.



***N*²-Benzyloxycarbonyl-*N*⁴-{2,3-di-*O*-acetyl-4-*O*-methyl-β-D-xylopyranosyl-(1→4)-[2,4-di-*O*-benzyl-3-*O*-methyl-α-L-rhamnopyranosyl-(1→3)]- }-[2,3-di-*O*-benzyl-α-D-galactopyranosyl-(1→2)]-α-L-fucopyranosyl-(1→3)-[2,3-di-*O*-benzyl-4-*O*-methyl-β-D-xylopyranosyl-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranosyl}-L-asparagine benzyl ester (2.77):** To a stirred solution of **2.76** (7.9 mg, 3.6 μmol) in THF–pyridine (1.5 mL, 1:1) was added HF·pyridine (0.15 mL, pyridine ~30%, hydrogen fluoride ~70%) at 0 °C under an Ar atmosphere. The reaction mixture was stirred for 1.5 h at 0 °C, and then poured into saturated $NaHCO_3$ (aq.). The aqueous layer was extracted with EtOAc (10 mL × 3), dried over Na_2SO_4, filtered and concentrated. The crude residue was purified by flash chromatography (2:1 hexane–EtOAc) to afford **2.77** (6.4 mg, 86%) as a syrup. R_f 0.34 (1:2 hexane–EtOAc); $[\alpha]_D$ –33.0 (*c* 0.30, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.36–7.26 (m,

29H), 7.24–7.18 (m, 19H), 7.00–6.99 (m, 2H), 6.21 (d, 1H, *J* = 8.9 Hz), 5.98 (d, 1H, *J* = 8.8 Hz), 5.47 (d, 1H, *J* = 3.2 Hz, Fuc-H-1), 5.14 (t, 1H, *J* = 9.1 Hz, Glc-H-1), 5.11–5.03 (m, 5H, Gal-H-1), 5.02–4.99 (m, 2H, Rha-H-1), 4.96 (dd, 1H, *J* = 9.3, 7.2 Hz), 4.82–4.73 (m, 5H), 4.72 (d, 1H, *J* = 11.1 Hz), 4.68 (d, 1H, *J* = 11.1 Hz), 4.62–4.51 (m, 9H), 4.47 (d, 1H, *J* = 7.2 Hz, Xyl-H-1), 4.41 (dd, 1H, *J* = 11.5, 5.2 Hz), 4.38 (d, 1H, *J* = 11.5 Hz), 4.34 (d, 1H, *J* = 11.9 Hz), 4.30 (d, 1H, *J* = 7.9 Hz, Xyl'-H-1), 4.14–4.10 (m, 2H), 4.07–4.02 (m, 2H), 4.00 (t,1H, *J* = 9.1 Hz), 3.89–3.86 (m, 2H), 3.83–3.74 (m, 6H), 3.71–3.69 (m, 2H), 3.65 (t, *J* = 8.7 Hz, 2H), 3.62–3.60 (m, 1H), 3.56 (dd, 1H, *J* = 10.7, 1.6 Hz), 3.46 (t, 1H, *J* = 9.4 Hz), 3.40–3.37 (m, 4H), 3.36–3.32 (m, 4H), 3.23 (t, 1H, *J* = 9.0 Hz), 3.18 (dd, 1H, *J* = 11.9, 9.7 Hz), 3.15–3.12 (m, 4H), 3.01 (dd, 1H, *J* = 8.9, 8.1 Hz), 2.83 (t, 1H, *J* = 11.0 Hz), 2.77 (dd, 1H, *J* = 16.5, 4.5 Hz), 2.54 (dd, 1H, *J* = 16.5, 4.1 Hz), 2.04 (s, 3H), 2.02 (s, 3H), 1.24 (d, 3H, *J* = 6.1 Hz), 1.20 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 170.8, 170.3, 170.12, 170.1, 156.1, 139.2, 139.0, 138.9, 138.5, 138.3, 138.11, 137.6, 137.4, 136.3, 135.4, 128.6, 128.5 (3 × C), 128.4 (2 × C), 128.3, 128.2 (2 × C), 128.1 (3 × C), 128.0, 127.9, 127.8 (2 × C), 127.7, 127.6, 127.5, 127.4, 127.2, 126.8, 102.9 (Xyl'-C-1), 101.5 (Xyl-C-1), 98.0 (Gal-C-1), 95.9 (Fuc-C-1), 93.3 (Rha-C-1), 83.7, 82.3, 81.7, 80.8, 80.5, 79.7, 77.7 (Glc-C-1), 77.6, 77.2, 76.3, 75.9, 75.8, 75.6, 75.4, 75.2, 74.8, 74.2, 74.1, 73.4, 73.3, 72.7, 72.4, 72.2, 71.5, 71.4, 70.1, 69.8, 68.0, 67.9, 67.6, 67.3, 67.0, 65.4, 63.2, 63.1, 62.4, 58.7 (2 × C), 57.2, 50.6, 37.7, 20.9, 20.8, 17.9, 16.8; HRMS (ESI) Calc. for $[M + 2Na]^{+2}$ $C_{116}H_{134}N_2Na_2O_{33}$: 1064.4327; Found 1064.4322.



N^4-{4-*O*-Methyl-β-D-xylopyranosyl-(1→4)-[3-*O*-methyl-α-L-rhamnopyranosyl-(1→3)]-[α-D-galactopyranosyl-(1→2)]-α-L-fucopyranosyl-(1→3)-[4-*O*-methyl-β-D-xylopyranosyl-(1→4)]-β-D-glucopyranosyl}-L-asparagine (2.1): To a stirred solution of **2.77** (7.7 mg, 3.7 μmol) in THF–H_2O (2.0 mL, 1:1) was added 20% palladium hydroxide on carbon (3.5 mg). After stirring overnight under an H_2 atmosphere, the reaction mixture was filtered through Celite and the filtrate was concentrated. The residue was then dissolved in H_2O (2.0 mL) and 50 mM NaOH (0.2 mL) was added. The reaction mixture was stirred overnight at room temperature, then neutralized by addition of Amberlite® IR-120 (H^+) cation exchange resin and filtered. After concentration of the filtrate, the residue was dissolved in water and then lyophilized to afford **2.1** (3.9 mg, quant.) as a white solid. R_f 0.42 (3:3:3:2 EtOAc–CH_3OH–AcOH–H_2O); $[\alpha]_D$ –104 (*c* 0.10, H_2O); ^{1}H NMR (700 MHz; D_2O): δ 5.70 (d, 1H, J = 3.8 Hz, Fuc-H-1), 5.27 (d, 1H, J = 3.4 Hz, Gal-H-1), 5.12 (s, 1H, Rha-H-1), 5.02 (d, 1H, J = 9.2 Hz, Glc-H-1), 4.74 (m, 1H), 4.45–4.39 (m, 4H, Xyl-H-1, Xyl'-H-1), 4.29 (d, 1H, J = 2.0 Hz), 4.24–4.21 (m, 2H), 4.17-4.11 (m, 2H), 4.06–4.05 (m, 2H), 4.00–3.97 (m, 2H), 3.93 (d, 1H, J = 11.9 Hz), 3.88–3.63 (m, 8H), 3.52–3.48 (m, 9H), 3.46–3.41 (m, 5H), 3.38 (dd, 1H, J = 9.8, 2.9 Hz), 3.26–3.14 (m, 4H), 3.01 (dd, 1H, *J*

= 17.3, 4.1 Hz), 2.96 (dd, 1H, *J* = 17.2, 7.1 Hz), 1.34 (d, 3H, *J* = 6.8 Hz), 1.32 (d, 3H, *J* = 6.1 Hz); ^{13}C NMR (125 MHz; D_2O): δ 173.9, 105.3 (Xyl-C-1), 103.5 (Xyl'-C-1), 99.3 (Gal-C-1), 98.2 (Fuc-C-1), 96.6 (Rha-C-1), 81.0, 80.3 (Glc-C-1), 80.1, 79.7, 77.8, 76.4, 75.9, 75.6, 75.5, 74.9, 74.7, 74.4 (2 × C), 72.9, 72.8, 72.0, 70.6, 70.2, 69.8, 69.3, 69.1, 67.4, 66.9, 63.7 (2 × C), 62.4, 60.3, 59.4, 59.2, 57.0, 52.0, 36.1, 17.8, 15.9; HRMS (ESI) Calc. for $[M - H]^-$ $C_{41}H_{69}N_2O_{29}$: 1053.3991; Found 1053.3995.

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Chapter 3

Synthesis of Highly Branched Chlorella Virus *N*-Glycans using a "Counter-Clockwise" Assembly Approach

3.1 Background

Motivated by the success I had in the synthesis of highly branched chlorovirus *N*-glycans described in Chapter 2, I investigated the accessibility of more complex targets using the developed "counter-clockwise" assembly approach. Reports on the structures of chlorovirus *N*-glycans[1–3] indicate that: 1) the size of the carbohydrate residue on the C-4 hydroxyl group of fucose varies from a monosaccharide to a tetrasaccharide; 2) with only two exceptions, the fucose C-3 hydroxyl group is glycosylated with a single rhamnose residue (D- or L-); 3) the C-2 hydroxyl group of the fucose is always glycosylated with a galactose residue.

The family of *N*-glycans isolated from *Paramecium bursaria* chlorella virus 1 (PBCV-1) is an exception with regard to the substitution on the C-3 hydroxyl group. These glycans are not functionalized with a monosaccharide at this position but rather with a larger oligosaccharide motif. Their structures were first elucidated by De Castro and co-workers in 2013.[4] They consist of 8–10 monosaccharide residues and exist as a total of four glycoforms. Among the four PBCV-1 *N*-glycans, the most abundant *N*-glycan **3.1** contains nine sugar residues as shown in Figure 3-1. In contrast with the ATCV-1 *N*-glycan (Chapter 2), these PBCV-1 glycans contain a disaccharide on the C-3 hydroxyl group of the fucose (shown in red) and a trisaccharide residue on the C-4 hydroxyl group of the fucose (shown in blue). The other exception to the general rule of O-3 fucose substitution is the *N*-glycan from *Paramecium bursaria* chlorella virus NY-2A$_1$ (**3.2**). Like the PBCV-1 structures, this glycan is also a nonasaccharide. The structure contains a tetrasaccharide residue (shown in

red) on the O-3 position of the fucose and a single xylose residue fucose O-4 (shown in blue).

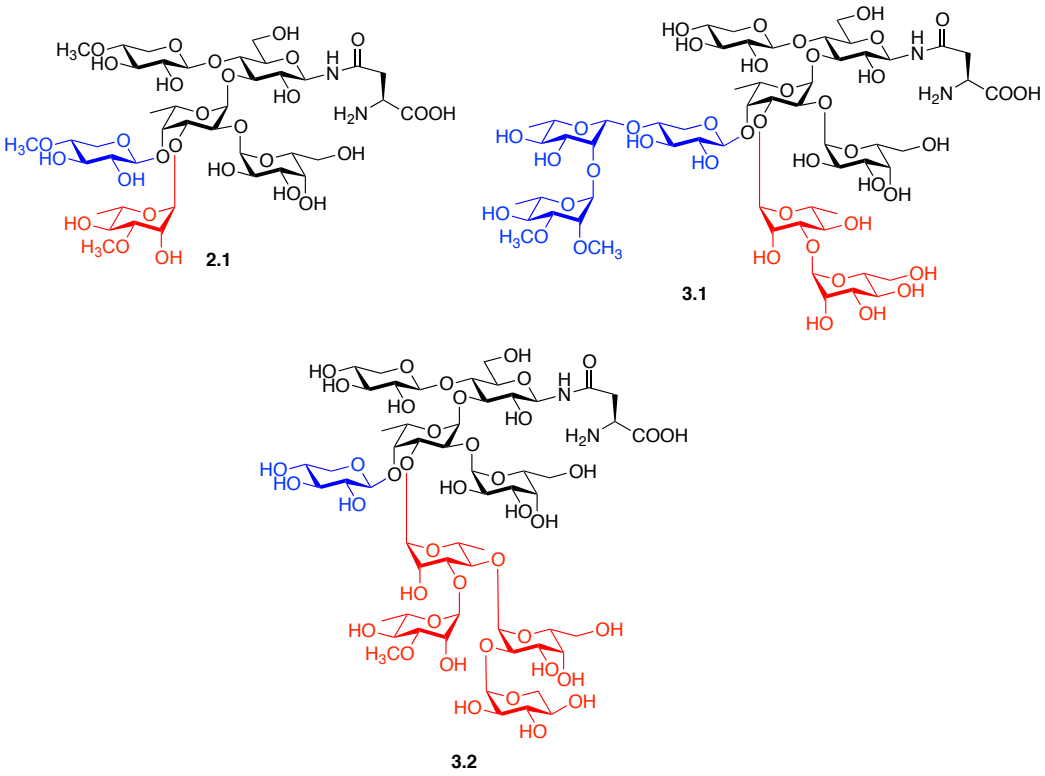


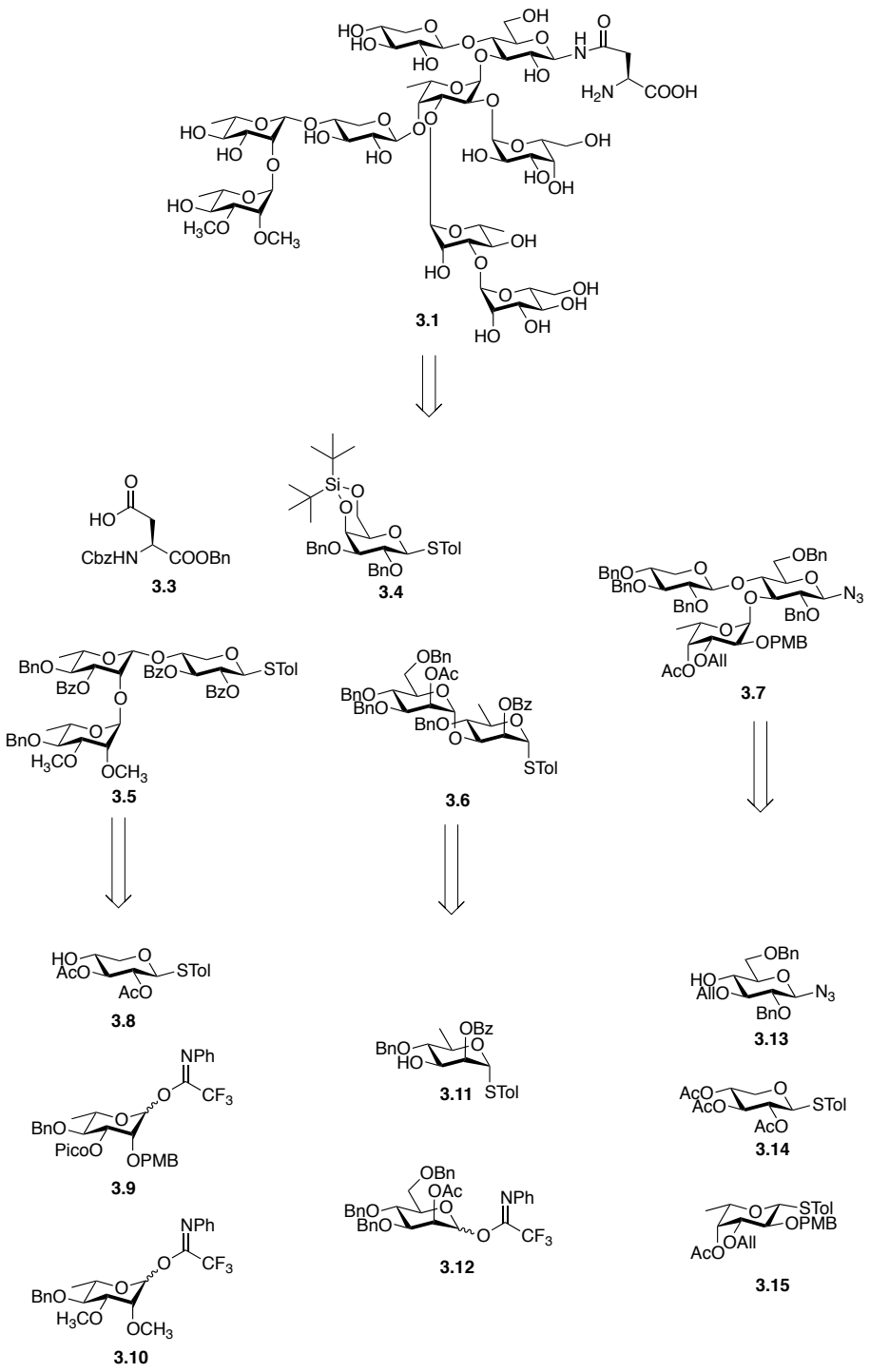
Figure 3-1: Structure of the major *N*-glycan **3.1** from chlorovirus PBCV-1 and the *N*-glycan **3.2** from chlorovirus NY-2A$_1$.

From a synthetic point of view, **3.1** and **3.2** are the most complex chlorovirus *N*-glycans reported to date.[1–3] Thus, if these structures could be obtained using the "counter-clockwise" assembly strategy, it would suggest that this approach could be feasible to access all types of these molecules. This chapter describes the extension of my approach, using *N*-glycans **3.1** and **3.2** as the targets.

3.2 Results and discussions

3.2.1 Synthesis of the nonasaccharide *N*-linked glycan from chlorella virus PBCV-1

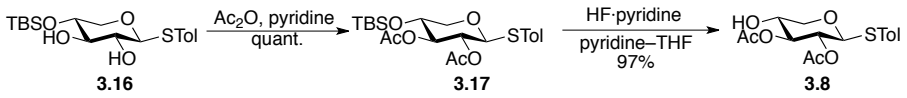
Compared to the ATCV-1 *N*-glycan, nonasaccharide **3.1** has some unique structural features including 1) a β-rhamnosidic linkage and 2) two rhamnose residues with opposite configurations (D- and L-). After the successful synthesis of **2.1**, I hypothesized that nonasaccharide **3.1** could also be achieved from a "counter-clockwise" introduction of the carbohydrate residues **3.4–3.6** onto the trisaccharide **3.7** (Scheme 3-1). The trisaccharide donor **3.5** could be prepared from three different monosaccharides (**3.8**–**3.10**) and the disaccharide donor could be derived from the glycosylation of **3.11** with **3.12**. In addition, the trisaccharide acceptor could be produced from monosaccharides **3.13**–**3.15**, in a similar way as described for **2.62** in Chapter 2. In total, nine different monosaccharide building blocks (**3.4**, **3.8**–**3.15**) needed to be prepared and three of them (**3.4**, **3.13** and **3.15**) were the same as used for ATCV-1 (Chapter 2; **3.4** = **2.10**; **3.13** = **2.12** and **3.15** = **2.63**).



Scheme 3-1: Retrosynthetic analysis of nonasaccharide **3.1**.

3.2.1.1 Synthesis of building blocks 3.8–3.15

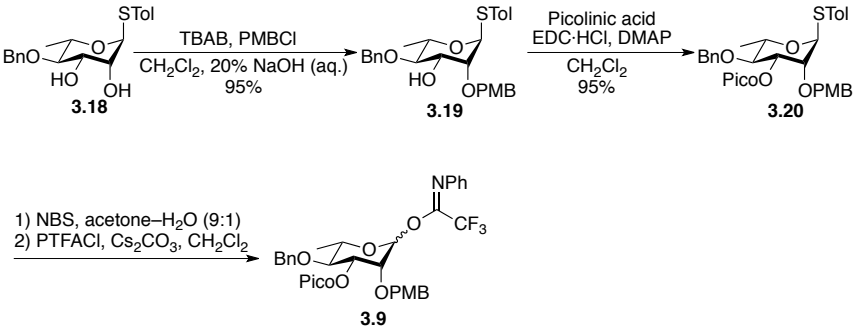
The synthesis of **3.8** started from thioglycoside **3.16**, which could be prepared from D-xylose in four steps as previously reported.[5] The acetylation of diol **3.16** (Scheme 3-2) was performed to provide **3.17** in quantitative yield. Then the *tert*-butyldimethylsilyl group was removed upon treatment with HF·pyridine at 0 °C to furnish the desired xylose acceptor **3.8** in 97% yield. As described in Chapter 2, the acetyl group was proposed to induce β-selectivity through neighbouring group participation during the glycosylation.



Scheme 3-2: Synthesis of xylose acceptor **3.8**.

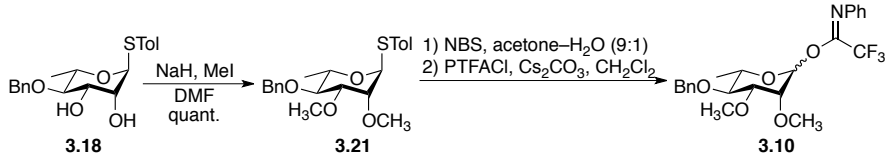
The synthesis of rhamnose donor **3.9** (Scheme 3-3) began from compound **3.18**, which was prepared from L-rhamnose in six steps as reported.[6] Regioselective protection of **3.18** via phase-transfer catalyzed reaction conditions was used. The C-2 hydroxyl group is more acidic than the C-3 hydroxyl group.[7–9] Therefore, treatment with 4-methoxybenzyl chloride and tetra-*n*-butylammonium bromide in the presence of 20% sodium hydroxide solution, allowed the C-2 hydroxyl group on **3.18** to be protected selectively affording **3.19** in 95% yield. The C-3 hydroxyl group was then protected as a picoloyl ester by treatment with 2-picolinic acid in the presence of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride and 4-(dimethylamino)pyridine to furnish thioglycoside **3.20** in 95% yield. The picoloyl group was introduced to help promote the β-selectivity during the

glycosylation by Hydrogen bond mediated Aglycone Delivery (HAD).[10–12] Finally, **3.20** was hydrolyzed with *N*-bromosuccinimide and water to generate the hemiacetal, which was then converted into its *N*-phenyl-trifluoroacetimidate derivative **3.9**, which, like all glycosyl imidates described in this thesis, were used immediately in the glycosylation and not characterized.



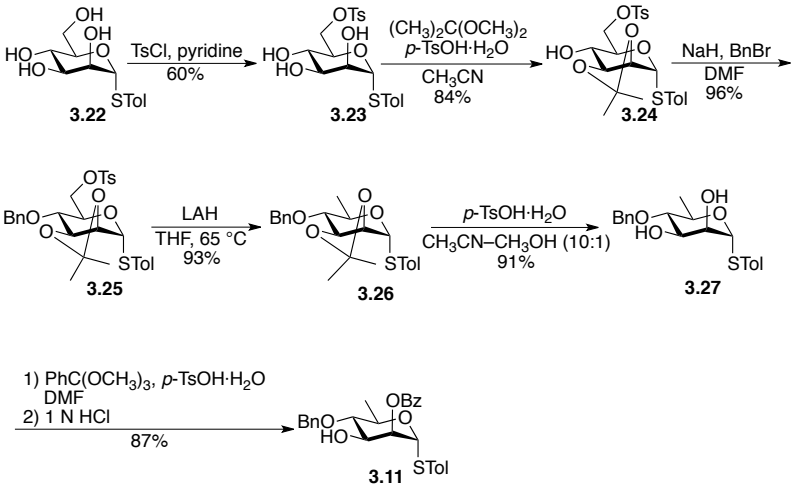
Scheme 3-3: Synthesis of L-rhamnose donor **3.9**.

The synthesis of **3.10** could also be completed from diol **3.18** (Scheme 3-4). Methylation of **3.18** in the presence of sodium hydride and methyl iodide yielded **3.21** quantitatively. This thioglycoside was then transformed into its corresponding *N*-phenyl-trifluoroacetimidate derivative **3.10** as described for **3.9**.



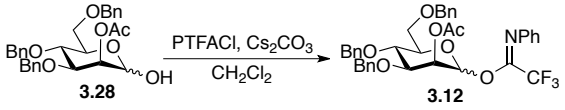
Scheme 3-4: Synthesis of L-rhamnose donor **3.10**.

The preparation of D-rhamnose acceptor **3.11** started from thiomannoside derivative **3.22** (Scheme 3-5), which was prepared from D-mannose in three steps as reported.[13] Regioselective tosylation of the primary hydroxyl group in **3.22** afforded the 6-*O*-tosylated mannoside derivative **3.23** in 60% yield. The C-2 and C-3 hydroxyl groups of **3.23** were then protected with an isopropylidene ketal using 2,2-dimethoxypropane in the presence of *p*-toluenesulfonic acid to afford **3.24** in 84% yield. The C-4 hydroxyl group was next benzylated to furnish compound **3.25** in 96% yield. Subsequent reduction of **3.25** with lithium aluminum hydride at 65 °C provided D-rhamnoside **3.26** in 93% yield. The ketal was then removed with *p*-toluenesulfonic acid to give diol **3.27** in 91% yield. Reaction of diol **3.27** with trimethyl orthobenzoate and acid allowed for the efficient formation of 2,3-*O*-orthoester intermediate, and subsequent treatment with 1 N hydrogen chloride resulted in the regioselective opening of the orthoester to afford the D-rhamnose acceptor **3.11** in 87% yield. The benzoyl group was chosen for the protection of the C-2 hydroxyl group, as compared to an acetyl group, because benzoyl groups are less prone to orthoester formation during the construction of glycosidic bonds. More practically, compounds protected by benzoyl groups are typically less polar than those with acetyl groups, and this could potentially help in purifications especially as the size of the molecule gets larger.



Scheme 3-5: Synthesis of D-rhamnose acceptor **3.11**.

The mannose donor **3.12** was derived from **3.28** (Scheme 3-6), which was synthesized from D-mannose in six steps as reported.[14] The galactose donor **3.4** and xylose donor **3.14** were prepared based on the protocols previously reported.[15,16] The glucose acceptor **3.13** and fucose donor **3.15** were generated using the methods described in Chapter 2.

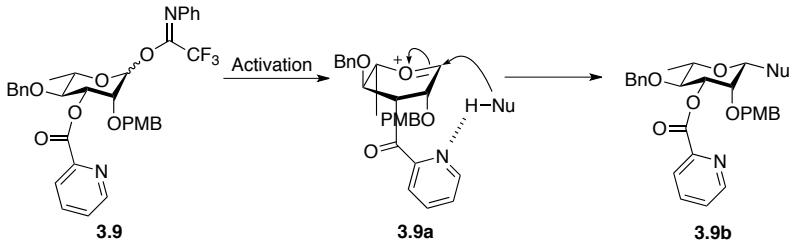


Scheme 3-6: Synthesis of mannose donor **3.12**.

3.2.1.2 Synthesis of intermediates 3.5–3.7

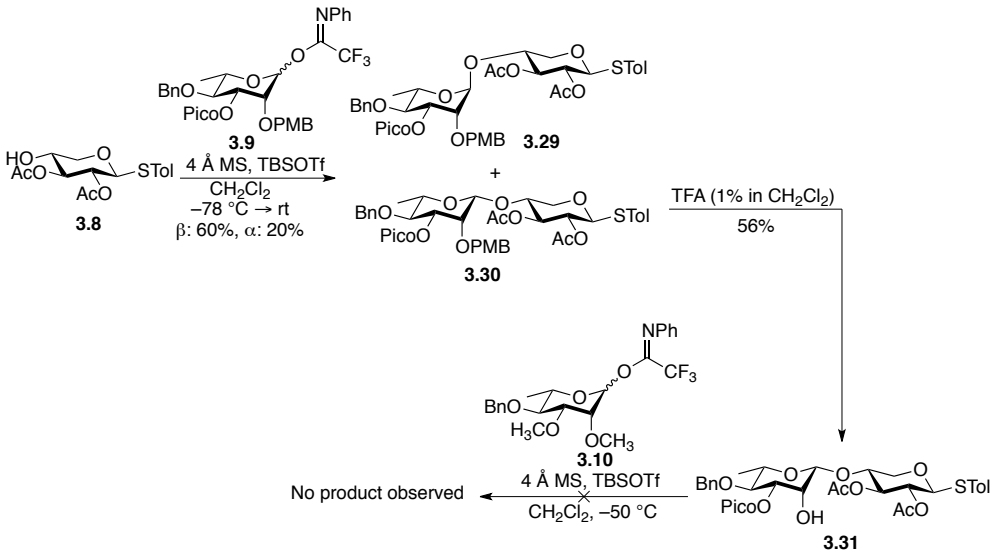
With all the necessary building blocks **3.8**–**3.10** constructed, the synthesis of trisaccharide donor **3.5** was first investigated. The attempted synthesis of **3.5** started with the construction of the challenging β-rhamnosidic linkage.[17–20] It was proposed that the

remote C-3 picoloyl group could promote the formation of this linkage with increased stereoselectivity through HAD as shown in Scheme 3-7.[10–12]



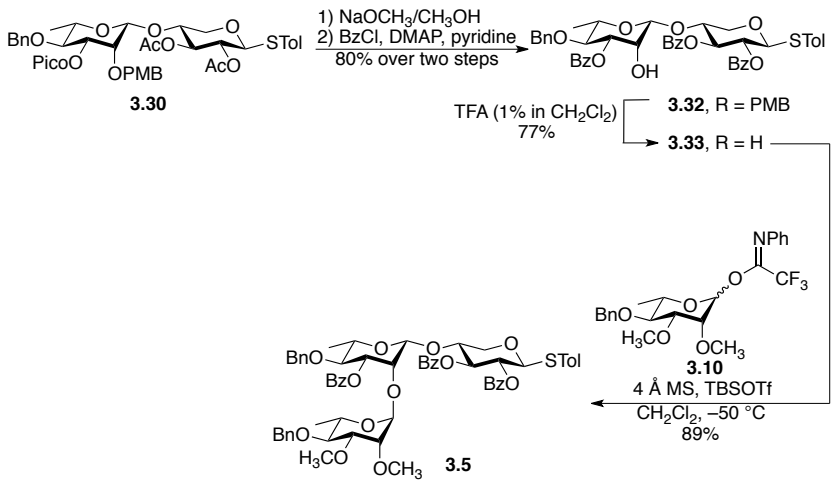
Scheme 3-7: HAD method for synthesizing β-rhamnosides.

To explore this strategy, a TBSOTf-catalyzed glycosylation of glycosyl acceptor **3.8** with glycosyl donor **3.9** was performed (Scheme 3-8). This reaction afforded the α-glycoside **3.29** in 20% yield and the desired β-glycoside **3.30** in 60% yield. The stereoselectivity was confirmed from the ^{1}H-coupled HSQC spectrum; the $^{1}J_{C\text{-}H}$ for the α-glycoside was 172.1 Hz and that for the β-glycoside was 156.1 Hz. Subsequent removal of the 4-methoxybenzyl group in **3.30** was implemented upon treatment with 1% TFA in dichloromethane, giving **3.31** in 56% yield. Some migration of the picoloyl group from rhamnose O-3 to rhamnose O-2 was observed during the purification process, resulting in a low yield of the target compound. With **3.31** in hand, its reaction with imidate **3.10** was investigated but, unfortunately, no desired product was observed and the acceptor was recovered.



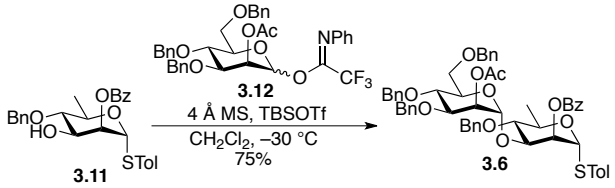
Scheme 3-8: Attempted the synthesis of trisaccharide donor **3.5**.

I hypothesized that the picoloyl group on **3.31** was responsible for preventing the glycosylation with **3.10**. According to the literature,[11,12] the picoloyl group is commonly replaced with other protecting groups immediately after the HAD glycosylation reaction, presumably as the basic pyridine nitrogen interferes with acid mediated-reactions. Thus, all the ester groups in **3.30** were replaced by benzoyl groups to afford **3.32** in 80% yield over two steps as shown in Scheme 3-9. Subsequent removal of the 4-methoxybenzyl group gave the disaccharide acceptor **3.33** in 77% yield. No migration of benzoyl group was observed in this case. Then, the coupling of disaccharide **3.33** to the rhamnose donor **3.10,** mediated by NIS and AgOTf, afforded the desired trisaccharide donor **3.5** in 89% yield with excellent α-selectivity. The stereochemistry was confirmed by the coupling constant between Rha-H-1 and Rha-C-1 ($^1J_{C\text{-}H}$ = 170.6 Hz) in the ^{1}H-coupled HSQC spectrum



Scheme 3-9: Synthesis of trisaccharide donor **3.5** after replacement of the picoloyl group.

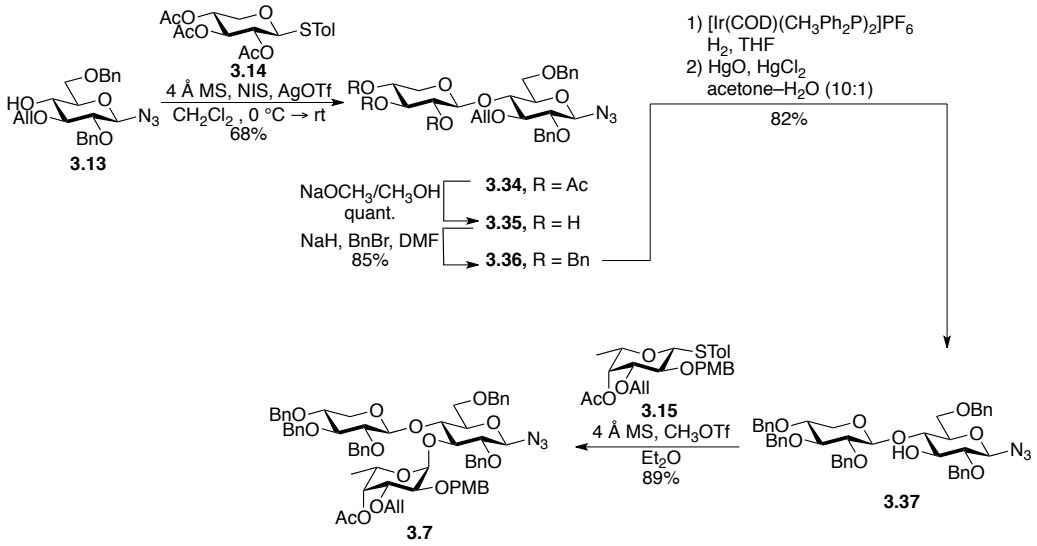
With **3.11** and **3.12** in hand, the synthesis of **3.6** (Scheme 3-10) was achieved by a straightforward glycosylation of **3.11** with **3.12** using TBSOTf at –30 °C to afford the desired disaccharide donor **3.6** in 75% yield. The assessment of α-selectivity was supported by the coupling constant of Man-C-1 to Man-H-1 ($^{1}J_{C\text{-}H}$ = 174.4 Hz) in the ^{1}H-coupled HSQC spectrum.



Scheme 3-10: Synthesis of disaccharide donor **3.6**.

After trisaccharide **3.5** and disaccharide **3.6** were obtained, the synthesis of **3.7** (Scheme 3-11) was done according to the route discussed in the Chapter 2. An NIS/AgOTf-

promoted glycosylation of **3.13** with **3.14** was carried out to achieve the desired disaccharide **3.34** in 68% yield. Subsequent Zemplén deacetylation and benzylation were performed successively, followed by removal of the allyl group to generate the desired disaccharide acceptor **3.37** in 70% yield over three steps. Then, the trisaccharide **3.7** was obtained by a CH_3OTf-catalyzed glycosylation with **3.15** in 89% yield with exclusive α-selectivity.[21,22]

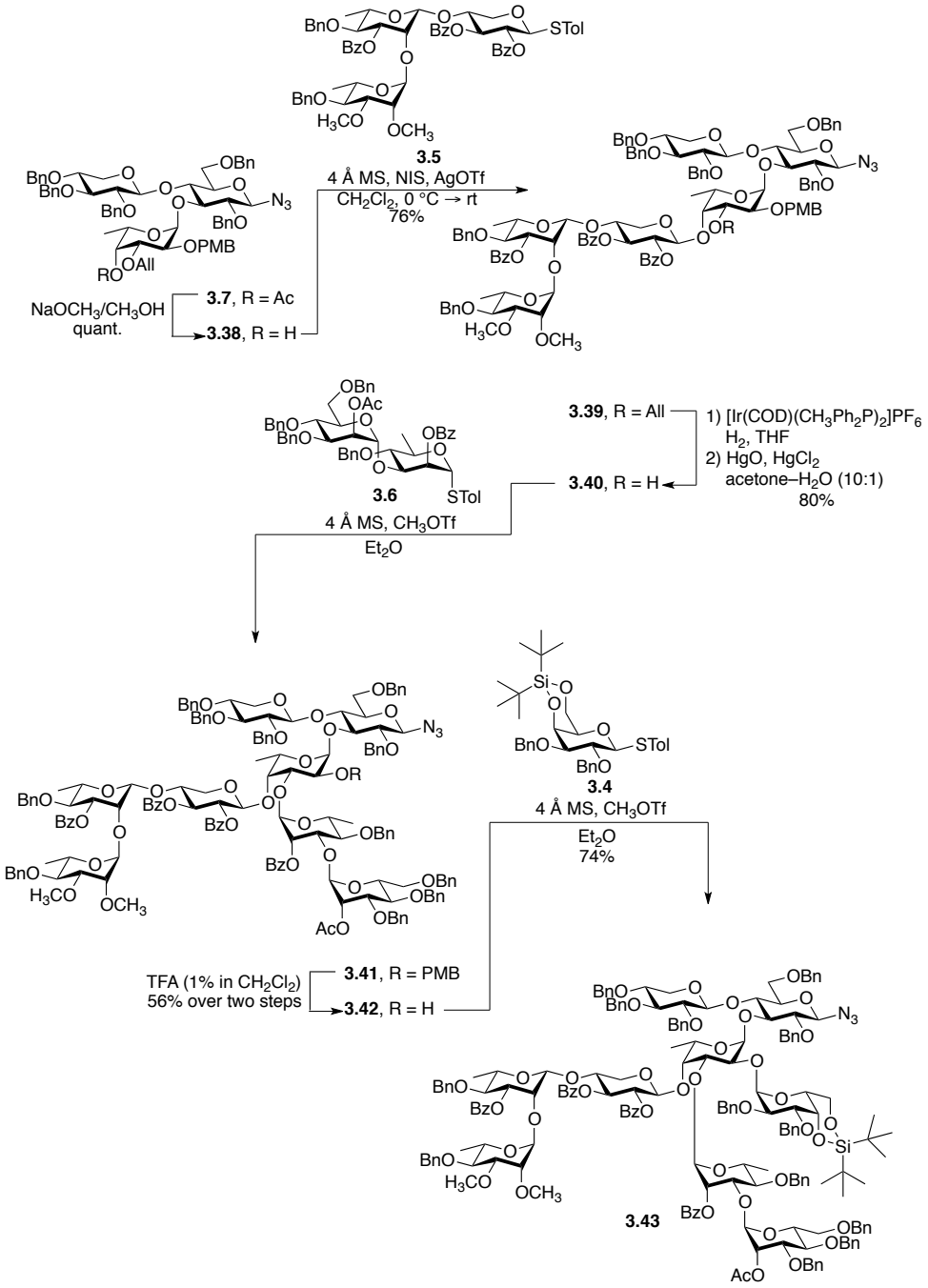


Scheme 3-11: Synthesis of trisaccharide **3.7**.

3.2.1.3 Assembly of nonasaccharide through a "counter-clockwise" sequence

Having a robust route to **3.5**, **3.6** and **3.7**, I turned my attention to investigate whether **3.5** and **3.6** were appropriate substrates in the "counter-clockwise" assembly sequence (Scheme 3-12). Thus, the acetyl group in **3.7** was first hydrolyzed under Zemplén

conditions to afford **3.38** in quantitative yield. The resulting alcohol **3.38** was then glycosylated using an NIS/AgOTf-promoted reaction with trisaccharide donor **3.5** to



Scheme 3-12: Synthesis of nonsaccharide **3.43** through a "counter-clockwise" assembly strategy.

produce hexasaccharide **3.39** in 76% yield. A single glycoside product was isolated with a Xyl-H-1 to Xyl-H-2 coupling constant ($^3J_{H1\text{-}H2}$) of 4.7 Hz. This value is intermediate between what would be expected for either a β-glycoside (~7–8 Hz) or an α-glycoside (~3–4 Hz) and suggests that the xylose residue in **3.39** does not adopt a chair conformation. This finding concerned me, but I nevertheless proceeded forward hoping that I could later obtain data that was more conclusive about the anomeric stereochemistry of this xylose residue.

After successfully obtaining hexasaccharide **3.39**, the allyl ether was first converted into the corresponding vinyl ether upon treatment with $[Ir(COD)(CH_3Ph_2P)_2]PF6$. Subsequent hydrolytic cleavage using HgO and $HgCl_2$ in wet acetone generated the hexasaccharide acceptor **3.40** in 80% yield. The β-selectivity of the previous glycosylation was confirmed at this stage by the Xyl-H-1 to Xyl-H-2 coupling constant ($^3J_{H1\text{-}H2}$), which was 7.4 Hz. Thus, it appears that the allyl group in **3.39** induces a conformational change in the adjacent xylose residue; upon removal of this group, a normal chair conformation is observed.

Next, hexasaccharide acceptor **3.40** was glycosylated with the disaccharide donor **3.6** using NIS/AgOTf-promoted reaction conditions as described in Chapter 2. However, the reaction yield was extremely low, the donor was completely decomposed in 1 h, and 90% of acceptor was recovered. I postulated that this was due to: 1) steric congestion around the C-3 hydroxyl group of **3.40**, which resulted in its low accessibility and low reactivity; 2) the size of donor might also affect its accessibility during the glycosylation reaction. I

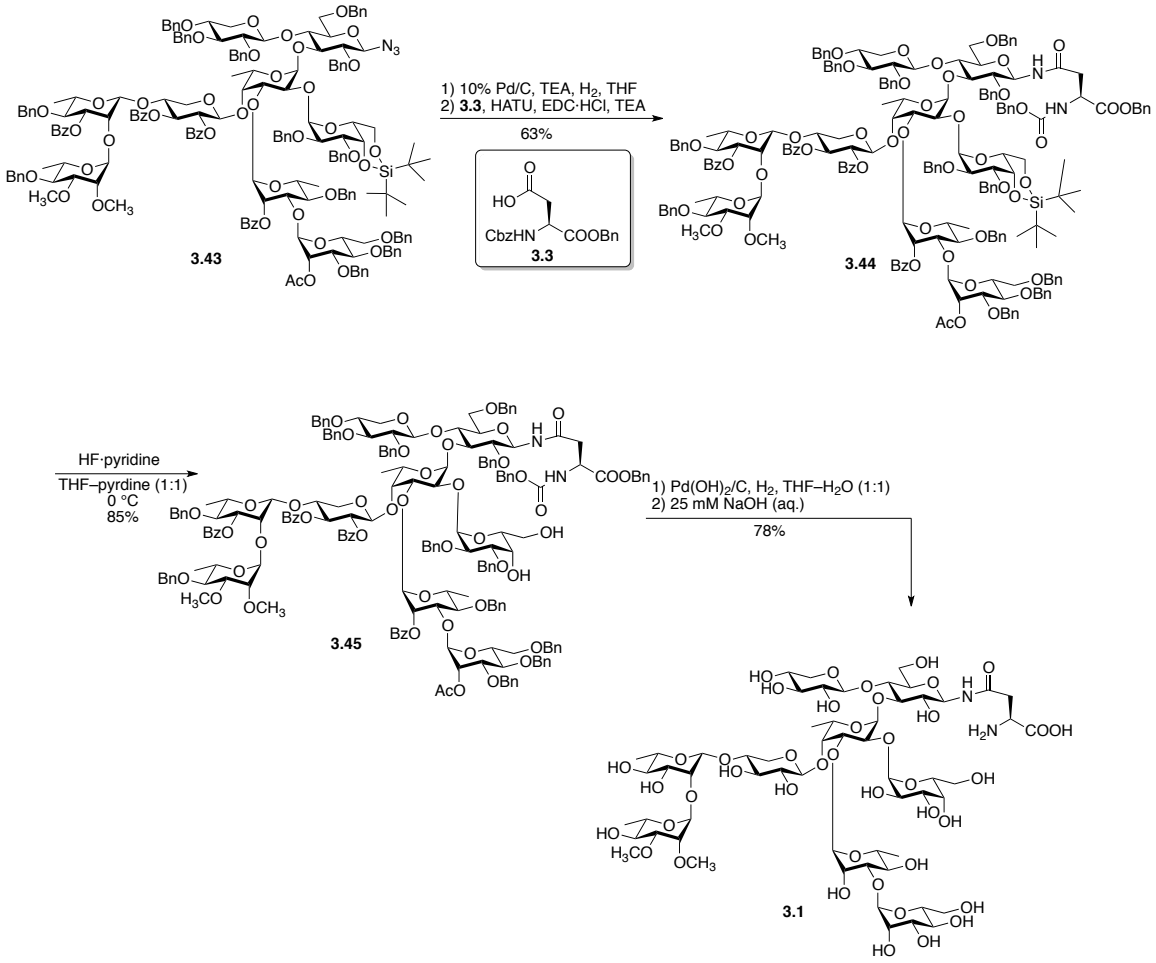
hypothesized that this problem might be addressed by a CH_3OTf-activated glycosylation of **3.6** with **3.40**. As I discussed in Chapter 2, when an unreactive acceptor is involved in a glycosylation, a milder activation of the donor usually helps to slow down the side reactions of the donor. As a result, a CH_3OTf-activated glycosylation of **3.6** was then investigated with **3.40**. After stirring at room temperature for four days a chromatography-inseparable mixture of the desired octasaccharide **3.41** and the methylated acceptor was produced. Subsequent treatment of this mixture with 1% TFA in dichloromethane removed the 4-methoxybenzyl group and afforded pure **3.42** in 56% yield over two steps. The stereochemistry was determined by the coupling constant between D-Rha-C-1 and D-Rha-H-1 ($^1J_{C\text{-}H}$ = 172.3 Hz) in the ^{1}H-coupled HSQC spectrum.

Having succeeded in producing the octasaccharide, the final glycosylation was the introduction of the galactose residue. Reaction of **3.4** and **3.42** was promoted by treatment with CH_3OTf leading to the desired nonasaccharide **3.43** in 74% yield with exclusive α-selectivity. The stereochemistry was confirmed by the coupling constant of Gal-C-1 to Gal-H-1 1 ($^1J_{C\text{-}H}$ = 170.1 Hz) in the ^{1}H-coupled HSQC spectrum

3.2.1.4 Reduction of glycosyl azide 3.43 and global deprotection

After successful construction of nonasaccharide **3.43**, the palladium-catalyzed hydrogenation of the azide was done in the presence of a stoichiometric amount of triethylamine as described in Chapter 2. The resulting free amine was immediately added to a solution of pre-activated amino acid **3.3** to afford the fully protected nonasaccharide

3.44 in 63% yield with stereochemical retention of the anomeric β-linkage (Scheme 3-13). To accomplish the deprotection of **3.44**, the di-*tert*-butylsilylene group was first removed with HF·pyridine at 0 °C to afford diol **3.45** in 85% yield. Then subsequent debenzylation was performed by catalytic hydrogenation using 20% palladium hydroxide on carbon in THF–H_2O (1:1) under 1 atm of H_2 to remove the 14 benzyl groups and the carboxybenzyl group simultaneously. Lastly, the ester groups were removed using 25 mM aqueous NaOH to generate the **3.1** in 66% yield over three steps. Overall, **3.1** was synthesized in 16 steps and in 4.4% overall yield from **3.13** using the "counter-clockwise" assembly strategy.



Scheme 3-13: Synthesis of nonasaccharide **3.1** from **3.43** through reduction, amidation and global deprotection.

3.2.1.5 Comparison of 3.1 and the isolated molecule via ^{1}H NMR spectroscopy

A comparison of the ^{1}H NMR spectrum of **3.1** with that reported for the natural product was made (Figure 3-2). The blue trace is the anomeric region of the ^{1}H NMR spectrum of the naturally-isolated glycan in D_2O measured at 600 MHz and 310 K (FID provided by Dr. Cristina de Castro, University of Naples). The black trace is the anomeric region of the

^{1}H NMR spectrum obtained from synthetic **3.1** in D_2O measured at 700 MHz and 300 K; I noticed that the anomeric proton of the Glc was missing. The addition of 0.1% TFA to the D_2O during the measurement allowed this problem to be overcome (red trace). Overall, based on the comparison of the chemical shift of the anomeric protons, I am confident that the structure of my chemically synthesized glycan **3.1** agrees with the natural product.

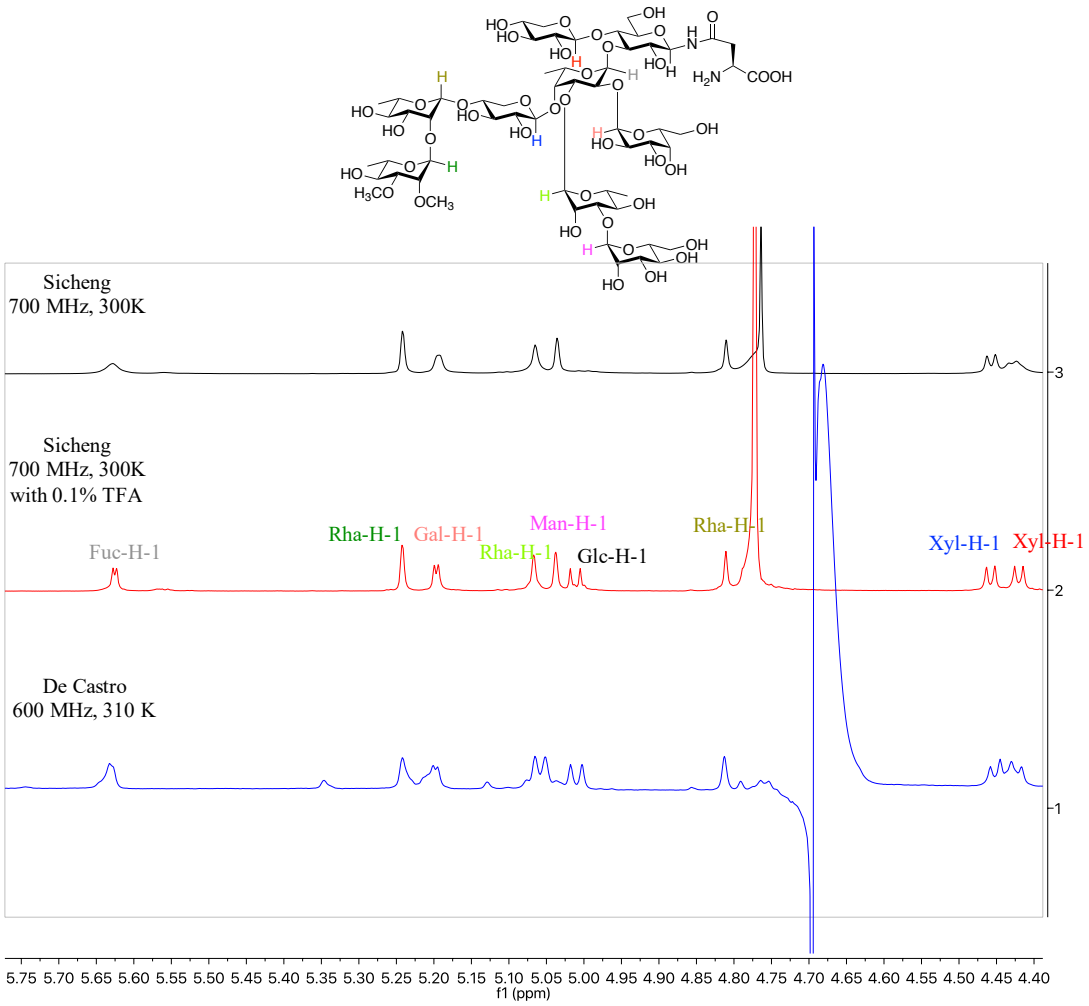


Figure 3-2: Comparison of the anomeric region of the ^{1}H NMR spectrum of **3.1** and the natural product.

3.2.1.6 Summary

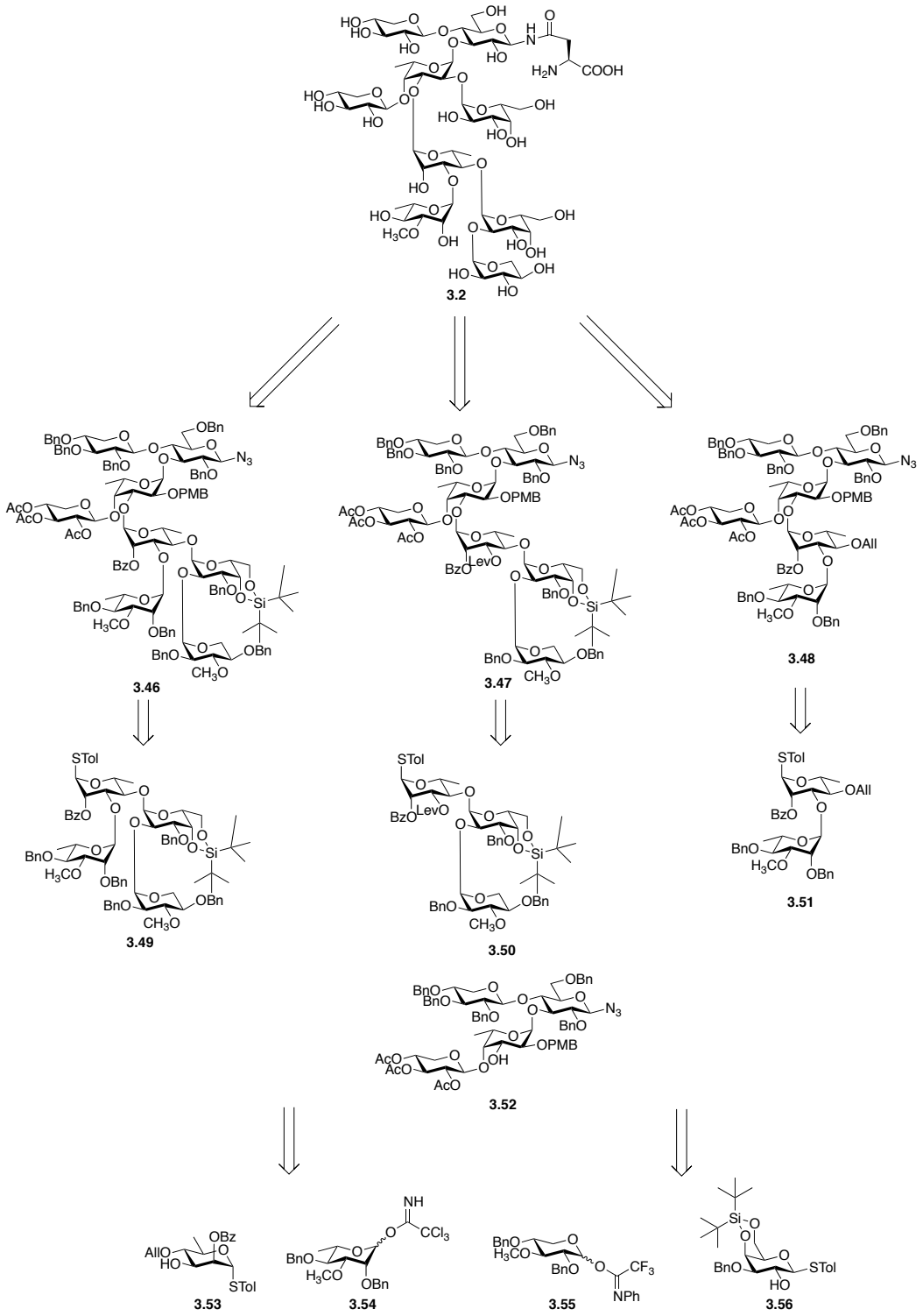
In summary, this section described the application of the "counter-clockwise" assembly approach to the successful synthesis of **3.1**, one of the most complex *N*-linked glycans isolated to date from chloroviruses. Compared to the synthesis of the ATCV-1 *N*-glycan (**2.1**, Chapter 2), the overall yield for the synthesis of the PBCV-1 *N*-glycan **3.1** was lower. The yield of the glycosylations of the fucose C-4 hydroxyl group with a trisaccharide donor and the fucose C-3 hydroxyl group with a disaccharide donor were reasonable and proceeded with good stereocontrol. These results further support my hypothesis that the method can be applied as a general strategy to access all chlorovirus *N*-glycans. The difficulty in the NIS/AgOTf-mediated incorporation of a disaccharide onto the C-3 hydroxyl group of the fucose was overcome using a CH_3OTf-promoted glycosylation. However, in Chapter 2, in the synthesis of the ATCV-1 *N*-glycan, I showed that the NIS/AgOTf-mediated glycosylation of a monosaccharide onto the O-3 position of the fucose was possible. Thus, the reactivity and accessibility of this hydroxyl group, as well as the size of donor and the activation conditions are crucial elements for success in this glycosylation reaction.

With the success of the syntheses of *N*-glycans **2.1** and **3.1**, I turned my attention to *N*-glycan **3.2**. This compound provides another challenging test for my "counter-clockwise" assembly method and to explore the effect of the donor size during the glycosylation of the C-3 hydroxyl group of fucose in these systems. If the "counter-clockwise" approach is to

be used for the synthesis of **3.2**, it would require the glycosylation of this hydroxyl group with a tetrasaccharide donor.

3.2.2 Synthesis of the nonasaccharide from chlorella virus NY-2A$_1$

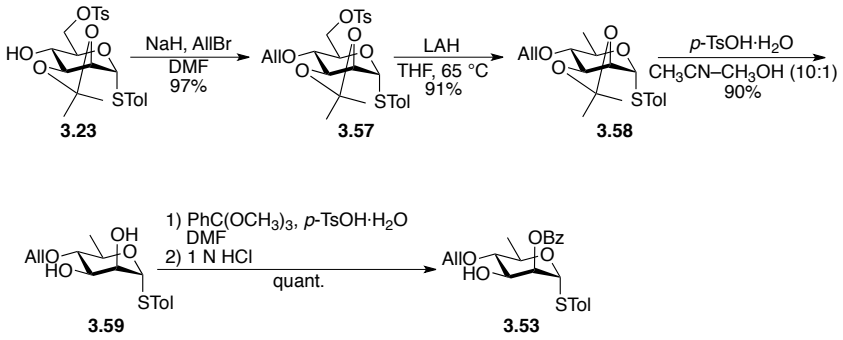
It was proposed that the nonasaccharide **3.2** could be prepared from three different precursors (Scheme 3-14): octasaccharide **3.46**, heptasaccharide **3.47** or hexasaccharide **3.48**. The most convergent of these approaches, via **3.46**, would require glycosylation of the fucose O-3 in tetrasaccharide **3.52** with tetrasaccharide donor **3.49**. Concerned about whether such an approach would be feasible given the size of the donor and acceptor, I also decided to explore if smaller donors, trisaccharide **3.50** or a disaccharide **3.51**, would be better. In the case of the latter two approaches, after the glycosylation of **3.52**, the product (either **3.47** or **3.48**) would need to undergo additional reactions to complete the bottom tetrasaccharide moiety. Donors **3.49**–**3.51** could be prepared from four different monosaccharide building blocks, **3.53**–**3.56**. The synthesis of L-rhamnose donor **3.54** was described in Section 2.2.2; the rest were prepared as discussed below.



Scheme 3-14: Retrosynthetic analysis of nonasaccharide **3.2** using di-, tri-, and tetrasaccharide donors.

3.2.2.1 Synthesis of building blocks 3.53, 3.55 and 3.56

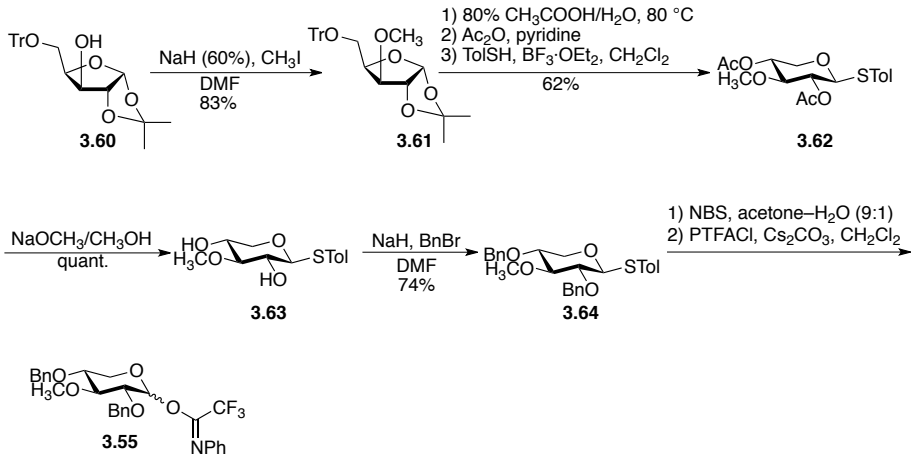
The preparation of D-rhamnose acceptor **3.53** started from mannose derivative **3.23**, whose synthesis was described in Section 3.2.1.1. The C-4 hydroxyl group in **3.23** was first protected by treatment with sodium hydride and allyl bromide to furnish compound **3.57** in 97% yield (Scheme 3-15). Subsequent reduction of **3.57** by lithium aluminum hydride at 65 °C provided D-rhamnoside **3.58** in 91% yield. The ketal was then removed by hydrolysis with *p*-toluenesulfonic acid in a 10:1 acetonitrile–methanol solution to give diol **3.59** in 90% yield. Reaction of **3.59** with trimethyl orthobenzoate and acid followed by treatment with 1 N hydrogen chloride led to the regioselective opening of the orthoester to afford the D-rhamnose acceptor **3.53** in quantitative yield.



Scheme 3-15: Synthesis of D-rhamnose acceptor **3.53**.

The synthesis of xylose donor **3.55** began from xylofuranose derivative **3.60**, which was obtained from D-xylose in two steps as reported.[23] The C-3 hydroxyl group was first methylated to give **3.61** in 83% yield (Scheme 3-16). Transformation from the furanose to pyranose ring form was done by hydrolysis with 80% aqueous acetic acid, followed by

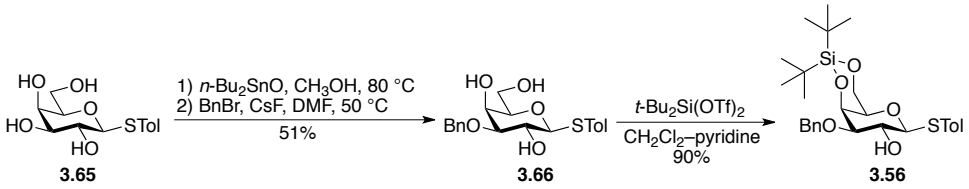
acetylation and thioglycoside formation to afford **3.62** in 62% yield over three steps. Subsequent exchange of the two acetyl groups with benzyl groups produced **3.64** in 74% yield over the two steps. Hydrolysis of thioglycoside **3.64** upon treatment with *N*-bromosuccinimide in wet acetone, gave a hemiacetal that was converted into its *N*-phenyl-trifluoroacetimidate derivative **3.55** with 2,2,2-trifluoro-*N*-phenylacetimidoyl chloride and cesium carbonate.



Scheme 3-16: Synthesis of xylose donor **3.55**.

Finally, acceptor **3.56** was prepared from **3.65**, which was produced in three steps from D-galactose.[24] Reaction of **3.65** (Scheme 3-17) with dibutyltin oxide at reflux in methanol with a Dean–Stark apparatus produced a stannylidene acetal that was regioselectively benzylated upon the addition of benzyl bromide and cesium fluoride and heating at 50 °C. This reaction afforded **3.66** in 51% yield. Also isolated was unreacted starting material and other benzylated compounds that were not characterized. The structure of **3.66** was

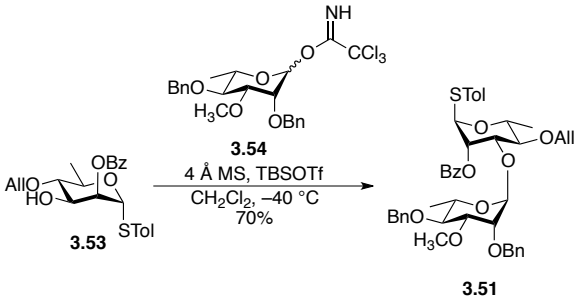
confirmed by the correlation between H-3 and the benzylic carbon in the HMBC spectrum. The C-4 and C-6 hydroxyl groups of **3.66** were next protected as a di-*tert*-butylsilylene acetal to give **3.56** in 90% yield.



Scheme 3-17: Synthesis of galactose acceptor **3.56**.

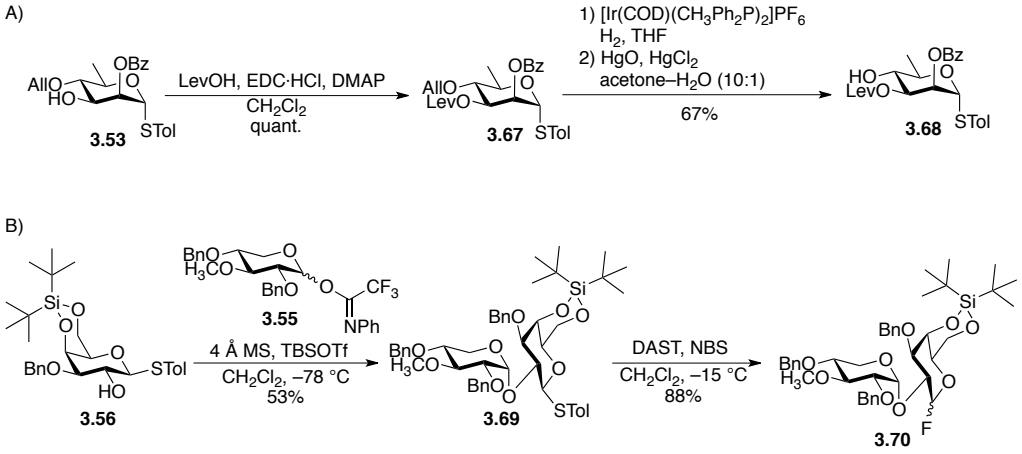
3.2.2.2 Synthesis of di-, tri-, tetrasaccharide donors 3.49–3.51

Disaccharide **3.51** was synthesized first because it could also be used as an intermediate for the construction of the tetrasaccharide donor. As shown in Scheme 3-18, the glycosylation of **3.53** with **3.54** was performed to afford the desired disaccharide donor **3.51** in 70% yield. The α-stereochemistry was determined by the coupling constant between C'-1 and H'-1 ($^1J_{C\text{-}H}$ = 169.3 Hz) in the ^{1}H-coupled HSQC spectrum.



Scheme 3-18: Synthesis of disaccharide donor **3.51**.

The synthesis of trisaccharide donor **3.50** started with the preparation of acceptor **3.68** and donor **3.70** as shown in Scheme 3-19. The acceptor **3.68** was prepared (Scheme 3-19A) in 67% yield over two steps by first protection of the C-3 hydroxyl group in **3.53** as a levulinate ester, followed by cleavage of O-4 allyl ether, liberating an alcohol.

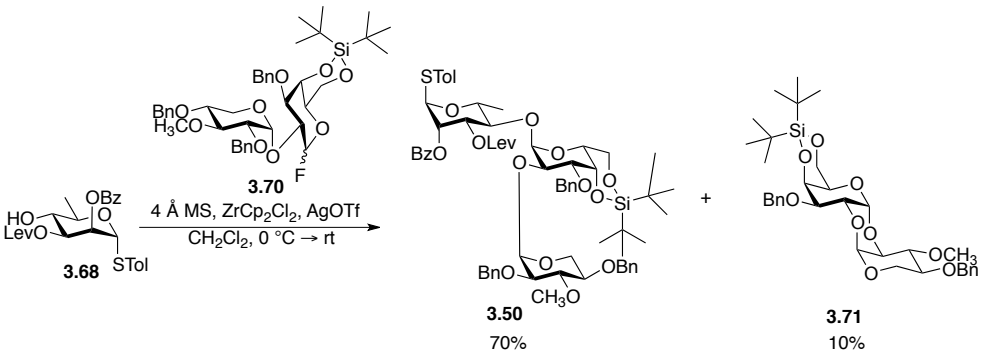


Scheme 3-19: Synthesis of A) acceptor **3.68** and B) donor **3.70**.

To minimize the difficulties associated in selectively producing an α-xylosidic linkage on complex oligosaccharide substrates, we sought to establish the 1,2-*cis* linkage early in the synthetic route. As a result, the preparation of donor **3.70** (Scheme 3-19B) started with a TBSOTf-promoted glycosylation of alcohol **3.56** with imidate **3.55** to furnish **3.69** in 53% yield. The low yield was due to the formation of β-anomer (~30% yield). My attempts to improve the selectivity were not successful. The α-configuration in **3.69** was determined by the coupling constant of Xyl-C-1 to Xyl-H-1 ($^1J_{C\text{-}H}$ = 172.1 Hz) in the ^{1}H-coupled HSQC spectrum. Then, the disaccharide thioglycoside **3.69** was subjected to diethylaminosulfur

trifluoride and *N*-bromosuccinimide at –15 °C to afford the expected glycosyl fluoride **3.70** in 88% yield.

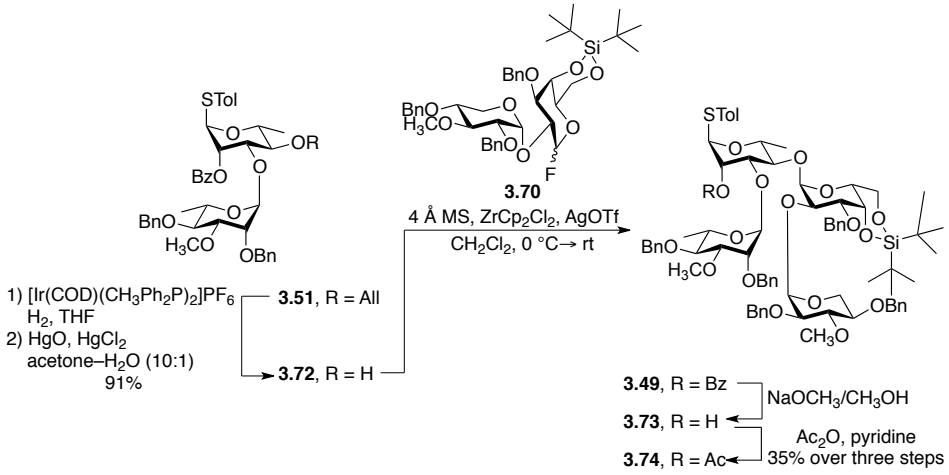
Subsequent glycosylation of acceptor **3.68** with donor **3.70** (Scheme 3-20), promoted by bis(cyclopentadienyl)zirconium(IV) dichloride and silver trifluoromethanesulfonate, resulted in the formation of trisaccharide **3.50** in 70% yield; tricyclic by-product **3.71** was also isolated in 10% yield. The stereochemistry of **3.50** was again confirmed by the coupling constant between Gal-H-1 and Gal-C-1 ($^1J_{C\text{-}H}$ = 172.4 Hz) in the ^{1}H-coupled HSQC spectrum. The formation of **3.71** is likely due to the low reactivity of the C-4 hydroxyl group in **3.68**. Upon activation of **3.70**, the O-2 of the xylose could act as a nucleophile forming an oxonium ion intermediate. Subsequent loss of a benzyl cation from this intermediate would result in **3.71**.



Scheme 3-20: Synthesis of tetrasaccharide donor **3.50**.

The tetrasaccharide donor **3.49** was synthesized from disaccharide **3.51** (Scheme 3-21). First, removal of the allyl ether on the C-4 hydroxyl group of **3.51** afforded acceptor **3.72** in 91% yield. Subsequent glycosylation of **3.72** with donor **3.70** (an intermediate in

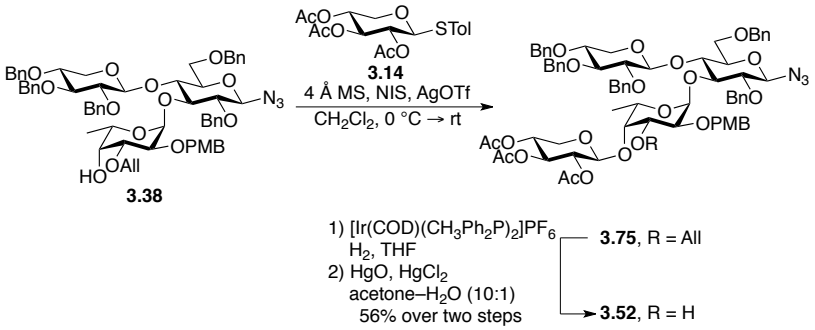
the synthesis of the trisaccharide donor **3.50**) then furnished tetrasaccharide **3.49** as an inseparable mixture with other by-products. To confirm the structure of the desired product, a portion of the material was subjected to deprotection of the benzoyl group. Purification of the product, **3.73**, was then possible. After acetylation, tetrasaccharide donor **3.74** was obtained in 35% yield over three steps. Both **3.74** and **3.49** are potentially useful as substrates for investigating glycosylation reactions leading to the target octasaccharide **3.46**. As discussed in the previous paragraph, the glycosylation of monosaccharide acceptor **3.68** with **3.70** gave the product **3.50** in 70% yield (Scheme 3-20). The decreased yield using a disaccharide acceptor **3.72** might result from a decrease in the reactivity of the C-4 hydroxyl group due to the adjacent carbohydrate residue.



Scheme 3-21: Synthesis of tetrasaccharide donors **3.49** and **3.74**.

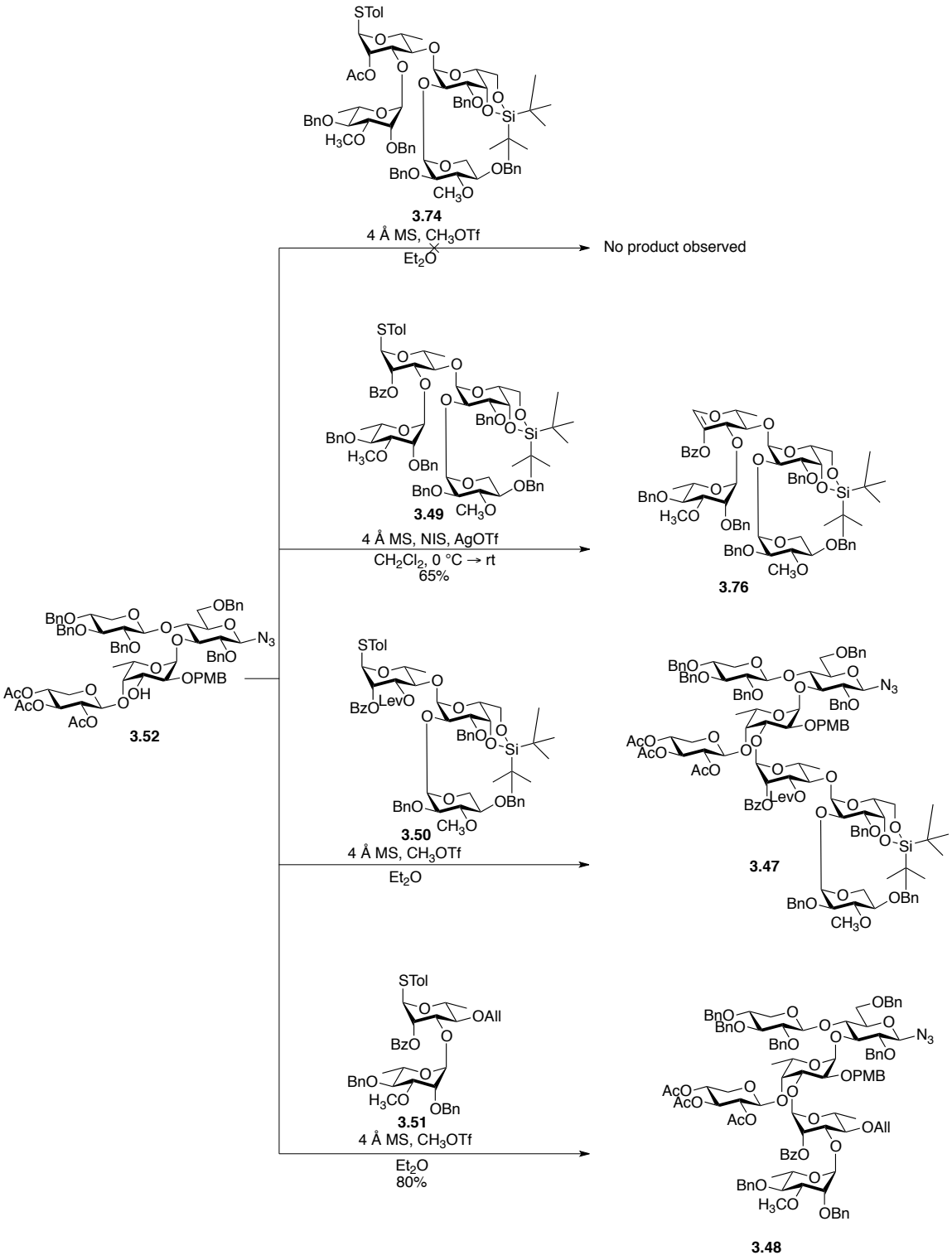
3.2.2.3 Investigating the effect of donor size in glycosylation with 3.49–3.51

Although the yield for making tetrasaccharide donor **3.49** was not satisfying, I wanted to investigate the effect of donor size in the glycosylation with an appropriate acceptor before optimization of the donor synthesis. Thus, tetrasaccharide acceptor **3.52** was prepared first from **3.38** by glycosylation with **3.14**, followed by removal of the allyl ether (Scheme 3-22). The reaction sequence afforded **3.52** in 56% yield over two steps.



Scheme 3-22: Synthesis of tetrasaccharide acceptor **3.52**.

Having all of the necessary intermediates constructed, the glycosylation between **3.52** with different-sized donors (**3.49**–**3.51** and **3.74**) was evaluated (Scheme 3-23). I used CH_3OTf as the promoter to perform the reactions at room temperature as these conditions were shown to be effective in other glycosylations of the C-3 hydroxyl group on the fucose when a carbohydrate residue was present at O-4 (Chapter 2 and Section 3.2.1.3). I first explored the most convergent approach, a 4+4 coupling. Attempted glycosylation of **3.52**



Scheme 3-23: Attempted coupling of donors **3.49**–**3.51** and **3.73** with acceptor **3.52**.

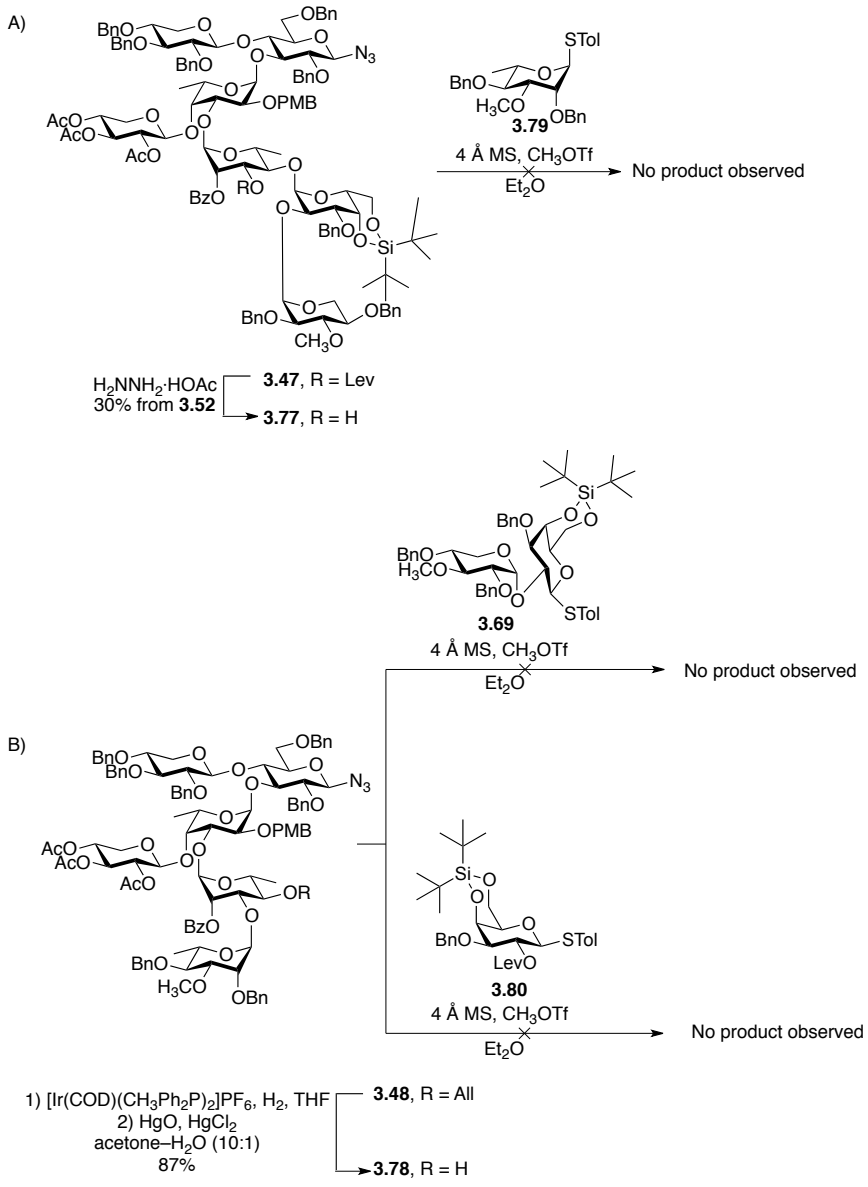
with **3.74** led to none of the desired octasaccharide product. Both the acceptor and donor were recovered. Moreover, an attempted NIS/AgOTf-activated glycosylation using **3.49** provided the elimination product **3.76** in 65% yield as the only isolated product. This result further suggests that the NIS/AgOTf-mediated glycosylation is not compatible with large donors as also observed in Section 3.2.1.3. Then I turned my attention to trisaccharide **3.50**, which afforded the desired heptasaccharide **3.47** using a CH_3OTf-promoted glycosylation. However, it contained inseparable by-products and gave a low yield of the product. Finally, the glycosylation of **3.52** with disaccharide **3.51** was performed and the desired hexasaccharide **3.48** was obtained in 80% yield.

With these results in mind, it can be concluded: 1) that a trisaccharide might be the largest donor that could be glycosylated on the fucose C-3 hydroxyl group of **3.52** under CH_3OTf-catalyzed conditions, albeit, in a low yield as observed; and 2) a disaccharide donor (**3.51**) was more efficient in the glycosylation.

3.2.2.4 Attempted synthesis of octasaccharide 3.46 from heptasaccharide 3.47 or hexasaccharide 3.48

Because the glycosylation of tetrasaccharide acceptor **3.52** with a tetrasaccharide donor (**3.49** or **3.74**) failed, I attempted the synthesis of octasaccharide **3.46** from heptasaccharide **3.47** and hexasaccharide **3.48**. To do this, the levulinoyl group in **3.47** was removed, which allowed for the purification of heptasaccharide acceptor **3.77** in 30% yield from **3.52** (two steps). Similarly, the removal of the allyl ether in **3.48** provided the

hexasaccharide acceptor **3.78** in 87% yield. With **3.77** in hand, its transformation to the desired octasaccharide **3.46** via a 7+1 glycosylation was investigated as shown in Scheme 3-24A. However, no product was obtained and only the starting materials were recovered.



Scheme 3-24: Attempted synthesis of octasaccharide **3.46** from A) heptasaccharide acceptor **3.77** and B) hexasaccharide acceptor **3.78**.

In addition, a 6+2 glycosylation of **3.78** with **3.69** or a 6+1 glycosylation with **3.80** (Scheme 2-24B) both failed to achieve the desired product. This outcome indicated that the synthesis of *N*-glycan from virus NY-2A$_1$ following these routes was not feasible.

3.3 Conclusion

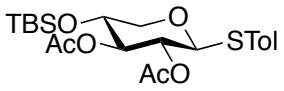
In conclusion, the work described in this chapter explored the extension of my "counter-clockwise" assembly approach for the synthesis of chlorovirus *N*-glycans. This work demonstrated that the approach can be applied to the successful synthesis of the PBCV-1 glycan **3.1**, but my attempts to produce the NY-2A$_1$ glycan **3.2** were unsuccessful. The successful synthesis of *N*-glycan **3.1**, which has a trisaccharide on the fucose C-4 hydroxyl group and a disaccharide on the fucose C-3 hydroxyl group, suggests that this method could be used as a general strategy to access most chlorovirus *N*-glycans because the majority of the chlorovirus *N*-glycans only have a monosaccharide on the fucose C-3 hydroxyl group and a mono- or disaccharide on the fucose O-4 position. Additionally, the investigation of the donor size in glycosylation with acceptor **3.52** during the synthesis of *N*-glycan **3.2** suggests that a trisaccharide is the largest donor that can be glycosylated onto the fucose C-3 hydroxyl group under CH_3OTf-catalyzed reaction conditions. However, disaccharide and monosaccharide donors are more suitable, giving higher yields. Even through it was possible to make two advanced precursors, hexasaccharide **3.48** and heptasaccharide **3.47**, their further elaboration to the NY-2A$_1$ target was not possible. Attempts to glycosylate either **3.77** or **3.78**, leading to octasaccharide **3.46**, and eventually a nonasaacharide, were unsuccessful. Unfortunately, due to the time constraints of my Ph.D. studies, I decide to stop at this point.

Aside from the total synthesis of these compounds (**2.1**, **3.1** and **3.2**), the Lowary group has engaged in a collaboration related to them with Dr. Cristina De Castro's group at the

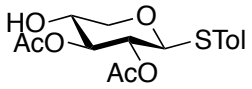
University of Napoli in Italy. Dr. De Castro's group determined the structure of these glycans[1–4] and also has a particular interest in understanding their biosynthesis. They have focused on the PBCV-1 *N*-glycan as a model system.[25] Fragments of the PBCV-1 structure are essential tools to probe the roles of the different biosynthetic enzymes (glycosyltransferases and methyl transferases). In the next chapter, access to fragments of the PBCV-1 glycan will be described.

3.4 Experimental section

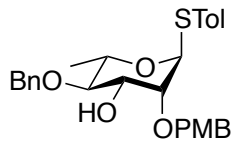
General methods: All reagents were purchased from commercial sources and were used without further purification unless noted. Reaction solvents were purified by successive passage through columns of alumina and copper under argon. Unless stated otherwise, all reactions were carried out at room temperature and under a positive pressure of argon and were monitored by TLC on Silica Gel G-25 F254 (0.25 mm). Visualization of the reaction components was achieved using UV fluorescence (254 nm) and/or by charring with acidified anisaldehyde solution in ethanol, acetic acid and sulfuric acid. Organic solvents were evaporated under reduced pressure, and the products were purified by column chromatography on silica gel (230−400 mesh) or size exclusion column chromatography (Sephadex-LH20). Optical rotations were measured in a microcell (1 cm, 1 mL) at ambient temperature and are in units of degrees·mL/(g·dm). ^{1}H NMR spectra were recorded at 400 MHz, 500 MHz, 600 MHz or 700 MHz and chemical shifts are referenced to residual $CHCl_3$ (7.26 ppm, $CDCl_3$), CHD_2OD (3.30 ppm, CD_3OD), HDO (4.78 ppm, D_2O). ^{13}C NMR spectra were recorded at 125 MHz or 175 MHz and chemical shifts are referenced to $CDCl_3$ (77.0 ppm) or CD_3OD (49.3 ppm). Reported splitting patterns are abbreviated as s = singlet, d = doublet, t = triplet, m = multiplet, br = broad, app = apparent. Assignments of NMR spectra were based on two-dimensional experiments (^{1}H–^{1}H COSY, HSQC and HMBC. High-resolution ESI-MS spectra (time-of-flight analyzer) were recorded on samples suspended in THF or CH_3OH and with added NaCl.



***p*-Tolyl 2,3-di-*O*-acetyl-4-*O*-*tert*-butyldimethylsilyl-1-thio-β-D-xylopyranoside (3.17):** To a stirred solution of *p*-tolyl 4-*O*-*tert*-butyldimethylsilyl-1-thio-β-D-xylopyranoside **3.16**[5] (1.29 g, 3.48 mmol) in pyridine (6.0 mL) was added acetic anhydride (3.0 mL) dropwise at room temperature. The reaction mixture was stirred overnight at room temperature, then the solvent was concentrated. The crude residue was diluted with CH_2Cl_2 (150 mL) and washed with 1N HCl and saturated $NaHCO_3$ (aq.). The organic layer was dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (8:1 hexane–EtOAc) to afford **3.17** (1.58 g, quant.) as a syrup. R_f 0.43 (6:1 hexane–EtOAc); $[\alpha]_D$ –46.7 (*c* 0.12, $CHCl_3$); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.40–7.37 (m, 2H, Ar), 7.16–7.13 (m, 2H, Ar), 5.05 (t, 1H, *J* = 9.0 Hz, H-3), 4.85 (dd, 1H, *J* = 9.7, 9.2 Hz, H-2), 4.63 (d, 1H, *J* = 9.8 Hz, H-1), 3.99 (dd, 1H, *J* = 11.6, 5.3 Hz, H-5a), 3.80 (ddd, 1H, *J* = 10.2, 8.9, 5.3 Hz, H-4), 3.30 (dd, 1H, *J* = 11.6, 10.2 Hz, H-5b), 2.36 (s, 3H, ArC$\underline{H}_3$), 2.10 (s, 3H, COC$\underline{H}_3$), 2.05 (s, 3H, COC$\underline{H}_3$), 0.85 (s, 9H, SiC(C$\underline{H}_3$)$_3$), 0.06 (s, 3H, SiC$\underline{H}_3$), 0.05 (s, 3H, SiC$\underline{H}_3$); ^{13}C NMR (125 MHz; $CDCl_3$): δ 170.0 (C=O), 169.7 (C=O), 138.4 (Ar), 133.3 (Ar), 129.8 (Ar), 128.4 (Ar), 86.9 (C-1), 76.5 (C-3), 70.4 (C-2), 70.1 (C-5), 68.7 (C-4), 25.5 (SiC($\underline{C}H_3$)$_3$), 21.2 (Ar$\underline{C}H_3$), 20.9 (2 × CO$\underline{C}H_3$), 17.8 (Si$\underline{C}$(CH$_3$)$_3$), -4.7 (Si$\underline{C}H_3$), -5.0 (Si$\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{22}H_{34}NaO_6SSi$: 477.1738; Found 477.1733.

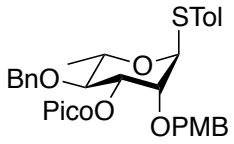


***p*-Tolyl 2,3-di-*O*-acetyl-1-thio-β-D-xylopyranoside (3.8):** To a stirred solution of **3.17** (1.58 g 3.48 mmol) in THF–pyridine (8.0 mL, 1:1) was added HF·pyridine (1.5 mL, pyridine ~30%, hydrogen fluoride ~70%) at 0 °C under an Ar atmosphere. The reaction mixture was stirred overnight at room temperature and then poured into saturated $NaHCO_3$ (aq.). The aqueous layer was extracted with EtOAc (50 mL × 3), dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (3:2 hexane–EtOAc) to afford **3.8** (1.15 g, 97%) as a syrup. R_f 0.24 (3:2 hexane–EtOAc); $[\alpha]_D$ –59.9 (*c* 0.22, $CHCl_3$); ^{1}H NMR (600 MHz; $CDCl_3$): δ 7.40–7.39 (m, 2H, Ar), 7.15–7.14 (m, 2H, Ar), 4.98–4.94 (m, 2H, H-2, H-3), 4.76 (d, 1H, J = 7.9 Hz, H-1), 4.27 (dd, 1H, J = 11.9, 4.6 Hz, H-5a), 3.81–3.77 (m, 1H, H-4), 3.43 (dd, 1H, J = 11.9, 8.5 Hz, H-5b), 2.50 (d, 1H, J = 6.5 Hz, 4-OH), 2.36 (s, 3H, ArC$\underline{H}_3$), 2.13 (s, 3H, COC$\underline{H}_3$), 2.13 (s, 3H, COC$\underline{H}_3$); ^{13}C NMR (125 MHz; $CDCl_3$): δ 171.2 (C=O), 169.3 (C=O), 138.4 (Ar), 133.1 (Ar), 129.8 (Ar), 128.9 (Ar), 86.8 (C-1), 75.5 (C-3), 69.7 (C-2), 68.2 (C-4), 67.8 (C-5), 21.2 (Ar$\underline{C}H_3$), 20.9 (2 × CO$\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{16}H_{20}NaO_6S$: 363.0873; Found 363.0875.



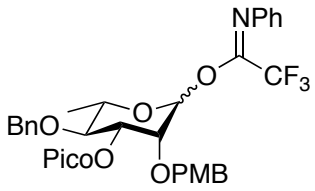
***p*-Tolyl 4-*O*-benzyl-2-*O*-(4-methoxybenzyl)-1-thio-α-L-rhamnopyranoside (3.19):** To a stirred solution of *p*-tolyl 4-*O*-benzyl-1-thio-α-L-rhamnopyranoside **3.18**[6] (3.14 g, 8.70

mmol) in CH_2Cl_2 (30 mL) was added tetrabutylammonium bromide (1.40 g, 4.36 mmol), 4-methoxybenzyl chloride (1.41 mL, 10.4 mmol) and aq. 20% NaOH (30 mL) successively. The reaction mixture was stirred overnight at room temperature and then poured into saturated $NaHCO_3$ (aq.) and extracted with CH_2Cl_2 (100 mL × 3). The combined organic layers were dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (4:1 hexane–EtOAc) to afford **3.19** (3.97 g, 95%) as a syrup. R_f 0.64 (2:1 hexane–EtOAc); $[\alpha]_D$ –32.3 (*c* 0.40, $CHCl_3$); ^1H NMR (600 MHz; $CDCl_3$): δ 7.40–7.26 (m, 9H, Ar), 7.13–7.12 (m, 2H, Ar), 6.91–6.89 (m, 2H, Ar), 5.46 (s, 1H, H-1), 4.94 (d, 1H, *J* = 11.1 Hz, PhC$\underline{H}_2$), 4.69, (d, 1H, *J* = 11.4 Hz, ArC$\underline{H}_2$), 4.68 (d, 1H, *J* = 11.1 Hz, PhC$\underline{H}_2$), 4.47 (d, 1H, *J* = 11.4 Hz, ArC$\underline{H}_2$), 4.17 (dq, 1H, *J* = 9.4, 6.1 Hz, H-5), 3.98–3.94 (m, 2H, H-2, H-3), 3.83 (s, 3H, ArOC$\underline{H}_3$), 3.38 (t, 1H, *J* = 9.1 Hz, H-4), 2.37 (d, 1H, *J* = 9.3 Hz, 3-OH), 2.35 (s, 3H, ArC$\underline{H}_3$), 1.35 (d, 3H, *J* = 6.2 Hz, H-6); ^{13}C NMR (125 MHz; $CDCl_3$): δ 159.6 (Ar), 138.5 (Ar), 137.7 (Ar), 132.2 (Ar), 130.6 (Ar), 129.8 (2 × Ar), 129.4 (Ar), 128.4 (Ar), 127.9 (Ar), 127.7 (Ar), 114.0 (Ar), 85.4 (C-1), 82.5 (C-4), 79.6 (C-2), 75.1 (Ph$\underline{C}H_2$), 72.1 (Ar$\underline{C}H_2$), 72.0 (C-3), 68.5 (C-5), 55.3 (ArO$\underline{C}H_3$), 21.1 (Ar$\underline{C}H_3$), 17.9 (C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{28}H_{32}NaO_5S$: 503.1863; Found 503.1862.

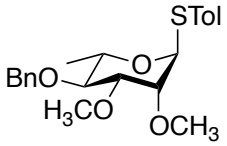


***p*-Tolyl 4-*O*-benzyl-2-*O*-(4-methoxybenzyl)-3-*O*-picoloyl-1-thio-α-L-rhamnopyranoside (3.20):** To a stirred solution of **3.19** (3.94 g, 8.20 μmol) in dry CH_2Cl_2

(40 mL) was added EDC·HCl (4.72 g. 24.6 mmol), 2-picolinic acid (3.03 g, 24.6 mmol) and 4-(dimethylamino)pyridine (301 mg, 2.46 mmol) successively. The reaction mixture was stirred overnight at room temperature. Then poured into the saturated $NaHCO_3$ (aq.) and extracted with CH_2Cl_2 (100 mL × 3). The combined organic layers were dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (2:1 hexane–EtOAc) to afford **3.20** (4.56 g, 95%) as a syrup. R_f 0.31 (2:1 hexane–EtOAc); $[\alpha]_D$ –13.4 (*c* 0.20, $CHCl_3$); ^{1}H NMR (600 MHz; $CDCl_3$): δ 8.81 (ddd, 1H, *J* = 4.7, 1.7, 0.9 Hz, Ar), 8.02 (dt, 1H, *J* = 7.8, 1.0 Hz, Ar), 7.82 (td, 1H, *J* = 7.7, 1.8 Hz, Ar), 7.50 (ddd, 1H, *J* = 7.6, 4.7, 1.2 Hz, Ar), 7.38–7.36 (m, 2H, Ar), 7.26–7.19 (m, 5H, Ar), 7.15–7.12 (m, 4H, Ar), 6.63–6.60 (m, 2H, Ar), 5.49 (dd, 1H, *J* = 9.4, 3.4 Hz, H-3), 5.41 (d, 1H, *J* = 1.8 Hz, H-1), 4.88 (d, 1H, *J* = 11.0 Hz, PhC$\underline{H}_2$), 4.71 (d, 1H, *J* = 11.0 Hz, PhC$\underline{H}_2$), 4.61 (d, 1H, *J* = 12.0 Hz, ArC$\underline{H}_2$), 4.44 (d, 1H, *J* = 12.0 Hz, ArC$\underline{H}_2$), 4.29 (dq, 1H, *J* = 9.3, 6.2 Hz, H-5), 4.24 (dd, 1H, *J* = 3.3, 1.9 Hz, H-2), 3.91 (t, 1H, *J* = 9.4 Hz, H-4), 3.71 (s, 3H, ArOC$\underline{H}_3$), 2.35 (s, 3H, ArC$\underline{H}_3$), 1.39 (d, 3H, *J* = 6.2 Hz, H-6); ^{13}C NMR (125 MHz; $CDCl_3$): δ 164.2 (C=O), 159.2 (Ar), 150.0 (Ar), 147.9 (Ar), 138.1 (Ar), 137.6 (Ar), 136.7 (Ar), 132.3 (Ar), 130.5 (Ar), 129.8 (Ar), 129.7 (Ar), 129.5 (Ar), 128.3 (Ar), 127.9 (Ar), 127.6 (Ar), 126.8 (Ar), 125.2 (Ar), 113.6 (Ar), 85.8 (C-1), 79.1 (C-4), 76.4 (C-2), 75.2 (C-3), 75.1 (Ph$\underline{C}H_2$), 72.0 (Ar$\underline{C}H_2$), 69.2 (C-5), 55.1 (ArO$\underline{C}H_3$), 21.1 (Ar$\underline{C}H_3$), 18.0 (C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{34}H_{35}NNaO_6S$: 608.2077; Found 608.2082.

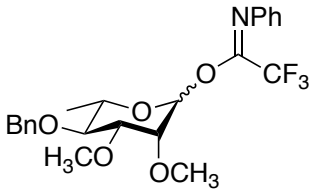


4-*O*-Benzyl-2-*O*-(4-methoxybenzyl)-3-*O*-picoloyl-α-L-rhamnopyranose 1-(*N*-phenyl)-2,2,2-trifluoroacetimidate (3.9): To a stirred solution of **3.20** (4.80 g, 8.20 mmol) in dry acetone–H_2O (22 mL, 10:1) was added and *N*-bromosuccinimide (4.38 g, 24.6 mmol) at 0 °C. The reaction mixture was stirred for 1 h at room temperature, then CH_3OH was added and the solution was concentrated. The residue was then diluted with CH_2Cl_2 and wash with saturated $NaHCO_3$ (aq.). The aqueous layer was extracted with CH_2Cl_2 (100 mL × 3), and combined organic layers were dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (2:3 hexane–EtOAc) to afford its hemiactal (3.93 g, quant.). Then to a solution of hemiactal (3.31 g, 6.90 mmol) in CH_2Cl_2 (15 mL) was added 2,2,2-trifluoro-*N*-phenylacetimidoyl chloride (1.64 mL, 10.4 mmol) and cesium carbonate (4.50 g, 13.8 mmol) successively. The reaction mixture was stirred overnight at room temperature. The crude residue was then filtered through Celite, the filtrate was concentrated to afford **3.9** and used without further purification.



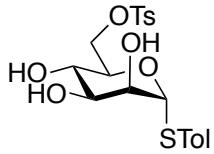
***p*-Tolyl 4-*O*-benzyl-2,3-di-*O*-methyl-1-thio-α-L-rhamnopyranoside (3.21):** To a stirred solution of *p*-tolyl 4-*O*-benzyl-1-thio-α-L-rhamnopyranoside **3.18**[6] (1.55 g, 4.29 mmol) in dry DMF (5.0 mL) was added sodium hydride (0.688 g, 17.2 mmol, 60% dispersion in

mineral oil) in one portion at 0 °C, After stirring for 30 min, methyl iodide (1.34 mL, 21.5 mmol) was added dropwise, and the reaction mixture was warmed to room temperature and stirred overnight under an Ar atmosphere. Then, CH_3OH was added at 0 °C and the solution was concentrated. The crude residue was diluted with CH_2Cl_2 (150 mL), washed with saturated $NaHCO_3$ (aq.), dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (4:1 hexane–EtOAc) to afford **3.21** (1.67 g, quant.) as a viscous oil. R_f 0.34 (4:1 hexane–EtOAc); $[\alpha]_D$ –207 (*c* 0.50, $CHCl_3$); ^{1}H NMR (600 MHz; $CDCl_3$): δ 7.40–7.35 (m, 6H, Ar), 7.32–7.29 (m, 1H, Ar), 7.15–7.14 (m, 2H, Ar), 5.54 (d, 1H, J = 1.4 Hz, H-1), 4.94 (d, 1H, J = 11.0 Hz, PhC$\underline{H}_2$), 4.64 (d, 1H, J = 11.0 Hz, PhC$\underline{H}_2$), 4.18 (dq, 1H, J = 9.3, 6.2 Hz, H-5), 3.89 (dd, 1H, J = 3.1, 1.7 Hz, H-2), 3.59 (dd, 1H, J = 9.4, 3.1 Hz, H-3), 3.55 (s, 3H, OC$\underline{H}_3$), 3.52 (t, 1H, J = 9.4, H-4), 3.50 (s, 3H, OC$\underline{H}_3$), 2.35 (s, 3H, ArC$\underline{H}_3$), 1.34 (d, 3H, J = 6.2 Hz, H-6); ^{13}C NMR (125 MHz; $CDCl_3$): δ 138.6 (Ar), 137.5 (Ar), 131.7 (Ar), 131.0 (Ar), 129.8 (Ar), 128.4 (Ar), 128.0 (Ar), 127.6 (Ar), 85.0 (C-1), 81.9 (C-3), 80.6 (C-4), 79.0 (C-2), 75.4 (Ph$\underline{C}H_2$), 68.9 (C-5), 58.2 (O$\underline{C}H_3$), 57.8 (O$\underline{C}H_3$), 21.1 (Ar$\underline{C}H_3$), 17.8 (C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{22}H_{28}NaO_4S$: 411.1601; Found 411.1595.



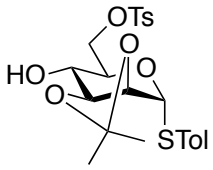
4-*O*-Benzyl-2,3-di-*O*-methyl-1-thio-α-L-rhamnopyranose 1-(*N*-phenyl)-2,2,2-trifluoroacetimidate (3.10): To a stirred solution of **3.21** (1.68 g, 4.41 mmol) in dry

acetone–H_2O (22 mL, 10:1) was added and *N*-bromosuccinimide (2.36 g, 13.2 mmol) at 0 °C. The reaction mixture was stirred for 1 h at room temperature, then CH_3OH was added and the solution was concentrated. The residue was then diluted with CH_2Cl_2 and wash with saturated $NaHCO_3$ (aq.). The aqueous layer was extracted with CH_2Cl_2 (100 mL × 3), and combined organic layers were dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (1:1 hexane–EtOAc) to afford its hemiactal (1.25 g, quant.). Then to a solution of hemiactal (460 mg, 1.63 mmol) in CH_2Cl_2 (20 mL) was added 2,2,2-trifluoro-*N*-phenylacetimidoyl chloride (0.39 mL, 2.5 mmol) and cesium carbonate (798 mg, 2.45 mmol) successively. The reaction mixture was stirred overnight at room temperature. The crude residue was then filtered through Celite, the filtrate was concentrated to afford **3.10** and used without further purification.



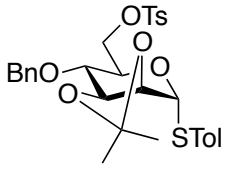
***p*-Tolyl 6-*O*-(*p*-toluenesulfonyl)-1-thio-α-D-mannopyranoside (3.23):** To a stirred solution of 1-thio-α-D-mannopyranoside **3.22**[13] (5.15 g, 18.0 mmol) in dry pyridine (60 mL) was added *p*-toluenesulfonyl chloride (5.15 g, 27.0 mmol) at 0 °C. The reaction mixture was stirred for 18 h at 0 °C. The solvent was evaporated and the crude residue was purified by flash chromatography (1:4 hexane–EtOAc) to afford **3.23** (4.76 g, 60%) as a white foam. R_f 0.53 (9:1 CH_2Cl_2–CH_3OH); $[\alpha]_D$ +142 (*c* 0.62, $CHCl_3$); ^1H NMR (400 MHz; $CDCl_3$): δ 7.80–7.77 (m, 2H, Ar), 7.32–7.29 (m, 4H, Ar), 7.10–7.08 (m, 2H, Ar), 5.42 (d, 1H, J = 1.1 Hz, H-1), 4.43 (dd, 1H, J = 11.0, 4.4 Hz, H-6a), 4.30 (ddd, 1H, J = 9.4, 4.4, 1.9

Hz, H-5), 4.25 (dd, 1H, J = 11.0, 2.0 Hz, H-6b), 4.21 (br s, 1H, H-2), 3.89 (t, 1H, J = 9.4 Hz, H-4), 3.83 (dd, 1H, J = 9.4, 2.7 Hz, H-3), 3.33 (br s, 2H, 3-OH, 4-OH), 3.16 (br s, 1H, 2-OH), 2.44 (s, 3H, ArC$\underline{H}_3$), 2.33 (s, 3H, ArC$\underline{H}_3$); ^{13}C NMR (125 MHz; $CDCl_3$): δ 145.0 (Ar), 137.9 (Ar), 132.6 (Ar), 132.2 (Ar), 129.9 (2 × Ar), 129.6 (Ar), 128.0 (Ar), 88.4 (C-1), 72.1 (C-3), 72.0 (C-2), 70.9 (C-5), 68.9 (C-6), 67.5 (C-4), 21.7 (Ar$\underline{C}H_3$), 21.1 (Ar$\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{20}H_{24}NaO_7S_2$: 463.0856; Found 463.0865.



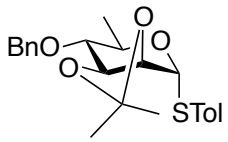
***p*-Tolyl 2,3-*O*-isopropylidene-6-*O*-(*p*-toluenesulfonyl)-1-thio-α-D-mannopyranoside (3.24):** To a stirred solution of **3.23** (3.75 g, 8.51 mmol) in dry CH_3CN (25 mL) were added 2,2-dimethoxypropane (1.56 mL, 12.8 mmol) and *p*-toluenesulfonic acid monohydrate (323 mg, 1.70 mmol) successively, the reaction mixture was stirred at room temperature for 2 h. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (3:1 hexane–EtOAc) to afford **3.24** (3.45 g, 84%) as a white foam. R_f 0.37 (2:1 hexane–EtOAc); $[\alpha]_D$ +98.3 (*c* 0.83, $CHCl_3$); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.75–7.73 (m, 2H, Ar), 7.36–7.34 (m, 2H, Ar), 7.32–7.30 (m, 2H, Ar), 7.13–7.12 (m, 2H, Ar), 5.65 (s, 1H, H-1), 4.35–4.31 (m, 2H, H-2, H-6a), 4.2–-4.18 (m, 2H, H-5, H-6b), 4.15 (dd, 1H, J = 7.5, 5.6 Hz, H-3), 3.72 (ddd, 1H, J = 10.3, 7.6, 4.2 Hz, H-4), 2.60 (d, 1H, J = 4.4 Hz, 4-OH), 2.46 (s, 3H, ArC$\underline{H}_3$), 2.35 (s, 3H, ArC$\underline{H}_3$), 1.52 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.38 (s, 3H, C(C$\underline{H}_3$)$_2$); ^{13}C NMR (125

MHz; $CDCl_3$): δ 144.9 (Ar), 138.2 (Ar), 132.8 (Ar), 132.7 (Ar), 129.9 (Ar), 129.8 (Ar), 128.8 (Ar), 128.0 (Ar), 110.0 ($\underline{C}(CH_3)_2$), 84.4 (C-1), 78.0 (C-3), 76.1 (C-2), 69.2 (C-4), 68.9 (C-5), 68.5 (C-6), 28.1 ($C(\underline{C}H_3)_2$), 26.3 ($C(\underline{C}H_3)_2$), 21.7 ($Ar\underline{C}H_3$), 21.2 ($Ar\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{23}H_{28}NaO_7S_2$: 503.1169; Found 503.1173.



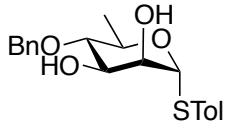
***p*-Tolyl 4-*O*-benzyl-2,3-*O*-isopropylidene-6-*O*-(*p*-toluenesulfonyl)-1-thio-α-D-mannopyranoside (3.25):** To a stirred solution of **3.24** (1.22 g, 2.55 mmol) in dry DMF (5.0 mL) was added sodium hydride (204 mg, 5.10 mmol, 60% dispersion in mineral oil) in one portion at 0 °C, After stirring for 30 min, benzyl bromide (0.36 mL, 3.1 mmol) was added dropwise and the reaction mixture was warmed to room temperature and stirred for 1 h under an Ar atmosphere. Then, CH_3OH was added at 0 °C and the solution was concentrated. The crude residue was diluted with CH_2Cl_2 (50 mL), washed with saturated $NaHCO_3$ (aq.), dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (6:1 hexane–EtOAc) to afford **3.25** (1.39 g, 96%) as a syrup. R_f 0.59 (3:1 hexane–EtOAc); $[\alpha]_D$ +141 (*c* 0.98, $CHCl_3$); ^1H NMR (500 MHz; $CDCl_3$): δ 7.70–7.69 (m, 2H, Ar), 7.37–7.29 (m, 7H, Ar), 7.26–7.25 (m, 2H, Ar), 7.12–7.11 (m, 2H, Ar), 5.60 (s, 1H, H-1), 4.89 (d, 1H, J = 11.3 Hz, $PhC\underline{H}_2$), 4.53 (d, 1H, J = 11.3 Hz, $PhC\underline{H}_2$), 4.34–4.28 (m, 3H, H-2, H-3, H-5), 4.23 (dd, 1H, J = 10.5, 1.9 Hz, H-6a), 4.18 (dd, 1H, J = 10.6, 5.3 Hz, H-6b), 3.51 (dd, 1H, J = 10.2, 6.5 Hz, H-4), 2.43 (s,

3H, ArC$\underline{H}_3$), 2.35 (s, 3H, ArC$\underline{H}_3$), 1.51 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.39 (s, 3H, C(C$\underline{H}_3$)$_2$); ^{13}C NMR (125 MHz; $CDCl_3$): δ 144.6 (Ar), 138.1 (Ar), 137.7 (Ar), 132.9 (Ar), 132.7 (Ar), 129.9 (Ar), 129.7 (Ar), 129.0 (Ar), 128.4 (Ar), 128.0 (3 × Ar), 127.8 (Ar), 109.7 ($\underline{C}(CH_3)_2$), 84.4 (C-1), 78.3 (C-3), 76.2 (C-2), 75.4 (C-4), 72.9 (Ph$\underline{C}H_2$), 68.9 (C-6), 67.9 (C-5), 28.0 (C($\underline{C}H_3$)$_2$), 26.4 (C($\underline{C}H_3$)$_2$), 21.6 (Ar$\underline{C}H_3$), 21.2 (Ar$\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{30}H_{34}NaO_7S_2$: 593.1638; Found 593.1641.

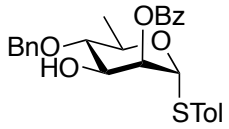


***p*-Tolyl 4-*O*-benzyl-2,3-*O*-isopropylidene-1-thio-α-D-rhamnopyranoside (3.26):** To a stirred solution of **3.25** (1.29 g, 2.26 mmol) in dry THF (20 mL) was added lithium aluminum hydride (214 mg, 5.65 mmol) at room temperature. The reaction mixture was stirred for 2.5 h at 65 °C, then cooled to 0 °C and ethyl acetate was added. The crude residue was then washed with 1N HCl and saturated $NaHCO_3$ (aq.), the aqueous layers were extracted with EtOAc (60 mL), and the combined organic layers were dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (15:1 hexane–EtOAc) to afford **3.26** (843 mg, 93%) as a white solid. R_f 0.54 (9:1 hexane–EtOAc); $[\alpha]_D$ +200 (*c* 2.4, $CHCl_3$); ^{1}H NMR (400 MHz; $CDCl_3$): δ 7.41–7.29 (m, 7H, Ar), 7.15–7.13 (m, 2H, Ar), 5.68 (d, 1H, J = 0.3 Hz, H-1), 4.94 (d, 1H, J = 11.6 Hz, PhC$\underline{H}_2$), 4.66 (d, 1H, J = 11.6 Hz, PhC$\underline{H}_2$), 4.38–4.32 (m, 2H, H-2, H-3), 4.18 (dq, 1H, J = 9.8, 6.1 Hz, H-5), 3.32 (dd, 1H, J = 9.8, 6.9 Hz, H-4), 2.35 (s, 3H, ArC$\underline{H}_3$), 1.54 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.41 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.26 (d, 3H, J = 6.2 Hz, H-6); ^{13}C NMR (125

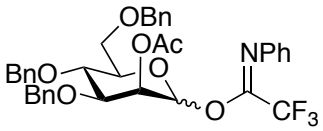
MHz; $CDCl_3$): δ 138.3 (Ar), 137.8 (Ar), 132.5 (Ar), 129.8 (Ar), 129.7 (Ar), 128.3 (Ar), 128.0 (Ar), 127.7 (Ar), 109.4 ($\underline{C}(CH_3)_2$), 84.2 (C-1), 81.5 (C-4), 78.5 (C-3), 76.7 (C-2), 73.1 (Ph$\underline{C}H_2$), 66.2 (C-5), 28.1 (C($\underline{C}H_3)_2$), 26.5 (C($\underline{C}H_3)_2$), 21.1 (Ar$\underline{C}H_3$), 17.7 (C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{23}H_{28}NaO_4S$: 423.1601; Found 423.1610.



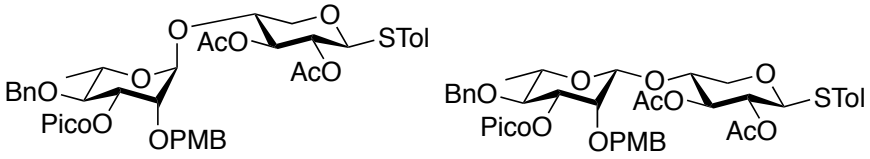
***p*-Tolyl 4-*O*-benzyl-1-thio-α-D-rhamnopyranoside (3.27):** To a stirred solution of **3.26** (3.84 g, 9.59 mmol) in CH_3CN–CH_3OH (55 mL, 10:1) was added *p*-toluenesulfonic acid monohydrate (5.47 g, 28.8 mmol) at room temperature. The reaction mixture was stirred for 2 h at room temperature. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (3:2 hexane–EtOAc) to afford **3.27** (3.13 g, 91%) as a white solid. R_f 0.18 (2:1 hexane–EtOAc); $[\alpha]_D$ +261 (*c* 0.33, $CHCl_3$); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.42–7.33 (m, 7H, Ar), 7.15–7.13 (m, 2H, Ar), 5.42 (d, 1H, *J* = 1.4 Hz, H-1), 4.80 (d, 1H, *J* = 11.4 Hz, PhC$\underline{H}_2$), 4.76 (d, 1H, *J* = 11.4 Hz, PhC$\underline{H}_2$), 4.25 (dq, 1H, *J* = 9.3, 6.2 Hz, H-5), 4.21 (td, 1H, *J* = 3.6, 1.6 Hz, H-2), 3.96 (ddd, 1H, *J* = 8.9, 5.2, 3.5 Hz, H-3), 3.44 (t, 1H, *J* = 9.2 Hz, H-4), 2.47 (d, 1H, *J* = 3.8 Hz, 2-OH), 2.35 (d, 1H, *J* = 3.5 Hz, 3-OH), 1.38 (d, 3H, *J* = 6.3 Hz, H-6); ^{13}C NMR (175 MHz; $CDCl_3$): δ 138.1 (Ar), 137.7 (Ar), 132.1 (Ar), 130.2 (Ar), 129.8 (Ar), 128.7 (Ar), 128.1 (Ar), 127.9 (Ar), 87.7 (C-1), 81.9 (C-4), 75.0 (Ph$\underline{C}H_2$), 72.5 (C-2), 71.8 (C-3), 68.5 (C-5), 21.1 (Ar$\underline{C}H_3$), 17.9 (C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{20}H_{24}NaO_4S$: 383.1288; Found 383.1283.



***p*-Tolyl 2-*O*-benzoyl-4-*O*-benzyl-1-thio-α-D-rhamnopyranoside (3.11):** To a stirred solution of **3.27** (2.22 g, 6.16 mmol) in dry DMF (1.0 mL) was treated with trimethyl orthobenzoate (7.0 mL), then evacuated for 5 min under high vacuum. *p*-Toluenesulfonic acid monohydrate (234 mg, 1.23 mmol) was added in one portion and vacuum was immediately restored. The reaction mixture was stirred for 10 min under high vacuum, then 1N HCl (20 mL) was added and stirred for 30 min. The reaction mixture was diluted with CH_2Cl_2 (100 mL), then the aqueous layer was extracted with CH_2Cl_2 (50 mL × 3) and combined organic layers were dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (6:1 hexane–EtOAc) to afford **3.11** (2.49 g, 87%) as a syrup. R_f 0.39 (4:1 hexane–EtOAc); $[\alpha]_D$ +118 (*c* 0.33, $CHCl_3$); ^{1}H NMR (500 MHz; $CDCl_3$): δ 8.06–8.04 (m, 2H, Ar), 7.63–7.59 (m, 1H, Ar), 7.50–7.47 (m, 2H, Ar), 7.43–7.32 (m, 7H, Ar), 7.14–7.12 (m, 2H, Ar), 5.63 (dd, 1H, J = 3.3, 1.5 Hz, H-2), 5.50 (d, 1H, J = 1.4 Hz, H-1), 4.88 (d, 1H, J = 11.2 Hz, PhC$\underline{H}_2$), 4.81 (d, 1H, J = 11.2 Hz, PhC$\underline{H}_2$), 4.34 (dq, 1H, J = 9.4, 6.2 Hz, H-5), 3.57 (t, 1H, J = 9.4 Hz, H-4), 2.34 (s, 3H, ArC$\underline{H}_3$), 2.21 (d, 1H, J = 5.0 Hz, H-4), 1.44 (d, 3H, J = 6.2 Hz, H-6); ^{13}C NMR (175 MHz; $CDCl_3$): δ 166.1 (C=O), 138.0 (Ar), 137.9 (Ar), 133.4 (Ar), 132.4 (Ar), 130.0 (Ar), 129.8 (2 × Ar), 129.6 (2 × Ar), 128.4, 128.0 (2 × Ar), 86.3 (C-1), 81.9 (C-4), 75.2 (Ph$\underline{C}H_2$), 74.8 (C-2), 71.1 (C-3), 68.7 (C-5), 21.1 (Ar$\underline{C}H_3$), 18.0 (C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{27}H_{28}NaO_5S$: 487.1550; Found 487.1562.



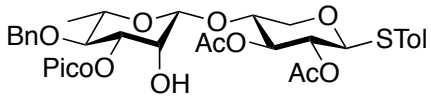
2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-D-mannopyranose 1-(*N*-phenyl)-2,2,2-trifluoroacetimidate (3.12): To a solution of 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-D-mannopyranose **3.28**[14] (947 mg, 1.92 mmol) in CH_2Cl_2 (20 mL) was added 2,2,2-trifluoro-*N*-phenylacetimidoyl chloride (0.46 mL, 2.9 mmol) and cesium carbonate (1.25 g, 3.84 mmol) successively. The reaction mixture was stirred overnight at room temperature. The crude residue was then filtered through Celite, the filtrate was concentrated to afford **3.12** and used without further purification.



***p*-Tolyl 4-*O*-benzyl-2-*O*-(4-methoxybenzyl)-3-*O*-picoloyl-α-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-acetyl-1-thio-β-D-xylopyranoside (3.29) & *p*-Tolyl 4-*O*-benzyl-2-*O*-(4-methoxybenzyl)-3-*O*-picoloyl-β-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-acetyl-1-thio-β-D-xylopyranoside (3.30):** To a stirred solution of acceptor **3.8** (1.09 g, 3.19 mmol) and donor **3.9** (4.49 g, 6.90 mmol) in dry CH_2Cl_2 (50 mL) was added molecular sieves (5.0 g, 4Å, powder). After stirring for 30 min at room temperature, the reaction mixture was cooled to 0 °C, and then *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.15 mL, 0.64 mmol) was added dropwise. The resulting solution was stirred for 1 h at 0 °C under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography

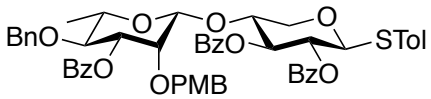
(3:2 hexane–EtOAc) to afford **3.29** (0.51 g, 20%) as a syrup and **3.30** (1.53 g, 60%) as a syrup. Data for **3.29**: R_f 0.24 (3:2 hexane–EtOAc); $[\alpha]_D$ –56.7 (*c* 0.57, $CHCl_3$); ^{1}H NMR (500 MHz; $CDCl_3$): δ 8.80 (ddd, 1H, *J* = 4.7, 1.6, 0.8 Hz, Ar), 8.01 (dt, 1H, *J* = 7.8, 1.0 Hz, Ar), 7.82 (td, 1H, *J* = 7.7, 1.7 Hz, Ar), 7.49 (ddd, 1H, *J* = 7.6, 4.7, 1.1 Hz, Ar), 7.40–7.38 (m, 2H, Ar), 7.24–7.14 (m, 9H, Ar), 6.73–6.70 (m, 2H, Ar), 5.33 (dd, 1H, *J* = 8.8, 3.3 Hz, Rha-H-3), 5.15 (t, 1H, *J* = 8.5 Hz, Xyl-H-3), 4.88 (t, 1H, *J* = 8.6 Hz, Xyl-H-2), 4.83 (d, 1H, *J* = 11.3 Hz, PhC$\underline{H}_2$), 4.77 (d, 1H, *J* = 2.0 Hz, Rha-H-1), 4.69 (d, 1H, *J* = 8.9 Hz, Xyl-H-1), 4.68 (d, 1H, *J* = 11.4 Hz, PhC$\underline{H}_2$), 4.58 (d, 1H, *J* = 11.9 Hz, ArC$\underline{H}_2$), 4.55 (d, 1H, *J* = 11.9 Hz, ArC$\underline{H}_2$), 4.11 (dd, 1H, *J* = 11.8, 4.8 Hz, Xyl-H-5a), 3.93 (dd, 1H, *J* = 3.2, 2.2 Hz, Rha-H-2), 3.85–3.78 (m, 3H, Xyl-H-4, Rha-H-5, Rha-H-4), 3.75 (s, 3H, ArOC$\underline{H}_3$), 2.37 (s, 3H, ArC$\underline{H}_3$), 2.12 (s, 3H, COC$\underline{H}_3$), 2.06 (s, 3H, COC$\underline{H}_3$), 1.34 (d, 3H, *J* = 5.8 Hz, Rha-H-6); ^{13}C NMR (175 MHz; $CDCl_3$): δ 169.8 (C=O), 169.7 (C=O), 164.1 (C=O), 159.3 (Ar), 150.0 (Ar), 147.9 (Ar), 138.5 (Ar), 138.2 (Ar), 136.7 (Ar), 133.4 (Ar), 129.7 (2 × Ar), 129.6 (Ar), 128.3 (Ar), 128.2 (Ar), 127.6 (Ar), 127.5 (Ar), 126.8 (Ar), 125.1 (Ar), 113.7 (Ar), 96.2 (Rha-C-1, $^1J_{C\text{-}H}$ = 172.1 Hz), 86.6 (Xyl-C-1), 78.7 (Rha-C-4), 75.2 (Rha-C-2), 74.9 (Rha-C-3), 74.8 (Ph$\underline{C}H_2$), 73.3 (Xyl-C-3), 72.9 (Ar$\underline{C}H_2$), 71.0 (Xyl-C-4), 70.2 (Xyl-C-2), 68.3 (Rha-C-5), 65.8 (Xyl-C-5), 55.1 (ArO$\underline{C}H_3$), 21.1 (Ar$\underline{C}H_3$), 20.9 (CO$\underline{C}H_3$), 20.8 (CO$\underline{C}H_3$), 17.9 (Rha-C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{43}H_{47}NNaO_{12}S$: 824.2711; Found 824.2715. Data for **3.30**: R_f 0.17 (3:2 hexane–EtOAc); $[\alpha]_D$ +28.1 (*c* 0.28, $CHCl_3$); ^{1}H NMR (500 MHz; $CDCl_3$): δ 8.80 (ddd, 1H, *J* = 4.7, 1.7, 0.9 Hz, Ar), 7.89 (dt, 1H, *J* = 7.8, 1.0 Hz, Ar), 7.80 (td, 1H, *J* = 7.7, 1.8 Hz, Ar), 7.50 (ddd, 1H, *J* = 7.6, 4.7, 1.2 Hz, Ar),

7.42–7.39 (m, 2H), 7.23–7.19 (m, 5H), 7.17–7.12 (m, 4H), 6.48–6.46 (m, 2H, Ar), 5.23 (t, 1H, J = 9.2 Hz, Xyl-H-3), 4.97 (dd, 1H, J = 9.9, 3.3 Hz, Rha-H-3), 4.90 (t, 1H, J = 9.4 Hz, Xyl-H-2), 4.83 (d, 1H, J = 10.9 Hz, PhC$\underline{H}_2$), 4.77 (d, 1H, J = 12.3 Hz, ArC$\underline{H}_2$), 4.67 (d, 1H, J = 11.0 Hz, PhC$\underline{H}_2$), 4.64 (d, 1H, J = 9.7 Hz, Xyl-H-1), 4.64 (s, 1H, Rha-H-1) 4.45–4.40 (m, 2H, ArC$\underline{H}_2$, Xyl-H-5a), 4.02 (d, 1H, J = 3.2 Hz, Rha-H-2), 3.82–3.76 (m, 2H, Rha-H-4, Xyl-H-4), 3.64 (s, 3H, ArOC$\underline{H}_3$), 3.48–3.41 (m, 2H, Rha-H-5, Xyl-H-5b), 2.37 (s, 3H, ArC$\underline{H}_3$), 2.11 (s, 3H, COC$\underline{H}_3$), 2.11 (s, 3H, COC$\underline{H}_3$), 1.41 (d, 3H, J = 6.1 Hz, Rha-H-6); ^{13}C NMR (175 MHz; $CDCl_3$): δ 170.1 (C=O), 169.5 (C=O), 164.0 (C=O), 158.9 (Ar), 149.9 (Ar), 147.5 (Ar), 138.6 (Ar), 137.9 (Ar), 136.6 (Ar), 133.6 (Ar), 130.0 (2 × Ar), 129.8 (Ar), 128.3 (Ar), 127.9 (2 × Ar), 127.7 (Ar), 126.8 (Ar), 125.1 (Ar), 113.3 (Ar), 102.4 (Rha-C-1, $^1J_{C\text{-}H}$ = 156.1 Hz), 86.5 (Xyl-C-1), 77.8 (Rha-C-4), 76.9 (Xyl-C-4), 76.8 (Rha-C-3), 75.2 (Ph$\underline{C}H_2$), 74.8 (Xyl-C-3), 74.3 (Rha-C-2), 74.1 (Ar$\underline{C}H_2$), 72.0 (Rha-C-5), 70.4 (Xyl-C-2), 69.1 (Xyl-C-5), 54.9 (ArO$\underline{C}H_3$), 21.2 (Ar$\underline{C}H_3$), 20.8 (2 × CO$\underline{C}H_3$), 17.9 (Rha-C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{43}H_{47}NNaO_{12}S$: 824.2711; Found 824.2704.



***p*-Tolyl 4-*O*-benzyl-3-*O*-picoloyl-β-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-acetyl-1-thio-β-D-xylopyranoside (3.31):** To a stirred solution of **3.30** (55.5 mg, 69.2 μmol) in dry CH_2Cl_2 (4.0 mL) was added trifluoroacetic acid (40 μL) dropwise at 0 °C. The reaction mixture was stirred for 1.5 h at room temperature under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was

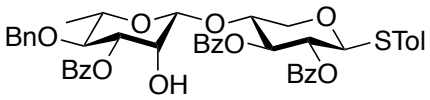
concentrated. The crude residue was purified by flash chromatography (1:6 hexane–EtOAc) to afford **3.31** (26.4 mg, 56%) as a syrup. R_f 0.11 (1:2 hexane–EtOAc); $[\alpha]_D$ +14.0 (*c* 0.58, $CHCl_3$); ^1H NMR (500 MHz; $CDCl_3$): δ 8.80 (d, 1H, *J* = 4.7, 1.7, 0.9 Hz, Ar), 8.10 (d, 1H, *J* = 7.9, 1.0 Hz, Ar), 7.84 (td, 1H, *J* = 7.7, 1.7 Hz, Ar), 7.50 (ddd, 1H, *J* = 7.5, 4.7, 0.9 Hz, Ar), 7.40–7.38 (m, 2H, Ar), 7.23–7.20 (m, 5H, Ar), 7.16–7.14 (m, 2H, Ar), 5.18–5.13 (m, 2H, Rha-H-3, Xyl-H-3), 4.88 (t, 1H, *J* = 9.2 Hz, Xyl-H-2), 4.80 (d, 1H, *J* = 11.0 Hz, PhC$\underline{H}_2$), 4.68 (d, 1H, *J* = 11.0 Hz, PhC$\underline{H}_2$), 4.66 (s, 1H, Rha-H-1), 4.63 (d, 1H, *J* = 9.5 Hz, Xyl-H-1), 4.35 (dd, 1H, *J* = 11.8, 5.3 Hz, Xyl-H-5a), 4.21 (d, 1H, *J* = 3.0 Hz, Rha-H-2), 3.88–3.81 (m, 2H, Xyl-H-4, Rha-H-4), 3.49 (dq, 1H, *J* = 9.3, 6.1 Hz, Rha-H-5), 3.41 (dd, 1H, *J* = 11.7, 10.1 Hz, Xyl-H-5b), 2.36 (s, 3H, ArC$\underline{H}_3$), 2.10 (s, 3H, COC$\underline{H}_3$), 2.08 (s, 3H, COC$\underline{H}_3$), 1.39 (d, 3H, *J* = 6.1 Hz, Rha-H-6); ^{13}C NMR (175 MHz; $CDCl_3$): δ 170.0 (C=O), 169.5 (C=O), 164.4 (C=O), 150.1 (Ar), 147.6 (Ar), 138.5 (Ar), 137.7 (Ar), 137.0 (Ar), 133.5 (Ar), 129.7 (Ar), 128.3 (Ar), 128.0 (2 × Ar), 127.8 (Ar), 127.1 (Ar), 125.3 (Ar), 100.3 (Rha-C-1), 86.5 (Xyl-C-1), 77.5 (Rha-C-4), 76.8 (Rha-C-3), 75.9 (Xyl-C-4), 75.3 (Ph$\underline{C}H_2$), 74.4 (Xyl-C-3), 71.8 (Rha-C-5), 70.3 (Xyl-C-2), 69.4 (Rha-C-2), 68.5 (Xyl-C-5), 21.2 (Ar$\underline{C}H_3$), 20.8 (2 × CO$\underline{C}H_3$), 17.9 (Rha-C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{35}H_{39}NNaO_{11}S$: 704.2136; Found 704.2139.



***p*-Tolyl 3-*O*-benzoyl-4-*O*-benzyl-2-*O*-(4-methoxybenzyl)-β-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-benzoyl-1-thio-β-D-xylopyranoside (3.32):** To a stirred solution of **3.30**

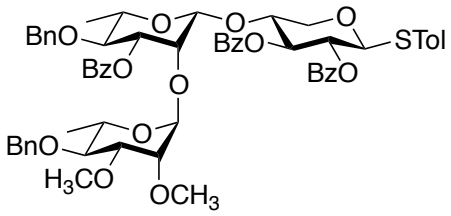
(1.29 g, 1.60 mmol) in CH_3OH (15 mL) was added a solution of $NaOCH_3$ in CH_3OH (3.0 mL, 0.5 M). The reaction mixture was stirred overnight at room temperature, then neutralized by addition of Amberlite® IR-120 (H^+) cation exchange resin, filtered and the filtrate was concentrated. The crude residue in pyridine (10 mL) was added benzoyl chloride (1.12 mL, 9.60 mmol) and 4-(dimethylamino)pyridine (98 mg, 0.80 mmol) successively at room temperature. The reaction mixture was stirred for 5 h at room temperature, then CH_3OH was added and the solution was concentrated. The crude residue was dilute with CH_2Cl_2 (150 mL) and wash with 1N HCl and saturated $NaHCO_3$ (aq.). The organic layer was dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (4:1 hexane–EtOAc) to afford **3.32** (1.18 g, 80%) as a white foam. R_f 0.19 (4:1 hexane–EtOAc); $[\alpha]_D$ +73.2 (*c* 0.34, $CHCl_3$); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.99–7.96 (m, 4H, Ar), 7.90–7.88 (m, 2H, Ar), 7.58–7.51 (m, 3H, Ar), 7.43–7.38 (m, 8H, Ar), 7.22–7.19 (m, 3H, Ar), 7.17–7.13 (m, 4H, Ar), 7.04–7.01 (m, 2H, Ar), 6.41–6.38 (m, 2H, Ar), 5.69 (t, 1H, J = 9.1 Hz, Xyl-H-3), 5.37 (t, 1H, J = 9.3 Hz, Xyl-H-2), 4.89 (d, 1H, J = 9.4 Hz, Xyl-H-1), 4.85 (dd, 1H, J = 9.9, 3.4 Hz, Rha-H-3), 4.76 (d, 1H, J = 12.1 Hz, PhC$\underline{H}_2$), 4.69 (d, 1H, J = 10.9 Hz, ArC$\underline{H}_2$), 4.64 (s, 1H, Rha-H-1), 4.60–4.55 (m, 2H, ArC$\underline{H}_2$, Xyl-H-5a), 4.40 (d, 1H, J = 12.2 Hz, ArC$\underline{H}_2$), 4.05–4.00 (m, 1H, Xyl-H-4), 3.85 (d, 1H, J = 3.4 Hz, Rha-H-2), 3.71 (t, 1H, J = 9.5 Hz, Rha-H-4), 3.64–3.60 (m, 4H, Xyl-H-5b, ArOC$\underline{H}_3$), 3.42 (dq, 1H, J = 9.2, 6.1 Hz, Rha-H-5), 2.37 (s, 3H, ArC$\underline{H}_3$), 1.41 (d, 3H, J = 6.1 Hz, Rha-H-6); ^{13}C NMR (175 MHz; $CDCl_3$): δ 165.7 (C=O), 165.2 (C=O), 165.1 (C=O), 158.8 (Ar), 138.5 (Ar), 137.7 (Ar), 133.6 (Ar), 133.3 (Ar),

133.2 (Ar), 132.9 (Ar), 130.0 (2 × Ar), 129.8 (2 × Ar), 129.7 (2 × Ar), 129.6 (Ar), 129.3 (Ar), 129.2 (Ar), 128.5 (Ar), 128.3 (3 × Ar), 128.2 (Ar), 127.9 (Ar), 127.8 (Ar), 113.2 (Ar), 102.2 (Rha-C-1), 87.0 (Xyl-C-1), 78.1 (Rha-C-4), 76.9 (Xyl-C-4), 75.5 (Rha-C-3), 75.2 (Ph<u>C</u>H_2), 74.7 (Xyl-C-3), 74.6 (Rha-C-2), 74.3 (Ar<u>C</u>H_2), 71.9 (Rha-C-5), 70.7 (Xyl-C-2), 69.2 (Xyl-C-5), 54.9 (ArO<u>C</u>H_3), 21.2 (Ar<u>C</u>H_3), 18.0 (Rha-C-6); HRMS (ESI) Calc. for [M + Na]$^+$ $C_{54}H_{52}NaO_{12}S$: 947.3072; Found 947.3072.



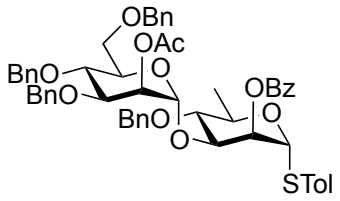
***p*-Tolyl 3-*O*-benzoyl-4-*O*-benzyl-β-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-benzoyl-1-thio-β-D-xylopyranoside (3.33):** To a stirred solution of **3.32** (1.18 g, 1.28 mmol) in dry CH_2Cl_2 (20 mL) was added trifluoroacetic acid (0.2 mL) dropwise at 0 °C. The reaction mixture was stirred for 2 h at room temperature under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (2:1 hexane–EtOAc) to afford **3.33** (0.79 g, 77%) as a syrup. R_f 0.22 (2:1 hexane–EtOAc); $[\alpha]_D$ +60.3 (*c* 0.47, $CHCl_3$); ^{1}H NMR (600 MHz; $CDCl_3$): δ 8.06–8.04 (m, 2H, Ar), 7.98–7.96 (m, 4H, Ar), 7.59–7.50 (m, 3H, Ar), 7.46–7.38 (m, 8H, Ar), 7.23–7.13 (m, 7H, Ar), 5.57 (t, 1H, J = 8.5 Hz, Xyl-H-3), 5.36 (t, 1H, J = 8.6 Hz, Xyl-H-2), 5.02 (dd, 1H, J = 9.7, 2.8 Hz, Rha-H-3), 4.92 (d, 1H, J = 8.7 Hz, Xyl-H-1), 4.70 (d, 1H, J = 10.9 Hz, PhC<u>H</u>$_2$), 4.67 (s, 1H, Rha-H-1), 4.60 (d, 1H, J = 11.0 Hz, PhC<u>H</u>$_2$), 4.51 (dd, 1H, J = 11.9, 5.0 Hz, Xyl-H-5a), 4.11–4.07 (m, 1H, Xyl-H-4), 4.05 (br s, 1H, Xyl-H-4), 3.75 (t, 1H, J = 9.4 Hz, Rha-H-4), 3.62 (dd,

1H, J = 11.9, 9.2 Hz, Xyl-H-5b), 3.46 (dq, 1H, J = 9.2, 6.1 Hz, Rha-H-5), 2.36 (s, 3H, ArC$\underline{H}_3$), 2.21 (br s, 1H, Rha-2-OH), 1.39 (d, 3H, J = 6.1 Hz, Rha-H-6); ^{13}C NMR (175 MHz; $CDCl_3$): δ 165.7 (C=O), 165.6 (C=O), 165.2 (C=O), 138.4 (Ar), 137.6 (Ar), 133.4 (2 × Ar), 133.2 (2 × Ar), 129.8 (Ar), 129.7 (3 × Ar), 129.3 (Ar), 129.0 (Ar), 128.5 (Ar), 128.4 (2 × Ar), 128.3 (Ar), 128.0 (Ar), 127.8 (Ar), 99.9 (Rha-C-1), 86.9 (Xyl-C-1), 77.8 (Rha-C-4), 75.6 (2 × C, Xyl-H-4, Rha-C-3), 75.3 (Ph$\underline{C}H_2$), 74.0 (Xyl-C-3), 71.7 (Rha-C-5), 70.4 (Xyl-C-2), 69.4 (Rha-C-2), 68.0 (Xyl-C-5), 21.2 (Ar$\underline{C}H_3$), 18.0 (Rha-C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{46}H_{44}NaO_{11}S$: 827.2497; Found 827.2495.



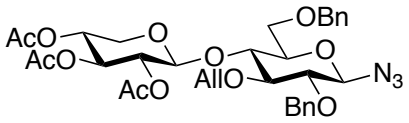
***p*-Tolyl 4-*O*-benzyl-2,3-di-*O*-methyl-α-L-rhamnopyranosyl-(1→2)-3-*O*-benzoyl-4-*O*-benzyl-β-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-benzoyl-1-thio-β-D-xylopyranoside (3.5):** To a stirred solution of acceptor **3.33** (525 mg, 0.652 mmol) and donor **3.10** (739 mg, 1.63 mmol) in dry CH_2Cl_2 (30 mL) was added molecular sieves (3.0 g, 4Å, powder). After stirring for 30 min at room temperature, the reaction mixture was cooled to –50 °C, and then *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.15 mL, 0.64 mmol) was added dropwise. The resulting solution was stirred for 1 h at –50 °C under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (2:1 hexane–EtOAc) to afford **3.5** (619 mg, 89%) as a white foam. R_f 0.27 (2:1 hexane–

EtOAc); $[\alpha]_D$ +34.4 (*c* 0.31, $CHCl_3$); ^1H NMR (600 MHz; $CDCl_3$): δ 7.99–7.95 (m, 6H, Ar), 7.58–7.51 (m, 3H, Ar), 7.43–7.31 (m, 13H, Ar), 7.22–7.20 (m, 3H, Ar), 7.17–7.15 (m, 2H, Ar), 7.12–7.10 (m, 2H, Ar), 5.53 (t, 1H, *J* = 8.8 Hz, Xyl-H-3), 5.32 (t, 1H, *J* = 9.0 Hz, Xyl-H-2), 5.03 (dd, 1H, *J* = 9.7, 2.9 Hz, Rha-H-3), 4.90 (d, 1H, *J* = 11.1 Hz, PhC$\underline{H}_2$), 4.86 (d, 1H, *J* = 1.4 Hz, Rha(OCH_3)-H-1), 4.82 (d, 1H, *J* = 9.1 Hz, Xyl-H-1), 4.68–4.61 (m, 4H, 3 × PhC$\underline{H}_2$, Rha-H-1), 4.44 (dd, 1H, *J* = 11.8, 5.2 Hz, Xyl-H-5a), 4.11–4.07 (m, 3H, Rha(OCH_3)-H-5, Xyl-H-4, Rha-H-2), 3.66 (dd, 1H, *J* = 9.3, 3.3 Hz, Rha(OCH_3)-H-3), 3.64–3.60 (m, 2H, Rha-H-4, Rha(OCH_3)-H-2), 3.54 (s, 3H, OC$\underline{H}_3$), 3.51 (dd, 1H, *J* = 11.8, 9.6 Hz, Xyl-H-5b), 3.44 (dq, 1H, *J* = 9.4, 6.1 Hz, Rha-H-5), 3.39 (t, 1H, *J* = 9.5 Hz, Rha(OCH_3)-H-4), 3.22 (s, 3H, OC$\underline{H}_3$), 2.36 (s, 3H, ArC$\underline{H}_3$), 1.41 (d, 3H, *J* = 6.1 Hz, Rha-H-6), 1.33 (d, 3H, *J* = 6.2 Hz, Rha(OCH_3)-H-6); ^{13}C NMR (175 MHz; $CDCl_3$): δ 165.3 (2 × C=O), 165.0 (C=O), 139.0 (Ar), 138.3 (Ar), 137.5 (Ar), 133.5 (Ar), 133.3 (2 × Ar), 133.2 (Ar), 129.9 (Ar), 129.7 (2 × Ar), 129.6 (Ar), 129.4 (Ar), 129.3 (Ar), 129.2 (Ar), 128.7 (Ar), 128.5 (Ar), 128.3 (3 × Ar), 127.9 (2 × Ar), 127.7 (Ar), 127.4 (Ar), 99.6 (Rha-C-1), 97.5 (Rha(OCH_3)-C-1, $^1J_{C\text{-}H}$ = 170.6 Hz), 86.9 (Xyl-C-1), 80.9 (Rha(OCH_3)-C-3), 80.8 (Rha(OCH_3)-C-4), 78.6 (Rha-C-4), 77.7 (Rha(OCH_3)-C-2), 75.9 (Rha-C-3), 75.2 (Ph$\underline{C}H_2$), 75.0 (Ph$\underline{C}H_2$), 74.6 (Xyl-C-3), 74.3 (Xyl-C-4), 73.8 (Rha-C-2), 71.9 (Rha-C-5), 70.7 (Xyl-C-2), 68.5 (Xyl-C-5), 68.0 (Rha(OCH_3)-C-5), 58.6 (O$\underline{C}H_3$), 57.9 (O$\underline{C}H_3$), 21.2 (Ar$\underline{C}H_3$), 18.0 (Rha-C-6), 17.8 (Rha(OCH_3)-C-6); HRMS (ESI) Calc. for $[M + NH_4]^+$ $C_{61}H_{68}NO_{15}S$: 1086.4304; Found 1086.4306.



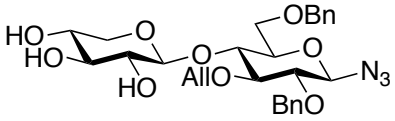
***p*-Tolyl 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-2-*O*-benzoyl-4-*O*-benzyl-1-thio-α-D-rhamnopyranoside (3.6):** To a stirred solution of acceptor **3.11** (307 mg, 0.661 mmol) and donor **3.12** (879 mg, 1.32 mmol) in dry CH_2Cl_2 (12 mL) was added molecular sieves (1.0 g, 4Å, powder). After stirring for 30 min at room temperature, the reaction mixture was cooled to –30 °C, and then *tert*-butyldimethylsilyl trifluoromethanesulfonate (44 μL, 0.64 mmol) was added dropwise. The resulting solution was stirred for 1 h at –30 °C under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (6:1 hexane–EtOAc) to afford **3.6** (465 mg, 75%) as a syrup. R_f 0.17 (6:1 hexane–EtOAc); $[\alpha]_D$ +62.6 (*c* 0.54, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 8.02–8.00 (m, 2H, Ar), 7.59–7.56 (m, 1H, Ar), 7.45–7.42 (m, 2H, Ar), 7.38–7.16 (m, 20H), 7.09–7.08 (m, 2H, Ar), 7.06–7.04 (m, 2H, Ar), 5.64 (dd, 1H, *J* = 3.1, 1.8 Hz, D-Rha-H-2), 5.46 (d, 1H, *J* = 1.5 Hz, D-Rha-H-1), 5.37 (dd, 1H, *J* = 3.1, 1.9 Hz, Man-H-2), 5.20 (d, 1H, *J* = 1.6 Hz, Man-H-1), 4.81 (d, 1H, *J* = 10.9 Hz, PhC$\underline{H}_2$), 4.75 (d, 1H, *J* = 11.2 Hz, PhC$\underline{H}_2$), 4.68 (d, 1H, *J* = 12.1 Hz, PhC$\underline{H}_2$), 4.65 (d, 1H, *J* = 10.9 Hz, PhC$\underline{H}_2$), 4.49 (d, 1H, *J* = 11.2 Hz, PhC$\underline{H}_2$), 4.43 (d, 1H, *J* = 12.1 Hz, PhC$\underline{H}_2$), 4.41 (d, 1H, *J* = 11.2 Hz, PhC$\underline{H}_2$), 4.33 (d, 1H, *J* = 11.2 Hz, PhC$\underline{H}_2$), 4.30–4.25 (m, 2H, D-Rha-H-5, D-Rha-H-3), 3.90 (t, 1H, *J* = 9.6 Hz, Man-H-4), 3.84–3.81 (m, 2H, Man-H-5, Man-H-3),

3.65–3.61 (m, 2H, D-Rha-H-4, Man-H-6a), 3.56 (dd, 1H, J = 11.0, 1.5 Hz, Man-H-6b), 2.30 (s, 3H, ArC$\underline{H}_3$), 2.08 (s, 3H, COC$\underline{H}_3$), 1.34 (d, 3H, J = 6.2 Hz, D-Rha-H-6); ^{13}C NMR (175 MHz; $CDCl_3$): δ 170.2 (C=O), 165.6 (C=O), 138.6 (Ar), 138.3 (Ar), 137.9 (Ar), 137.8 (Ar), 137.7 (Ar), 133.3 (Ar), 132.4 (Ar), 129.9 (Ar), 129.8 (2 × Ar), 129.7 (Ar), 128.5 (2 × Ar), 128.2 (2 × Ar), 128.1 (Ar), 128.0 (Ar), 127.9 (2 × Ar), 127.7 (Ar), 127.6 (Ar), 127.4 (2 × Ar), 127.3 (Ar), 99.6 (Man-C-1, $^1J_{C\text{-}H}$ = 174.4 Hz), 86.0 (D-Rha-C-1), 80.8 (D-Rha-C-4), 77.7 (Man-C-3), 77.3 (D-Rha-C-3), 75.5 (Ph$\underline{C}H_2$), 74.5 (Ph$\underline{C}H_2$), 74.3 (D-Rha-C-2), 73.9 (Man-C-4), 73.4 (Ph$\underline{C}H_2$), 72.4 (Man-C-5), 71.9 (Ph$\underline{C}H_2$), 69.1 (D-Rha-C-5), 69.0 (Man-C-2), 68.3 (Man-C-6), 21.1 (Ar$\underline{C}H_3$), 21.0 (CO$\underline{C}H_3$), 17.9 (D-Rha-C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{56}H_{58}NaO_{11}S$: 961.3592; Found 961.3595.



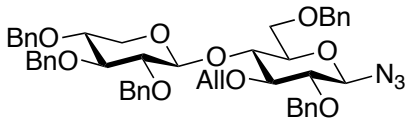
2,3,4-Tri-*O*-acetyl-β-D-xylopyranosyl-(1→4)-3-*O*-allyl-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (3.34): To a stirred solution of acceptor **3.13** (2.04 g, 4.79 mmol) and *p*-tolyl 2,3,4-tri-*O*-acetyl-1-thio-β-D-xylopyranoside **3.14**[16] (2.20 g, 5.75 mmol) in dry CH_2Cl_2 (40 mL) was added molecular sieves (4.0 g, 4Å, powder). After stirring for 30 min at room temperature, the reaction mixture was cooled to 0 °C, and then *N*-iodosuccinimide (1.62 g, 7.19 mmol) and silver trifluoromethanesulfonate (246 mg, 0.957 mmol) were added successively. The resulting solution was stirred for 1 h at room temperature under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was washed with saturated $Na_2S_2O_3$ (aq.) and saturated $NaHCO_3$

(aq.), the aqueous layer was extracted with CH_2Cl_2 (100 mL × 3), dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (3:1 hexane–EtOAc) to afford **3.34** (2.23 g, 68%) as a syrup. R_f 0.40 (2:1 hexane–EtOAc); $[\alpha]_D$ –32.1 (*c* 0.36, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.39–7.27 (m, 10H, Ar), 5.92 (ddt, 1H, *J* = 17.2, 10.3, 5.9 Hz, $OCH_2C\underline{H}=CH_2$), 5.24 (dq,1H, *J* = 17.2, 1.6 Hz, $OCH_2CH=C\underline{H}_2$), 5.15 (dq, 1H, *J* = 10.4, 1.4 Hz, $OCH_2CH=C\underline{H}_2$), 5.03 (t, 1H, *J* = 8.9 Hz, Xyl-H-3), 4.91 (td, 1H, *J* = 9.2, 5.2 Hz, Xyl-H-4), 4.83 (dd, 1H, *J* = 9.0, 7.4 Hz, Xyl-H-2), 4.78 (d, 1H, *J* = 10.7 Hz, $PhC\underline{H}_2$), 4.76 (d, 1H, *J* = 10.7 Hz, $PhC\underline{H}_2$), 4.71 (d, 1H, *J* = 12.0 Hz, $PhC\underline{H}_2$), 4.55 (d, 1H, *J* = 7.4 Hz, Xyl-H-1), 4.53 (d, 1H, *J* = 8.6 Hz, Glc-H-1), 4.48 (d, 1H, *J* = 12.0 Hz, $PhC\underline{H}_2$), 4.35 (ddt, 1H, *J* = 11.8, 5.8, 1.3 Hz, $OC\underline{H}_2CH=CH_2$), 4.23 (ddt, 1H, *J* = 11.9, 5.9, 1.3 Hz, $OC\underline{H}_2CH=CH_2$), 4.06 (dd, 1H, *J* = 11.8, 5.4 Hz, Xyl-H-5a), 3.87 (t, 1H, *J* = 9.5 Hz, Glc-H-4), 3.74–3.70 (m, 2H, Glc-H-6), 3.40 (t, 1H, *J* = 9.1 Hz, Glc-H-3), 3.36 (dt, 1H, *J* = 9.9, 2.5 Hz, Glc-H-5), 3.26 (t, 1H, *J* = 8.9 Hz, Glc-H-2), 3.13 (dd, 1H, *J* = 11.8, 9.5 Hz, Xyl-H-5b), 2.03 (s, 3H, $COC\underline{H}_3$), 2.01 (s, 3H, $COC\underline{H}_3$), 1.96 (s, 3H, $COC\underline{H}_3$); ^{13}C NMR (125 MHz; $CDCl_3$): δ 170.1 (C=O), 169.9 (C=O), 169.3 (C=O), 137.8 (2 × Ar), 134.9 ($OCH_2\underline{C}H=CH_2$), 128.6 (Ar), 128.4 (Ar), 128.2 (Ar), 128.0 (Ar), 127.9 (Ar), 117.2 ($OCH_2CH=\underline{C}H_2$), 100.3 (Xyl-C-1, $^1J_{C\text{-}H}$ = 165.0 Hz), 90.1 (Glc-C-1), 82.5 (Glc-C-3), 81.2 (Glc-C-2), 76.9 (Glc-C-5), 76.1 (Glc-C-4), 75.4 ($Ph\underline{C}H_2$), 74.7 ($O\underline{C}H_2CH=CH_2$), 73.7 ($Ph\underline{C}H_2$), 72.1 (Xyl-C-3), 71.6 (Xyl-C-2), 68.9 (Xyl-C-4), 67.3 (Glc-C-6), 62.3 (Xyl-C-5), 20.8 ($CO\underline{C}H_3$), 20.7 ($CO\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{34}H_{41}N_3NaO_{12}$: 706.2582; Found 706.2568.



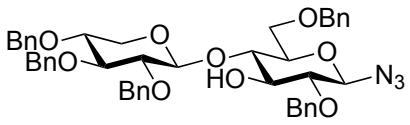
β-D-Xylopyranosyl-(1→4)-3-*O*-allyl-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (3.35): To a stirred solution of **3.34** (2.23 g, 3.26 mmol) in CH_3OH (25 mL) was added a solution of $NaOCH_3$ in CH_3OH (5.0 mL, 0.5 M). The reaction mixture was stirred overnight at room temperature, then neutralized by addition of Amberlite® IR-120 (H^+) cation exchange resin, filtered and the filtrate was concentrated to afford **3.35** (1.82 g, quant.) as a syrup. R_f 0.24 (15:1 CH_2Cl_2–CH_3OH); $[\alpha]_D$ –16.1 (*c* 0.34, CH_3OH); ^1H NMR (700 MHz; CD_3OD): δ 7.38–7.31 (m, 8H, Ar), 7.30–7.26 (m, 2H, Ar), 5.94 (ddt, 1H, J = 17.2, 10.5, 5.8 Hz, $OCH_2C\underline{H}=CH_2$), 5.22 (dq, 1H, J = 17.3, 1.8 Hz, $OCH_2CH=C\underline{H}_2$), 5.09 (dq, 1H, J = 10.4, 1.6 Hz, $OCH_2CH=C\underline{H}_2$), 4.80 (d, 1H, J = 10.9 Hz, $PhC\underline{H}_2$), 4.75 (d, 1H, J = 11.0 Hz, $PhC\underline{H}_2$), 4.66 (d, 1H, J = 8.6 Hz, Glc-H-1), 4.62 (d, 1H, J = 11.7 Hz, $PhC\underline{H}_2$), 4.57 (d, 1H, J = 11.7 Hz, $PhC\underline{H}_2$), 4.43 (ddt, 1H, J = 12.0, 5.5, 1.5 Hz, $OC\underline{H}_2CH=CH_2$), 4.33 (d, 1H, J = 7.7 Hz, Xyl-H-1), 4.19 (ddt, 1H, J = 12.0, 6.0, 1.3 Hz, $OCH_2CH=C\underline{H}_2$), 3.97 (dd, 1H, J = 11.3, 3.8 Hz, Glc-H-6a), 3.85 (dd, 1H, J = 11.3, 1.8 Hz, Glc-H-6b), 3.83–3.79 (m, 2H, Glc-H-4, Xyl-H-5a), 3.59 (ddd, 1H, J = 9.9, 3.8, 1.8 Hz, Glc-H-5), 3.49–3.43 (m, 2H, Glc-H-3, Xyl-H-4), 3.24 (t, 1H, J = 9.0 Hz, Xyl-H-3), 3.20 (t, 1H, J = 8.9 Hz, Glc-H-2), 3.14 (dd, 1H, J = 9.2, 7.7 Hz, Xyl-H-2), 3.04 (dd, 1H, J = 11.5, 10.4 Hz, Xyl-H-5b); ^{13}C NMR (125 MHz; CD_3OD): δ 139.6 (Ar), 139.5 (Ar), 136.8 ($OCH_2\underline{C}H=CH_2$), 129.4 (Ar), 129.3 (Ar), 129.1 (Ar), 128.9 (Ar), 128.8 (Ar), 128.7 (Ar), 116.8 ($OCH_2CH=\underline{C}H_2$), 105.0 (Xyl-C-1), 91.2 (Glc-C-1), 84.2 (Glc-C-3), 82.4 (Glc-C-2), 78.1 (Glc-C-5), 78.0 (Xyl-C-3), 77.7

(Glc-C-4), 76.1 (Ph<u>C</u>H_2), 75.5 (O<u>C</u>H_2CH=CH_2, Xyl-C-2), 74.3 (OCH$_2$C<u>H</u>=CH_2), 71.3 (Xyl-C-4), 69.3 (Glc-C-6), 67.1 (Xyl-C-5); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{28}H_{35}N_3Na$-O_9: 580.2266; Found 580.2255.



2,3,4-Tri-*O*-benzyl-β-D-xylopyranosyl-(1→4)-3-*O*-allyl-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (3.36): To a stirred solution of **3.35** (1.82 g, 3.26 mmol) in dry DMF (15 mL) was added sodium hydride (0.784 g, 19.6 mmol, 60% dispersion in mineral oil) in one portion at 0 °C, After stirring for 30 min, benzyl bromide (1.74 mL, 14.7 mmol) was added dropwise, and the reaction mixture was warmed to room temperature and stirred overnight under an Ar atmosphere. Then, CH_3OH was added at 0 °C and the solution was concentrated. The crude residue was diluted with CH_2Cl_2 (100 mL), washed with saturated $NaHCO_3$ (aq.), dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (6:1 hexane–EtOAc) to afford **3.36** (2.29 g, 85%) as a syrup. R_f 0.20 (6:1 hexane–EtOAc); $[\alpha]_D$ +9.8 (*c* 0.65, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.37–7.25 (m, 25H, Ar), 5.93 (ddt, 1H, *J* = 16.9, 10.7, 6.1 Hz, OCH$_2$C<u>H</u>=CH_2), 5.20 (dq, 1H, *J* = 17.2, 1.8 Hz, OCH$_2$CH=C<u>H</u>$_2$), 5.12 (d, 1H, *J* = 10.3, 1.6 Hz, OCH$_2$C<u>H</u>=CH_2), 4.88–4.70 (m, 7H, 7 × PhC<u>H</u>$_2$), 4.61 (d, 1H, *J* = 11.7 Hz, PhC<u>H</u>$_2$), 4.55–4.53 (m, 2H, Glc-H-1, PhC<u>H</u>$_2$), 4.39–4.35 (m, 3H, PhC<u>H</u>$_2$, OC<u>H</u>$_2$CH=CH_2, Xyl-H-1), 4.19 (ddt, 1H, *J* = 11.7, 6.1, 1.3 Hz, 1H), 3.90–3.86 (m, 2H, Xyl-H-5a, Glc-H-4), 3.78 (dd, 1H, *J* = 11.2, 3.7 Hz, Glc-H-6a), 3.64 (d, 1H, *J* = 11.1, 1.8 Hz, Glc-H-6b), 3.57–3.54

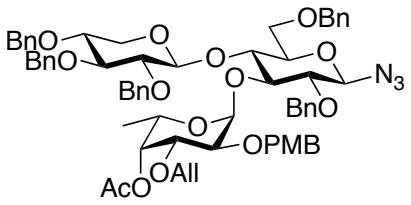
(m, 1H, Xyl-H-4), 3.46 (t, 1H, J = 9.0 Hz, Xyl-H-3), 3.39 (t, 1H, J = 9.1 Hz, Glc-H-3), 3.34 (dt, 1H, J = 9.8, 1.7 Hz, Glc-H-5), 3.27–3.23 (m, 2H, Glc-H-2, Xyl-H-2), 3.03 (t, 1H, J = 11.0 Hz, Xyl-H-5b); ^{13}C NMR (125 MHz; $CDCl_3$): δ 138.6 (Ar), 138.4 (Ar), 138.2 (Ar), 138.0 (2 × Ar), 135.3 ($OCH_2\underline{C}H=CH_2$), 128.5 (Ar), 128.4 (3 × Ar), 128.3 (Ar), 128.2 (Ar), 127.9 (Ar), 127.8 (3 × Ar), 127.7 (Ar), 127.6 (2 × Ar), 117.1 ($O\underline{C}H_2CH=CH_2$), 103.1 (Xyl-C-1), 90.1 (Glc-C-1), 84.1 (Xyl-C-3), 82.8 (Glc-C-3), 82.3 (Xyl-C-2), 81.0 (Glc-C-2), 78.2 (Xyl-C-4), 77.2 (Glc-C-5), 76.0 (Glc-C-4), 75.6 ($Ph\underline{C}H_2$), 75.4 ($Ph\underline{C}H_2$), 75.2 ($Ph\underline{C}H_2$), 74.7 ($O\underline{C}H_2CH=CH_2$), 73.3 ($Ph\underline{C}H_2$), 73.2 ($Ph\underline{C}H_2$), 67.6 (Glc-C-6), 63.9 (Xyl-C-5); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{49}H_{53}N_3NaO_9$: 850.3674; Found 850.3669.



2,3,4-Tri-*O*-benzyl-β-D-xylopyranosyl-(1→4)-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (3.37): To a stirred solution of **3.36** (1.12 g, 1.35 mmol) in dry THF (24 mL), degassed under vacuum, and stirring under an Ar atmosphere, (1,5-cyclooctadiene)bis(methyldiphenylphosphine)iridium (I) hexafluorophosphate catalyst (68.7 mg, 81.2 μmol) was added, followed by further degassing of the reaction mixture. The suspension was stirred for 15 min at 0 °C, and the catalyst was then activated with hydrogen (2 min under hydrogen atmosphere). The excess hydrogen was removed by three cycles of vacuum/Ar. The reaction mixture was then stirred for 2 h at room temperature under an Ar atmosphere. The solvent was then evaporated, and the residue was dissolved in acetone–water (10:1, 11 mL) before HgO (410 mg, 1.89 mmol) and $HgCl_2$ (440 mg,

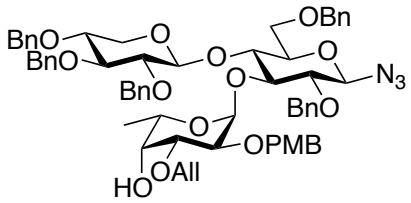
1.62 mmol) were added. The reaction mixture was stirred for 2 h at room temperature, then the solvent was concentrated, and the residue was diluted with EtOAc (150 mL), washed with 10% KI, saturated $Na_2S_2O_3$ (aq.) and water. The aqueous layers were extracted with EtOAc (100 mL), and the combined organic layers were dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (4:1 hexane–EtOAc) to afford **3.37** (872 mg, 82%) as a syrup. R_f 0.26 (4:1 hexane–EtOAc); $[\alpha]_D$ +5.6 (*c* 0.42, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.41–7.40 (m, 2H, Ar), 7.34–7.26 (m, 20H, Ar), 7.23–7.21 (m, 2H, Ar), 4.89 (d, 1H, J = 11.0 Hz, PhC$\underline{H}_2$), 4.88 (d, 1H, J = 10.9 Hz, PhC$\underline{H}_2$), 4.84 (d, 1H, J = 10.9 Hz, PhC$\underline{H}_2$), 4.79 (d, 1H, J = 10.9 Hz, PhC$\underline{H}_2$), 4.78 (d, 1H, J = 11.0 Hz, PhC$\underline{H}_2$), 4.71 (d, 2H, J = 11.1 Hz, 2 × PhC$\underline{H}_2$), 4.59 (d, 1H, J = 11.7 Hz, PhC$\underline{H}_2$), 4.57 (d, 1H, J = 8.6 Hz, Glc-H-1), 4.42 (d, 1H, J = 12.0 Hz, PhC$\underline{H}_2$), 4.30 (d, 1H, J = 12.0 Hz, PhC$\underline{H}_2$), 4.22 (d, 1H, J = 7.8 Hz, Xyl-H-1), 3.96 (s, 1H, 3-OH), 3.91 (dd, 1H, J = 11.6, 5.4 Hz, Xyl-H-5a), 3.67 (td, 1H, J = 8.9, 0.4 Hz, Glc-H-3), 3.63–3.63 (m, 2H, Glc-H-6), 3.60–3.57 (m, 2H, Glc-H-4, Xyl-H-4), 3.50 (t, 1H, J = 9.0 Hz, Xyl-H-3), 3.48–3.45 (m, 1H, Glc-H-5), 3.30 (dd, 1H, J = 9.2, 7.9 Hz, Xyl-H-2), 3.25 (t, 1H, J = 8.8 Hz, Glc-H-2), 3.14 (dd, 1H, J = 11.6, 10.6 Hz, Xyl-H-5b); ^{13}C NMR (125 MHz; $CDCl_3$): δ 138.4 (Ar), 138.1 (2 × Ar), 138.0 (2 × Ar), 128.5 (Ar), 128.4 (2 × Ar), 128.1 (Ar), 128.0 (Ar), 127.9 (Ar), 127.8 (3 × Ar), 127.7 (4 × Ar), 103.7 (Xyl-C-1), 89.6 (Glc-C-1), 83.9 (Xyl-C-3), 81.5 (Xyl-C-2), 80.9 (Glc-C-2), 79.3 (Glc-C-4), 77.6 (Xyl-C-4), 76.2 (Glc-C-5), 75.7 (Ph$\underline{C}H_2$), 75.5 (Glc-C-3), 75.4 (PhC$\underline{H}_2$), 74.9 (PhC$\underline{H}_2$), 73.5 (PhC$\underline{H}_2$), 73.3

(PhC$\underline{H}_2$), 67.7 (Glc-C-6), 64.1 (Xyl-C-5); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{46}H_{49}N_3NaO_9$: 810.3361; Found 810.3352.



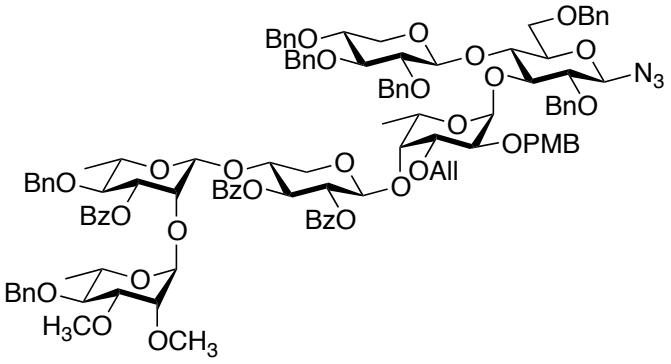
2,3,4-Tri-*O*-benzyl-β-D-xylopyranoside-(1→4)-[4-*O*-acetyl-3-*O*-allyl-2-*O*-(4-methoxybenzyl)-α-L-fucopyranosyl-(1→3)]-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (3.7): To a stirred solution of acceptor **3.37** (0.804 g, 1.02 mmol) and donor **3.15** (1.04 g, 2.20 mmol) in dry Et_2O (30 mL) was added molecular sieves (3.0 g, 4Å, powder). After stirring for 30 min at room temperature, the methyl trifluoromethanesulfonate (0.42 mL, 3.7 mmol) was added dropwise. The resulting solution was stirred for 24 h at room temperature under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (4:1 hexane–EtOAc) to afford **3.7** (1.03 g, 89%) as a syrup. R_f 0.25 (4:1 hexane–EtOAc); $[\alpha]_D$ –21.3 (*c* 0.39, $CHCl_3$); ^1H NMR (700 MHz; $CDCl_3$): δ 7.35–7.26 (m, 21H), 7.23–7.21 (m, 2H, Ar), 7.20–7.19 (m, 2H, Ar), 7.06–7.03 (m, 2H, Ar), 6.65–6.63 (m, 2H, Ar), 5.88 (ddt, 1H, J = 17.2, 10.5, 5.3 Hz, $OCH_2C\underline{H}=CH_2$), 5.51 (d, 1H, J = 3.7 Hz, Fuc-H-1), 5.27 (dq, 1H, J = 17.2, 1.7 Hz, $OCH_2CH=C\underline{H}_2$), 5.14–5.11 (m, 2H, Fuc-H-4, $OCH_2CH=C\underline{H}_2$), 4.85–4.80 (m, 4H, Fuc-H-5, 3 × PhC$\underline{H}_2$), 4.75 (d, 1H, J = 11.1 Hz, PhC$\underline{H}_2$), 4.73 (d, 1H, J = 11.7 Hz, PhC$\underline{H}_2$), 4.70 (d, 1H, J = 11.1 Hz, PhC$\underline{H}_2$), 4.67 (d, 1H, J = 11.1 Hz, PhC$\underline{H}_2$), 4.64 (d, 1H, J = 11.5 Hz, ArC$\underline{H}_2$), 4.62 (d, 1H, J = 11.9 Hz,

PhC$\underline{H}_2$), 4.57 (d, J = 8.6, Glc-H-1), 4.57 (d, 1H, J = 11.7 Hz, PhC$\underline{H}_2$), 4.54 (d, 1H, J = 11.5 Hz, ArC$\underline{H}_2$), 4.39 (d, 1H, J = 11.5 Hz, PhC$\underline{H}_2$), 4.38 (d, 1H, J = 7.9 Hz, Xyl-H-1), 4.07 (ddt, 1H, J = 12.4, 5.3, 1.5 Hz, OC$\underline{H}_2$CH=CH$_2$), 4.04 (t, 1H, J = 9.7 Hz, Glc-H-4), 3.99 (dd, 1H, J = 10.1, 3.3 Hz, Fuc-H-3), 3.92–3.86 (m, 3H, OC$\underline{H}_2$CH=CH$_2$, Glc-H-6a, Glc-H-3), 3.77 (dd, 1H, J = 11.7, 5.5 Hz, Xyl-H-5a), 3.71–3.69 (m, 4H, ArOC$\underline{H}_3$, Fuc-H-2), 3.62 (dd, 1H, J = 11.3, 1.6 Hz, Glc-H-6b), 3.45 (ddd, 1H, J = 10.7, 9.0, 5.4 Hz, Xyl-H-4), 3.42–3.35 (m, 3H, Glc-H-2, Xyl-H-3, Glc-H-5), 3.05 (dd, 1H, J = 8.9, 8.2 Hz, Xyl-H-2), 2.94 (dd, 1H, J = 11.6, 10.8 Hz, Xyl-H-5b), 2.12 (s, 3H, COC$\underline{H}_3$), 1.06 (d, 3H, J = 6.6 Hz, Fuc-H-6); ^{13}C NMR (125 MHz; $CDCl_3$): δ 170.7 (C=O), 159.1 (Ar), 138.4 (Ar), 138.1 (Ar), 138.0 (Ar), 137.9 (Ar), 135.0 (OCH$_2$C$\underline{H}$=CH$_2$), 130.3 (Ar), 129.9 (Ar), 128.5 (2 × Ar), 128.4 (Ar), 128.0 (Ar), 127.9 (2 × Ar), 127.8 (Ar), 127.7 (4 × Ar), 127.5 (Ar), 127.1 (Ar), 116.3 (OCH$_2$CH=C$\underline{H}_2$), 113.5 (Ar), 103.2 (Xyl-C-1), 97.6 (Fuc-C-1, $^1J_{C\text{-}H}$ = 174.9 Hz), 90.2 (Glc-C-1), 84.1 (Xyl-C-3), 82.6 (Glc-C-2), 82.5 (Xyl-C-2), 78.4 (Xyl-C-4), 77.3 (Glc-C-5), 76.5 (Fuc-C-3), 75.8 (PhC$\underline{H}_2$), 75.3 (PhC$\underline{H}_2$), 74.8 (Glc-C-3), 74.1 (Glc-C-4), 74.0 (PhC$\underline{H}_2$), 73.6 (Fuc-C-2), 73.5 (PhC$\underline{H}_2$), 73.4 (ArC$\underline{H}_2$, PhC$\underline{H}_2$), 71.4 (Fuc-C-4), 70.4 (OC$\underline{H}_2$CH=CH$_2$), 67.3 (Glc-C-6), 64.2 (Fuc-C-5), 64.1 (Xyl-C-5), 55.2 (ArOC$\underline{H}_3$), 20.9 (COC$\underline{H}_3$), 16.1 (Fuc-C-6); HRMS (ESI) Calc. for $[M + NH_4]^+$ $C_{65}H_{77}N_4O_{15}$: 1153.5380; Found 1153.5379.



2,3,4-Tri-*O*-benzyl-β-D-xylopyranoside-(1→4)-[3-*O*-allyl-2-*O*-(4-methoxybenzyl)-α-L-fucopyranosyl-(1→3)]-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (3.38): To a stirred solution of **3.7** (1.03 g, 0.906 mmol) in CH_3OH (15 mL) was added a solution of $NaOCH_3$ in CH_3OH (3.0 mL, 0.5 M). The reaction mixture was stirred overnight at room temperature, then neutralized by addition of Amberlite® IR-120 (H^+) cation exchange resin, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (4:1 hexane–EtOAc) to afford **3.38** (0.99 g, quant.) as a syrup. R_f 0.25 (4:1 hexane–EtOAc); $[\alpha]_D$ –29.5 (*c* 0.39, $CHCl_3$); ^1H NMR (700 MHz; $CDCl_3$): δ 7.35–7.25 (m, 21H, Ar), 7.24–7.23 (m, 2H, Ar), 7.19–7.18 (m, 2H, Ar), 7.03–7.01 (m, 2H, Ar), 6.65–6.63 (m, 2H, Ar), 5.92 (ddt, 1H, *J* = 17.1, 10.9, 5.6 Hz, $OCH_2C\underline{H}=CH_2$), 5.54 (d, 1H, *J* = 3.7 Hz, Fuc-H-1), 5.28 (dq, 1H, *J* = 17.2, 1.6 Hz, $OCH_2CH=C\underline{H}_2$), 5.15 (dq, 1H, *J* = 10.5, 1.4 Hz, $OCH_2CH=C\underline{H}_2$), 4.86 (d, 1H, *J* = 11.2 Hz, $PhC\underline{H}_2$), 4.82 (s, 2H, 2 × $PhC\underline{H}_2$), 4.73–4.68 (m, 5H, Fuc-H-5, 4 × $PhC\underline{H}_2$), 4.62 (d, 1H, *J* = 11.9 Hz, $PhC\underline{H}_2$), 4.58 (d, 1H, *J* = 8.6 Hz, Glc-H-1), 4.56 (d, 1H, *J* = 11.8 Hz, $PhC\underline{H}_2$), 4.51 (s, 2H, 2 × $PhC\underline{H}_2$), 4.39 (d, 1H, *J* = 12.0 Hz, $PhC\underline{H}_2$), 4.37 (d, 1H, *J* = 8.0 Hz, Xyl-H-1), 4.09 (ddt, 1H, *J* = 12.7, 5.2, 1.5 Hz, $OC\underline{H}_2CH=CH_2$), 4.06–4.03 (m, 2H, $OCH_2CH=C\underline{H}_2$, Glc-H-4), 3.93 (t, 1H, *J* = 9.2 Hz, Glc-H-3), 3.90–3.88 (m, 2H, Glc-H-6a, Fuc-H-3), 3.74 (dd, 1H, *J* = 11.7, 4.9 Hz, Xyl-H-5a), 3.71–3.69 (m, 4H, $ArOC\underline{H}_3$, Fuc-H-2), 3.65 (t, 1H, *J* = 1.5 Hz, Fuc-H-4), 3.62 (dd, 1H, *J*

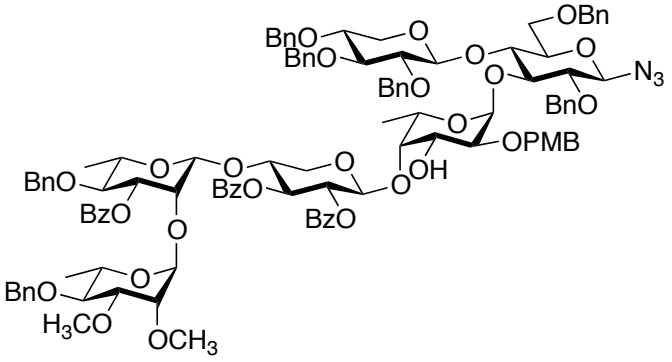
= 11.2, 1.4 Hz, Glc-H-6b), 3.42 (t, 1H, *J* = 8.9 Hz, Glc-H-2), 3.39–3.35 (m, 3H, Xyl-H-3, Glc-H-5, Xyl-H-4), 3.07 (t, 1H, *J* = 8.3 Hz, Xyl-H-2), 2.94 (dd, 1H, *J* = 11.5, 10.3 Hz, Xyl-H-5b), 2.30 (s, 1H, Fuc-4-OH), 1.22 (d, 3H, *J* = 6.7 Hz, Fuc-H-6); ^{13}C NMR (125 MHz; $CDCl_3$): δ 159.1 (Ar), 138.4 (Ar), 138.1 (2 × Ar), 137.9 (2 × Ar), 135.0 ($OCH_2\underline{C}H=CH_2$), 130.2 (Ar), 129.7 (Ar), 128.5 (2 × Ar), 128.4 (3 × Ar), 128.0 (Ar), 127.9 (2 × Ar), 127.7 (Ar), 127.6 (2 × Ar), 127.5 (Ar), 126.9 (Ar), 116.6 ($OCH_2CH=\underline{C}H_2$), 113.6 (Ar), 103.1 (Xyl-C-1), 97.1 (Fuc-C-1), 90.2 (Glc-C-1), 84.0 (Xyl-C-3), 82.6 (2 × C, Glc-C-2, Xyl-C-2), 78.2 (Xyl-C-4), 78.0 (Fuc-C-3), 77.3 (Glc-C-5), 75.8 ($Ph\underline{C}H_2$), 75.3 ($Ph\underline{C}H_2$), 74.5 (Glc-C-3), 74.0 (Glc-C-4), 73.9 (2 × C, Fuc-C-2, $Ph\underline{C}H_2$), 73.4 (2 × C, $Ph\underline{C}H_2$), 73.0 ($Ar\underline{C}H_2$), 70.9 ($O\underline{C}H_2CH=CH_2$), 70.5 (Fuc-C-4), 67.3 (Glc-C-6), 64.6 (Fuc-C-5), 64.0 (Xyl-C-5), 55.2 ($ArO\underline{C}H_3$), 16.2 (Fuc-C-6); HRMS (ESI) Calc. for $[M + NH_4]^+$ $C_{63}H_{75}N_4O_{14}$: 1111.5274; Found 1111.5271.



4-*O*-Benzyl-2,3-di-*O*-methyl-α-L-rhamnopyranosyl-(1→2)-3-*O*-benzoyl-4-*O*-benzyl-β-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-3-*O*-allyl-2-*O*-(4-methoxybenzyl)-α-L-fucopyranosyl-(1→3)-[2,3,4-tri-*O*-benzyl-β-D-xylopyranoside-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (3.39): To a stirred solution of

acceptor **3.38** (359 mg, 328 μmol) and donor **3.5** (574 mg, 536 μmol) in dry CH_2Cl_2 (20 mL) was added molecular sieves (2.0 g, 4Å, powder). After stirring for 30 min at room temperature, the reaction mixture was cooled to 0 °C, and then *N*-iodosuccinimide (146 mg, 649 μmol) and silver trifluoromethanesulfonate (16.9 mg, 65.6 μmol) were added successively. The resulting solution was stirred for 2 h at room temperature under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was washed with saturated $Na_2S_2O_3$ (aq.) and saturated $NaHCO_3$ (aq.), the aqueous layer was extracted with CH_2Cl_2 (50 mL × 3), dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (2:1 hexane–EtOAc) to afford **3.39** (505 mg, 76%) as a syrup. R_f 0.37 (2:1 hexane–EtOAc); $[\alpha]_D$ –10.2 (*c* 0.20, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 8.02–8.01 (m, 2H), 7.99–7.97 (m, 2H), 7.93–7.92 (m, 2H), 7.57–7.54 (m, 1H), 7.43–7.38 (m, 4H), 7.34–7.15 (m, 39H), 6.99–6.96 (m, 2H), 6.52–6.50 (m, 2H), 5.90 (ddt, 1H, *J* = 17.2, 10.5, 5.3 Hz), 5.44 (d, 1H, *J* = 3.6 Hz, Fuc-H-1), 5.39 (t, 1H, *J* = 6.1 Hz), 5.32 (dd, 1H, *J* = 6.1, 4.7 Hz), 5.27 (dq, 1H, *J* = 17.2, 1.7 Hz), 5.06 (dd, 1H, *J* = 9.7, 3.0 Hz), 5.02 (dq, 1H, *J* = 10.4, 1.5 Hz), 4.87–4.76 (m, 8H, L-Rha(Bz)-H-1, L-Rha(OCH_3)-H-1, Xyl(Bz)-H-1), 4.70–4.55 (m, 11H, Glc-H-1), 4.50 (d, 1H, *J* = 11.6 Hz), 4.41 (dd, 1H, *J* = 12.6, 4.1 Hz), 4.37 (d, 1H, *J* = 12.0 Hz), 4.35 (d, 1H, *J* = 8.0 Hz, Xyl(Bn)-H-1), 4.18 (dq, 1H, *J* = 9.7, 6.2 Hz), 4.13–4.09 (m, 2H), 4.07-4.04 (m, 1H), 4.01 (t, 1H, *J* = 9.6 Hz), 3.93–3.90 (m, 2H), 3.88–3.85 (m, 3H), 3.74 (dd, 1H, *J* = 11.8, 5.5 Hz), 3.70–3.59 (m, 8H), 3.56–3.48 (m, 5H), 3.39–3.31 (m, 5H), 3.14 (s, 3H), 2.98 (t, 1H, *J* = 8.4 Hz), 2.91 (t, 1H, *J* = 11.0 Hz), 1.39 (d, 3H, *J* = 6.1 Hz), 1.32 (d, 3H, *J*

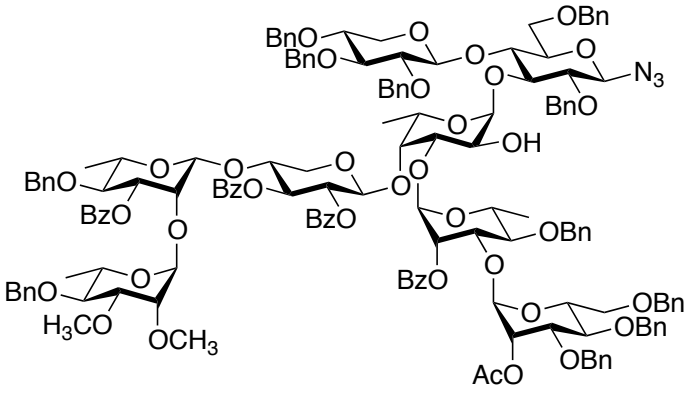
= 6.2 Hz), 1.07 (d, 3H, J = 6.6 Hz); ^{13}C NMR (175 MHz; $CDCl_3$): δ 165.4 (2 × C), 165.1, 158.8, 138.9, 138.5, 138.1 (2 × C), 138.0, 137.9 (2 × C), 137.6, 135.1, 133.5, 133.3, 133.2, 130.4, 129.9, 129.8 (2 × C), 129.6, 129.5, 129.4, 129.3, 128.5 (2 × C), 128.4 (2 × C), 128.3 (3 × C), 128.2, 128.0 (2 × C), 127.9 (2 × C), 127.8 (3 × C), 127.7 (2 × C), 127.6 (2 × C), 127.5 (2 × C), 127.4, 127.0, 116.4, 113.3, 103.0 (Xyl(Bn)-C-1), 100.6 (Xyl(Bz)-C-1), 98.2 (L-Rha(OCH_3)-C-1), 98.1 (L-Rha(Bz)-C-1), 97.7 (Fuc-C-1), 90.2 (Glc-C-1), 84.0, 82.6, 82.5, 81.1, 80.8, 79.8, 78.7, 78.0, 77.9, 77.8, 77.3, 77.2, 76.5, 76.2, 75.8, 75.3, 75.2, 75.0, 74.7, 74.0, 73.9, 73.8, 73.5, 73.4, 73.2, 72.0, 71.6, 70.6, 70.4, 70.2, 68.2, 67.3, 65.5, 63.9, 62.6, 58.5, 57.9, 55.0, 18.1, 17.7, 16.4; HRMS (ESI) Calc. for $[M + NH_4]^+$ $C_{117}H_{131}N_4O_{29}$: 2055.8894; Found 2055.8893.



4-*O*-Benzyl-2,3-di-*O*-methyl-α-L-rhamnopyranosyl-(1→2)-3-*O*-benzoyl-4-*O*-benzyl-β-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-2-*O*-(4-methoxybenzyl)-α-L-fucopyranosyl-(1→3)-[2,3,4-tri-*O*-benzyl-β-D-xylopyranoside-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (3.40): To a stirred solution of **3.39** (505 mg, 248 μmol) in dry THF (20 mL), degassed under vacuum, and stirring under an Ar atmosphere, (1,5-cyclooctadiene)bis(methyldiphenylphosphine)iridium (I)

hexafluorophosphate catalyst (12.6 mg, 14.9 μmol) was added, followed by further degassing of the reaction mixture. The suspension was stirred for 15 min at 0 °C, and the catalyst was then activated with hydrogen (2 min under hydrogen atmosphere). The excess hydrogen was removed by three cycles of vacuum/Ar. The reaction mixture was then stirred overnight at room temperature under an Ar atmosphere. The solvent was then evaporated, and the residue was dissolved in acetone–water (10:1, 11 mL) before HgO (75.2 mg, 347 μmol) and $HgCl_2$ (80.9 mg, 298 μmol) were added. The reaction mixture was stirred for 2 h at room temperature, then the solvent was concentrated, and the residue was diluted with EtOAc (100 mL), washed with 10% KI, saturated $Na_2S_2O_3$ (aq.) and water. The aqueous layers were extracted with EtOAc (100 mL), and the combined organic layers were dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (3:2 hexane–EtOAc) to afford **3.40** (397 mg, 80%) as a white solid. R_f 0.29 (3:2 hexane–EtOAc); $[\alpha]_D$ –22.0 (*c* 0.47, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.95–7.94 (m, 2H), 7.91–7.89 (m, 4H), 7.55–7.53 (m, 1H), 7.50–7.48 (m, 1H), 7.44–7.42 (m, 1H), 7.40–7.24 (m, 30H), 7.19–7.16 (m, 9H), 7.13–7.12 (m, 2H), 7.10–7.08 (m, 2H), 6.69–6.67 (m, 2H), 5.50 (t, 1H, *J* = 9.1 Hz), 5.47 (d, 1H, *J* = 3.7 Hz, Fuc-H-1), 5.38 (dd, 1H, *J* = 9.3, 7.4 Hz), 5.00 (dd, 1H, *J* = 9.7, 3.0 Hz), 4.86–4.76 (m, 5H, L-Rha(OCH_3)-H-1), 4.71–4.53 (m, 14H, L-Rha(Bz)-H-1, Xyl(Bz)-H-1), 4.52 (d, 1H, *J* = 8.6 Hz, Glc-H-1), 4.37 (d, 1H, *J* = 11.9 Hz), 4.34 (d, 1H, *J* = 8.0 Hz, Xyl(Bn)-H-1), 4.27 (dd, 1H, *J* = 11.9, 5.2 Hz), 4.13–3.98 (m, 5H), 3.91–3.86 (m, 2H), 3.79 (t, 1H, *J* = 9.2 Hz), 3.72 (s, 3H), 3.62–3.54 (m, 6H), 3.50–3.47 (m, 4H), 3.45–3.41 (m, 2H), 3.38–3.30 (m, 5H), 3.19

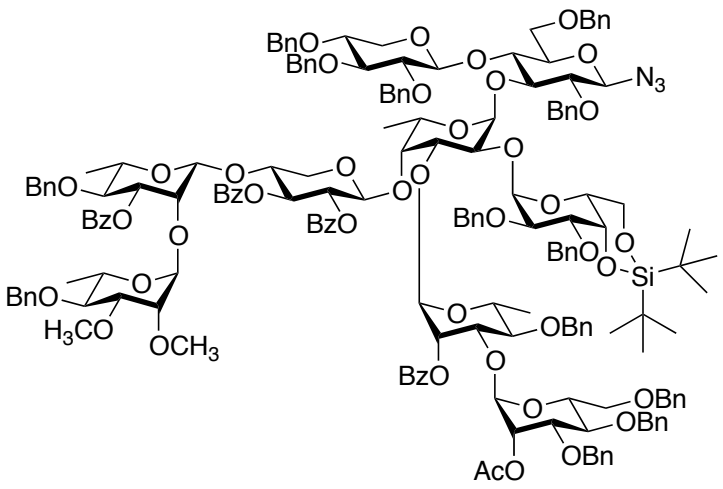
(s, 3H), 2.99–2.93 (m, 2H), 1.40 (d, 3H, J = 6.1 Hz), 1.29 (d, 3H, J = 6.2 Hz), 0.87 (d, 3H, J = 6.6 Hz); ^{13}C NMR (175 MHz; $CDCl_3$): δ 165.3, 165.1, 165.0, 159.0, 139.0, 138.5, 138.1, 138.0, 137.9, 137.4, 133.5, 133.3, 133.1, 130.6, 129.8, 129.7 (2 × C), 129.6, 129.4, 129.2, 129.1, 128.5 (2 × C), 128.4 (3 × C), 128.3 (4 × C), 128.0, 127.9 (2 × C), 127.8 (2 × C), 127.7 (2 × C), 127.6 (3 × C), 127.5, 127.4, 126.9, 113.5, 103.1 (Xyl(Bn)-C-1), 102.5 (Xyl(Bz)-C-1), 99.8 (L-Rha(Bz)-C-1), 97.6 (L-Rha(OCH_3)-C-1), 97.5 (Fuc-C-1), 90.1 (Glc-C-1), 85.6, 84.0, 82.5, 82.2, 81.0, 80.7, 78.5, 78.2, 77.7, 77.3, 76.1, 75.9, 75.8, 75.2, 75.1, 75.0 (2 × C), 74.3, 74.1, 73.9 (2 × C), 73.6, 73.4, 73.3, 73.1, 72.0, 71.9, 69.0, 68.0, 67.2, 65.1, 64.9, 63.9, 58.6, 57.8, 55.2, 18.1, 17.9, 16.0; HRMS (ESI) Calc. for $[M + Na]^+$ $C_{114}H_{123}N_3NaO_{29}$: 2020.8135; Found 2020.8131.



4-*O*-Benzyl-2,3-di-*O*-methyl-α-L-rhamnopyranosyl-(1→2)-3-*O*-benzoyl-4-*O*-benzyl-β-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-[2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-2-*O*-benzoyl-4-*O*-benzyl-α-D-rhamnopyranosyl-(1→3)]-α-L-fucopyranosyl-(1→3)-[2,3,4-tri-*O*-benzyl-β-D-xylopyranoside-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (3.42): To a stirred solution of acceptor **3.40** (62.0 mg, 31.0 μmol) and donor **3.6** (72.8 mg, 77.5 μmol) in dry Et_2O (6.0 mL) was added

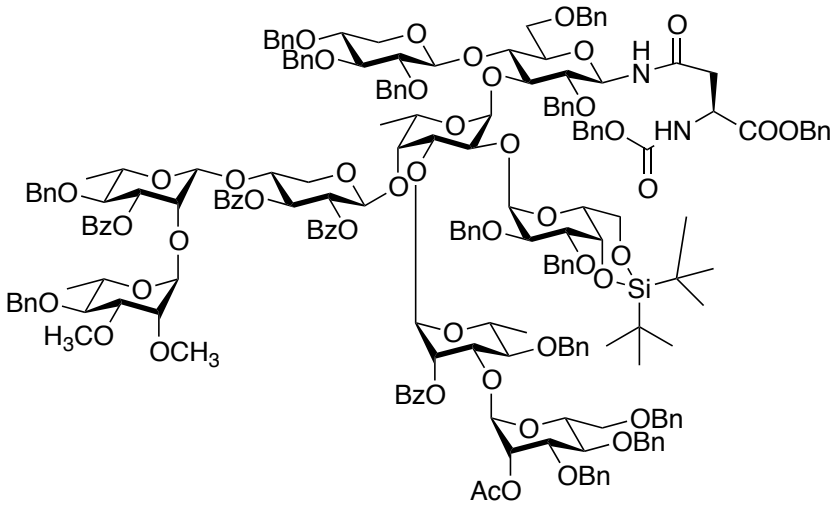
molecular sieves (600 mg, 4Å, powder). After stirring for 30 min at room temperature, the methyl trifluoromethanesulfonate (14.6 μL, 129 μmol) was added dropwise. The resulting solution was stirred for 4 days at room temperature under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (2:1 hexane–EtOAc) to afford **3.41** with methylated acceptor as inseparable impurity. To a stirred solution of the mixture was added dry CH_2Cl_2 (5.0 mL) was added trifluoroacetic acid (50 μL) dropwise at 0 °C. The reaction mixture was stirred for 3.5 h at room temperature under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (2:1 hexane–EtOAc) to afford **3.42** (46.8 mg, 56% over two steps) as a syrup. R_f 0.57 (3:2 hexane–EtOAc); $[\alpha]_D$ –21.4 (*c* 0.69, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 8.02–8.01 (m, 2H), 7.96–7.95 (m, 4H), 7.88–7.87 (m, 2H), 7.57–7.52 (m, 2H), 7.46–7.44 (m, 1H), 7.41–7.10 (m, 62H), 7.04–7.02 (m, 1H), 5.59 (dd, 1H, J = 1.9, 0.2 Hz), 5.51 (t, 1H, J = 8.4 Hz), 5.40 (dd, 1H, J = 8.7, 6.7 Hz), 5.33 (d, 1H, J = 3.0 Hz, Fuc-H-1), 5.32 (dd, 1H, J = 2.9, 1.9 Hz), 5.23 (s, 1H, D-Rha-H-1), 5.13 (d, 1H, J = 0.6 Hz, Man-H-1), 4.97 (dd, 1H, J = 9.7, 3.0 Hz), 4.88 (d, 1H, J = 1.1 Hz, L-Rha(OCH_3)-H-1), 4.81–4.36 (m, 28H, Xyl(Bz)-H-1, L-Rha(Bz)-H-1, Glc-H-1), 4.31–4.27 (m, 2H, Xyl(Bn)-H-1), 4.24 (d, 1H, J = 11.1 Hz), 4.15 (td, 1H, J = 8.4, 5.3 Hz), 4.07–4.03 (m, 2H), 3.99–3.81 (m, 8H), 3.73–3.71 (m, 2H), 3.59–3.44 (m, 9H), 3.36–3.25 (m, 7H), 3.19 (s, 3H), 3.00 (t, 1H, J = 8.6 Hz), 2.91 (t, 1H, J = 11.2 Hz), 2.00 (s, 3H), 1.31 (d, J = 6.2 Hz, 2H), 1.18 (d, J = 5.9 Hz, 3H), 1.17 (d, J = 5.8

Hz, 3H), 1.04 (d, J = 6.7 Hz, 2H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 170.1, 165.6, 165.5, 165.3, 165.1, 139.1, 138.7, 138.5, 138.4 (2 × C), 138.2, 138.1, 138.0, 137.9, 137.7, 137.5, 133.4, 133.3, 133.2, 132.8, 130.0, 129.8, 129.7 (2 × C), 129.6 (2 × C), 129.5, 128.6, 128.5 (2 × C), 128.4 (3 × C), 128.3 (3 × C), 128.2 (3 × C), 128.1 (2 × C), 128.0, 127.9 (3 × C), 127.8 (2 × C), 127.7 (4 × C), 127.6 (2 × C), 127.5 (3 × C), 127.4 (3 × C), 127.3, 103.4 (Xyl(Bn)-C-1), 101.2 (Xyl(Bz)-C-1), 99.7 (2 × C, L-Rha(Bz)-C-1, Man-C-1), 99.0 (D-Rha-C-1, $^1J_{C\text{-}H}$ = 172.3 Hz), 97.8 (Fuc-C-1), 97.7 (L-Rha(OCH_3)-C-1), 90.1 (Glc-C-1), 84.0, 82.5, 82.4, 80.9, 80.8, 80.6, 79.5, 78.6 (2 × C), 78.2, 78.0, 77.8, 77.3, 75.9, 75.8, 75.2, 75.0, 74.9 (3 × C), 74.6, 74.5, 74.4, 74.2, 73.9, 73.4, 73.2 (2 × C), 73.1, 72.9, 72.3, 71.8 (2 × C), 71.7, 69.1, 68.3, 68.1, 68.0, 67.9, 67.2, 66.0, 64.2, 63.8, 58.6, 57.7, 21.0, 18.6, 18.0 (2 × C), 16.7; HRMS (ESI) Calc. for $[M + 2NH_4]^{+2}$ $C_{155}H_{173}N_5O_{39}$: 1364.0848; Found 1364.0842.



4-*O*-Benzyl-2,3-di-*O*-methyl-α-L-rhamnopyranosyl-(1→2)-3-*O*-benzoyl-4-*O*-benzyl-β-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-[2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-2-*O*-benzoyl-4-*O*-benzyl-α-D-rhamnopyranosyl-(1→3)]-[2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranosyl-(1→2)]-α-L-fucopyranosyl-(1→3)-[2,3,4-tri-*O*-benzyl-β-D-xylopyranoside-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (3.43): To a stirred solution of acceptor **3.42** (40.5 mg, 15.0 μmol) and *p*-tolyl 2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranoside **3.4**[15] (36.4 mg, 60.0 μmol) in dry Et_2O (5.0 mL) was added molecular sieves (500 mg, 4Å, powder). After stirring for 30 min at room temperature, the methyl trifluoromethanesulfonate (11.3 μL, 100 μmol) was added dropwise. The resulting solution was stirred for 24 h at room temperature under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (2:1 hexane–EtOAc, then 2:1 hexane–Actone) to afford **3.43** (35.5 mg, 74%) as a syrup. R_f 0.38 (2:1 hexane–EtOAc); $[\alpha]_D$ –37.4 (*c* 0.50, $CHCl_3$); ^1H NMR (700 MHz; $CDCl_3$): δ 7.97–7.93 (m, 6H), 7.82–7.80

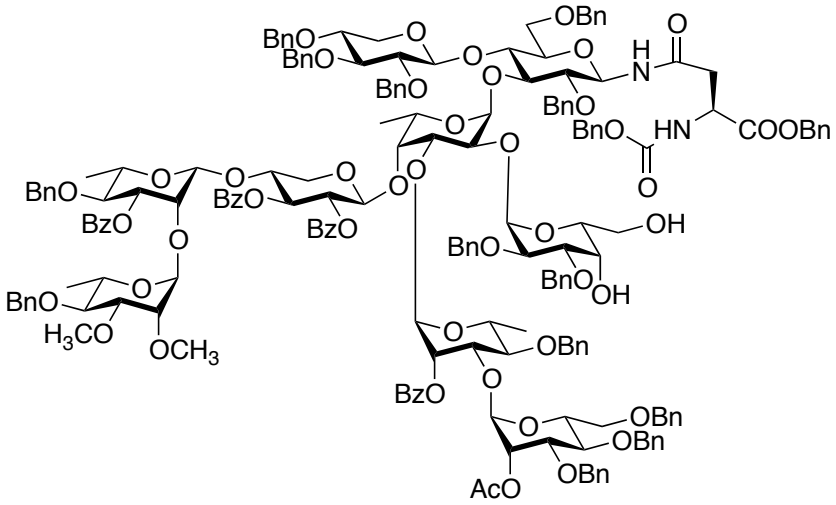
(m, 2H), 7.54–7.51 (m, 1H), 7.45–7.05 (m, 71H), 7.03–6.98 (m, 3H), 6.91–6.90 (m, 2H), 5.70 (dd, 1H, J = 3.2, 1.4 Hz), 5.55 (t, 1H, J = 9.5 Hz), 5.47 (dd, 1H, J = 9.9, 7.6 Hz), 5.22–5.20 (m, 3H, 3 × H-1 (α)), 5.17 (s, 1H, D-Rha-H-1), 5.14 (dd, 1H, J = 3.2, 1.6 Hz), 5.01 (d, 1H, J = 12.4 Hz), 4.89 (d, 1H, J = 1.4 Hz, H-1 (α)), 4.86–4.73 (m, 7H, Xyl(Bz)-H-1 (β)), 4.71–4.59 (m, 14H, Glc-H-1 (β)), 4.56–4.44 (m, 11H), 4.41–4.37 (m, 4H, Xyl(Bn)-H-1 (β)), 4.30–4.28 (m, 2H), 4.21 (d, 1H, J = 2.6 Hz), 4.15–3.80 (m, 16H, L-Rha(Bz)-H-1 (β)), 3.76–3.72 (m, 2H), 3.62–3.58 (m, 4H), 3.54 (dd, 1H, J = 3.2, 1.8 Hz), 3.49 (t, 1H, J = 9.6 Hz), 3.46 (t, 1H, J = 9.4 Hz), 3.43–3.39 (m, 3H), 3.38–3.35 (m, 4H), 3.34–3.33 (m, 2H), 3.22 (s, 3H), 3.16 (t, 1H, J = 7.9 Hz), 3.09 (t, 1H, J = 8.6 Hz), 3.03 (t, 1H, J = 11.0 Hz), 2.90 (dq, 1H, J = 9.2, 6.1 Hz), 1.70 (s, 3H), 1.36 (d, 3H, J = 6.2 Hz), 1.24 (d, 3H, J = 6.3 Hz), 1.08 (d, 6H, J = 6.2 Hz), 0.98 (s, 9H), 0.95 (s, 9H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 169.8, 165.9, 165.0, 164.9, 164.7, 139.5, 139.4, 139.2, 139.1, 138.7, 138.6, 138.5, 138.3, 138.2 (2 × C), 137.9, 137.8 (2 × C), 133.4, 133.0, 132.8, 132.7, 130.3, 129.8, 129.6, 129.5 (2 × C), 128.8, 128.6, 128.5 (3 × C), 128.4 (2 × C), 128.3 (2 × C), 128.2 (4 × C), 128.1 (3 × C), 127.9 (3 × C), 127.8 (5 × C), 127.7 (4 × C), 127.6 (3 × C), 127.5 (2 × C), 127.4 (2 × C), 127.2, 127.1, 127.0, 126.7 (2 × C), 125.9, 103.5, 100.8, 100.4, 99.9, 98.4, 98.3, 97.4, 96.1, 89.6, 84.1, 82.4, 82.2, 81.6, 80.9, 78.6, 78.4, 78.3, 78.1, 77.8, 77.2, 77.0, 76.4, 75.8, 75.7, 75.6, 75.3, 75.0, 74.8, 74.7, 74.5 (2 × C), 74.4, 74.3, 74.0 (2 × C), 73.5, 73.4, 72.9 (2 × C), 72.8, 72.7, 72.5, 72.3, 72.2, 71.8, 71.4, 71.1, 70.7, 69.1, 68.3, 68.1, 67.6, 67.5, 67.4, 66.5, 65.9, 65.5, 63.9, 58.7, 57.7, 27.8, 27.4, 23.3, 20.82, 20.62, 18.4, 17.96, 17.95, 16.6; HRMS (ESI) Calc. for $[M + 2NH_4]^{+2}$ $C_{183}H_{211}N_5O_{44}Si$: 1605.2093; Found 1605.2109.



N^2-Benzyloxycarbonyl-N^4-{4-*O*-benzyl-2,3-di-*O*-methyl-α-L-rhamnopyranosyl-(1→2)-3-*O*-benzoyl-4-*O*-benzyl-β-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-[2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-2-*O*-benzoyl-4-*O*-benzyl-α-D-rhamnopyranosyl-(1→3)]-[2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranosyl-(1→2)]-α-L-fucopyranosyl-(1→3)-[2,3,4-tri-*O*-benzyl-β-D-xylopyranoside-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranosyl}-L-asparagine benzyl ester (3.44): To a stirred solution of **3.43** (59.7 mg, 18.8 μmol) in dry THF (6.0 mL) was added triethylamine (2.9 μL, 21 μmol) and 10% palladium on carbon (10.0 mg) at room tempertature. After stirring for 2 h under an H_2 atmosphere (1 atm), the reaction mixture was filtered through Celite. The filtrate (glycosyl amine) was concentrated and used directly in the next step. To a stirred solution of *N*-benzyloxycarbonyl-L-aspartic acid 1-benzyl ester **3.3** (16.8 mg, 47.0 μmol) in dry THF (2.0 mL) was added HATU (17.9 mg, 47.0 μmol) at 0 °C. The reaction mixture was stirred for 1 h at 0 °C, then a solution of glycosyl amine in dry THF (2.0 mL) was added followed by triethylamine (3.0 μL). The

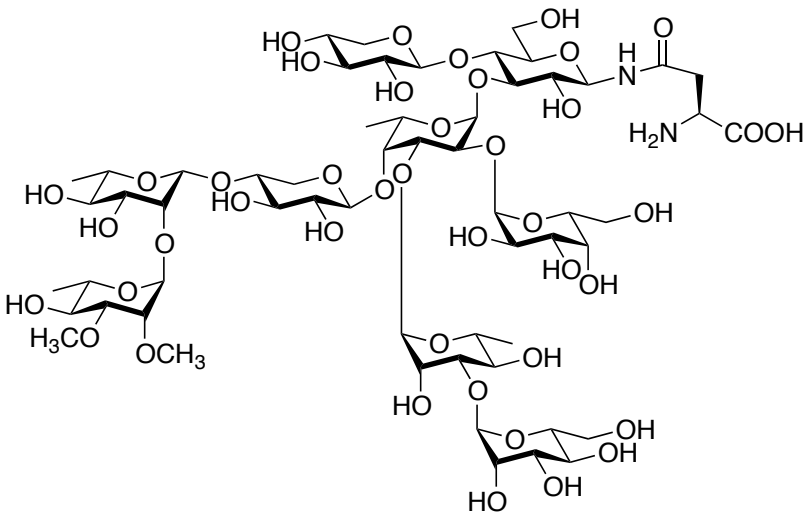
reaction mixture was stirred for 2 h at room temperature under an Ar atmosphere, then dilute with CH_2Cl_2 (30 mL) and wash with brine. The aqueous layer was extracted with CH_2Cl_2 (20 mL × 3), dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (3:2 hexane–EtOAc) to afford **3.44** (41.2 mg, 63%) as a white amorphous solid. R_f 0.31 (3:2 hexane–EtOAc); $[\alpha]_D$ –28.2 (*c* 0.50, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.95–7.94 (m, 5H), 7.91–7.88 (m, 4H), 7.54–7.52 (m, 1H), 7.47–7.45 (m, 1H), 7.40–7.05 (m, 82H), 7.02–7.00 (m, 2H), 5.94 (d, 2H, J = 8.6 Hz), 5.71 (d, 1H, J = 1.4 Hz), 5.55 (t, 1H, J = 9.4 Hz), 5.51 (dd, 1H, J = 9.8, 7.5 Hz), 5.22–4.28 (m, 48H), 4.25 (d, 1H, J = 8.0 Hz), 4.19–4.15 (m, 2H), 4.09–4.03 (m, 3H), 3.99–3.66 (m, 14H), 3.61 (dd, 1H, J = 9.4, 3.3 Hz), 3.56–3.35 (m, 14H), 3.31 (t, 1H, J = 9.0 Hz), 3.24–3.23 (m, 4H), 3.07–3.02 (m, 2H), 2.91 (t, 1H, J = 11.0 Hz), 2.79 (dd, 1H, J = 16.0, 3.2 Hz), 2.62 (dd, 1H, J = 15.7, 2.7 Hz), 1.80 (s, 3H), 1.35 (d, 3H, J = 6.2 Hz), 1.25 (d, 3H, J = 5.5 Hz), 1.07 (d, 3H, J = 6.1 Hz), 1.03 (d, 3H, J = 6.7 Hz), 0.99 (s, 9H), 0.93 (s, 9H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 170.8, 170.2, 169.9, 165.8, 165.0 (2 × C), 164.9, 156.1, 139.6, 139.4, 139.1 (2 × C), 138.7, 138.5 (2 × C), 138.4 (2 × C), 138.3, 138.2 (2 × C), 137.8, 137.7, 137.5, 136.3, 135.4, 133.4, 133.0, 132.9, 132.8, 130.1, 130.0, 129.7, 129.6 (3 × C), 129.5, 128.6 (2 × C), 128.5 (3 × C), 128.4 (2 × C), 128.3 (3 × C), 128.2 (3 × C), 128.1 (3 × C), 128.0 (2 × C), 127.9 (3 × C), 127.8 (3 × C), 127.7 (2 × C), 127.6 (2 × C), 127.5 (2 × C), 127.4 (3 × C), 127.2, 127.1 (2 × C), 127.0, 103.7, 101.3, 100.1, 100.0, 98.5, 98.4, 97.4, 96.6, 83.9, 82.3, 81.8, 80.9 (2 × C), 80.5, 78.9, 78.5, 78.4, 78.3, 78.1, 77.8, 77.5, 77.2, 76.0, 75.9, 75.8, 75.6, 75.2, 75.1, 75.0 (2 × C), 74.8, 74.5, 74.4, 74.3, 74.1, 73.9, 73.5, 73.0,

72.9, 72.6, 72.5, 71.8, 71.5, 71.1, 70.8, 70.6, 69.1, 68.4, 68.1, 67.8, 67.7 (2 × C), 67.2, 67.0, 66.9, 65.9, 65.3, 63.8, 58.7, 57.7, 50.5, 37.7, 27.8, 27.4, 23.3, 20.9, 20.6, 18.5, 18.01, 17.92, 16.4; HRMS (ESI) Calc. for $[M + 2NH_4]^{+2}$ $C_{202}H_{230}N_4O_{49}Si$: 1761.7693; Found 1761.7705.



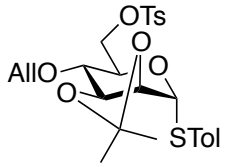
***N*²-Benzyloxycarbonyl-*N*⁴-{4-*O*-benzyl-2,3-di-*O*-methyl-α-L-rhamnopyranosyl-(1→2)-3-*O*-benzoyl-4-*O*-benzyl-β-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-[2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-2-*O*-benzoyl-4-*O*-benzyl-α-D-rhamnopyranosyl-(1→3)]-[2,3-di-*O*-benzyl-α-D-galactopyranosyl-(1→2)]-α-L-fucopyranosyl-(1→3)-[2,3,4-tri-*O*-benzyl-β-D-xylopyranoside-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranosyl}-L-asparagine benzyl ester (3.45):** To a stirred solution of **3.44** (41.1 mg, 11.8 μmol) in THF–pyridine (2.0 mL, 1:1) was added HF·pyridine (0.2 mL, pyridine ~30%, hydrogen fluoride ~70%) at 0 °C under an Ar atmosphere. The reaction mixture was stirred for 1.5 h at 0 °C, the reaction mixture was then poured into saturated $NaHCO_3$ (aq.), the aqueous layer was extracted with EtOAc (20 mL × 3), dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue

was purified by flash chromatography (1:1 hexane–EtOAc) to afford **3.45** (33.6 mg, 85%) as a syrup. R_f 0.41 (1:1 hexane–EtOAc); $[\alpha]_D$ –27.4 (*c* 0.48, $CHCl_3$); ^1H NMR (700 MHz; $CDCl_3$): δ 7.96–7.92 (m, 7H), 7.89–7.88 (m, 2H), 7.55–7.52 (m, 1H), 7.50–7.47 (m, 2H), 7.40–7.07 (m, 81H), 7.05–7.03 (m, 2H), 6.19 (d, 1H, J = 6.6 Hz), 5.97 (d, 1H, J = 8.7 Hz), 5.68 (d, 1H, J = 0.2 Hz), 5.59 (t, 1H, J = 9.5 Hz), 5.52 (dd, 1H, J = 9.8, 7.7 Hz), 5.24–5.00 (m, 10H), 4.90–4.85 (m, 4H), 4.81–4.76 (m, 3H), 4.72–4.68 (m, 4H), 4.66–4.16 (m, 29H), 4.05 (dq, 1H, J = 9.6, 6.2 Hz), 4.00 (d, 1H, J = 3.0 Hz), 3.97–3.94 (m, 3H), 3.91–3.73 (m, 10H), 3.63–3.42 (m, 13H), 3.39–3.36 (m, 4H), 3.32 (t, 1H, J = 9.0 Hz), 3.23 (s, 3H), 3.15 (dq, 1H, J = 9.2, 6.1 Hz), 3.08 (t, 1H, J = 8.5 Hz), 2.95 (t, 1H, J = 10.9 Hz), 2.75 (dd, 1H, J = 16.3, 3.7 Hz), 2.52 (dd, 1H, J = 15.8, 3.2 Hz), 1.87 (s, 3H), 1.34 (d, 3H, J = 6.2 Hz), 1.20 (d, 3H, J = 6.2 Hz), 1.06 (d, 6H, J = 6.1 Hz); ^{13}C NMR (125 MHz; $CDCl_3$): δ 170.8, 170.2, 170.1, 165.6, 165.5, 165.0 (2 × C), 156.2, 139.3, 139.1, 139.0, 138.7, 138.4 (2 × C), 138.2, 138.1, 137.8, 137.6 (2 × C), 136.3, 135.4, 133.4, 133.2, 133.0, 132.9, 129.9, 129.8, 129.7 (2 × C), 129.6 (2 × C), 129.4, 128.6 (2 × C), 128.5 (4 × C), 128.4 (2 × C), 128.3 (3 × C), 128.2 (3 × C), 128.1 (2 × C), 128.0 (3 × C), 127.9 (3 × C), 127.8 (2 × C), 127.7 (3 × C), 127.6 (3 × C), 127.5 (4 × C), 127.4 (2 × C), 127.3, 127.1, 103.5, 101.6, 100.3, 100.1, 98.5 (2 × C), 97.5, 96.2, 83.9, 82.2, 81.4, 80.9 (2 × C), 79.6, 78.9, 78.5 (2 × C), 78.2, 77.8, 77.6, 77.2, 76.3, 76.2, 7.1, 75.9, 75.6 (2 × C), 75.1, 75.0 (3 × C), 74.9, 74.5, 74.4, 74.3, 74.1, 73.9, 73.5, 73.1, 73.0, 72.6, 72.5, 72.3, 71.9, 71.6, 71.3, 69.2, 68.3, 68.1, 67.9, 67.8, 67.3, 66.9, 66.0, 65.1, 63.9, 62.6, 58.7, 57.7, 50.6, 37.6, 21.0, 18.5, 18.0, 17.9, 16.6; HRMS (ESI) Calc. for $[M + 2Na]^{+2}$ $C_{194}H_{206}N_2Na_2O_{49}$: 1696.6737; Found 1696.6779.



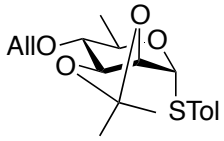
***N*^{4}-{2,3-Di-*O*-methyl-α-L-rhamnopyranosyl-(1→2)-β-L-rhamnopyranosyl-(1→4)-2,3-β-D-xylopyranosyl-[α-D-mannopyranosyl-α-D-rhamnopyranosyl-(1→3)]-[α-D-galactopyranosyl-(1→2)]-α-L-fucopyranosyl-(1→3)-[β-D-xylopyranoside-(1→4)]-β-D-glucopyranosyl}-L-asparagine (3.1):** To a stirred solution of **3.45** (12.2 mg, 3.64 μmol) in THF–H_2O (3.0 mL, 1:1) was added 20% palladium hydroxide on carbon (4.0 mg). After stirring for 24 h under an H_2 atmosphere (1 atm), the reaction mixture was filtered through Celite and concentrate. The residue was then dissolved in H_2O (1.5 mL) and 50 mM NaOH (1.5 mL) was added. The reaction mixture was stirred for 3 days at room temperature, then neutralized by addition of Amberlite® IR-120 (H^+) cation exchange resin, filtered. The crude residue was purified by size exclusion column chromatography (Sephadex LH-20, CH_3OH–H_2O, 1:1) and lyophilized to afford **3.1** (4.2 mg, 78%) as a white solid. R_f 0.29 (3:3:3:2 EtOAc–CH_3OH–AcOH–H_2O); $[\alpha]_D$ +13.6 (*c* 0.10, $CHCl_3$); ^{1}H NMR (700 MHz; 0.1% TFA in D_2O): δ 5.63 (d, 1H, J = 3.3 Hz), 5.24 (s, 1H), 5.20 (d, 1H, J = 3.7 Hz), 5.07 (s, 1H), 5.04 (s, 1H), 5.01 (d, 1H, J = 9.2 Hz), 4.81 (s, 1H), 4.76 (m, 1H) 4.46 (d, 1H, J =

7.8 Hz), 4.42 (d, 1H, J = 7.9 Hz), 4.36–4.33 (m, 2H), 4.22–4.18 (m, 4H), 4.14–4.08 (m, 3H), 4.05–3.90 (m, 7H), 3.88–3.66 (m, 14H), 3.65–3.54 (m, 6H), 3.52–3.47 (m, 4H), 3.46–3.43 (m, 5H), 3.41–3.37 (m, 2H), 3.30–3.24 (m, 2H), 3.17–3.10 (m, 2H), 3.07 (dd, 1H, J = 17.5, 4.3 Hz), 1.33 (d, 3H, J = 6.1 Hz), 1.30 (d, 3H, J = 6.3 Hz), 1.30 (d, 3H, J = 6.3 Hz), 1.27 (d, J = 6.2 Hz, 3H); ^{13}C NMR (125 MHz; 0.1% TFA in D_2O): δ 173.0, 172.1, 105.0, 103.9, 103.8, 103.1, 102.2, 99.7, 99.1, 98.3, 81.6, 80.8, 80.4, 79.9, 79.5, 78.0, 77.8, 76.9 (2 × C), 76.6, 75.8, 75.5, 74.8, 74.7 (2 × C), 74.6, 74.5, 74.0, 73.3, 73.0, 72.3 (2 × C), 72.0, 71.7, 71.4, 71.2, 70.91, 70.8, 70.7, 70.2 (2 × C), 69.4, 69.3, 68.2, 68.1, 65.8, 65.6, 62.6, 62.3, 60.3, 59.1, 57.6, 50.5, 35.5, 18.1, 17.9, 17.5, 15.7; HRMS (ESI) Calc. for $[M - H]^-$ $C_{58}H_{97}N_2O_{42}$: 1493.5521; Found 1493.5512.



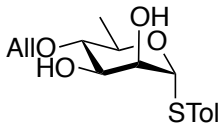
***p*-Tolyl 4-*O*-allyl-2,3-*O*-isopropylidene-6-*O*-(*p*-toluenesulfonyl)-1-thio-α-D-mannopyranoside (3.57):** To a stirred solution of **3.23** (4.38 g, 9.11 mmol) in dry DMF (15 mL) was added sodium hydride (0.728 g, 18.2 mmol, 60% dispersion in mineral oil) in one portion at 0 °C, After stirring for 30 min, allyl bromide (0.94 mL, 11 mmol) was added dropwise, and the reaction mixture was warmed to room temperature and stirred for 1.5 h under an Ar atmosphere. Then, CH_3OH was added at 0 °C and the solution was concentrated. The crude residue was diluted with CH_2Cl_2 (200 mL), washed with saturated $NaHCO_3$ (aq.), dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude

residue was purified by flash chromatography (6:1 hexane–EtOAc) to afford **3.57** (4.60 g, 97%) as a syrup. R_f 0.71 (2:1 hexane–EtOAc); $[\alpha]_D$ +130 (*c* 0.42, $CHCl_3$); ^1H NMR (700 MHz; $CDCl_3$): δ 7.68–7.67 (m, 2H, Ar), 7.32–7.31 (m, 2H, Ar), 7.26–7.25 (m, 2H, Ar), 7.09–7.07 (m, 2H, Ar), 5.82 (ddt, 1H, *J* = 17.1, 10.4, 5.8 Hz, $OCH_2C\underline{H}=CH_2$), 5.56 (s, 1H, H-1), 5.22 (dq, 1H, *J* = 17.2, 1.6 Hz, $OCH_2CH=C\underline{H}_2$), 5.15 (dq, *J* = 10.4, 1.4 Hz, $OCH_2CH=C\underline{H}_2$), 4.30 (ddt, 1H, *J* = 12.5, 5.5, 1.3 Hz, $OC\underline{H}_2CH=CH_2$), 4.27 (dd, 1H, *J* = 5.7, 0.7 Hz, H-2), 4.24–4.19 (m, 3H, H-5, H-3, H-6a), 4.17 (dd, 1H, *J* = 10.6, 5.5 Hz, H-6b), 3.99 (ddt, 1H, *J* = 12.5, 5.9, 1.4 Hz, $OC\underline{H}_2CH=CH_2$), 3.40 (dd, 1H, *J* = 10.2, 7.0 Hz, H-4), 2.42 (s, 3H, $ArC\underline{H}_3$), 2.32 (s, 3H, $ArC\underline{H}_3$), 1.48 (s, 3H, $C(C\underline{H}_3)_2$), 1.33 (s, 3H, $C(C\underline{H}_3)_2$); ^{13}C NMR (125 MHz; $CDCl_3$): δ 144.5 (Ar), 138.1 (Ar), 134.3 ($OCH_2\underline{C}H=CH_2$), 132.9 (Ar), 132.7 (Ar), 129.9 (Ar), 129.7 (Ar), 129.0 (Ar), 128.0 (Ar), 117.4 ($OCH_2CH=\underline{C}H_2$), 109.6 ($\underline{C}(CH_3)_2$), 84.4 (C-1), 78.2 (C-3), 76.2 (C-2), 75.2 (C-4), 71.9 ($O\underline{C}H_2CH=CH_2$), 68.8 (C-6), 67.9 (C-5), 27.9 ($C(\underline{C}H_3)_2$), 26.3 ($C(\underline{C}H_3)_2$), 21.6 ($Ar\underline{C}H_3$), 21.2 ($Ar\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{26}H_{32}NaO_7S_2$: 543.1482; Found 543.1471.



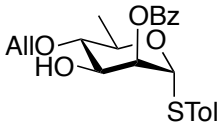
***p*-Tolyl 4-*O*-allyl-2,3-*O*-isopropylidene-1-thio-α-D-rhamnopyranoside (3.58):** To a stirred solution of **3.57** (4.60 g, 8.83 mmol) in dry THF (80 mL) was added lithium aluminum hydride (0.839 g, 22.1 mmol) at room temperature. The reaction mixture was stirred for 2.5 h at 65 °C, then cooled to 0 °C and ethyl acetate was added. The crude residue

was then washed with 1N HCl and saturated $NaHCO_3$ (aq.), the aqueous layers were extracted with EtOAc (200 mL), and the combined organic layers were dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (15:1 hexane–EtOAc) to afford **3.58** (2.83 g, 91%) as a viscous oil. R_f 0.55 (6:1 hexane–EtOAc); $[\alpha]_D$ +232 (*c* 0.81, $CHCl_3$); ^1H NMR (500 MHz; $CDCl_3$): δ 7.39–7.36 (m, 2H, Ar), 7.15–7.13 (m, 2H, Ar), 5.95 (dddd, 1H, J = 17.2, 10.4, 6.0, 5.4 Hz, $OCH_2C\underline{H}=CH_2$), 5.67 (d, 1H, J = 0.6 Hz, H-1), 5.31 (dq, 1H, J = 17.2, 1.7 Hz, $OCH_2CH=C\underline{H}_2$), 5.20 (dq, 1H, J = 10.4, 1.5 Hz, $OCH_2CH=C\underline{H}_2$), 4.38 (ddt, 1H, J = 12.7, 5.4, 1.4 Hz, $OC\underline{H}_2CH=CH_2$), 4.34 (dd, 1H, J = 5.6, 0.8 Hz, H-2), 4.24 (dd, 1H, J = 7.1, 5.7 Hz, H-3), 4.17–4.10 (m, 2H, $OC\underline{H}_2CH=CH_2$, H-5), 3.24 (dd, 1H, J = 9.8, 7.2 Hz, H-4), 2.35 (s, 3H, $ArC\underline{H}_3$), 1.55 (s, 3H, $C(C\underline{H}_3)_2$), 1.38 (s, 3H, $C(C\underline{H}_3)_2$), 1.25 (d, 3H, J = 6.2 Hz, H-6); ^{13}C NMR (125 MHz; $CDCl_3$): δ 137.8 (Ar), 134.9 ($OCH_2\underline{C}H=CH_2$), 132.5 (Ar), 129.8 (Ar), 129.7 (Ar), 117.1 ($OCH_2CH=\underline{C}H_2$), 109.3 ($\underline{C}(CH_3)_2$), 84.2 (C-1), 81.4 (C-4), 78.3 (C-3), 76.7 (C-2), 72.2 ($O\underline{C}H_2CH=CH_2$), 66.2 (C-5), 28.0 ($C(\underline{C}H_3)_2$), 26.5 ($C(\underline{C}H_3)_2$), 21.1 ($Ar\underline{C}H_3$), 17.6 (C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{19}H_{26}NaO_4S$: 373.1444; Found 373.1453.



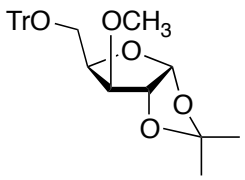
***p*-Tolyl 4-*O*-allyl-1-thio-α-D-rhamnopyranoside (3.59):** To a stirred solution of **3.58** (2.83 g, 8.07 mmol) in CH_3CN–CH_3OH (55 mL, 10:1) was added *p*-toluenesulfonic acid monohydrate (4.60 g, 24.2 mmol) at room temperature. The reaction mixture was stirred

for 3 h at room temperature. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (3:2 hexane–EtOAc) to afford **3.59** (2.26 g, 90%) as a white solid. R_f 0.29 (3:2 hexane–EtOAc); $[\alpha]_D$ +252 (*c* 0.48, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.34–7.33 (m, 2H, Ar), 7.11–7.09 (m, 2H, Ar), 5.95 (ddt, 1H, *J* = 17.2, 10.4, 5.7 Hz, $OCH_2C\underline{H}=CH_2$), 5.38 (d, 1H, *J* = 1.4 Hz, H-1), 5.31 (dq, 1H, *J* = 17.2, 1.6 Hz, $OCH_2CH=C\underline{H}_2$), 5.21 (dq, 1H, *J* = 10.4, 1.4 Hz, $OCH_2CH=C\underline{H}_2$), 4.22 (dt, 2H, *J* = 5.7, 1.4 Hz, $OC\underline{H}_2CH=CH_2$), 4.20–4.15 (m, 2H, H-2, H-5), 3.89 (ddd, 1H, *J* = 8.9, 5.2, 3.5 Hz, H-3), 3.30 (t, 1H, *J* = 9.3 Hz, H-4), 2.49 (d, 1H, *J* = 5.2 Hz, 3-OH), 2.48 (d, 1H, *J* = 3.9 Hz, 2-OH), 2.32 (s, 3H, $ArC\underline{H}_3$), 1.31 (d, 3H, *J* = 6.3 Hz, H-6); ^{13}C NMR (125 MHz; $CDCl_3$): δ 137.7 (Ar), 134.7 ($OCH_2\underline{C}H=CH_2$), 132.1 (Ar), 130.2 (Ar), 129.8 (Ar), 117.6 ($OCH_2CH=\underline{C}H_2$), 87.8 (C-1), 81.7 (C-4), 73.9 ($O\underline{C}H_2CH=CH_2$), 72.5 (C-2), 71.8 (C-3), 68.5 (C-5), 21.1 ($Ar\underline{C}H_3$), 17.9 (C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{16}H_{22}NaO_4S$: 333.1131; Found 333.1135.

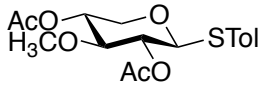


***p*-Tolyl 4-*O*-allyl-2-*O*-benzoyl-1-thio-α-D-rhamnopyranoside (3.53)**: To a stirred solution of **3.59** (1.58 g, 5.09 mmol) in dry DMF (0.7 mL) was treated with trimethyl orthobenzoate (4.9 mL), then evacuated for 5 min under high vacuum. *p*-Toluenesulfonic acid monohydrate (194 mg, 1.02 mmol) was added in one portion and vacuum was immediately restored. The reaction mixture was stirred for 10 min under high vacuum, then

1N HCl (20 mL) was added and stirred for 30 min. The reaction mixture was diluted with CH_2Cl_2 (100 mL), then the aqueous layer was extracted with CH_2Cl_2 (50 mL × 3) and combined organic layers were dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (6:1 hexane–EtOAc) to afford **3.53** (2.11 g, quant.) as a syrup. R_f 0.38 (4:1 hexane–EtOAc); $[\alpha]_D$ +116 (*c* 0.36, $CHCl_3$); ^{1}H NMR (600 MHz; $CDCl_3$): δ 8.07–8.05 (m, 2H, Ar), 7.61–7.58 (m, 1H, Ar), 7.48–7.46 (m, 2H, Ar), 7.40–7.38 (m, 2H, Ar), 7.14–7.13 (m, 2H, Ar), 6.00 (ddt, 1H, *J* = 17.2, 10.4, 5.7 Hz, $OCH_2C\underline{H}=CH_2$), 5.64 (dd, 1H, *J* = 3.4, 1.6 Hz, H-2), 5.48 (d, 1H, *J* = 1.2 Hz, H-1), 5.35 (dq, 1H, *J* = 17.2, 1.6 Hz, $OCH_2CH=C\underline{H}_2$), 5.24 (dq, 1H, *J* = 10.4, 1.4 Hz, $OCH_2CH=C\underline{H}_2$), 4.35 (ddt, 1H, *J* = 12.5, 5.8, 1.3 Hz, $OC\underline{H}_2CH=CH_2$), 4.31–4.26 (m, 2H, $OC\underline{H}_2CH=CH_2$, H-5), 4.19 (ddd, 1H, *J* = 9.3, 4.9, 3.4 Hz, H-3), 3.45 (t, 1H, *J* = 9.4 Hz, H-4), 2.34 (s, 3H, $ArC\underline{H}_3$), 2.30 (d, 1H, *J* = 4.9 Hz, 3-OH), 1.41 (d, 3H, *J* = 6.2 Hz, H-6); ^{13}C NMR (125 MHz; $CDCl_3$): δ 166.1 (C=O), 138.0 (Ar), 134.7 ($OCH_2\underline{C}H=CH_2$), 133.4 (Ar), 132.4 (Ar), 130.0 (Ar), 129.9 (Ar), 129.8 (Ar), 129.7 (Ar), 128.5 (Ar), 117.4 ($OCH_2CH=\underline{C}H_2$), 86.4 (C-1), 82.0 (C-4), 74.7 (C-2), 74.1 ($O\underline{C}H_2CH=CH_2$), 71.0 (C-3), 68.8 (C-5), 21.1 ($Ar\underline{C}H_3$), 18.0 (C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{23}H_{26}NaO_5S$: 437.1393; Found 437.1396.

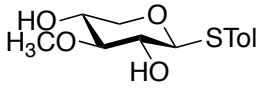


1,2-*O*-Isopropylidene-3-*O*-methyl-5-*O*-triphenylmethyl-α-D-xylofuranoside (3.61): To a stirred solution of 1,2-*O*-isopropylidene-5-*O*-triphenylmethyl-α-D-xylofuranoside **3.60**[23] (45.8 g, 106 mmol) in dry DMF (40 mL) was added sodium hydride (10.6 g, 265 mmol, 60% dispersion in mineral oil) in one portion at 0 °C, After stirring for 30 min, methyl iodide (13.2 mL, 212 mmol) was added dropwise, and the reaction mixture was warmed to room temperature and stirred for 3 h under an Ar atmosphere. Then, CH_3OH was added at 0 °C and the solution was concentrated. The crude residue was diluted with CH_2Cl_2 (500 mL), washed with saturated $NaHCO_3$ (aq.), dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (6:1 hexane–EtOAc) to afford **3.61** (39.2 g, 83%) as a white foam. R_f 0.47 (4:1 hexane–EtOAc); $[\alpha]_D$ –49.6 (*c* 0.40, $CHCl_3$); ^{1}H NMR (400 MHz; $CDCl_3$): δ 7.49–7.46 (m, 6H, Ar), 7.33–7.22 (m, 9H, Ar), 5.87 (d, 1H, J = 3.8 Hz, H-1), 4.56 (d, 1H, J = 3.8 Hz, H-2), 4.35 (ddd, 1H, J = 7.3, 5.5, 3.1 Hz, H-4), 3.80 (d, 1H, J = 3.1 Hz, H-3), 3.45 (dd, 1H, J = 9.1, 5.6 Hz, H-5a), 3.35 (s, 3H, OC$\underline{H}_3$), 3.33 (dd, 1H, J = 9.1, 7.3 Hz, H-5b), 1.55 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.35 (s, 3H, C(C$\underline{H}_3$)$_2$); ^{13}C NMR (125 MHz; $CDCl_3$): δ 143.9 (Ar), 128.7 (Ar), 127.8 (Ar), 127.0 (Ar), 111.6 (C(CH$_3$)$_2$), 104.9 (C-1), 86.7 (C(Ph)$_3$), 83.9 (C-3), 81.7 (C-2), 79.3 (C-4), 60.5 (C-5), 58.0 (OCH$_3$), 26.8 (C(CH$_3$)$_2$), 26.2 (C(CH$_3$)$_2$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{28}H_{30}NaO_5$: 469.1985; Found 469.1990.

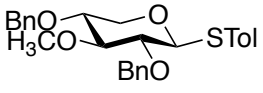


***p*-Tolyl 2,4-di-*O*-acetyl-3-*O*-methyl-1-thio-β-D-xylopyranoside (3.62):** To a stirred solution of **3.61** (38.9 g 87.0 mmol) in AcOH–H_2O (150 mL) was heated at 80 °C for 4 h and then cooled to room temperature. The mixture was concentrated, then co-evaporated with toluene (3 ×) and used without further purification. To a crude residue (38.9 g, 87.0 mmol) in pyridine (100 mL) was added acetic anhydride (60 mL) dropwise at room temperature. The reaction mixture was stirred for overnight at room temperature, then the solvent was concentrated. The crude residue was dilute with CH_2Cl_2 (500 mL) and wash with 1N HCl and saturated $NaHCO_3$ (aq.). The organic layer was dried over Na_2SO_4, filtered, the filtrate was concentrated and used without further purification. To a crude residue (23.8 g, 81.9 mmol) in dry CH_2Cl_2 (150 mL) was added *p*-thiocresol (12.2 g, 98.3 mmol) and boron trifluoride diethyl etherate (20.2 mL, 164 mmol) successively. The reaction mixture was stirred overnight at room temperature under an Ar atmosphere. Then poured into the saturated $NaHCO_3$ (aq.) and extracted with CH_2Cl_2 (300 mL × 3). The combined organic layers were dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (4:1 hexane–EtOAc) to afford **3.62** (19.1 g, 62%) as a syrup. R_f 0.42 (2:1 hexane–EtOAc); $[\alpha]_D$ –60.4 (*c* 0.60, $CHCl_3$); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.40–7.38 (m, 2H, Ar), 7.14–7.11 (m, 2H, Ar), 5.03 (t, 1H, J = 5.8 Hz, H-2), 4.96 (d, 1H, J = 5.7 Hz, H-1), 4.86 (td, 1H, J = 6.1, 3.8 Hz, H-4), 4.41 (dd, 1H, J = 12.3, 3.8 Hz, H-5a), 3.52–3.47 (m, 5H, OC$\underline{H}_3$, H-3, H-5), 2.35 (s, 3H, ArC$\underline{H}_3$),

2.15 (s, 3H, COC<u>H</u>$_3$), 2.12 (s, 3H, COC<u>H</u>$_3$); ^{13}C NMR (125 MHz; $CDCl_3$): δ 169.9 (C=O), 169.4 (C=O), 137.8 (Ar), 132.2 (Ar), 130.3 (Ar), 129.7 (Ar), 86.3 (C-1), 77.9 (C-3), 69.8 (C-2), 68.9 (C-4), 62.7 (C-5), 59.0 (O<u>C</u>H$_3$), 21.1 (Ar<u>C</u>H$_3$), 21.0 (2 × CO<u>C</u>H$_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{17}H_{22}NaO_6S$: 377.1029; Found 377.1028.

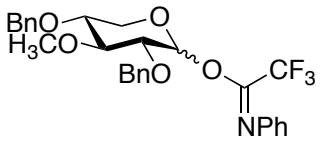


***p*-Tolyl 3-*O*-methyl-1-thio-β-D-xylopyranoside (3.63):** To a stirred solution of **3.62** (12.5 g, 35.2 mmol) in CH_3OH (50 mL) was added a solution of $NaOCH_3$ in CH_3OH (10 mL, 0.5 M). The reaction mixture was stirred for 3 h at room temperature, then neutralized by addition of Amberlite® IR-120 (H^+) cation exchange resin, filtered and the filtrate was concentrated to afford **3.63** (9.52 g, quant.) as a solid. R_f 0.58 (9:1 CH_2Cl_2–CH_3OH); $[\alpha]_D$ –63.9 (*c* 0.76, CH_3OH); ^{1}H NMR (500 MHz; CD_3OD): δ 7.41–7.38 (m, 2H, Ar), 7.13–7.11 (m, 2H, Ar), 4.47 (d, 1H, *J* = 9.1 Hz, H-1), 3.91 (dd, 1H, *J* = 11.4, 5.2 Hz, H-5a), 3.61 (s, 3H, OC<u>H</u>$_3$), 3.48 (ddd, 1H, *J* = 9.8, 8.5, 5.2 Hz, H-4), 3.24 (dd, 1H, *J* = 8.9, 8.4 Hz, H-2), 3.20 (dd, 1H, *J* = 11.4, 9.9 Hz, H-5b), 3.05 (t, 1H, *J* = 8.4 Hz, H-3), 2.31 (s, 3H, ArC<u>H</u>$_3$); ^{13}C NMR (125 MHz; CD_3OD): δ 139.1 (Ar), 134.0 (Ar), 130.8 (Ar), 130.5 (Ar), 90.4 (C-1), 88.6 (C-3), 73.1 (C-2), 70.6 (C-4), 70.1 (C-5), 61.1 (O<u>C</u>H$_3$), 21.1 (Ar<u>C</u>H$_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{13}H_{18}NaO_4S$: 293.0818; Found 293.0822.



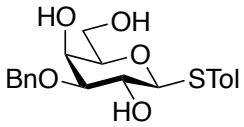
***p*-Tolyl 2,4-di-*O*-benzyl-3-*O*-methyl-1-thio-β-D-xylopyranoside (3.64):** To a stirred solution of **3.63** (1.67 g, 6.18 mmol) in dry DMF (22 mL) was added sodium hydride (1.20

g, 30.9 mmol, 60% dispersion in mineral oil) in one portion at 0 °C, After stirring for 30 min, benzyl bromide (1.76 mL, 14.8 mmol) was added dropwise, and the reaction mixture was warmed to room temperature and stirred overnight under an Ar atmosphere. Then, CH_3OH was added at 0 °C and the solution was concentrated. The crude residue was diluted with CH_2Cl_2 (100 mL), washed with saturated $NaHCO_3$ (aq.), dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (9:1 hexane–EtOAc) to afford **3.64** (2.06 g, 74%) as a syrup. R_f 0.27 (9:1 hexane–EtOAc); $[\alpha]_D$ –16.5 (*c* 0.63, $CHCl_3$); ^{1}H NMR (400 MHz; $CDCl_3$): δ 7.48–7.29 (m, 12H, Ar), 7.13–7.11 (m, 2H, Ar), 4.87 (d, 1H, *J* = 10.4 Hz, PhC$\underline{H}_2$), 4.76 (d, 1H, *J* = 10.4 Hz, PhC$\underline{H}_2$), 4.74 (d, 1H, *J* = 11.7 Hz, PhC$\underline{H}_2$), 4.64 (d, 1H, *J* = 11.7 Hz, PhC$\underline{H}_2$), 4.57 (d, 1H, *J* = 9.0 Hz, H-1), 4.02 (dd, 1H, *J* = 11.6, 5.2 Hz, H-5a), 3.68 (s, 3H, OC$\underline{H}_3$), 3.56–3.50 (m, 1H, H-4), 3.38–3.30 (m, 2H, H-3, H-2), 3.19 (dd, 1H, *J* = 11.4, 10.1 Hz, H-5b), 2.35 (s, 3H, ArC$\underline{H}_3$); ^{13}C NMR (125 MHz; $CDCl_3$): δ 138.2 (Ar), 137.8 (Ar), 132.6 (Ar), 129.8 (Ar), 129.7 (Ar), 128.5 (Ar), 128.4 (Ar), 128.3 (Ar), 127.9 (Ar), 127.8 (Ar), 127.7 (Ar), 88.7 (C-1), 87.4 (C-3), 80.5 (C-2), 77.6 (C-4), 75.4 (Ph$\underline{C}H_2$), 73.2 (Ph$\underline{C}H_2$), 67.5 (C-5), 61.2 (O$\underline{C}H_3$), 21.1 (Ar$\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{27}H_{30}NaO_4S$: 473.1757; Found 473.1753.



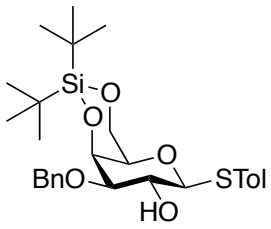
2,4-Di-*O*-benzyl-3-*O*-methyl-1-thio-β-D-xylopyranose 1-(*N*-phenyl)-2,2,2-trifluoroacetimidate (3.55): To a stirred solution of **3.64** (510 mg, 1.13 mmol) in dry acetone–H_2O (11 mL, 10:1) was added and *N*-bromosuccinimide (603 mg, 3.39 mmol) at

0 °C. The reaction mixture was stirred for 2 h at 0 °C, then CH_3OH was added and the solution was concentrated. The residue was then diluted with CH_2Cl_2 and wash with saturated $NaHCO_3$ (aq.). The aqueous layer was extracted with CH_2Cl_2 (50 mL × 3), and combined organic layers were dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (2:1 hexane–EtOAc) to afford its hemiacetal (379 mg, 97%). Then to a solution of hemiacetal (379 mg, 1.10 mmol) in CH_2Cl_2 (12 mL) was added 2,2,2-trifluoro-*N*-phenylacetimidoyl chloride (0.34 mL, 2.2 mmol) and cesium carbonate (538 mg, 1.65 mmol) successively. The reaction mixture was stirred overnight at room temperature. The crude residue was then filtered through Celite, the filtrate was concentrated to afford **3.55** and used without further purification.



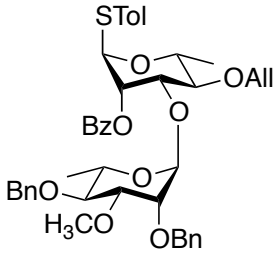
***p*-Tolyl 3-*O*-benzyl-1-thio-α-D-galactopyranoside (3.66):** To a stirred solution of *p*-tolyl 1-thio-α-D-galactopyranoside **3.65**[24] (1.06 g, 3.69 mmol) in CH_3OH (15 mL) was added dibutyltin oxide (1.01 g, 4.06 mmol) at room temperature. The reaction mixture was heated at reflux for 2 h at 80 °C under an Ar atmosphere. The reaction mixture was cooled to room temperature, concentrated and dried under high vacuum for 5 h. To a solution of the tin acetal in dry DMF (12 mL) was added cesium fluoride (0.62 g, 4.1 mmol) and allyl bromide (0.48 mL, 4.1 mmol) successively at room temperature. The reaction mixture was stirred overnight at 50 °C under an Ar atmosphere. Then the reaction mixture was diluted with EtOAc (200 mL) and washed with brine. The aqueous layer was extracted with EtOAc (50

mL × 3), and combined organic layers were dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (1:2 hexane–EtOAc) to afford **3.66** (703 mg, 51%) as a white solid. R_f 0.32 (1:2 hexane–EtOAc); $[\alpha]_D$ –20.2 (*c* 0.49, $CHCl_3$); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.48–7.46 (m, 2H, Ar), 7.40–7.31 (m, 5H, Ar), 7.15–7.12 (m, 2H, Ar), 4.76 (s, 2H, PhC$\underline{H}_2$), 4.48 (d, 1H, J = 9.7 Hz, H-1), 4.06–4.05 (m, H-4), 3.99 (ddd, 1H, J = 11.8, 6.7, 4.1 Hz, H-6a), 3.84–3.76 (m, 2H, H-6b, H-2), 3.55 (ddt, 1H, J = 6.7, 4.4, 1.1 Hz, H-5), 3.48 (dd, 1H, J = 9.0, 3.4 Hz, H-3), 2.50 (dd, 1H, J = 2.0, 1.2 Hz, 4-OH), 2.45 (d, 1H, J = 2.1 Hz, 2-OH), 2.35 (s, 3H, ArC$\underline{H}_3$), 2.14 (dd, 1H, J = 8.7, 4.0 Hz, 6-OH); ^{13}C NMR (125 MHz; $CDCl_3$): δ 138.4 (Ar), 137.5 (Ar), 133.2 (Ar), 129.8 (Ar), 128.7 (Ar), 128.2 (Ar), 128.0 (Ar), 127.9 (Ar), 88.7 (C-1), 81.3 (C-3), 78.4 (C-5), 72.3 (Ph$\underline{C}H_2$), 68.8 (C-2), 67.5 (C-4), 62.8 (C-6), 21.2 (Ar$\underline{C}H_3$); HRMS (ESI) Calc. for $[M + NH_4]^+$ $C_{20}H_{28}NO_5S$: 394.1683; Found 394.1689.



***p*-Tolyl 3-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-1-thio-α-D-galactopyranoside (3.56):** To a stirred solution of **3.66** (697 mg, 1.85 mmol) in CH_2Cl_2–pyridine (17.6 mL, 1:1.2) was added di-tert-butylsilyl bis(trifluoromethanesulfonate) (0.66 mL, 2.0 mmol) at 0 °C. The reaction mixture was stirred for 1 h at room temperature under Ar atmosphere. The crude residue was dilute with CH_2Cl_2 (100 mL) and wash with 1N HCl and saturated $NaHCO_3$ (aq.). The organic layer was dried over Na_2SO_4, filtered and the filtrate was

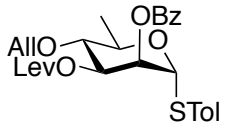
concentrated. The crude residue was purified by flash chromatography (4:1 hexane–EtOAc) to afford **3.56** (858 mg, 90%) as a white foam. R_f 0.27 (4:1 hexane–EtOAc); $[\alpha]_D$ –23.0 (*c* 0.48, $CHCl_3$); ^1H NMR (500 MHz; $CDCl_3$): δ 7.50–7.47 (m, 2H, Ar), 7.44–7.42 (m, 2H, Ar), 7.39–7.36 (m, 2H, Ar), 7.34–7.30 (m, 1H, Ar), 7.13–7.11 (m, 2H, Ar), 4.83 (d, 1H, *J* = 11.6 Hz, PhC$\underline{H}_2$), 4.64 (d, 1H, *J* = 11.7 Hz, PhC$\underline{H}_2$), 4.58 (dd, 1H, *J* = 3.0, 0.7 Hz, H-4), 4.53 (d, 1H, *J* = 9.8 Hz, H-1), 4.27 (dd, 1H, *J* = 12.4, 1.6 Hz, H-6a), 4.23 (dd, 1H, *J* = 12.4, 2.3 Hz, H-6b), 4.02 (td, 1H, *J* = 9.4, 1.7 Hz, H-2), 3.39–3.35 (m, 2H, H-3, H-5), 2.58 (d, 1H, *J* = 1.8 Hz, 2-OH), 2.35 (s, 3H, ArC$\underline{H}_3$), 1.08 (s, 18H, 2 × C(C$\underline{H}_3$)$_3$); ^{13}C NMR (125 MHz; $CDCl_3$): δ 138.0 (2 × Ar), 133.4 (Ar), 129.6 (Ar), 129.5 (Ar), 128.5 (Ar), 127.9 (2 × Ar), 89.6 (C-1), 81.9 (C-3), 75.2 (C-5), 70.3 (Ph$\underline{C}H_2$), 69.3 (C-4), 68.5 (C-2), 67.5 (C-6), 27.6 (C($\underline{C}H_3$)$_3$), 27.5 (C($\underline{C}H_3$)$_3$), 23.4 ($\underline{C}(CH_3)_3$), 21.1 (Ar$\underline{C}H_3$), 20.6 ($\underline{C}(CH_3)_3$); HRMS (ESI) Calc. for $[M + NH_4]^+$ $C_{28}H_{44}NO_5SSi$: 534.2704; Found 534.2694.



***p*-Tolyl 2,4-di-*O*-benzyl-3-*O*-methyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-allyl-2-*O*-benzoyl-1-thio-α-D-rhamnopyranoside (3.51):** To a stirred solution of acceptor **3.53** (47.8 mg, 115 μmol) and donor **3.54** (79.1 mg, 157 μmol) in dry CH_2Cl_2 (4.0 mL) was added molecular sieves (400 mg, 4Å, powder). After stirring for 30 min at room temperature, the reaction mixture was cooled to –40 °C, and then *tert*-butyldimethylsilyl

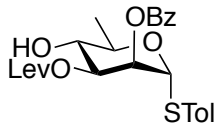
trifluoromethanesulfonate (3.6 μL, 16 μmol) was added dropwise. The resulting solution was stirred for 1 h at –40 °C under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (6:1 hexane–EtOAc) to afford **3.51** (61.3 mg, 70%) as a syrup. R_f 0.41 (6:1 hexane–EtOAc); $[\alpha]_D$ +33.4 (*c* 0.24, $CHCl_3$); ^{1}H NMR (600 MHz; $CDCl_3$): δ 8.03–8.01 (m, 2H, Ar), 7.62–7.59 (m, 1H, Ar), 7.48–7.45 (m, 4H, Ar), 7.40–7.38 (m, 2H, Ar), 7.34–7.31 (m, 6H, Ar), 7.27–7.25 (m, 2H, Ar), 7.15–7.13 (m, 2H, Ar), 5.96 (ddt, 1H, *J* = 16.9, 10.6, 6.2 Hz, $OCH_2C\underline{H}=CH_2$), 5.81 (dd, 1H, *J* = 3.1, 1.7 Hz, D-Rha-H-2), 5.44 (d, 1H, *J* = 1.5 Hz, D-Rha-H-1), 5.28 (dq, 1H, *J* = 17.2, 1.5 Hz, $OCH_2CH=C\underline{H}_2$), 5.23 (d, 1H, *J* = 1.6 Hz, L-Rha-H-1), 5.13 (dq, 1H, *J* = 10.3, 1.5 Hz, $OCH_2CH=C\underline{H}_2$), 4.92 (d, 1H, *J* = 11.6 Hz, $PhC\underline{H}_2$), 4.82 (d, 1H, *J* = 12.5 Hz, $PhC\underline{H}_2$), 4.70 (d, 1H, *J* = 12.5 Hz, $PhC\underline{H}_2$), 4.63 (d, 1H, *J* = 11.6 Hz, $PhC\underline{H}_2$), 4.35–4.27 (m, 2H, D-Rha-H-5, $OC\underline{H}_2CH=CH_2$), 4.21 (dd, 1H, *J* = 9.5, 3.2 Hz, D-Rha-H-3), 4.07 (ddt, *J* = 11.6, 6.1, 1.1 Hz, 1H), 3.91 (dq, 1H, *J* = 9.4, 6.2 Hz, L-Rha-H-5), 3.57 (dd, 1H, *J* = 3.3, 1.8 Hz, L-Rha-H-2), 3.51 (t, 1H, *J* = 9.4 Hz, L-Rha-H-4), 3.40 (dd, 1H, *J* = 9.4, 3.3 Hz, L-Rha-H-3), 3.37 (t, 1H, *J* = 9.5 Hz, D-Rha-H-4), 3.13 (s, 3H, $OC\underline{H}_3$), 2.34 (s, 3H, $ArC\underline{H}_3$), 1.41 (d, 3H, *J* = 6.2 Hz, D-Rha-H-6), 1.35 (d, 3H, *J* = 6.2 Hz, L-Rha-H-6); ^{13}C NMR (125 MHz; $CDCl_3$): δ 165.4 (C=O), 139.4 (Ar), 138.4 (Ar), 138.0 (Ar), 134.1 ($OCH_2\underline{C}H=CH_2$), 133.3 (Ar), 132.5 (Ar), 130.0 (Ar), 129.9 (Ar), 129.8 (2 × Ar), 128.5 (Ar), 128.2 (Ar), 128.1 (2 × Ar), 127.4 (Ar), 127.2 (Ar), 127.1 (Ar), 118.0 ($OCH_2CH=\underline{C}H_2$), 93.8 (L-Rha-C-1, $^1J_{C\text{-}H}$ = 169.8 Hz), 86.5 (D-Rha-C-1), 81.4 (L-Rha-C-3), 80.3 (L-Rha-C-4), 79.7 (D-Rha-C-4), 74.8

(O<u>C</u>H$_2$CH=CH$_2$), 74.7 (Ph<u>C</u>H$_2$), 73.5 (L-Rha-C-2), 73.0 (D-Rha-C-3), 72.0 (Ph<u>C</u>H$_2$), 70.1 (D-Rha-C-2), 69.1 (D-Rha-C-5), 68.1 (L-Rha-C-5), 57.2 (O<u>C</u>H$_3$), 21.1 (Ar<u>C</u>H$_3$), 18.2 (L-Rha-C-6), 17.9 (D-Rha-C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{44}H_{50}NaO_9S$: 777.3068; Found 777.3061.



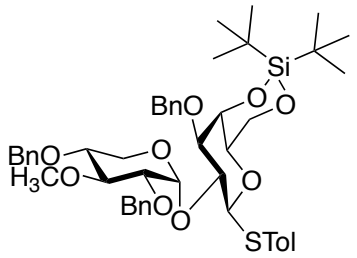
***p*-Tolyl 4-*O*-allyl-2-*O*-benzoyl-3-*O*-levulinoyl-1-thio-α-D-rhamnopyranoside (3.67):** To a stirred solution of **3.53** (744 mg, 1.80 mmol) in dry CH_2Cl_2 (10 mL) was added EDC·HCl (689 mg, 3.59 mmol), levulinic acid (417 mg, 3.59 mmol) and 4-(dimethylamino)pyridine (22 mg, 0.18 mmol) successively. The reaction mixture was stirred for 2 h at room temperature. Then poured into the saturated $NaHCO_3$ (aq.) and extracted with CH_2Cl_2 (100 mL × 3). The combined organic layers were dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (4:1 hexane–EtOAc) to afford **3.67** (923 mg, quant.) as a syrup. R_f 0.21 (4:1 hexane–EtOAc); $[\alpha]_D$ +57.8 (*c* 0.47, $CHCl_3$); ^{1}H NMR (600 MHz; $CDCl_3$): δ 8.06–8.04 (m, 2H, Ar), 7.63–7.60 (m, 1H, Ar), 7.50–7.47 (m, 2H, Ar), 7.41–7.39 (m, 2H, Ar), 7.14–7.13 (m, 2H, Ar), 5.93 (ddt, 1H, *J* = 17.2, 10.4, 5.7 Hz, OCH$_2$C<u>H</u>=CH$_2$), 5.73 (dd, 1H, *J* = 3.2, 1.7 Hz, H-2), 5.43 (d, 1H, *J* = 1.7 Hz, H-1), 5.37 (dd, 1H, *J* = 9.6, 3.3 Hz, H-3), 5.30 (dq, 1H, *J* = 17.2, 1.6 Hz, OCH$_2$CH=C<u>H</u>$_2$), 5.20 (dq, 1H, *J* = 10.4, 1.4 Hz, OCH$_2$CH=C<u>H</u>$_2$), 4.36 (dq, 1H, *J* = 9.4, 6.2 Hz, H-5), 4.25 (ddt, 1H, *J* = 12.4, 5.5, 1.4 Hz, OC<u>H</u>$_2$CH=CH$_2$), 4.15 (ddt, 1H, *J* = 12.4, 5.9, 1.3 Hz, OC<u>H</u>$_2$CH=CH$_2$), 3.58 (t, 1H, *J* = 9.5

Hz, H-4), 2.83 (dt, 1H, J = 18.3, 7.2 Hz, $COCH_2C\underline{H}_2COCH_3$), 2.69 (dt, 1H, J = 18.3, 6.4 Hz, $COCH_2C\underline{H}_2COCH_3$), 2.61 (ddd, 1H, J = 17.2, 7.3, 6.9 Hz, $COC\underline{H}_2CH_2COCH_3$), 2.49 (ddd, 1H, J = 17.2, 6.9, 6.1 Hz, $COC\underline{H}_2CH_2COCH_3$), 2.34 (s, 3H, $ArC\underline{H}_3$), 2.15 (s, 3H, $COCH_2CH_2COC\underline{H}_3$), 1.42 (d, 3H, J = 6.2 Hz, H-6); ^{13}C NMR (125 MHz; $CDCl_3$): δ 206.2 (C=O), 171.7 (C=O), 165.4 (C=O), 138.0 (Ar), 134.6 ($OCH_2\underline{C}H=CH_2$), 133.4 (Ar), 132.6 (Ar), 129.9 (Ar), 129.8 (2 × Ar), 129.6 (Ar), 128.5 (Ar), 117.2 ($OCH_2CH=\underline{C}H_2$), 86.1 (C-1), 78.7 (C-4), 74.0 ($O\underline{C}H_2CH=CH_2$), 72.4 (C-3), 72.3 (C-2), 69.1 (C-5), 37.8 ($COCH_2\underline{C}H_2COCH_3$), 29.8 ($COCH_2CH_2CO\underline{C}H_3$), 28.0 ($CO\underline{C}H_2CH_2COCH_3$), 21.1 ($Ar\underline{C}H_3$), 18.0 (C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{28}H_{32}NaO_7S$: 535.1761; Found 535.1762.



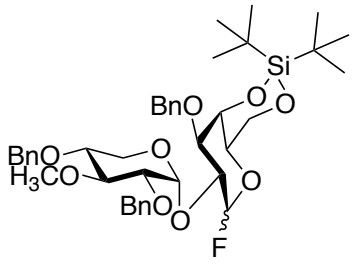
***p*-Tolyl 2-*O*-benzoyl-3-*O*-levulinoyl-1-thio-α-D-rhamnopyranoside (3.68):** To a stirred solution of **3.67** (198 mg, 386 mol) in dry THF (6.0 mL), degassed under vacuum, and stirring under an Ar atmosphere, (1,5-cyclooctadiene)bis(methyldiphenylphosphine)iridium (I) hexafluorophosphate catalyst (19.6 mg, 23.2 μmol) was added, followed by further degassing of the reaction mixture. The suspension was stirred for 15 min at 0 °C, and the catalyst was then activated with hydrogen (2 min under hydrogen atmosphere). The excess hydrogen was removed by three cycles of vacuum/Ar. The reaction mixture was then stirred for 2 h at room temperature under an Ar atmosphere. The solvent was then evaporated, and the residue was dissolved

in acetone–water (10:1, 11 mL) before HgO (117 mg, 540 μmol) and $HgCl_2$ (126 mg, 465 μmol) were added. The reaction mixture was stirred for 2 h at room temperature, then the solvent was concentrated, and the residue was diluted with EtOAc (100 mL), washed with 10% KI, saturated $Na_2S_2O_3$ (aq.) and water. The aqueous layers were extracted with EtOAc (100 mL), and the combined organic layers were dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (3:2 hexane–EtOAc) to afford **3.68** (122 mg, 67%) as a syrup. R_f 0.16 (2:1 hexane–EtOAc); $[\alpha]_D$ +59.2 (*c* 0.30, $CHCl_3$); ^{1}H NMR (600 MHz; $CDCl_3$): δ 8.06–8.05 (m, 2H, Ar), 7.62–7.60 (m, 1H, Ar), 7.49–7.47 (m, 2H, Ar), 7.42–7.40 (m, 2H, Ar), 7.15–7.14 (m, 2H, Ar), 5.71 (dd, 1H, *J* = 3.3, 1.6 Hz, H-2), 5.48 (d, 1H, *J* = 1.2 Hz, H-1), 5.33 (dd, 1H, *J* = 9.7, 3.3 Hz, H-3), 4.36 (dq, 1H, *J* = 9.4, 6.1 Hz, H-5), 3.88 (td, 1H, *J* = 9.6, 4.0 Hz, H-4), 2.86 (ddd, 1H, *J* = 18.5, 8.5, 5.6 Hz, $COCH_2C\underline{H}_2COCH_3$), 2.70 (dt, 1H, *J* = 18.5, 5.9 Hz, $COCH_2C\underline{H}_2COCH_3$), 2.66 (d, 1H, *J* = 4.1 Hz, 4-OH), 2.60 (ddd, 1H, *J* = 16.8, 8.5, 5.3 Hz, $COC\underline{H}_2CH_2COCH_3$), 2.49 (ddd, 1H, *J* = 16.8, 6.3, 5.7 Hz, $COC\underline{H}_2CH_2COCH_3$), 2.34 (s, 3H, $ArC\underline{H}_3$), 2.14 (s, 3H, $COCH_2CH_2COC\underline{H}_3$), 1.45 (d, 3H, *J* = 6.2 Hz, H-6); ^{13}C NMR (125 MHz; $CDCl_3$): δ 207.3 (C=O), 172.5 (C=O), 165.4 (C=O), 138.1 (Ar), 133.4 (Ar), 132.6 (Ar), 129.9 (Ar), 129.8 (Ar), 129.7 (Ar), 129.5 (Ar), 128.5 (Ar), 86.3 (C-1), 72.9 (C-3), 72.2 (C-2), 71.7 (C-4), 69.7 (C-5), 38.3 ($COCH_2\underline{C}H_2COCH_3$), 29.7 ($COCH_2CH_2CO\underline{C}H_3$), 28.1 ($CO\underline{C}H_2CH_2COCH_3$), 21.1 ($Ar\underline{C}H_3$), 17.6 (C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{25}H_{28}NaO_7S$: 495.1448; Found 495.1444.



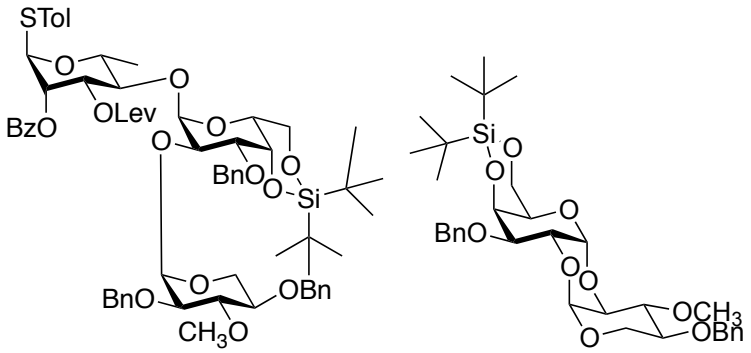
***p*-Tolyl 2,4-di-*O*-benzyl-3-*O*-methyl-α-D-xylopyranosyl-(1→2)-3-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-1-thio-α-D-galactopyranoside (3.69):** To a stirred solution of acceptor **3.56** (312 mg, 0.604 mmol) and donor **3.55** (567 g, 1.10 mmol) in dry CH_2Cl_2 (6.0 mL) was added molecular sieves (600 mg, 4Å, powder). After stirring for 30 min at room temperature, the reaction mixture was cooled to –78 °C, and then *tert*-butyldimethylsilyl trifluoromethanesulfonate (28 μL, 0.12 mmol) was added dropwise. The resulting solution was stirred for 1 h at –78 °C under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (4:1 hexane–EtOAc) to afford **3.69** (270 mg, 53%) as a white solid. R_f 0.31 (4:1 hexane–EtOAc); $[\alpha]_D$ +18.3 (*c* 0.52, $CHCl_3$); ^{1}H NMR (600 MHz; $CDCl_3$): δ 7.45–7.43 (m, 2H, Ar), 7.37–7.24 (m, 15H, Ar), 7.04–7.03 (m, 2H, Ar), 5.65 (d, 1H, J = 3.7 Hz, Xyl-H-1), 4.89 (d, 1H, J = 11.8 Hz, PhC$\underline{H}_2$), 4.77 (d, 1H, J = 11.2 Hz, PhC$\underline{H}_2$), 4.77 (d, 1H, J = 9.8 Hz, Gal-H-1), 4.73 (d, 1H, J = 11.8 Hz, PhC$\underline{H}_2$), 4.64 (d, 1H, J = 11.9 Hz, PhC$\underline{H}_2$), 4.59 (d, 1H, J = 11.2 Hz, PhC$\underline{H}_2$), 4.59 (d, 1H, J = 3.1 Hz, Gal-H-4), 4.53 (d, 1H, J = 11.9 Hz, PhC$\underline{H}_2$), 4.19 (d, 2H, J = 1.8 Hz, Gal-H-6), 4.15–4.07 (m, 2H, Xyl-H-5a, Gal-H-2), 3.71 (s, 3H, OC$\underline{H}_3$), 3.64 (t, 1H, J = 9.2 Hz, Xyl-H-3), 3.52 (dd, 1H, J = 8.9, 3.2 Hz, Gal-H-3), 3.44–3.38 (m, 3H, Xyl-H-4, Xyl-H-2, Xyl-H-5b),

3.28 (s, 1H, Gal-H-5), 2.32 (s, 3H, ArC$\underline{H}_3$), 1.13 (s, 9H, C(C$\underline{H}_3$)$_3$), 1.08 (s, 9H, C(C$\underline{H}_3$)$_3$); ^{13}C NMR (125 MHz; $CDCl_3$): δ 138.8 (Ar), 138.3 (Ar), 137.8 (Ar), 137.4 (Ar), 132.2 (Ar), 130.4 (Ar), 129.5 (Ar), 128.5 (Ar), 128.4 (Ar), 128.3 (Ar), 128.2 (Ar), 128.0 (Ar), 127.7 (Ar), 127.5 (Ar), 127.4 (Ar), 96.5 (Xyl-C-1, $^1J_{C\text{-}H}$ = 172.1 Hz), 88.1 (Gal-C-1), 82.7 (Xyl-C-3), 80.8 (Gal-C-3), 79.6 (Xyl-C-2), 78.2 (Xyl-C-4), 74.3 (Gal-C-5), 73.1 (Ph$\underline{C}H_2$), 72.8 (Ph$\underline{C}H_2$), 72.3 (Gal-C-2), 70.4 (Ph$\underline{C}H_2$), 69.1 (Gal-C-4), 67.3 (Gal-C-6), 61.2 (O$\underline{C}H_3$), 60.5 (Xyl-C-5), 27.7 (C($\underline{C}H_3$)$_3$), 27.6 (C($\underline{C}H_3$)$_3$), 23.4 ($\underline{C}$(CH$_3$)$_3$), 21.1 (Ar$\underline{C}H_3$), 20.7 ($\underline{C}$(CH$_3$)$_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{48}H_{62}NaO_9SSi$: 865.3776; Found 865.3773.



2,4-Di-*O*-benzyl-3-*O*-methyl-α-D-xylopyranosyl-(1→2)-3-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-1-thio-α-D-galactopyranosyl fluoride (3.70): To a stirred solution of **3.69** (74.1 mg, 87.9 μmol) in dry CH_2Cl_2 (5.0 mL) was added (dimethylamino)sulfur trifluoride (0.106 mL, 106 μmol, 1.0 M in CH_2Cl_2) and *N*-bromosuccinimide (18.8 mg, 106 μmol) successively at –15 °C. The reaction mixture was stirred for 1 h at –15 °C, then CH_3OH was added and the solution was concentrated. The residue was then diluted with CH_2Cl_2 and wash with saturated $NaHCO_3$ (aq.). The aqueous layer was extracted with CH_2Cl_2 (20 mL × 3), and combined organic layers were dried over Na_2SO_4, filtered and the filtrate was

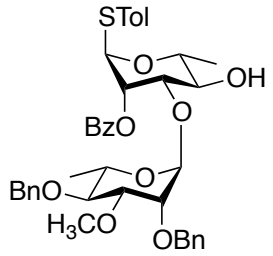
concentrated. The crude residue was purified by flash chromatography (4:1 hexane–EtOAc) to afford **3.70** (56.9 mg, 88%) as a white solid.



***p*-Tolyl 2,4-di-*O*-benzyl-3-*O*-methyl-α-D-xylopyranosyl-(1→2)-3-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranosyl-(1→4)-2-*O*-benzoyl-3-*O*-levulinoyl-1-thio-α-D-rhamnopyranoside (3.50) & 4-*O*-benzyl-3-*O*-methyl-α-D-xylopyranose 3-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranose 1,2':1':2 anhydride (3.71):** To a stirred solution of acceptor **3.68** (80.1 mg, 170 μmol) and donor **3.70** (56.9 mg, 77.0 μmol) in dry CH_2Cl_2 (4.0 mL) was added molecular sieves (400 mg, 4Å, powder). After stirring for 30 min at room temperature, the reaction mixture was cooled to 0 °C, and then bis(cyclopentadienyl)zirconium(IV) dichloride (27.0 mg, 92.4 μmol) and silver trifluoromethanesulfonate (47.5 mg, 185 μmol) were added successively. The resulting solution was stirred for 1.5 h at room temperature under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was washed with saturated $NaHCO_3$ (aq.), the aqueous layer was extracted with CH_2Cl_2 (50 mL × 3), dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (4:1 hexane–EtOAc) to afford **3.50** (64.4 mg, 70%) as a

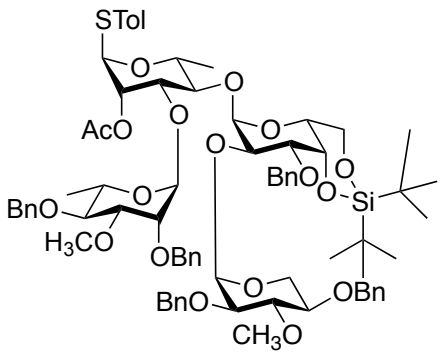
syrup and **3.71** as a byproduct (4.8 mg, 10%). Data for **3.50**: R_f 0.15 (4:1 hexane–EtOAc); $[\alpha]_D$ +82.0 (*c* 0.19, $CHCl_3$); ^1H NMR (600 MHz; $CDCl_3$): δ 8.05–8.03 (m, 2H, Ar), 7.62–7.59 (m, 1H, Ar), 7.50–7.45 (m, 6H, Ar), 7.35–7.20 (m, 13H, Ar), 7.12–7.11 (m, 2H, Ar), 5.77 (dd, 1H, *J* = 3.2, 2.1 Hz, D-Rha-H-2), 5.56 (d, 1H, *J* = 3.7 Hz, Gal-H-1), 5.44 (dd, 1H, *J* = 9.2, 3.3 Hz, D-Rha-H-3), 5.38 (d, 1H, *J* = 1.9 Hz, D-Rha-H-1), 5.13 (d, 1H, *J* = 3.5 Hz, Xyl-H-1), 4.82 (d, 1H, *J* = 11.9 Hz, PhC$\underline{H}_2$), 4.76 (s, 2H, PhC$\underline{H}_2$), 4.69 (d, 1H, *J* = 11.8 Hz, PhC$\underline{H}_2$), 4.63 (d, 1H, *J* = 11.9 Hz, PhC$\underline{H}_2$), 4.59–4.57 (m, 2H, PhC$\underline{H}_2$, Gal-H-4), 4.38 (dq, 1H, *J* = 9.1, 6.1 Hz, D-Rha-H-5), 4.31–4.27 (m, 2H, Gal-H-2, Gal-H-6a), 4.17 (dd, 1H, *J* = 12.4, 1.4 Hz, Gal-H-6b), 4.09 (t, 1H, *J* = 9.2 Hz, D-Rha-H-4), 3.88 (t, 1H, *J* = 11.0 Hz, Xyl-H-5a), 3.82 (dd, 1H, *J* = 10.2, 2.9 Hz, Gal-H-3), 3.74–3.71 (m, 2H, Gal-H-5, Xyl-H-3), 3.61 (s, 3H, OC$\underline{H}_3$), 3.57 (dd, 1H, *J* = 11.1, 5.8 Hz, Xyl-H-5b), 3.54–3.47 (m, 2H, Xyl-H-2, Xyl-H-4), 2.76 (ddd, 1H, *J* = 18.0, 8.4, 5.7 Hz, $COCH_2C\underline{H}_2COCH_3$), 2.62 (ddd, 1H, *J* = 17.2, 8.5, 5.5 Hz, $COC\underline{H}_2CH_2COCH_3$), 2.53 (dt, 1H, *J* = 18.0, 5.6 Hz, $COCH_2C\underline{H}_2COCH_3$), 2.43 (dt, 1H, *J* = 17.2, 5.6 Hz, $COC\underline{H}_2CH_2COCH_3$), 2.33 (s, 3H, ArC$\underline{H}_3$), 2.06 (s, 3H, $COCH_2CH_2COC\underline{H}_3$), 1.33 (d, 3H, *J* = 6.2 Hz, D-Rha-H-6), 1.08 (s, 9H, C(C$\underline{H}_3$)$_3$), 1.05 (s, 9H, C(C$\underline{H}_3$)$_3$); ^{13}C NMR (125 MHz; $CDCl_3$): δ 206.0 (C=O), 171.9 (C=O), 165.5 (C=O), 138.9 (Ar), 138.8 (Ar), 138.0 (Ar), 133.4 (Ar), 132.6 (Ar), 129.9 (2 × Ar), 129.5 (2 × Ar), 128.5 (Ar), 128.2 (2 × Ar), 127.9 (Ar), 127.6 (Ar), 127.5 (Ar), 127.4 (2 × Ar), 127.2 (Ar), 95.2 (Gal-C-1, $^1J_{C\text{-}H}$ = 172.4 Hz), 94.4 (Xyl-C-1), 85.8 (D-Rha-C-1), 82.8 (Xyl-C-3), 79.5 (Xyl-C-2), 78.2 (Xyl-C-4), 75.7 (Gal-C-3), 73.4 (D-Rha-C-3), 73.2 (D-Rha-C-4), 72.9 (Ph$\underline{C}H_2$), 72.4 (Ph$\underline{C}H_2$), 71.6 (D-Rha-C-2), 71.2 (Ph$\underline{C}H_2$), 70.9 (Gal-C-4), 70.4 (Gal-C-2),

68.4 (D-Rha-C-5), 68.0 (Gal-C-5), 67.1 (Gal-C-6), 61.1 ($O\underline{C}H_3$), 60.1 (Xyl-C-5), 37.5 ($COCH_2\underline{C}H_2COCH_3$), 29.7 ($COCH_2CH_2CO\underline{C}H_3$), 28.1 ($CO\underline{C}H_2CH_2COCH_3$), 27.7 ($C(\underline{C}H_3)_3$), 27.3 ($C(\underline{C}H_3)_3$), 23.4 ($\underline{C}(CH_3)_3$), 21.1 ($Ar\underline{C}H_3$), 20.7 ($\underline{C}(CH_3)_3$), 19.0 (D-Rha-C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{66}H_{82}NaO_{16}SSi$: 1213.4985; Found 1213.4984. Data for **3.71**: R_f 0.21 (4:1 hexane–EtOAc); $[\alpha]_D$ +46.1 (*c* 0.16, $CHCl_3$); ^1H NMR (700 MHz; $CDCl_3$): δ 7.48–7.47 (m, 2H, Ar), 7.32–7.30 (m, 2H, Ar), 7.26–7.16 (m, 6H), 5.01 (d, 1H, J = 3.4 Hz, Gal-H-1), 4.79 (s, 2H, 2 × $PhC\underline{H}_2$), 4.76 (d, 1H, J = 1.9 Hz, Xyl-H-1), 4.51 (d, 1H, J = 11.1 Hz, $PhC\underline{H}_2$), 4.50 (d, 1H, J = 11.0 Hz, $PhC\underline{H}_2$), 4.44 (dd, 1H, J = 10.1, 3.0 Hz, Gal-H-3), 4.09 (d, 1H, J = 12.7, 1.9 Hz, Xyl-H-5a), 4.07–4.05 (m, 2H, Gal-H-2, Gal-H-4), 3.91 (dd, 1H, J = 12.5, 1.6 Hz, Gal-H-6a), 3.88 (br s, 1H, Xyl-H-2), 3.78 (dd, 1H, J = 12.7, 1.0 Hz, Xyl-H-5b), 3.72 (dd, 1H, J = 12.5, 2.0 Hz, Gal-H-6b), 3.67 (q, 1H, J = 2.2 Hz, Xyl-H-4), 3.43 (s, 3H, $OC\underline{H}_3$), 3.39 (d, 1H, J = 1.3 Hz, Xyl-H-3), 3.23 (br s, 1H, Gal-H-5), 0.99 (s, 9H, $C(C\underline{H}_3)_3$), 0.98 (s, 9H, $C(C\underline{H}_3)_3$); ^{13}C NMR (125 MHz; $CDCl_3$): δ 139.4 (Ar), 138.3 (Ar), 128.3 (Ar), 128.1 (2 × Ar), 127.6 (Ar), 127.5 (Ar), 127.4 (Ar), 95.2 (Gal-C-1), 90.5 (Xyl-C-1), 77.1 (Xyl-C-4), 76.1 (Gal-C-3), 71.5 (Xyl-C-2), 71.4 (Xyl-C-3), 71.2 (2 × C, $Ph\underline{C}H_2$, Gal-C-4), 70.1 ($Ph\underline{C}H_2$), 69.8 (Gal-C-2), 69.5 (Gal-C-5), 67.1 (Gal-C-6), 63.5 (Xyl-C-5), 58.3 ($O\underline{C}H_3$), 27.6 ($C(\underline{C}H_3)_3$), 27.3 ($C(\underline{C}H_3)_3$), 23.4 ($\underline{C}(CH_3)_3$), 20.7 ($\underline{C}(CH_3)_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{34}H_{48}NaO_9Si$: 651.2960; Found 651.2965.



***p*-Tolyl 2,4-di-*O*-benzyl-3-*O*-methyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-benzoyl-1-thio-α-D-rhamnopyranoside (3.72):** To a stirred solution of **3.51** (29.6 mg, 39.2 μmol) in dry THF (2.0 mL), degassed under vacuum, and stirring under an Ar atmosphere, (1,5-cyclooctadiene)bis(methyldiphenylphosphine)iridium (I) hexafluorophosphate catalyst (2.0 mg, 2.4 μmol) was added, followed by further degassing of the reaction mixture. The suspension was stirred for 15 min at 0 °C, and the catalyst was then activated with hydrogen (2 min under a hydrogen atmosphere). The excess hydrogen was removed by three cycles of vacuum/Ar. The reaction mixture was then stirred for 2 h at room temperature under an Ar atmosphere. The solvent was then evaporated, and the residue was dissolved in acetone–water (10:1, 2.2 mL) before HgO (11.9 mg, 54.9 μmol) and $HgCl_2$ (12.8 mg, 47.0 μmol) were added. The reaction mixture was stirred for 2 h at room temperature, then the solvent was concentrated, and the residue was diluted with EtOAc (150 mL), washed with 10% KI, saturated $Na_2S_2O_3$ (aq.) and water. The aqueous layers were extracted with EtOAc (100 mL), and the combined organic layers were dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (4:1 hexane–EtOAc) to afford **3.72** (25.5 mg, 91%) as a syrup. R_f 0.34 (4:1 hexane–EtOAc); $[\alpha]_D$ +36.6 (*c* 0.38, $CHCl_3$); ^{1}H NMR (600 MHz; $CDCl_3$): δ 8.02–8.00 (m, 2H, Ar), 7.58–7.56 (m, 1H, Ar),

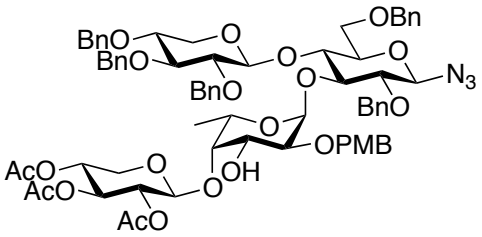
7.45–7.39 (m, 6H, Ar), 7.37–7.28 (m, 8H, Ar), 7.16–7.14 (m, 2H, Ar), 5.74 (dd, 1H, *J* = 3.3, 1.5 Hz, D-Rha-H-2), 5.48 (d, 1H, *J* = 1.2 Hz, D-Rha-H-1), 5.05 (d, 1H, *J* = 1.9 Hz, L-Rha-H-1), 4.84 (d, 1H, *J* = 11.0 Hz, PhC$\underline{H}_2$), 4.76 (s, 2H, 2 × PhC$\underline{H}_2$), 4.58 (d, 1H, *J* = 11.0 Hz, PhC$\underline{H}_2$), 4.27 (dq, 1H, *J* = 9.3, 6.1 Hz, 1H, D-Rha-H-5), 3.95 (dd, 1H, *J* = 9.2, 3.4 Hz, D-Rha-H-3), 3.80 (dq, 1H, *J* = 9.3, 6.2 Hz, L-Rha-H-5), 3.70 (dd, 1H, *J* = 3.1, 1.9 Hz, L-Rha-H-2), 3.67 (td, 1H, *J* = 9.3, 2.5 Hz, D-Rha-H-4), 3.52 (t, 1H, *J* = 9.2 Hz, L-Rha-H-4), 3.34 (dd, 1H, *J* = 9.1, 3.1 Hz, L-Rha-H-3), 3.19 (s, 3H, OC$\underline{H}_3$), 3.11 (d, 1H, *J* = 2.2 Hz, D-Rha-4-OH), 2.35 (s, 3H, ArC$\underline{H}_3$), 1.42 (d, 3H, *J* = 6.2 Hz, D-Rha-H-6), 1.36 (d, 3H, *J* = 6.2 Hz, L-Rha-H-6); ^{13}C NMR (125 MHz; $CDCl_3$): δ 165.6 (C=O), 138.6 (Ar), 138.2 (Ar), 138.1 (Ar), 133.4 (Ar), 132.5 (Ar), 129.9 (Ar), 129.8 (2 × Ar), 129.6 (Ar), 128.5 (Ar), 128.3 (2 × Ar), 128.0 (Ar), 127.8 (Ar), 127.7 (Ar), 127.6 (Ar), 97.0 (L-Rha-C-1), 86.5 (D-Rha-C-1), 81.2 (L-Rha-C-3), 79.8 (L-Rha-C-4), 77.6 (D-Rha-C-3), 74.9 (Ph$\underline{C}H_2$), 74.3 (L-Rha-C-2), 72.7 (Ph$\underline{C}H_2$), 72.3 (D-Rha-C-4), 71.5 (D-Rha-C-2), 69.3 (D-Rha-C-5), 69.1 (L-Rha-C-5), 57.4 (O$\underline{C}H_3$), 21.1 (Ar$\underline{C}H_3$), 18.1 (L-Rha-C-6), 17.7 (D-Rha-C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{41}H_{46}NaO_9S$: 737.2755; Found 737.2749.



***p*-Tolyl 2,4-di-*O*-benzyl-3-*O*-methyl-α-D-xylopyranosyl-(1→2)-3-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranosyl-(1→4)-[2,4-di-*O*-benzyl-3-*O*-methyl-α-L-rhamnopyranosyl-(1→3)]-2-*O*-acetyl-1-thio-α-D-rhamnopyranoside (3.74):** To a stirred solution of acceptor **3.72** (4.3 mg, 6.03 μmol) and donor **3.70** (5.67 mg, 7.67 μmol) in dry CH_2Cl_2 (1.5 mL) was added molecular sieves (100 mg, 4Å, powder). After stirring for 30 min at room temperature, the reaction mixture was cooled to 0 °C, and then bis(cyclopentadienyl)zirconium(IV) dichloride (2.69 mg, 9.20 μmol) and silver trifluoromethanesulfonate (4.73 mg, 18.4 μmol) were added successively. The resulting solution was stirred for 1 h at room temperature under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was washed with saturated $NaHCO_3$ (aq.), the aqueous layer was extracted with CH_2Cl_2 (20 mL × 3), dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (6:1 hexane–EtOAc) to afford **3.49** with inseparable byproducts. To a stirred solution of **3.49** (1.97 mg) in CH_3OH (1 mL) was added a solution of $NaOCH_3$ in CH_3OH (0.2 mL, 0.5 M). The reaction mixture was stirred overnight at room temperature, then neutralized by addition of Amberlite® IR-120 (H^+) cation exchange resin,

filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (4:1 hexane–EtOAc) to afford **3.73** (2.81 mg, 35% over two steps) as a syrup. To a stirred solution of **3.73** (2.81 mg, 2.11 μmol) in pyridine (1.0 mL) was added acetic anhydride (0.5 mL) dropwise at room temperature. The reaction mixture was stirred for 2 h at room temperature, then the solvent was concentrated. The crude residue was dilute with CH_2Cl_2 (20 mL) and wash with 1N HCl and saturated $NaHCO_3$ (aq.). The organic layer was dried over Na_2SO_4, filtered and the filtrate was concentrated to afford **3.74** (2.90 mg, quant.) as a syrup. R_f 0.50 (3:1 hexane–EtOAc); $[\alpha]_D$ +59.9 (*c* 0.17, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.42–7.39 (m, 4H), 7.34–7.16 (m, 23H), 7.09–7.08 (m, 2H), 5.63 (br s, 1H, Gal-H-1), 5.27 (t, 1H, *J* = 3.4 Hz), 5.18–5.16 (m, 2H, Xyl-H-1, D-Rha-H-1), 4.92 (d, 1H, *J* = 1.8 Hz, L-Rha-H-1), 4.86 (d, 1H, *J* = 11.1 Hz), 4.82 (d, 1H, *J* = 11.9 Hz), 4.70 (d, 1H, *J* = 12.5 Hz), 4.66 (s, 2H), 4.64–4.59 (m, 4H), 4.51–4.50 (m, 2H), 4.27 (dd, 1H, *J* = 10.1, 3.6 Hz), 4.21 (dd, 1H, *J* = 12.4, 1.9 Hz), 4.15–4.10 (m, 2H), 4.07 (dd, 1H, *J* = 6.9, 3.1 Hz), 3.81–3.76 (m, 3H), 3.74–3.69 (m, 2H), 3.64 (t, 1H, *J* = 9.2 Hz), 3.59 (s, 1H), 3.57 (s, 3H), 3.51–3.49 (m, 2H), 3.46 (dd, 1H, *J* = 11.1, 5.7 Hz), 3.36–3.30 (m, 5H), 2.31 (s, 3H), 1.95 (s, 3H), 1.29 (d, 3H, *J* = 6.2 Hz), 1.21 (d, 3H, *J* = 6.3 Hz), 1.04 (s, 9H), 1.00 (s, 9H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 169.7, 138.89, 138.8 (2 × C), 138.7, 138.2, 137.9, 132.6, 129.8 (2 × C), 128.4, 128.3 (2 × C), 128.2 (2 × C), 127.8 (2 × C), 127.7 (2 × C), 127.6, 127.5, 127.4 (2 × C), 127.2, 97.8 (L-Rha-C-1), 95.0 (Gal-C-1), 94.1 (Xyl-C-1), 85.3 (D-Rha-C-1), 82.8, 81.4, 80.2, 79.0, 78.0, 76.5, 75.7, 75.0, 74.5, 72.9, 72.8, 72.0, 70.8 (2 × C), 70.6, 69.4, 68.6, 68.0, 67.0, 60.9, 60.1, 57.7, 31.9, 27.7, 27.4, 22.7, 21.1, 21.0,

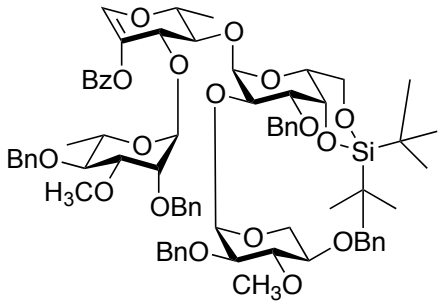
18.9, 18.1; HRMS (ESI) Calc. for $[M + NH_4]^+$ $C_{77}H_{102}NO_{18}SSi$: 1388.6581; Found 1388.6572.



2,3,4-Tri-*O*-acetyl-β-D-xylopyranosyl-(1→4)-2-*O*-(4-methoxybenzyl)-α-L-fucopyranosyl-(1→3)-[2,3,4-tri-*O*-benzyl-β-D-xylopyranosyl-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (3.52): To a stirred solution of acceptor **3.38** (319 mg, 291 μmol) and *p*-tolyl 2,3,4-tri-*O*-acetyl-1-thio-β-D-xylopyranoside **3.14**[16] (268 mg, 699 μmol) in dry CH_2Cl_2 (8.0 mL) was added molecular sieves (800 mg, 4Å, powder). After stirring for 30 min at room temperature, the reaction mixture was cooled to 0 °C, and then *N*-iodosuccinimide (189 mg, 839 μmol) and silver trifluoromethanesulfonate (22.5 mg, 87.4 mmol) were added successively. The resulting solution was stirred for 1 h at 0 °C under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was washed with saturated $Na_2S_2O_3$ (aq.) and saturated $NaHCO_3$ (aq.), the aqueous layer was extracted with CH_2Cl_2 (100 mL × 3), dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (2:1 hexane–EtOAc) to afford **3.75** with glycal as an inseparable byproduct. To a stirred solution of **3.75** (302 mg, 224 μmol) in dry THF (7.0 mL), degassed under vacuum, and stirring under an Ar atmosphere, (1,5-cyclooctadiene)bis(methyldiphenylphosphine)iridium (I) hexafluorophosphate catalyst

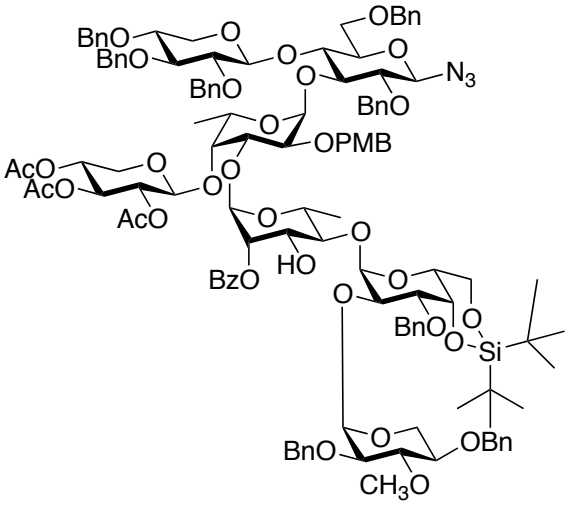
(11.3 mg, 13.4 μmol) was added, followed by further degassing of the reaction mixture. The suspension was stirred for 15 min at 0 °C, and the catalyst was then activated with hydrogen (2 min under hydrogen atmosphere). The excess hydrogen was removed by three cycles of vacuum/Ar. The reaction mixture was then stirred for 2 h at room temperature under an Ar atmosphere. The solvent was then evaporated, and the residue was dissolved in acetone–water (10:1, 5.5 mL) before HgO (67.8 mg, 313 μmol) and $HgCl_2$ (72.8 mg, 268 μmol) were added. The reaction mixture was stirred for 2 h at room temperature, then the solvent was concentrated, and the residue was diluted with EtOAc (100 mL), washed with 10% KI, saturated $Na_2S_2O_3$ (aq.) and water. The aqueous layers were extracted with EtOAc (60 mL), and the combined organic layers were dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (4:1 hexane–EtOAc) to afford **3.52** (215 mg, 56% over two steps) as a syrup. R_f 0.44 (1:1 hexane–EtOAc); $[\alpha]_D$ –64.5 (*c* 0.28, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.36–7.26 (m, 21H), 7.25–7.24 (m, 2H), 7.21–7.20 (m, 2H), 7.11–7.09 (m, 2H), 6.72–6.70 (m, 2H), 5.49 (d, 1H, J = 3.7 Hz, Fuc-H-1), 5.17 (t, 1H, J = 9.2 Hz), 4.99–4.94 (m, 2H), 4.83–4.80 (m, 3H), 4.77 (q, 1H, J = 6.7 Hz), 4.73 (d, 1H, J = 11.2 Hz), 4.72 (t, 1H, J = 11.4 Hz), 4.68 (d, 1H, J = 11.1 Hz), 4.67 (d, 1H, J = 11.4 Hz), 4.62 (d, 1H, J = 11.4 Hz), 4.61 (d, 1H, J = 11.9 Hz), 4.57 (d, 1H, J = 8.6 Hz, Glc-H-1), 4.55 (d, 1H, J = 11.7 Hz), 4.52 (d, 1H, J = 11.7 Hz), 4.45 (d, 1H, J = 7.5 Hz, Xyl-H-1), 4.39 (d, 1H, J = 11.9 Hz), 4.38 (d, 1H, J = 8.0 Hz, Xyl'-H-1), 4.11 (td, 1H, J = 10.1, 3.0 Hz), 4.07 (dd, 1H, J = 11.7, 5.4 Hz), 4.03 (t, 1H, J = 9.6 Hz), 3.93–3.88 (m, 2H), 3.86 (t, 1H, J = 9.3 Hz), 3.73 (s, 3H), 3.61 (dd, 1H, J = 11.2,

1.6 Hz), 3.56 (d, 1H, J = 2.2 Hz), 3.52 (dd, 1H, J = 10.3, 3.7 Hz), 3.43–3.35 (m, 4H), 3.29 (dd, 1H, J = 11.7, 9.8 Hz), 3.04 (t, 1H, J = 8.4 Hz), 3.01 (d, 1H, J = 9.9 Hz), 2.96 (dd, 1H, J = 11.6, 10.4 Hz), 2.03 (s, 3H), 2.03 (s, 3H), 2.01 (s, 3H), 1.10 (d, 3H, J = 6.6 Hz); ^{13}C NMR (125 MHz; $CDCl_3$): δ 170.2, 169.7, 169.3, 159.1, 138.3, 138.1 (2 × C), 138.0, 137.9, 130.4, 129.9, 128.5 (2 × C), 128.4 (2 × C), 128.1, 127.9, 127.8 (2 × C), 127.7, 127.6, 127.5, 127.0, 113.5, 103.2 (Xyl'-C-1), 102.4 (Xyl-C-1, $^1J_{C\text{-}H}$ = 162.7 Hz), 97.4 (Fuc-C-1), 90.2 (Glc-C-1), 85.0, 84.0, 82.6, 82.5, 78.4, 77.4, 77.2, 76.0, 75.8, 75.2, 75.0, 74.0, 73.5, 73.3, 73.2, 72.1, 71.6, 68.9, 68.6, 67.3, 65.0, 64.0, 62.6, 55.2, 20.8, 20.7 (2 × C), 16.1; HRMS (ESI) Calc. for $[M + NH_4]^+$ $C_{71}H_{85}N_4O_{21}$: 1329.5701; Found 1329.5712.



2,4-di-*O*-benzyl-3-*O*-methyl-α-D-xylopyranosyl-(1→2)-3-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranosyl-(1→4)-[2,4-di-*O*-benzyl-3-*O*-methyl-α-L-rhamnopyranosyl-(1→3)]-2-*O*-benzoyl-1-thio-α-D-rhamnopyransyl glycal (3.76): To a stirred solution of acceptor **3.52** (2.1 mg, 1.6 μmol) and donor **3.49** (4.5 mg, 3.1 μmol) in dry CH_2Cl_2 (1.5 mL) was added molecular sieves (100 mg, 4Å, powder). After stirring for 30 min at room temperature, the reaction mixture was cooled to 0 °C, and then *N*-iodosuccinimide (0.85 mg, 3.8 μmol) and silver trifluoromethanesulfonate (0.1 mg, 0.3 μmol) were added successively. The resulting solution was stirred for 1 h at room

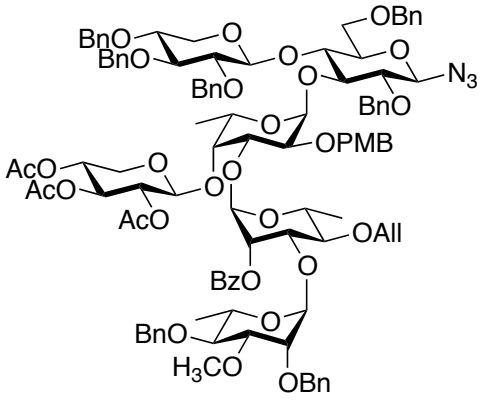
temperature under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was washed with saturated $Na_2S_2O_3$ (aq.) and saturated $NaHCO_3$ (aq.), the aqueous layer was extracted with CH_2Cl_2 (10 mL × 3), dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (3:1 hexane–EtOAc) to afford **3.76** (2.7 mg, 65%) as a syrup. R_f 0.50 (3:1 hexane–EtOAc); $[\alpha]_D$ –3.0 (*c* 0.10, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 8.02–8.01 (m, 2H), 7.55–7.53 (m, 1H), 7.41–7.40 (m, 2H), 7.36–7.23 (m, 17H), 7.20–7.17 (m, 3H), 7.15–7.14 (m, 3H), 7.06–7.04 (m, 2H), 6.56 (s, 1H, D-Rha-H-1), 5.34 (d, 1H, J = 3.6 Hz, Gal-H-1), 5.01 (d, 1H, J = 1.8 Hz, L-Rha-H-1), 4.88 (d, 1H, J = 3.4 Hz, Xyl-H-1), 4.84 (d, 1H, J = 11.0 Hz), 4.73–4.69 (m, 3H), 4.66 (d, 1H, J = 11.8 Hz), 4.62 (d, 1H, J = 11.8 Hz), 4.56 (d, 1H, J = 11.0 Hz), 4.54–4.52 (m, 2H), 4.48 (br s, 1H), 4.38–4.35 (m, 1H), 4.28 (d, 1H, J = 12.1 Hz), 4.23–4.21 (m, 2H), 4.13–4.11 (m, 2H), 3.98 (t, 1H, J = 2.0 Hz), 3.82–3.77 (m, 2H), 3.74–3.70 (m, 2H), 3.67 (t, 1H, J = 9.2 Hz), 3.58 (dd, 1H, J = 2.7, 2.2 Hz), 3.57 (s, 3H), 3.47–3.38 (m, 4H), 3.33 (dd, 1H, J = 9.5, 3.4 Hz), 3.27 (s, 3H), 1.40 (d, 3H, J = 7.0 Hz), 1.28 (d, 3H, J = 6.2 Hz), 1.04 (s, 9H), 1.03 (s, 9H); ^{13}C NMR (175 MHz; $CDCl_3$): δ 165.3, 138.9, 138.7, 138.4, 138.1, 137.8, 137.4 (D-Rha-C-1), 137.4, 133.5, 130.0, 129.4, 128.9, 128.5, 128.3 (2 × C), 128.2, 128.1, 128.0 (2 × C), 127.7, 127.6, 127.5 (2 × C), 127.3 (2 × C), 99.6 (L-Rha-C-1), 99.7 (Gal-C-1), 99.6 (Xyl-C-1), 82.8, 81.4, 80.2, 78.9, 78.2, 76.9, 76.3, 75.1, 75.0, 73.0, 72.9, 72.8, 72.5, 72.3, 71.2, 71.1, 70.9, 69.1, 68.0, 67.1, 61.0, 60.3, 57.4, 27.6, 27.4, 18.0, 15.4; HRMS (ESI) Calc. for $[M + Na]^+$ $C_{75}H_{92}NaO_{18}Si$: 1331.5945; Found 1331.5950.



2,4-Di-*O*-benzyl-3-*O*-methyl-α-D-xylopyranosyl-(1→2)-3-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranosyl-(1→4)-2-*O*-benzoyl-α-D-rhamnopyranosyl-(1→3)-[2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl-(1→4)]-2-*O*-(4-methoxybenzyl)-α-L-fucopyranosyl-(1→3)-[2,3,4-tri-*O*-benzyl-β-D-xylopyranosyl-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (3.77): To a stirred solution of acceptor **3.52** (2.1 mg, 1.6 μmol) and donor **3.50** (7.7 mg, 6.5 μmol) in dry Et_2O (1.5 mL) was added molecular sieves (100 mg, 4Å, powder). After stirring for 30 min at room temperature, the methyl trifluoromethanesulfonate (1.2 μL, 11 μmol) was added dropwise. The resulting solution was stirred for 24 h at room temperature under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (3:1 hexane–EtOAc) to afford **3.47** with inseparable byproducts. To a stirred solution of **3.47** (3.0 mg) in CH_2Cl_2–CH_3OH (1.0 mL, 9:1) was added hydrazine acetate (0.29 mg, 3.2 μmol) at room temperature. The reaction mixture was stirred overnight at room temperature. The reaction mixture was then

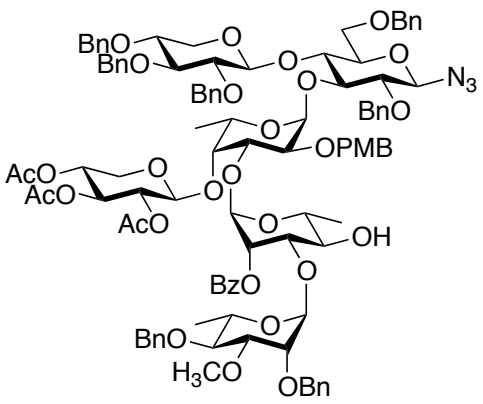
concentrated and the crude residue was purified by flash chromatography (2.5:1 hexane–EtOAc) to afford **3.77** (2.2 mg, 30% over two steps) as a syrup. R_f 0.42 (2:1 hexane–EtOAc); $[\alpha]_D$ –10.2 (*c* 0.22, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 8.00–7.99 (m, 2H), 7.50–7.48 (m, 1H), 7.41–7.40 (m, 2H), 7.32–7.18 (m, 39H), 7.14–7.11 (m, 3H), 6.68–6.66 (m, 2H), 5.44–5.43 (m, 2H, Fuc-H-1), 5.33 (d, 1H, J = 3.6 Hz, Gal-H-1), 5.11–5.09 (m, 2H, D-Rha-H-1), 5.02 (dd, 1H, J = 7.0, 5.3 Hz), 4.85 (td, 1H, J = 6.7, 4.3 Hz), 4.78–4.64 (m, 13H, Xyl(Me)-H-1, Xyl(Ac)-H-1), 4.62–4.57 (m, 3H), 4.54–4.49 (m, 6H, Glc-H-1), 4.44 (d, 1H, J = 11.8 Hz), 4.37–4.34 (m, 2H, Xyl(Bn)-H-1), 4.26 (dd, 1H, J = 10.3, 2.5 Hz), 4.23 (dd, 1H, J = 12.2, 4.2 Hz), 4.19 (dd, 1H, J = 10.4, 3.6 Hz), 4.14 (dd, 1H, J = 12.5, 1.8 Hz), 4.12–4.00 (m, 5H), 3.92–3.85 (m, 4H), 3.80 (dd, 1H, J = 10.4, 2.9 Hz), 3.77 (br s, 1H), 3.64–3.59 (m, 7H), 3.55 (s, 3H), 3.44–3.32 (m, 6H), 3.27 (dd, 1H, J = 9.7, 3.7 Hz), 3.05 (t, 1H, J = 8.6 Hz), 2.92 (t, 1H, J = 11.1 Hz), 2.05 (s, 3H), 1.92 (s, 3H), 1.88 (s, 3H), 1.27 (d, 3H, J = 6.2 Hz), 1.17 (d, 3H, J = 6.7 Hz), 1.01 (s, 9H), 1.01 (s, 9H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 169.9, 169.7, 169.4, 165.4, 159.1, 138.7, 138.6, 138.5, 138.3, 138.2, 137.9, 137.8, 137.3, 132.9, 130.3, 130.2, 130.0, 129.8, 128.9, 128.5, 128.4 (4 × C), 128.3, 128.2 (2 × C), 128.1, 128.0, 127.9, 127.7 (3 × C), 127.6, 127.5, 127.4 (2 × C), 127.3, 127.2, 113.7, 103.3 (Xyl(Bn)-C-1), 101.0 (D-Rha-C-1, $^1J_{C\text{-}H}$ = 172.7 Hz), 100.3 (Xyl(Ac)-C-1), 99.6 (Gal-C-1), 97.4 (Xyl(Me)-C-1), 96.8 (Fuc-C-1), 90.2 (Glc-C-1), 84.0, 83.3, 83.2, 82.6, 82.5, 82.0, 78.8, 78.6, 78.1, 76.1, 75.8, 75.2, 74.5, 74.4, 74.1 (2 × C), 73.8, 73.6, 73.5, 73.2, 73.0, 72.9, 72.5, 70.6 (2 × C), 69.8, 69.7, 69.1, 68.7, 67.8, 67.2, 67.1, 66.9, 65.7, 64.0, 60.9, 60.8, 60.1,

55.0, 31.9, 27.7, 27.3, 22.7, 20.9, 20.8, 20.7, 19.1, 16.7; HRMS (ESI) Calc. for [M + 2(NH_4)]$^{+2}$ $C_{125}H_{157}N_5O_{35}Si$: 1158.0209; Found 1158.0222.



2,4-Di-*O*-benzyl-3-*O*-methyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-allyl-2-*O*-benzoyl-α-D-rhamnopyranosyl-(1→3)-[2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl-(1→4)]-2-*O*-(4-methoxybenzyl)-α-L-fucopyranosyl-(1→3)-[2,3,4-tri-*O*-benzyl-β-D-xylopyranosyl-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (3.48): To a stirred solution of acceptor **3.52** (170 mg, 130 μmol) and donor **3.51** (188 mg, 249 μmol) in dry CH_2Cl_2 (5.0 mL) was added molecular sieves (500 mg, 4Å, powder). After stirring for 30 min at room temperature, the methyl trifluoromethanesulfonate (47.0 μL, 415 μmol) was added dropwise. The resulting solution was stirred for 24 h at room temperature under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (2:1 hexane–EtOAc) to afford **3.48** (200 mg, 80%) as a syrup. R_f 0.38 (2:1 hexane–EtOAc); $[\alpha]_D$ –56.7 (*c* 0.51, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.95–7.94 (m, 2H), 7.57–7.54 (m, 1H), 7.44–7.43 (m, 2H), 7.38–7.19 (m, 35H), 7.06–7.04 (m, 2H), 6.71–6.69 (m, 2H), 5.87 (ddt, 1H, J = 17.0, 10.4, 5.9 Hz), 5.70 (dd, 1H, J = 3.1, 1.7 Hz), 5.53 (d, 1H, J = 3.7

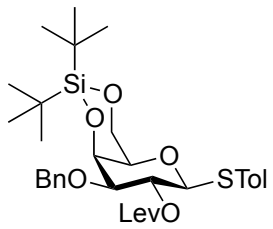
Hz, Fuc-H-1), 5.23 (d, 1H, J = 1.6 Hz, L-Rha-H-1), 5.18-5.17 (dq, 1H, J = 17.0, 1.6 Hz), 5.17 (d, 1H, J = 1.4 Hz, D-Rha-H-1), 5.03 (dq, 1H, J = 10.4, 1.6 Hz), 4.98–4.93 (m, 3H), 4.87 (d, 1H, J = 11.7 Hz), 4.83–4.76 (m, 5H), 4.73 (d, 1H, J = 11.1 Hz), 4.69–4.66 (m, 3H), 4.62–4.57 (m, 6H, Xyl(Ac)-H-1, Glc-H-1), 4.53 (d, 1H, J = 12.0 Hz), 4.40–4.37 (m, 3H, Xyl(Bn)-C-1), 4.27 (dd, 1H, J = 10.4, 2.4 Hz), 4.19 (ddt, 1H, J = 11.9, 5.7, 1.3 Hz, 1H), 4.16 (dd, 1H, J = 9.6, 3.3 Hz), 4.13–4.07 (m, 3H), 4.03 (t, 1H, J = 9.6 Hz), 3.97–3.91 (m, 3H), 3.89–3.83 (m, 2H), 3.64–3.59 (m, 5H), 3.56 (dd, 1H, J = 12.4, 5.2 Hz), 3.52–3.50 (m, 2H), 3.45–3.35 (m, 4H), 3.33 (dd, 1H, J = 9.4, 3.4 Hz), 3.21 (t, 1H, J = 9.5 Hz), 3.09–3.05 (m, 4H), 2.96 (t, 1H, J = 11.1 Hz), 2.07 (s, 3H), 2.01 (s, 3H), 1.88 (s, 3H), 1.31 (d, 3H, J = 6.3 Hz), 1.24 (d, 3H, J = 6.1 Hz), 1.15 (d, 3H, J = 6.6 Hz); ^{13}C NMR (125 MHz; $CDCl_3$): δ 169.8, 169.6, 169.5, 165.3, 159.2, 139.5, 138.6, 138.5 (2 × C), 138.1, 137.9 (2 × C), 134.5, 133.1, 130.0, 129.7, 129.6 (2 × C), 128.5, 128.4 (4 × C), 128.2, 128.1, 128.0 (2 × C), 127.9, 127.7 (2 × C), 127.6, 127.5, 127.3, 127.1 (2 × C), 126.7, 117.4, 113.7, 103.4 (Xyl(Bn)-C-1), 101.0 (D-Rha-C-1, $^{1}J_{C\text{-}H}$ = 173.8 Hz), 100.1 (Xyl(Ac)-C-1), 96.2 (Fuc-C-1), 93.6 (L-Rha-C-1), 90.2 (Glc-C-1), 84.2, 83.4, 82.7, 82.6, 81.4, 80.3, 79.3, 78.7, 77.4, 76.9, 75.7, 75.3, 74.6, 74.2, 74.0, 73.8, 73.7 (2 × C), 73.5, 73.2, 72.5, 72.1, 72.0, 69.1, 68.8, 68.6, 68.2, 67.9, 67.7, 67.2, 66.0, 64.1, 60.1, 57.1, 55.1, 21.0, 20.8, 20.6, 18.7, 18.1, 16.4; HRMS (ESI) Calc. for $[M + Na]^+$ $C_{108}H_{123}N_3NaO_{30}$: 1964.8084; Found 1964.8103.



2,4-Di-*O*-benzyl-3-*O*-methyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-benzoyl-α-D-rhamnopyranosyl-(1→3)-[2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl-(1→4)]-2-*O*-(4-methoxybenzyl)-α-L-fucopyranosyl-(1→3)-[2,3,4-tri-*O*-benzyl-β-D-xylopyranosyl-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranosyl azide (3.78): To a stirred solution of **3.48** (11.7 mg, 6.02 μmol) in dry THF (1.5 mL), degassed under vacuum, and stirring under an Ar atmosphere, (1,5-cyclooctadiene)bis(methyldiphenylphosphine)iridium (I) hexafluorophosphate catalyst (0.30 mg, 0.36 μmol) was added, followed by further degassing of the reaction mixture. The suspension was stirred for 15 min at 0 °C, and the catalyst was then activated with hydrogen (2 min under hydrogen atmosphere). The excess hydrogen was removed by three cycles of vacuum/Ar. The reaction mixture was then stirred for 2 h at room temperature under an Ar atmosphere. The solvent was then evaporated, and the residue was dissolved in acetone–water (10:1, 2.2 mL) before HgO (1.83 mg, 8.43 μmol) and $HgCl_2$ (1.96 mg, 7.22 μmol) were added. The reaction mixture was stirred overnight at room temperature, then the solvent was concentrated, and the residue was diluted with EtOAc (20 mL), washed with 10% KI, saturated $Na_2S_2O_3$ (aq.) and water. The aqueous layers were extracted with EtOAc (20 mL), and the combined

organic layers were dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (2:1 hexane–EtOAc) to afford **3.78** (10.0 mg, 87%) as a syrup. R_f 0.26 (2:1 hexane–EtOAc); $[\alpha]_D$ –49.8 (*c* 0.50, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.94–7.93 (m, 2H), 7.53–7.50 (m, 1H), 7.42–7.41 (m, 2H), 7.35–7.21 (m, 33H), 7.19–7.18 (m, 2H), 7.11–7.10 (m, 2H), 6.71–6.69 (m, 2H), 5.66 (dd, 1H, *J* = 3.4, 1.7 Hz), 5.51 (d, 1H, *J* = 3.7 Hz, Fuc-H-1), 5.18 (d, 1H, *J* = 1.2 Hz, D-Rha-H-1), 5.12 (d, 1H, *J* = 1.6 Hz, L-Rha-H-1), 5.02 (t, 1H, *J* = 6.3 Hz), 4.99 (dd, 1H, *J* = 6.2, 4.9 Hz), 4.91 (d, 1H, *J* = 11.3 Hz), 4.86 (td, 1H, *J* = 6.1, 4.4 Hz), 4.82–4.80 (m, 3H), 4.77–4.66 (m, 6H), 4.61–4.57 (m, 5H), 4.55–4.52 (m, 2H), 4.47 (d, 1H, *J* = 11.8 Hz), 4.38–4.36 (m, 2H), 4.28 (dd, 1H, *J* = 10.4, 2.6 Hz), 4.13–4.06 (m, 3H), 4.02 (t, 1H, *J* = 9.6 Hz), 3.97 (dd, 1H, *J* = 9.3, 3.5 Hz), 3.93–3.90 (m, 2H), 3.82 (dd, 1H, *J* = 10.4, 3.7 Hz), 3.76 (dq, 1H, *J* = 9.4, 6.1 Hz), 3.64–3.60 (m, 6H), 3.54–3.50 (m, 2H), 3.48–3.35 (m, 5H), 3.30 (dd, 1H, *J* = 9.3, 3.1 Hz), 3.10 (s, 3H), 3.07 (t, 1H, *J* = 8.6 Hz), 2.95 (t, 1H, *J* = 11.1 Hz), 2.75 (d, 1H, *J* = 3.1 Hz), 2.07 (s, 3H), 2.01 (s, 3H), 1.93 (s, 3H), 1.35 (d, 3H, *J* = 6.3 Hz), 1.28 (d, 3H, *J* = 6.2 Hz), 1.17 (d, 3H, *J* = 6.6 Hz); ^{13}C NMR (125 MHz; $CDCl_3$): δ 169.9, 169.6, 169.5, 165.4, 159.2, 138.7, 138.5, 138.4, 138.2, 137.9 (2 × C), 133.2, 129.8 (3 × C), 129.6, 128.5, 128.4 (4 × C), 128.3, 128.2, 128.0 (2 × C), 127.9, 127.8, 127.7 (3 × C), 127.6 (2 × C), 127.5 (2 × C), 127.3, 126.8, 113.7, 103.4 (Xyl(Bn)-C-1), 100.8 (D-Rha-C-1), 100.5 (Xyl(Ac)-C-1), 96.3 (Fuc-C-1), 96.1 (L-Rha-C-1), 90.2 (Glc-C-1), 84.2, 83.0, 82.7, 82.6, 81.2, 79.9, 78.7, 77.4, 76.5, 76.1, 75.7, 75.3, 74.9, 74.3, 74.2, 74.1, 74.0, 73.8, 73.5, 73.2, 72.6, 72.5, 72.1, 69.8, 69.4 (2 × C), 68.8, 68.1, 67.9, 67.2, 65.9, 64.1, 60.6, 57.2, 55.0, 20.9, 20.8, 20.7, 18.6,

18.0, 16.4; HRMS (ESI) Calc. for $[M + Na]^+$ $C_{105}H_{119}N_3NaO_{30}$: 1924.7771; Found 1924.7793.



***p*-Tolyl 3-*O*-benzyl-4,6-2-*O*-levulinoyl-*O*-di-*tert*-butylsilylene-1-thio-α-D-galactopyranoside (3.80):** To a stirred solution of **3.56** (54.5 mg, 106 μmol) in dry CH_2Cl_2 (2.5 mL) was added EDC·HCl (40.4 mg. 211 μmol), levulinic acid (24.5 mg, 211 μmol) and 4-(dimethylamino)pyridine (1.3 mg, 11 μmol) successively. The reaction mixture was stirred overnight at room temperature. Then poured into the saturated $NaHCO_3$ (aq.) and extracted with CH_2Cl_2 (30 mL × 3). The combined organic layers were dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (4:1 hexane–EtOAc) to afford **3.80** (63.9 mg, 99%) as a white amorphous solid. R_f 0.21 (4:1 hexane–EtOAc); $[\alpha]_D$ +28.7 (*c* 0.43, $CHCl_3$); ^{1}H NMR (600 MHz; $CDCl_3$): δ 7.42–7.40 (m, 2H, Ar), 7.38–7.35 (m, 4H, Ar), 7.31–7.29 (m, 1H, Ar), 7.11–7.10 (m, 2H, Ar), 5.42 (t, 1H, J = 9.8 Hz, H-2), 4.74 (d, 1H, J = 12.5 Hz, PhC$\underline{H}_2$), 4.64 (d, 1H, J = 12.5 Hz, PhC$\underline{H}_2$), 4.59 (d, 1H, J = 10.1 Hz, H-1), 4.53 (d, 1H, J = 2.8 Hz, H-4), 4.25 (dd, 1H, J = 12.4, 1.6 Hz, H-6a), 4.20 (dd, 1H, J = 12.4, 2.2 Hz, H-6b), 3.44 (dd, 1H, J = 9.5, 3.0 Hz, H-3), 3.31 (br s, 1H, H-5), 2.86–2.75 (m, 2H, $COCH_2C\underline{H}_2COCH_3$), 2.71–2.62 (m, 2H, $COC\underline{H}_2CH_2COCH_3$), 2.34 (s, 3H, $ArC\underline{H}_3$), 2.21 (s, 3H, $COCH_2CH_2COC\underline{H}_3$), 1.13 (s, 9H, $C(C\underline{H}_3)_3$), 1.07 (s, 9H, $C(C\underline{H}_3)_3$); ^{13}C NMR (125 MHz; $CDCl_3$): δ 206.4 (C=O),

171.7 (C=O), 138.1 (Ar), 137.8 (Ar), 132.8 (Ar), 130.6 (Ar), 129.6 (Ar), 128.4 (Ar), 127.7 (2 × Ar), 87.8 (C-1), 79.5 (C-3), 75.1 (C-5), 70.4 (Ph<u>C</u>H_2), 70.0 (C-4), 69.2 (C-2), 67.3 (C-6), 38.0 ($COCH_2$<u>C</u>H_2COCH_3), 29.9 ($COCH_2CH_2CO$<u>C</u>H_3), 28.1 (CO<u>C</u>$H_2CH_2COCH_3$), 27.6 (2 × C(<u>C</u>H_3)$_3$), 23.4 (<u>C</u>(CH_3)$_3$), 21.1 (Ar<u>C</u>H_3), 20.7 (<u>C</u>(CH_3)$_3$); HRMS (ESI) Calc. for [M + NH_4]$^+$ $C_{33}H_{50}NO_7SSi$: 632.3072; Found 632.3060.

3.5 References

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Chapter 4

Synthesis of PBCV-1 *N*-Glycan Fragments as Biosynthetic Probes

4.1 Background

As described in Chapter 1, PBCV-1 produces six putative glycosyltransferases (GTs): A064R (638 amino acids), A111/114R (860 aa), A219/222/226R (677 aa), A473L (517 aa), A546L (396aa), and A075L (280 aa).[1] Given the complexity of this *N*-glycan (**3.1**), which has nine different monosaccharide linkages, this is a small number of GTs. One possibility to explain this is that one or more of these six enzymes has multiple functionalities. Another possibility is that other viral genes, which are not similar to GTs in the databases, encode these enzymes. A final possibility is that host-encoded GTs might also be involved in the biosynthesis.[2]

Among the six candidate GTs, the protein encoded by gene *a064r* attracted interest because it is only found in PBCV-1 and not in other chloroviruses for which the *N*-glycan structure is known.[3] This suggested that the protein encoded by this gene, A064R, was involved in the assembly of a structural moiety that was not present in other chlorovirus *N*-glycans.[4–6] In addition, it turned out that 18 of 21 antigenic variants of the PBCV-1 glycans, which have structural differences with the parent compound, had mutations in gene *a064r*. Inspired by this finding, De Castro and co-workers analyzed a combination of structural data and genetic information to propose the activity of the A064R protein. On the basis of this analysis, they postulated that the protein is a GT with three domains[2] as shown in Figure 4-1: 1) domain 1 is a β-L-rhamnosyltransferase that installs the rhamnose onto O-4 of the distal xylose unit; 2) domain 2 attaches the second L-rhamnose, via an α-glycosidic linkage, to O-2 of first L-rhamnose unit; and 3) domain 3 is a methyltransferase that

modifies one or both positions in the terminal α-L-rhamnose unit. To probe the activity of A064R, *N*-glycans isolated from the antigenic variants or synthetic compounds can be used as potential substrates. The latter would be preferred as this would overcome limitations due to the small amounts of material that are typically available from nature. This chapter focuses on the synthesis of such compounds.

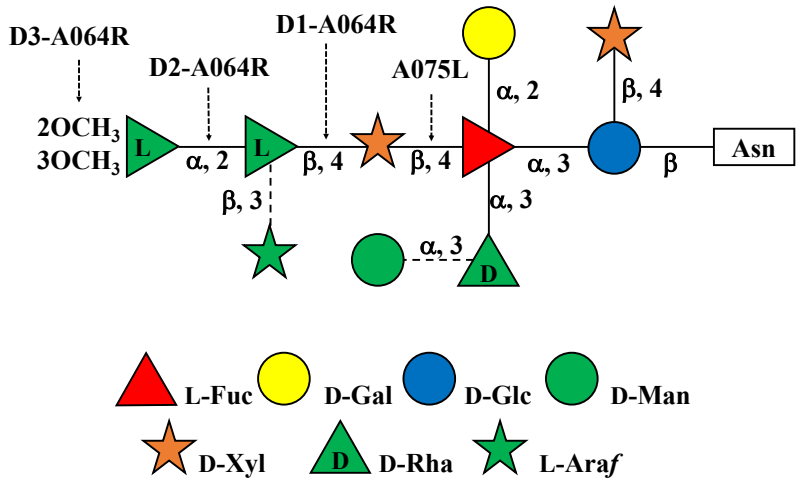


Figure 4-1: PBCV-1 *N*-glycan structure with the predicted glycosyltransferases involved in glycosidic bond formation (D = domain).

The isolated chlorovirus *N*-glycans contain a small peptide at the reducing end, resulting from enzymatic digestion of the capsid protein. On the basis of known biosynthetic pathways, De Castro hypothesized[3] that the oligosaccharide substrates for these GTs are linked to a lipid moiety. The GTs would assemble the oligosaccharide on this lipid-carrier before 'en block' transfer of the entire structure to the major capsid protein, Vp54. Thus, a lipophilic group (an octyl group) was designed to be installed at the reducing

end of the synthetic targets. In addition to mimicking the natural lipid, the octyl group could help facilitate purification of the deprotected molecules, particularly after enzymatic reactions, via a C_{18} column.[7]

As target probes of the A064R GT, we chose oligosaccharides **4.1**–**4.4** (Figure 4-2), which could be accessed in multi-milligram quantities thus overcoming the limitation of the insufficient quantities available from natural *N*-glycan substrates. Furthermore, a synthetic approach allows access to substrates of different sizes, i.e. tetra-, tri-, di- and monosaccharide, which will lead to better mapping of the substrates recognized by the enzyme.

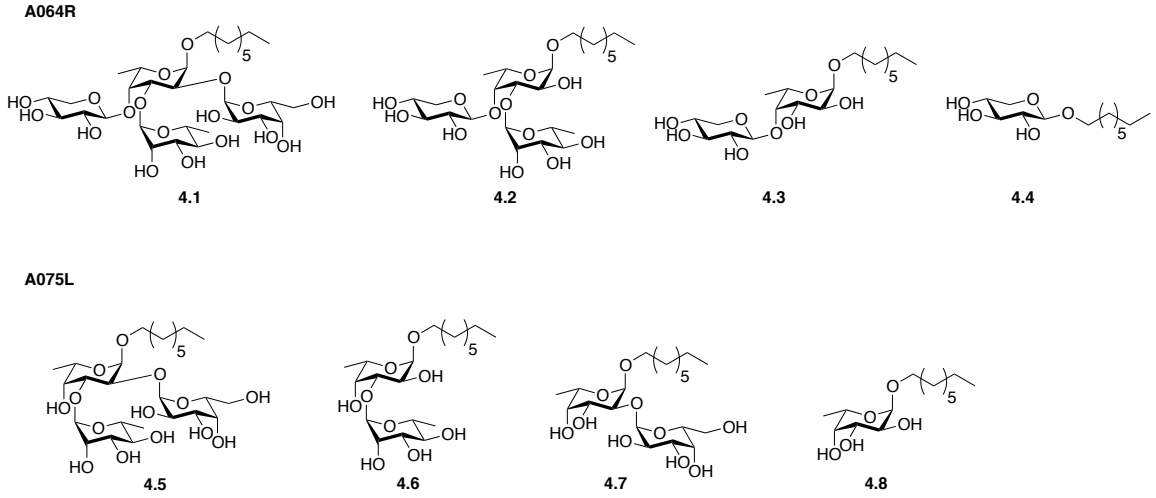


Figure 4-2: Designed synthetic PBCV-1 fragments **4.1**–**4.8**.

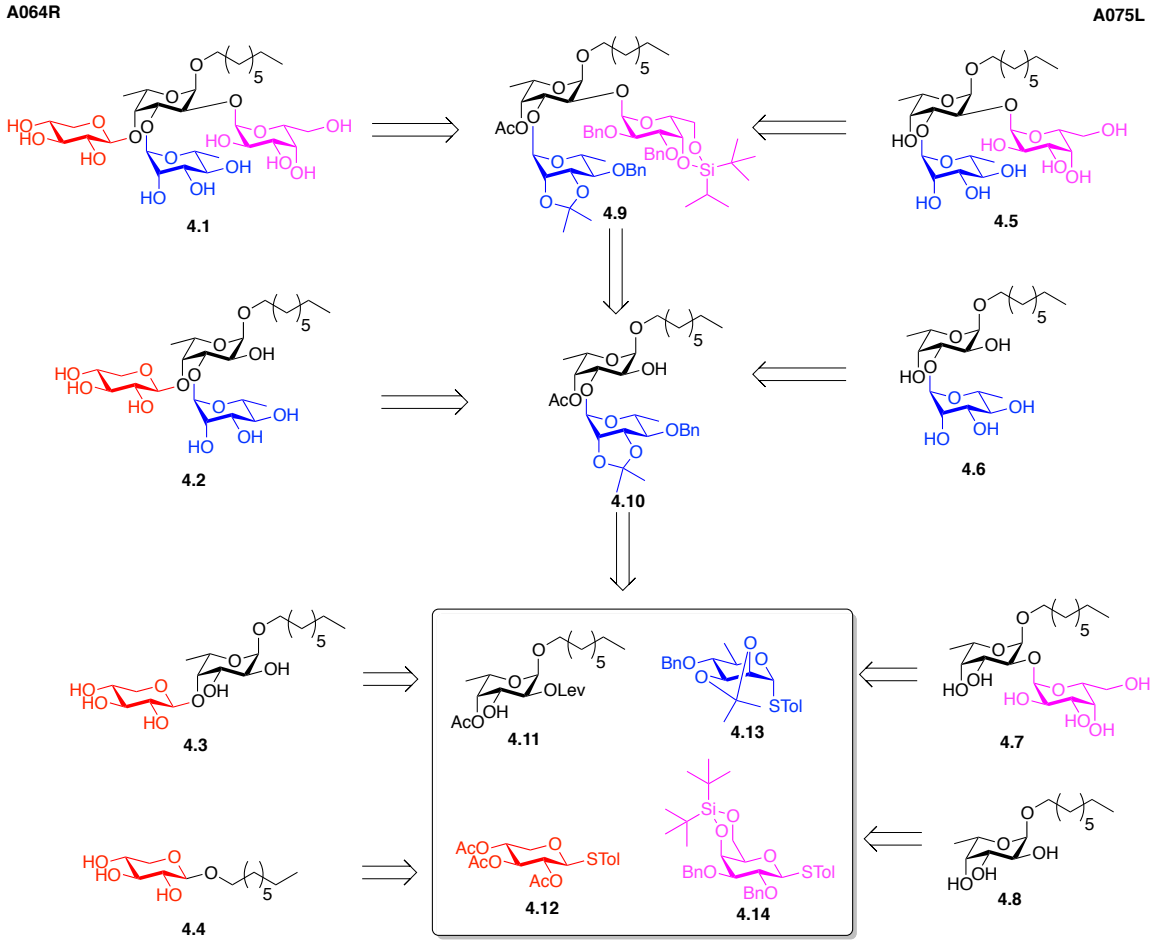
In addition, the A075L GT was another target of this study; this enzyme is predicted to be a β-xylosyltransferase that attaches the distal D-xylose unit to the O-4 of L-fucose.

Thus, the tri-, di- and monosaccharide substrates **4.5**–**4.8** (Figure 4-2), which lack this xylose residue, were also targeted for synthesis.

4.2 Results and discussions

4.2.1 Retrosynthetic analysis of the PBCV-1 fragments

The retrosynthetic analysis of **4.1**–**4.8** is shown in Scheme 4-1. To minimize the number of building blocks and to simplify the synthetic route, I proposed that all of the target molecules could be achieved from four monosaccharide building blocks (**4.11**–**4.14**).



Scheme 4-1: Retrosynthetic analysis of the seven PBCV-1 fragments **4.1**–**4.8**.

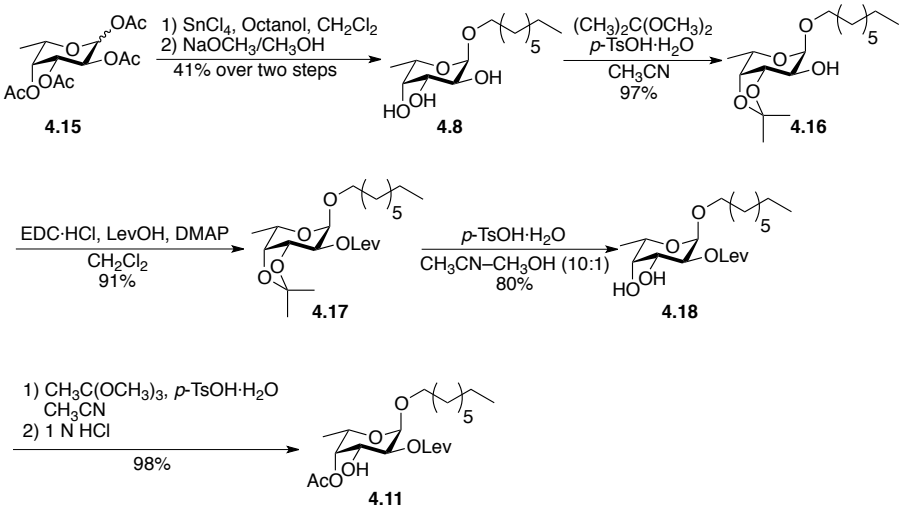
The synthesis of tetrasaccharide **4.1** could be achieved using the approach for the synthesis of 'hyper-branched' fucose derivative **2.30** (Scheme 2-8), because the aglycone on the fucose contains an octyl group, which is small. Thus, the "counter-clockwise" assembly sequence discussed in Section 2.2.2 will not be required here. In addition, use of the "counter-clockwise" sequence requires extra protection steps, so I decided not to perform this addition sequence here.

Moreover, manipulations on the intermediates involved in the synthesis of **4.1** (i.e., trisaccharide **4.9** and disaccharide **4.10**) could lead to the generation of other oligosaccharide targets (**4.2**, **4.5** and **4.6**). The disaccharide target **4.3** could be prepared from the fucose acceptor derivatized from **4.11** and glycosyl donor **4.12**. In addition, the disaccharide target **4.7** could be obtained from the coupling between a modified fucose acceptor and galactose donor **4.14**. The monosaccharide target **4.8** could be produced during the preparation of **4.11**, and monosaccharide **4.4** could be derived from **4.12** directly through glycosylation of octanol and deprotection.

4.2.2 Synthesis of the fragments for understanding the role A064R (4.1–4.4)

The synthesis of D-rhamnose donor **4.13** was prepared as described in Chapter 3. In addition, galactose donor **4.14**[8] and xylose donor **4.12**[9] were prepared as reported. Thus, only the synthesis of fucose acceptor **4.11** will be discussed. This compound was prepared starting from peracetylated fucose derivative **4.15**[9] as shown in Scheme 4-2. The glycosylation of octanol with **4.15** under the activation of tin (IV) chloride afforded octyl

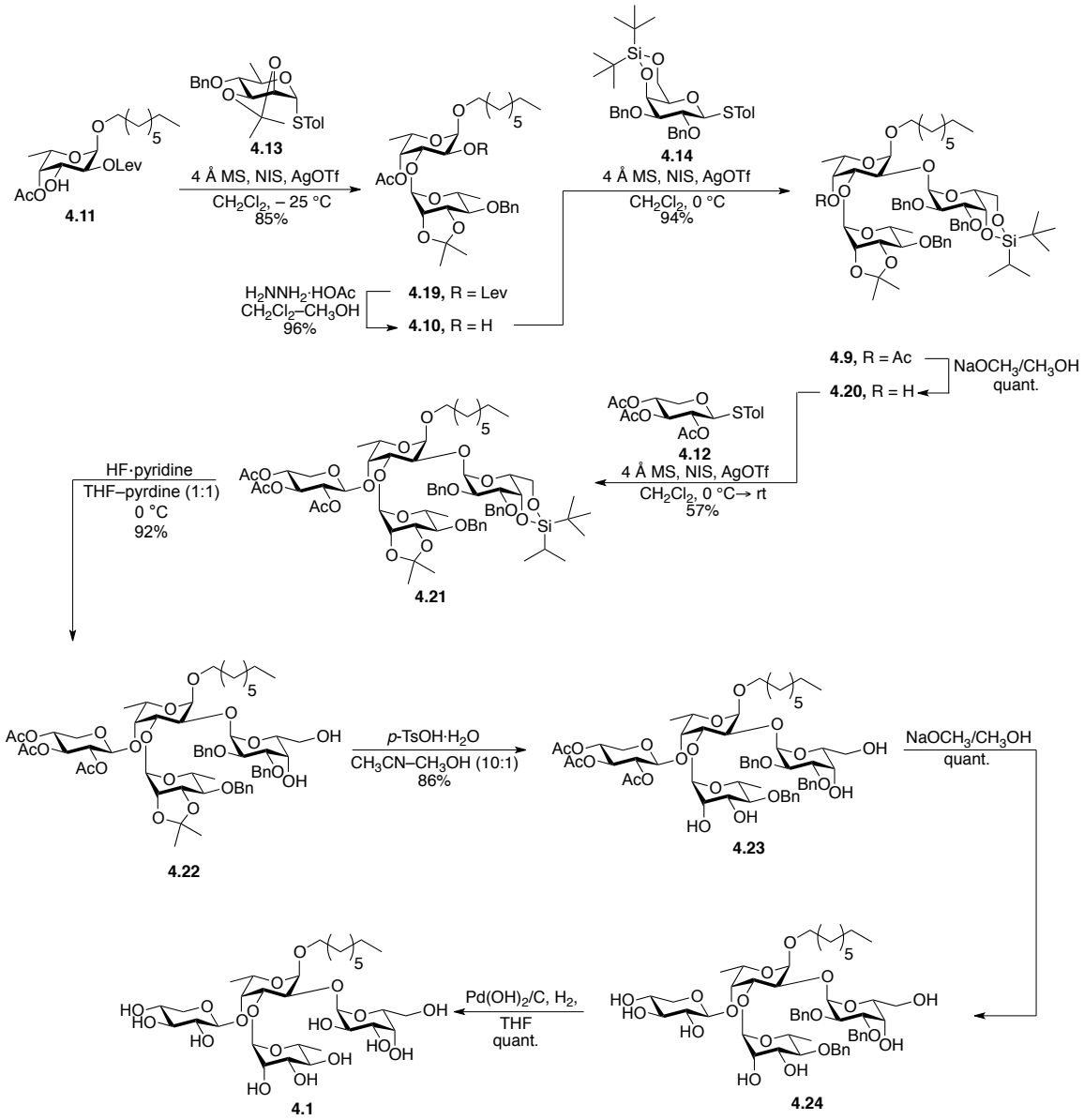
2,3,4-tri-*O*-acetyl-α-D-fucopyranoside, which could not be separated from the excess octanol. Subsequent removal of the acetyl groups under Zemplén conditions facilitated purification, giving **4.8** in 41% yield over two steps. The $^{3}J_{H1\text{-}H2}$ was 2.7 Hz, indicative of the α-stereochemistry. The C-3 and C-4 hydroxyl groups of **4.8** were then protected as an isopropylidene ketal to afford **4.16** in 97% yield. Alcohol **4.16** was next treated with levulinic acid in the presence of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride and 4-(dimethylamino)pyridine to furnish **4.17** in 91% yield. The ketal was then removed using *p*-toluenesulfonic acid and water to give **4.18**, which was converted via reaction with trimethyl orthoacetate and then 1 N hydrogen chloride, to acceptor **4.11** in 78% yield over the three steps.



Scheme 4-2: Synthesis of octyl fucoside acceptor **4.11**.

Having the building blocks **4.11**–**4.14** in hand, the glycosylation between glycosyl acceptor **4.11** and glycosyl donor **4.13** provided the disaccharide **4.19** in 85% yield with

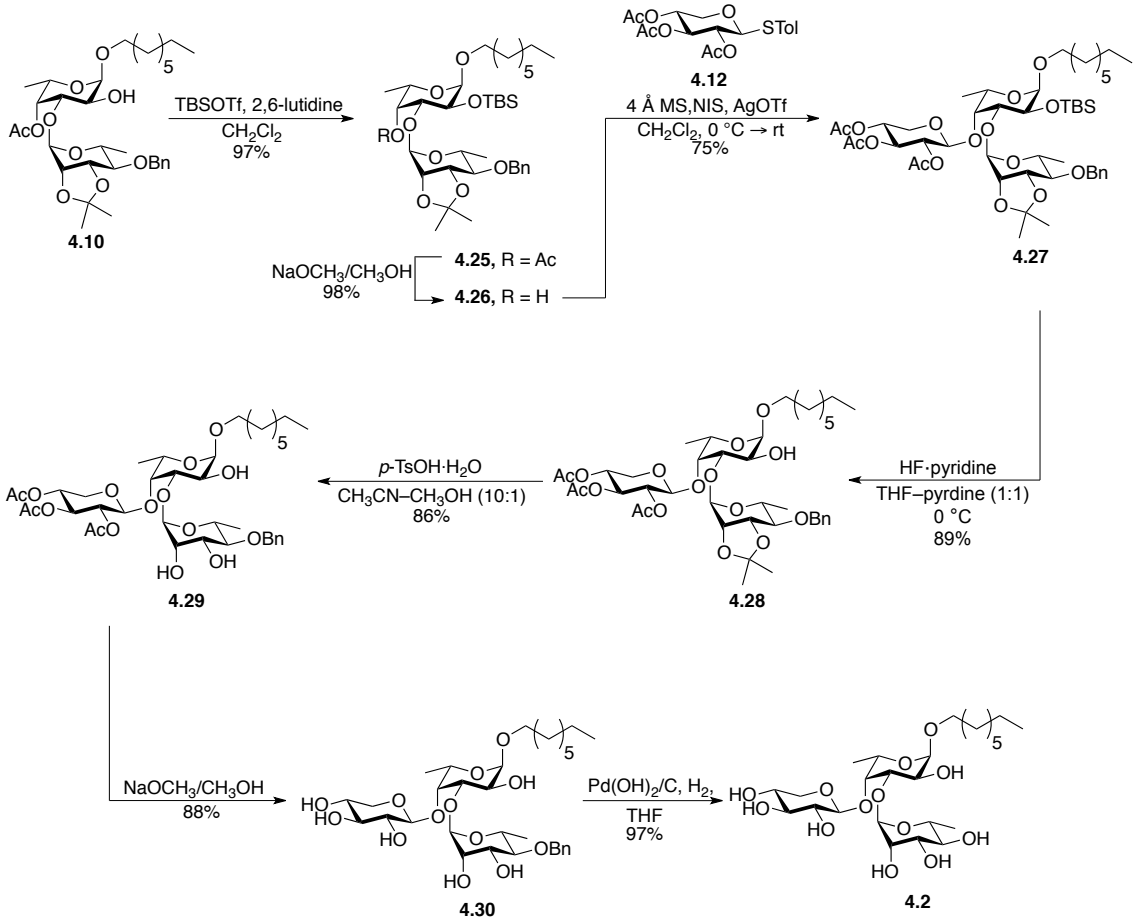
excellent α-selectivity (Scheme 4-3). The stereochemistry was confirmed by the coupling constant between Rha-C-1 and Rha-H-1 ($^1J_{C\text{-}H}$ = 172.2 Hz) in the ^{1}H-coupled HSQC spectrum. Chemoselective deprotection of levulinoyl group was performed upon treatment with hydrazine acetate to give disaccharide acceptor **4.10** in 96% yield. Glycosylation of **4.10** with galactose donor **4.14** was done first to generate trisaccharide **4.9** in 94% yield. The α-selectivity was confirmed by the coupling constant between Gal-H-1 and Gal-C-1 ($^1J_{C\text{-}H}$ = 169.5 Hz) in the ^{1}H-coupled HSQC spectrum. Subsequent Zemplén deacetylation of **4.9**, followed by glycosylation with **4.12**, afforded tetrasaccharide **4.21** in 57% yield over two steps. These results further suggest, as detailed in Chapter 2 (Schemes 2-8, 2-15, 2-17 and 2-18), that the size of the aglycone on the fucose impacts the required addition sequence of the monosaccharides to this 'hyper-branched' residue. The "counter-clockwise" assembly sequence is not required when 'small' groups are present, but is required in molecules in which this group is a larger glycan-containing species. Global deprotection was performed via removal of di-*tert*-butylsilylene group and ketal hydrolysis to afford **4.23** in 79% yield over two steps. Lastly, the deacetylation and debenzylation were performed to provide tetrasaccharide **4.1** quantitatively.



Scheme 4-3: Synthesis of tetrasaccharide **4.1**.

The synthesis of trisaccharide **4.2** was achieved using an intermediate prepared in course of accessing **4.1** (Scheme 4-4). The C-2 hydroxyl group in disaccharide **4.10** was treated with *tert*-butyldimethylsilyl trifluoromethanesulfonate and 2,6-lutidine to give **4.25** in 97% yield. The acetate group on **4.25** as then removed in 98% yield to generate **4.26**.

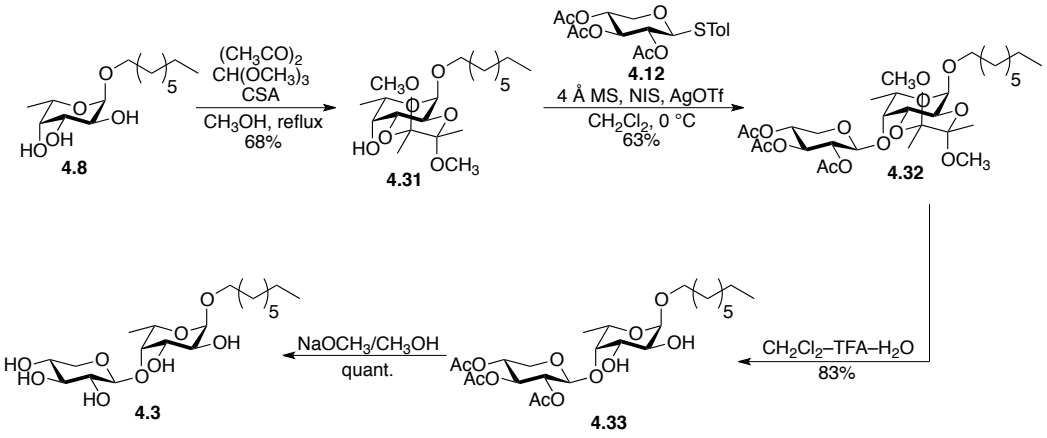
An NIS/AgOTf-catalyzed glycosylation of this alcohol using donor **4.12** afforded trisaccharide **4.27** in 75% yield. Cleavage of the *tert*-butyldimethylsilyl ether followed by hydrolysis of ketal group generated triol **4.29** in 77% yield over two steps. Subsequent deacetylation and debenzylation of **4.29** furnished the trisaccharide **4.2** in 85% yield over two steps.



Scheme 4-4: Synthesis of trisaccharide **4.2**.

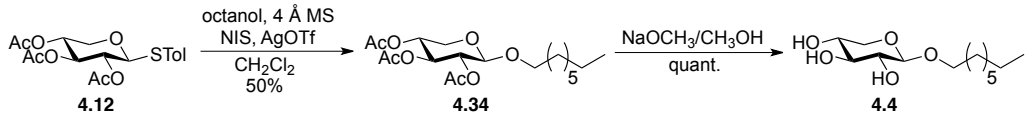
The synthesis of disaccharide **4.3** began from the conversion, in 68% yield, of octyl α-D-fucopyranoside (**4.8**) into diactal **4.31** upon reaction with butane-2,3-dione and (+)-

camphorsulfonic acid (Scheme 4-5). Subsequent glycosylation with **4.12**, activated with NIS/AgOTf, afforded disaccharide **4.32** in 63% yield. After cleavage of the diacetal in **4.32**, the remaining acetyl groups were removed under Zemplén conditions to afford **4.3** in 83% yield over the two steps.



Scheme 4-5: Synthesis of disaccharide **4.3**.

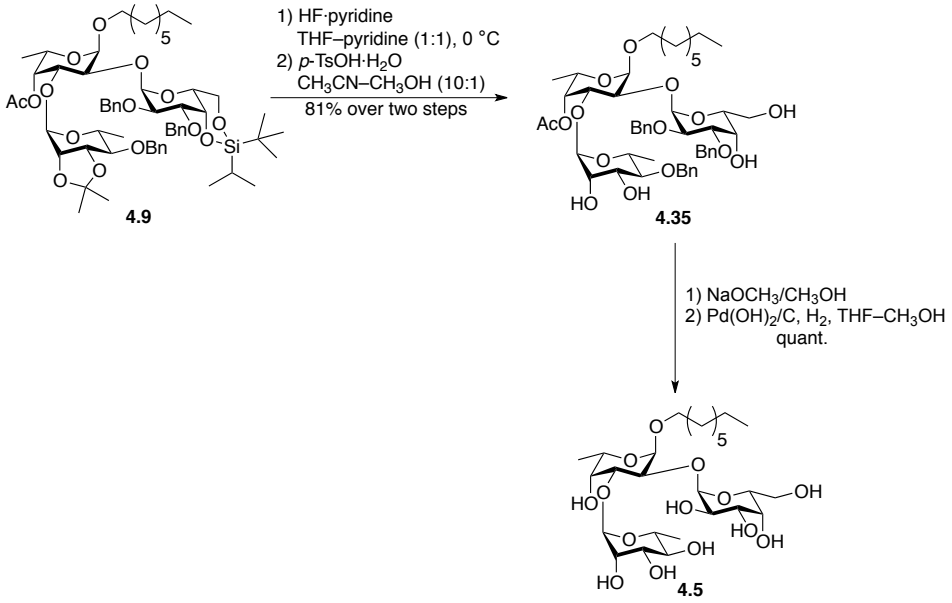
Lastly, the monosaccharide **4.4** was synthesized by a glycosylation between octanol and **4.12**. The product, **4.34**, was obtained in 50% yield, which was then subjected to a Zemplén deacetylation, providing the monosaccharide **4.4** in quantitative yield.



Scheme 4-6: Synthesis of monosaccharide **4.4**.

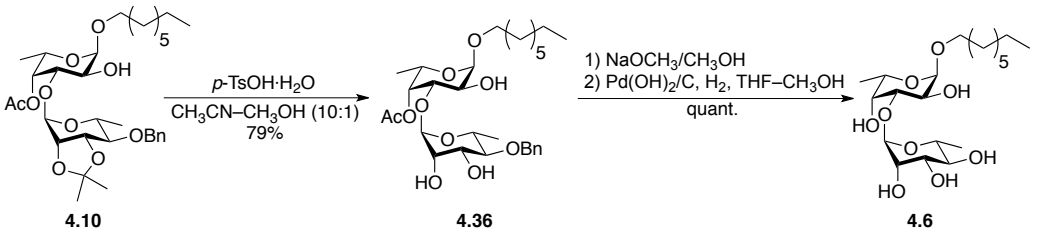
4.2.3 Synthesis of the fragments for understanding the role A075L (4.5–4.8)

The preparation of **4.5** was achieved by deprotection of trisaccharide **4.9**, which was prepared as described previously (Scheme 4-3). This was completed (Scheme 4-7) in four steps and in 81% overall yield: 1) removal of the di-*tert*-butylsilylene group; 2) hydrolysis of the ketal; 3) deacetylation; and 4) debenzylation.



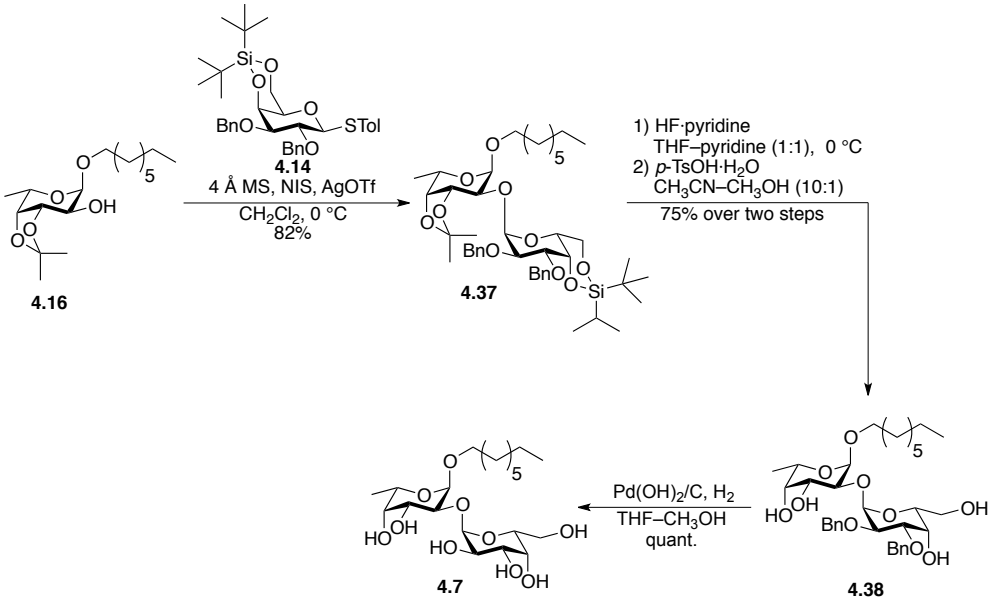
Scheme 4-7: Synthesis of trisaccharide **4.5**.

Disaccharide **4.6** was synthesized (Scheme 4-8) by deprotection of **4.10**, an intermediate in the synthesis of **4.1**. Removal of the ketal in **4.10** by *p*-toluenesulfonic acid-catalyzed hydrolysis gave **4.36** in 79% yield. Then, deacetylation followed by debenzylation was performed to provide a quantitative yield of **4.6**.



Scheme 4-8: Synthesis of disaccharide **4.6**.

Intermediate **4.16**, which was generated in the course of preparing fucose acceptor **4.11** (Scheme 4-2), was used for the preparation of disaccharide **4.7**. As shown in Scheme 4-9, glycosylation of **4.16** with galactose donor **4.14** led to the formation of disaccharide **4.37** in 82% yield with exclusive α-selectivity ($^3J_{H\text{-}1,H\text{-}2} = 3.8$ Hz). A three-step deprotection sequence analogous to that used for the other targets gave **4.7** in 75% overall yield.



Scheme 4-9: Synthesis of disaccharide **4.7**.

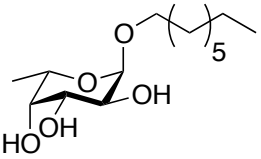
Monosaccharide **4.8** was prepared during the synthesis of **4.11** as illustrated in Scheme 4-2.

4.3 Conclusion

In conclusion, this chapter details the chemical synthesis of eight different fragments of the PBCV-1 *N*-glycan. The synthesis proceeded without any challenges and the work described in Chapters 2 and 3 laid the groundwork for these syntheses. All of the synthetic targets have been sent to laboratory of our collaborator, Prof. Cristina De Castro, at University of Napoli in Italy for biochemical assays. Preliminary data in testing these compounds as substrates for the A064R and A075L GTs confirmed the hypothesis put forward in Figure 4-1.

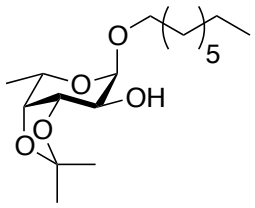
4.4 Experimental section

General Methods: All reagents were purchased from commercial sources and were used without further purification unless noted. Reaction solvents were purified by successive passage through columns of alumina and copper under argon. Unless stated otherwise, all reactions were performed at room temperature and under a positive pressure of argon and were monitored by TLC on Silica Gel G-25 F254 (0.25 mm). Visualization of the reaction components was achieved using UV fluorescence (254 nm) and/or by charring with acidified anisaldehyde solution in ethanol, acetic acid and sulfuric acid. Organic solvents were evaporated under reduced pressure, and the products were purified by column chromatography on silica gel (230−400 mesh). Optical rotations were measured in a microcell (1 cm, 1 mL) at ambient temperature and are in units of degrees·mL/(g·dm). ^{1}H NMR spectra were recorded at 400 MHz, 500 MHz, 600 MHz or 700 MHz and chemical shifts are referenced to residual $CHCl_3$ (7.26 ppm, $CDCl_3$) or CHD_2OD (3.30 ppm, CD_3OD). ^{13}C NMR spectra were recorded at 125 MHz and chemical shifts are referenced to $CDCl_3$ (77.0 ppm) or CD_3OD (49.3 ppm). Reported splitting patterns are abbreviated as s = singlet, d = doublet, t = triplet, m = multiplet, br = broad, app = apparent. Assignments of NMR spectra were based on two-dimensional experiments (^{1}H−^{1}H COSY, HSQC and HMBC. High-resolution ESI-MS spectra (time-of-flight analyzer) were recorded on samples suspended in THF or CH_3OH and with added NaCl.



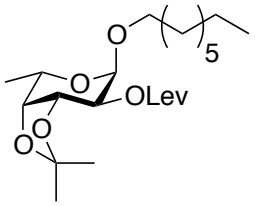
Octyl α-L-fucopyranoside (**4.8**)**:** To a stirred solution of octanol (6.04 mL, 38.5 mmol) and 1,2,3,4-tetra-*O*-acetyl-L-fucopyranose **4.15**[9] (5.12 g, 15.4 mmol) in dry CH_2Cl_2 (40 mL) was added tin (IV) chloride at 0 °C. The resulting solution was stirred for 1 h at room temperature under an Ar atmosphere. The crude residue was diluted with CH_2Cl_2 (200 mL), then washed with saturated $NaHCO_3$ (aq.). The organic layer was dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (4:1 hexane–EtOAc) to afford octyl 2,3,4-tri-*O*-acetyl-α-L-fucopyranoside which was contaminated with octanol. To a stirred mixture in CH_3OH (60 mL) was added a solution of $NaOCH_3$ in CH_3OH (6.0 mL, 0.5 M). The reaction mixture was stirred for 3 h at room temperature then neutralized by addition of Amberlite® IR-120 (H^+) cation exchange resin, filtered and the filtrate was concentrated to afford **4.8** (1.70 g, 41%) as a white amorphous solid. R_f 0.41 (9:1 CH_2Cl_2–CH_3OH); $[\alpha]_D$ –106 (*c* 0.64, CH_3OH); ^{1}H NMR (400 MHz; CD_3OD): δ 4.72 (d, 1H, J = 2.7 Hz, H-1), 3.93 (qd, 1H, J = 6.6, 0.7 Hz, H-5), 3.71–3.70 (m, 2H, H-2, H-3), 3.67–3.61 (m, 2H, H-4, $OC\underline{H}_2CH_2(CH_2)_5CH_3$), 3.43 (dt, 1H, J = 9.7, 6.4 Hz, $OC\underline{H}_2CH_2(CH_2)_5CH_3$), 1.66–1.56 (m, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.39–1.27 (m, 10H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 1.19 (d, 3H, J = 6.6 Hz, H-6), 0.89 (t, 1H, J = 6.9 Hz, $OCH_2CH_2(CH_2)_5C\underline{H}_3$); ^{13}C NMR (125 MHz; CD_3OD): δ 100.5 (C-1), 73.7 (C-4), 71.8 (C-2 or C-3), 70.1 (C-2 or C-3), 69.3 ($O\underline{C}H_2(CH_2)_6CH_3$), 67.5 (C-5), 33.0 ($OCH_2(\underline{C}H_2)_6CH_3$), 30.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 30.5 ($OCH_2(\underline{C}H_2)_6CH_3$),

30.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 27.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 23.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 16.6 (C-6), 14.4 ($OCH_2(CH_2)_6\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{14}H_{28}NaO_5$: 299.1829; Found 299.1833.



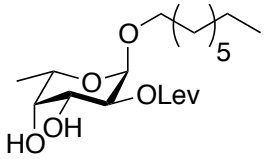
Octyl 3,4-*O*-isopropylidene-α-L-fucopyranoside (4.16): To a stirred solution of **4.8** (783 mg, 2.83 mmol) in dry CH_3CN (24 mL) were added 2,2-dimethoxypropane (0.54 mL, 4.3 mmol) and *p*-toluenesulfonic acid monohydrate (53 mg, 0.28 mmol) successively, the reaction mixture was stirred at room temperature for 2 h. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (4:1 hexane–EtOAc) to afford **4.16** (873 mg, 97%) as a viscous oil. R_f 0.69 (1:1 hexane–EtOAc); $[\alpha]_D$ –105 (*c* 1.17, $CHCl_3$); ^{1}H NMR (400 MHz; $CDCl_3$): δ 4.82 (d, 1H, J = 4.0 Hz, H-1), 4.21 (t, 1H, J = 6.2 Hz, H-3), 4.13 (qd, 1H, J = 6.7, 2.2 Hz, H-5), 4.07 (dd, 1H, J = 6.0, 2.3 Hz, H-4), 3.82–3.73 (m, 2H, H-2, $OC\underline{H}_2CH_2(CH_2)_5CH_3$), 3.48 (dt, 1H, J = 9.7, 6.6 Hz, $OC\underline{H}_2CH_2(CH_2)_5CH_3$), 2.26 (d, 1H, J = 7.2 Hz, 2-OH), 1.65–1.59 (m, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.53 (s, 3H, $C(C\underline{H}_3)_2$), 1.37-1.29 (m, 16H, $C(C\underline{H}_3)_2$, C-6, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 0.90 (t, 3H, J = 6.9 Hz, $OCH_2CH_2(CH_2)_5C\underline{H}_3$); ^{13}C NMR (125 MHz; $CDCl_3$): δ 109.2 ($\underline{C}(CH_3)_2$), 97.3 (C-1), 76.3 (C-3), 75.7 (C-4), 69.4 (C-2), 68.3 ($O\underline{C}H_2(CH_2)_6CH_3$), 63.8 (C-5), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.5 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 27.8 ($C(\underline{C}H_3)_2$),

26.1 ($OCH_2(\underline{C}H_2)_6CH_3$), 25.9 ($C(\underline{C}H_3)_2$), 22.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 16.3 (C-6), 14.1 ($OCH_2(CH_2)_6\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{17}H_{32}NaO_5$: 339.2142; Found 339.2147.



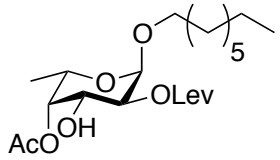
Octyl 3,4-*O*-isopropylidene-2-*O*-levulinoyl-α-L-fucopyranoside (4.17): To a stirred solution of **4.16** (873 mg, 2.76 mmol) in dry CH_2Cl_2 (20 mL) was added EDC·HCl (1.06 g, 5.52 mmol), levulinic acid (0.641 g, 5.52 mmol) and 4-(dimethylamino)pyridine (34 mg, 0.28 mmol) successively. The reaction mixture was stirred overnight at room temperature. Then poured into the saturated $NaHCO_3$ (aq.) and extracted with CH_2Cl_2 (60 mL × 3). The combined organic layers were dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (4:1 hexane–EtOAc) to afford **4.17** (1.04 g, 91%) as a viscous oil. R_f 0.23 (4:1 hexane–EtOAc); $[\alpha]_D$ –134 (*c* 0.58, $CHCl_3$); ^{1}H NMR (400 MHz; $CDCl_3$): δ 4.90–4.87 (m, 2H, H-1, H-1), 4.34–4.30 (m, 1H, H-3), 4.14 (qd, 1H, J = 6.7, 2.5 Hz, H-5), 4.09 (dd, 1H, J = 5.4, 2.6 Hz, H-4), 3.65 (dt, 1H, J = 9.8, 6.8 Hz, $OC\underline{H}_2CH_2(CH_2)_5CH_3$), 3.42 (dt, 1H, J = 9.8, 6.6 Hz, $OC\underline{H}_2CH_2(CH_2)_5CH_3$), 2.86–2.73 (m, 2H, $COCH_2C\underline{H}_2COCH_3$), 2.72–2.62 (m, 2H, $COC\underline{H}_2CH_2COCH_3$), 2.20 (s, 3H, $COC\underline{H}_3$), 1.60–1.55 (m, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.54 (s, 3H, $C(C\underline{H}_3)_2$), 1.38-1.27 (m, 16H, $C(C\underline{H}_3)_2$, C-6, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 0.90 (t, 3H, J = 6.9 Hz, $OCH_2CH_2(CH_2)_5C\underline{H}_3$); ^{13}C NMR (125 MHz; $CDCl_3$): δ 206.2 (C=O), 172.3 (C=O), 109.3 ($\underline{C}(CH_3)_2$), 96.0 (C-1),

76.2 (C-4), 73.5 (C-3), 72.3 (C-2), 68.5 ($O\underline{C}H_2(CH_2)_6CH_3$), 63.1 (C-5), 38.0 ($COCH_2\underline{C}H_2COCH_3$), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.8 ($CO\underline{C}H_3$), 29.4 (2 × $OCH_2(\underline{C}H_2)_6CH_3$), 29.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 28.0 ($C(\underline{C}H_3)_2$, $CO\underline{C}H_2CH_2COCH_3$), 26.4 ($C(\underline{C}H_3)_2$), 26.1 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 16.3 (C-6), 14.1 ($OCH_2(CH_2)_6\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{22}H_{38}NaO_7$: 437.2510; Found 437.2509.



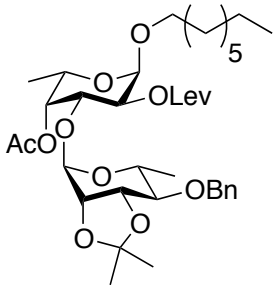
Octyl 3,4-*O*-isopropylidene-2-*O*-levulinoyl-α-L-fucopyranoside (4.18): To a stirred solution of **4.17** (1.12 g, 2.70 mmol) in CH_3CN–CH_3OH (22 mL, 10:1) was added *p*-toluenesulfonic acid monohydrate (1.54 g, 8.10 mmol) at room temperature. The reaction mixture was stirred for 3 h at room temperature. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (1:2 hexane–EtOAc) to afford **4.18** (809 mg, 80%) as a viscous oil. R_f 0.17 (1:2 hexane–EtOAc); $[\alpha]_D$ –120 (*c* 0.85, $CHCl_3$); ^{1}H NMR (500 MHz; $CDCl_3$): δ 5.03 (dd, 1H, J = 10.1, 3.8 Hz, H-2), 4.93 (d, 1H, J = 3.8 Hz, H-1), 4.08–4.01 (m, 2H, H-3, H-5), 3.85–3.84 (m, 1H, H-4), 3.66 (dt, 1H, J = 9.8, 6.8 Hz, $OC\underline{H}_2CH_2(CH_2)_5CH_3$), 3.43 (dt, 1H, J = 9.8, 6.6 Hz, $OC\underline{H}_2CH_2(CH_2)_5CH_3$), 2.99 (d, 1H, J = 5.2 Hz, 3-OH), 2.88–2.76 (m, 2H, $COCH_2C\underline{H}_2COCH_3$), 2.71–2.58 (m, 2H, $COC\underline{H}_2CH_2COCH_3$), 2.44 (br s, 1H, 4-OH), 2.21 (s, 3H, $COC\underline{H}_3$), 1.63–1.57 (m, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.37–1.26 (m, 13H, C-6, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 0.90 (t, 3H, J =

7.0 Hz, $OCH_2CH_2(CH_2)_5C\underline{H}_3$); ^{13}C NMR (125 MHz; $CDCl_3$): δ 207.2 (C=O), 173.1 (C=O), 96.2 (C-1), 72.2 (C-4), 72.0 (C-2), 68.7 (C-3), 68.4 ($O\underline{C}H_2(CH_2)_6CH_3$), 65.4 (C-5), 38.3 ($COCH_2\underline{C}H_2COCH_3$), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.8 ($CO\underline{C}H_3$), 29.5 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 28.2 ($CO\underline{C}H_2CH_2COCH_3$), 26.1 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 16.1 (C-6), 14.1 ($OCH_2(CH_2)_6\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{19}H_{34}NaO_7$: 397.2197; Found 397.2195.



Octyl 4-*O*-acetyl-2-*O*-levulinoyl-α-L-fucopyranoside (4.11): To a stirred solution of **4.18** (690 mg, 1.84 mmol) in dry CH_3CN (18 mL) was added trimethyl orthoacetate (0.34 mL, 2.8 mmol) and *p*-toluenesulfonic acid monohydrate (35 mg, 0.18 mmol) at 0 °C. The reaction mixture was stirred for 1 h under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The reaction was then dissolved in CH_2Cl_2 (50 mL) and 1N HCl was added (50 mL). The reaction mixture was stirred for 1 h at room temperature, then the aqueous layer was extracted with CH_2Cl_2 (50 mL × 3) and combined organic layers were dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (1:1 hexane–EtOAc) to afford **4.11** (748 mg, 98%) as a white solid. R_f 0.23 (1:1 hexane–EtOAc); $[\alpha]_D$ –122 (*c* 0.59, $CHCl_3$); ^1H NMR (400 MHz; $CDCl_3$): δ 5.27 (dd, 1H, J = 3.6, 1.3 Hz, H-4), 5.01 (dd, 1H, J = 10.1, 3.7 Hz, H-2), 4.97 (d, 1H, J = 3.8 Hz, H-1), 4.24 (dt, 1H, J = 9.9, 4.1 Hz, 1H), 4.10 (qd, 1H, J = 6.6, 0.9 Hz, H-5), 3.66 (dt,

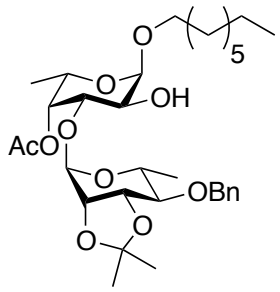
1H, *J* = 9.8, 6.7 Hz, $OCH_2CH_2(CH_2)_5CH_3$), 3.44 (dt, 1H, *J* = 9.8, 6.6 Hz, $OCH_2CH_2(CH_2)_5CH_3$), 2.81–2.78 (m, 2H, $COCH_2CH_2COCH_3$), 2.67–2.63 (m, 2H, $COCH_2CH_2COCH_3$), 2.34 (d, 1H, *J* = 5.0 Hz, 3-OH), 2.20 (s, 3H, $COCH_3$), 2.20 (s, 3H, $COCH_3$), 1.62–1.56 (m, 2H, $OCH_2CH_2(CH_2)_5CH_3$), 1.37–1.27 (m, 10H, $OCH_2CH_2(CH_2)_5CH_3$), 1.16 (d, 3H, *J* = 6.6 Hz, H-6), 0.90 (t, 3H, *J* = 6.9 Hz, $OCH_2CH_2(CH_2)_5CH_3$); ^{13}C NMR (125 MHz; $CDCl_3$): δ 206.7 (C=O), 172.9 (C=O), 171.3 (C=O), 96.3 (C-1), 73.5 (C-4), 71.8 (C-2), 68.6 ($OCH_2(CH_2)_6CH_3$), 67.1 (C-3), 64.7 (C-5), 38.1 ($COCH_2CH_2COCH_3$), 31.8 ($OCH_2(CH_2)_6CH_3$), 29.8 ($COCH_3$), 29.5 ($OCH_2(CH_2)_6CH_3$), 29.4 ($OCH_2(CH_2)_6CH_3$), 29.3 ($OCH_2(CH_2)_6CH_3$), 28.1 ($COCH_2CH_2COCH_3$), 26.1 ($OCH_2(CH_2)_6CH_3$), 22.7 ($OCH_2(CH_2)_6CH_3$), 20.8 ($COCH_3$), 16.2 (C-6), 14.1 ($OCH_2(CH_2)_6CH_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{21}H_{36}NaO_8$: 439.2302; Found 439.2304.



Octyl 4-*O*-benzyl-2,3-*O*-isopropylidene-α-D-rhamnopyranosyl-(1→3)-4-*O*-acetyl-2-*O*-levulinoyl-α-L-fucopyranoside (4.19): To a stirred solution of acceptor **4.11** (748 mg, 1.80 mmol) and donor **4.13** (826 mg, 2.06 μmol) in dry CH_2Cl_2 (20 mL) was added molecular sieves (2.0 g, 4Å, powder). After stirring for 30 min at room temperature, the reaction mixture was cooled to –25 °C, and then *N*-iodosuccinimide (567 mg, 2.52 mmol)

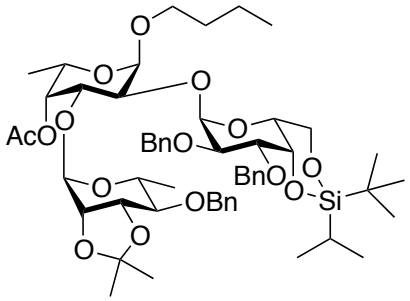
and silver trifluoromethanesulfonate (93 mg, 0.36 mmol) were added successively. The resulting solution was stirred for 1 h at –25 °C under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was washed with saturated $Na_2S_2O_3$ (aq.) and saturated $NaHCO_3$ (aq.). The aqueous layer was extracted with CH_2Cl_2 (30 mL × 3), dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (4:1 hexane–EtOAc) to afford **4.19** (1.06 g, 85%) as a syrup. R_f 0.51 (2:1 hexane–EtOAc); $[\alpha]_D$ –50.1 (*c* 1.3, $CHCl_3$); ^{1}H NMR (400 MHz; $CDCl_3$): δ 7.39–7.26 (m, 5H, Ar), 5.24 (dd, 1H, J = 3.6, 1.1 Hz, Fuc-H-4), 5.14 (s, 1H, Rha-H-1), 5.09 (dd, 1H, J = 10.5, 3.7 Hz, Fuc-H-2), 4.99 (d, 1H, J = 3.7 Hz, Fuc-H-1), 4.88 (d, 1H, J = 11.8 Hz, PhC$\underline{H}_2$), 4.65 (d, 1H, J = 11.8 Hz, PhC$\underline{H}_2$), 4.26 (dd, 1H, J = 10.5, 3.5 Hz, Fuc-H-3), 4.20–4.15 (m, 2H, Rha-H-3, Rha-H-2), 4.10 (qd, 1H, J = 6.8, 0.8 Hz, Fuc-H-5), 3.73 (dq, 1H, J = 9.8, 6.1 Hz, Rha-H-5), 3.65 (dt, 1H, J = 9.8, 6.6 Hz, OC$\underline{H}_2$CH$_2$(CH$_2$)$_5$CH$_3$), 3.42 (dt, 1H, J = 9.8, 6.6 Hz, OC$\underline{H}_2$CH$_2$(CH$_2$)$_5$CH$_3$), 3.18 (dd, 1H, J = 9.8, 6.7 Hz, Rha-H-4), 2.84–2.70 (m, 2H, COCH$_2$C$\underline{H}_2$COCH$_3$), 2.68–2.55 (m, 2H, COC$\underline{H}_2$CH$_2$COCH$_3$), 2.19 (s, 3H, COC$\underline{H}_3$), 2.16 (s, 3H, COC$\underline{H}_3$), 1.60–1.55 (m, 2H, OCH$_2$C$\underline{H}_2$(CH$_2$)$_5$CH$_3$), 1.49 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.36–1.27 (m, 16H, C(C$\underline{H}_3$)$_2$, Rha-H-6, OCH$_2$CH$_2$(C$\underline{H}_2$)$_5$CH$_3$), 1.12 (d, 3H, J = 6.6 Hz, Fuc-H-6), 0.90 (t, 3H, J = 6.9 Hz, OCH$_2$CH$_2$(CH$_2$)$_5$C$\underline{H}_3$); ^{13}C NMR (125 MHz; $CDCl_3$): δ 205.8 (C=O), 172.2 (C=O), 170.5 (C=O), 138.5 (Ar), 128.2 (Ar), 128.0 (Ar), 127.5 (Ar), 108.9 ($\underline{C}$(CH$_3$)$_2$), 99.7 (Rha-C-1, $^1J_{C\text{-}H}$ = 172.2 Hz), 96.2 (Fuc-C-1), 80.7 (Rha-C-4), 78.4 (Rha-C-3), 76.2 (Rha-C-2), 73.3 (Fuc-C-4), 72.9 (Ph$\underline{C}$H$_2$), 72.8 (Fuc-C-3), 71.2 (Fuc-C-2), 68.6 (O$\underline{C}$H$_2$(CH$_2$)$_6$CH$_3$), 65.4

(Rha-C-5), 65.0 (Fuc-C-5), 37.8 ($COCH_2\underline{C}H_2COCH_3$), 31.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.8 ($CO\underline{C}H_3$), 29.5 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 28.0 ($CO\underline{C}H_2CH_2COCH_3$, $C(\underline{C}H_3)_2$), 26.3 ($C(\underline{C}H_3)_2$), 26.1 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 20.8 ($CO\underline{C}H_3$), 17.7 (Rha-C-6), 16.1 (Fuc-C-6), 14.1 ($OCH_2(CH_2)_6\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{37}H_{56}NaO_{12}$: 715.3664; Found 715.3661.



Octyl 4-*O*-benzyl-2,3-*O*-isopropylidene-α-D-rhamnopyranosyl-(1→3)-4-*O*-acetyl-α-L-fucopyranoside (4.10): To a stirred solution of **4.19** (989 mg, 1.43 mmol) in CH_2Cl_2–CH_3OH (20 mL, 9:1) was added hydrazine acetate (263 mg, 2.86 mmol) at room temperature. The reaction mixture was stirred for 2 h at room temperature. The reaction mixture was then concentrated and the crude residue was purified by flash chromatography (3:1 hexane–EtOAc) to afford **4.10** (814 mg, 96%) as a syrup. R_f 0.13 (4:1 hexane–EtOAc); $[\alpha]_D$ –53.2 (*c* 1.20, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.35–7.30 (m, 4H, Ar), 7.27–7.24 (m, 1H, Ar), 5.28 (s, 1H, Rha-H-1), 5.15 (d, 1H, J = 2.9 Hz, Fuc-H-4), 4.88–4.85 (m, 2H, $PhC\underline{H}_2$, Fuc-H-1), 4.63 (d, 1H, J = 11.8 Hz, $PhC\underline{H}_2$), 4.21–4.17 (m, 2H, Rha-H-2, Rha-H-3), 4.02 (q, 1H, J = 6.6 Hz, Fuc-H-5), 3.92 (dd, 1H, J = 10.0, 3.3 Hz, Fuc-H-3), 3.88 (td, 1H, J = 10.1, 3.9 Hz, Fuc-H-2), 3.74–3.68 (m, 2H, Rha-H-5, $OC\underline{H}_2CH_2(CH_2)_5CH_3$), 3.44

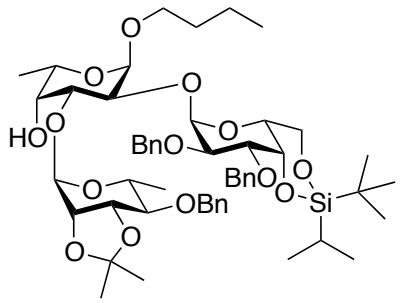
(dt, 1H, J = 9.7, 6.6 Hz, OC<u>H</u>$_2$CH$_2$(CH$_2$)$_5$CH$_3$), 3.17 (dd, 1H, J = 9.8, 7.1 Hz, Rha-H-4), 2.12 (s, 3H, COC<u>H</u>$_3$), 1.94 (d, 1H, J = 10.3 Hz, 2-OH), 1.62–1.58 (m, 2H, OCH$_2$C<u>H</u>$_2$(CH$_2$)$_5$CH$_3$), 1.47 (s, 3H, C(C<u>H</u>$_3$)$_2$), 1.35–1.24 (m, 16H, C(C<u>H</u>$_3$)$_2$, Rha-H-6, OCH$_2$CH$_2$(C<u>H</u>$_2$)$_5$CH$_3$), 1.10 (d, 3H, J = 6.6 Hz, Fuc-H-6), 0.88 (t, 3H, J = 7.1 Hz, OCH$_2$CH$_2$(CH$_2$)$_5$C<u>H</u>$_3$); ^{13}C NMR (175 MHz; CDCl$_3$): δ 170.4 (C=O), 138.5 (Ar), 128.2 (Ar), 127.9 (Ar), 127.5 (Ar), 108.9 (<u>C</u>(CH$_3$)$_2$), 99.3 (Rha-C-1), 98.6 (Fuc-C-1), 80.8 (Rha-C-4), 78.4 (Rha-C-3), 76.1 (Rha-C-2), 75.4 (Fuc-C-3), 73.1 (Fuc-C-4), 72.9 (Ph<u>C</u>H$_2$), 69.3 (Fuc-C-2), 68.5 (O<u>C</u>H$_2$(CH$_2$)$_6$CH$_3$), 65.4 (Fuc-C-5), 65.3 (Rha-C-5), 31.8 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 29.5 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 29.3 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 29.2 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 28.0 (C(<u>C</u>H$_3$)$_2$), 26.4 (C(<u>C</u>H$_3$)$_2$), 26.1 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 22.6 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 20.8 (CO<u>C</u>H$_3$), 17.7 (Rha-C-6), 16.2 (Fuc-C-6), 14.1 (OCH$_2$(CH$_2$)$_6$<u>C</u>H$_3$); HRMS (ESI) Calc. for [M + Na]$^+$ C$_{32}$H$_{50}$NaO$_{10}$: 617.3296; Found 617.3294.



Octyl 4-*O*-benzyl-2,3-*O*-isopropylidene-α-D-rhamnopyranosyl-(1→3)-[2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranosyl-(1→2)]-4-*O*-acetyl-α-L-fucopyranoside (4.9): To a stirred solution of acceptor **4.10** (259 mg, 435 μmol) and 2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranoside **4.14**[9] (317 mg, 522 μmol)

in dry CH_2Cl_2 (10 mL) was added molecular sieves (1.0 g, 4Å, powder). After stirring for 30 min at room temperature, the reaction mixture was cooled to –10 °C, and then *N*-iodosuccinimide (147 mg, 653 μmol) and silver trifluoromethanesulfonate (22.4 mg, 87.0 μmol) were added successively. The resulting solution was stirred for 1 h at 0 °C under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was washed with saturated $Na_2S_2O_3$ (aq.) and saturated $NaHCO_3$ (aq.), the aqueous layer was extracted with CH_2Cl_2 (30 mL × 3), dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (8:1 hexane–EtOAc) to afford **4.9** (439 mg, 94%) as a syrup. R_f 0.56 (4:1 hexane–EtOAc); $[\alpha]_D$ –3.4 (*c* 1.3, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.43–7.42 (m, 2H, Ar), 7.36–7.24 (m, 12H, Ar), 5.48 (s, 1H, Rha-H-1), 5.17 (d, 1H, J = 2.6 Hz, Fuc-H-4), 4.89 (d, 1H, J = 3.6 Hz, Fuc-H-1), 4.87 (d, 1H, J = 11.9 Hz, PhC$\underline{H}_2$), 4.81 (d, 1H, J = 12.4 Hz, PhC$\underline{H}_2$), 4.73–4.70 (m, 3H, Gal-H-1, PhC$\underline{H}_2$), 4.68 (d, 1H, J = 12.4 Hz, PhC$\underline{H}_2$), 4.63 (d, 1H, J = 11.9 Hz, PhC$\underline{H}_2$), 4.38 (d, 1H, J = 2.6 Hz, Gal-H-4), 4.24 (d, 1H, J = 5.6 Hz, Rha-H-2), 4.21 (dd, 1H, J = 10.2, 3.5 Hz, Fuc-H-3), 4.14 (dd, 1H, J = 12.3, 2.0 Hz, Gal-H-6a), 4.08 (dd, 1H, J = 7.3, 5.7 Hz, Rha-H-3), 4.00–3.96 (m, 2H, Fuc-H-5, Gal-H-6b), 3.88 (dd, 1H, J = 10.1, 3.5 Hz, Gal-H-2), 3.83–3.78 (m, 2H, Fuc-H-2, Rha-H-5), 3.77–3.74 (m, 2H, Gal-H-5, Gal-H-3), 3.57 (dt, 1H, J = 9.5, 7.0 Hz, OC$\underline{H}_2$CH$_2$(CH$_2$)$_5$CH$_3$), 3.19–3.14 (m, 2H, Rha-H-4, OC$\underline{H}_2$CH$_2$(CH$_2$)$_5$CH$_3$), 2.20 (s, 3H, COC$\underline{H}_3$), 1.53–1.45 (m, 2H, OCH$_2$C$\underline{H}_2$(CH$_2$)$_5$CH$_3$), 1.41 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.28–1.22 (m, 13H, Rha-H-6, OCH$_2$CH$_2$(C$\underline{H}_2$)$_5$CH$_3$), 1.11 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.09 (d, 3H, J = 6.6 Hz, Fuc-H-6), 1.02 (s, 9H, C(C$\underline{H}_3$)$_3$), 0.91 (s, 9H, C(C$\underline{H}_3$)$_3$),

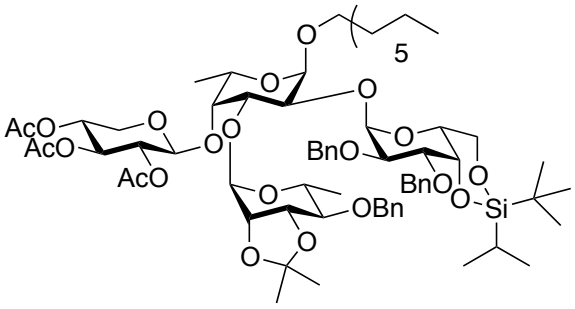
0.87 (t, 3H, J = 7.1 Hz, $OCH_2CH_2(CH_2)_5C\underline{H}_3$); ^{13}C NMR (175 MHz; $CDCl_3$): δ 170.4 (C=O), 139.4 (Ar), 138.9 (Ar), 138.7 (Ar), 128.3 (Ar), 128.2 (2 × Ar), 128.1 (Ar), 127.9 (Ar), 127.7 (Ar), 127.4 (2 × Ar) , 127.3 (Ar), 108.7 ($\underline{C}(CH_3)_2$), 101.2 (Gal-C-1, $^1J_{C\text{-}H}$ = 169.5 Hz), 98.7 (Rha-C-1), 98.3 (Fuc-C-1), 81.0 (Rha-C-4), 79.3 (Fuc-C-2), 78.3 (Rha-C-3), 77.6 (Gal-C-3), 76.0 (Rha-C-2), 73.9 (Gal-C-2), 73.5 (Fuc-C-4), 73.2 ($Ph\underline{C}H_2$), 72.7 ($Ph\underline{C}H_2$), 71.6 (Gal-C-4), 71.3 ($Ph\underline{C}H_2$), 71.0 (Fuc-C-3), 68.1 ($O\underline{C}H_2(CH_2)_6CH_3$), 68.0 (Gal-C-5), 67.3 (Gal-C-6), 64.9 (Rha-C-5), 64.6 (Fuc-C-5), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 28.1 ($C(\underline{C}H_3)_2$), 27.6 ($C(\underline{C}H_3)_3$), 27.2 ($C(\underline{C}H_3)_3$), 26.4 ($C(\underline{C}H_3)_2$), 26.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 23.4 ($\underline{C}(CH_3)_3$), 22.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 20.8 ($CO\underline{C}H_3$), 20.6 ($\underline{C}(CH_3)_3$), 17.8 (Rha-C-6), 16.1 (Fuc-C-6), 14.1 ($OCH_2(CH_2)_6\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{60}H_{88}NaO_{15}Si$: 1099.5785; Found 1099.5790.



Octyl 4-*O*-benzyl-2,3-*O*-isopropylidene-α-D-rhamnopyranosyl-(1→3)-[2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranosyl-(1→2)]-α-L-fucopyranoside (4.20): To a stirred solution of **4.9** (439 mg, 407 μmol) in CH_3OH (8.0 mL) was added a solution of $NaOCH_3$ in CH_3OH (1.0 mL, 0.5 M). The reaction mixture was stirred for 7 h at room temperature, then neutralized by addition of Amberlite® IR-120 (H^+) cation

exchange resin, filtered and the filtrate was concentrated to afford **4.20** (421 mg, quant.) as a syrup. R_f 0.37 (4:1 hexane–EtOAc); $[\alpha]_D$ +6.4 (*c* 0.89, $CHCl_3$); ^1H NMR (700 MHz; $CDCl_3$): δ 7.44–7.43 (m, 2H, Ar), 7.36–7.23 (m, 13H, Ar), 5.61 (s, 1H, Rha-H-1), 4.90 (d, 1H, J = 11.6 Hz, PhC$\underline{H}_2$), 4.86 (d, 1H, J = 3.6 Hz, Fuc-H-1), 4.81 (d, 1H, J = 12.5 Hz, PhC$\underline{H}_2$), 4.72–4.70 (m, 4H, 3 × PhC$\underline{H}_2$, Gal-H-1), 4.61 (d, 1H, J = 11.6 Hz, PhC$\underline{H}_2$), 4.40 (d, 1H, J = 2.6 Hz, Gal-H-4), 4.32 (d, 1H, J = 5.7 Hz, Rha-H-2), 4.21 (t, 1H, J = 6.3 Hz, Rha-H-3), 4.13 (dd, 1H, J = 12.3, 1.9 Hz, Gal-H-6a), 4.10 (dd, 1H, J = 10.0, 3.3 Hz, Fuc-H-3), 3.97 (dd, 1H, J = 12.3, 1.3 Hz, Gal-6-Hb), 3.91–3.84 (m, 3H, Fuc-H-5, Gal-H-2, Fuc-H-2), 3.79–3.70 (m, 4H, Gal-H-3, Gal-H-5, Rha-H-5, Fuc-H-4), 3.58 (dt, 1H, J = 9.5, 7.0 Hz, OC$\underline{H}_2CH_2(CH_2)_5CH_3$), 3.24 (dd, 1H, J = 9.6, 7.1 Hz, Rha-H-4), 3.14 (dt, 1H, J = 9.4, 6.8 Hz, OC$\underline{H}_2CH_2(CH_2)_5CH_3$), 2.23 (s, 1H, Fuc-4-OH), 1.52–1.45 (m, 5H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$, $C(C\underline{H}_3)_2$), 1.29–1.24 (m, 16H, Rha-H-6, Fuc-H-6, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 1.14 (s, 3H, $C(C\underline{H}_3)_2$), 1.01 (s, 9H, $C(C\underline{H}_3)_3$), 0.88–0.86 (m, 12H, $C(C\underline{H}_3)_3$, $OCH_2CH_2(CH_2)_5C\underline{H}_3$); ^{13}C NMR (125 MHz; $CDCl_3$): δ 139.4 (Ar), 138.8 (Ar), 138.3 (Ar), 128.3 (3 × Ar), 128.17 (Ar), 128.0 (Ar), 127.7 (Ar), 127.6 (Ar), 127.4 (Ar), 127.3 (Ar), 109.0 ($\underline{C}(CH_3)_2$), 101.4 (Gal-C-1), 98.5 (Rha-C-1), 98.2 (Fuc-C-1), 81.2 (Rha-C-4), 78.8 (Fuc-C-2), 78.3 (Rha-C-3), 77.7 (Gal-C-3), 75.8 (Gal-C-4), 73.4 (Gal-C-2), 73.3 (Fuc-C-3), 73.0 (2 × Ph$\underline{C}H_2$), 72.3 (Fuc-C-4), 71.5 (Gal-C-4), 71.1 (Ph$\underline{C}H_2$), 68.0 (Gal-C-5, O$\underline{C}H_2(CH_2)_6CH_3$), 67.3 (Gal-C-6), 65.0 (Rha-C-5, Fuc-C-5), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 28.1 ($C(\underline{C}H_3)_2$), 27.6 ($C(\underline{C}H_3)_3$), 27.2 ($C(\underline{C}H_3)_3$), 26.4 ($C(\underline{C}H_3)_2$, $OCH_2(\underline{C}H_2)_6CH_3$), 23.4 ($\underline{C}(CH_3)_3$), 22.7

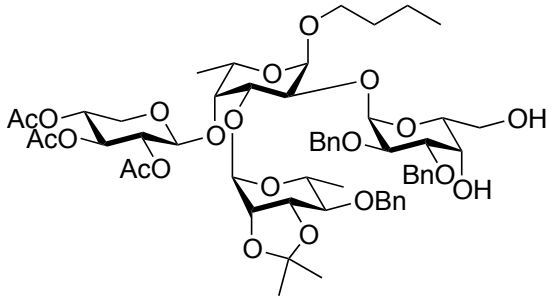
($OCH_2(\underline{C}H_2)_6CH_3$), 20.6 ($\underline{C}(CH_3)_3$), 18.0 (Rha-C-6), 16.0 (Fuc-C-6), 14.1 ($OCH_2(CH_2)_6\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{58}H_{86}NaO_{14}Si$: 1057.5679; Found 1057.5681.



Octyl 2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl-(1→4)-[4-*O*-benzyl-2,3-*O*-isopropylidene-α-D-rhamnopyranosyl-(1→3)]-[2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranosyl-(1→2)]-α-L-fucopyranoside (4.21): To a stirred solution of acceptor **4.20** (384 mg, 371 μmol) and *p*-tolyl 2,3,4-tri-*O*-acetyl-1-thio-β-D-xylopyranoside **4.12**[8] (352 mg, 920 μmol) in dry CH_2Cl_2 (8.0 mL) was added molecular sieves (800 mg, 4Å, powder). After stirring for 30 min at room temperature, the reaction mixture was cooled to 0 °C, and then *N*-iodosuccinimide (32.2 mg, 143 μmol) and silver trifluoromethanesulfonate (4.9 mg, 19 μmol) were added successively. The resulting solution was stirred for 1 h at room temperature under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was washed with saturated $Na_2S_2O_3$ (aq.) and saturated $NaHCO_3$ (aq.), the aqueous layer was extracted with CH_2Cl_2 (25 mL × 3), dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (4:1 hexane–EtOAc) to afford **4.21** (274 mg, 57%) as a syrup. R_f 0.32 (3:1 hexane–EtOAc); $[\alpha]_D$ –21.2 (*c* 0.92,

$CHCl_3$); ^1H NMR (700 MHz; $CDCl_3$): δ 7.43–7.42 (m, 2H, Ar), 7.35–7.23 (m, 13H, Ar), 5.51 (s, 1H, Rha-H-1), 5.11 (t, 1H, J = 7.4 Hz, Xyl-H-3), 5.05 (dd, 1H, J = 7.4, 5.7 Hz, Xyl-H-2), 4.98 (td, 1H, J = 7.0, 4.6 Hz, Xyl-H-4), 4.89 (d, 1H, J = 11.7 Hz, PhC$\underline{H}_2$), 4.82 (d, 1H, J = 3.6 Hz, Fuc-H-1), 4.81 (d, 1H, J = 12.4 Hz, PhC$\underline{H}_2$), 4.74–4.69 (m, 4H, Gal-H-1, 3 × PhC$\underline{H}_2$), 4.59–4.58 (m, 2H, PhC$\underline{H}_2$, Xyl-H-1), 4.37 (d, 1H, J = 2.7 Hz, Gal-H-4), 4.34–4.31 (m, 2H, Xyl-H-5a, Rha-H-2), 4.15–4.10 (m, 3H, Rha-H-3, Gal-H-6a, Fuc-H-3), 3.96–3.91 (m, 2H, Gal-H-6b, Rha-H-5), 3.88–3.82 (m, 3H, Gal-H-2, Fuc-H-5, Fuc-H-2), 3.76 (br s, 1H, Gal-H-5), 3.74 (dd, 1H, J = 10.1, 2.8 Hz, Gal-H-3), 3.63 (d, 1H, J = 2.9 Hz, Fuc-H-4), 3.5 (dt, 1H, J = 9.5, 7.1 Hz, OC$\underline{H}_2CH_2(CH_2)_5CH_3$), 3.36 (dd, 1H, J = 12.2, 7.1 Hz, Xyl-H-5b), 3.20 (dd, 1H, J = 9.7, 7.1 Hz, Rha-H-4), 3.12 (dt, 1H, J = 9.3, 6.9 Hz, OC$\underline{H}_2CH_2(CH_2)_5CH_3$), 2.06 (s, 3H, COC$\underline{H}_3$), 2.03 (s, 3H, COC$\underline{H}_3$), 1.99 (s, 3H, COC$\underline{H}_3$), 1.49–1.41 (m, 5H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$, C(C$\underline{H}_3$)$_2$), 1.29–1.24 (m, 13H, Rha-H-6, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 1.18 (d, 3H, J = 6.6 Hz, Fuc-H-6), 1.11 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.01 (s, 9H, C(C$\underline{H}_3$)$_3$), 0.89 (s, 9H, C(C$\underline{H}_3$)$_3$), 0.86 (t, 3H, J = 7.0 Hz, $OCH_2CH_2(CH_2)_5C\underline{H}_3$); ^{13}C NMR (125 MHz; $CDCl_3$): δ 170.0 (C=O), 169.7 (C=O), 169.4 (C=O), 139.5 (Ar), 138.8 (2 × Ar), 128.4 (Ar), 128.3 (Ar), 128.1 (Ar), 127.9 (Ar), 127.8 (Ar), 127.4 (2 × Ar), 127.2 (Ar), 108.9 ($\underline{C}(CH_3)_2$), 101.2 (Gal-C-1), 100.9 (Xyl-C-1, $^1J_{C\text{-}H}$ = 165.6 Hz), 98.4 (Rha-C-1), 98.3 (Fuc-C-1), 81.5 (Rha-C-4), 80.4 (Fuc-C-4), 79.2 (Fuc-C-2), 78.5 (Rha-C-3), 77.9 (Gal-C-3), 75.8 (Rha-C-2), 73.7 (Gal-C-2), 73.1 (Ph$\underline{C}H_2$), 72.7 (Ph$\underline{C}H_2$), 71.7 (Gal-C-4), 71.4 (Ph$\underline{C}H_2$), 71.3 (Fuc-C-3), 70.6 (Xyl-C-3), 70.3 (Xyl-C-2), 68.6 (Xyl-C-4), 68.0 (Gal-C-5), 67.9 ($O\underline{C}H_2(CH_2)_6CH_3$), 67.4 (Gal-C-6), 65.7 (Fuc-C-5), 64.5 (Rha-C-5), 61.2 (Xyl-

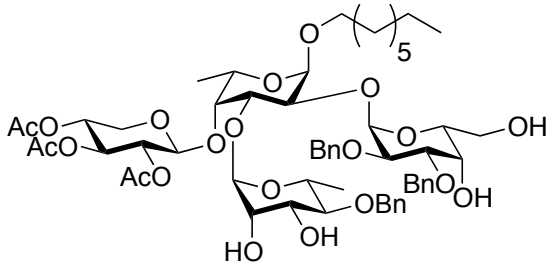
C-5), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 28.2 ($C(\underline{C}H_3)_2$), 27.6 ($C(\underline{C}H_3)_3$), 27.2 ($C(\underline{C}H_3)_3$), 26.5 ($C(\underline{C}H_3)_2$), 26.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 23.4 ($\underline{C}(CH_3)_3$), 22.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 20.80 (3 × $CO\underline{C}H_3$), 20.6 ($\underline{C}(CH_3)_3$), 18.0 (Rha-C-6), 16.3 (Fuc-C-6), 14.1 ($OCH_2(CH_2)_6\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{69}H_{100}NaO_{21}Si$: 1315.6419; Found 1315.6430.



Octyl 2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl-(1→4)-[4-*O*-benzyl-2,3-*O*-isopropylidene-α-D-rhamnopyranosyl-(1→3)]-[2,3-di-*O*-benzyl-α-D-galactopyranosyl-(1→2)]-α-L-fucopyranoside (4.22): To a stirred solution of **4.21** (226 mg 174 μmol) in THF–pyridine (6.0 mL, 1:1) was added HF·pyridine (0.6 mL, pyridine ~30%, hydrogen fluoride ~70%) at 0 °C under an Ar atmosphere. The reaction mixture was stirred for 1 h at 0 °C, before being poured into saturated $NaHCO_3$ (aq.). The aqueous layer was extracted with EtOAc (25 mL × 3), dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (2:3 hexane–EtOAc) to afford **4.22** (181 mg, 92%) as a syrup. R_f 0.21 (1:1 hexane–EtOAc); $[\alpha]_D$ –25.1 (*c* 1.3, $CHCl_3$); ^1H NMR (700 MHz; $CDCl_3$): δ 7.36–7.23 (m, 15H, Ar), 5.52 (s, 1H, Rha-H-1), 5.12 (t, 1H, J = 7.3 Hz, Xyl-H-3), 5.05 (dd, 1H, J = 7.5, 5.6 Hz, Xyl-H-2), 4.98 (td, 1H, J = 7.0, 4.6 Hz, Xyl-H-4), 4.93–4.91 (m, 2H, Gal-H-1, Fuc-H-1), 4.88 (d, 1H, J = 11.8 Hz, $PhC\underline{H}_2$), 4.82 (d, 1H, J =

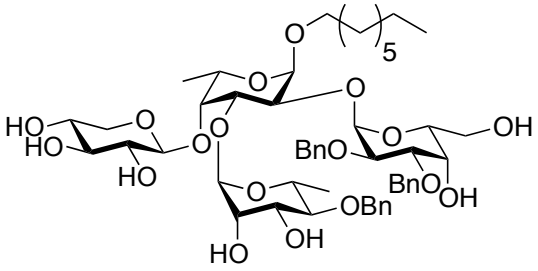
11.5 Hz, PhC$\underline{H}_2$), 4.76 (d, 1H, J = 12.5 Hz, PhC$\underline{H}_2$), 4.71 (d, 1H, J = 12.5 Hz, PhC$\underline{H}_2$), 4.66 (d, 1H, J = 11.5 Hz, PhC$\underline{H}_2$), 4.60 (d, 1H, J = 5.5 Hz, Xyl-H-1), 4.58 (d, 1H, J = 11.8 Hz, PhC$\underline{H}_2$), 4.34 (dd, 1H, J = 12.2, 4.5 Hz, Xyl-H-5a), 4.28 (d, 1H, J = 5.7 Hz, Rha-H-2), 4.18 (dd, 1H, J = 10.3, 3.1 Hz, Fuc-H-3), 4.13 (t, 1H, J = 6.3 Hz, Rha-H-3), 4.03 (d, 1H, J = 2.0 Hz, Gal-H-4), 3.99 (t, 1H, J = 4.2 Hz, Gal-H-5), 3.95–3.84 (m, 5H, Rha-H-5, Fuc-H-5, Fuc-H-2, Gal-H-3, Gal-H-6a), 3.77 (dd, 1H, J = 9.9, 3.4 Hz, Gal-H-2), 3.71 (dd, 1H, J = 11.8, 4.4 Hz, Gal-H-6b), 3.65 (d, 1H, J = 3.0 Hz, Fuc-H-4), 3.57 (dt, 1H, J = 9.4, 7.0 Hz, OC$\underline{H}_2$CH$_2$(CH$_2$)$_5$CH$_3$), 3.37 (dd, 1H, J = 12.2, 7.1 Hz, Xyl-H-5b), 3.31 (dt, 1H, J = 9.4, 6.8 Hz, OC$\underline{H}_2$CH$_2$(CH$_2$)$_5$CH$_3$), 3.19 (dd, 1H, J = 9.8, 7.1 Hz, Rha-H-4), 2.07 (s, 3H, COC$\underline{H}_3$), 2.03 (s, 3H, COC$\underline{H}_3$), 2.00 (s, 3H, COC$\underline{H}_3$), 1.57–1.51 (m, 2H, OCH$_2$C$\underline{H}_2$(CH$_2$)$_5$CH$_3$), 1.38 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.30–1.25 (m, 13H, Rha-H-6, OCH$_2$CH$_2$(C$\underline{H}_2$)$_5$CH$_3$), 1.20 (d, 3H, J = 6.6 Hz, Fuc-H-6), 1.01 (s, 3H, C(C$\underline{H}_3$)$_2$), 0.87 (t, 3H, J = 7.0 Hz, OCH$_2$CH$_2$(CH$_2$)$_5$C$\underline{H}_3$); ^{13}C NMR (125 MHz; CDCl$_3$): δ 169.9 (C=O), 169.7 (C=O), 169.4 (C=O), 138.7 (Ar), 138.5 (Ar), 138.4 (Ar), 128.5 (2 × Ar), 128.1 (Ar), 128.0 (Ar), 127.9 (2 × Ar), 127.8 (Ar), 127.7 (2 × Ar), 108.9 (C(CH$_3$)$_2$), 100.9 (Xyl-C-1), 100.7 (Gal-C-1), 98.4 (Rha-C-1), 98.1 (Fuc-C-1), 81.4 (Rha-C-4), 80.6 (Fuc-C-4), 79.5 (Fuc-C-2), 78.5 (Rha-C-3), 75.8 (Rha-C-2), 75.3 (Gal-C-2), 73.2 (Ph$\underline{C}$H$_2$), 72.9 (Ph$\underline{C}$H$_2$), 72.7 (Ph$\underline{C}$H$_2$), 71.3 (Fuc-C-3), 70.6 (Xyl-C-3), 70.3 (Xyl-C-2), 70.2 (Gal-C-4), 69.3 (Gal-C-5), 68.6 (Xyl-C-4), 67.8 (O$\underline{C}$H$_2$(CH$_2$)$_6$CH$_3$), 65.7 (Fuc-C-5), 64.6 (Rha-C-5), 63.5 (Gal-C-6), 61.2 (Xyl-C-5), 31.8 (OCH$_2$($\underline{C}$H$_2$)$_6$CH$_3$), 29.8 (OCH$_2$($\underline{C}$H$_2$)$_6$CH$_3$), 29.5 (OCH$_2$($\underline{C}$H$_2$)$_6$CH$_3$), 29.3 (OCH$_2$($\underline{C}$H$_2$)$_6$CH$_3$), 28.1 (C($\underline{C}$H$_3$)$_2$), 26.43 (OCH$_2$($\underline{C}$H$_2$)$_6$CH$_3$), 26.4 (C($\underline{C}$H$_3$)$_2$), 22.7

($OCH_2(\underline{C}H_2)_6CH_3$), 20.8 (3 × $CO\underline{C}H_3$), 18.0 (Rha-C-6), 16.3 (Fuc-C-6), 14.1 ($OCH_2(CH_2)_6\underline{C}H_3$); HRMS (ESI) Calc. for $[M + NH_4]^+$ $C_{61}H_{88}NO_{21}$: 1170.5843; Found 1170.5862.



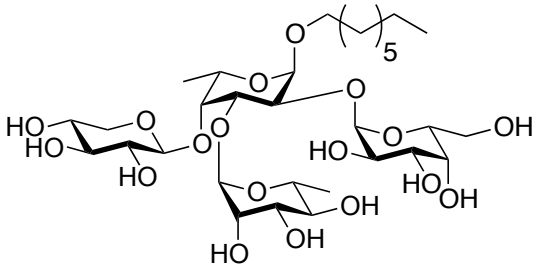
Octyl 2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl-(1→4)-[4-*O*-benzyl-α-D-rhamnopyranosyl-(1→3)]-[2,3-di-*O*-benzyl-α-D-galactopyranosyl-(1→2)]-α-L-fucopyranoside (4.23): To a stirred solution of **4.22** (181 mg, 157 μmol) in CH_3CN–CH_3OH (18 mL, 10:1) was added *p*-toluenesulfonic acid monohydrate (89.5 mg, 470 μmol) at room temperature. The reaction mixture was stirred for 3.5 h at room temperature. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (1:2 hexane–EtOAc) to afford **4.23** (150 mg, 86%) as a white amorphous solid. R_f 0.31 (1:2 hexane–EtOAc); $[\alpha]_D$ –10.9 (*c* 0.57, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.39–7.23 (m, 15H), 5.11–5.08 (m, 2H, Rha-H-1), 5.04 (dd, 1H, J = 8.3, 6.5 Hz), 4.99–4.95 (m, 2H, Gal-H-1), 4.92 (d, 1H, J = 3.5 Hz, Fuc-H-1), 4.81–4.75 (m, 3H), 4.70–4.67 (m, 2H), 4.58 (d, 1H, J = 11.4 Hz), 4.52 (d, 1H, J = 6.4 Hz, Xyl-H-1), 4.21 (dd, 1H, J = 12.0, 4.9 Hz), 4.11 (d, 1H, J = 1.6 Hz), 4.06–4.03 (m, 2H), 3.92–3.80 (m, 7H), 3.75–3.72 (m, 2H), 3.67 (d, 1H, J = 3.0 Hz), 3.56 (dt, 1H, J = 9.4, 6.9 Hz), 3.31 (dt, 1H, J = 9.4, 6.8 Hz), 3.23 (dd, 1H, J = 12.0,

8.4 Hz), 3.18 (t, 1H, J = 8.7 Hz), 2.71 (s, 1H), 2.41 (dd, 1H, J = 6.4, 0.4 Hz), 2.05 (s, 3H), 2.02 (s, 3H), 1.96 (s, 3H), 1.89 (d, 1H, J = 3.7 Hz), 1.87 (d, 1H, J = 6.1 Hz), 1.55-1.51 (m, 2H), 1.30–1.24 (m, 13H), 1.18 (d, 3H, J = 6.6 Hz), 0.87 (t, 3H, J = 7.0 Hz); ^{13}C NMR (125 MHz; $CDCl_3$): δ 170.1, 169.6, 169.5, 138.8, 138.2, 138.0, 128.7, 128.6, 128.3 (3 × C), 128.0, 127.8, 127.7, 127.5, 101.3 (Xyl-C-1), 101.3 (Rha-C-1), 100.9 (Gal-C-1), 98.1 (Fuc-C-1), 81.9, 80.5, 79.7, 77.6, 76.2, 74.5, 74.1, 72.8, 71.9, 71.5, 71.2, 71.0, 70.6, 69.5, 69.2, 68.7, 67.7, 67.4, 65.5, 63.4, 61.7, 31.9, 29.8, 29.5, 29.3, 26.5, 22.7, 20.8 (2 × C), 20.7, 18.3, 16.2, 14.1; HRMS (ESI) Calc. for $[M + Na]^+$ $C_{58}H_{80}NaO_{21}$: 1135.5084; Found 1135.5090.



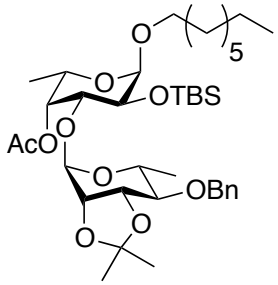
Octyl β-D-xylopyranosyl-(1→4)-[4-*O*-benzyl-α-D-rhamnopyranosyl-(1→3)]-[2,3-di-*O*-benzyl-α-D-galactopyranosyl-(1→2)]-α-L-fucopyranoside (4.24): To a stirred solution of **4.23** (104 mg, 93.0 μmol) in CH_3OH (4.0 mL) was added a solution of $NaOCH_3$ in CH_3OH (0.4 mL, 0.5 M). The reaction mixture was stirred for 4 h at room temperature, then neutralized by addition of Amberlite® IR-120 (H^+) cation exchange resin, filtered and the filtrate was concentrated to afford **4.24** (91.8 mg, quant.) as a white amorphous solid. R_f 0.32 (9:1 CH_2Cl_2–CH_3OH); $[\alpha]_D$ +2.7 (*c* 1.5, CH_2Cl_2–CH_3OH); ^{1}H NMR (700 MHz; CD_3OD): δ 7.46–7.44 (m, 4H), 7.38–7.23 (m, 11H), 5.30 (d, 1H, J = 1.1 Hz, Rha-H-1), 5.02 (d, 1H, J = 3.6 Hz, Gal-H-1), 4.95 (d, 1H, J = 11.4 Hz), 4.87 (d, 1H, J = 12.8 Hz),

4.83–4.81 (m, 2H, Fuc-H-1), 4.77 (d, 1H, J = 11.6 Hz), 4.71 (d, 1H, J = 11.6 Hz), 4.63 (d, 1H, J = 11.4 Hz), 4.29 (d, 1H, J = 7.4 Hz, Xyl-H-1), 4.13–4.08 (m, 3H), 4.06–4.05 (m, 2H), 4.00–3.94 (m, 3H), 3.87–3.82 (m, 4H), 3.65–3.61 (m, 3H), 3.53 (ddd, 1H, J = 10.0, 8.8, 5.4 Hz), 3.47 (dt, 1H, J = 9.4, 6.5 Hz), 3.39–3.34 (m, 2H), 3.32–3.30 (m, 1H), 3.09 (t, 1H, J = 11.0 Hz), 1.60 (quintet, 2H, J = 6.9 Hz), 1.39–1.27 (m, 13H), 1.24 (d, 3H, J = 6.3 Hz), 0.90 (t, 3H, J = 6.9 Hz); ^{13}C NMR (125 MHz; CD_3OD): δ 140.5, 140.3, 140.2, 129.6, 129.5, 129.3 (2 × C), 128.9 (2 × C), 128.7, 128.5, 128.4, 106.3 (Xyl-C-1), 102.6 (Rha-C-1), 102.5 (Fuc-C-1), 99.8 (Gal-C-1), 83.0, 81.0, 80.3, 79.2, 78.0, 76.1, 75.7, 75.5, 74.0, 73.0, 72.8, 72.6, 72.5, 72.3, 71.3, 69.3, 68.7 (2 × C), 67.8, 66.8, 62.5, 33.1, 30.8, 30.6 (2 × C), 27.6, 23.8, 18.4, 16.5, 14.5; HRMS (ESI) Calc. for $[M + Na]^+$ $C_{52}H_{74}NaO_{18}$: 1009.4767; Found 1009.4772.



Octyl β-D-xylopyranosyl-(1→4)-[α-D-rhamnopyranosyl-(1→3)]-[α-D-galactopyranosyl-(1→2)]-α-L-fucopyranoside (4.1): To a stirred solution of **4.24** (91.8 mg, 93.0 μmol) in dry THF (5.0 mL) was added 20% palladium hydroxide on carbon (10.0 mg). After stirring for 24 h under an H_2 atmosphere (1 atm), the reaction mixture was filtered through Celite and concentrated. The residue was dissolved in water and then lyophilized to afford **4.1** (66.7 mg, quant.) as a white solid. R_f 0.28 (1:2:1 CH_2Cl_2–CH_3OH–

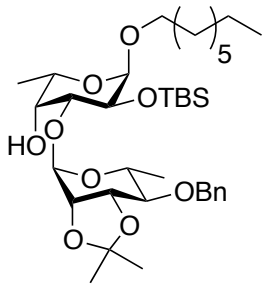
H_2O); $[\alpha]_D$ +2.9 (*c* 0.42, CH_2Cl_2–CH_3OH); ^1H NMR (700 MHz; CD_3OD): δ 5.14 (d, 1H, *J* = 1.2 Hz, Rha-H-1), 5.04 (d, 1H, *J* = 3.7 Hz, Fuc-H-1), 4.97 (d, 1H, *J* = 3.8 Hz, Gal-H-1), 4.28 (d, 1H, *J* = 7.1 Hz, Xyl-H-1), 4.08 (dd, 1H, *J* = 11.6, 5.4 Hz), 4.04 (dd, 1H, *J* = 10.4, 3.1 Hz), 4.00 (q, 1H, *J* = 6.7 Hz), 3.98 (dd, 1H, *J* = 3.3, 1.6 Hz), 3.96–3.92 (m, 3H), 3.88 (d, 1H, *J* = 2.6 Hz), 3.84 (d, 1H, *J* = 3.1 Hz), 3.81–3.78 (m, 2H), 3.75 (dd, 1H, *J* = 10.2, 3.2 Hz), 3.73–3.65 (m, 3H), 3.53–3.48 (m, 2H), 3.40 (t, 1H, *J* = 9.4 Hz), 3.33–3.28 (m, 2H), 3.10 (t, 1H, *J* = 11.0 Hz), 1.62 (dt, 2H, *J* = 14.0, 7.0 Hz), 1.42–1.40 (m, 2H), 1.36–1.27 (m, 11H), 1.24 (d, 3H, *J* = 6.3 Hz), 0.91 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR (125 MHz; CD_3OD): δ 106.3 (Xyl-C-1), 103.4 (Rha-C-1), 103.2 (Gal-C-1), 99.9 (Fuc-C-1), 81.2, 78.4, 77.9, 75.5, 74.3, 74.1, 72.7, 71.9, 71.3, 71.2, 71.1, 70.1, 68.9, 68.0, 66.7, 62.8, 33.1, 30.8, 30.6, 30.5, 27.6, 23.7, 18.0, 16.6, 14.4; HRMS (ESI) Calc. for $[M + Na]^+$ $C_{31}H_{56}NaO_{18}$: 739.3359; Found 739.3364.



Octyl 4-*O*-benzyl-2,3-*O*-isopropylidene-α-D-rhamnopyranosyl-(1→3)-4-*O*-acetyl-2-*O*-*tert*-butyldimethylsilyl-α-L-fucopyranoside (4.25): To a stirred solution of **4.10** (161 mg, 272 μmol) in dry CH_2Cl_2 (5.0 mL) was added *tert*-butyldimethylsilyl trifluoromethanesulfonate (93.0 μL, 406 μmol) and 2,6-lutidine (63.0 μL, 541 μmol) at 0 °C. The reaction mixture was stirred for 2 h at room temperature. The crude residue was

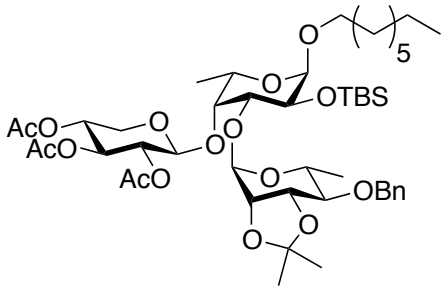
diluted with CH_2Cl_2 (50 mL), then washed with 1N HCl and saturated $NaHCO_3$ (aq.). The organic layer was dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (8:1 hexane–EtOAc) to afford **4.25** (186 mg, 97%) as a viscous oil. R_f 0.63 (4:1 hexane–EtOAc); $[\alpha]_D$ –40.7 (*c* 0.45, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.35–7.30 (m, 4H, Ar), 7.26–7.24 (m, 1H, Ar), 5.17 (s, 1H, Rha-H-1), 5.15 (dd, 1H, J = 3.6, 1.2 Hz, Fuc-H-4), 4.86 (d, 1H, J = 11.8 Hz, PhC$\underline{H}_2$), 4.71 (d, 1H, J = 3.7 Hz, Fuc-H-1), 4.63 (d, 1H, J = 11.8 Hz, PhC$\underline{H}_2$), 4.15–4.12 (m, 2H, Rha-H-2, Rha-H-3), 4.07–4.04 (m, 2H, Fuc-H-3, Fuc-H-5), 3.94 (dd, 1H, J = 9.9, 3.7 Hz, Fuc-H-2), 3.73 (dq, 1H, J = 9.8, 6.2 Hz, Rha-H-5), 3.63 (dt, 1H, J = 9.7, 6.6 Hz, OC$\underline{H}_2$CH$_2$(CH$_2$)$_5$CH$_3$), 3.36 (dt, 1H, J = 9.7, 6.7 Hz, OC$\underline{H}_2$CH$_2$(CH$_2$)$_5$CH$_3$), 3.15 (dd, 1H, J = 9.8, 6.6 Hz, Rha-H-4), 2.13 (s, 3H, COC$\underline{H}_3$), 1.58 (quintet, 2H, J = 7.2 Hz, OCH$_2$C$\underline{H}_2$(CH$_2$)$_5$CH$_3$), 1.45 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.36–1.25 (m, 16H, C(C$\underline{H}_3$)$_2$, OCH$_2$CH$_2$(C$\underline{H}_2$)$_5$CH$_3$, Rha-H-6), 1.07 (d, 3H, J = 6.6 Hz, Fuc-H-6), 0.88–0.86 (m, 12H, SiC(C$\underline{H}_3$)$_3$, OCH$_2$CH$_2$(CH$_2$)$_5$C$\underline{H}_3$), 0.07 (s, 3H, SiC$\underline{H}_3$), 0.07 (s, 3H, SiC$\underline{H}_3$); ^{13}C NMR (125 MHz; $CDCl_3$): δ 170.5 (C=O), 138.6 (Ar), 128.2 (Ar), 127.9 (Ar), 127.5 (Ar), 108.7 (C(CH$_3$)$_2$), 99.5 (2 × C, Fuc-H-1, Rha-H-1), 80.9 (Rha-C-4), 78.5 (Rha-C-3), 76.1 (Rha-C-2), 75.0 (Fuc-C-3), 73.8 (Fuc-C-4), 72.9 (PhCH$_2$), 70.1 (Fuc-C-2), 68.6 (OCH$_2$(CH$_2$)$_6$CH$_3$), 65.1 (Rha-C-5), 64.9 (Fuc-C-5), 31.9 (OCH$_2$(CH$_2$)$_6$CH$_3$), 29.6 (OCH$_2$(CH$_2$)$_6$CH$_3$), 29.4 (OCH$_2$(CH$_2$)$_6$CH$_3$), 29.3 (OCH$_2$(CH$_2$)$_6$CH$_3$), 28.0 (C(CH$_3$)$_2$), 26.3 (OCH$_2$(CH$_2$)$_6$CH$_3$), 26.2 (C(CH$_3$)$_2$), 25.8 (SiC(CH$_3$)$_3$), 22.7 (OCH$_2$(CH$_2$)$_6$CH$_3$), 20.9 (COCH$_3$), 18.0 (SiC(CH$_3$)$_3$), 17.6 (Rha-C-6),

16.2 (Fuc-C-6), 14.1 ($OCH_2(CH_2)_6\underline{C}H_3$), -4.4 ($Si\underline{C}H_3$), -4.8 ($Si\underline{C}H_3$); HRMS (ESI) Calc. for $[M + NH_4]^+$ $C_{38}H_{68}NO_{10}Si$: 726.4607; Found 726.4604.



Octyl 4-*O*-benzyl-2,3-*O*-isopropylidene-α-D-rhamnopyranosyl-(1→3)-2-*O*-*tert*-butyldimethylsilyl-α-L-fucopyranoside (4.26): To a stirred solution of **4.25** (182 mg, 257 μmol) in CH_3OH (6.0 mL) was added a solution of $NaOCH_3$ in CH_3OH (0.6 mL, 0.5 M). The reaction mixture was stirred for 6 h at room temperature, then neutralized by addition of Amberlite® IR-120 (H^+) cation exchange resin, filtered and the filtrate was concentrated to afford **4.26** (168 mg, 98%) as a viscous oil. R_f 0.40 (4:1 hexane–EtOAc); $[\alpha]_D$ –30.8 (*c* 0.31, $CHCl_3$); ^{1}H NMR (600 MHz; $CDCl_3$): δ 7.38–7.34 (m, 4H), 7.31–7.28 (m, 1H), 5.28 (s, 1H, Rha-C-1), 4.92 (d, 1H, J = 11.6 Hz, $PhC\underline{H}_2$), 4.71 (d, 1H, J = 2.5 Hz, Fuc-H-1), 4.64 (d, 1H, J = 11.6 Hz, $PhC\underline{H}_2$), 4.30–4.25 (m,2H, Rha-H-3, Rha-H-2), 4.02–3.97 (m, 3H, Fuc-H-5, Fuc-H-2, Fuc-H-3), 3.79–3.74 (m, 2H, Rha-H-5, Fuc-H-4), 3.67 (dt, 1H, J = 9.7, 6.6 Hz, $OC\underline{H}_2CH_2(CH_2)_5CH_3$), 3.40 (dt, 1H, J = 9.7, 6.7 Hz, $OC\underline{H}_2CH_2(CH_2)_5CH_3$), 3.24 (dd, 1H, J = 9.7, 7.0 Hz, Rha-H-4), 2.15 (br s, 1H, 4-OH), 1.61 (quintet, 2H, J = 7.1 Hz, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.51 (s, 3H, $C(C\underline{H}_3)_2$), 1.39–1.26 (m, 19H, $C(C\underline{H}_3)_2$, $OCH_2CH_2(C\underline{H}_2)_5CH_3$, Rha-H-6, Fuc-H-6), 0.91–0.89 (m, 12H, $SiC(C\underline{H}_3)_3$, $OCH_2CH_2(CH_2)_5C\underline{H}_3$), 0.09 (s, 3H, $SiC\underline{H}_3$), 0.08 (s, 3H, $SiC\underline{H}_3$); ^{13}C NMR (125 MHz

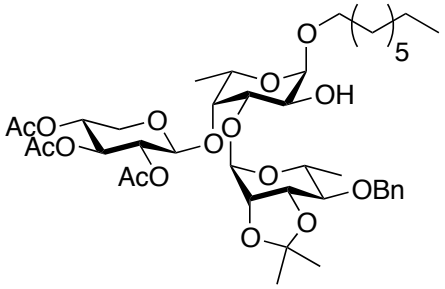
$CDCl_3$): δ 138.3 (Ar), 128.3 (Ar), 128.0 (Ar), 127.6 (Ar), 109.0 ($\underline{C}(CH_3)_2$), 99.3 (Fuc-C-1), 99.1 (Rha-C-1), 80.9 (Rha-C-4), 78.3 (Rha-C-3), 77.9 (Fuc-C-3), 75.9 (Rha-C-2), 73.0 ($Ph\underline{C}H_2$), 72.4 (Fuc-C-4), 69.3 (Fuc-C-2), 68.4 ($O\underline{C}H_2(CH_2)_6CH_3$), 65.3 (Rha-C-5), 65.1 (Fuc-C-5), 31.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 27.9 ($C(\underline{C}H_3)_2$), 26.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 26.1 ($C(\underline{C}H_3)_2$), 25.7 ($SiC(\underline{C}H_3)_3$), 22.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 18.0 ($Si\underline{C}(CH_3)_3$), 17.9 (Rha-C-6), 16.1 (Fuc-C-6), 14.1 ($OCH_2(CH_2)_6\underline{C}H_3$), -4.4 ($Si\underline{C}H_3$), -4.7 ($Si\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{36}H_{62}NaO_9Si$: 689.4055; Found 689.4056.



Octyl 2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl-(1→4)-[4-*O*-benzyl-2,3-*O*-isopropylidene-α-D-rhamnopyranosyl-(1→3)]-2-*O*-*tert*-butyldimethylsilyl-α-L-fucopyranoside (4.27): To a stirred solution of acceptor **4.26** (136 mg, 204 μmol) and *p*-tolyl 2,3,4-tri-*O*-acetyl-1-thio-β-D-xylopyranoside **4.12**[8] (156 mg, 409 μmol) in dry CH_2Cl_2 (5.0 mL) was added molecular sieves (500 mg, 4Å, powder). After stirring for 30 min at room temperature, the reaction mixture was cooled to 0 °C, and then *N*-iodosuccinimide (110 mg, 491 μmol) and silver trifluoromethanesulfonate (10.5 mg, 40.9 μmol) were added successively. The resulting solution was stirred for 1 h at room temperature under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was

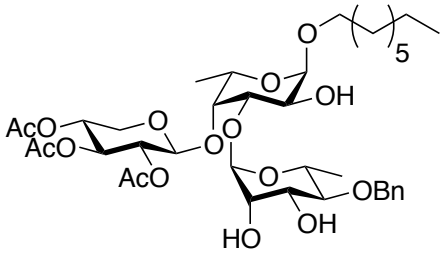
washed with saturated $Na_2S_2O_3$ (aq.) and saturated $NaHCO_3$ (aq.), the aqueous layer was extracted with CH_2Cl_2 (30 mL × 3), dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (4:1 hexane–EtOAc) to afford **4.27** (141 mg, 75%) as a white solid. R_f 0.24 (4:1 hexane–EtOAc); $[\alpha]_D$ –62.1 (*c* 0.47, $CHCl_3$); ^{1}H NMR (600 MHz; $CDCl_3$): δ 7.35–7.30 (m, 4H, Ar), 7.27–7.24 (m, 1H, Ar), 5.25 (s, 1H, Rha-H-1), 5.06 (t, 1H, J = 6.4 Hz, Xyl-H-3), 4.98 (dd, 1H, J = 6.4, 4.7 Hz, Xyl-H-2), 4.93–4.88 (m, 2H, Xyl-H-4, PhC$\underline{H}_2$), 4.65 (d, 1H, J = 3.0 Hz, Fuc-H-1), 4.62–4.60 (m, 2H, PhC$\underline{H}_2$, Xyl-H-1), 4.33 (dd, 1H, J = 12.3, 4.0 Hz, Xyl-H-5a), 4.21–4.17 (m, 2H, Rha-H-2, Rha-H-3), 4.02–3.98 (m, 2H, Fuc-H-3, Fuc-H-2), 3.96–3.92 (m, 2H, Rha-H-5, Fuc-H-5), 3.63-3.59 (m, 2H, OC$\underline{H}_2$CH$_2$(CH$_2$)$_5$CH$_3$, Fuc-H-4), 3.39 (dd, 1H, J = 12.3, 5.9 Hz, Xyl-H-5b), 3.34 (dt, 1H, J = 9.6, 6.7 Hz, OC$\underline{H}_2$CH$_2$(CH$_2$)$_5$CH$_3$), 3.18 (dd, 1H, J = 9.8, 7.0 Hz, Rha-H-4), 2.07 (s, 3H, COC$\underline{H}_3$), 2.06 (s, 3H, COC$\underline{H}_3$), 2.02 (s, 3H, COC$\underline{H}_3$), 1.59–1.54 (m, 2H, OCH$_2$C$\underline{H}_2$(CH$_2$)$_5$CH$_3$), 1.48 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.34–1.23 (m, 16H, C(C$\underline{H}_3$)$_2$, OCH$_2$CH$_2$(C$\underline{H}_2$)$_5$CH$_3$, Rha-H-6), 1.19 (d, 3H, J = 6.6 Hz, Fuc-H-6), 0.89–0.87 (m, 12H, SiC(C$\underline{H}_3$)$_3$, OCH$_2$CH$_2$(CH$_2$)$_5$C$\underline{H}_3$), 0.08 (s, 3H, SiC$\underline{H}_3$), 0.06 (s, 3H, SiC$\underline{H}_3$); ^{13}C NMR (125 MHz $CDCl_3$): δ 169.8 (C=O), 169.7 (C=O), 169.4 (C=O), 138.7 (Ar), 128.1 (Ar), 127.9 (Ar), 127.4 (Ar), 108.9 ($\underline{C}$(CH$_3$)$_2$), 100.3 (Xyl-C-1), 99.4 (Fuc-C-1), 98.9 (Rha-C-1), 81.3 (Fuc-C-4), 81.2 (Rha-C-4), 78.7 (Rha-C-3), 75.9 (Rha-C-2), 74.8 (Fuc-C-3), 72.7 (Ph$\underline{C}$H$_2$), 70.0 (Fuc-C-2), 69.8 (Xyl-C-3), 69.6 (Xyl-C-2), 68.4 (O$\underline{C}$H$_2$(CH$_2$)$_6$CH$_3$), 68.1 (Xyl-C-4), 66.0 (Fuc-C-5), 64.6 (Rha-C-5), 60.5 (Xyl-C-5), 31.9 (OCH$_2$($\underline{C}$H$_2$)$_6$CH$_3$), 29.6 (OCH$_2$($\underline{C}$H$_2$)$_6$CH$_3$), 29.4 (OCH$_2$($\underline{C}$H$_2$)$_6$CH$_3$), 29.3 (OCH$_2$($\underline{C}$H$_2$)$_6$CH$_3$), 28.0 (C($\underline{C}$H$_3$)$_2$),

26.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 26.2 ($C(\underline{C}H_3)_2$), 25.8 ($SiC(\underline{C}H_3)_3$), 22.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 20.9 ($CO\underline{C}H_3$), 20.8 (2 × $CO\underline{C}H_3$), 17.9 ($Si\underline{C}(CH_3)_3$), 17.8 (Rha-C-6), 16.3 (Fuc-C-6), 14.1 ($OCH_2(CH_2)_6\underline{C}H_3$), -4.4 ($Si\underline{C}H_3$), -4.8 ($Si\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{47}H_{76}NaO_{16}Si$: 947.4795; Found 947.4802.



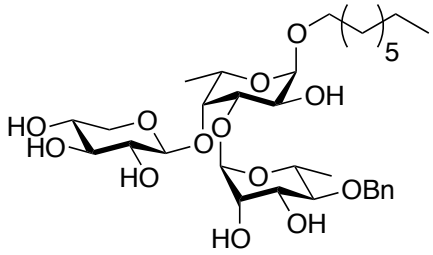
Octyl 2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl-(1→4)-[4-*O*-benzyl-2,3-*O*-isopropylidene-α-D-rhamnopyranosyl-(1→3)]-α-L-fucopyranoside (4.28): To a stirred solution of **4.27** (141 mg 153 μmol) in THF–pyridine (12 mL, 1:1) was added HF·pyridine (2.0 mL, pyridine ~30%, hydrogen fluoride ~70%) at 0 °C under an Ar atmosphere. The reaction mixture was stirred overnight at room temperature, before being poured into saturated $NaHCO_3$ (aq.). The aqueous layer was extracted with EtOAc (30 mL × 3), dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (3:2 hexane–EtOAc) to afford **4.28** (110 mg, 89%) as a viscous oil. R_f 0.20 (2:1 hexane–EtOAc); $[\alpha]_D$ –81.8 (*c* 0.11, $CHCl_3$); ^1H NMR (600 MHz; $CDCl_3$): δ 7.37–7.32 (m, 4H, Ar), 7.29–7.26 (m, 1H, Ar), 5.35 (s, 1H, Rha-H-1), 5.09 (t, 1H, J = 6.8 Hz, Xyl-H-3), 5.01 (dd, 1H, J = 6.9, 5.1 Hz, Xyl-H-2), 4.93–4.90 (m, 2H, $PhC\underline{H}_2$, Xyl-H-4), 4.82 (d, 1H, J = 4.0 Hz, Fuc-H-1), 4.63 (d, 1H, J = 11.8 Hz, $PhC\underline{H}_2$), 4.60 (d, 1H, J = 5.0 Hz, Xyl-H-1), 4.36–4.32 (m, 2H, Xyl-H-5a, Rha-H-2), 4.24 (t, 1H, J = 6.4 Hz, Rha-H-

3), 3.98–3.90 (m, 3H, Rha-H-5, Fuc-H-2, Fuc-H-5), 3.86 (dd, 1H, *J* = 10.1, 2.9 Hz, Fuc-H-3), 3.69 (dt, 1H, *J* = 9.8, 6.8 Hz, $OC\underline{H}_2CH_2(CH_2)_5CH_3$), 3.63 (d, 1H, *J* = 2.8 Hz, Fuc-H-4), 3.45 (dt, 1H, *J* = 9.8, 6.6 Hz, $OC\underline{H}_2CH_2(CH_2)_5CH_3$), 3.39 (dd, 1H, *J* = 12.3, 6.4 Hz, Xyl-H-5b), 3.22 (dd, 1H, *J* = 9.8, 7.1 Hz, Rha-H-4), 2.08 (s, 3H, $COC\underline{H}_3$), 2.07 (s, 3H, $COC\underline{H}_3$), 2.03 (s, 3H, $COC\underline{H}_3$), 1.94 (d, 1H, *J* = 10.3 Hz, 2-OH), 1.63–1.58 (m, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.51 (s, 3H, $C(C\underline{H}_3)_2$), 1.40 (s, 3H, $C(C\underline{H}_3)_2$), 1.35–1.26 (m, 13H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$, Rha-H-6), 1.24 (d, 3H, *J* = 6.6 Hz, Fuc-H-6), 0.90 (t, 3H, *J* = 7.0 Hz, $OCH_2CH_2(CH_2)_5C\underline{H}_3$); ^{13}C NMR (125 MHz $CDCl_3$): δ 169.9 (C=O), 169.7 (C=O), 169.3 (C=O), 138.6 (Ar), 128.2 (Ar), 127.9 (Ar), 127.4 (Ar), 109.1 ($\underline{C}(CH_3)_2$), 100.7 (Xyl-C-1), 99.0 (Rha-C-1), 98.5 (Fuc-C-1), 81.1 (Rha-C-4), 80.8 (Fuc-C-4), 78.6 (Rha-C-3), 75.9 (Rha-C-2), 75.8 (Fuc-C-3), 72.7 ($Ph\underline{C}H_2$), 69.9 (Xyl-C-3), 69.7 (Xyl-C-2), 69.2 (Fuc-C-2), 68.4 ($O\underline{C}H_2(CH_2)_6CH_3$), 68.2 (Xyl-C-4), 66.5 (Fuc-C-5), 64.8 (Rha-C-5), 60.9 (Xyl-C-5), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.5 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 28.0 ($C(\underline{C}H_3)_2$), 26.4 ($C(\underline{C}H_3)_2$), 26.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 20.8 (3 × $CO\underline{C}H_3$), 17.9 (Rha-C-6), 16.4 (Fuc-C-6), 14.1 ($OCH_2(CH_2)_6\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{41}H_{62}NaO_{16}$: 833.3930; Found 833.3934.



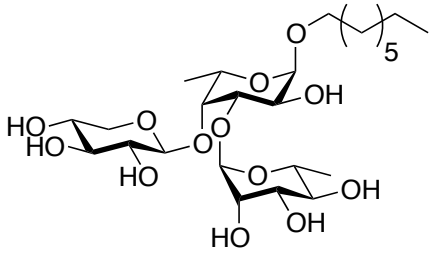
Octyl 2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl-(1→4)-[4-*O*-benzyl-α-D-rhamnopyranosyl-(1→3)]-α-L-fucopyranoside (4.29): To a stirred solution of **4.28** (110 mg, 136 μmol) in CH_3CN–CH_3OH (6.0 mL, 10:1) was added *p*-toluenesulfonic acid monohydrate (77.5 mg, 408 μmol) at room temperature. The reaction mixture was stirred for 2 h at room temperature. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (15:1 CH_2Cl_2–CH_3OH) to afford **4.29** (97.6 mg, 93%) as a syrup. R_f 0.33 (15:1 CH_2Cl_2–CH_3OH); $[\alpha]_D$ –60.7 (*c* 0.26, $CHCl_3$); ^{1}H NMR (600 MHz; $CDCl_3$): δ 7.38–7.34 (m, 4H, Ar), 7.32–7.29 (m, 1H, Ar), 5.19 (d, 1H, J = 1.6 Hz, Rha-H-1), 5.11 (t, 1H, J = 7.7 Hz, Xyl-H-3), 5.03 (dd, 1H, J = 7.8, 6.0 Hz, Xyl-H-2), 4.93 (td, 1H, J = 7.6, 4.7 Hz, Xyl-H-4), 4.80 (d, 1H, J = 11.5 Hz, PhC$\underline{H}_2$), 4.80 (d, 1H, J = 4.0 Hz, Fuc-H-1), 4.73 (d, 1H, J = 11.5 Hz, PhC$\underline{H}_2$), 4.56 (d, 1H, J = 5.9 Hz, Xyl-H-1), 4.29 (dd, 1H, J = 12.1, 4.6 Hz, Xyl-H-5a), 4.12–4.11 (m, 1H, Rha-H-2), 4.03–4.01 (m, 1H, Rha-H-3), 3.97–3.87 (m, 3H, Rha-H-5, Fuc-H-5, Fuc-H-2), 3.82 (dd, 1H, J = 10.1, 3.0 Hz), 3.70–3.66 (m, 2H, OC$\underline{H}_2$CH$_2$(CH$_2$)$_5$CH$_3$, Fuc-H-4), 3.44 (dt, 1H, J = 9.8, 6.6 Hz, OC$\underline{H}_2$CH$_2$(CH$_2$)$_5$CH$_3$), 3.37 (t, 1H, J = 9.1 Hz, Rha-H-4), 3.32 (dd, 1H, J = 12.1, 7.7 Hz, Xyl-H-5b), 2.33–2.33 (m, 2H, Rha-2-OH, Rha-3-OH), 2.08 (s, 3H, COC$\underline{H}_3$), 2.05 (s, 3H, COC$\underline{H}_3$), 2.01 (s, 3H, COC$\underline{H}_3$),

1.93 (d, 1H, J = 10.5 Hz, Fuc-2-OH), 1.63–1.59 (m, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.36-1.27 (m, 13H, Rha-H-6, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 1.23 (d, 3H, J = 6.6 Hz, Fuc-H-6), 0.90 (t, 3H, J = 7.0 Hz, $OCH_2CH_2(CH_2)_5C\underline{H}_3$); ^{13}C NMR (125 MHz $CDCl_3$): δ 170.1 (C=O), 169.6 (C=O), 169.3 (C=O), 138.6 (Ar), 128.5 (Ar), 127.8 (Ar), 127.7 (Ar), 101.2 (Xyl-C-1), 101.0 (Rha-C-1), 98.5 (Fuc-C-1), 81.8 (Rha-C-4), 80.5 (Fuc-C-4), 75.4 (Fuc-C-3), 74.9 ($Ph\underline{C}H_2$), 71.3 (Rha-C-3), 71.1 (Rha-C-2), 70.8 (Xyl-C-3), 70.5 (Xyl-C-2), 69.3 (Fuc-C-2), 68.4 (Xyl-C-4, $O\underline{C}H_2(CH_2)_6CH_3$), 67.6 (Rha-C-5), 66.4 (Fuc-C-5), 61.4 (Xyl-C-5), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.5 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 26.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 20.8 (3 × $CO\underline{C}H_3$), 18.2 (Rha-C-6), 16.3 (Fuc-C-6), 14.1 ($OCH_2(CH_2)_6\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{38}H_{58}NaO_{16}$: 793.3617; Found 793.3618.



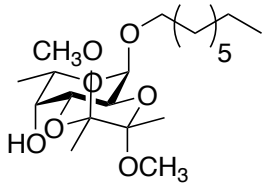
Octyl β-D-xylopyranosyl-(1→4)-[4-*O*-benzyl-α-D-rhamnopyranosyl-(1→3)]-α-L-fucopyranoside (4.30): To a stirred solution of **4.29** (97.6 mg, 127 μmol) in CH_3OH (5.0 mL) was added a solution of $NaOCH_3$ in CH_3OH (0.5 mL, 0.5 M). The reaction mixture was stirred for 2 h at room temperature, then neutralized by addition of Amberlite® IR-120 (H^+) cation exchange resin, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (9:1⟶5:1 CH_2Cl_2–CH_3OH) to afford **4.30** (72.0 mg,

88%) as a white amorphous solid. R_f 0.13 (9:1 CH_2Cl_2–CH_3OH); $[\alpha]_D$ –44.1 (*c* 0.17, CH_3OH); ^1H NMR (600 MHz; CD_3OD): δ 7.37–7.36 (m, 2H), 7.31–7.29 (m, 2H), 7.24–7.21 (m, 1H), 5.02 (d, 1H, *J* = 1.5 Hz, Rha-H-1), 4.94 (d, 1H, *J* = 11.5 Hz), 4.75 (s, 1H, Fuc-H-1), 4.63 (d, 1H, *J* = 11.5 Hz), 4.24 (d, 1H, *J* = 7.1 Hz, Xyl-H-1), 4.05–3.98 (m, 4H), 3.94 (dd, 1H, *J* = 3.3, 1.7 Hz), 3.87–3.86 (m, 2H), 3.80 (br s, 1H), 3.67–3.63 (m, 1H), 3.49–3.44 (m, 2H), 3.35 (t, 1H, *J* = 9.4 Hz), 3.29–3.24 (m, 2H), 3.06 (dd, 1H, *J* = 11.5, 10.4 Hz), 1.68–1.59 (m, 2H), 1.40–1.27 (m, 13H), 1.20 (d, 3H, *J* = 6.3 Hz), 0.89 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR (125 MHz; CD_3OD): δ 140.5, 129.2, 128.8, 128.4, 106.3 (Xyl-C-1), 103.1 (Rha-C-1), 100.7 (Fuc-C-1), 82.9, 81.0, 77.9, 76.1, 75.4 (2 × C), 72.7, 72.6, 71.3, 70.2, 69.6, 69.2, 68.3, 66.7, 33.0, 30.6, 30.5, 30.4, 27.3, 23.7, 18.3, 16.5, 14.4; HRMS (ESI) Calc. for $[M + Na]^+$ $C_{32}H_{52}NaO_{13}$: 667.3300; Found 667.3296.



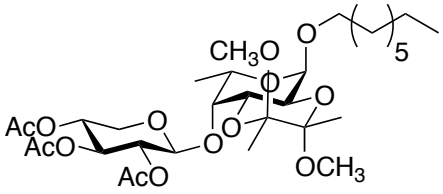
Octyl β-D-xylopyranosyl-(1→4)-[α-D-rhamnopyranosyl-(1→3)]-α-L-fucopyranoside (4.2): To a stirred solution of **4.30** (72.0 mg, 112 μmol) in dry THF (5.0 mL) was added 20% palladium hydroxide on carbon (8.0 mg). After stirring overnight under an H_2 atmosphere (1 atm), the reaction mixture was filtered through Celite and concentrated. The residue was dissolved in water and then lyophilized to afford **4.2** (60.3 mg, 97%) as a white solid. R_f 0.49 (2:1 CH_2Cl_2–CH_3OH); $[\alpha]_D$ –55.9 (*c* 0.33, CH_3OH); ^1H NMR (600 MHz;

CD_3OD): δ 5.03 (d, 1H, J = 1.3 Hz, Rha-H-1), 4.75 (s, 1H, Fuc-H-1), 4.26 (d, 1H, J = 7.2 Hz, Xyl-H-1), 4.05 (dd, 1H, J = 11.6, 5.4 Hz), 4.01 (q, 1H, J = 6.7 Hz), 3.96–3.91 (m, 2H), 3.88–3.87 (m, 2H), 3.82 (s, 1H), 3.80 (dd, 1H, J = 9.5, 3.4 Hz), 3.66 (dt, 1H, J = 9.7, 7.0 Hz), 3.51–3.46 (m, 2H), 3.39 (t, 1H, J = 9.4 Hz), 3.29–3.25 (m, 2H), 3.10 (dd, 1H, J = 11.4, 10.4 Hz), 1.68–1.59 (m, 2H), 1.41–1.29 (m, 13H), 1.23 (d, 3H, J = 6.3 Hz), 0.90 (t, 3H, J = 7.0 Hz); ^{13}C NMR (125 MHz; CD_3OD): δ 106.2 (Xyl-C-1), 103.3 (Rha-C-1), 100.7 (Fuc-C-1), 81.0, 77.9, 75.5, 75.4, 74.0, 72.2, 72.0, 71.3, 70.2, 70.1, 69.6, 68.4, 66.7, 33.0, 30.6, 30.5, 30.4, 27.3, 23.7, 18.0, 16.6, 14.4; HRMS (ESI) Calc. for $[M + Na]^+$ $C_{25}H_{46}NaO_{13}$: 577.2831; Found 577.2827.



Octyl 2,3-*O*-(2',3'-dimethoxybutane-2',3'-diyl)-α-L-fucopyranoside (4.31): To a solution of **4.8** (61.0 mg, 221 μmol) in dry CH_3OH (5.0 mL) was added butane-2,3-dione (23.3 μL, 265 μmol), trimethyl orthoformate (96.6 μL, 883 μmol) and camphorsulfonic acid (2.6 mg, 11 μmol) successively. The reaction mixture was stirred overnight under reflux. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (2:1 hexane–EtOAc) to afford **4.31** (58.5 mg, 68%) as a viscous oil. R_f 0.37 (2:1 hexane–EtOAc); $[\alpha]_D$ +21.0 (*c* 0.34, $CHCl_3$); ^{1}H NMR (600 MHz; $CDCl_3$): δ 4.86 (d, 1H, J = 3.5 Hz, H-1), 4.13 (dd, 1H, J = 10.5, 3.6 Hz, H-2), 4.07 (dd, 1H, J = 10.5, 3.2 Hz, H-3), 4.01

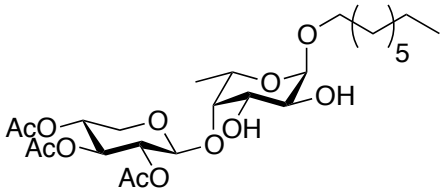
(q, 1H, J = 6.6 Hz, H-5), 3.76–3.76 (m, 1H, H-4), 3.64 (dt, 1H, J = 9.9, 7.4 Hz, $OC\underline{H}_2CH_2(CH_2)_5CH_3$), 3.58 (dt, 1H, J = 9.9, 6.9 Hz, $OC\underline{H}_2CH_2(CH_2)_5CH_3$), 3.28 (s, 3H, $C(CH_3)OC\underline{H}_3$), 3.25 (s, 3H, $C(CH_3)OC\underline{H}_3$), 2.30 (s, 1H, 4-OH), 1.66 (quintet, 2H, J = 7.0 Hz, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.33–1.26 (m, 19H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$, 2 × $C(C\underline{H}_3)OCH_3$, H-6), 0.90 (t, 3H, J = 7.0 Hz, $OCH_2CH_2(CH_2)_5C\underline{H}_3$); ^{13}C NMR (175 MHz $CDCl_3$): δ 100.0 (2 × $\underline{C}(CH_3)OCH_3$), 97.3 (C-1), 70.5 (C-4), 68.4 ($O\underline{C}H_2(CH_2)_6CH_3$), 66.6 (C-3), 66.3 (C-5), 65.0 (C-2), 47.8 (2 × $C(CH_3)O\underline{C}H_3$), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 (2 × $OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 26.0 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 17.8 ($C(\underline{C}H_3)OCH_3$), 17.7 ($C(\underline{C}H_3)OCH_3$), 16.1 (C-6), 14.1 ($OCH_2(CH_2)_6\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{20}H_{38}NaO_7$: 413.2510; Found 413.2505.



Octyl 2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl-(1→4)-2,3-*O*-(2',3'-dimethoxybutane-2',3'-diyl)-α-L-fucopyranoside (4.32): To a stirred solution of acceptor **4.31** (58.5 mg, 142 μmol) and *p*-tolyl 2,3,4-tri-*O*-acetyl-1-thio-β-D-xylopyranoside **4.12**[8] (109 mg, 284 μmol) in dry CH_2Cl_2 (4.0 mL) was added molecular sieves (400 mg, 4Å, powder). After stirring for 30 min at room temperature, the reaction mixture was cooled to 0 °C, and then *N*-iodosuccinimide (76.6 mg, 341 μmol) and silver trifluoromethanesulfonate (7.3 mg, 28 μmol) were added successively. The resulting solution was stirred for 1 h at 0 °C under an

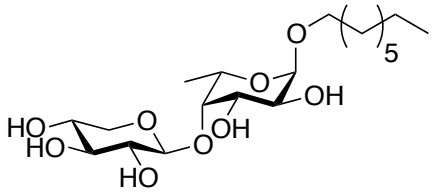
Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was washed with saturated $Na_2S_2O_3$ (aq.) and saturated $NaHCO_3$ (aq.), the aqueous layer was extracted with CH_2Cl_2 (20 mL × 3), dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (2:1 hexane–EtOAc) to afford **4.32** (57.7 mg, 63%) as a syrup. R_f 0.27 (2:1 hexane–EtOAc); $[\alpha]_D$ –34.5 (*c* 0.17, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 5.04 (t, 1H, *J* = 5.8 Hz, Xyl-H-3), 4.95 (dd, 1H, *J* = 5.9, 4.0 Hz, Xyl-H-2), 4.88–4.86 (m, 1H, Xyl-H-4), 4.80 (d, 1H, *J* = 3.7 Hz, Fuc-H-1), 4.76 (d, 1H, *J* = 3.9 Hz, Xyl-H-1), 4.55 (dd, 1H, *J* = 13.0, 3.7 Hz, Xyl-H-5a), 4.12 (dd, 1H, *J* = 10.7, 3.7 Hz, Fuc-H-2), 4.04 (dd, 1H, *J* = 10.7, 2.9 Hz, Fuc-H-3), 3.96 (q, 1H, *J* = 6.6 Hz, Fuc-H-5), 3.67 (d, 1H, *J* = 2.6 Hz, Fuc-H-4), 3.59–3.53 (m, 2H, $OC\underline{H}_2CH_2(CH_2)_5CH_3$), 3.41 (dd, 1H, *J* = 12.9, 4.5 Hz, Xyl-H-5b), 3.23 (s, 3H, $C(CH_3)OC\underline{H}_3$), 3.21 (s, 3H, $C(CH_3)OC\underline{H}_3$), 2.08 (s, 3H, $COC\underline{H}_3$), 2.07 (s, 3H, $COC\underline{H}_3$), 2.06 (s, 3H, $COC\underline{H}_3$), 1.61 (quintet, 2H, *J* = 7.0 Hz, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.29–1.24 (m, 16H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$, 2 × $C(C\underline{H}_3)OCH_3$), 1.18 (d, 3H, *J* = 6.6 Hz, Fuc-H-6), 0.87 (t, 3H, *J* = 7.1 Hz, $OCH_2CH_2(CH_2)_5C\underline{H}_3$); ^{13}C NMR (175 MHz $CDCl_3$): δ 170.0 (C=O), 169.8(C=O), 169.3 (C=O), 99.6 ($\underline{C}(CH_3)OCH_3$), 99.5 (Xyl-C-1, $\underline{C}(CH_3)OCH_3$), 97.3 (Fuc-C-1), 78.6 (Fuc-C-4), 69.4 (Xyl-C-2), 69.3 (Xyl-C-3), 68.5 (Xyl-C-4), 68.4 ($O\underline{C}H_2(CH_2)_6CH_3$), 66.6 (Fuc-C-5), 66.1 (Fuc-C-3), 65.3 (Fuc-C-2), 60.5 (Xyl-C-5), 47.8 (2 × $C(CH_3)O\underline{C}H_3$), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 26.0 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 20.9 ($CO\underline{C}H_3$), 20.8 (2 × $CO\underline{C}H_3$), 17.9 ($C(\underline{C}H_3)OCH_3$), 17.8

($C(\underline{C}H_3)OCH_3$), 16.3 (Fuc-C-6), 14.1 ($OCH_2(CH_2)_6\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{31}H_{52}NaO_{14}$: 671.3249; Found 671.3241.



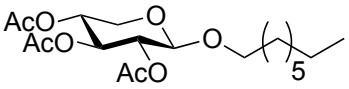
Octyl 2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl-(1→4)-α-L-fucopyranoside (4.33): To a solution of **4.32** (51.4 mg, 79.2 μmol) in CH_2Cl_2 (1.5 mL) was added TFA (1.3 mL) and H_2O (0.1 mL). The reaction mixture was stirred for 1 h at room temperature, then diluted with CH_2Cl_2 (40 mL) and washed with saturated $NaHCO_3$ (aq.). The organic layer was dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (1:2 hexane–EtOAc) to afford **4.33** (35.0 mg, 83%) as a syrup. R_f 0.22 (1:2 hexane–EtOAc); $[\alpha]_D$ –100 (*c* 0.35, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 5.19 (t, 1H, J = 9.3 Hz, Xyl-H-3), 5.02–4.98 (m, 2H, Xyl-H-2, Xyl-H-4), 4.81 (d, 1H, J = 3.8 Hz, Fuc-H-1), 4.49 (d, 1H, J = 7.6 Hz, Xyl-H-1), 4.18 (dd, 1H, J = 11.7, 5.5 Hz, Xyl-H-5a), 3.95 (q, 1H, J = 6.6 Hz, Fuc-H-5), 3.72–3.69 (m, 2H, Fuc-H-4, Fuc-H-3), 3.67–3.62 (m, 2H, Fuc-H-2, $OC\underline{H}_2CH_2(CH_2)_5CH_3$), 3.43 (dt, 1H, J = 9.7, 6.5 Hz, $OC\underline{H}_2CH_2(CH_2)_5CH_3$), 3.36 (dd, 1H, J = 11.7, 10.0 Hz, Xyl-H-5b), 3.28 (d, 1H, J = 9.8 Hz, 3-OH), 2.04–2.02 (m, 9H, $COC\underline{H}_3$, 2-OH), 1.60–1.57 (m, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.33–1.24 (m, 10H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 1.19 (d, 3H, J = 6.6 Hz, Fuc-H-6), 0.87 (t, 3H, J = 7.1 Hz, $OCH_2CH_2(CH_2)_5C\underline{H}_3$); ^{13}C NMR (175 MHz $CDCl_3$): δ 170.2 (C=O), 169.6 (C=O), 169.1 (C=O), 102.3 (Xyl-C-1), 98.5 (Fuc-C-1), 83.6 (Fuc-C-4), 71.9 (Xyl-C-3),

71.5 (Xyl-C-2), 70.2 (Fuc-C-3), 70.0 (Fuc-C-2), 68.5 (Xyl-C-4), 68.4 ($O\underline{C}H_2(CH_2)_6CH_3$), 65.9 (Fuc-C-5), 62.7 (Xyl-C-5), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.5 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 26.1 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 20.7 ($CO\underline{C}H_3$), 20.6 (2 × $CO\underline{C}H_3$), 16.1 (Fuc-C-6), 14.1 ($OCH_2(CH_2)_6\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{25}H_{42}NaO_{12}$: 557.2568; Found 557.2574.



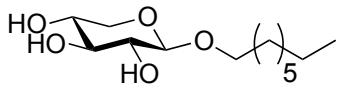
Octyl β-D-xylopyranosyl-(1→4)-α-L-fucopyranoside (4.3): To a stirred solution of **4.33** (35.0 mg, 65.5 μmol) in CH_3OH (3.0 mL) was added a solution of $NaOCH_3$ in CH_3OH (0.3 mL, 0.5 M). The reaction mixture was stirred for 2 h at room temperature, then neutralized by addition of Amberlite® IR-120 (H^+) cation exchange resin, filtered and the filtrate was concentrated. The residue was dissolved in water and then lyophilized to afford **4.3** (26.7 mg, quant.) as a white solid. R_f 0.51 (5:1 CH_2Cl_2–CH_3OH); $[\alpha]_D$ –92.9 (*c* 0.18, CH_3OH); ^1H NMR (600 MHz; $CDCl_3$): δ 4.74 (d, 1H, J = 3.8 Hz, Fuc-H-1), 4.23 (d, 1H, J = 7.4 Hz, Xyl-H-1), 4.02 (q, 1H, J = 6.7 Hz, Fuc-H-5), 3.89 (dd, 1H, J = 11.4, 5.5 Hz, Xyl-H-5a), 3.84 (d, 1H, J = 3.0 Hz, Fuc-H-4), 3.72 (dd, 1H, J = 10.2, 3.2 Hz, Fuc-H-3), 3.66–3.61 (m, 2H, $OC\underline{H}_2CH_2(CH_2)_5CH_3$, Fuc-H-2), 3.51 (ddd, 1H, J = 10.4, 8.6, 5.5 Hz, Xyl-H-4), 3.44 (dt, 1H, J = 9.7, 6.4 Hz, $OC\underline{H}_2CH_2(CH_2)_5CH_3$), 3.33–3.22 (m, 3H, Xyl-H-3, Xyl-H-3, Xyl-H-5b), 1.66–1.57 (m, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.39–1.26 (m, 13H,

$OCH_2CH_2(C\underline{H}_2)_5CH_3$, Fuc-H-6), 0.89 (t, 3H, J = 7.0 Hz, $OCH_2CH_2(CH_2)_5C\underline{H}_3$); ^{13}C NMR (125 MHz; CD_3OD): δ 106.1 (Xyl-C-1), 100.6 (Fuc-C-1), 82.9 (Fuc-C-4), 77.7 (Xyl-C-3), 75.0 (Xyl-C-2), 71.0 (2 × C, Fuc-C-2, Xyl-C-4), 70.6 (Fuc-C-3), 69.5 ($O\underline{C}H_2(CH_2)_6CH_3$), 67.8 (Fuc-C-5), 67.1 (Xyl-C-5), 33.0 ($OCH_2(\underline{C}H_2)_6CH_3$), 30.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 30.5 ($OCH_2(\underline{C}H_2)_6CH_3$), 30.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 27.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 23.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 16.4 (Fuc-C-6), 14.4 ($OCH_2(CH_2)_6\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{19}H_{36}NaO_9$: 431.2252; Found 431.2253.



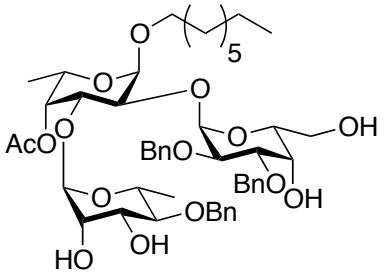
Octyl 2,3,4-tri-*O*-acetyl-β-D-xylopyranoside (4.34): To a stirred solution of octanol (48.0 μL, 306 μmol) and *p*-tolyl 2,3,4-tri-*O*-acetyl-1-thio-β-D-xylopyranoside **4.12**[8] (130 mg, 367 μmol) in dry CH_2Cl_2 (4.0 mL) added molecular sieves (400 mg, 4Å, powder). After stirring for 30 min at room temperature, the reaction mixture was cooled to 0 °C, and then *N*-iodosuccinimide (103 mg, 459 μmol) and silver trifluoromethanesulfonate (15.7 mg, 61.2 μmol) were added successively. The resulting solution was stirred for 1 h at room temperature under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was washed with saturated $Na_2S_2O_3$ (aq.) and saturated $NaHCO_3$ (aq.), the aqueous layer was extracted with CH_2Cl_2 (25 mL × 3), dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (3:1 hexane–EtOAc) to afford **4.34** (59.4 mg, 50%) as a white amorphous solid. R_f 0.51 (2:1 hexane–EtOAc); $[\alpha]_D$ –48.5 (c 0.74, $CHCl_3$); ^1H NMR (600

MHz; $CDCl_3$): δ 5.17 (t, 1H, J = 8.6 Hz, H-3), 4.96 (td, 1H, J = 8.7, 5.1 Hz, H-4), 4.93 (dd, 1H, J = 8.7, 6.8 Hz, H-2), 4.48 (d, 1H, J = 6.8 Hz, H-1), 4.13 (dd, 1H, J = 11.8, 5.1 Hz, H-5a), 3.82 (dt, 1H, J = 9.6, 6.5 Hz, $OC\underline{H}_2CH_2(CH_2)_5CH_3$), 3.47 (dt, 1H, J = 9.6, 6.7 Hz, $OC\underline{H}_2CH_2(CH_2)_5CH_3$), 3.37 (dd, 1H, J = 11.8, 8.8 Hz, H-5b), 2.07 (s, 3H, $COC\underline{H}_3$), 2.06 (s, 3H, $COC\underline{H}_3$), 2.05 (s, 3H, $COC\underline{H}_3$), 1.60–1.55 (m, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.34–1.28 (m, 10H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 0.89 (t, 3H, J = 7.0 Hz, $OCH_2CH_2(CH_2)_5C\underline{H}_3$); ^{13}C NMR (125 MHz; $CDCl_3$): δ 170.1 (C=O), 169.8 (C=O), 169.4 (C=O), 100.7 (C-1), 71.5 (C-3), 70.9 (C-2), 69.7 ($O\underline{C}H_2(CH_2)_6CH_3$), 69.0 (C-4), 62.0 (C-5), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.5 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.3 (2 × $OCH_2(\underline{C}H_2)_6CH_3$), 25.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 20.8 ($CO\underline{C}H_3$), 20.7 (2 × $CO\underline{C}H$), 14.1 ($OCH_2(CH_2)_6\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{19}H_{32}NaO_8$: 411.1989; Found 411.1984.



Octyl β-D-xylopyranoside (4.4): To a stirred solution of **4.34** (25.9 mg, 66.7 μmol) in CH_3OH (4.0 mL) was added a solution of $NaOCH_3$ in CH_3OH (0.4 mL, 0.5 M). The reaction mixture was stirred for 4 h at room temperature, then neutralized by addition of Amberlite® IR-120 (H^+) cation exchange resin, filtered and the filtrate was concentrated. The residue was dissolved in water and then lyophilized to afford **4.4** (17.5 mg, quant.) as a white solid. R_f 0.49 (9:1 CH_2Cl_2–CH_3OH); $[\alpha]_D$ –38.6 (c 0.20, CH_2Cl_2–CH_3OH); ^{1}H NMR (600 MHz; CD_3OD): δ 4.17 (d, 1H, J = 7.6 Hz, H-1), 3.83 (dd, 1H, J = 11.5, 5.4 Hz, H-5a), 3.79 (dt, 1H, J = 9.5, 6.8 Hz, $OC\underline{H}_2CH_2(CH_2)_5CH_3$), 3.51 (dt, 1H, J = 9.6, 6.7 Hz,

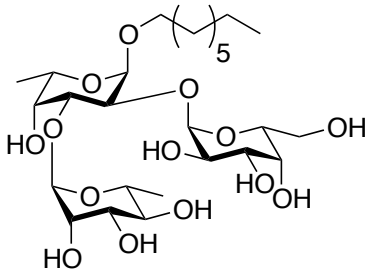
$OC\underline{H}_2CH_2(CH_2)_5CH_3$), 3.46 (ddd, 1H, J = 10.2, 8.8, 5.4 Hz, H-4), 3.28 (t, 1H, J = 8.9 Hz, H-3), 3.17 (dd, 1H, J = 11.2, 10.1 Hz, H-5b), 3.14 (dd, 1H, J = 9.0, 7.5 Hz, H-2), 1.62–1.57 (m, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.38–1.27 (m, 10H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 0.89 (t, 3H, J = 7.0 Hz, $OCH_2CH_2(CH_2)_5C\underline{H}_3$); ^{13}C NMR (125 MHz; CD_3OD): δ 105.1 (C-1), 77.9 (C-3), 74.9 (C-2), 71.2 (C-4), 70.9 ($O\underline{C}H_2(CH_2)_6CH_3$), 66.9 (C-5), 33.0 ($OCH_2(\underline{C}H_2)_6CH_3$), 30.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 30.5 ($OCH_2(\underline{C}H_2)_6CH_3$), 30.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 27.1 ($OCH_2(\underline{C}H_2)_6CH_3$), 23.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 14.4 ($OCH_2(CH_2)_6\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{13}H_{26}NaO_5$: 285.1672; Found 285.1670.



Octyl 4-*O*-benzyl-α-D-rhamnopyranosyl-(1→3)-[2,3-di-*O*-benzyl-*O*-α-D-galactopyranosyl-(1→2)]-4-*O*-acetyl-α-L-fucopyranoside (4.35): To a stirred solution of **4.9** (145 mg 135 μmol) in THF–pyridine (3.0 mL, 1:1) was added HF·pyridine (0.3 mL, pyridine ~30%, hydrogen fluoride ~70%) at 0 °C under an Ar atmosphere. The reaction mixture was stirred for 1 h at 0 °C, before being poured into saturated $NaHCO_3$ (aq.). The aqueous layer was extracted with EtOAc (25 mL × 3), dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was then dissolved in CH_3CN–CH_3OH (3.3 mL, 10:1) and *p*-toluenesulfonic acid monohydrate (74.1 mg, 390 μmol) was added at room temperature. The reaction mixture was stirred for 3.5 h at room temperature. Excess

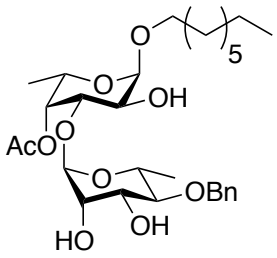
triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (1:2 hexane–EtOAc) to afford **4.35** (97.9 mg, 81%) as a syrup. R_f 0.30 (2:3 hexane–EtOAc); $[\alpha]_D$ +3.9 (*c* 0.50, $CHCl_3$); ^1H NMR (600 MHz; $CDCl_3$): δ 7.40–7.29 (m, 15H, Ar), 5.26 (d, 1H, J = 3.0 Hz, Fuc-H-4), 5.13 (d, 1H, J = 1.9 Hz, Rha-H-1), 5.02 (d, 1H, J = 3.4 Hz, Fuc-H-1), 4.94 (d, 1H, J = 3.2 Hz, Gal-H-1), 4.82 (dd, 1H, J = 11.9 Hz, PhC$\underline{H}_2$), 4.81 (dd, 1H, J = 11.4 Hz, PhC$\underline{H}_2$), 4.74–4.66 (m, 4H, PhC$\underline{H}_2$), 4.22 (dd, 1H, J = 10.2, 3.5 Hz, Fuc-H-3), 4.15 (br s, 1H, Gal-H-4), 4.06–4.02 (m, 2H, Gal-H-5, Fuc-H-5), 3.95–3.91 (m, 2H, Gal-H-3, Gal-H-6a), 3.87 (dd, 1H, J = 10.0, 3.1 Hz, Gal-H-2), 3.84–3.77 (m, 4H, Fuc-H-2, Rha-H-5, Rha-H-2, Gal-H-6b), 3.72 (d, 1H, J = 7.4 Hz, Rha-H-3), 3.64 (dt, 1H, J = 9.4, 6.8 Hz, OC$\underline{H}_2CH_2(CH_2)_5CH_3$), 3.37 (dt, 1H, J = 9.4, 6.7 Hz, OC$\underline{H}_2CH_2(CH_2)_5CH_3$), 3.26 (t, 1H, J = 8.7 Hz, Rha-H-4), 2.21 (s, 3H, COC$\underline{H}_3$), 1.62–1.57 (m, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.35–1.28 (m, 13H, Rha-H-6, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 1.12 (d, 3H, J = 6.5 Hz, Fuc-H-6), 0.91 (t, 3H, J = 7.0 Hz, $OCH_2CH_2(CH_2)_5C\underline{H}_3$); ^{13}C NMR (125 MHz $CDCl_3$): δ 170.4 (C=O), 138.6 (Ar), 138.1 (Ar), 138.0 (Ar), 128.6 (2 × Ar), 128.4 (Ar), 128.3 (Ar), 128.0 (Ar), 127.9 (Ar), 127.8 (Ar), 127.7 (Ar), 101.7 (Rha-C-1), 100.9 (Gal-C-1), 98.1 (Fuc-C-1), 81.6 (Rha-C-4), 80.0 (Fuc-C-2), 77.4 (Gal-C-3), 76.0 (Gal-C-2), 74.0 (Ph$\underline{C}H_2$), 73.6 (Ph$\underline{C}H_2$), 73.5 (Fuc-C-4), 72.9 (Ph$\underline{C}H_2$), 71.6 (Fuc-C-3), 70.7 (Rha-C-3), 70.6 (Rha-C-2), 69.6 (Gal-C-4), 69.3 (Gal-C-5), 68.0 ($O\underline{C}H_2(CH_2)_6CH_3$), 67.5 (Rha-C-5), 64.5 (Fuc-C-5), 63.4 (Gal-C-6), 31.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.5 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 26.5 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 20.9 ($CO\underline{C}H_3$), 18.3

(Rha-C-6), 16.0 (Fuc-C-6), 14.1 ($OCH_2(CH_2)_6\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{49}H_{68}NaO_{15}$: 919.4450; Found 919.4451.



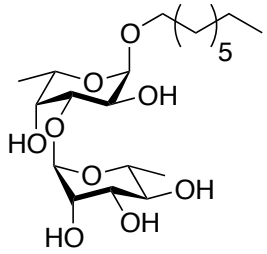
Octyl α-D-rhamnopyranosyl-(1→3)-[α-D-galactopyranosyl-(1→2)]-α-L-fucopyranoside (4.5): To a stirred solution of **4.35** (94.6 mg, 106 μmol) in CH_3OH (3.0 mL) was added a solution of $NaOCH_3$ in CH_3OH (0.3 mL, 0.5 M). The reaction mixture was stirred overnight at room temperature, then neutralized by addition of Amberlite® IR-120 (H^+) cation exchange resin, filtered and the filtrate was concentrated. The residue was then dissolved in THF–CH_3OH (1:1, 3.0 mL) and 20% palladium hydroxide on carbon (10.0 mg) was added. After stirring for 4 h under an H_2 atmosphere (1 atm), the reaction mixture was filtered through Celite and concentrated. The residue was dissolved in water and then lyophilized to afford **4.5** (61.6 mg, quant.) as a white solid. R_f 0.25 (3:1 CH_2Cl_2–CH_3OH); $[\alpha]_D$ +21.6 (*c* 0.52, CH_3OH); ^1H NMR (600 MHz; CD_3OD): δ 5.07 (d, 1H, J = 1.6 Hz, Rha-H-1), 4.98–4.97 (m, 2H, Gal-H-1, Fuc-H-1), 4.00 (dd, 1H, J = 3.4, 1.7 Hz), 3.97–3.89 (m, 4H), 3.87 (dd, 1H, J = 2.9, 1.1 Hz), 3.77–3.64 (m, 8H), 3.48 (dt, 1H, J = 9.7, 6.5 Hz), 3.38 (t, 1H, J = 9.5 Hz), 1.63–1.58 (m, 2H), 1.34–1.30 (m, 10H), 1.24 (d, 3H, J = 6.2 Hz), 1.19 (d, 3H, J = 6.6 Hz), 0.90 (t, 3H, J = 7.0 Hz); ^{13}C NMR (125 MHz CD_3OD): δ 104.0 (Rha-C-1), 103.0 (Gal-C-1), 99.7 (Fuc-C-1), 78.1, 76.9, 74.1, 73.7, 72.8, 72.2, 71.9,

71.4, 71.2, 70.4, 70.2, 68.8, 67.2, 62.8, 33.1, 30.8, 30.6, 30.5, 27.6, 23.7, 18.0, 16.6, 14.5; HRMS (ESI) Calc. for $[M + Na]^+$ $C_{26}H_{48}NaO_{14}$: 607.2936; Found 607.2934.



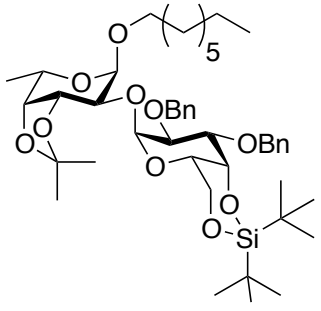
Octyl 4-*O*-benzyl-α-D-rhamnopyranosyl-(1→3)-4-*O*-acetyl-α-L-fucopyranoside (4.36): To a stirred solution of **4.10** (148 mg, 249 μmol) in CH_3CN–CH_3OH (5.5 mL, 10:1) was added *p*-toluenesulfonic acid monohydrate (142 mg, 748 μmol) at room temperature. The reaction mixture was stirred for 3.5 h at room temperature. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (1:2 hexane–EtOAc) to afford **4.36** (110 mg, 79%) as a syrup. R_f 0.29 (1:2 hexane–EtOAc); $[\alpha]_D$ –58.3 (*c* 0.50, $CHCl_3$); ^1H NMR (600 MHz; $CDCl_3$): δ 7.39–7.36 (m, 4H, Ar), 7.34–7.31 (m, 1H, Ar), 5.20 (dd, 1H, *J* = 3.3, 0.8 Hz, Fuc-H-4), 5.17 (d, 1H, *J* = 1.5 Hz, Rha-H-1), 4.87 (d, 1H, *J* = 3.9 Hz, Fuc-H-1), 4.78 (d, 1H, *J* = 11.6 Hz, PhC$\underline{H}_2$), 4.68 (d, 1H, *J* = 11.6 Hz, PhC$\underline{H}_2$), 4.07–4.03 (m, 2H, Fuc-H-5, Rha-H-2), 3.94 (dd, 1H, *J* = 9.9, 3.4 Hz, Fuc-H-3), 3.90–3.84 (m, 2H, Fuc-H-2, Rha-H-5), 3.81 (dd, 1H, *J* = 9.2, 3.4 Hz, Rha-H-3), 3.72 (dt, 1H, *J* = 9.7, 6.8 Hz, OC$\underline{H}_2CH_2(CH_2)_5CH_3$), 3.47 (dt, 1H, *J* = 9.7, 6.7 Hz, OC$\underline{H}_2CH_2(CH_2)_5CH_3$), 3.37 (t, 1H, *J* = 9.3 Hz, Rha-H-4), 2.15 (s, 3H, COC$\underline{H}_3$), 1.66–1.61 (m, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.37–1.27 (m, 13H, Rha-H-6, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 1.14 (d, 3H, *J* = 6.6 Hz, Fuc-H-6), 0.91 (t,

3H, J = 7.0 Hz, $OCH_2CH_2(CH_2)_5C\underline{H}_3$); ^{13}C NMR (125 MHz $CDCl_3$): δ 170.5 (C=O), 138.4 (Ar), 128.6 (Ar), 128.0 (2 × Ar), 101.0 (Rha-C-1), 98.6 (Fuc-C-1), 81.2 (Rha-C-4), 74.8 (Fuc-C-3), 74.2 ($Ph\underline{C}H_2$), 73.0 (Fuc-C-4), 71.0 (Rha-C-2), 70.6 (Rha-C-3), 69.5 (Fuc-C-2), 68.6 ($O\underline{C}H_2(CH_2)_6CH_3$), 67.8 (Rha-C-5), 65.3 (Fuc-C-5), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.5 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 26.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 20.8 ($CO\underline{C}H_3$), 18.0 (Rha-C-6), 16.1 (Fuc-C-6), 14.1 ($OCH_2(CH_2)_6\underline{C}H_3$); HRMS (ESI) Calc. for $[M + NH_4]^+$ $C_{29}H_{50}NO_{10}$: 572.3429; Found 572.3431.



Octyl α-D-rhamnopyranosyl-(1→3)-α-L-fucopyranoside (4.6): To a stirred solution of **4.36** (104 mg, 188 μmol) in CH_3OH (4.0 mL) was added a solution of $NaOCH_3$ in CH_3OH (0.4 mL, 0.5 M). The reaction mixture was stirred overnight at room temperature, then neutralized by addition of Amberlite® IR-120 (H^+) cation exchange resin, filtered and the filtrate was concentrated. The residue was then dissolved in THF–CH_3OH (1:1, 3.0 mL) and 20% palladium hydroxide on carbon (10.0 mg) was added. After stirring for 24 h under an H_2 atmosphere (1 atm), the reaction mixture was filtered through Celite and concentrated. The residue was dissolved in water and then lyophilized to afford **4.6** (79.3 mg, quant.) as a white solid. R_f 0.45 (5:1 CH_2Cl_2–CH_3OH); $[\alpha]_D$ –16.7 (c 0.40, CH_3OH);

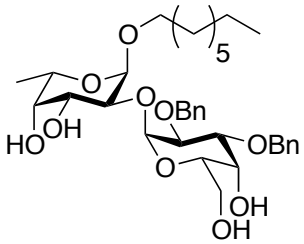
^{1}H NMR (600 MHz; CD_3OD): δ 5.01 (d, 1H, J = 1.5 Hz, Rha-H-1), 4.72 (d, 1H, J = 3.8 Hz, Fuc-H-1), 3.97–3.93 (m, 2H, Rha-H-2, Fuc-H-5), 3.86 (dd, 1H, J = 10.2, 3.9 Hz, Fuc-H-2), 3.80–3.73 (m, 3H, Fuc-H-3, Rha-H-3, Rha-H-5), 3.71 (d, 1H, J = 2.8 Hz, Fuc-H-4), 3.65 (dt, 1H, J = 9.7, 7.0 Hz, $OC\underline{H}_2CH_2(CH_2)_5CH_3$), 3.45 (dt, 1H, J = 9.7, 6.4 Hz, $OC\underline{H}_2CH_2(CH_2)_5CH_3$), 3.38 (t, 1H, J = 9.5 Hz, Rha-H-4), 1.66–1.59 (m, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.35–1.28 (m, 10H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 1.24 (d, 3H, J = 6.3 Hz, Rha-H-6), 1.19 (d, 3H, J = 6.6 Hz, Fuc-H-6), 0.89 (t, 3H, J = 7.0 Hz, $OCH_2CH_2(CH_2)_5C\underline{H}_3$); ^{13}C NMR (125 MHz CD_3OD): δ 103.8 (Rha-C-1), 100.5 (Fuc-C-1), 78.9 (Fuc-C-3), 74.1 (Rha-C-4), 73.5 (Fuc-C-4), 72.2 (Rha-C-2), 72.1 (Rha-C-3), 70.1 (Rha-C-5), 69.4 (2 × C, Fuc-C-2, $O\underline{C}H_2(CH_2)_6CH_3$), 67.6 (Fuc-C-5), 33.0 ($OCH_2(\underline{C}H_2)_6CH_3$), 30.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 30.5 ($OCH_2(\underline{C}H_2)_6CH_3$), 30.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 27.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 23.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 18.0 (Rha-C-5), 16.6 (Fuc-C-5), 14.4 ($OCH_2(CH_2)_6\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{20}H_{38}NaO_9$: 445.2408; Found 445.2406.



Octyl 2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranosyl-(1→2)-3,4-*O*-isopropylidene-α-L-fucopyranoside (4.37): To a stirred solution of acceptor **4.16** (152 mg, 480 μmol) and 2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranoside

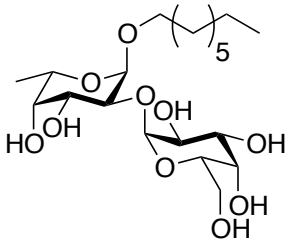
4.14[9] (565 mg, 932 μmol) in dry CH_2Cl_2 (5.0 mL) was added molecular sieves (500 mg, 4Å, powder). After stirring for 30 min at room temperature, the reaction mixture was cooled to –10 °C, and then *N*-iodosuccinimide (252 mg, 1.12 mmol) and silver trifluoromethanesulfonate (23.1 mg, 89.0 μmol) were added successively. The resulting solution was stirred for 1 h at 0 °C under an Ar atmosphere. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was washed with saturated $Na_2S_2O_3$ (aq.) and saturated $NaHCO_3$ (aq.), the aqueous layer was extracted with CH_2Cl_2 (50 mL × 3), dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was purified by flash chromatography (8:1 hexane–EtOAc) to afford **4.37** (316 mg, 82%) as a syrup. R_f 0.24 (8:1 hexane–EtOAc); $[\alpha]_D$ +17.6 (*c* 0.26, $CHCl_3$); ^{1}H NMR (600 MHz; $CDCl_3$): δ 7.46–7.44 (m, 4H, Ar), 7.36–7.30 (m, 6H, Ar), 5.10 (d, 1H, *J* = 3.8 Hz, Gal-H-1), 4.84–4.82 (m, 2H, PhC$\underline{H}_2$, Fuc-H-1), 4.76 (d, 1H, *J* = 12.6 Hz, PhC$\underline{H}_2$), 4.75 (s, 2H, PhC$\underline{H}_2$) 4.55 (d, 1H, *J* = 2.7 Hz, Gal-H-4), 4.36 (dd, 1H, *J* = 7.8, 5.6 Hz, Fuc-H-3), 4.22 (dd, 1H, *J* = 12.3, 2.1 Hz, Gal-H-6a), 4.10–4.05 (m, 3H, Fuc-H-5, Gal-H-6b, Fuc-H-4), 4.01 (dd, 1H, *J* = 10.1, 3.8 Hz, Gal-H-2), 3.88 (dd, 1H, *J* = 10.1, 3.0 Hz, Gal-H-3), 3.82 (br s, 1H, Gal-H-5), 3.71 (dd, 1H, *J* = 7.8, 3.5 Hz, Fuc-H-2), 3.65 (dt, 1H, *J* = 9.6, 6.8 Hz, OC$\underline{H}_2$CH$_2$(CH$_2$)$_5$CH$_3$), 3.25 (dt, 1H, *J* = 9.6, 6.7 Hz, OC$\underline{H}_2$CH$_2$(CH$_2$)$_5$CH$_3$), 1.56 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.55–1.51 (m, 2H, OCH$_2$C$\underline{H}_2$(CH$_2$)$_5$CH$_3$), 1.39 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.35 (d, 3H, *J* = 6.6 Hz, Fuc-H-6), 1.32–1.27 (m, 10H, OCH$_2$CH$_2$(C$\underline{H}_2$)$_5$CH$_3$), 1.08 (s, 9H, C(C$\underline{H}_3$)$_3$), 1.00 (s, 9H, C(C$\underline{H}_3$)$_3$), 0.90 (t, 3H, *J* = 7.0 Hz, OCH$_2$CH$_2$(CH$_2$)$_5$C$\underline{H}_3$); ^{13}C NMR (125 MHz $CDCl_3$): δ 139.2 (Ar), 138.9 (Ar), 128.3 (Ar), 128.1 (2 × Ar), 127.5 (Ar), 127.4 (Ar), 127.3

(Ar), 108.8 (<u>C</u>(CH_3)$_2$), 99.9 (Gal-H-1, $^1J_{C\text{-}H}$ = 170.6 Hz), 98.1 (Fuc-C-1), 78.4 (Fuc-C-2), 77.5 (Gal-C-3), 76.3 (Fuc-C-4), 74.6 (Fuc-C-3), 74.3 (Gal-C-2), 72.5 (Ph<u>C</u>H_2), 71.2 (Gal-C-4), 71.1 (Ph<u>C</u>H_2), 68.1 (O<u>C</u>H_2(CH_2)$_6$$CH_3$), 67.5 (Gal-C-5), 67.4 (Gal-C-6), 63.3 (Fuc-C-5), 31.9 (OCH$_2$(<u>C</u>H_2)$_6$$CH_3$), 29.6 (OCH$_2$(<u>C</u>$H_2$)$_6$$CH_3$), 29.4 (OCH$_2$(<u>C</u>$H_2$)$_6$$CH_3$), 29.3 (OCH$_2$(<u>C</u>$H_2$)$_6$$CH_3$), 28.4 (C(<u>C</u>$H_3$)$_2$), 27.6 (C(<u>C</u>$H_3$)$_3$), 27.3 (C(<u>C</u>$H_3$)$_3$), 26.4 (C(<u>C</u>$H_3$)$_2$), 26.2 (OCH$_2$(<u>C</u>$H_2$)$_6$$CH_3$), 23.4 (<u>C</u>($CH_3$)$_3$), 22.7 (OCH$_2$(<u>C</u>$H_2$)$_6$$CH_3$), 20.7 (<u>C</u>($CH_3$)$_3$), 16.4 (Fuc-C-6), 14.1 (OCH$_2$(CH_2)$_6$<u>C</u>H_3); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{45}H_{70}NaO_{10}Si$: 821.4630; Found 821.4632.



Octyl 2,3-di-*O*-benzyl-α-D-galactopyranosyl-(1→2)-α-L-fucopyranoside (4.38): To a stirred solution of **4.37** (316 mg 395 μmol) in THF–pyridine (6.0 mL, 1:1) was added HF·pyridine (0.6 mL, pyridine ~30%, hydrogen fluoride ~70%) at 0 °C under an Ar atmosphere. The reaction mixture was stirred for 1 h at 0 °C, before being poured into saturated $NaHCO_3$ (aq.). The aqueous layer was extracted with EtOAc (40 mL × 3), dried over Na_2SO_4, filtered and the filtrate was concentrated. The crude residue was then dissolved in CH_3CN–CH_3OH (5.5 mL, 10:1) and *p*-toluenesulfonic acid monohydrate (223 mg, 1.17 mmol) was added at room temperature. The reaction mixture was stirred for 3.5 h at room temperature. Excess triethylamine was added to quench the acid, the mixture was filtered and the filtrate was concentrated. The crude residue was purified by flash

chromatography (1:2 hexane–EtOAc) to afford **4.38** (183 mg, 75%) as a syrup. R_f 0.15 (2:3 hexane–EtOAc); $[\alpha]_D$ –1.5 (*c* 0.45, $CHCl_3$); ^1H NMR (600 MHz; $CDCl_3$): δ 7.41–7.31 (m, 10H, Ar), 4.95 (d, 1H, *J* = 3.7 Hz, Gal-H-1), 4.93 (d, 1H, *J* = 3.7 Hz, Fuc-H-1), 4.87 (d, 1H, *J* = 11.6 Hz, PhC$\underline{H}_2$), 4.79 (d, 1H, *J* = 11.4 Hz, PhC$\underline{H}_2$), 4.73 (d, 1H, *J* = 11.4 Hz, PhC$\underline{H}_2$), 4.69 (d, 1H, *J* = 11.6 Hz, PhC$\underline{H}_2$), 4.15 (dd, 1H, *J* = 3.2, 1.0 Hz, Gal-H-4), 4.04–3.99 (m, 3H, Fuc-H-3, Gal-H-5, Gal-H-3), 3.97–3.92 (m, 2H, Fuc-H-5, Gal-H-6a), 3.90 (t, 1H, *J* = 4.9 Hz, Gal-H-2), 3.85 (d, 1H, *J* = 2.4 Hz, Fuc-H-4), 3.78 (dd, 1H, *J* = 11.6, 4.0 Hz, Gal-H-6b), 3.74 (dd, 1H, *J* = 9.9, 3.7 Hz, Fuc-H-2), 3.68 (dt, 1H, *J* = 9.7, 6.8 Hz, OC$\underline{H}_2CH_2(CH_2)_5CH_3$), 3.42 (dt, 1H, *J* = 9.7, 6.7 Hz, OC$\underline{H}_2CH_2(CH_2)_5CH_3$), 1.61–1.56 (m, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.35–1.28 (m, 10H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 0.91 (t, 3H, *J* = 7.0 Hz, $OCH_2CH_2(CH_2)_5C\underline{H}_3$); ^{13}C NMR (175 MHz $CDCl_3$): δ 137.8 (Ar), 137.6 (Ar), 128.6 (2 × Ar), 128.2 (Ar), 128.1 (Ar), 128.0 (Ar), 127.7 (Ar), 101.5 (Gal-C-1), 98.0 (Fuc-C-1), 80.5 (Fuc-C-2), 78.0 (Gal-C-3), 75.9 (Gal-C-2), 74.3 (Ph$\underline{C}H_2$), 72.4 (Ph$\underline{C}H_2$), 71.3 (Fuc-C-4), 69.7 (Fuc-C-3), 69.1 (Gal-C-5), 68.8 (Gal-C-4), 68.2 (O$\underline{C}H_2(CH_2)_6CH_3$), 65.3 (Fuc-C-5), 63.2 (Gal-C-6), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 26.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 16.1 (Fuc-C-6), 14.1 ($OCH_2(CH_2)_6\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{34}H_{50}NaO_{10}$: 641.3296; Found 641.3297.



Octyl α-D-galactopyranosyl-(1→2)-α-L-fucopyranoside (4.7): To a stirred solution of **4.38** (129 mg, 208 μmol) in THF–CH_3OH (1:1, 4.0 mL) and 20% palladium hydroxide on carbon (15.0 mg) was added. After stirring for 24 h under an H_2 atmosphere (1 atm), the reaction mixture was filtered through Celite and concentrated. The residue was dissolved in water and then lyophilized to afford **4.7** (91.3 mg, quant.) as a white solid. R_f 0.29 (4:1 CH_2Cl_2–CH_3OH); $[\alpha]_D$ –5.4 (*c* 0.52, CH_3OH); ^{1}H NMR (600 MHz; CD_3OD): δ 5.00 (d, 1H, J = 3.7 Hz, Fuc-H-1), 4.99 (d, 1H, J = 3.0 Hz, Gal-H-1), 3.99–3.97 (m, 1H), 3.95–3.91 (m, 2H), 3.88 (t, 1H, J = 1.3 Hz), 3.76–3.75 (m, 2H), 3.74–3.69 (m, 3H), 3.68–3.63 (m, 2H), 3.48 (dt, 1H, J = 9.6, 6.5 Hz), 1.59 (quintet, 2H, J = 7.0 Hz), 1.40–1.28 (m, 10H), 1.20 (d, 3H, J = 6.6 Hz), 0.90 (t, 3H, J = 7.1 Hz); ^{13}C NMR (125 MHz CD_3OD): δ 103.7 (Gal-C-1), 99.8 (Fuc-C-1), 80.0, 73.6, 72.8, 71.6, 71.2, 70.8, 70.4, 68.6, 67.2, 62.7, 33.1, 30.8, 30.6, 30.5, 27.6, 23.7, 16.6, 14.4; HRMS (ESI) Calc. for $[M + Na]^+$ $C_{20}H_{38}NaO_{10}$: 461.2357; Found 461.2356.

4.5 References

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Chapter 5

Summary and Future Work

5.1 Summary and future work

In this thesis, I have investigated the synthesis of highly branched *N*-glycans isolated from chloroviruses. This includes the development of a reliable approach to the core structure of the molecules via the synthesis of the simplest of these compounds, the ATCV-1 *N*-glycan (Chapter 2), the assessment of this approach as a means to synthesize more complex *N*-glycans (Chapter 3), and the synthesis of PBCV-1 fragments as probes for understanding its biosynthetic pathways (Chapter 4).

5.1.1 Synthesis of highly branched *N*-glycans in chloroviruses

The structure of chlorovirus *N*-glycans is species specific, but all of them share a common pentasaccharide as shown in Figure 5-1. This motif is further elaborated with either a D-rhamnose or L-rhamnose forming a semi-conserved hexasaccharide core structure. These *N*-glycans have a highly branched architecture in which every hydroxyl group on the fucose is glycosylated.

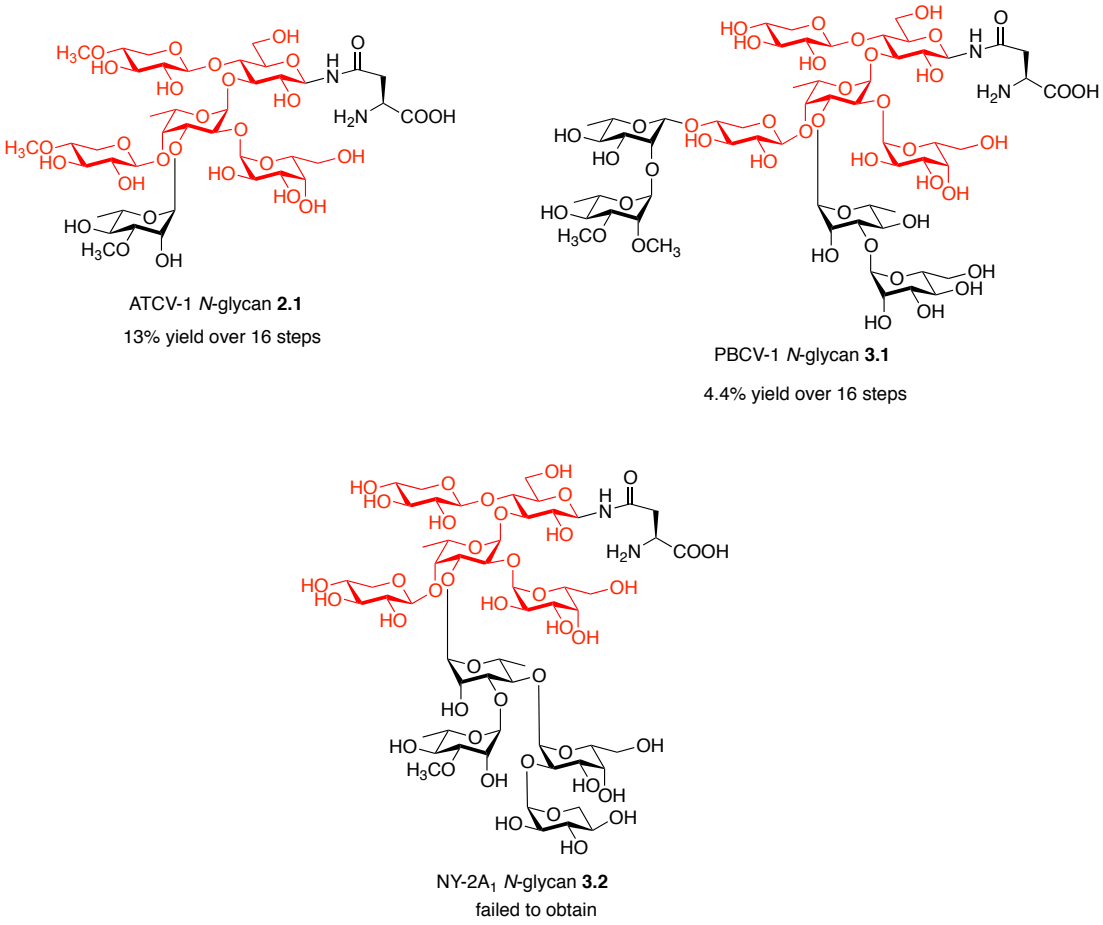
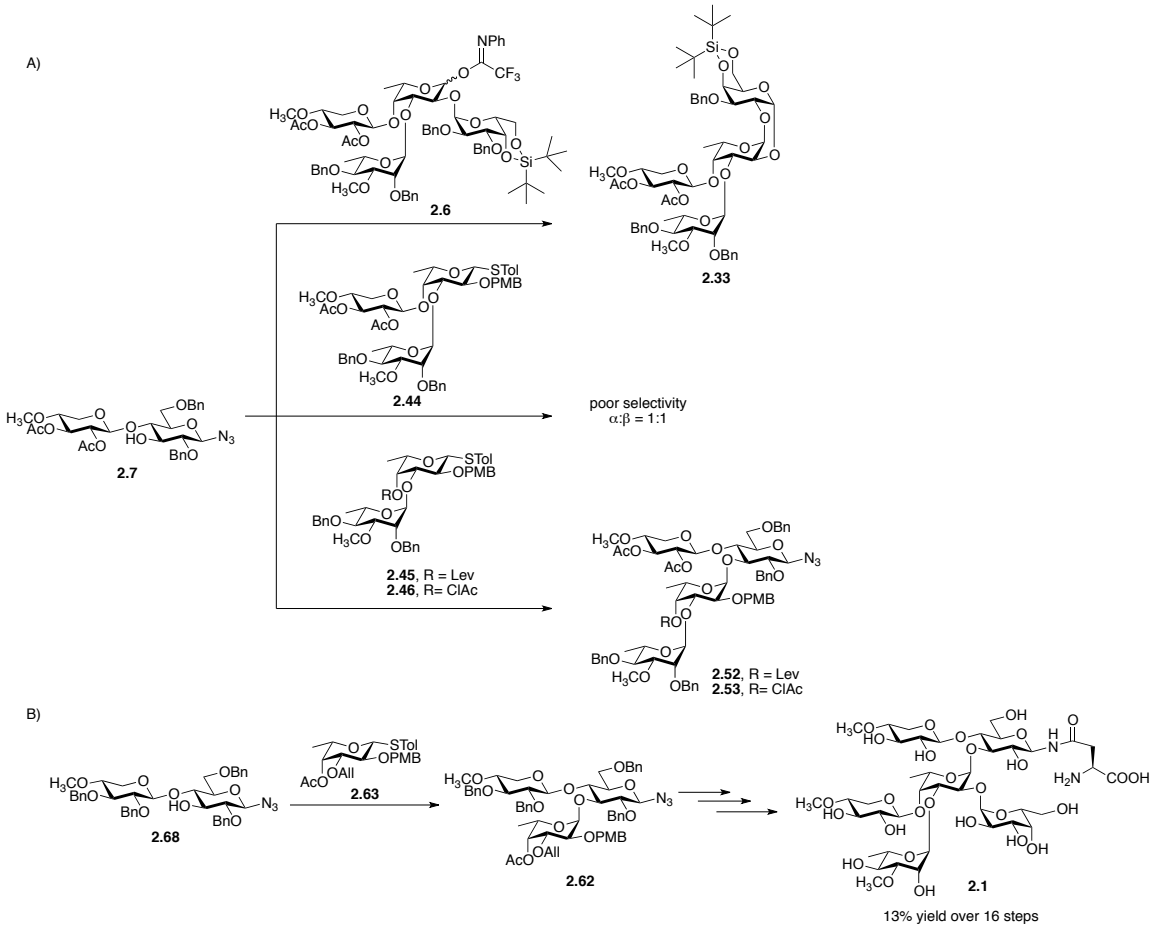


Figure 5-1: Structure of *N*-glycans from three different chloroviruses.

In Chapter 2, I described the synthesis of *N*-glycan **2.1** isolated from *Acanthocystis turfacea* chlorella virus 1 (ATCV-1), which has the simplest hexasaccharide motif. It was initially envisioned to be obtained from a convergent 4+2 approach. This route was abandoned due to the formation of a tricyclic by-product **2.33** (Scheme 5-1A). I postulated that this approach failed because of the high reactivity of donor **2.6** and steric hinderance of the hydroxyl group at the C-3 position in acceptor **2.7.** Alternatively, a 2+3 and 2+2

glycosylation approach were attempted. The synthesis of trisaccharide donor **2.44** gave very low yield and the 2+3 glycosylation provided poor selectivity; thus, this approach was also abandoned, and a 2+2 glycosylation with **2.45** or **2.46** was attempted. Although the tetrasaccharide could be achieved successfully, the presence of a rhamnose moiety at the C-3 position of the fucose was found to be problematic for further functionalization of the C-4 hydroxyl group.

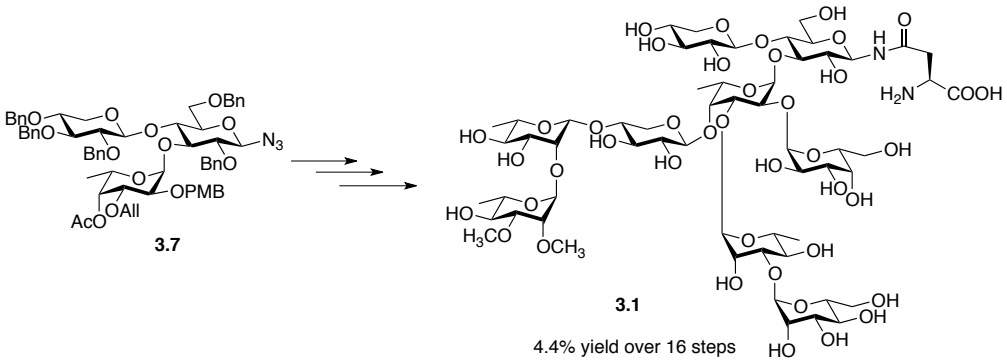


Scheme 5-1: A) Attempted convergent syntheses of hexasaccharide **2.1**, which were unsuccessful; B) Successful linear synthesis of hexasaccharide **2.1**.

As a result, a linear approach was investigated (Scheme 5-1B). Trisaccharide **2.62**, containing three orthogonal protecting groups on each of the fucose hydroxyl groups was synthesized. The distal xylose residue was glycosylated first on the presumed least reactive C-4 hydroxyl group. The C-3 and C-2 hydroxyl groups were then glycosylated, in that order, using an L-rhamnose and galactose donor, respectively. Subsequent azide reduction, coupling with a commercially-available protected amino acid, and global deprotection afforded the desired target **2.1** in 13% overall yield in 16 steps. A key feature for the success of this approach was a "counter-clockwise" introduction of the carbohydrate residues onto the fucose moiety. At this point I considered this to be a versatile approach to access any highly branched chlorovirus *N*-glycans.

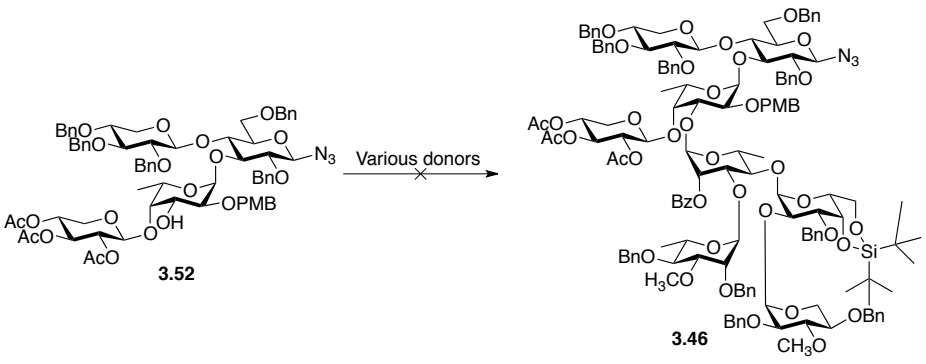
To approve the feasibility of my developed "counter-clockwise" assembly method, in Chapter 3, I extended this approach to the synthesis of complex *N*-glycans **3.1** and **3.2** from the chlorovirus strains PBCV-1 and NY-2A$_1$, respectively. Glycan **3.1** and **3.2** are the most complex among the characterized chlorovirus *N*-glycans, and thus I hypothesized that if my developed approach is applicable to those, this will be a general strategy to access all of the others.

The synthesis of PBCV-1 *N*-glycan **3.1** containing a trisaccharide residue on the fucose C-4 hydroxyl group and a disaccharide residue on the fucose C-3 hydroxyl group was successful. The target was obtained in 4.4% overall yield in 16 steps (Scheme 5-2). This yield is lower compared to the synthesis of the ATCV glycan **2.1**.



Scheme 5-2: Successful approach to nonasaccharide **3.1**.

Unfortunately, the synthesis of the NY-2A$_1$ *N*-glycan **3.2** could not be achieved due to the failure in attempting the formation of octasaccharide **3.46** with various donors (Scheme 5-3). Work I did in the course of these studies suggested that a trisaccharide was the largest donor that could be glycosylated on the C-3 hydroxyl group of fucose when a carbohydrate residue is on the adjacent C-4 hydroxyl group. Although a trisaccharide could be added, disaccharide and monosaccharide donors gave better yields in this glycosylation. I propose that the synthetic challenge for the nonasaccharide **3.2** might be addressed by: 1) addition of large excess of donor under a high concentration to push the reaction to completion to achieve **3.46**; 2) using a different assembly sequence; 3) optimizing glycosylation conditions to adjust the reactivity between the donor and the acceptor; 4) increasing the reactivity of the acceptor by manipulation of protecting groups.



Scheme 5-3: Attempted synthesis of **3.46** with various donors.

Overall, I believe that the developed "counter-clockwise" assembly approach can be applied to most chlorovirus *N*-glycans (except NY-2A$_1$) reported to date. Moreover, I hope the problems I encountered could also provide some insights for the synthesis of the highly congested oligosaccharides. The project of my colleague, Mikel Allas, involves the synthesis of the glycan **5.1**, isolated from the parasite *Trypanosoma cruzi*[1] (Figure 5-2). The presence of two highly branched carbohydrate units (shown in red) in this structure makes its synthesis even more of a challenge.

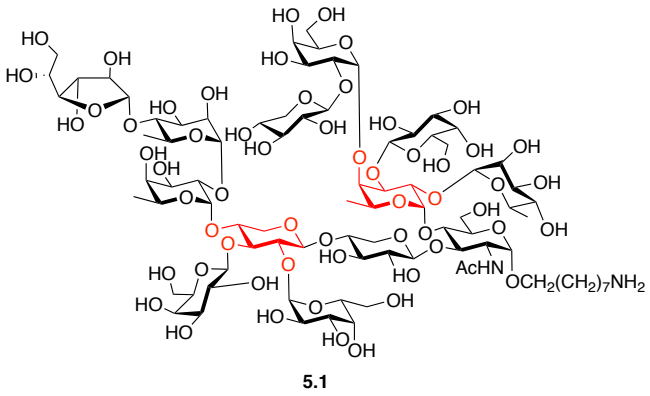


Figure 5-2: Glycan structure found on gp72 glycoprotein of *T. cruzi*.

5.1.2 Synthesis of the PBCV-1 fragments for understanding its biosynthetic pathway

It has been predicted that PBCV-1 encodes at least six glycosyltransferases. To understand how these glycans are assembled, one of the questions that need to be addressed is: What are the roles of the six glycosyltransferases encoded by the virus? In Chapter 4, I performed the chemical synthesis of eight different fragments **4.1**–**4.8** from PBCV-1. These compounds are currently being studied with two glycosyltransferases – A064R and A075L – in collaboration with the Prof. Cristina De Castro, at University of Napoli in Italy. In the future, other PBCV-1 encoded glycosyltransferases can also be discovered with suitable synthetic targets using biochemical assays.

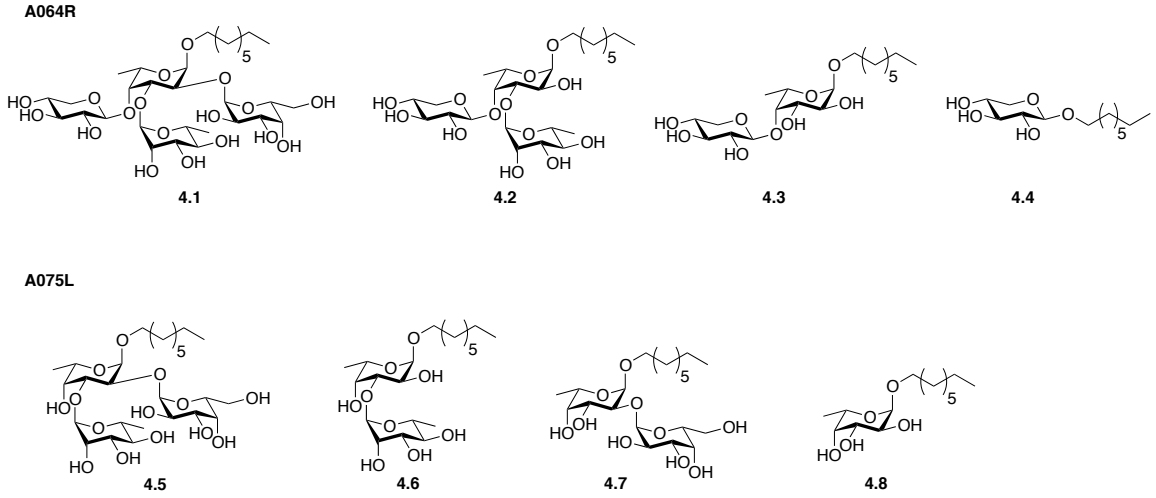


Figure 5-3: Structure of the synthetic probes **4.1**–**4.8** related to the PBCV-1 *N*-glycan.

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