Synthesis of Chlorovirus PBCV-1 *N*-Glycan Analogs

by

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Abstract

Chloroviruses are a group of water-borne viruses that infect eukaryotic, chlorella-like green algae. Unlike most other viruses, chloroviruses come equipped with their own carbohydrate-processing enzymes; they do not rely on the host's biosynthetic machinery for glycoprotein assembly. Chloroviruses express a set of unique *N*-linked glycans, which, at their core, contain a conserved pentasaccharide comprised of a highly branched fucose residue situated on an uncommon *β*-glucose residue that is *N*-linked to asparagine.

This thesis will focus on the synthesis of six *N*-glycan analogs from the chlorovirus PBCV-1, for their use as probes in the viral *N*-glycan biosynthetic pathway. Three of the target structures are derived from truncated *N*-glycans expressed by antigenic PBCV-1 mutants while the additional three are putative biosynthetic intermediates. The six structures range from tetra- and pentasaccharides to a highly branched hexasaccharide. Each structure was successfully accessed from a core α-L-Fuc*p*-(1→3)-[β-D-Xyl*p*- (1→4)]-β-D-Glc*p* trisaccharide using a linear synthetic approach. The strategy hinged on the use of orthogonal protecting groups on the central fucose residue to assemble the branched structures.

Acknowledgments

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$[\alpha]_D$	specific rotation (sodium D Line)
Å	angstrom
Ara*f*	arabinofuranose
Ac	acetyl
Ac_2O	acetic anhydride
AgOTf	silver trifluoromethanesulfonate
All	allyl
AllBr	allyl bromide
app	apparent (NMR spectra)
Ar	aromatic
Asn	asparagine
ATCV-1	*Acanthocystis turfacea* chlorella virus 1
BDA	benzaldehyde dimethyl acetal
$BF_3 \cdot OEt_2$	boron trifluoride etherate
Bn	benzyl
BnBr	benzyl bromide
br s	broad singlet (NMR spectrum)

Bz	benzoyl
Cbz	benzyloxycarbonyl
$(CH_3)C(OCH_3)_3$	trimethyl orthoacetate
CH_3OTf	methyl trifluoromethanesulfonate
C.jejuni	*Campylobacter jejuni*
$ClC(NPh)CF_3$	*N*-phenyltrifluoroacetimidoyl chloride
COSY	correlation spectroscopy
CSA	camphorsulfonic acid
Cs_2CO_3	cesium carbonate
CsF	cesium fluoride
Cys	cysteine
d	doublet (NMR spectra)
ddd	doublet of doublet of doublet (NMR spectra)
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
ddt	doublet of doublet of triplet (NMR spectra)
DMF	dimethylformamide
DNA	deoxyribonucleic acid
Dol-P	dolichol phosphate

Dol-P-P	dolichyl pyrophosphate
dq	doublet of quartet (NMR spectra)
dsDNA	double-stranded DNA
dt	doublet of triplet (NMR spectra)
DTBS	di-*tert*-butylsilyl
$(t\text{-Bu})_2Si(OTf)_2$	di-*tert*-butylsilyl bis (trifluoromethanesulfonate)
EDC·HCl	*N*-(3-dimethylaminopropyl)-*N*'-ethylcarbodiimide hydrochloride
ER	endoplasmic reticulum
ESI	electrospray ionization
Et_2O	diethyl ether
Et_2SiH	triethylsilane
EtOAc	ethyl acetate
Fuc*p* (Fuc)	fucopyranose (fucose)
Gal*p* (Gal)	galactopyranose (galactose)
GlcNAc*p* (GlcNAc)	(acetylamino)-2-deoxy-glucopyranose, (*N*-acetylglucosamine)
Glc*p* (Glc)	glucopyranose (glucose)

GT	glycosyltransferase
HATU	1-[bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxide hexafluorophosphate
Hbt. salinarum	*Halobacterium salinarum*
HOAc	acetic acid
HRMS	high-resolution mass spectrometry
HSQC	heteronuclear signal quantum coherence
$[Ir(COD)(CH_3Ph_2P)_2]PF_6$	(1,5-cyclooctadiene)bis (methyldiphenylphosphine)iridium(I) hexafluorophosphate
kb	kilobase
Lev	levulinoyl
$LiAlH_4$	lithium aluminium hydride
m	multiplet (NMR spectra)
Man*p*	mannopyranose
MCP	major capsid protein
MS	molecular sieves
NaH	sodium hydride

NaOAc	sodium acetate
$NaOCH_3$	sodium methoxide
NBS	*N*-bromosuccinimide
n-Bu_2SnO	di-*n*-butyltin oxide
NIS	*N*-iodosuccinimide
NMR	nuclear magnetic resonance
OST	oligosaccharyltransferase
PBCV-1	*Paramecium bursaria* chlorella virus 1
pent	pentet (NMR spectra)
PFU	plaque-forming units
PG	protecting group
Ph	phenyl
PMB	*para*-methoxybenzyl
PMBCl	*para*-methoxybenzyl chloride
ppm	parts per million
p-TolSCl	*para*-toluenesulfonyl chloride
p-Tolyl	4-methylphenyl
p-TsOH	*para*-toluenesulfonic acid

q	quartet (NMR spectra)
R_f	retention factor
Rha*p* (Rha)	rhamnopyranose (rhamnose)
RNA	ribonucleic acid
rRNA	ribosomal RNA
s	singlet (NMR spectra)
Ser	serine
TBAI	tetrabutylammonium iodide
TBSOTf	*tert*-butyldimethylsilyl trifluoromethanesulfonate
t-Bu	*tert*-butyl
TEA	triethylamine
TFA	trifluoroacetic acid
TfOH	trifluoromethanesulfonic acid
THF	tetrahydrofuran
Thr	threonine
TLC	thin layer chromatography
Tol	*para*-tolyl
TPP	triphenylphosphine

tRNA	transfer RNA
Ts	toluenesulfonyl
TsCl	toluenesulfonyl chloride
TTBP	2,4,6-tri-*tert*-butylpyrimidine
UDP	uridine diphosphate
Und-PP	undecaprenyl-diphosphate
Xyl*p* (Xyl)	xylopyranose (xylose)

Chapter 1

Introduction

1.1 Carbohydrates in biological systems

Carbohydrates are one of four major classes of biomolecules found in nature.[1, 2, 3] The simplest carbohydrate unit is the monosaccharide.[4] They can be connected together through glycosidic bonds to produce large, polymeric molecules known as polysaccharides. In biological systems, when oxidised, they provide energy for various cellular processes such as protein synthesis, movement, and transportation.[3] Furthermore, carbohydrates are prominently found covalently attached to numerous macromolecules forming complexes known as glycoconjugates.[4] The sugar moieties of such complexes are referred to as glycans while the attached noncarbohydrate moieties (such as proteins or lipids) are known as aglycones.[4] The roles of carbohydrates and glycoconjugates in biological systems are vast: from energy and energy storage, to structural support and the mediation of cellular events and processes.[3, 4] Unlike proteins whose form and function are defined by the DNA template that controls their synthesis; the structures and roles of glycans are less explicitly described. The non-templated assembly generates enormous biological complexities that are crucial to growth, development, and function.[4, 5] The study of such systems and interactions is important to further describe and unify the underlying concepts and models of molecular biology.

1.2 Glycoproteins

The glycosylation of proteins is a post translational modification found throughout all domains of life.[4, 6, 7, 8] The process involves the covalent attachment of glycans to a peptide backbone, typically, through *N*- or *O*- glycosidic bonds, and, in rarer cases, *C*- linked (e.g., *C*-mannosylation).[4, 8, 9] Of the commonly found linkage types, *N*-linked glycans are covalently

attached to the amide nitrogen of an asparagine residue while *O*-linked glycans are attached to the hydroxyl group of either a serine or a threonine residue.[4, 8] Protein glycosylation is an important post-translational process vital to protein folding, stability, and bioactivity.[7, 10, 11, 12] For a long time, it was thought that *N*-glycosylation was a post translational process unique to eukaryotes.[4, 13, 14] However, in the past few decades it has been discovered that both bacteria and archaea express their own forms of *N*-glycosylation.[9, 12]

1.2.1 *N*-Glycosylation of eukaryotes

In eukaryotes, *N*-linked glycans express structural diversity across species and even cell types, while maintaining a conserved core structure of α-D-Man*p*-(1→3)-[(α-D-Man*p*-(1→6)]-β-D-Man*p*-(1→4)-β-D-GlcNAc*p*-(1→4)-β-D-GlcNAc*p*-Asn.[4, 6, 11, 13] In the initial stages of *N*-glycan synthesis (**Figure 1-1**), the oligosaccharide is assembled on a phosphorylated lipid carrier, dolichol phosphate (Dol-P), found in the endoplasmic reticulum (ER) membrane.[4, 6] Initially on the cytosolic face, GlcNAc-1-P is transferred from UDP-GlcNAc to Dol-P to form dolichol pyrophosphate *N*-acetylglucosamine (Dol-P-P-GlcNAc).[4] The glycan is further elongated to $Man_5GlcNAc_2$-P-P-Dol before it is "flipped" into the ER lumen where an additional three glucose and four mannose residues are added.[4] An oligosaccharyltransferase (OST) then transfers the oligosaccharide to an asparagine of a peptide acceptor.[4,6] Further elaboration of the glycan is done in the ER lumen and is continued in the Golgi apparatus, resulting in the observed structural diversity.[4, 6] Most *N*-glycosylation sites of eukaryotic proteins follow the acceptor peptide sequence Asn-X-Ser/Thr (where X is an amino acid other than proline) with the occasional case of having Asn-X-Cys.[4, 6, 11, 12] However, not all sequons have the asparagine *N*-

glycosylated; conformational changes during protein folding may render some sequons inaccessible.[4]

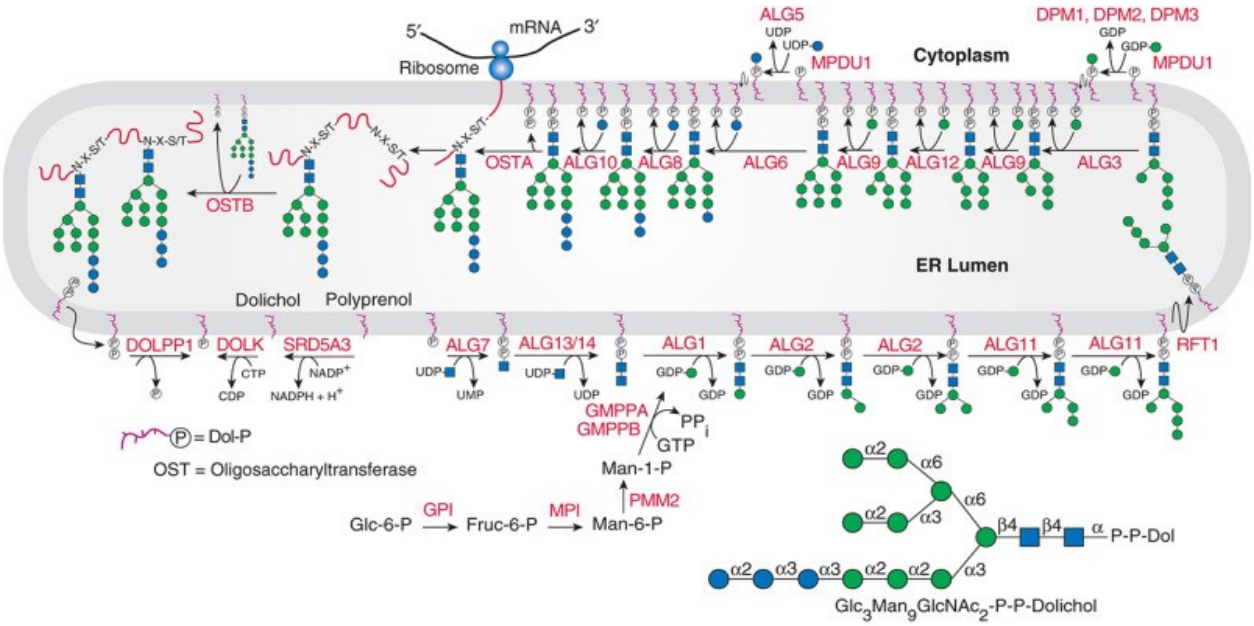


Figure 1-1: The biosynthesis of eukaryotic *N*-linked glycans in the ER. Image used with permission from Varki, A.; Cummings, R. D.; Esko, J. D.; et al. Essentials of Glycobiology [Internet]. 3rd edition; Cold Springs Harbor Laboratory Press, 2015–2017.[4]

1.2.2 *N*-Glycosylation of prokaryotes

In prokaryotes, both bacteria and archaea have been observed to express forms of *N*-glycosylation. *N*-glycosylation in bacteria was first identified and described for the Gram-native bacterium *Campylobacter jejuni*.[4, 9] Since then, several other bacterial species have been identified to express *N*-linked glycans but overall diversity remains rather limited.[6, 10, 15] The *N*-linked protein glycosylation pathway of *C. jejuni* remains the most studied and best characterized bacterial system.[16]

Archaeal *N*-linked glycans were first found in the extreme halophile, *Halobacterium salinarum.*[4, 5, 13] At the time, Archaea were not recognized as a separate domain of life.[4, 5, 13] *Hbt. salinarum* was thought to be a rather bizarre bacterium due to its extreme habitat and expression of *N*-linked glycans.[5, 13] It was not until the advent of 16S rRNA analysis that life on Earth was restructured into three distinct domains.[4, 13] The reclassification of *Hbt. salinarum* and early glycobiological studies helped disprove the idea that *N*-glycosylation was a post translational process unique to eukaryotes.[4, 13] The studies also further supported the idea of Archaea being a distinct domain from Bacteria as Archaea were found to not contain peptidoglycan.[4] Since then, numerous examples of *N*-glycosylated proteins have been identified throughout archaeal species.[4, 6, 13] They have been found to express an impressive array of *N*-glycan diversity, not only in structure but in unique sugar residues and modifications used – possibly reflecting the unique niches these organisms occupy.[4, 6, 13] However, only a handful of archaeal *N*-glycosylation pathways have been described.[13]

Similar to that of their eukaryotic counterpart, *N*-glycan synthesis in prokaryotes involve the assembly of the oligosaccharide substrate on a phosphorylated polyisoprenoid lipid carrier.[4, 6] Bacteria, however, typically use the phosphorylated polyprenol carrier, undecaprenyl-diphosphate (Und-PP) while archaea and eukaryotes use phosphorylated dolichols.[17, 18] Assembly of the lipid-linked oligosaccharides in prokaryotes takes place on the cytosolic face of the plasma membrane. Membrane-bound OSTs (homologous to the catalytic subunit of eukaryotic OTases) then catalyze the transfer of the oligosaccharide unit to an asparagine of a peptide acceptor in the periplasm.[4, 6, 13, 14, 16, 18] The acceptor peptide sequon found in Archaea is reminiscent of that found in eukaryotes but in bacteria it is somewhat more elaborate.[6, 13] In Archaea, the peptide acceptor sequon appears to follow the Asn-X-Ser/Thr sequence (where X

cannot be proline).[5, 6, 13] However, in bacteria an extended sequon, Asp/Glu-Z-Asn-X-Ser/Thr (where X and Z are amino acids other than proline) is observed (as seen in *C. jejuni*).[5, 16, 19]

1.2.3 Glycosylation in viruses

Outside the three main domains of life, exist viruses – whose origins remain a mystery.[20, 21] Viruses are parasites of cellular life [21]; incapable of self replication, they nevertheless are the most abundant biological entities on the planet.[22, 23] Unable to replicate on their own, viruses must rely on the appropriation of their hosts' own molecular machinery.[24, 25] Consequentially, viruses express their own forms of glycosylation – however, it is usually host-specific, as they are dependent on the same processes as the host's own glycoproteins.[26] Viral proteins, especially those that comprise the viral envelope or capsid express both *O*- and *N*- linked glycans.[25, 27] The role of the viral glycosylation is found to aid in infectivity, virion formation, and immune evasion.[25] While most viruses rely on host-encoded glycosyltransferases and glycosidases for post translational modification, a group of viruses known as chloroviruses encode their own means of glycosylation.[26] As such, they produce unique glycan structures, currently not found elsewhere in life.[28]

1.3 Chloroviruses

1.3.1 *Phycodnaviridae*

Phycodnaviridae is a family of viruses that infect eukaryotic algae.[29] Unlike viruses of higher-order plants – which are typically small and contain plus-stranded RNA; viruses of

Phycodnaviridae are large and contain double-stranded DNA (dsDNA), which are predicted to incorporate several hundred protein-encoding genes and a variety of tRNA genes.[29, 30] While genetically diverse, members of *Phycodnaviridae* are icosahedral in shape and often share similar morphological features.[31, 32] These viruses can be found globally in aqueous environments and have an active role in regulating aquatic systems.[29, 30] *Phycodnaviridae* is further divided into six genera of which one particular group, *Chlorovirus*, has been the subject of numerous investigations.[29, 31, 32]

1.3.2 *Chlorovirus*

Chloroviruses are viruses of the *Chlorella* genus and are unicellular, eukaryotic, chlorella-like green algae.[29, 30] Most *Chlorella* species are freestanding while a few exist as endosymbionts that are associated with one of three hosts: *Paramecium bursaria*, *Hydra viridis*, or *Acanthocystis turfacea*.[29, 30] The nature of such relationship is that of mutualism; the chlorellae provides a source of energy by way of photosynthesis while the host provides protection from environmental elements – including resistance to chloroviruses themselves.[29, 30] The *Chlorovirus* genus is further divided into four species that are aptly named after the hosts they infect: NC64A viruses, infect *Chlorella variabilis* NC64A; Osy viruses, infect *Chlorella variabilis* Syngen 2-3; SAG viruses, infect *Chlorella heliozoae* SAG 3.83; and Pbi viruses, infect *Micractinium conductrix* Pbi.[28, 29] Of the currently identified chloroviruses, the chlorovirus *Paramecium bursaria* chlorella virus 1 (PBCV-1) – a virus of *Chlorella variabilis* NC64A – is the type member of the genus.[28, 29, 30]

Chloroviruses can be found throughout inland waters, world wide.[29, 30] Typical chlorovirus titers range from 1 to 100 plaque-forming units (PFU) per millilitre, and in some cases, as high as 1000's of PFU/mL.[29, 30] Analysis of marine metagenomes suggests the presence of chloroviruses in such environments, however, none have been isolated.[29, 30] Given their prevalence in nature, one particular chlorovirus – *Acanthocystis turfacea* chlorella virus 1 (ATCV-1) – has been found in association with humans.[33] Yolken and colleagues had sequenced the metagenomes from throat mucosal samples of several individuals, identifying the presence of genomic sequences belonging to ATCV-1.[33] Viral studies conducted on mouse models revealed a modest (albeit statistically significant) reduction in several cognitive function domains including recognition memory and sensory-motor gating.[33]

Chloroviruses have genomes that range from 290 to 370 kb in length and contain more than 300 protein-encoding genes. [29] Approximately half of the genes have unknown function and do not resemble homologs in known databases (except as orthologs to those present in other chloroviruses, phycodnaviruses, or large DNA viruses) – with many being unexpected for viruses. [29] Proteomic analysis of PBCV-1 virions has revealed at least 148 different viral encoded proteins – accounting for approximately 35% of the viral coding capacity and are typically the smallest of their protein class. [29] Functions of the identified viral encoded proteins range from structural to enzymatic, chromatin modifying, and signal transduction. [29] Given their gene coding capacity, chloroviruses express a number of unique and unexpected characteristics not found in other viruses.[29]

1.3.3 *N*-Glycans of *Chlorovirus*

A large portion of the chlorovirus genes encode carbohydrate-processing enzymes involved in both synthesis and metabolism.[34] Unlike most previously studied viruses, which rely on host-encoded biosynthetic machinery for post translational modifications, chloroviruses encode their own glycosyltransferases and glycosidases responsible for glycan assembly. This alleviates dependency on host glycosylation pathways.[26, 35] Collectively, of the current 43 genetically sequenced chloroviruses, a total of eight putative glycosyltransferases have been identified.[34] Six of the glycosyltransferase-encoding genes are found in the Chlorovirus PBCV-1 and are not found to contain any discernible ER localizing signal peptides.[34] As a result, the glycans are not attached to the typical Asn-X-Ser/Thr acceptor peptide sequence, commonly recognized by the glycosyltransferases and glycosidases of the ER and Golgi apparatus.[34] Instead, the glycans are assembled in the cytoplasm, bypassing the host's ER and Golgi altogether.[34] In addition to the acceptor peptide sequence variations, chloroviruses express unique *N*-linked glycan structures.[34, 35] The major capsid protein (MCP) of chloroviruses is a glycoprotein, with *N*-linked glycans linked to asparagine through an uncommon β-glucosyl linkage.[34, 35] The dominant glycoforms are species-specific but share a common, conserved core (**Figure 1-2**). The conserved core is a pentasaccharide comprised of four different sugars: an Asn-linked glucose coupled to a proximal xylose and a highly branched fucose residue, which in turn has a galactose residue coupled to the O-2 position.[29] The fucose residue is further elaborated with an additional distal xylose residue at the O-4 position. A semi-conserved L- or D-rhamnose residue is found at the O-3 position of the central fucose residue, making up the extended core region.[29] Further elaboration of the core structure is specie dependent with variations in the substitution of additional sugar residues; typically, extending from the proximal

and distal xylose as well as the semi-conserved rhamnose. Moreover, the glycoforms contain varying degrees of methylation, typically found on capping rhamnose residues.[34, 35]

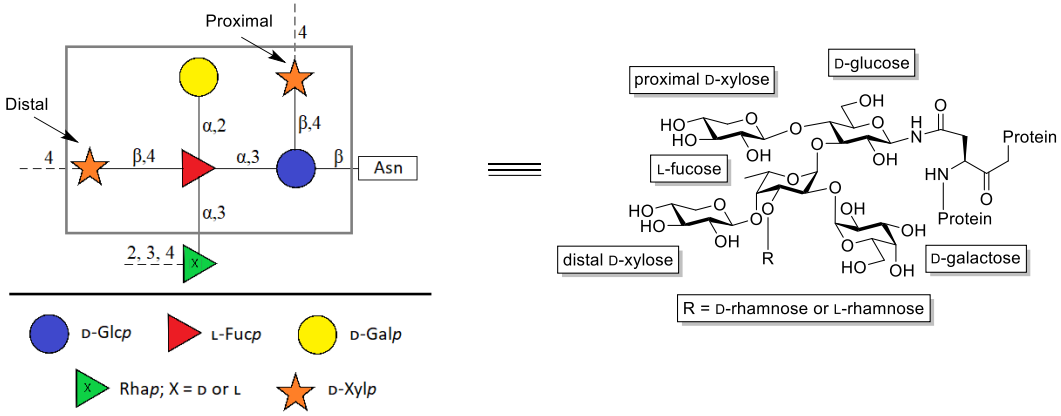


Figure 1-2: The structure of the conserved *N*-glycan core of chloroviruses[35] in both pictorial and bond-line form. Inclusion of the semi-conserved rhamnose residue makes up the "extended core region". Dashed lines represent sites of further elaboration; the extent is virus specific.

1.3.4 The paradox of PBCV-1 viral-encoded glycosyltransferases

MCPs of the chlorovirus PBCV-1 express four *N*-linked glycans.[34] The predominant glycoform is a nonasaccharide in which the conserved glycan core is further elongated at the O-4 position of the distal xylose with an additional three sugar residues: 2,3-*O*-methyl-α-L-Rha*p*-(1→2)-[β-L-Ara*f*-(1→3)]-β-L-Rha*p*.[35] Furthermore, the O-3 position of the core region galactose is substituted with α-D-mannose residue.[35] Both the mannose (red) and arabinose (blue) residues occur as nonstoichiometric substituents, generating four glycoforms (**Figure 1-3**).[35] A total of six GTs are predicted to be encoded by PBCV-1.[28, 34] While a small number, compared to the number of different glycosidic linkages, they are thought to be responsible for the observed

structural complexity of the expressed *N*-glycans.[28] This discrepancy between the restricted glycosylation capabilities and the glycan structural complexity lends itself to several theories. First, is that one (or more) of the predicted GTs may be responsible for multiple processes; that is, they have more than one functional domain. Second, is the possibility of misidentified viral GT genes, which have no homologs in databases. Finally, there exists the possibility of host-encoded GT(s) involvement.[28]

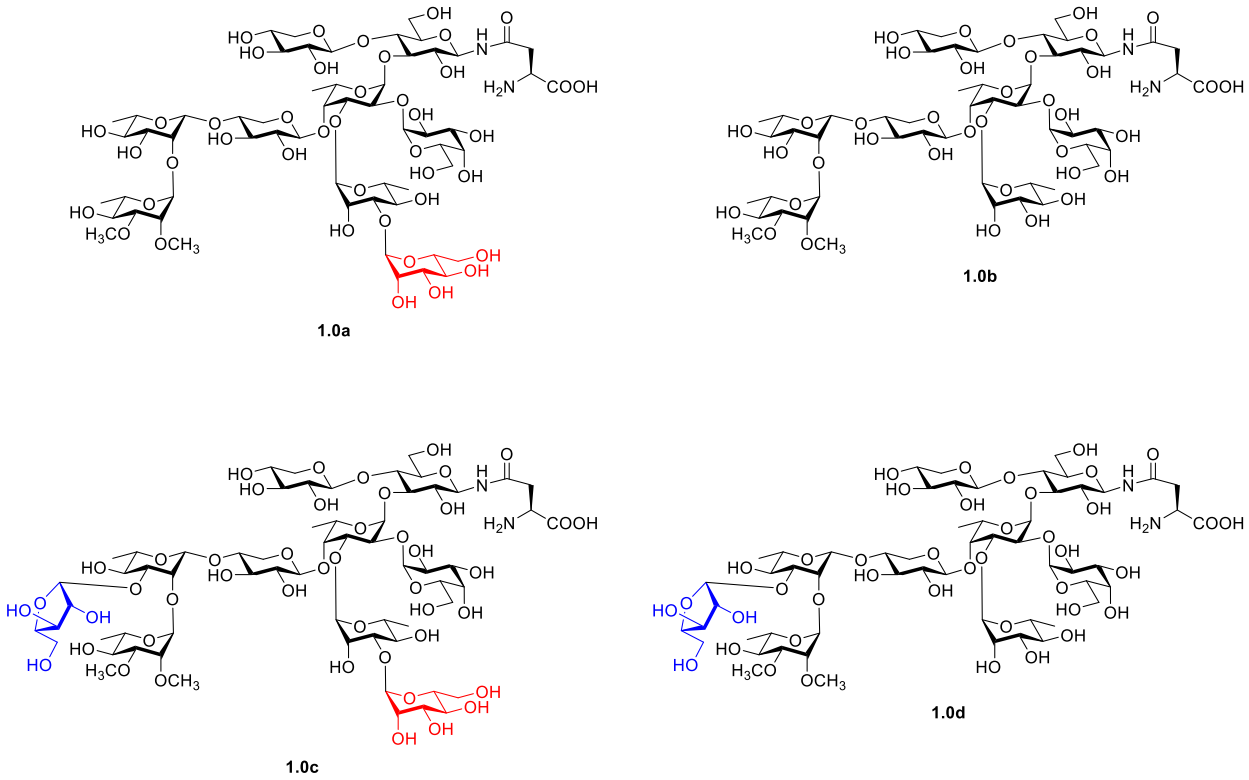


Figure 1-3: Structures of the four MCP *N*-glycans (**1.0a–b**) expressed by the chlorovirus PBCV-1. The two left structures are the most abundant glycoforms. The mannose (red) and arabinose (blue) residues appear as nonstoichiometric substituents.

1.4 Synthetic efforts towards glycans of the major capsid protein of chloroviruses

1.4.1 Linear approach

The first synthesis of a natural glycan found on the MCP of a chlorovirus was accomplished in 2018 by Lin and Lowary.[7] The target was the *N*-linked hexasaccharide **1.1** expressed by the chlorovirus ATCV-1 (**Figure 1-4**). The glycan consists of the conserved pentasaccharide core (composed of D-glucose, L-fucose, D-galactose, and two D-xylose residues) and the semi conserved L-rhamnose. In addition, the O-4 positions of both xylose residues as well as O-3 of the rhamnose residue are methylated. Given the rather complex structure, the hyperbranched fucose residue proved to be a challenge to introduce.[7]

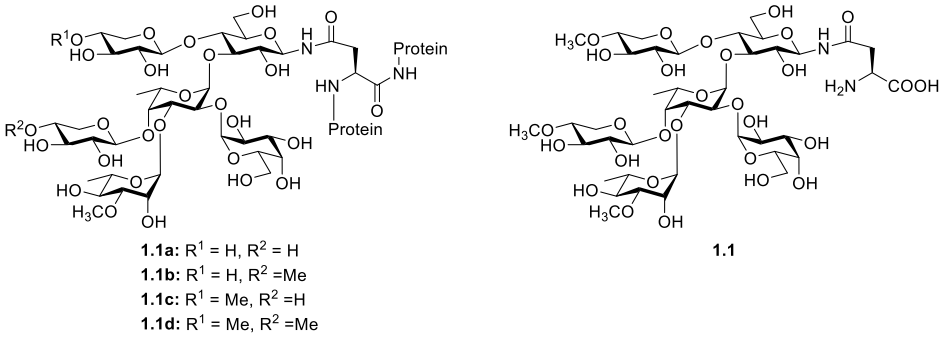
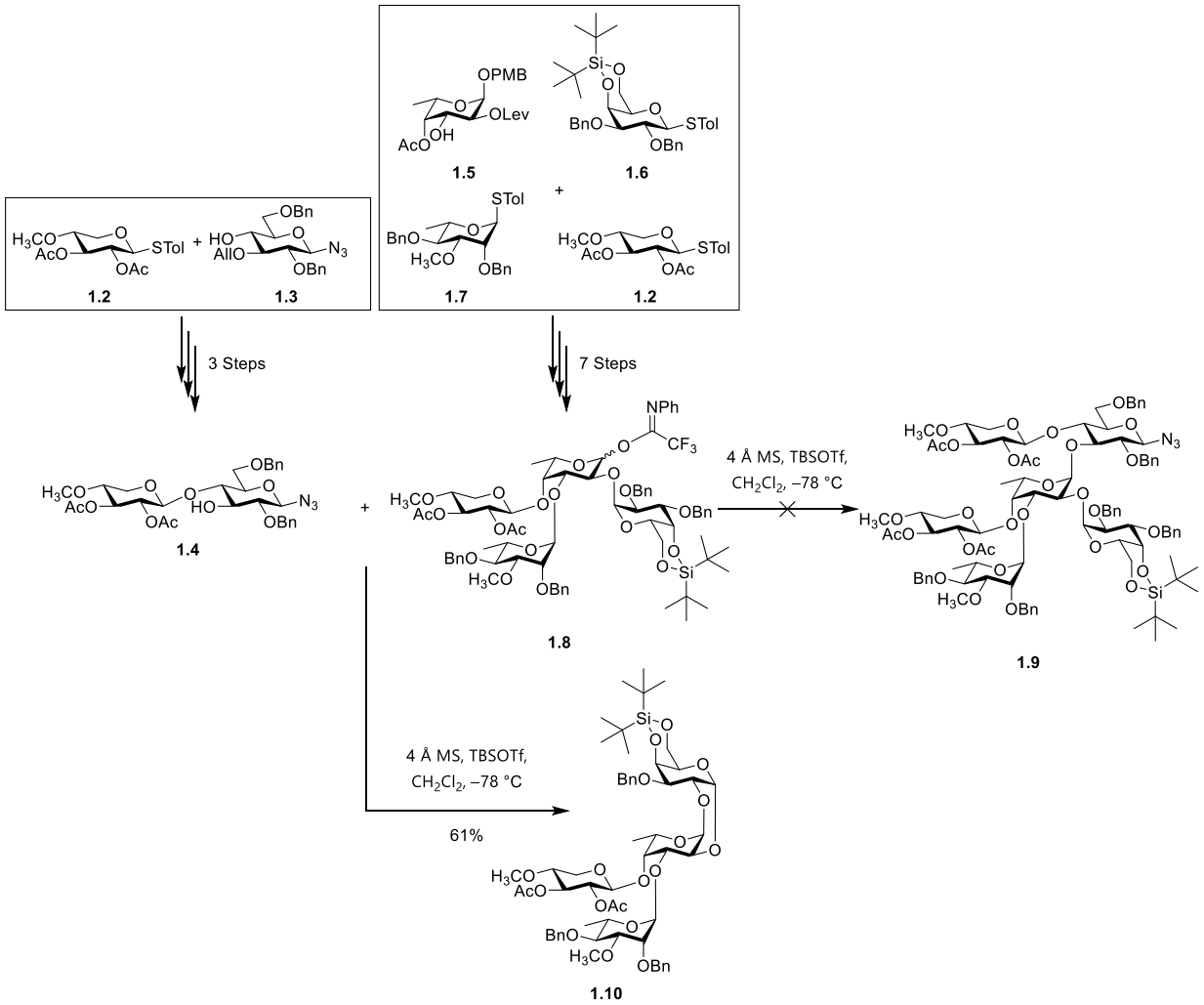


Figure 1-4: Structure of chlorovirus ATCV-1 *N*-glycans (**1.1a–d**) and the glycan structure used as synthetic target (**1.1**).[7]

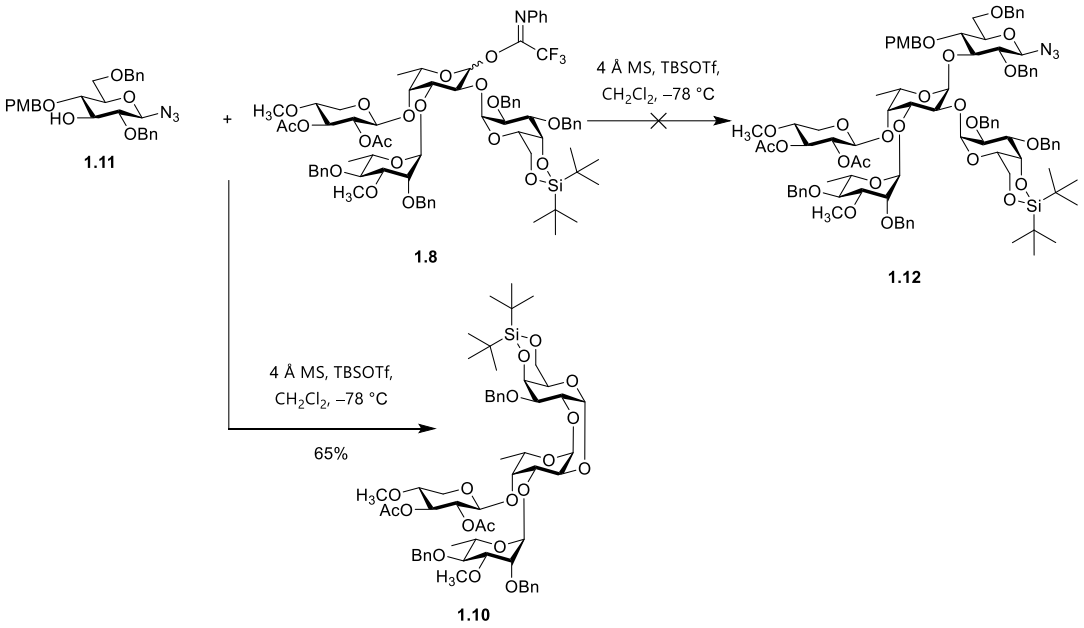
Initially, a convergent 4 + 2 strategy was explored (**Scheme 1-1**). The *N*-phenyl-trifluoroacetimidate tetrasaccharide donor **1.9** (prepared from the monosaccharides **1.2** and **1.5**–**1.7**) was glycosylated with the disaccharide acceptor **1.4** (prepared from the monosaccharides **1.2**

and **1.3**) using *tert*-butyldimethylsilyl trifluoromethanesulfonate as the promotor (TBSOTf). However, the desired hexasaccharide **1.9** was not observed. Instead, the major product was the anhydride **1.10**. Formation of the product was thought to be due to steric congestion surrounding the glycosylation site. Thus, in the event of imidate activation, the O-2 of the galactose residue proved a better nucleophile for the resulting oxonium ion intermediate than the alcohol. Then loss of the benzyl group would afford **1.10**.[7]



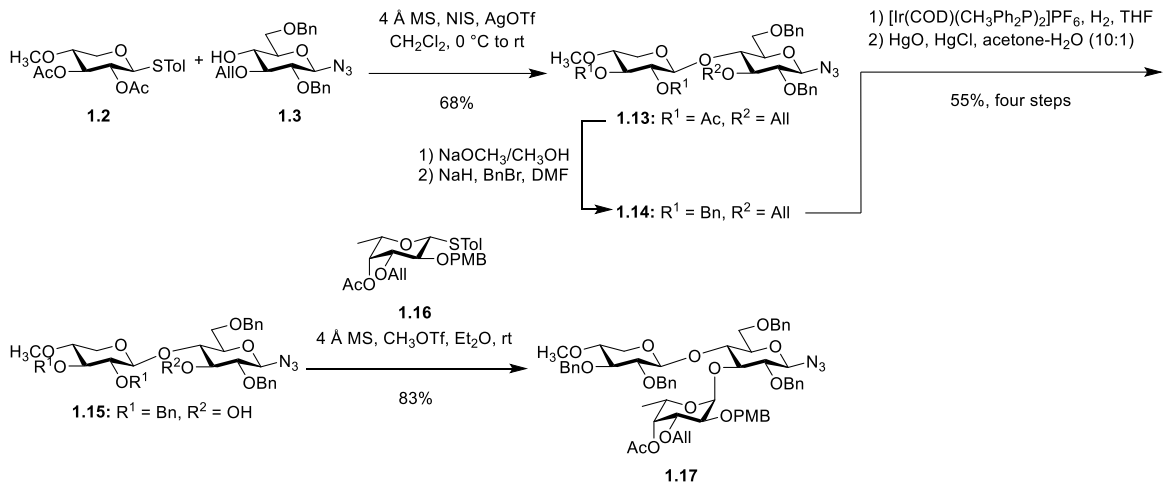
Scheme 1-1: Attempted convergent 4 + 2 strategy by Lin and Lowary.[7]

A convergent 4 + 1 strategy was also explored using the same the *N*-phenyl-trifluoroacetimidate tetrasaccharide donor **1.8** and the glucosyl azide acceptor **1.11** (**Scheme 1-2**). The outcome was the same; the desired glucoside product **1.12** was not observed, and **1.10** was the major product.[7]



Scheme 1-2: Attempted convergent 4 + 1 strategy by Lin and Lowary.[7]

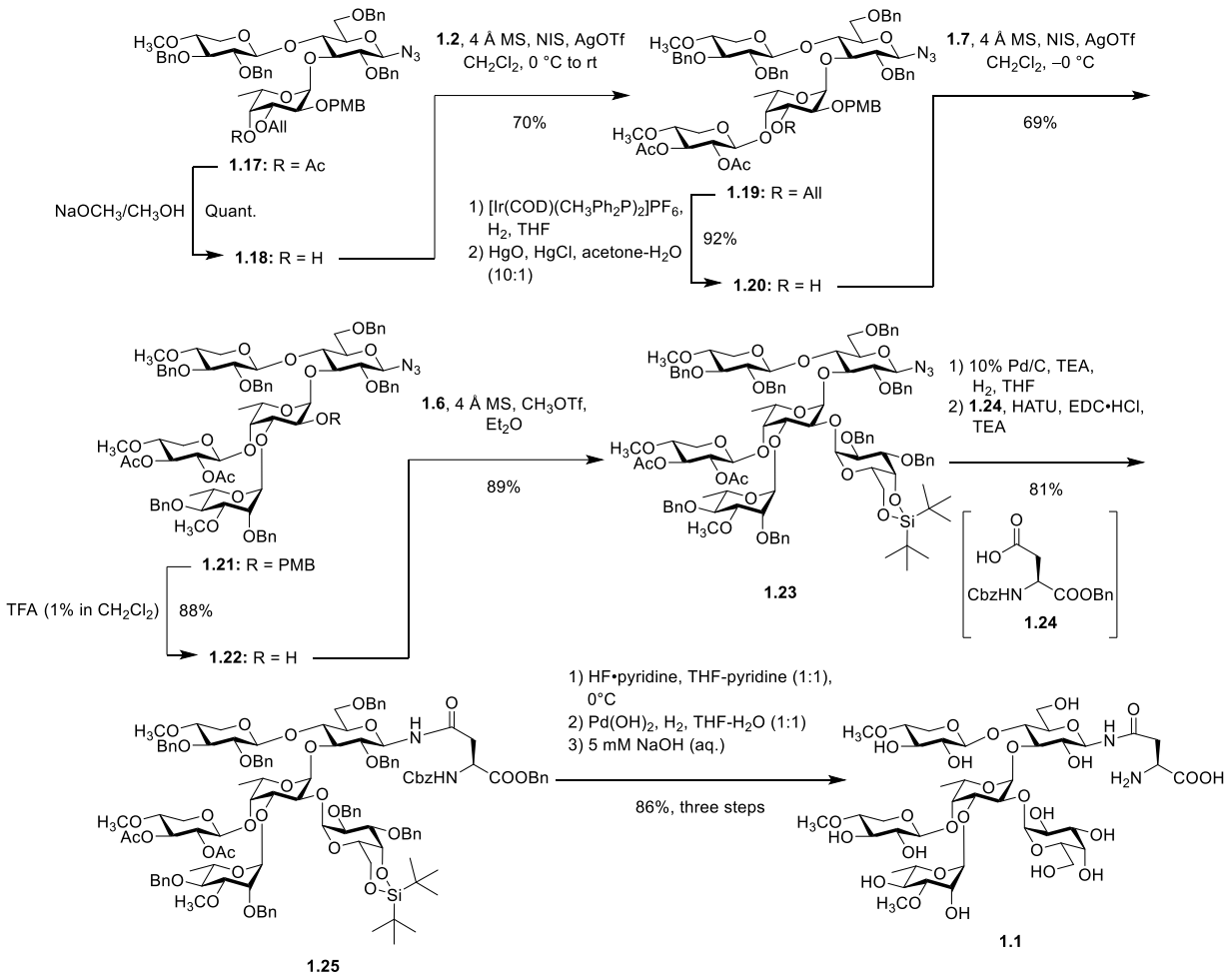
With the lack of success using a convergent approach, a linear synthetic strategy was adopted. Rather than coupling two, large, bulky subunits together, the individual monosaccharides were attached one at a time. The previous attempts suggested that the formation of the Fuc*p*-(1→3)-Glc*p* linkage had to be made prior to the introduction of the galactose residue. Thus, to prevent the formation of **1.10**, trisaccharide **1.17** was first synthesised as described below (**Scheme 1-3**).[7]



Scheme 1-3: Synthesis of orthogonally protected trisaccharide **1.17** by Lin and Lowary.[7]

The intent was to have the fucose residue contain three orthogonal protecting groups, allowing for sequential deprotection (**Scheme 1-4**). However, this approach required protecting group modification of the previously used disaccharide acceptor (**1.4**). The acetyl groups of the xylose residue were exchanged for benzyl groups to allow selective remove the acetyl group of the fucose later in the synthesis. The glycosylation of the disaccharide acceptor **1.15** with the fucose donor **1.16** yielded (83%) the desired trisaccharide **1.17** with high α-selectivity. The acetyl group of the fucose O-4 was proposed to aid in the selectivity via remote participation.[36] It was found that the order in which the remaining residues surrounding the fucose unit were added, mattered. The introduction of the remaining residues had to start with the xylose at O-4 of the fucose and follow a counter clockwise pattern. Introduction of the rhamnose residue at O-3 prior to the xylose at O-4 was explored but proved to be unsuccessful, likely due to steric congestion of the glycosylation site.[7] Thus, the trisaccharide **1.17** was deacetylated using

standard Zemplén conditions to yield **1.18.** The resulting acceptor **1.18** was glycosylated with the xylose donor **1.2** using *N*-iodosuccinimide and silver triflate to give **1.19** in 70% yield. Following a counter clockwise pattern, the allyl group was removed and the revealed hydroxyl group glycosylated with **1.7** to give the pentasaccharide **1.21**. Acidic treatment of **1.21** with 1% trifluoracetic acid in dichloromethane gave the acceptor **1.22** in 88% yield and was then glycosylated with **1.6** to give the desired hexasaccharide **1.23**. The α-product was insured through the use of the di-*tert*-butylsilylene group.[37] The final major step in the synthesis involved the amino acid coupling. The azide was reduced using palladium-catalyzed hydrogenation and the resulting glucosyl amine coupled with the protected protein **1.24**. A stochiometric amount of triethylamine was required to prevent hydrogenolysis of the benzyl ethers as well as minimizing the anomerization of the glycosyl amine intermediate. Finally, global deprotection of **1.25** gave the desired product **1.1** with an overall yield of 13% over 16 steps, starting from **1.3**.[7]

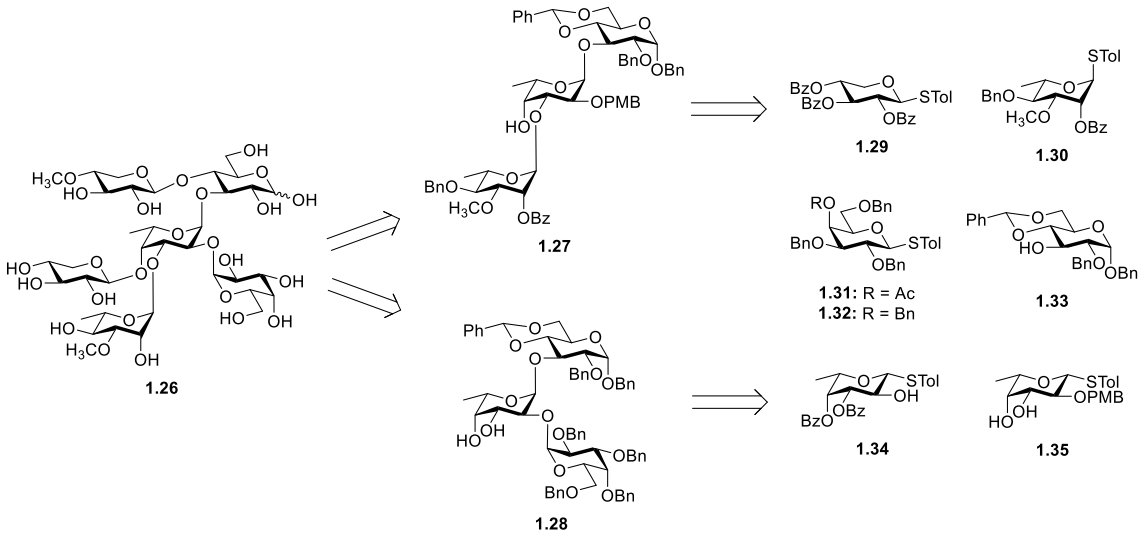


Scheme 1-4: Synthesis ATCV-1 *N*-glycan **1.1** by Lin and Lowary.[7]

1.4.2 Preactivation-based one-pot approach

In another, more recent study, Ye and coworkers set out to synthesize hexasaccharide **1.26**, an analog of the ATCV-1 *N*-glycan (**Scheme 1-5**), using a 4-toluenesulfonyl chloride/silver triflate preactivation-based one-pot strategy with a focus on reducing the number of protecting group manipulations. Several synthetic routes were explored before settling on an

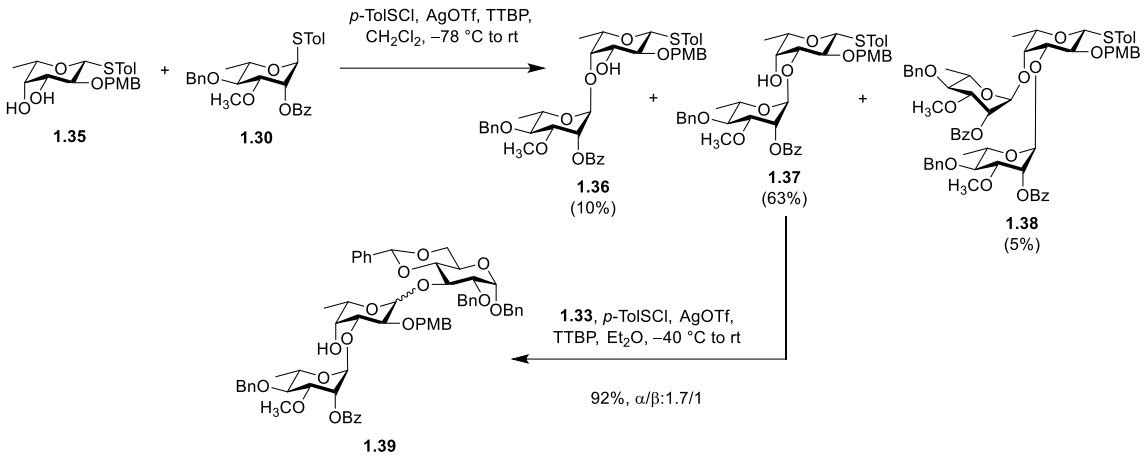
optimal route that was able to effectively make use of a three-component one-pot glycosylation.[11]



Scheme 1-5: Retrosynthetic analysis of target synthetic ATCV-1 glycan analog by Ye and coworkers.[11]

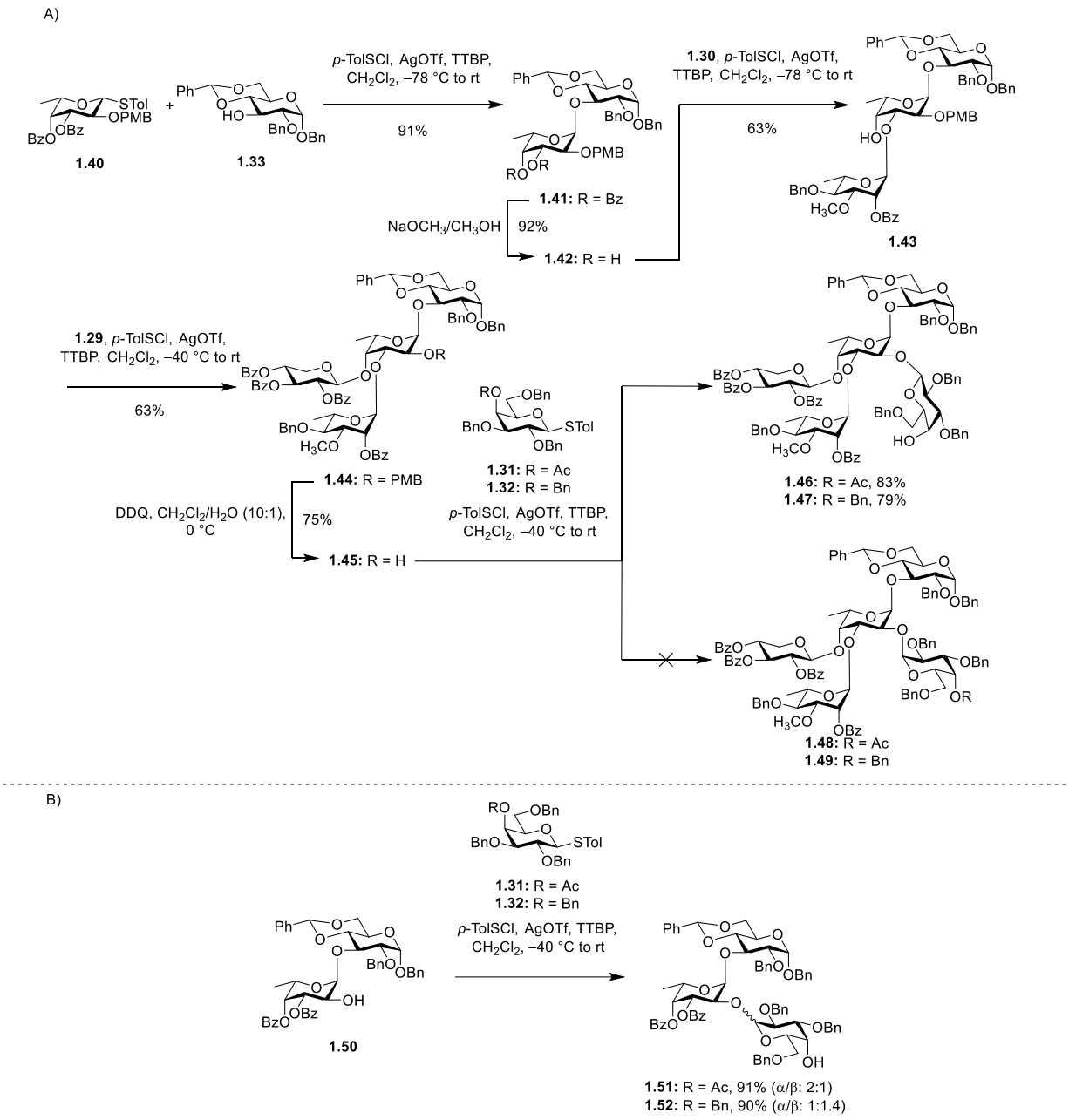
Initially, the synthesis of the trisaccharide intermediate **1.27** using the fucoside acceptor **1.35** and the thiorhamnoside donor **1.31** was envisioned (**Scheme 1-6**). In attempts to minimize protecting group manipulations, the route relied on the regioselectivity resulting from the reactive differences between the axial and equatorial hydroxyl groups in **1.35**. When glycosylated using 4-toluenesulfonyl chloride/silver triflate activation, the desired disaccharide **1.37** was obtained (63% yield) along with the di-glycosylated product **1.38** (5%) and O-4 glycosylated product **1.36** (10%). Disaccharide donor **1.37** was then coupled with the glucose acceptor **1.33**; however, the glycosylation lacked stereocontrol and an anomeric mixture of **1.39**

was obtained (α/β ratio 1.7/1, 92%). Ultimately, the low efficiency of the synthetic route led to its abandonment.[11]



Scheme 1-6: Attempted synthesis of trisaccharide intermediate **1.39** of ATCV-1 glycan analog by Ye and coworkers.[11]

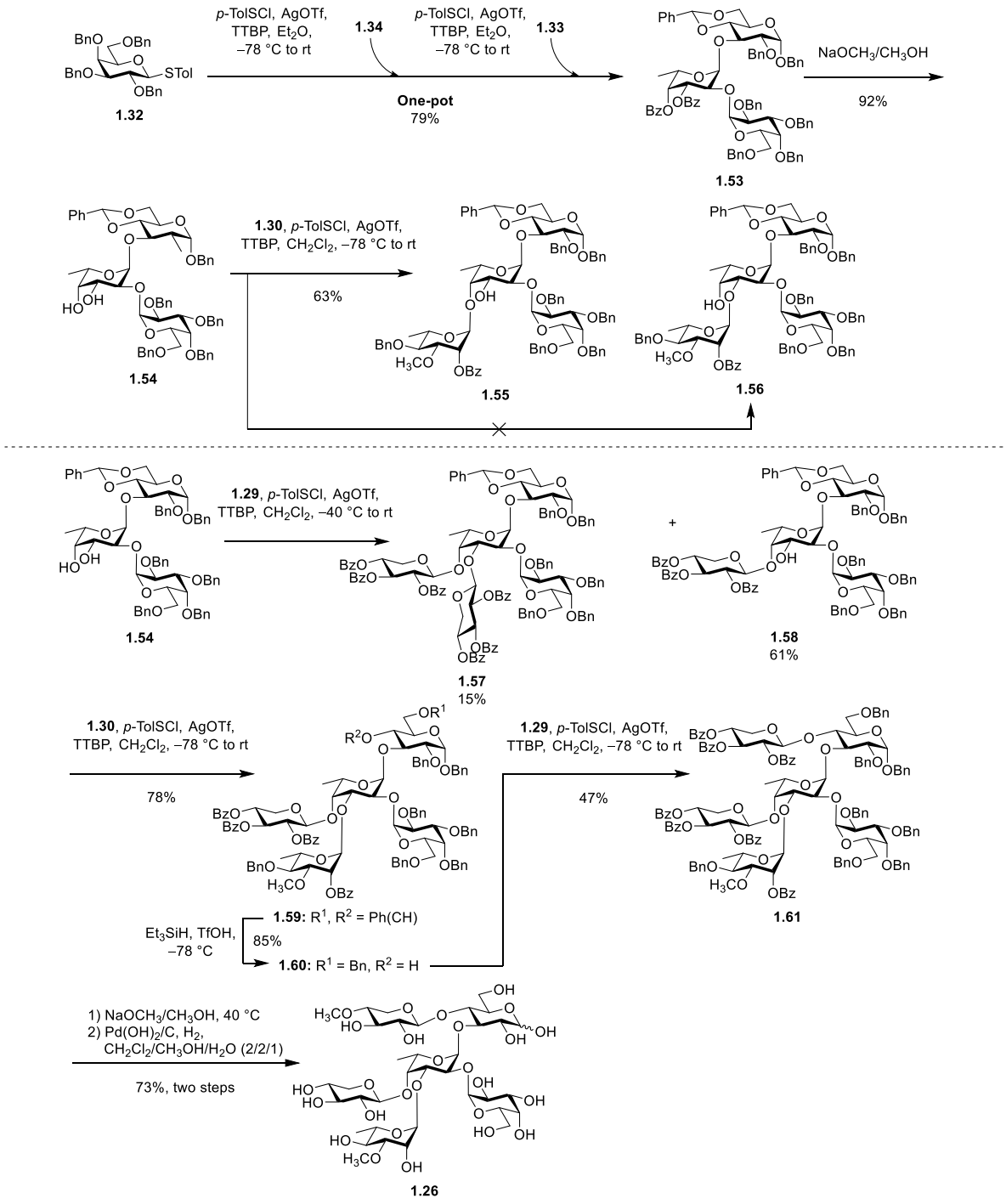
After establishing the need for stereocontrol in the introduction of the glucose residue, a second synthetic route was explored (**Scheme 1-7**). The use of a remote participating acyl group at the fucosyl O-4 position was required to ensure *α*-selectivity of the product. Disaccharide **1.41** was obtained through the glycosylation of thiofucoside donor **1.40** with glucoside acceptor **1.33** (91%) with exclusive *α*-selectivity. Again, relying on regioselectivity of the hydroxyl reactivity, the benzoyl groups were removed and the subsequent disaccharide **1.42** glycosylated with **1.30** to give the trisaccharide **1.43** (63%). The obtained product was then coupled with thioxyloside donor **1.29** to give the tetrasaccharide **1.44** (79%) and this compound subjected to PMB deprotection using DDQ. The resulting tetrasaccharide acceptor **1.45** was glycosylated with



Scheme 1-7: A) Attempted synthesis of pentasaccharide intermediate of ATCV-1 glycan analog by Ye and coworkers. B) Attempted galactose glycosylation with less sterically hindered disaccharide acceptor by Ye and coworkers.[11]

per-benzylated thiogalactoside donor **1.32**; however, the desired product **1.49** was not observed – only the product with the *β*-galactosyl linkage (**1.47**) was obtained. The O-4 acetylated thiogalactoside donor **1.31** was also explored in hopes that remote participation of the acetyl group would promote *α*-selectivity. Again, only the *β*-product (**1.46**) was observed. It was speculated that steric congestion surrounding the hydroxyl group prevented *α*-attack. Further exploration supported this supposition. Two galactose donors (**1.31** and **1.32**) were tested with the less sterically hindered disaccharide **1.50**. While *α*-isomers were observed, they were formed in lesser amounts then the *β*-isomers (**1.51** and **1.52**). Thus, this approach was also abandoned.[11]

A third synthetic route was proposed. This time, the synthesis began with the two 1,2-*cis* glycosylations, using a 4-toluenesulfonyl chloride/silver triflate preactivation one-pot strategy (**Scheme 1-8**). The preactivated per-benzylated thiogalactoside donor **1.32** was first glycosylated with the fucoside acceptor **1.34**. After complete consumption of the acceptor, a second round of preactivation was performed followed by the addition of the glucoside acceptor **1.33**. The desired tetrasaccharide **1.53** was obtained in 79% yield with high *α*-selectivity. The benzoyl groups were then removed and **1.54** was coupled with the thiorhamnoside donor **1.30**. However, unlike the previous attempts where substitution at the O-3 position was regioselectively favoured, **1.30** was added to the O-4 position giving the tetrasaccharide **1.55**. This was attributed to the O-4 position being less sterically hindered. Instead, **1.54** was glycosylated with the thioxyloside donor **1.29**, giving the desired tetrasaccharide **1.58** (61%) as well as a small amount of di-glycosylated product **1.57** (15%). Tetrasaccharide **1.58** was then coupled with **1.30** to give the target pentasaccharide **1.59** (78%). Finally, the benzylidene ring of **1.59** was selectively opened, giving the acceptor **1.60** (85%), which was subsequently glycosylated with the thioxyloside **1.29**. The hexasaccharide **1.61** was obtained in 47% yield. Global deprotection of **1.61** generated the final



Scheme 1-8: Synthesis of target hexasaccharide analog **1.26** of ATCV-1 glycan by Ye and coworkers.[11]

target hexasaccharide **1.26** in 73% (two steps). Overall, this preactivation-based one-pot strategy gave the desired hexasaccharide product in eight steps with a total yield of 10% – from the initial monosaccharide building blocks.[11]

1.5 Project aims

Chloroviruses express uniquely structured *N*-glycans, a result of their encoded glycosylation capabilities – a rare phenomenon among viruses.[28, 29, 35] At first glance, the number of encoded GTs seems small in respect to the structural complexity of the expressed glycans.[28] This ambiguity has prompted investigations into the viral glycosylation pathway, looking to further probe the function of the predicted GTs.[28] Moreover, the enzymatic properties of these encoded GTs may prove to have application in the chemo-enzymatic synthesis of glycans.[38]

The aim of the project is to synthesis several potential biosynthetic intermediates of the MCP *N*-glycan expressed by the chlorovirus PBCV-1 (**Figure 1-5**). The glycan analogs **1.62–1.64** are based on observed truncated glycans expressed by mutant PBCV-1 virions.[28] In doing so, the methodologies previously established by Dr. Sicheng Lin will be employed.[7] The target oligosaccharides are to be synthesised using a similar, linear approach. The use of an orthogonally protected fucose residue, will allow for selective protecting group removal and subsequent glycosylation to access the desired structures. Additional structural intermediates **1.65–1.67** were also targeted for synthesis as they could be readily accessed during the synthesis of the previous three compounds.

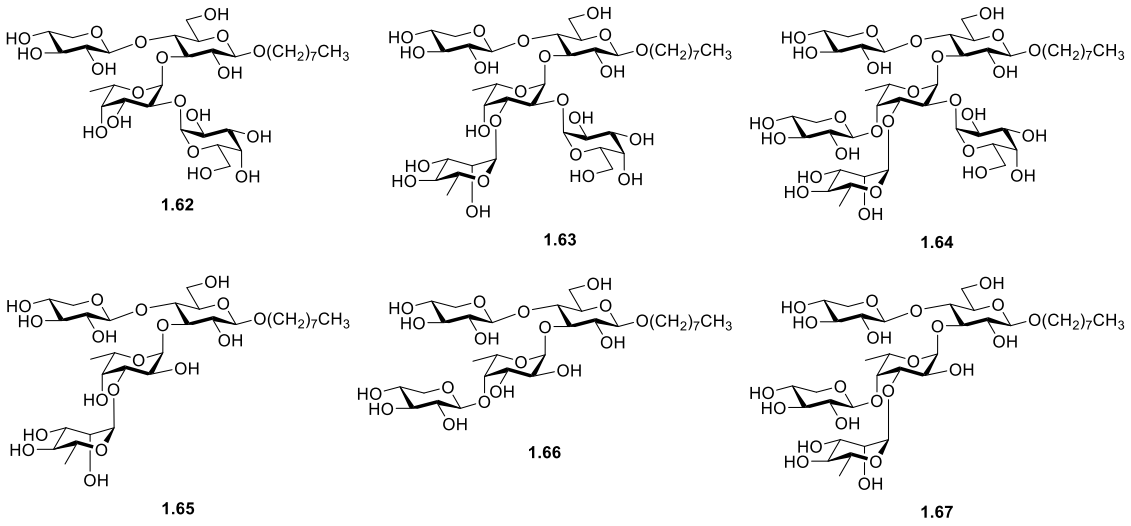


Figure 1-5: Structures of target analogs of the major MCP *N*-glycan of chlorovirus PBCV-1.

The compounds are of interest to the group of Dr. Cristina De Castro (University of Naples), a collaborator of the Lowary group, who are looking to further investigate the viral *N*-glycan biosynthetic pathway of the chlorovirus PBCV-1.

1.6 References

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Chapter 2

Synthesis of Chlorovirus PBCV-1 *N*-Glycan Analogs

2.1 Background

Since the discovery of their unique *N*-glycans [1, 2], chloroviruses have been the subject of several studies trying to probe the viral glycosylation biosynthetic pathways.[1–7] Notably, analysis of the chlorovirus PBCV-1 genome has revealed several carbohydrate processing genes, six of which are thought to be putative glycosyltransferases: *a064r*, *a111/114r*, *a219/222/226r*, *a4731*, *a5461*, and *a0751*.[7, 8] Furthermore, based on their amino acid sequences, computational predictions have suggested the protein products to be soluble and localized in the cytoplasm.[7] The current hypothesis is that the viral glycan assembly takes place in the host's cytoplasm and the six putative GTs are responsible for the formation of most, if not all, the glycosidic bonds.[7]

A recent study conducted by De Castro and co-workers focused on exploring the roles of the putative GT gene products of the chlorovirus PBCV-1.[7] Predicted protein function was inferred from observed antigenic variants (**Figure 2-1**), resulting from spontaneous mutations.[7]

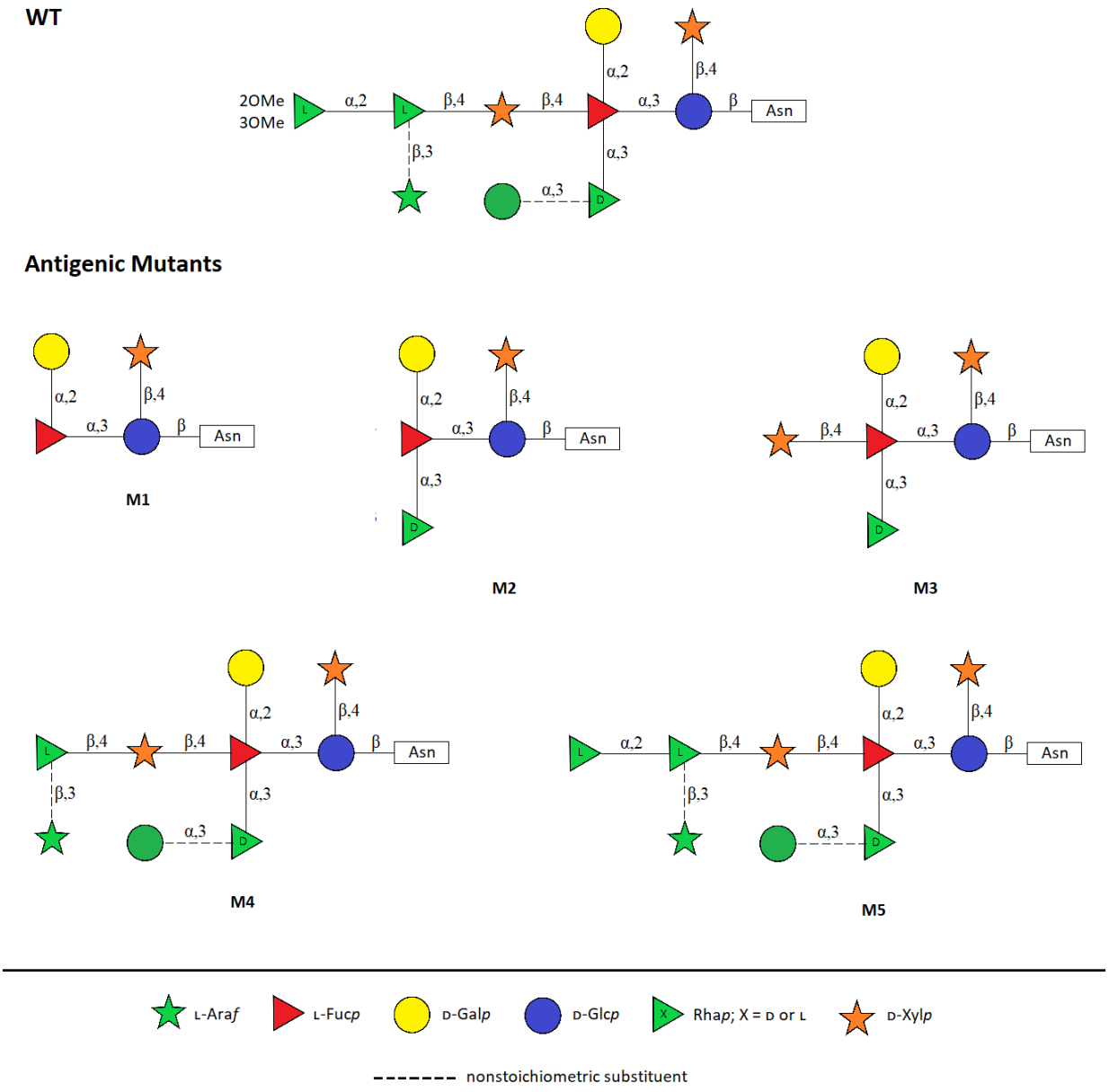


Figure 2-1: The observed truncated MCP *N*-glycan structures of PBCV-1 antigenic mutants along with the wild type (WT) structure.[7]

PBCV-1 mutants were identified based on their reaction with polyclonal antibodies; their MCP *N*-glycans characterized, and the associated genetic mutations mapped.[7] The truncated

glycan structures along with the associated genetic mutations were used to infer the protein functions of the putative GT genes: *a064r*, *a0751, a111/114r*, as well as the previously unrecognized *a075r* gene (**Figure 2-2**).[7] The *a064r* gene, a unique gene to PBCV-1, was proposed to encode a protein with three domains: domain 1 a *β*-L-rhamnosyltransferase, domain 2 an *α*-L-rhamnosyltransferase, and domain 3 a methyltransferase.[7] The *a075r* gene, while previously unrecognized as a putative GT by initial genomic database comparisons, was proposed to encode a GT responsible in the addition of the semi-conserved rhamnose to the fucose of the conserved glycan core.[7] Both the *a0751* and *a111/114r* genes are found throughout all currently sequenced chloroviruses, suggesting they are responsible for the introduction of shared glycan elements.[7, 8] The *a0751* gene was found to encode a *β*-xylosyltransferase; responsible for the attachment of the distal xylose to the central fucose residue, making up part of the conserved glycan core.[7] Lastly, it was suggested that the putative GT from the *a111/114r* gene is responsible for the assembly of the remainder of the conserved glycan core. However, to what extent, remains unknown.[7] Furthermore, it is still unclear whether or not additional PBCV-1 encoded proteins or host-encoded enzymes are involved in the assembly of the glycan core and its attachment to the viral MCP.[7]

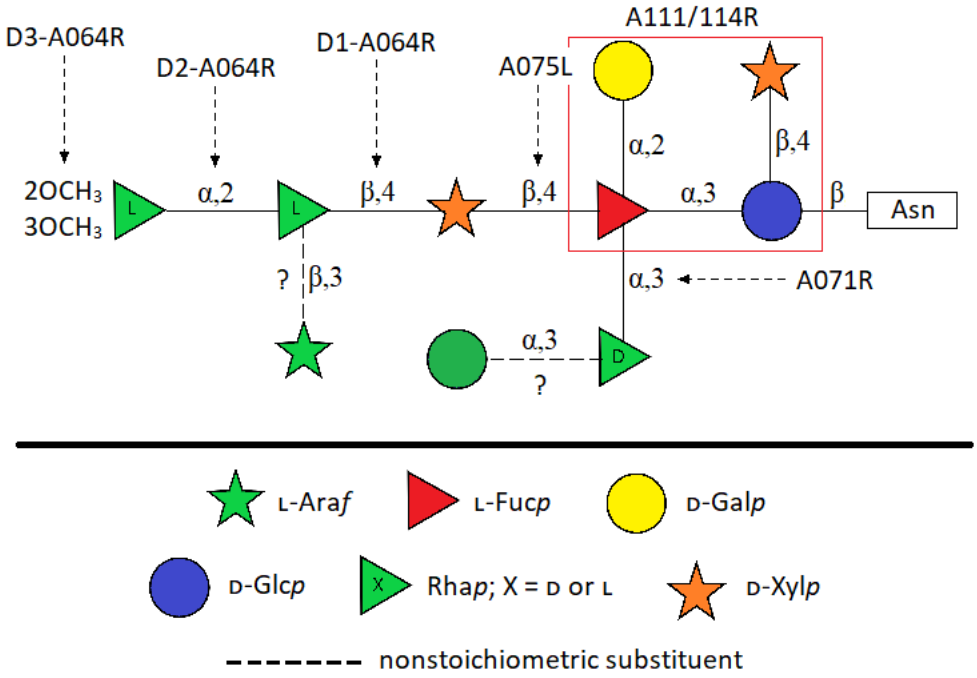


Figure 2-2: Diagram of chlorovirus PBCV-1 MCP *N*-glycan structure anointed with predicted GT activity (red box: conserved glycan core; D = domain).[7]

The three truncated glycans **2.1**, **2.2**, **2.3** (**Figure 2-3**) were chosen as biologically significant synthetic targets and served as the basis of this thesis. These structures are of interest for the group of Dr. Cristina De Castro, and are to be used as probes to investigate the viral glycan biosynthetic pathway. In this chapter, the synthesis of PBCV-1 *N*-glycan analogs will be described.

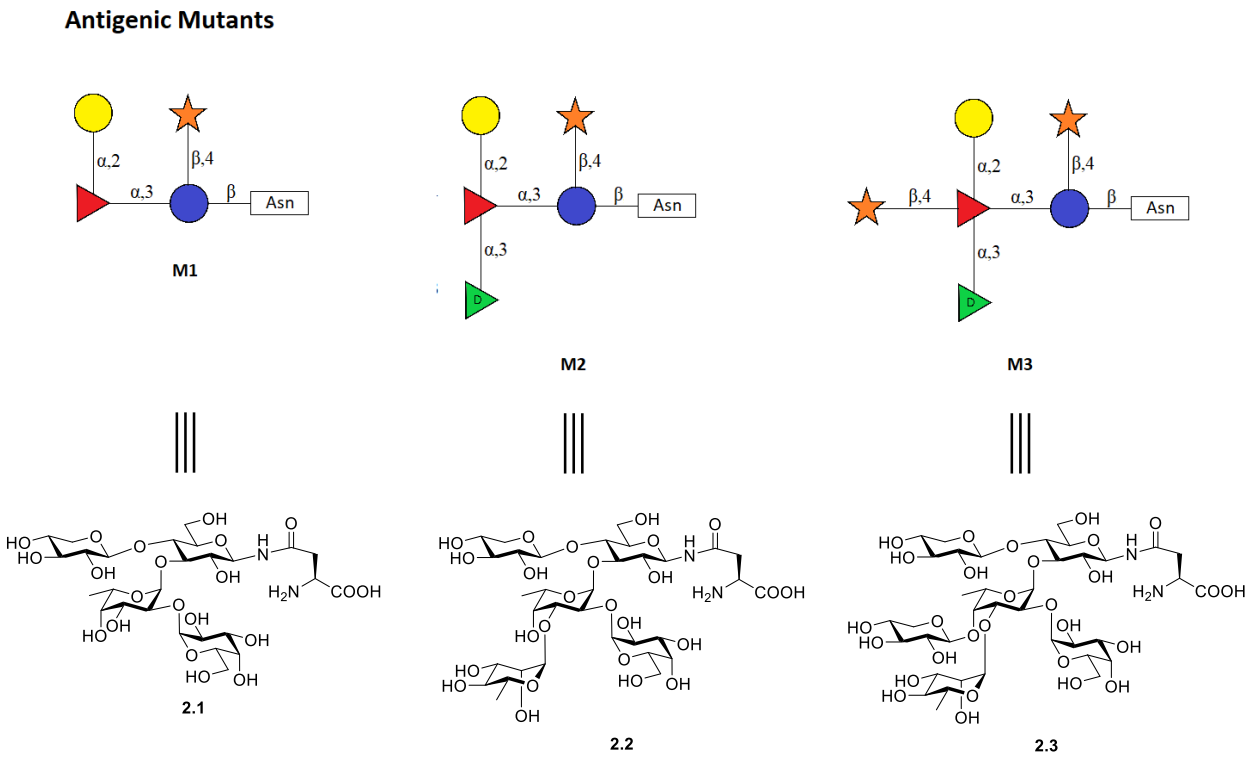
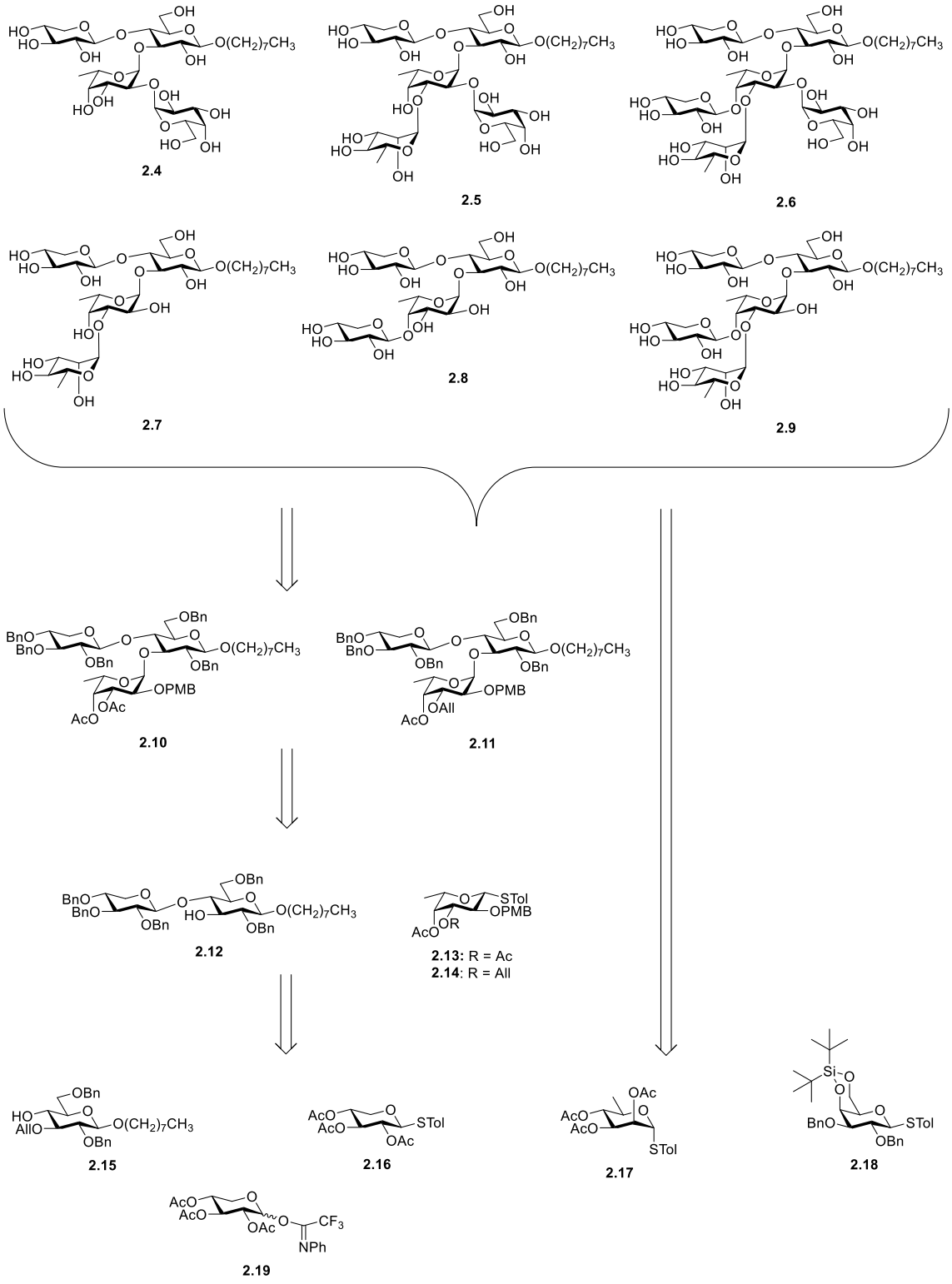


Figure 2-3: Structure of antigenic mutant PBCV-1 *N*-glycans used to design synthetic targets, in both pictorial and line-bond form.

2.2 Results and discussion

2.2.1 Retrosynthetic analysis

As mentioned in Chapter 1, the six target *N*-glycan analogs (**Figure 2-4**) include the octyl glycosides **2.4**, **2.5**, and **2.6** derived from three truncated MCP *N*-glycans of mutant PBCV-1 viruses (**2.1**, **2.2**, and **2.3**). Moreover, the additional three structures **2.7**, **2.8**, and **2.9** – which are deprotected versions of synthetic intermediates – were to be produced, as these molecules could be of use in probing the viral glycan biosynthetic pathway.



Scheme 2-1: Retrosynthetic analysis of target PBCV-1 *N*-glycan analogs (**2.4–2.9**).

In nature, these glycan structures are found attached to a peptide (Asn) at the reducing end.[8] However, during their synthesis in vivo, they are assembled first on a lipid carrier then transferred "en bloc" to the target protein acceptor.[8] To mimic the structural intermediates of this biosynthetic process, a lipophilic group (an octyl group) was to be incorporated at the reducing end of the synthetic targets.[9]

In synthesis of the target oligosaccharides, the linear approach developed by Lin and Lowary was to be applied.[9, 10] A total of five unique monosaccharides make up the target structures (**Scheme 2-1**), with each structure being based on a central α-L-Fuc*p*-(1→3)-[β-D-Xyl*p*-(1→4)]-β-D-Glc*p* trisaccharide. The branched structures could be obtained through selective glycosylations at the appropriate positions around the fucose residue. The use of orthogonal protecting groups (an acetate ester, allyl ether, and a 4-methoxybenzyl ether) would allow for selective access to the desired hydroxyl groups and subsequent glycosylation. As initially planned, the targets were thought obtainable from the seven monosaccharide building blocks **2.13–2.19**. In doing so, the use of acetate protecting groups were employed as often as possible due to their ease of preparation and deprotection, as well as, their ability to control glycosylation stereochemistry through neighboring group participation. The C-2 acetate groups of the proposed xylose and rhamnose donors would be required to ensure the *β*- and *α*-selectivity, respectively, in their corresponding glycosylated products.[11]

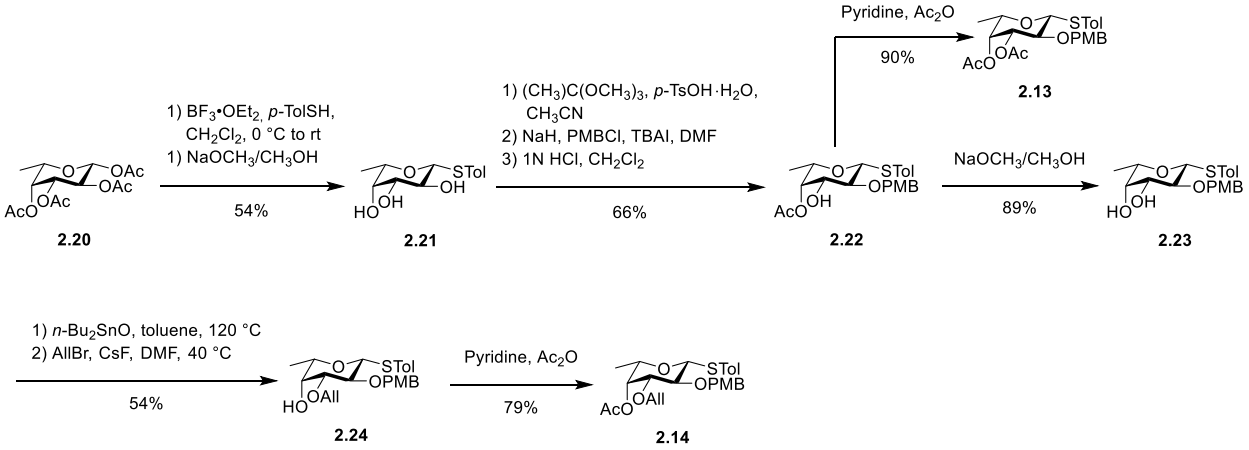
With the α-L-Fuc*p*-(1→3)-[β-D-Xyl*p*-(1→4)]-β-D-Glc*p* trisaccharide comprising the core structure of the target oligosaccharides, two intermediates – **2.10** and **2.11 –** were proposed. As discussed in Chapter 1, the formation of the Fuc*p*-(1→3)-Glc*p* linkage was required, before introduction of the galactose residue. This was done to avoid the formation of a tricyclic by-product from the intramolecular reaction with the O-2 of the galactose residue.[10] The two

proposed trisaccharides differed from one another by the protecting group situated at O-3 of the fucose residue. The intent of using **2.10** (instead of just **2.11**) was to 1) reduce the number of protecting group manipulations later in the syntheses for some targets; and 2) minimize the handling of toxic reagents used in the allyl ether deprotection, to access the tetrasaccharide **2.4**. As planned, both trisaccharide intermediates could be obtained from the glycosylation of the fucose donors **2.13** or **2.14** with the disaccharide **2.12**. Previous work found that thioglycosides with methyl triflate activation were best suited for the formation of the Fuc*p*-(1→3)-Glc*p* linkage.[9] Furthermore, the disaccharide **2.12** could be generated from the monosaccharide building blocks **2.15** and **2.16**. Initially, the thioxyloside **2.16** was proposed as the donor in this glycosylation, however, it was later found to result in poor product formation, thus the imidate version **2.19** was also explored. The use of acetyl protecting groups of the proposed xylose donors (**2.16** and **2.19**) were to help ensure *β*-selectivity of the resulting glycosidic bond through neighboring group participation. However, they would need to be exchanged for benzyl ethers later, as an acetate makes up one of the three orthogonal protecting groups of the fucose residue. From the two trisaccharides **2.10** and **2.11** the desired targets could be generated through selective deprotections and subsequent glycosylations with the monosaccharide building blocks **2.16–2.19**.

2.2.2 Synthesis of monosaccharide building blocks 2.13–2.19

The synthesis of the thiofucoside donor **2.14** [9, 10] started from per-acetylated L-fucose (**2.20**). The related donor **2.13** was straightforwardly accessed from this synthetic route (**Scheme 2-2**). Per-acetylated L-fucose (**2.20**) was first coupled with 4-methoxybenzenethiol using boron trifluoride ethyl etherate activation, then deacetylated using Zemplén conditions to furnish **2.21**

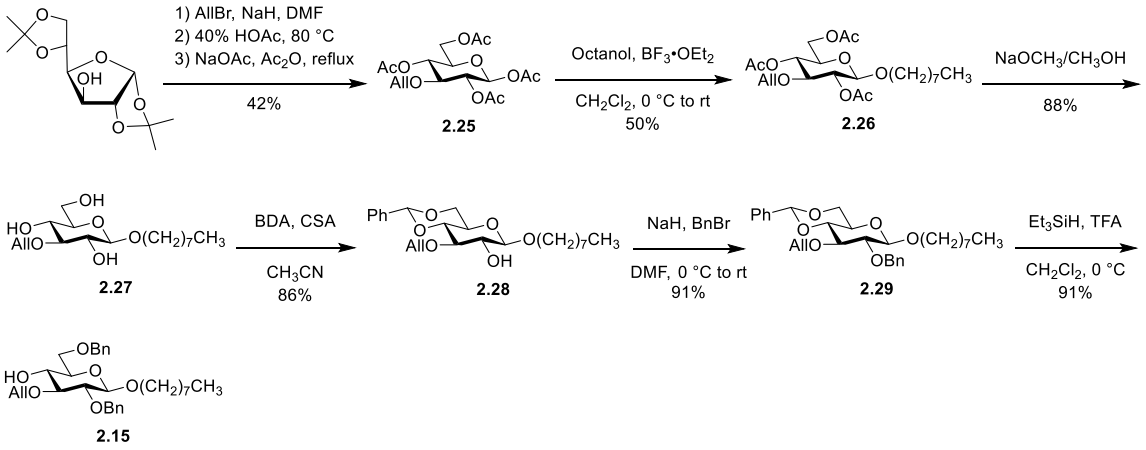
in 54% yield. The resulting triol was reacted with trimethyl orthoacetate in the presence of *p*-toluenesulfonic acid, generating a 3,4-*O*-orthoester intermediate. A subsequent reaction with 4-methoxybenzyl chloride using sodium hydride and tetra-*n*-butylammonium iodide was followed by an acid catalyzed, regioselective opening of the orthoester gave the desired product **2.22** in 66% yield over three steps. At this point, the thiofucoside donor **2.13** was obtained by acetylation of the free hydroxyl group, affording **2.13** in 90% yield. The synthesis of **2.14** involved the deacetylation of the O-4 acetate group in **2.22** to give diol **2.23** in 89% yield. A regioselective alkylation of the equatorial C-3 hydroxyl group was accomplished through the formation of a 3,4-stannylene acetal using di-*n*-butyltin oxide at reflux followed by the subsequent addition of allyl bromide and cesium fluoride at 40 °C to generate **2.24** in 54% yield. Lastly, the C-4 hydroxyl group was acetylated and the desired, orthogonally protected thiofucoside donor **2.14** was obtained in 79% yield.



Scheme 2-2: Synthesis of fucose donors **2.13** and **2.14.**

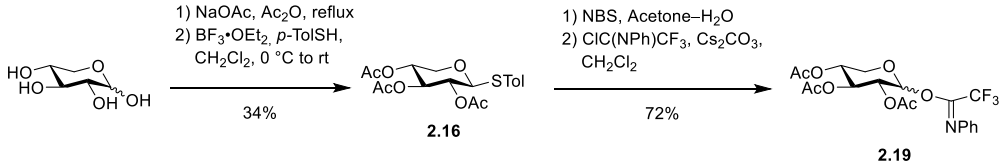
The synthesis of the glucosyl acceptor **2.15** was achieved over eight steps, starting from diacetone glucose (**Scheme 2-3**). As reported in the literature,[12] diacetone glucose was first

alkylated with allyl bromide using sodium hydride. The isopropylidene group was removed and the furanose form isomerised to the pyranose form under acidic conditions. The resulting residue was acetylated using sodium acetate in acetic anhydride at reflux to give **2.25** in 43% yield, over the three steps. Compound **2.25** was glycosylated with octanol in the presence of boron trifluoride ethyl etherate, generating the octyl glucoside **2.26** in 50% yield. Even with the *β*-directing effect of the O-2 acetyl group, a substantial portion of the *α*-glycoside was produced due to anomerization. This is known side effect of prolonged treatment with boron trifluoride.[13] Fortunately, the two anomers could be separated without much difficulty. A subsequent Zemplén deacetylation of **2.26** gave the triol **2.27** in 88% yield. Treatment of **2.27** with benzaldehyde dimethyl acetal and camphorsulfonic acid generated the desired 4,6-*O*-benzylidene acetal protected glucoside **2.28** in 86% yield. This transformation was followed by benzylation of the C-2 hydroxyl group, furnishing **2.29** in 91% yield. The final step involved the regioselective opening of the benzylidene acetal to afford a 91% yield of the octyl glucoside acceptor **2.15**.



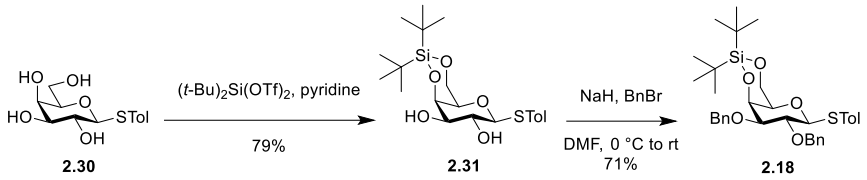
Scheme 2-3: Synthesis of glucose acceptor **2.15**.

The thioxyloside donor **2.16** was prepared from D-xylose over two steps (**Scheme 2-4**).[14] D-Xylose was first acetylated using sodium acetate in acetic anhydride at reflux. The resulting per-acetylated xylose was coupled with 4-methoxybenzenethiol using boron trifluoride ethyl etherate activation to generate **2.16** in 34% yield, over two steps. It was later determined, that the thioxyloside **2.16** was not a suitable donor. Instead, the thioglycoside donor was converted to the more reactive[15] *N*-phenyl-trifluoroacetimidate donor **2.19** over two steps (**Scheme 2-4**). To access this compound, first, **2.16** was hydrolysed with *N*-bromosuccinimide in 10:1 acetone-H_2O, then, the resulting product coupled with *N*-phenyl-trifluoroacetimidate using cesium carbonate to give **2.19** in 72% yield as a mixture of stereoisomers.



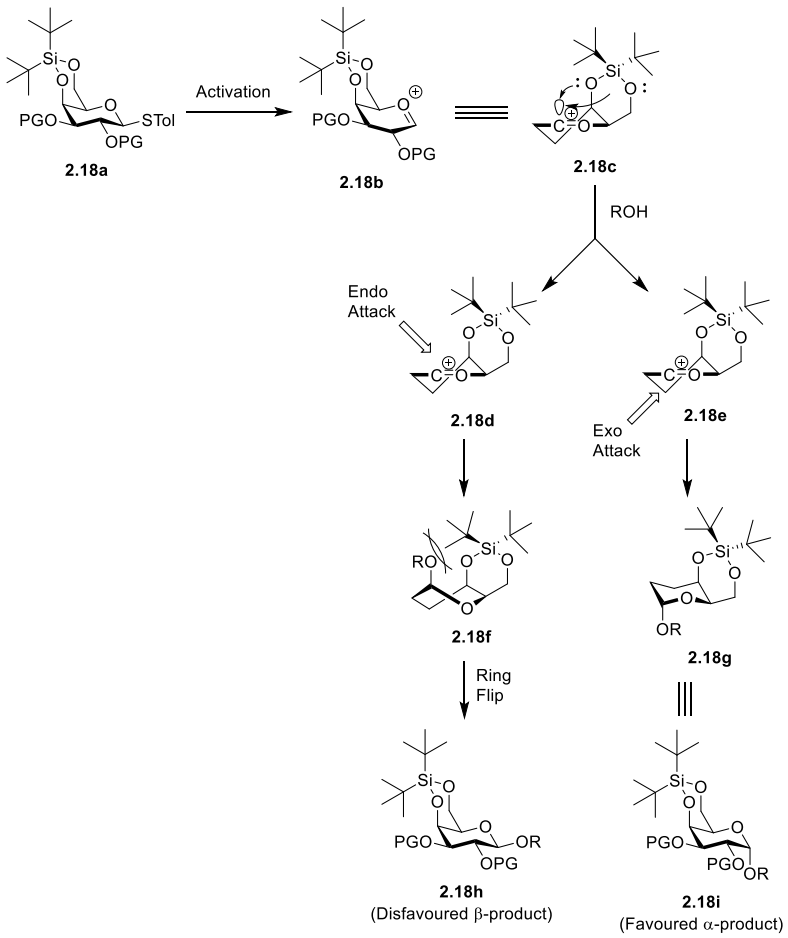
Scheme 2-4: Synthesis of xylose donors **2.16** and **2.19**.

The galactose donor **2.18** was synthesised from *p*-tolyl 1-thio-β-D-galactopyranoside (**2.30**) over two steps, as reported in literature (**Scheme 2-5**).[16] The 4,6-di-*tert*-butylsilylene (DTBS) group was first installed by treatment of **2.30** with di-*tert*-butylsilyl bis(trifluoromethanesulfonate) in pyridine, generating **2.31** in 79% yield. The resulting diol was then benzylated to give, in 71% yield, the desired thiogalactoside donor **2.18**.



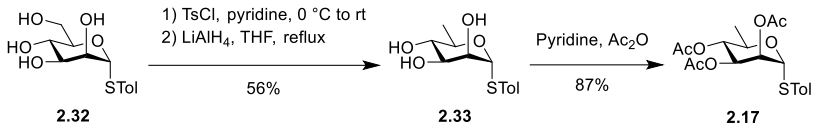
Scheme 2-5: Synthesis of galactose donor **2.18**.

The use of the di-*tert*-butylsilylene group in **2.18** was to ensure high α-selectivity in the glycosylation (**Scheme 2-6**).[17] The rationale is that, when the thioglycoside is activated, and the oxocarbenium ion formed, a structural conformational change is induced. It is proposed that C-4 and C-6 adopt such a conformation that electron density of O-4 and O-6 can act to stabilize the oxocarbenium ion by through-space electron donation (**2.18c**). The oxocarbenium ion could be approached on either the β-face (endo, **2.18d**) or the α-face (exo, **2.18e**) by an incoming nucleophile. An endo attack would be met with steric hindrance from the *tert*-butyl groups, while proceeding through a twist-boat-like conformer (**2.18f**). An additional ring flip would be required to obtain the more stable β-product (**2.18h**). On the other hand, an exo attack would proceed through a more favorable, chair-like conformer with less steric hindrance (**2.18g**). Hence there is a preference for exo attack, generating the α-glycosidic linkage as the favoured product (**2.18i**).



Scheme 2-6: Proposed mechanism of 4,6-di-*tert*-butylsilylene-directed *α*-glycosylation.[17]

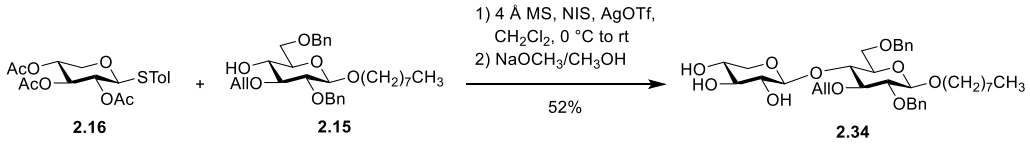
The rhamnose donor **2.17** was synthesised from *p*-tolyl 1-thio-α-D-mannopyranoside (**2.32**) using the procedure reported by Emmadi and Kulkarni (**Scheme 2-7**).[18] Deoxygenation of the C-6 position was done over two steps. First, the primary alcohol was tosylated using 4-toluenesulfonyl chloride in pyridine and the product reduced with lithium aluminum hydride to generate **2.33** in 56% yield. The final step involved the acetylation of **2.33** using acetic anhydride in pyridine to give the desired donor **2.17** in 87% yield.



Scheme 2-7: Synthesis of rhamnose donor **2.17**.

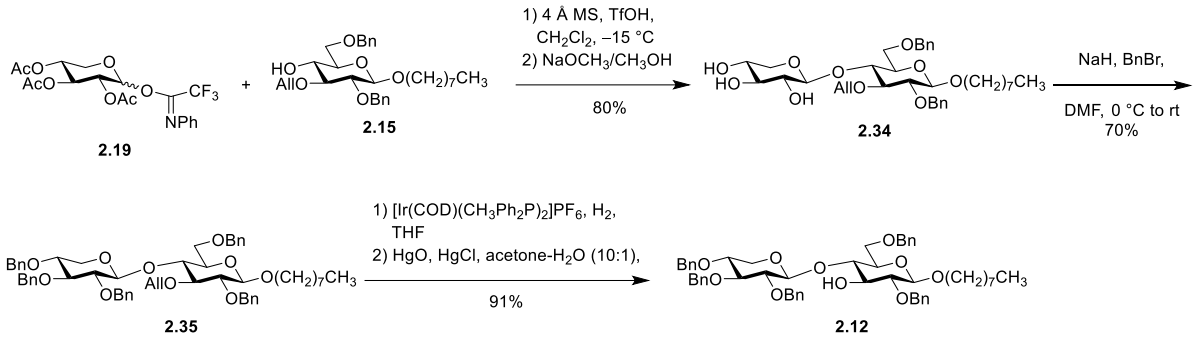
2.2.3 Synthesis of disaccharide 2.12.

With the acceptor **2.15** and donor **2.16** in hand, the disaccharide **2.12** was accessed through the glycosylation of the two residues. The glycosylation was carried out using silver triflate and *N*-iodosuccinimide activation; however, purification proved to be difficult as the excess donor had a similar R_f to that of the product. A subsequent deacetylation of the mixture improved separation, and was, fortunately, the next required step in the synthesis. The desired triol **2.34** was obtained in 52% yield over the two steps; the *β*-stereochemistry confirmed with coupling constant of Xyl-H-1 with Xyl-H-2 ($^3J_{\text{H-1, H-2}}$ = 7.4 Hz) (**Scheme 2-8**). Unsatisfied with the rather poor yield, both methyl triflate and *N*-iodosuccinimide/triflic acid promotor systems were explored, but I saw no significant increase in yield. The poor product yield may be attributed to the rather unreactive nature of the donor. The electron withdrawing acetate groups destabilize the oxocarbenium ion intermediate, leading to a decrease in reactivity.



Scheme 2-8: Glycosylation of acceptor **2.15** with **2.16**.

To improve the yield, the thioxyloside donor **2.16** was swapped with *N*-phenyl-trifluoroacetimidate donor **2.19** (**Scheme 2-9**). A triflic acid promoted glycosylation between the imidate donor **2.19** and the octyl glucoside acceptor **2.15**, followed by the deacetylation of the resulting mixture gave the desired triol **2.34** in 80% yield over the two steps. Having improved the glycosylation leading to **2.34,** I converted it to the disaccharide acceptor **2.12** in two steps. First, triol **2.34** was benzylated to afford a 70% yield of **2.35**. Then the allyl group deprotected using (1,5-cyclooctadiene)bis(methyldiphenylphosphine)iridium(I) hexafluorophosphate catalyzed isomerization followed by the hydrolytic cleavage of the resulting vinyl ether with aqueous mercuric salts gave the desired disaccharide acceptor **2.12** in 91% yield. The loss of the allyl protons was obvious in the proton NMR spectrum of **2.12**.

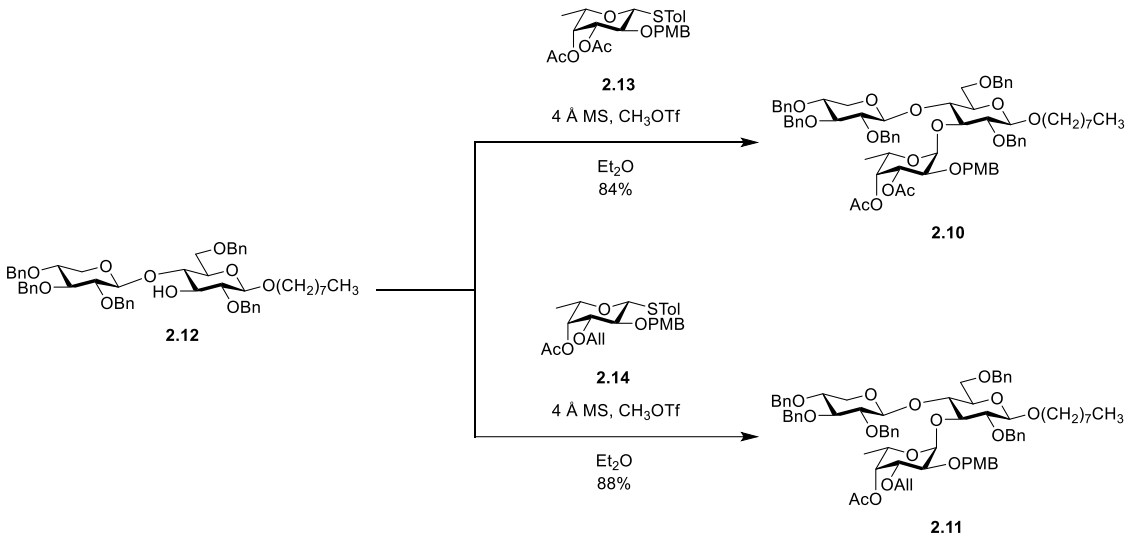


Scheme 2-9: Synthesis of disaccharide acceptor **2.12**.

2.2.4 Synthesis of trisaccharides intermediates 2.10 and 2.11

Access to both trisaccharides **2.10** and **2.11** was achieved by methyl triflate promoted glycosylation of the disaccharide acceptor **2.12** and the corresponding thiofucoside donors, **2.13** or **2.14** (**Scheme 2-10**). Trisaccharide **2.10** was obtained in 84% yield while **2.11** was obtained in

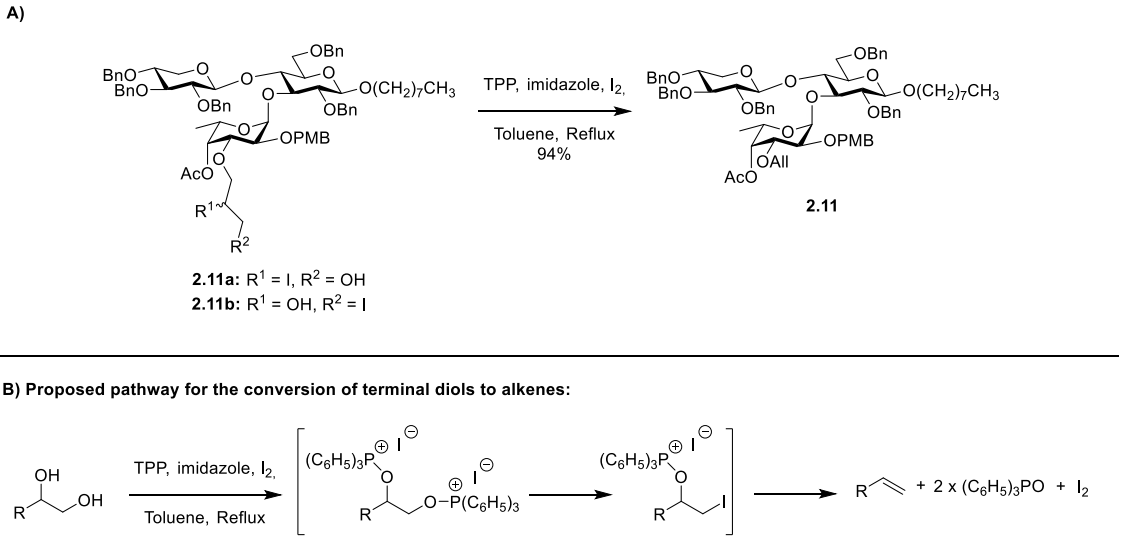
88% yield, both with high α-selectivity (confirmed via a fucose $^{3}J_{\text{H-1, H-2}}$ of 3.5 and 3.7 Hz, in **2.10** and **2.11**, respectively). The high α-selectivity can be rationalized through remote participation of the C-4 acetate group of the fucose residue.[9,10]



Scheme 2-10: Synthesis of trisaccharide intermediates **2.10** and **2.11**.

As an aside, on larger scales, **2.11** became difficult to separate from remaining excess donor. In an attempt to alleviate the separation issue post reaction, the crude mixture was treated with *N*-iodosuccinimide and silver triflate in wet diethyl ether, with the intention of hydrolyzing the remaining donor and in turn making it more polar and easier to separate. The excess donor was successfully hydrolyzed; however, the allyl group was iodohydroxylated, effectively eliminating the ability to remove the once temporary protecting group. Fortunately, a paper published by Mereyala and co-workers was found and provided a solution.[19] The study reported the transformation of terminal diols to either alkenes or epoxides using triphenylphosphine

(TPP), imidazole, and iodine. As reported, conversion of terminal diols to alkenes required elevated temperatures (reflux in toluene) and a molar excess of reagents (4:1, per mole diol), while epoxides could be generated at lower temperatures (between –8 °C and 15 °C) with a 2:1 molar ratio of reagents for each mole of diol. The significance of the reaction was that the proposed pathway for alkene formation was through an iodohydrin intermediate, with elimination of HI, generating the alkene (**Scheme 2-11**). With that in mind, the iodohydrin isomeric mixture (**2.11a** and **2.11b**) was treated with triphenylphosphine, imidazole, and iodine at reflux in toluene (**Scheme 2-11**). Gratifyingly, the iodohydrin was successfully converted to the alkene in good yield (94%). Thus, it was possible to recover **2.11** from the mishap.



Scheme 2-11: A) Conversion of iodohydrin to alkene (**2.11a** and **2.11b**) and B) the proposed pathway of alkene formation from terminal diols using TPP, imidazole and iodine.[19]

2.2.5 Synthesis of final products

Having both trisaccharides **2.10** and **2.11** available, the target oligosaccharides could be accessed through selective deprotections and subsequent glycosylations to generate the desired structures. In synthesising the more branched structures, the monosaccharide residues were introduced around the central fucose, one at a time, and in a counter-clockwise fashion. Essentially, the distal xylose at the O-4 position of the fucose had to be added prior to the rhamnose residue, as mentioned in Chapter 1 (**Figure 2-4**).[9,10]

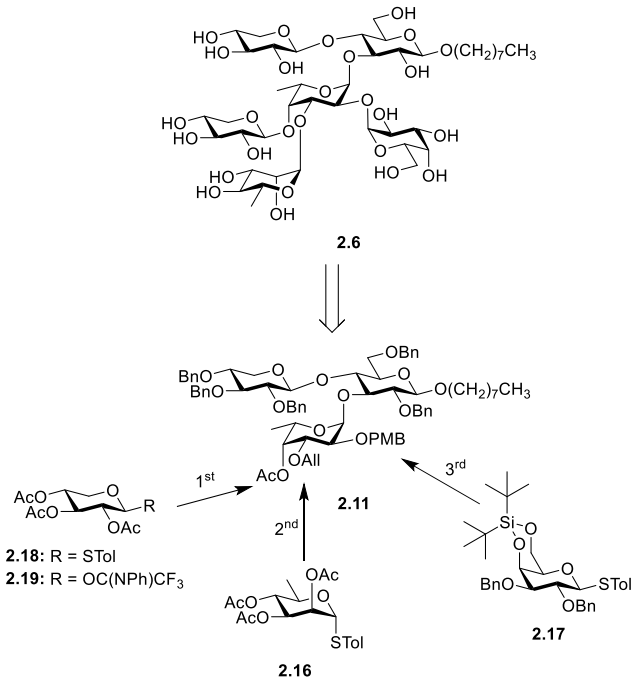


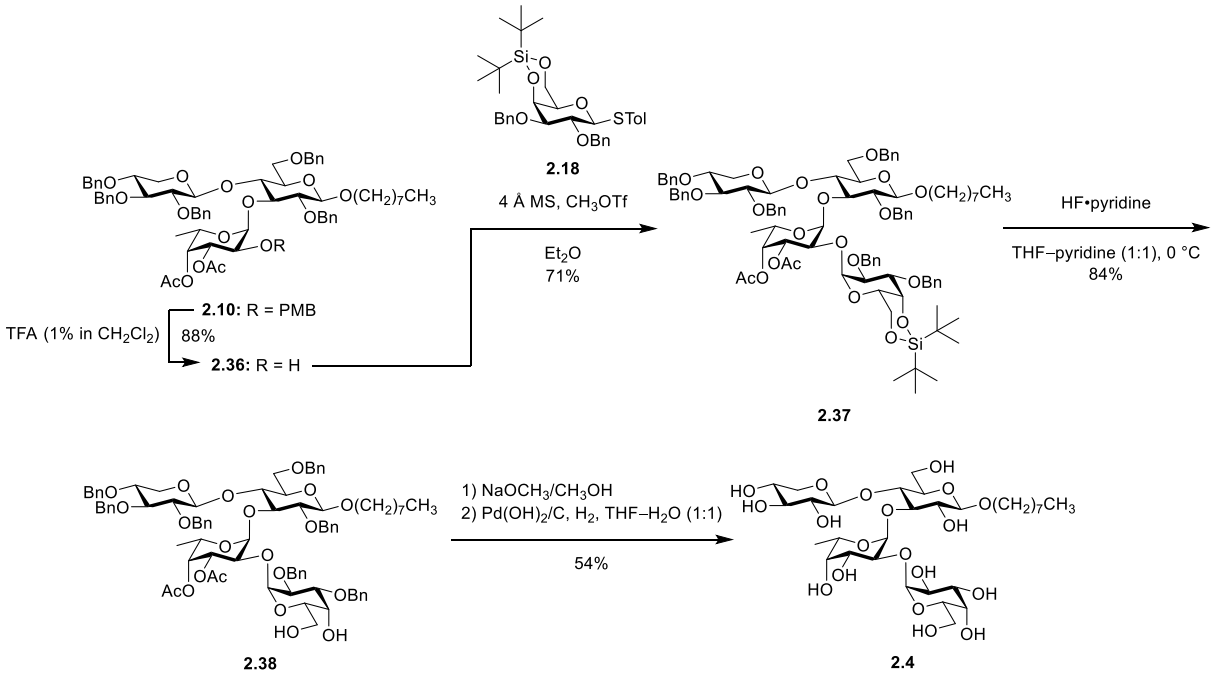
Figure 2-4: Example counter-clockwise assembly of the branched oligosaccharide synthetic targets.

2.2.5.1 Synthesis of tetrasaccharide 2.4

To avoid an extra protecting group manipulation, the trisaccharide **2.10** was used as the starting point for the synthesis of the tetrasaccharide **2.4** (**Scheme 2-12**). A single 4-methoxybenzyl group deprotection was needed to access the trisaccharide acceptor **2.36**. Acid treatment of **2.10** with 1% trifluoroacetic acid in dichloromethane gave the desired acceptor **2.36** in 88% yield. Glycosylation of acceptor **2.36** with the thiogalactoside donor **2.18** using methyl triflate afforded the tetrasaccharide **2.37** with a tentative yield of 71%. Proton NMR spectroscopy indicated trace contamination with a compound that was inseparable from the desired product. Later glycosylations using **2.18** as a donor showed similar issues, suggesting a purity issue originating in the galactoside donor supply. Global deprotection of **2.37** began with the removal of the silylene acetal using HF·pyridine, furnishing the diol **2.38** in 84% yield. The impurities from the previous step were no longer present. Left remaining, was the removal of the acetyl groups using sodium hydroxide in methanol, and a hydrogenolysis of the benzyl ethers with 20% palladium hydroxide on carbon in THF–H_2O (1:1).

After the final debenzylation, a portion of the recovered product had additional molecular weight. Product signals with an extra 70 m/z and 140 m/z were observed in the high-resolution mass spectrum. Compounds with analogous masses were not seen after the deacetylation step. Proton NMR spectroscopy also confirmed the presence of additional peaks, albeit, poorly resolved. As such, characterization based on NMR spectroscopy proved to be inconclusive. It was speculated that the extra molecular weight may have come from a butyric ester(s) attached to the product; possibly, having originated from butyric acid or gamma hydroxybutyrate, if present in the used THF solvent. Unfortunately, deacetylation attempts proved to have no effect. This issue, however, would show up again in later benzyl deprotections, possibly suggesting a

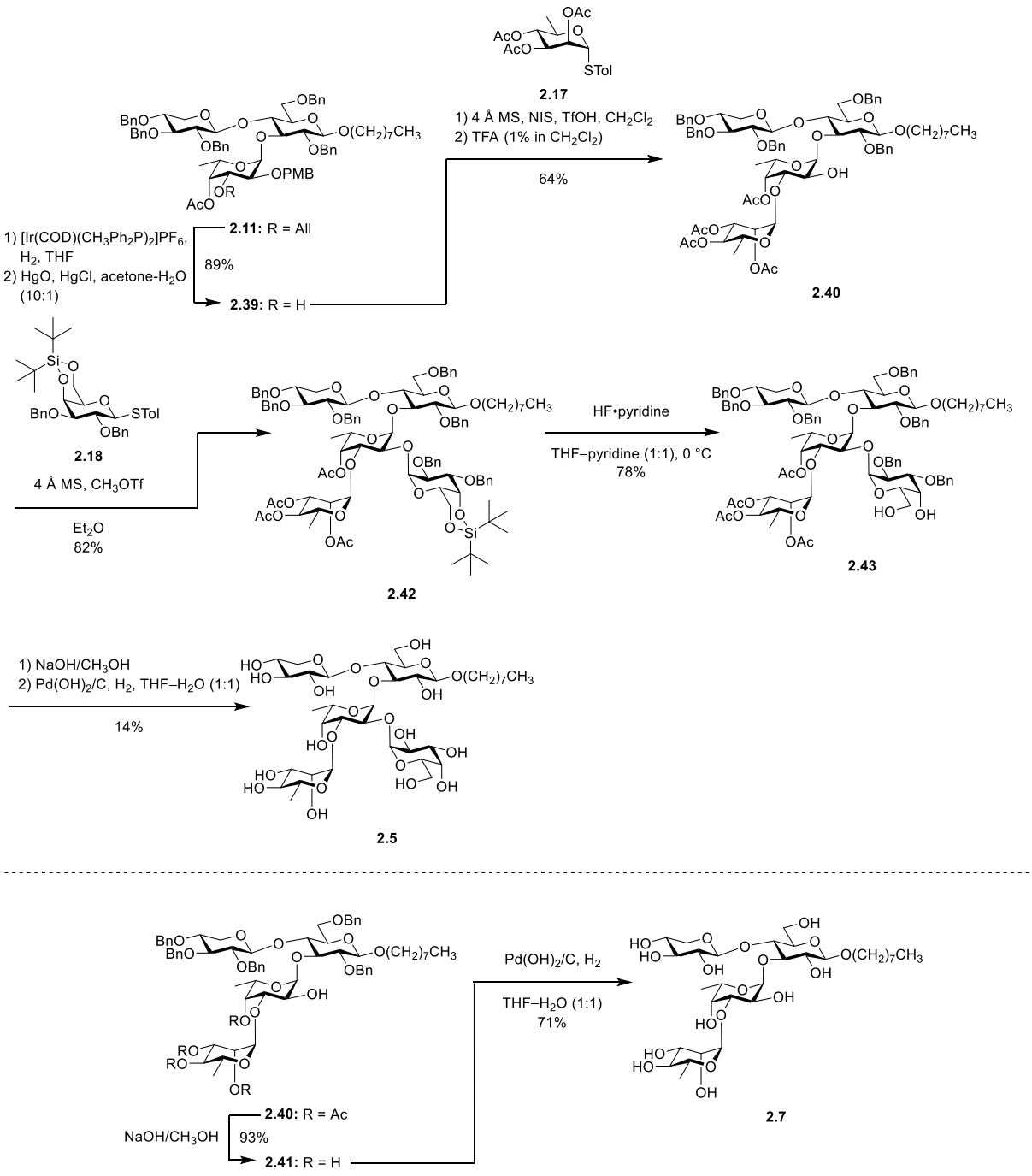
reagent issue. Fortunately, the desired compound **2.4** was successfully isolated in 54% using Iatrobead column chromatography. The α-stereochemistry of the galactose glycosidic linkage was confirmed by the corresponding Gal-C-1 and Gal-H-1 coupling constants of 175.5 Hz in the proton coupled HSQC spectrum.



Scheme 2-12: Synthesis of tetrasaccharide target **2.4**.

2.2.5.2 Synthesis of tetrasaccharide 2.7 and pentasaccharide 2.5

Both the tetra- and pentasaccharide targets **2.7** and **2.5**, respectively, were derived from trisaccharide **2.11** (**Scheme 2-13**). The initial step involved the cleavage of the allyl ether to give the acceptor **2.39** in 89% yield. The glycosylation of acceptor **2.39** with the thiorhamnoside donor **2.17** was performed at room temperature using *N*-iodosuccinimide and silver triflate activation. Isolation of the product proved difficult as any remaining trace amounts of acceptor



Scheme 2-13: Synthesis of target tetrasaccharide **2.7** and pentasaccharide **2.5**.

had an extremely similar R_f. Instead, the mixture was treated with 1% trifluoroacetic acid in dichloromethane and the 4-methoxybenzyl group removed. Having generated the more polar compound via deprotection, the desired acceptor **2.40** was successfully isolated in a 64% yield over the two steps. The α-stereochemistry of the glycosidic bond of the introduced rhamnose residue was confirmed with the Rha-C-1 and Rha-H-1 coupling constant of 177.4 Hz. At this point, the target tetrasaccharide **2.7** was easily obtained upon removal of both the acetyl and benzyl groups. The deacetylated product **2.41** was obtained with a 93% yield using sodium hydroxide in methanol, followed by the hydrogenolysis of the benzyl ethers using palladium hydroxide on carbon in THF–H_2O (1:1), generating the final tetrasaccharide **2.7** in 71% yield. Again, prior to purification, a product with additional molecular weight (an extra 70 m/z) was observed in the high-resolution mass spectrum as well as additional peaks were present in the proton NMR spectrum, albeit, to a lesser extent than seen previously with **2.4**.

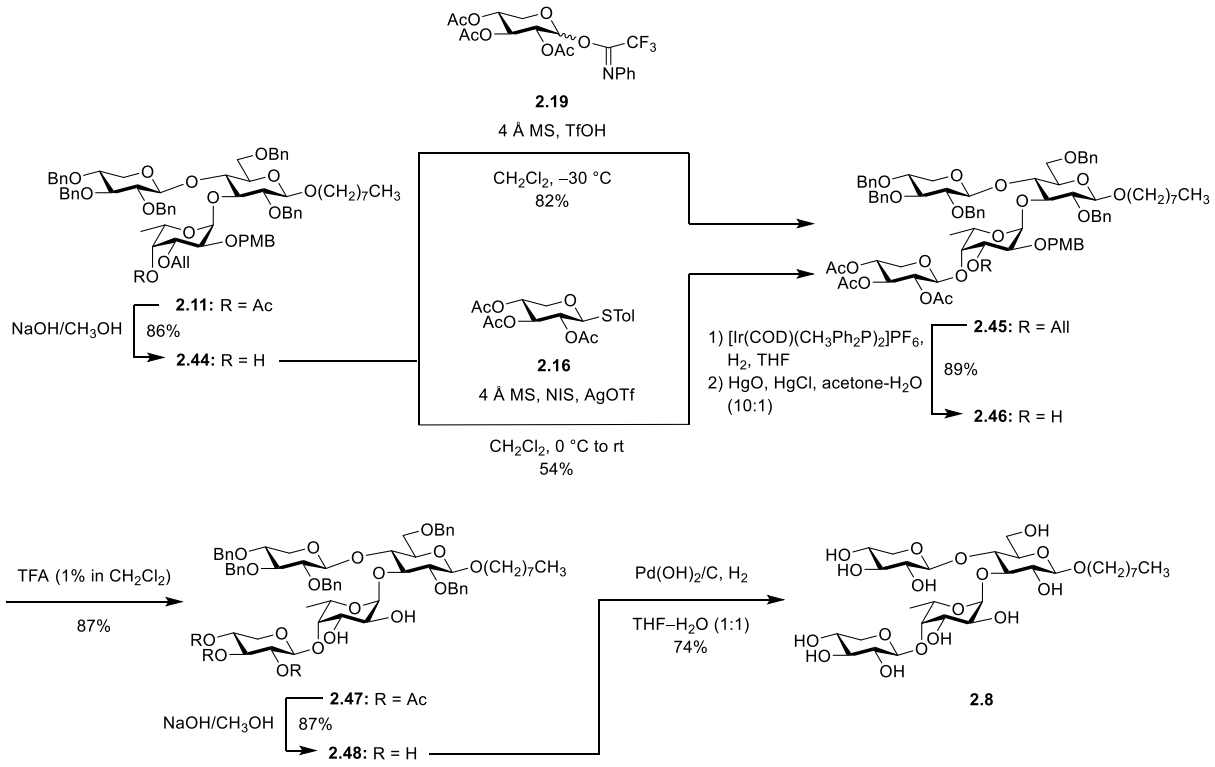
The final steps in the synthesis of pentasaccharide **2.5** first involved the glycosylation of the acceptor **2.40** with the thiogalactoside donor **2.18** using methyl triflate. The pentasaccharide **2.42** was obtained in a tentative yield of 82%. The α-stereochemistry of the introduced galactose residue would be later confirmed from the Gal-C-1 and Gal-H-1 coupling constant of 176.8 Hz; measured from the final deprotected product, **2.5**. Unfortunately, similar to what was observed in the synthesis of **2.37**, trace amounts of contamination were observed in the proton NMR spectrum, likely originating from the donor supply. However, upon removal of the di-*tert*-butylsilylene group with HF·pyridine, **2.43** was obtained in 78% yield as a pure compound. The deacetylation and subsequent debenzylation of **2.43** afforded the desired target pentasaccharide **2.5**. As seen with the previous debenzylation reactions, a significant portion of the recovered product had the higher molecular weight peaks (the additional 70 m/z and 140 m/z were

observed in the high-resolution mass spectrum); moreover, it was evident from TLC that at least two extra compounds were present. Loss of product from multiple purification attempts using both reverse phase and Iatrobead column chromatography and from the extent of contamination, resulted in an 14% isolated yield of the desired pentasaccharide **2.5** in pure form.

2.2.5.3 Synthesis of tetrasaccharide 2.8, pentasaccharide 2.9, and hexasaccharide 2.6.

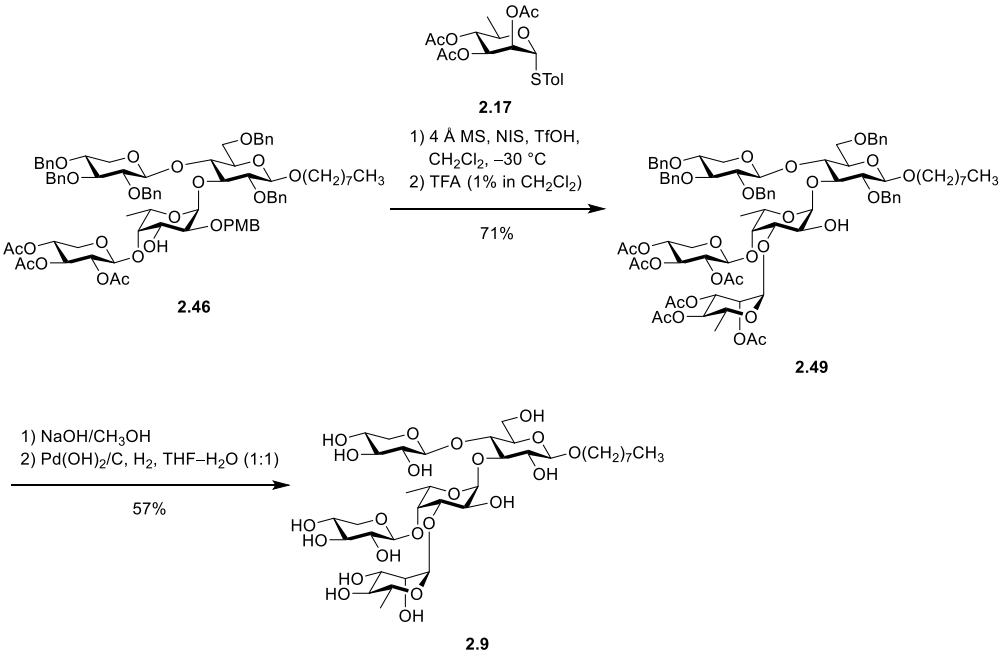
As with the synthesis of **2.5** and **2.7**, targets **2.8, 2.9,** and **2.6** were produced from the trisaccharide intermediate **2.11** (**Scheme 2-14).** Selective removal of the acetyl group revealed the O-4 position of the fucose for glycosylation. Upon deacetylation of **2.11**, acceptor **2.44** was obtained in 86% yield. In an initial attempt to obtain the tetrasaccharide **2.45**, the thioxyloside donor **2.16** was used to glycosylate the trisaccharide acceptor **2.44** using *N*-iodosuccinimide and silver triflate activation. The reaction was met with poor success (54% yield). Furthermore, purification proved difficult. Both excess donor and any residual acceptor had similar R_f values to that of the product, requiring additional protecting group manipulations. A subsequent deacetylation, purification, and reacetylation was required to obtain the pure tetrasaccharide **2.45**. With the previous success of the imidate donor **2.19** in the synthesis of the disaccharide **2.34**, glycosylation attempts using **2.19** were explored. The ensuing glycosylation between **2.44** and **2.19** was carried out at –30 °C using triflic acid promotion; the reaction generated the desired tetrasaccharide **2.45** in 82% yield. The β-stereochemistry of the Xyl*p*-(1→4)-Fuc*p* glycosidic linkage was confirmed by the coupling constant between Xyl-H-1 and Xyl-H-2 ($^3J_{\text{H-1, H-2}}$ = 7.6 Hz). The polarity difference of the imidate donor and thioglycoside donor was enough to ease purification; additional protecting group manipulations were no longer required. Cleavage of the allyl ether furnished the acceptor **2.46** in 79% yield. At this point, global

deprotection of the tetrasaccharide **2.46** gave the desired target **2.8**. First, the 4-methoxybenzyl ether was removed using 1% trifluoroacetic acid in dichloromethane, affording **2.47** in 87% yield. Deacetylation of the resulting product using sodium hydroxide in methanol generated **2.48** in 87% and a final benzyl ether hydrogenolysis gave the desired product **2.8,** in 74% yield. Due to time constraints, it was not confirmed whether the extra molecular weight product was present, prior to final purification. But given the prevalence of the issue, it was suspected, albeit in small quantities as reflected by the greater isolated yield.



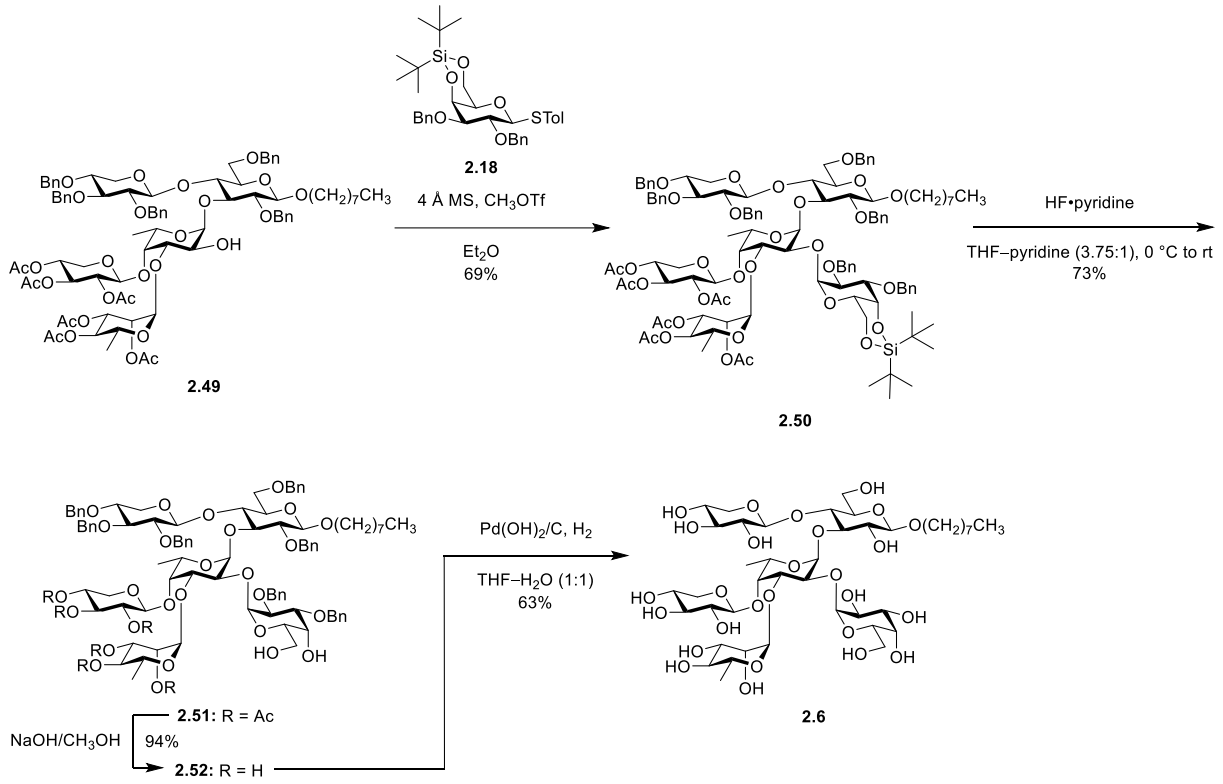
Scheme 2-14: Synthesis of tetrasaccharide target **2.8**.

To synthesize **2.9**, the tetrasaccharide **2.46** was glycosylated with the thiorhamnoside donor **2.17** using *N*-iodosuccinimide and triflic acid at –30 °C (**Scheme 2-15**). To aid in purification, the subsequent mixture was treated with 1% trifluoroacetic acid in dichloromethane and the 4-methoxybenzyl group removed. The acceptor **2.49** was obtained in 71% yield over the two steps. The α-stereochemistry of newly introduced rhamnose residue was confirmed by the coupling constant between Rha-C-1 and Rha-H-1 ($^1J_{C\text{-}H}$ = 175.5 Hz). Lastly, a deacetylation and debenzylation of the resulting product generated the desired pentasaccharide **2.9** in 57% yield over the two steps. Again, product with the additional molecular weight (extra 70 m/z present in the high-resolution mass spectrum) was observed following the debenzylation using palladium hydroxide on carbon in THF–H_2O (1:1).



Scheme 2-15: Synthesis of pentasaccharide target **2.9**.

The final hexasaccharide target **2.6** was obtained from the glycosylation of the thiogalactoside donor **2.18** with the pentasaccharide acceptor **2.49** using methyl triflate activation (**Scheme 2-16**). The desired hexasaccharide **2.50** was obtained in a tentative yield of 69%, and the α-selectivity of the Gal*p*-(1→2)-Fuc*p* glycosidic bond was confirmed by the coupling constant between Gal-C-1 and Gal-H-1 ($^1J_{C\text{-}H}$ = 172.6 Hz). Again, trace contamination was observed in the proton NMR spectrum, likely originating from the donor supply. The removal of the silylene acetal was carried out using HF·pyridine, generating the diol **2.51** in 73% yield. Deprotection of the acetate groups was done using sodium hydroxide in methanol, giving **2.52** in 94% yield. Finally, **2.52** was debenzylated to afford the deprotected hexasaccharide **2.6**. While not initially confirmed, product with the additional molecular weight was suspected to be present. The decision was made to acetylate the product in hopes of aiding in purification. Unfortunately, this proved to be a futile endeavour; acetylation only exacerbated the separation issue. Of the obtained fractions, the desired product was identified using high-resolution mass spectrometry (at this point, product with the additional 70 m/z was confirmed) and the appropriate mixtures deacetylated. The resulting residue was purified using Iatrobead chromatography. Due to time constraints, the hexasaccharide target **2.6** was obtained in a yield of 63%; the proton NMR spectrum confirms the presence of unidentifiable trace impurities.

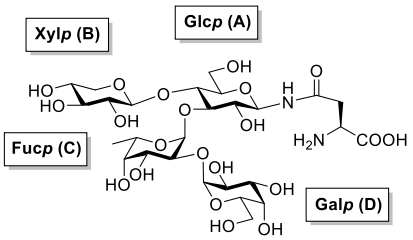


Scheme 2-16: Synthesis of target hexasaccharide target **2.6**.

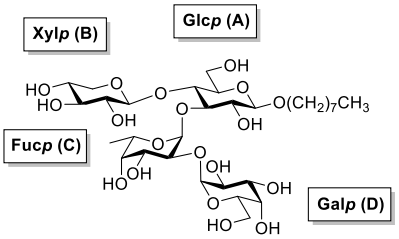
2.2.6 Proton NMR comparison of 2.4, 2.5, and 2.6 with their corresponding natural products

A comparison of the proton NMR chemical shifts between the synthesised glycan analogs and their natural product counter parts were made (**Table 2.1**, **Table 2.2**, and **Table 2.3**). The proton NMR spectra of **2.4**, **2.5**, and **2.6** were obtained in D_2O measured at 700 MHz and 300 K. The proton NMR spectrum of the natural products **2.1**, **2.2**, and **2.3** were acquired from naturally-isolated glycans in D_2O measured at 600 MHz and 310 K. The latter data was reported by De Castro and co-workers.[7] The nature of the attached aglycone of the glucose residue resulted in slight discrepancies in the comparison with that of the respective chemical shifts

reported. However, the remainder of the proton chemical shifts of the unmodified residues of both the synthetic analogs and the natural products, were in accordance. Based on these comparisons, the structures of the synthetic analogs were in agreement with that of the natural products.



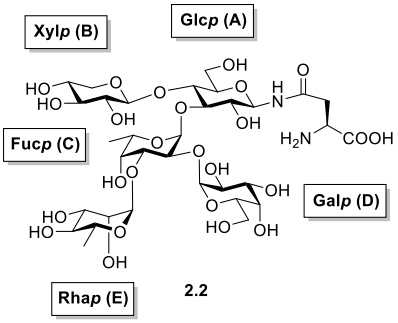
2.1



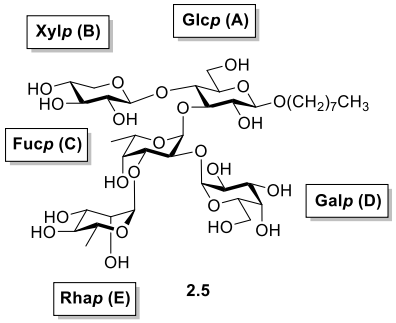
2.4

		H-1	H-2	H-3	H-4	H-5 (5a;5b)	H-6 (6a;6b)
Natural *N*-glycan **2.1**[7]	**Glc*p* (A)**	4.97	3.58	3.92	3.75	3.64	3.96;3.89
	Xyl*p* (B)	4.42	3.15	3.44	3.49	3.93;3.26	--
	Fuc*p* (C)	5.61	3.94	4.16	3.78	4.73	1.20
	Gal*p* (D)	5.28	3.84	3.90	4.02	4.05	3.73 x 2
Synthetic target **2.4**	**Glc*p* (A)**	4.45	3.45	3.86	3.72	3.58	3.99;3.82
	Xyl*p* (B)	4.42	3.15	3.44	3.51	3.93;3.27	--
	Fuc*p* (C)	5.62	3.93	4.15	3.78	4.73	1.20
	Gal*p* (D)	5.27	3.84	3.93	4.03	4.07	3.74 x 2

Table 2-1: Chemical shifts (ppm) comparison between the proton NMR of **2.4** and the natural product **2.1**.



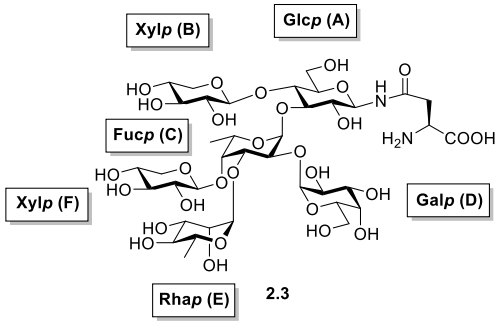
2.2



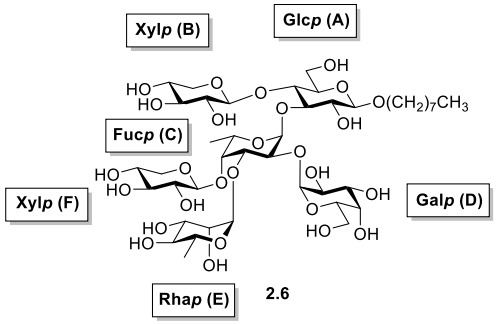
2.5

		H-1	H-2	H-3	H-4	H-5 (5a;5b)	H-6 (6a;6b)
Natural *N*-glycan **2.2**[7]	**Glc*p* (A)**	5.03	3.61	3.96	3.75	3.67	3.96;3.85
	Xyl*p* (B)	4.46	3.18	3.48	3.60	3.99;3.30	--
	Fuc*p* (C)	5.64	4.09	4.24	3.79	4.76	1.23
	Gal*p* (D)	5.23	3.85	3.90	4.06	4.06	3.75 x 2
	Rha*p* (E)	5.01	4.11	3.87	3.50	3.82	1.32
Synthetic target **2.5**	**Glc*p* (A)**	4.46	3.45	3.89	3.71	3.59	3.99; 3.83
	Xyl*p* (B)	4.43	3.15	3.45	3.57	3.97;3.29	--
	Fuc*p* (C)	5.63	4.05	4.22	3.78	4.74	1.20
	Gal*p* (D)	5.22	3.82	3.88	4.04	4.05	3.73 x 2
	Rha*p* (E)	4.99	4.10	3.85	3.49	3.79	1.30

Table 2-2: Chemical shifts (ppm) comparison between the proton NMR of **2.5** and the natural product **2.2**.



2.3



2.6

		H-1	H-2	H-3	H-4	H-5 (5a;5b)	H-6 (6a;6b)
Natural *N*-glycan **2.3**[7]	**Glc*p* (A)**	5.01	3.58	3.95	3.72	3.66	3.94;3.83
	Xyl*p* (B)	4.42	3.14	3.45	3.59	4.03;3.27	--
	Fuc*p* (C)	5.63	4.18	4.22	3.86	4.75	1.31
	Gal*p* (D)	5.23	3.82	3.86	4.03	4.03	3.74;3.71
	Rha*p* (E)	5.04	4.04	3.75	3.50	4.10	1.30
	Xyl*p* (F)	4.46	3.39	3.45	3.66	4.03;3.23	--
Synthetic target **2.6**	**Glc*p* (A)**	4.45	3.45	3.90	3.69	3.58	3.99;3.83
	Xyl*p* (B)	4.41	3.15	3.46	3.60	4.04;3.28	--
	Fuc*p* (C)	5.64	4.15	4.22	3.87	4.76	1.31
	Gal*p* (D)	5.23	3.81	3.86	4.04	4.06	3.74; 3.72
	Rha*p* (E)	5.05	4.04	3.76	3.50	4.11	1.29
	Xyl*p* (F)	4.47	3.39	3.45	3.67	4.04;3.24	--

Table 2-3: Chemical shifts (ppm) comparison between the proton NMR of **2.6** and the natural product **2.3**.

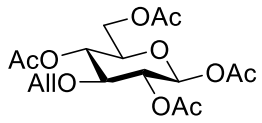
2.3 Conclusion

In conclusion, the work contained in this chapter describes the synthesis of six glycan analogs of the chlorovirus PBCV-1 MCP *N*-glycans. Three of the target structures were derived from truncated *N*-glycans expressed by PBCV-1 antigenic mutants (**2.4**, **2.5**, **2.6**), while the additional three targets (**2.7**, **2.8**, **2.9**) were deprotected derivatives of intermediates obtained along the applied synthetic routes. The general approach involved the synthesis of the trisaccharide cores **2.10** and **2.11**, both essential structural foundations of the six targets. The success of this approach relied on the use of orthogonal protection around the central fucose residue. Thus, selective access to the glycosylation sites could be achieved, and the branched structures generated. Unfortunately, in the final steps of deprotection, side-products were formed (or impurities unknowingly introduced) that were difficult to remove. This complicated access to several of the desired targets, significantly reducing the isolated yield.

Furthermore, it is also worth noting the useful application of transformation described by Mereyala and co-workers[19] which allowed the conversion of side-product iodohydrins to the corresponding alkene. This proved to be an invaluable transformation when faced with the issue of iodohydroxylation of alkenes; a concern when using *N*-iodosuccinimide promoted glycosylations in the presence of allyl groups.

2.4 Experimental section

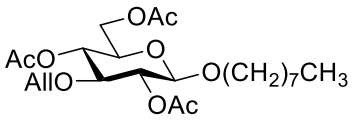
General methods: All reagents were purchased from commercial sources and were used without further purification unless noted. Reaction solvents were purified by successive passage through columns of alumina and copper under argon. Unless stated otherwise, all reactions were carried out at room temperature under a positive pressure of argon and were monitored by TLC on Silica Gel G-25 F254 (0.25 mm). Spots were visualized using UV fluorescence (254 nm) and/or by charring with acidified anisaldehyde solution in ethanol, acetic acid and sulfuric acid. Unless otherwise stated, products were purified by column chromatography on silica gel (230─400 mesh). Iatrobeads refers to a beaded silica gel 6RS─8060, manufactured by Iatron Laboratories (Tokyo). Optical rotation was measure at 22 ± 2 ˚C at the sodium D line (589 nm) and are in units of degree·mL(g·dm)$^{-1}$. ^{1}H NMR spectra were recorded at 500 MHz or 700 MHz and chemical shifts were referenced to residual $CHCl_3$ (7.26 ppm, $CDCl_3$) or CHD_2OD (3.30 ppm, CD_3OD) or external acetone (2.23 ppm, D_2O). ^{13}C NMR spectra were recorded at 126 or 176 MHz and chemical shifts were referenced to internal $CDCl_3$ (77.0 ppm, $CDCl_3$) or CD_3OD (49.3 ppm, CD_3OD) or external acetone (31.1 ppm, D_2O). Splitting patterns were reported as abbreviations: s = singlet, d = doublet, t = triplet, pent = pentet, m = multiplet, br = broad, app = apparent. Assignments of NMR spectra were based on two-dimensional experiments (^{1}H─^{1}H COSY and HSQC). Structural assignment labeling of the two xylose residues were as follows: Xyl = xylose-(1→4)-glucose, Xyl' = xylose-(1→4)-fucose. High-resolution ESI-MS spectra (time-of-flight analyzer) were recorded on samples in mixtures of THF or CH_3OH and added NaCl.



1,2,4,6-Tetra-*O*-acetyl-3-*O*-allyl-β-D-glucopyranoside (2.25)[12]

To a stirred solution of 1,2:5,6-di-O-isopropylidene-α-D-glucofuranose (6.579 g, 25.28 mmol) in dry DMF (60.0 mL) was added sodium hydride (2.053 g, 51.33 mmol, 60% dispersion in mineral oil) in one portion at 0 ˚C, under an Ar atmosphere. The mixture was stirred at 0 ˚C for 30 min and then allyl bromide (4.4 mL, 51 mmol) was added drop-wise. The reaction mixture was slowly warmed to room temperature and stirred for 1 h. The mixture was chilled to 0 ˚C and CH_3OH was added, poured into water, and the aqueous layer extracted with Et_2O (120 mL × 3). The combined organic layers were dried over Na_2SO_4, filtered, and the filtrate was then concentrated. The crude residue was purified via flash chromatography (5:1 hexanes─EtOAc). The resulting residue was dissolved in 40% acetic acid (40.0 mL) and stirred at 80 ˚C for 12 h. The reaction mixture was cooled to room temperature and then concentrated via co-evaporated with toluene and the resulting residue was dissolved in acetic anhydride (100.0 mL). Sodium acetate (6.478 g) was added at room temperature, and the reaction mixture was stirred at reflux for 1 h, cooled to room temperature, concentrated and then poured into water. The aqueous layer was extracted with $CHCl_3$ (50 mL × 3) and the combined organic layers dried over Na_2SO_4, filtered and then concentrated. The residue was recrystallized from ethanol to give **2.25** (4.146 g, 42%) as a white solid. R_f 0.21 (3:1 hexanes─ EtOAc); $[\alpha]_D$ ─ 1.7 (*c* 1.5, $CHCl_3$); ^{1}H NMR (500 MHz; $CDCl_3$): δ 5.79 (ddt, 1H, *J* = 17.3, 10.4, 5.6 Hz, $OCH_2C\underline{H}=CH_2$), 5.66 (d, 1H, *J* = 8.2 Hz, C-1), 5.23 (app dq, 1H, *J* = 17.2, 1.6 Hz, $OCH_2CH=C\underline{H}_2$), 5.17 (app dq, 1H, *J* = 10.4, 1.4 Hz, $OCH_2CH=C\underline{H}_2$), 5.13 (dd, 1H, *J* = 9.4, 8.2 Hz, H-2), 5.11 (app t, 1H, *J* = 9.6 Hz, H-4), 4.24 (dd, 1H, *J* = 12.4, 5.0 Hz, H-6a), 4.15 – 4.08 (m, 3H, H-6b, $OC\underline{H}_2CH=CH_2$), 3.75 (ddd, 1H, *J* = 9.9,

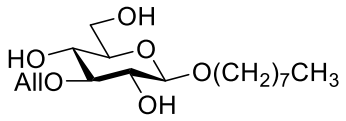
5.0, 2.4 Hz, H-5), 3.66 (app t, 1H, J = 9.3 Hz, H-3), 2.12 (s, 3H, COC<u>H</u>$_3$), 2.11 (s, 3H, COC<u>H</u>$_3$), 2.10 (s, 6H, COC<u>H</u>$_3$); ^{13}C NMR (126 MHz; $CDCl_3$): δ 170.7 (<u>C</u>OCH$_3$), 169.3 (<u>C</u>OCH$_3$), 169.2 (<u>C</u>OCH$_3$), 169.1 (<u>C</u>OCH$_3$), 134.1 (OCH$_2$<u>C</u>H=CH$_2$), 117.3 (OCH$_2$CH=<u>C</u>H$_2$), 92.0 (C-1), 79.7 (C-3), 73.1 (O<u>C</u>H$_2$CH=CH$_2$), 73.0 (C-5), 71.5 (C-2), 69.0 (C-4), 61.8 (C-6), 20.9 (CO<u>C</u>H$_3$), 20.8(3) (CO<u>C</u>H$_3$), 20.8 (CO<u>C</u>H$_3$), 20.7(6) (CO<u>C</u>H$_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{17}H_{24}NaO_{10}$: 411.1262; Found 411.1257.



Octyl 2,3,6-tri-*O*-acetyl-3-*O*-allyl-β-D-glucopyranoside (2.26)

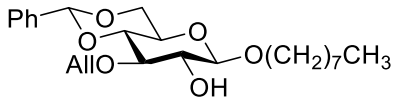
To a stirred solution of **2.25** (5.272 g, 13.57 mmol) and octanol (6.2 mL, 40 mmol) in dry CH_2Cl_2 (35.0 mL) was added boron trifluoride ethyl etherate (4.2 mL, 34 mmol) drop-wise at 0 ˚C, under an Ar atmosphere. The reaction mixture was stirred at 0 ˚C for 1 h then warmed to room temperature and stirred for 16 h and then poured into saturated $NaHCO_3$ (aq). The aqueous layer was extracted with CH_2Cl_2 (60 mL × 3) and the combined organic layers washed with brine, dried over Na_2SO_4, filtered and the filtrate wasthen concentrated. The resulting residue was dissolved in pyridine (50.0 mL) and acetic anhydride (42.0 mL) was added at 0 ˚C. The reaction mixture was warmed to room temperature and stirred for 20 h and then concentrated. The residue was diluted with CH_2Cl_2 (150 mL) and washed with 10% HCl (aq), saturated $NaHCO_3$ (aq), and brine. The organic layer was dried over Na_2SO_4, filtered and the filtrate was then concentrated. The crude residue was purified via flash chromatography (2.5:1 hexanes─

EtOAc) to give **2.26** (3.086 g, 50%) as a colourless syrup. R_f 0.57 (2:1 hexanes─ EtOAc); [α]D ─ 26.5 (*c* 1.1, $CHCl_3$); ^{1}H NMR (500 MHz; $CDCl_3$): δ 5.79 (ddt, 1H, *J* = 17.2, 10.4, 5.6 Hz, $OCH_2C\underline{H}=CH_2$), 5.22 (app dq, 1H, *J* = 17.2, 1.6 Hz, $OCH_2CH=C\underline{H}_2$), 5.15 (app dq, 1H, *J* = 10.4, 1.4 Hz, $OCH_2CH=C\underline{H}_2$), 5.08 (app t, 1H, *J* = 9.6 Hz, H-4), 5.00 (dd, 1H, *J* = 9.6, 7.9 Hz, H-2), 4.41 (d, 1H, *J* = 7.9 Hz, H-1), 4.23 (dd, 1H, *J* = 12.2, 5.1 Hz. H-6a), 4.14 (dd, 1H, *J* = 12.2, 2.7 Hz, H-6b), 4.12 – 4.04 (m, 2H, $OC\underline{H}_2CH=CH_2$), 3.87 (dt, 1H, *J* = 9.6, 6.3 Hz, $OC\underline{H}_2(CH_2)_6CH_3$), 3.61 (app t, 1H, *J* = 9.4 Hz, H-3), 3.63 – 3.56 (m, 1H, H-5), 3.46 (dt, 1H, *J* = 9.6, 6.8 Hz, $OC\underline{H}_2(CH_2)_6CH_3$), 2.11 (s, 3H, $COC\underline{H}_3$), 2.10 – 2.07 (m, 6H, $COC\underline{H}_3$), 1.63 – 1.49 (m, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.36 – 1.26 (m, 10H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 0.90 (t, 3H, *J* = 6.9 Hz, $O(CH_2)_7C\underline{H}_3$); ^{13}C NMR (126 MHz; $CDCl_3$): δ 170.8 ($\underline{C}OCH_3$), 169.3 ($\underline{C}OCH_3$), 169.1 ($\underline{C}OCH_3$), 134.3 ($OCH_2\underline{C}H=CH_2$), 116.9 ($OCH_2CH=\underline{C}H_2$), 101.1 (C-1), 79.8 (C-3), 72.6 ($O\underline{C}H_2CH=CH_2$), 72.5 (C-2), 72.0 (C-5), 70.0 ($O\underline{C}H_2(CH_2)_6CH_3$), 69.7 (C-4), 62.4 (C-6), 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(5) ($OCH_2(\underline{C}H_2)_6CH_3$), 25.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 20.9 ($CO\underline{C}H_3$), 20.8(5) ($CO\underline{C}H_3$), 20.8 ($CO\underline{C}H_3$), 14.1 ($O(CH_2)_7\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{23}H_{38}NaO_9$: 481.2408; Found 481.2408.



Octyl 3-*O*-allyl-β-D-glucopyranoside (2.27)

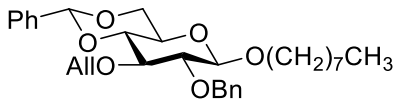
To a stirred solution of **2.26** (3.017 g, 6.579 mmol) in CH_3OH (20.0 mL) was added $NaOCH_3$ in CH_3OH (20.0 mL, 0.9 M). The reaction mixture was stirred at room temperature for 17 h. Amberlite® IR-120 (H^+) cation exchange resin was added, the mixture filtered and then the filtrate was concentrated. The crude residue was purified via flash chromatography (18:1 CH_2Cl_2─ CH_3OH) to give **2.27** (1.915 g, 88%) as a white solid. R_f 0.67 (9:1 CH_2Cl_2─ CH_3OH); $[\alpha]_D$ ─ 21.5 (*c* 2.8, CH_3OH); ^1H NMR (500 MHz; CD_3OD): δ 5.99 (ddt, 1H, *J* = 17.3, 10.4, 5.8 Hz, $OCH_2C\underline{H}=CH_2$), 5.26 (app dq, 1H, *J* = 17.3, 1.7 Hz, $OCH_2CH=C\underline{H}_2$), 5.10 (app dt, 1H, *J* = 10.4, 1.5 Hz, $OCH_2CH=C\underline{H}_2$), 4.40 – 4.28 (m, 2H, $OC\underline{H}_2CH=CH_2$), 4.23 (d, 1H, *J* = 7.4 Hz, H-1), 3.88 (dt, 1H, *J* = 10.0, 7.1 Hz, $OC\underline{H}_2(CH_2)_6CH_3$), 3.84 (dd, 1H, *J* = 11.8, 2.4 Hz, H-6a), 3.65 (dd, 1H, *J* = 11.9, 5.7 Hz, H-6b), 3.52 (dt, 1H, *J* = 9.5, 6.8 Hz, $OC\underline{H}_2(CH_2)_6CH_3$), 3.39 – 3.32 (m, 1H, H-4), 3.28 – 3.18 (m, 3H, H-2, H-5, H-3), 1.65 – 1.55 (m, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.42 – 1.23 (m, 10H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 0.89 (t, 3H, *J* = 6.9 Hz, $O(CH_2)_7C\underline{H}_3$); ^{13}C NMR (126 MHz; CD_3OD): δ 137.1 ($OCH_2\underline{C}H=CH_2$), 116.7 ($OCH_2CH=\underline{C}H_2$), 104.4 (C-1), 86.0 (C-3), 77.8, 75.2 (C-5 & C-2), 75.1 ($O\underline{C}H_2CH=CH_2$), 71.4 (C-4), 71.0 ($O\underline{C}H_2(CH_2)_6CH_3$), 62.8 (C-6), 33.0 ($OCH_2(\underline{C}H_2)_6CH_3$), 30.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 30.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 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 ($O(CH_2)_7\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{17}H_{32}NaO_6$: 355.2091; Found 355.2091.



Octyl 3-*O*-allyl-4,6-*O*-benzylidene-β-D-glucopyranoside (2.28)

To a stirred solution of **2.27** (1.890 g, 5.686 mmol) in dry CH_3CN (25.0 mL) was added benzaldehyde dimethyl acetal (2.56 mL, 17.1 mmol) and camphorsulfonic acid (397.7 mg, 1.712 mmol) at room temperature, under an Ar atmosphere. The reaction mixture was stirred at room temperature for 23 h before triethylamine was added and the solvent evaporated. The crude residue was purified via flash chromatography (6:1 hexanes─ EtOAc) to give **2.28** (2.066 g, 86%) as a white solid. R_f 0.55 (4:1 hexanes─ EtOAc); $[\alpha]_D$ ─ 38.6 (*c* 0.3, $CHCl_3$); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.54 – 7.48 (m, 2H, Ar), 7.44 – 7.35 (m, 3H, Ar), 5.99 (ddt, 1H, *J* = 17.3, 10.4, 5.8 Hz, $OCH_2CH=C\underline{H}_2$), 5.57 (s, 1H, $ArC\underline{H}$), 5.33 (app dq, 1H, *J* = 17.2, 1.7 Hz, OCH_2-$CH=C\underline{H}_2$), 5.21 (app dq, 1H, *J* = 10.3, 1.4 Hz, $OCH_2CH=C\underline{H}_2$), 4.46 (app ddt, 1H, *J* = 12.8, 5.6, 1.5 Hz, $OC\underline{H}_2CH=CH_2$), 4.42 (d, 1H, *J* = 7.6 Hz, H-1), 4.37 (dd, 1H, *J* = 10.5, 5.0 Hz, H-6a), 4.31 (app ddt, 1H, *J* = 12.8, 6.0, 1.4 Hz, $OC\underline{H}_2CH=CH_2$), 3.91 (dt, 1H, *J* = 9.5, 6.9 Hz, $OC\underline{H}_2(CH_2)_6CH_3$), 3.82 (app t, 1H, *J* = 10.3 Hz, H-6b), 3.67 (app t, 1H, *J* = 9.1 Hz, H-4), 3.61 (app t, 1H, *J* = 8.8 Hz, H-3), 3.61 – 3.57 (m, 1H, $OC\underline{H}_2(CH_2)_6CH_3$), 3.55 (app td, 1H, *J* = 8.2, 2.1 Hz, H-2), 3.46 (ddd, 1H, *J* = 10.1, 9.0, 5.0 Hz, H-5), 2.51 (d, 1H, *J* = 2.3 Hz, 2-O$\underline{H}$), 1.73 – 1.61 (m, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.41 – 1.25 (m, 10H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 0.91 (t, 3H, *J* = 6.8 Hz, $O(CH_2)_7C\underline{H}_3$); ^{13}C NMR (126 MHz; $CDCl_3$): δ 137.3 (Ar), 134.4 ($OCH_2\underline{C}H=CH_2$), 129.0 (Ar), 128.3 (Ar), 126.0 (Ar), 117.3 ($OCH_2CH=\underline{C}H_2$), 103.3 (C-1), 101.3 ($Ar\underline{C}H$), 81.5 (C-4), 80.0 (C-3), 74.2 (C-2), 73.6 ($O\underline{C}H_2CH=CH_2$), 70.6 ($O\underline{C}H_2(CH_2)_6CH_3$), 68.8 (C-6), 66.5 (C-5), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2

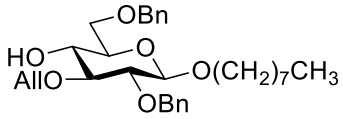
($OCH_2(\underline{C}H_2)_6CH_3$), 25.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 14.1 ($O(CH_2)_7\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{24}H_{36}NaO_6$: 443.2404; Found 443.2401.



Octyl 3-*O*-allyl-2-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranoside (2.29)

To a stirred solution of **2.28** (2.032 g, 4.831 mmol) in dry DMF was added sodium hydride (389.1 mg, 9.727 mmol, 60% dispersion in mineral oil) in one portion at 0 ˚C, under an Ar atmosphere. The mixture was stirred at 0 ˚C for 30 min and then benzyl bromide (1.2 mL, 10 mmol) was added drop-wise. The reaction mixture was slowly warm to room temperature and stirred for 19 h. The mixture was chilled to 0 ˚C and CH_3OH was added. The solution was diluted with CH_2Cl_2 (100 mL) and washed with saturated $NaHCO_3$ (aq) and water. The aqueous layers were extracted with CH_2Cl_2 (70 mL × 3) and the combined organic layers were dried over Na_2SO_4, filtered and then the filtrate was concentrated. The crude residue was purified via flash chromatography (12:1 hexanes─ EtOAc) to give **2.29** (2.244 g, 91%) as a white solid. R_f 0.58 (5:1 hexanes─ EtOAc); $[\alpha]_D$ ─ 31.1 (*c* 2.5, $CHCl_3$); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.55 – 7.49 (m, 2H, Ar), 7.45 – 7.29 (m, 8H, Ar), 5.98 (ddt, 1H, *J* = 17.3, 10.4, 5.7 Hz, $OCH_2CH=C\underline{H}_2$), 5.57 (s, 1H, Ar$C\underline{H}$), 5.32 (app dq, 1H, *J* = 17.2, 1.7 Hz, $OCH_2CH=C\underline{H}_2$), 5.19 (app dq, 1H, *J* = 10.4, 1.4 Hz, $OCH_2CH=C\underline{H}_2$), 4.92 (d, 1H, *J* = 10.9 Hz, Ar$C\underline{H}_2$), 4.80 (d, 1H, *J* = 10.9 Hz, Ar$C\underline{H}_2$), 4.52 (d, 1H, *J* = 7.7 Hz, H-1), 4.42 (app ddt, 1H, *J* = 12.6, 5.7, 1.5 Hz, $OC\underline{H}_2CH=CH_2$), 4.37 (dd, 1H, *J* = 10.5, 5.0 Hz, H-6a), 4.30 (app ddt, 1H, *J* = 12.6, 5.8, 1.5 Hz, $OC\underline{H}_2CH=CH_2$), 3.95 (dt,

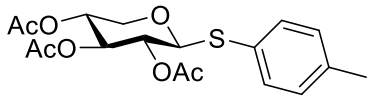
1H, J = 9.4, 6.5 Hz, OC<u>H</u>$_2$(CH$_2$)$_6$CH$_3$), 3.81 (app t, 1H, J = 10.3 Hz, H-6b), 3.70 – 3.62 (m, 2H, H-3, H-4), 3.59 (dt, 1H, J = 9.5, 6.9 Hz, OC<u>H</u>$_2$(CH$_2$)$_6$CH$_3$), 3.48 – 3.37 (m, 2H, H-2, H-5), 1.75 – 1.61 (m, 2H, OCH$_2$C<u>H</u>$_2$(CH$_2$)$_5$CH$_3$), 1.50 – 1.25 (m, 10H, OCH$_2$CH$_2$(C<u>H</u>$_2$)$_5$CH$_3$), 0.91 (t, 3H, J = 6.9 Hz, O(CH$_2$)$_7$C<u>H</u>$_3$); ^{13}C NMR (126 MHz; CDCl$_3$): δ 138.5 (Ar), 137.4 (Ar), 135.2 (OCH$_2$<u>C</u>H=CH$_2$), 128.9 (Ar), 128.3 (Ar), 128.3 (Ar), 128.2 (Ar), 127.7 (Ar), 126.0 (Ar), 116.8 (OCH$_2$CH=<u>C</u>H$_2$), 104.2 (C-1), 101.1 (Ar<u>C</u>H), 82.1 (C-2), 81.5, 80.7 (C-3 & C-4), 75.4 (Ar<u>C</u>H$_2$), 74.1 (O<u>C</u>H$_2$CH=CH$_2$), 70.7 (O<u>C</u>H$_2$(CH$_2$)$_6$CH$_3$), 68.9 (C-6), 66.1 (C-5), 31.9 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 29.8 (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$_3$), 26.2 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 22.7 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 14.1 (O(CH$_2$)$_7$<u>C</u>H$_3$); HRMS (ESI) Calc. for [M + Na]$^+$ C$_{31}$H$_{42}$NaO$_6$: 533.2874; Found 533.2873.



Octyl 3-*O*-allyl-2,6-*O*-benzyl-β-D-glucopyranoside (2.15)

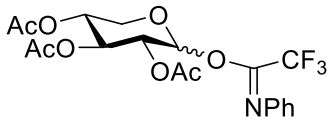
To a stirred solution of **2.29** (1.312 g, 2.569 mmol) in dry CH_2Cl_2 (10.0 mL) was added triethylsilane (1.6 mL, 20 mmol) and trifluoroacetic acid (2.4 mL, 15 mmol) successively at 0 ˚C, under an Ar atmosphere. The reaction mixture was stirred at 0 ˚C for 3 h and then poured into saturated $NaHCO_3$ (aq). The aqueous layer was extracted with CH_2Cl_2 (70 mL × 3) and the combined organic layers dried over Na_2SO_4, filtered and then the filtrate was concentrated. The crude residue was purified via flash chromatography (4:1 hexanes─ EtOAc) to give **2.15** (1.095 g, 83%) as a colourless syrup. R_f 0.26 (4:1 hexanes─ EtOAc); [α]D ─ 23.2 (*c* 2.4, $CHCl_3$); ^{1}H NMR

(500 MHz; $CDCl_3$): δ 7.40 – 7.30 (m, 10H, Ar), 5.97 (ddt, 1H, *J* = 17.2, 10.3, 5.8 Hz, $OCH_2C\underline{H}=CH_2$), 5.30 (app dq, 1H, *J* = 17.2, 1.5 Hz, $OCH_2CH=C\underline{H}_2$), 5.20 (app dq, 1H, *J* = 10.4, 1.3 Hz, $OCH_2CH=C\underline{H}_2$), 4.95 (d, 1H, *J* = 11.0 Hz, $Ar\underline{C}H_2$), 4.72 (d, 1H, *J* = 11.0 Hz, $Ar\underline{C}H_2$), 4.64, 4.61 (ABq, 2H, J_{AB} = 12.1 Hz, $Ar\underline{C}H_2$), 4.45 – 4.40 (m, 2H, $OC\underline{H}_2CH=CH_2$, H-1), 4.27 (app ddt, 1H, *J* = 12.6, 6.1, 1.3 Hz, $OC\underline{H}_2CH=CH_2$), 3.96 (dt, 1H, *J* = 9.4, 6.5 Hz, $OC\underline{H}_2(CH_2)_6CH_3$), 3.82 (dd, 1H, *J* = 10.4, 4.0 Hz, H-6a), 3.75 (dd, 1H, *J* = 10.4, 5.4 Hz, H-6b), 3.61 – 3.56 (m, 1H, H-4), 3.54 (dt, 1H, *J* = 9.4, 6.7 Hz, $OC\underline{H}_2(CH_2)_6CH_3$), 3.48 (ddd, 1H, *J* = 9.5, 5.4, 4.1 Hz, H-5), 3.39 – 3.35 (m, 2H, H-3, H-2), 2.73 (br s, 1H, 4-O<u>H</u>), 1.70 – 1.64 (m, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.45 – 1.29 (m, 10H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 0.90 (t, 3H, *J* = 7.0 Hz, $O(CH_2)_7C\underline{H}_3$); ^{13}C NMR (126 MHz; $CDCl_3$): δ 138.5 (Ar), 138.0 (Ar), 135.2 ($OCH_2\underline{C}H=CH_2$), 128.4 (Ar), 128.3 (Ar), 128.1 (Ar), 127.7(4) (Ar), 127.7(2) (Ar), 127.6 (Ar), 117.1 ($OCH_2CH=\underline{C}H_2$), 103.7 (C-1), 83.8, 81.7 (C-2 & C-3), 74.7 ($Ar\underline{C}H_2$), 74.2 ($O\underline{C}H_2CH=CH_2$), 73.9 (C-5), 73.7 ($Ar\underline{C}H_2$), 71.8 (C-4), 70.5 (C-6), 70.2 ($O\underline{C}H_2(CH_2)_6CH_3$), 31.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 26.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 14.1 ($O(CH_2)_7\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{31}H_{44}NaO_6$: 535.3030; Found 535.3030.



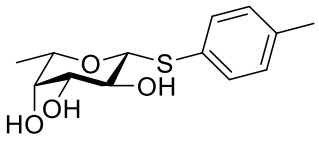
_p_-Tolyl 2,3,4-tri-_O_-acetyl-1-thio-β-D-xylopyranoside (2.16)[14]

To a stirred solution of D-xylose (10.75 g, 71.61 mmol) in acetic anyhdride (50.0 mL) was added sodium acetate (11.53 g, 140.6 mmol). The reaction mixture was heated at reflux for 2 h and then poured into ice water. The aqueous layer was extracted with CH_2Cl_2 (100 mL × 3) and the combined organic layers washed with brine, dried over Na_2SO_4, filtered and then the filtrate was concentrated. The crude residue was purified via flash chromatography (3:2 hexanes─EtOAc). The resulting residue was dissolved in dry CH_2Cl_2 (60.0 mL) and 4-methylbenzenethiol (5.0 g, 40 mmol) was added. The solution was chilled to ─ 20 ˚C and boron trifluoride ethyl etherate (8.3 mL, 67 mmol) was added drop wise over 15 min, under an Ar atmosphere. The reaction mixture was stirred at ─ 20 ˚C for 5 h and then diluted with CH_2Cl_2 (200 mL) and washed with saturated $NaHCO_3$ (aq) and brine. The organic layer was dried over Na_2SO_4, filtered and then the filtrate was concentrated. The residue was recrystallized from hexanes/EtOAc to give **2.16** (9.41 g, 34%) as a white solid. R_f 0.24 (3:1 hexanes─ EtOAc); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.43 – 7.37 (m, 2H, Ar), 7.18 – 7.13 (m, 2H, Ar), 5.20 (app t, 1H, J = 8.3 Hz, H-3), 4.93 (app t, 1H, J = 8.4 Hz, H-2), 4.93 (app td, 1H, J = 8.7, 5.0 Hz, H-4), 4.74 (d, 1H, J = 8.5 Hz, H-1), 4.28 (dd, 1H, J = 11.7, 5.0 Hz, H-5a), 3.42 (dd, 1H, J = 11.7, 9.0 Hz, H-5b), 2.37 (s, 3H, ArC$\underline{H}_3$), 2.12 (s, 3H, COC$\underline{H}_3$), 2.06 (s, 3H, COC$\underline{H}_3$), 2.06 (s, 3H, COC$\underline{H}_3$); ^{13}C NMR (126 MHz; $CDCl_3$): δ 170.0 ($\underline{C}OCH_3$), 169.8 ($\underline{C}OCH_3$), 169.4 ($\underline{C}OCH_3$), 138.7 (Ar), 133.5 (Ar), 129.8 (Ar), 128.1 (Ar), 86.4 (C-1), 77.3 (C-3), 69.9, 68.5 (C-4 & C-2), 65.4 (C-5), 21.2 (Ar$\underline{C}H_3$), 20.8 (CO$\underline{C}H_3$), 20.7 (CO$\underline{C}H_3$ × 2); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{18}H_{22}NaO_7S$: 405.0978; Found 405.0974.



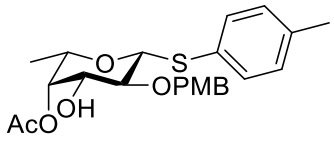
2,3,4-tri-*O*-acetyl-1-thio-β-D-xylopyranose 1-(*N*-phenyl)-2,2,2-trifluoroacetimidate (2.19)

To a stirred solution of **2.16** (2.159 g, 5.645 mmol) in acetone─ H_2O (9:1, 45.0 mL acetone, 5.0 mL H_2O) was added *N*-bromosuccinimide (4.013 g, 22.55 mmol). The reaction mixture was stirred at room temperature for 1.5 h and then poured to a saturated solution of $Na_2S_2O_3$ (40 mL). The aqueous layer was extracted with EtOAc (80 mL × 3) and the combined organic layers were washed with saturated $NaHCO_3$ (aq), water, and brine; dried over Na_2SO_4, filtered and then the filtrate was concentrated. The crude residue was passed through a silica column (2:1→1:1 hexanes─ EtOAc). The resulting residue was dissolved dry CH_2Cl_2 (30.0 mL) and 2,2,2-trifluoro-*N*-phenylacetimidoyl chloride (1.80 mL, 11.4 mmol) and cesium carbonate (5.010 g, 15.38 mmol) were added under an Ar atmosphere. The reaction mixture was stirred at room temperature for 16 h and then filtered and the filtrate was concentrated. The crude residue was purified via flash chromatography (3:1 hexanes─ EtOAc) to give **2.19** (1.815 g, 72%) as an off white solid. The product was confirmed by HRMS (ESI). R_f 0.32 (3:1 hexanes─ EtOAc). HRMS (ESI) Calc. for $[M + Na]^+$ $C_{19}H_{20}F_3NNaO_8$: 470.1033; Found 470.1028.



***p*-Tolyl 1-thio-β-L-fucopyranoside (2.21)[20]**

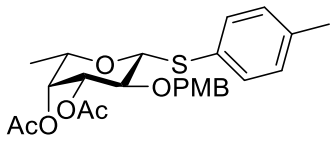
To a stirred solution of 1,2,3,4-*O*-acetyl-L-fucopyranoside (6.519 g, 19.62 mmol) and 4-methylbenzenethiol (2.7 g, 22 mmol) in dry CH_2Cl_2 (60.0 mL) was added boron trifluoride ethyl etherate (4.8 mL, 39 mmol) drop-wise at 0 ˚C, under an Ar atmosphere. The reaction mixture was stirred at 0 ˚C for 1 h and then warmed to room temperature and stirred for 16 h, being then diluted with CH_2Cl_2 (100 mL) and washed with saturated $NaHCO_3$ (aq) and brine. The organic layer was dried over Na_2SO_4, filtered, and the filtrate was concentrated. The crude residue was passed through a silica column (2:1 hexanes─ EtOAc). The resulting mixture was dissolved in CH_3OH (50.0 mL) and $NaOCH_3$ in CH_3OH (10.0 mL, 0.5 M) was added. The reaction mixture was stirred at room temperature for 15 h. Amberlite® IR-120 (H^+) cation exchange resin was added, the mixture filtered and then the filtrate was concentrated. The crude residue was purified via flash chromatography (10:1 CH_2Cl_2─ CH_3OH) to give **2.21** (2.865 g, 54%) as a white solid. R_f 0.38 (8:1 CH_2Cl_2─ CH_3OH); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.46 – 7.40 (m, 2H, Ar), 7.11 – 7.04 (m, 2H, Ar), 4.51 (d, 1H, J = 9.4 Hz, H-1), 3.83 (dd, 1H, J = 3.1, 1.1 Hz, H-4), 3.72 (app t, 1H, J = 9.3 Hz, H-2), 3.67 (dd, 1H, J = 9.2, 3.1 Hz, H-3), 3.60 (app q, 1H, J = 6.5 Hz, H-5), 2.33 (s, 3H, Ar$\underline{C}H_3$), 1.31 (d, 3H, J = 6.4 Hz, H-6); ^{13}C NMR (126 MHz; $CDCl_3$): δ 137.8 (Ar), 132.6 (Ar), 129.7 (Ar), 129.5 (Ar), 89.0 (C-1), 75.1 (C-3), 74.8 (C-4), 71.8 (C-5), 69.8 (C-2), 21.1 (Ar$\underline{C}H_3$), 16.7 (C-6).



***p*-Tolyl 4-*O*-acetyl-2-*O*-(4-methoxybenzyl)-1-thio-β-L-fucopyranoside (2.22)[9,10]**

To a stirred solution of **2.21** (1.954 g, 7.227 mmol) in dry CH_3CN (60.0 mL) was added trimethyl orthoacetate (1.10 mL, 8.64 mmol) and *p*-toluenesulfonic acid monohydrate (137.3 mg, 0.7218 mmol) successively at 0˚C, under an Ar atmosphere. The reaction mixture was stirred at 0 ˚C for 3 h and then triethylamine was added, and the solvent evaporated. The crude residue was passed through a silica column (3:2 hexanes─ EtOAc) and the resulting residue (1.762 g, 5.398 mmol) dissolved in dry DMF (40.0 mL) and sodium hydride (440.5 mg, 11.01 mmol, 60% dispersion in mineral oil) was added in one portion at 0 ˚C, under an Ar atmosphere. The mixture was stirred at 0 ˚C for 30 min and then tetra-*n*-butylammonium iodide (198.3 mg, 0.5469 mmol) and 4-methoxybenzyl chloride (0.88 mL, 6.5 mmol) were added successively. The reaction mixture was slowly warm to room temperature and stirred for 1 h then was chilled to 0 ˚C and CH_3OH was added. The solvent was co-evaporated with toluene and the crude residue was dissolved in CH_2Cl_2 (100 mL), washed with saturated $NaHCO_3$ (aq), dried over Na_2SO_4, filtered and then the filtrate was concentrated. The resulting residue was dissolved in CH_2Cl_2 (40.0 mL) and 1N HCl (aq) (40.0 mL) was added. The reaction mixture was stirred at room temperature for 1 h and then the aqueous layer was extracted with CH_2Cl_2 (40 mL × 2). The combined organic layers were washed with saturated $NaHCO_3$ (aq) and water, dried over Na_2SO_4, filtered and then the filtrate was concentrated. The crude residue was purified via flash chromatography (3:2 hexanes─ EtOAc) to give **2.22** (2.057 g, 66%) as a colourless syrup. R_f 0.26 (3:2 hexanes─ EtOAc); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.55 – 7.47 (m, 2H, Ar), 7.37 – 7.30 (m, 2H, Ar), 7.18 –

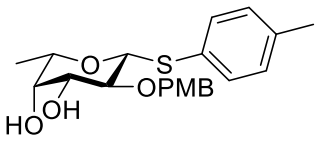
7.12 (m, 2H, Ar), 6.94 – 6.87 (m, 2H, Ar), 5.19 (dd, 1H, *J* = 3.5, 1.1 Hz, H-4), 4.92 (d, 1H, *J* = 10.5 Hz, ArC$\underline{H}_2$), 4.61 (d, 1H, *J* = 10.5 Hz, ArC$\underline{H}_2$), 4.59 (d, 1H, *J* = 9.6 Hz, H-1), 3.83 (s, 3H, ArOC$\underline{H}_3$), 3.80 (dd, 1H, *J* = 9.2, 3.4 Hz, H-3), 3.70 (qd, 1H, *J* = 6.4, 1.1 Hz, H-5), 3.58 (app t, 1H, *J* = 9.4 Hz, H-2), 2.37 (s, 3H, ArC$\underline{H}_3$), 2.19 (s, 3H, COC$\underline{H}_3$), 1.23 (d, 3H, *J* = 6.4 Hz, H-6); ^{13}C NMR (126 MHz; $CDCl_3$): δ 171.3 ($\underline{C}OCH_3$), 159.6 (Ar), 137.7 (Ar), 132.3 (Ar), 130.2 (Ar), 130.0 (Ar), 129.7 (Ar), 114.0 (Ar), 87.9 (C-1), 77.6 (C-2), 75.0 (Ar$\underline{C}H_2$), 73.9 (C-3), 73.2 (C-5), 72.7 (C-4), 55.3 (ArO$\underline{C}H_3$), 21.2 (Ar$\underline{C}H_3$), 20.9 (CO$\underline{C}H_3$), 16.8 (C-6); HRMS (ESI) Calc. for [M + Na]$^+$ $C_{23}H_{28}NaO_6S$: 455.1499; Found 455.1494.



***p*-Tolyl 3,4-*O*-acetyl-2-*O*-(4-methoxybenzyl)-1-thio-β-L-fucopyranoside (2.13)**

To a stirred solution of **2.22** (997.5mg, 2.306 mmol) in pyridine (10.0 mL) was added acetic anhydride (8.0 mL) at 0 ˚C. The reaction mixture was warmed to room temperature and stirred for 16 h and then concentrated. The residue was dissolved in CH_2Cl_2 (70 mL) and washed with 10% HCl (aq), saturated $NaHCO_3$ (aq), and brine. The organic layer was dried over Na_2SO_4, filtered and then the filtrate was concentrated to give **2.13** (979.1 mg, 90%) as a syrup, which was not further purified. R_f 0.37 (4:1 hexanes─ EtOAc); [α]D ─ 10.0 (*c* 1.3, $CHCl_3$); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.54 – 7.49 (m, 2H, Ar), 7.31 – 7.25 (m, 2H, Ar), 7.16 – 7.11 (m, 2H, Ar),

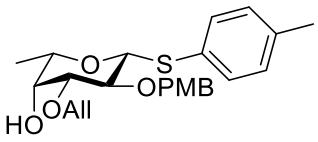
6.91 – 6.85 (m, 2H, Ar), 5.23 (app d, 1H, J = 3.4 Hz, H-4), 5.02 (dd, 1H, J = 9.7, 3.3 Hz, H-3), 4.77 (d, 1H, J = 10.5 Hz, ArC$\underline{H}_2$), 4.65 (d, 1H, J = 9.7 Hz, H-1), 4.54 (d, 1H, J = 10.5 Hz, ArC$\underline{H}$-$_2$), 3.79 (s, 3H, ArOC$\underline{H}_3$), 3.75 – 3.65 (m, 2H, H-5, H-2), 2.35 (s, 3H, COC$\underline{H}_3$), 2.16 (s, 3H, ArC$\underline{H}_3$), 1.98 (s, 3H, COC$\underline{H}_3$), 1.20 (d, 3H, J = 6.3 Hz, H-6); ^{13}C NMR (126 MHz; $CDCl_3$): δ 170.5 ($\underline{C}OCH_3$), 169.9 ($\underline{C}OCH_3$), 159.4 (Ar), 137.7 (Ar), 132.5 (Ar), 130.2 (Ar), 129.9 (Ar), 129.7 (Ar), 113.8 (Ar), 87.9 (C-1), 75.0 (Ar$\underline{C}H_2$), 74.8, 74.7 (C-2 & C-3), 72.7 (C-5), 71.0 (C-4), 55.3 (ArO$\underline{C}H_3$), 21.2 (Ar$\underline{C}H_3$), 20.8 (CO$\underline{C}H_3$), 20.8 (CO$\underline{C}H_3$), 16.6 (C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{25}H_{30}NaO_7S$: 497.1604; Found 497.1601.



***p*-Tolyl 2-*O*-(4-methoxybenzyl)-1-thio-β-L-fucopyranoside (2.23)[9,10]**

To a stirred solution of **2.22** (2.828 g, 6.538 mmol) in CH_3OH (15.0 mL) was added $NaOCH_3$ in CH_3OH (10.0 mL, 0.2 M). The reaction mixture was stirred at room temperature for 17 h. Amberlite® IR-120 (H^+) cation exchange resin was added, the mixture filtered and then the filtrate was concentrated. The crude residue was purified via flash chromatography (1:1 hexanes─ EtOAc) to give **2.23** (2.264 g, 89%) as a syrup. R_f 0.16 (3:2 hexanes─ EtOAc); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.53 – 7.48 (m, 2H, Ar), 7.37 – 7.32 (m, 2H, Ar), 7.18 – 7.13 (m, 2H, Ar), 6.95 – 6.89 (m, 2H, Ar), 4.92 (d, 1H, J = 10.8 Hz, ArC$\underline{H}_2$), 4.64 (d, 1H, J = 10.8 Hz,

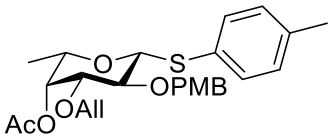
ArC<u>H</u>$_2$), 4.55 (d, 1H, *J* = 9.6 Hz, H-1), 3.83 (s, 3H, ArOC<u>H</u>$_3$), 3.74 (app d, 1H, *J* = 3.3 Hz, H-4), 3.66 – 3.58 (m, 2H, H-3, H-5), 3.52 (app t, 1H, *J* = 9.3 Hz, H-2), 2.37 (s, 3H, ArC<u>H</u>$_3$), 1.36 (d, 3H, *J* = 6.5 Hz, H-6); ^{13}C NMR (126 MHz; $CDCl_3$): δ 159.6 (Ar), 137.7 (Ar), 132.4 (Ar), 130.3 (Ar), 130.2 (Ar), 130.0 (Ar), 129.7 (Ar), 114.1 (Ar), 87.8 (C-1), 77.7 (C-2), 75.3 (C-3), 74.9 (Ar<u>C</u>H$_2$), 74.4 (C-5), 71.7 (C-4), 55.3 (ArO<u>C</u>H$_3$), 21.2 (Ar<u>C</u>H$_3$), 16.7 (C-6).



***p*-Tolyl 3-*O*-allyl-2-*O*-(4-methoxybenzyl)-1-thio-β-L-fucopyranoside (2.24)[9,10]**

To a stirred solution of **2.23** (210.0 mg, 0.5478 mmol) in dry toluene (12.0 mL) was added di-*n*-butyltin oxide (163.4 mg, 0.6564 mmol) at room temperature. The reaction mixture was heated at reflux 26 h under Ar. The reaction mixture was cooled to room temperature and the solvent evaporated. The residue was dissolved in dry DMF (3.0 mL) and cesium fluoride (132.1 mg, 0.8697 mmol) and allyl bromide (0.10 mL, 1.2 mmol) were added at room temperature, under an Ar atmosphere. The reaction mixture was stirred at 60 ˚C for 15 h, cooled to room temperature and diluted with EtOAc (60 mL). The organic layer was washed with brine and the aqueous layer extracted with EtOAc (40 mL × 3). The combined organic layers were dried over Na_2SO_4, filtered and then the filtrate was concentrated. The crude residue was purified via flash chromatography (2:1 hexanes─ EtOAc) to give **2.24** (125.5 mg, 54%) as a syrup. R_f 0.55 (3:2 hexanes─ EtOAc); ^{1}H NMR (498 MHz; $CDCl_3$): δ 7.54 – 7.48 (m, 2H, Ar), 7.42 – 7.35 (m, 2H,

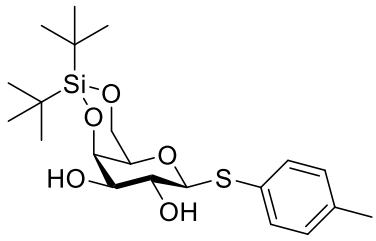
Ar), 7.16 – 7.10 (m, 2H, Ar), 6.94 – 6.88 (m, 2H, Ar), 5.96 (ddt, 1H, J = 17.3, 10.4, 5.7 Hz, $OCH_2C\underline{H}=CH_2$), 5.33 (app dq, 1H, J = 17.2, 1.6 Hz, $OCH_2CH=C\underline{H}_2$), 5.23 (app dq, 1H, J = 10.4, 1.3 Hz, $OCH_2CH=C\underline{H}_2$), 4.77 (d, 1H, J = 9.9 Hz, $ArC\underline{H}_2$), 4.67 (d, 1H, J = 9.9 Hz, $ArC\underline{H}_2$), 4.53 (d, 1H, J = 9.7 Hz, H-1), 4.26 – 4.17 (m, 2H, $OC\underline{H}_2CH=CH_2$) , 3.83 (s, 3H, $ArOC\underline{H}_3$), 3.84 – 3.81 (m, 1H, H-4), 3.61 (dd, 1H, J = 9.7, 9.0 Hz, H-2), 3.57 (app q, 1H, J = 6.4 Hz, H-5), 3.48 (dd, 1H, J = 9.0, 3.3 Hz, H-3), 2.35 (s, 3H, $ArC\underline{H}_3$), 2.24 (d, 1H, J = 2.6 Hz, 4-O$\underline{H}$), 1.39 (d, 3H, J = 6.5 Hz, H-6); ^{13}C NMR (125 MHz; $CDCl_3$): δ 159.4 (Ar), 137.5 (Ar), 134.6 ($OCH_2\underline{C}H=CH_2$), 132.7 (Ar), 130.6 (Ar), 130.1 (Ar), 130.0 (Ar), 129.6 (Ar), 117.5 ($OCH_2CH=\underline{C}H_2$), 113.8 (Ar), 87.9 (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 ($ArO\underline{C}H_3$), 21.1 ($Ar\underline{C}H_3$), 16.8 (C-6).



***p*-Tolyl 4-*O*-acetyl-3-*O*-allyl-2-*O*-(4-methoxybenzyl)-1-thio-β-L-fucopyranoside (2.14)[9,10]**

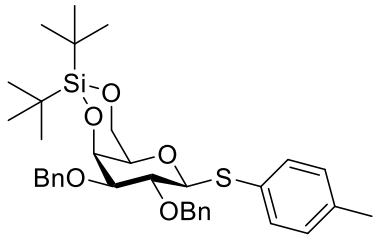
To a stirred solution of **2.24** (2.237 g, 5.196 mmol) in pyridine (10.0 mL) was added acetic anhydride (5.0 mL) at room temperature. The reaction mixture was stirred at room temperature for 8 h and then concentrated. The residue was dissolved in EtOAc (150 mL) and washed with 10% HCl (aq), saturated $NaHCO_3$ (aq), and brine. The organic layer was dried over Na_2SO_4, filtered and then the filtrate was concentrated. The crude residue was purified via flash

chromatography (4:1 hexanes─ EtOAc) to give **2.14** (1.945 g, 79%) as a syrup. R_f 0.55 (3:2 hexanes─ EtOAc); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.54 – 7.49 (m, 2H, Ar), 7.42 – 7.36 (m, 2H, Ar), 7.15 – 7.10 (m, 2H, Ar), 6.94 – 6.87 (m, 2H, Ar), 5.92 (ddt, 1H, J = 17.1, 10.2, 5.7 Hz, $OCH_2C\underline{H}=CH_2$), 5.35 – 5.27 (m, 2H, $OCH_2CH=C\underline{H}_2$, H-4), 5.20 (app dq, 1H, J = 10.4, 1.4 Hz, $OCH_2CH=C\underline{H}_2$), 4.73, 4.69 (ABq, 2H, J_{AB} = 9.8 Hz, $ArC\underline{H}_2$), 4.59 (d, 1H, J = 9.4 Hz, H-1), 4.20 (app ddt, 1H, J = 12.5, 5.6, 1.4 Hz, $OC\underline{H}_2CH=CH_2$), 4.06 (app ddt, 1H, J = 12.6, 5.8, 1.4 Hz, $OC\underline{H}_2CH=CH_2$), 3.83 (s, 3H, $ArOC\underline{H}_3$), 3.67 (app q, 1H, J = 6.4 Hz, H-5), 3.60 (app t, 1H, J = 9.3 Hz, H-2), 3.55 (dd, 1H, J = 9.1, 3.3 Hz, H-4), 2.36 (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 (126 MHz; $CDCl_3$): δ 170.8 ($\underline{C}OCH_3$), 159.4 (Ar), 137.6 (Ar), 134.5 ($OCH_2\underline{C}H=CH_2$), 132.6 (Ar), 130.6 (Ar), 130.1 (Ar), 130.0 (Ar), 129.6 (Ar), 117.5 ($OCH_2CH=\underline{C}H_2$), 113.8 (Ar), 88.0 (C-1), 81.0 (C-3), 76.4 (C-2), 75.4 ($Ar\underline{C}H_2$), 73.0 (C-5), 70.9 ($O\underline{C}H_2CH=CH_2$), 70.0 (C-4), 55.3 ($ArO\underline{C}H_3$), 21.2 ($Ar\underline{C}H_3$), 20.9 ($CO\underline{C}H_3$), 16.9 (C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{26}H_{32}NaO_6S$: 495.1812; Found 495.1808.



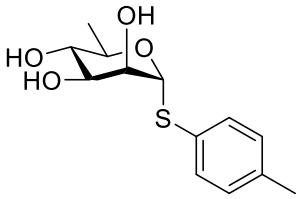
_p_-Tolyl 4,6-_O_-di-_tert_-butylsilylene-1-thio-β-D-galactopyranoside (2.31)[16]

To a stirred solution of *p*-tolyl 1-thio-β-D-galactopyranoside (1.492 g, 5.211 mmol) in pyridine (6.0 mL) was added di-*tert*-butylsilyl bis(trifluoromethanesulfonate) (1.84 mL, 5.64 mmol) at room temperature, under an Ar atmosphere. The reaction mixture was stirred at room temperature for 1 h and then concentrated. The residue was dissolved in EtOAc (60 mL), washed with water and brine, dried over Na_2SO_4, filtered and then the filtrate was concentrated. The crude residue was purified via flash chromatography (3:2 hexanes─ EtOAc) to give **2.31** (1.738 g, 79%) as a colourless film. R_f 0.23 (3:2 hexanes─ EtOAc); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.51 – 7.46 (m, 2H), 7.16 – 7.11 (m, 2H), 4.49 (d, 1H, J = 9.7 Hz, H-1), 4.45 (dd, 1H, J = 3.6, 1.2 Hz, H-4), 4.32 – 4.23 (m, 2H, H6a, H-6b), 3.74 (dd, 1H, J = 9.8, 8.8 Hz, H-2), 3.54 (dd, 1H, J = 9.0, 3.5 Hz, H-3), 3.48 – 3.45 (m, 1H, H-5), 2.36 (s, 3H, ArC$\underline{H}_3$), 1.08 (s, 9H, C(C$\underline{H}_3$)$_3$), 1.05 (s, 9H, C(C$\underline{H}_3$)$_3$); ^{13}C NMR (126 MHz; $CDCl_3$): δ 138.3 (Ar), 133.4 (Ar), 129.7 (Ar), 129.2 (Ar), 89.5 (C-1), 75.3 (C-5), 75.1 (C-3), 72.6 (C-4), 70.7 (C-2), 67.1 (C-6), 27.6 (C($\underline{C}$H$_3$)$_3$), 27.4 (C($\underline{C}$H$_3$)$_3$), 23.4 ($\underline{C}$(CH$_3$)$_3$), 21.2 (Ar$\underline{C}$H$_3$), 20.7 ($\underline{C}$(CH$_3$)$_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{21}H_{34}NaO_5SSi$: 449.1788; Found 449.1786.



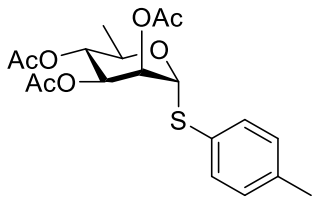
***p*-Tolyl 2,3-di-*O*-benzy-4,6-*O*-di-*tert*-butylsilylene-1-thio-β-D-galactopyranoside (2.18)[16]**

To a stirred solution of **2.31** (201.8 mg, 0.4730 mmol) and benzyl bromide (0.26 mL, 2.2 mmol) in dry DMF was added sodium hydride (75.0 mg, 1.88 mmol, 60% dispersion in mineral oil) in small portions over 30 min at 0 ˚C, under an Ar atmosphere. The mixture was stirred at 0 ˚C for 30 min and then warmed to room temperature and stirred for 1 h. The reaction mixture was diluted with EtOAc (50 mL) and poured into ice water. The organic layer was washed with brine, dried over Na_2SO_4, filtered and then the filtrate was concentrated. The crude residue was purified via flash chromatography (9:1 hexanes─ EtOAc) to give **2.18** (204.3 mg, 71%) as a white solid. R_f 0.58 (5:1 hexanes─ EtOAc); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.53 – 7.44 (m, 6H, Ar), 7.43 – 7.30 (m, 6H, Ar), 7.16 – 7.11 (m, 2H, Ar), 5.00, 4.96 (ABq, 2H, J = 10.3 Hz, ArC$\underline{H}_2$), 4.83, 4.75 (ABq, 2H, J = 12.0 Hz, ArC$\underline{H}_2$), 4.65 (d, 1H, J = 9.8 Hz, H-1), 4.54 (app d, 1H, J = 3.1 Hz, H-4), 4.29 – 4.18 (m, 2H, H-6a, H-6b), 3.89 (app t, 1H, J = 9.4 Hz, H-2), 3.52 (dd, 1H, J = 9.0, 3.0 Hz, H-3), 3.29 (app s, 1H, H-5), 2.37 (s, 3H, ArC$\underline{H}_3$), 1.20 (s, 9H, C(C$\underline{H}_3$)$_3$), 1.14 (s, 9H, C(C$\underline{H}_3$)$_3$); ^{13}C NMR (126 MHz; $CDCl_3$): δ 138.5 (Ar), 138.5 (Ar), 137.6 (Ar), 132.9 (Ar), 131.0 (Ar), 129.6 (Ar), 128.5 (Ar), 128.4(9) (Ar), 128.4 (Ar), 127.9 (Ar), 127.8 (Ar), 89.1 (C-1), 82.9 (C-3), 77.4 (C-2), 76.0 (Ar$\underline{C}H_2$), 74.8 (C-5), 71.1 (Ar$\underline{C}H_2$), 70.1 (C-4), 67.5 (C-6), 27.8 (C($\underline{C}H_3$)$_3$), 27.7 (C($\underline{C}H_3$)$_3$), 23.5 ($\underline{C}$(CH$_3$)$_3$), 21.2 (Ar$\underline{C}H_3$), 20.8 ($\underline{C}$(CH$_3$)$_3$); HRMS (ESI) Calc. for [M + Na]$^+$ $C_{35}H_{46}NaO_5SSi$: 629.2727; Found 629.2725.



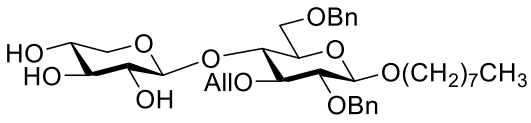
***p*-Tolyl 1-thio-α-D-rhamnopyranoside (2.33)[18]**

To a stirred solution of *p*-tolyl 1-thio-α-D-mannopyranoside (201.6 mg, 0.7041 mmol) in dry pyridine (8.0 mL) was added a solution of 4-toluenesulfonyl chloride (162.7 mg, 0.8534 mmol) in dry pyridine (5.0 mL) drop-wise under an Ar atmosphere at 0 ˚C. The reaction mixture was warmed to room temperature and stirred for 7 h then the solvent evaporated. The residue was dissolved in chloroform (20.0 mL) and washed with brine, dried over Na_2SO_4, filtered and then the filtrate was concentrated. The resulting residue was dissolved in dry THF (7.0 mL) and was slowly added drop-wise at 0 ˚C to a solution of $LiAlH_4$ (80.5 mg, 2.12 mmol) in dry THF (8.0 mL) under an Ar atmosphere. The reaction mixture was heated at reflux for 3.5 h and then chilled to 0 ˚C before slowly adding water, followed by 2N H_2SO_4 (10.0 mL). The aqueous layer was extracted with EtOAc (20 mL × 3) and the combined organic layers were dried over Na_2SO_4, filtered and then the filtrate was concentrated. The crude residue was purified via flash chromatography (3:1 EtOAc─ hexanes) to give **2.33** (105.6 mg, 56%) as a white solid. R_f 0.71 (6:1 CH_2Cl_2─ CH_3OH); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.36 – 7.31 (m, 2H, Ar), 7.11 – 7.05 (m, 2H, Ar), 5.43 (d, 1H, *J* = 1.4 Hz, H-1), 4.23 (dd, 1H, *J* = 3.3, 1.5 Hz, H-2), 4.19 (dq, 1H, *J* = 9.7, 6.7 Hz, H-5), 3.83 (dd, 1H, *J* = 9.6, 3.3 Hz, H-3), 3.58 (app t, 1H, *J* = 9.5 Hz, H-4), 2.32 (s, 3H, COC<u>H</u>$_3$), 1.34 (d, 3H, *J* = 6.2 Hz, H-6); ^{13}C NMR (126 MHz; $CDCl_3$): δ 137.6 (Ar), 132.1 (Ar), 130.2 (Ar), 129.9 (Ar), 88.3 (C-1), 73.2 (C-4), 72.5 (C-2), 72.1 (C-3), 69.3 (C-5), 21.1 (Ar<u>C</u>H$_3$), 17.5 (C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{13}H_{18}NaO_4S$: 293.0818; Found 293.0816.



***p*-Tolyl 2,3,4-*O*-acetyl-1-thio-α-D-rhamnopyranoside (2.17)**

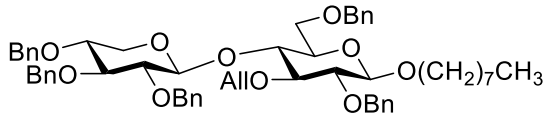
To a stirred solution of **2.33** (750.7 mg, 2.777 mmol) in pyridine (6.0 mL) was added acetic anhydride (3.0 mL) at 0 ˚C. The reaction mixture was warmed to room temperature, stirred for 21 h and then concentrated. The residue was dissolved in EtOAc (20 mL) and washed with 1M HCl (aq), saturated $NaHCO_3$ (aq), and water. The organic layer was dried over Na_2SO_4, filtered and then the filtrate wasconcentrated. The crude residue was purified via flash chromatography (3:1 hexanes─ EtOAc) to give **2.17** (956.1 mg, 87%) as a white solid. R_f 0.75 (1:1 hexanes─ EtOAc); $[\alpha]_D$ +104.7 (*c* 2.5, $CHCl_3$); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.41 – 7.35 (m, 2H, Ar), 7.17 – 7.12 (m, 2H, Ar), 5.51 (dd, 1H, *J* = 3.4, 1.7 Hz, H-2), 5.35 (d, 1H, *J* = 1.6 Hz, H-1), 5.32 (dd, 1H, *J* = 10.0, 3.4 Hz, H-3), 5.16 (app t, 1H, *J* = 9.9 Hz, H-4), 4.39 (dq, 1H, *J* = 9.7, 6.2 Hz, H-5), 2.35 (s, 3H, ArC$\underline{H}_3$), 2.15 (s, 3H, COC$\underline{H}_3$), 2.10 (s, 3H, COC$\underline{H}_3$), 2.03 (s, 3H, COC$\underline{H}_3$), 1.26 (d, 3H, *J* = 6.2 Hz, H-6); ^{13}C NMR (126 MHz; $CDCl_3$): δ 170.0 ($\underline{C}OCH_3$), 170.0 ($\underline{C}OCH_3$), 169.9 ($\underline{C}OCH_3$), 138.2 (Ar), 132.5 (Ar), 130.0 (Ar), 129.4 (Ar), 86.1 (C-1), 71.3, 71.2 (C-2 & C-4), 69.4 (C-3), 67.7 (C-5), 21.1 (Ar$\underline{C}H_3$), 20.9 (CO$\underline{C}H_3$), 20.8 (CO$\underline{C}H_3$), 20.7 (CO$\underline{C}H_3$), 17.4 (C-6); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{19}H_{24}NaO_7S$: 419.1135; Found 419.1137.



Octyl β-D-xylopyranosyl-(1→4)-3-*O*-allyl-2,6-di-*O*-benzyl-β-D-glucopyranoside (2.34)

To a stirred solution of acceptor **2.15** (1.106 g, 2.158 mmol) and donor **2.16** (1.355 g, 3.028 mmol) in dry CH_2Cl_2 (24.0 mL) was added oven-dried molecular sieves (2.4 g, 4Å, powder) under an Ar atmosphere. After stirring at room temperature for 30 min, the solution was chilled to ─ 30 ˚C and trifluoromethanesulfonic acid (0.04 mL, 0.5 mmol) was added drop-wise. The resulting solution was slowly warmed to ─ 25 ˚C and stirred for a total of 25 min before triethylamine was added. The solution was filtered through Celite and the filtrate was concentrated. The crude residue was passed through a silica column (2:1 hexanes─ EtOAc). The resulting product was dissolved in CH_3OH (30.0 mL) and $NaOCH_3$ in CH_3OH (5.0 mL, 1.0 M) was added. The reaction mixture was stirred at room temperature for 13 h. Amberlite® IR-120 (H^+) cation exchange resin was added, the mixture filtered and then the filtrate was concentrated. The crude residue was purified via flash chromatography (12:1 CH_2Cl_2─ CH_3OH) to give **2.34** (1.117 g, 80%) as a white solid. R_f 0.58 (9:1 CH_2Cl_2─ CH_3OH); $[\alpha]_D$ +12.1 (*c* 1.9, $CHCl_3$); ^1H NMR (700 MHz; $CDCl_3$): δ 7.37 – 7.22 (m, 10H, Ar), 5.93 (ddt, 1H, *J* = 17.4, 10.4, 5.8 Hz, $OCH_2C\underline{H}=CH_2$), 5.23 (app dq, 1H, *J* = 17.2, 1.7 Hz, $OCH_2CH=C\underline{H}_2$), 5.12 (app dq, 1H, *J* = 10.4, 1.4 Hz, $OCH_2CH=C\underline{H}_2$), 4.88 (d, 1H, *J* = 10.9 Hz, $ArC\underline{H}_2$), 4.68 (d, 1H, *J* = 11.0 Hz, $ArC\underline{H}_2$), 4.66 (d, 1H, *J* = 12.0 Hz, $ArC\underline{H}_2$), 4.57 (d, 1H, *J* = 12.1 Hz, $ArC\underline{H}_2$), 4.46 (d, 1H, *J* = 7.5 Hz, Xyl-H-1), 4.34 – 4.28 (m, 2H, $OC\underline{H}_2CH=CH_2$), 4.30 (d, 1H, *J* = 7.8 Hz, Glc-H-1), 3.91 – 3.84 (m, 3H, Xyl-H-5a, Glc-H-6a, $OC\underline{H}_2(CH_2)_6CH_3$), 3.82 (app t, 1H, *J* = 9.3 Hz, Glc-H-4), 3.75 (dd, 1H, *J* = 11.7, 2.4 Hz, Glc-H-6b), 3.56 (ddd, 1H, *J* = 10.2, 8.7, 5.4 Hz, Xyl-H-4), 3.48 (dt, 1H, *J* =

9.4, 6.8 Hz, OC<u>H</u>$_2$(CH$_2$)$_6$CH$_3$), 3.44 (app t, 1H, *J* = 9.2 Hz, Glc-H-3), 3.41 – 3.37 (m, 1H, Glc-H-5), 3.38 (app t, 1H, *J* = 9.0 Hz, Xyl-H-3), 3.35 (dd, 1H, *J* = 9.2, 7.8 Hz, Glc-H-2), 3.25 (dd, 1H, *J* = 9.1, 7.5 Hz, Xyl-H-2), 3.12 (dd, 1H, *J* = 11.7, 10.1 Hz, Xyl-H-5b), 1.67 – 1.57 (m, 2H, , OCH$_2$C<u>H</u>$_2$(CH$_2$)$_5$CH$_3$), 1.44 – 1.20 (m, 10H, OCH$_2$CH$_2$(C<u>H</u>$_2$)$_5$CH$_3$), 0.87 (t, 3H, *J* = 7.0 Hz, O(CH$_2$)$_7$C<u>H</u>$_3$); ^{13}C NMR (176 MHz; CDCl$_3$): δ 138.5 (Ar), 137.6 (Ar), 135.3 (OCH$_2$<u>C</u>H=CH$_2$), 128.4 (Ar), 128.3 (Ar), 128.1 (Ar), 128.0 (Ar), 127.9 (Ar), 127.7 (Ar), 116.7 (OCH$_2$CH=<u>C</u>H$_2$), 103.8 (Xyl-C-1), 103.6 (Glc-C-2), 82.9 (Glc-C-3), 82.1 (Glc-C-2), 77.7 (Glc-C-4), 76.5 (Xyl-C-3), 74.9 (Ar<u>C</u>H$_2$), 74.4 (O<u>C</u>H$_2$CH=CH$_2$), 74.3, 74.2 (Xyl-C-5 & Glc-C-5), 73.6 (Ar<u>C</u>H$_2$), 70.1 (O<u>C</u>H$_2$(CH$_2$)$_6$CH$_3$), 69.5 (Xyl-C-4), 68.7 (Glc-C-6), 65.8 (Xyl-C-5), 31.8 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 29.8 (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$_3$), 26.2 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 22.7 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 14.1 (O(CH$_2$)$_7$<u>C</u>H$_3$); HRMS (ESI) Calc. for [M + Na]$^+$ C$_{36}$H$_{52}$NaO$_{10}$: 667.3453; Found 667.3451.

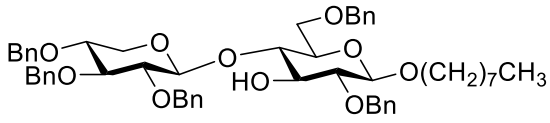


Octyl 2,3,4-*O*-benzyl-β-D-xylopyranosyl-(1→4)-3-*O*-allyl-2,6-di-*O*-benzyl-β-D-glucopyranoside (2.35)

To a stirred solution of **2.34** (1.117 g, 1.732 mmol) in dry DMF was added sodium hydride (0.250 g, 6.25 mmol, 60% dispersion in mineral oil) in one portion at 0 ˚C, under an Ar

atmosphere. The mixture was stirred at 0 ˚C for 1 h then benzyl bromide (0.72 mL, 8.9 mmol) was added drop-wise. The reaction mixture was slowly warmed to room temperature and stirred for 19.5 h. The mixture was chilled to 0 ˚C, CH_3OH was added and then poured into a saturated $NaHCO_3$ (aq). The aqueous layer was extracted with Et_2O (120 mL × 3) and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered and then the filtrate was concentrated. The crude residue was purified via flash chromatography (6:1 hexanes─ EtOAc) to give **2.35** (1.104 g, 70%) as a colourless syrup. R_f 0.53 (4:1 hexanes─ EtOAc); [α]ᴅ +11.0 (*c* 1.7, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.43 – 7.26 (m, 25H, Ar), 5.99 (ddt, 1H, *J* = 17.4, 10.4, 6.0 Hz, $OCH_2C\underline{H}=CH_2$), 5.25 (app dq, 1H, *J* = 17.3, 1.7 Hz, $OCH_2CH=C\underline{H}_2$), 5.15 (app dt, 1H, *J* = 10.3, 1.6 Hz, $OCH_2CH=C\underline{H}_2$), 4.91 (d, 1H, *J* = 11.0 Hz, $ArC\underline{H}_2$), 4.91, 4.87 (ABq, 2H, J_{AB} = 11.0 Hz, $ArC\underline{H}_2$), 4.81, 4.79 (ABq, 2H, J_{AB} = 11.2 Hz, $ArC\underline{H}_2$), 4.76 (d, 1H, *J* = 11.2 Hz, $ArC\underline{H}_2$), 4.74 (d, 1H, *J* = 11.6 Hz, $ArC\underline{H}_2$), 4.65 (d, 1H, *J* = 11.7 Hz, $ArC\underline{H}_2$), 4.58 (d, 1H, *J* = 12.1 Hz, $ArC\underline{H}_2$), 4.44 (d, 1H, *J* = 12.1 Hz, $ArC\underline{H}_2$), 4.43 (d, 1H, *J* = 7.8 Hz, Xyl-H-1), 4.39 (app ddt, 1H, *J* = 11.8, 6.0, 1.4 Hz, $OC\underline{H}_2CH=CH_2$), 4.36 (d, 1H, *J* = 7.7 Hz, Glc-H-1), 4.28 (app ddt, 1H, *J* = 11.9, 6.0, 1.4 Hz, $OC\underline{H}_2CH=CH_2$), 3.96 (dt, 1H, *J* = 9.6, 6.7 Hz, $OC\underline{H}_2(CH_2)_6CH_3$), 3.94 (dd, 1H, *J* = 11.3, 4.9 Hz, Xyl-H-5a), 3.87 (dd, 1H, *J* = 9.8, 8.8 Hz, Glc-H-4), 3.80 (dd, 1H, *J* = 10.9, 4.4 Hz, Glc-H-6a), 3.73 (dd, 1H, *J* = 10.9, 1.9 Hz, Glc-H-6b), 3.61 (ddd, 1H, *J* = 10.2, 8.8, 5.3 Hz, Xyl-H-4), 3.54 (dt, 1H, *J* = 9.4, 6.8 Hz, $OC\underline{H}_2(CH_2)_6CH_3$), 3.52 (app t, 1H, *J* = 8.6 Hz, Xyl-H-3), 3.43 (app t, 1H, *J* = 9.0 Hz, Glc-H-3), 3.40 – 3.35 (m, 2H, Glc-H-2, Glc-H-5), 3.31 (dd, 1H, *J* = 9.2, 7.7 Hz, Xyl-H-2), 3.10 (dd, 1H, *J* = 11.8, 10.2 Hz, Xyl-H-5b), 1.72 – 1.62 (m, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.48 – 1.27 (m, 10H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 0.92 (t, 3H, *J* = 7.0 Hz, $O(CH_2)_7C\underline{H}_3$); ^{13}C NMR (176 MHz; $CDCl_3$): δ 138.8 (Ar), 138.7 (Ar), 138.5 (Ar), 138.3(4) (Ar), 138.3 (Ar), 135.7 ($OCH_2\underline{C}H=CH_2$), 128.5 (Ar), 128.4 (Ar), 128.3(3) (Ar), 128.3 (Ar), 128.2(8)

(Ar), 128.2 (Ar), 127.9 (Ar), 127.8 (Ar), 127.7(9) (Ar), 127.7(6) (Ar), 127.7 (Ar), 127.6 (Ar), 127.5(9) (Ar), 127.5(7) (Ar), 127.5 (Ar), 116.7 ($OCH_2CH=\underline{C}H_2$), 103.6 (Glc-C-1), 103.2 (Xyl-C-1), 84.1 (Xyl-C-3), 82.5 (Glc-C-3), 82.4 (Xyl-C-2), 81.7 (Glc-C-2), 78.3 (Xyl-C-4), 76.9 (Glc-C-4), 75.6 ($Ar\underline{C}H_2$), 75.1(3) (Glc-C-5), 75.1 ($Ar\underline{C}H_2$), 75.0(8) ($Ar\underline{C}H_2$), 74.6 ($O\underline{C}H_2CH=CH_2$), 73.3 ($Ar\underline{C}H_2$), 73.2 ($Ar\underline{C}H_2$), 70.1 ($O\underline{C}H_2(CH_2)_6CH_3$), 68.3 (Glc-C-6), 63.9 (Xyl-C-5), 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 ($OCH_2(\underline{C}H_2)_6CH_3$), 26.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 14.2 ($O(CH_2)_7\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{57}H_{70}NaO_{10}$: 937.4861; Found 937.4864.

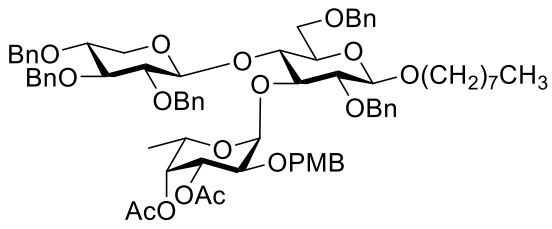


Octyl 2,3,4-*O*-benzyl-β-D-xylopyranosyl-(1→4)-2,6-di-*O*-benzyl-β-D-glucopyranoside (2.12)

A solution of **2.35** (1.104 g, 1.206 mmol) in dry THF (10.0 mL) was degassed via vacuum and (1,5-Cyclooctadiene)bis(methyldiphenylphosphine)iridium(I) hexafluorophosphate (61.8 mg, 73.1 μmol) was added under an Ar atmosphere. The resulting mixture was stirred at 0 ˚C for 20 min before the catalyst was activated with hydrogen (stirring for 2 min under a hydrogen atmosphere). Excess hydrogen was removed by three cycles of vacuum purging with Ar. The reaction mixture was stirred at room temperature for 3 h under an Ar atmosphere and then concentrated. The residue was dissolved in acetone─ water (10:1, 11.0 mL) and HgO (0.368 g, 1.70 mmol) and $HgCl_2$ (0.398 g, 1.47 mmol) were added. The reaction mixture was stirred at

room temperature for 2.5 h and then concentrated. The residue was diluted with EtOAc (100 mL) and was washed with 10% KI (aq), 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 then the filtrate was concentrated. The crude residue was purified via flash chromatography (5:1 hexanes─ EtOAc) to give **2.12** (0.960 g, 91%) as a syrup. R_f 0.57 (3:1 hexanes─ EtOAc); $[\alpha]_D$ +12.5 (*c* 0.7, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.44 – 7.40 (m, 2H, Ar), 7.38 – 7.23 (m, 23H, Ar), 4.91 (d, 1H, J = 11.4 Hz, ArC$\underline{H}_2$), 4.90, 4.87 (ABq, 2H, J_{AB} = 11.0 Hz, ArC$\underline{H}_2$), 4.82 (d, 1H, J = 11.4 Hz, ArC$\underline{H}_2$), 4.79, 4.78 (ABq, 2H, J_{AB} = 11.1 Hz, ArC$\underline{H}_2$), 4.73 (d, 1H, J = 11.7 Hz, ArC$\underline{H}_2$), 4.61 (d, 1H, J = 11.7 Hz, ArC$\underline{H}_2$), 4.44 (d, 1H, J = 12.1 Hz, ArC$\underline{H}_2$), 4.39 (d, 1H, J = 7.8 Hz, Xyl-H-1), 4.33 (d, 1H, J = 12.1 Hz, ArC$\underline{H}_2$), 4.26 (d, 1H, J = 7.8 Hz, Glc-H-1), 3.96 – 3.89 (m, 3H, OC$\underline{H}_2(CH_2)_6CH_3$, Xyl-H-5a, Glc-3-O$\underline{H}$), 3.70 (dd, 1H, J = 10.6, 1.7 Hz, Glc-H-6a), 3.68 (app t, 1H, J = 8.9 Hz, Xyl-H-3), 3.66 (dd, 1H, J = 10.7, 4.6 Hz, Glc-H-6b), 3.61 (ddd, 1H, J = 10.4, 8.9, 5.4 Hz, Xyl-H-4), 3.57 (dd, 1H, J = 9.8, 8.7 Hz, Glc-H-4), 3.52 (app t, 1H, J = 9.1 Hz, Glc-H-3), 3.53 – 3.49 (m, 1H, OC$\underline{H}_2(CH_2)_6CH_3$), 3.46 (ddd, 1H, J = 9.8, 4.6, 1.8 Hz, Glc-H-5), 3.33 (dd, 1H, J = 9.4, 7.7 Hz, Glc-H-2), 3.33 (dd, 1H, J = 9.2, 7.7 Hz, Xyl-H-2), 3.16 (dd, 1H, J = 11.7, 10.4 Hz, Xyl-H-5b), 1.70 – 1.60 (m, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.45 – 1.23 (m, 10H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 0.89 (t, 3H, J = 7.0 Hz, $O(CH_2)_7C\underline{H}_3$); ^{13}C NMR (176 MHz; $CDCl_3$): δ 138.8 (Ar), 138.5 (Ar), 138.3 (Ar), 138.2 (Ar), 138.0 (Ar), 128.5 (Ar), 128.4 (Ar), 128.3(5) (Ar), 128.3 (Ar), 128.2 (Ar), 128.0 (Ar), 127.9(3) (Ar), 127.9 (Ar), 127.8 (Ar), 127.7(4) (Ar), 127.7(3) (Ar), 127.7 (Ar), 127.6(6) (Ar), 127.5(3) (Ar), 127.5 (Ar), 103.8 (Glc-C-1), 103.1 (Xyl-C-1), 83.9 (Glc-C-3), 81.5, 81.4 (Glc-C-2 & Xyl-C-2), 80.2 (Glc-C-4), 77.7 (Xyl-C-4), 75.7 (Ar$\underline{C}H_2$), 75.3 (Ar$\underline{C}H_2$), 74.8 (Xyl-C-3), 74.6 (Ar$\underline{C}H_2$), 74.3 (Glc-C-5), 73.5 (Ar$\underline{C}H_2$), 73.2 (Ar$\underline{C}H_2$), 70.2 (O$\underline{C}H_2(CH_2)_6CH_3$), 68.3 (Glc-C-6),

64.0 (Xyl-C-5), 31.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 26.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 14.1 ($O(CH_2)_7\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{54}H_{66}NaO_{10}$: 897.4548; Found 897.4552.

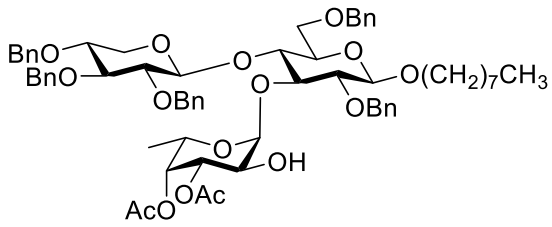


Octyl 3,4-di-*O*-acetyl-2-*O*-(4-methoxybenzyl)-α-L-fucopyranosyl-(1→3)-[2,3,4-tri-*O*-benzyl-β-D-xylopyranosyl-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranoside (2.10)

To a stirred solution of acceptor **2.12** (51.1 mg, 58.4 μmol) and donor **S3-7** (56.8 mg, 120 μmol) in dry Et_2O (5.0 mL) was added oven-dried molecular sieves (0.5 g, 4Å, powder) under an Ar atmosphere. After stirring at room temperature for 45 min, methyl trifluoromethanesulfonate (0.06 mL, 548 μmol) was added drop-wise at room temperature. The reaction mixture was stirred at room temperature for 18 h before triethylamine was added. The solution was filtered through Celite and the filtrate was concentrated. The crude residue was purified via flash chromatography (3.5:1 hexanes─ EtOAc) to give **2.10** (60.3 mg, 84%) as a colourless film. R_f 0.49 (3:1 hexanes─ EtOAc); $[\alpha]_D$ ─ 22.2 (*c* 0.7, $CHCl_3$); ^1H NMR (700 MHz; $CDCl_3$): δ 7.40 – 7.36 (m, 2H, Ar), 7.35 – 7.21 (m, 23H, Ar), 7.06 – 7.00 (m, 2H, Ar), 6.72 – 6.67 (m, 2H, Ar), 5.72 (d, 1H, *J* = 3.6 Hz, Fuc-H-1), 5.52 (dd, 1H, *J* = 10.7, 3.2 Hz, Fuc-H-3), 5.19 (dd, 1H, *J* = 3.4, 1.4 Hz, Fuc-H-4),

5.09 (d, 1H, J = 11.6 Hz, ArC$\underline{H}_2$), 5.01 (qd, 1H, J = 6.5, 1.5 Hz, Fuc-H-5), 4.86 (d, 1H, J = 10.9 Hz, ArC$\underline{H}_2$), 4.77 (d, 1H, J = 10.9 Hz, ArC$\underline{H}_2$), 4.77 (d, 1H, J = 11.6 Hz, ArC$\underline{H}_2$), 4.73 (ABq, 2H, J_{AB} = 11.0 Hz, ArC$\underline{H}_2$), 4.68 (d, 1H, J = 11.0 Hz, ArC$\underline{H}_2$), 4.65 (d, 1H, J = 11.6 Hz, ArC$\underline{H}_2$), 4.60 (d, 1H, J = 12.0 Hz, ArC$\underline{H}_2$), 4.52 (d, 1H, J = 12.1 Hz, ArC$\underline{H}_2$), 4.45 (dd, 1H, J = 11.4, 5.3 Hz, Xyl-H-5a), 4.41 (d, 1H, J = 11.9 Hz, ArC$\underline{H}_2$), 4.40 (d, 1H, J = 7.9 Hz, Xyl-H-1), 4.39 (d, 1H, J = 7.9 Hz, Glc-H-1), 4.36 (d, 1H, J = 12.1 Hz, ArC$\underline{H}_2$), 4.04 (app t, 1H, J = 9.6 Hz, Glc-H-4), 3.94 (app t, 1H, J = 9.4 Hz, Glc-H-3), 3.90 (dt, 1H, J = 9.6, 6.5 Hz, OC$\underline{H}_2$(CH$_2$)$_6$CH$_3$), 3.87 (dd, 1H, J = 10.9, 3.7 Hz, Glc-H-6a), 3.77 (dd, 1H, J = 10.7, 3.6 Hz, Fuc-H-2), 3.73 (s, 3H, ArOC$\underline{H}_3$), 3.67 (dd, 1H, J = 10.8, 1.8 Hz, Glc-H-6b), 3.64 (ddd, 1H, J = 10.6, 9.1, 5.3 Hz, Xyl-H-4), 3.53 (dd, 1H, J = 9.3, 7.8 Hz, Glc-H-2), 3.45 (dt, 1H, J = 9.4, 6.8 Hz, OC$\underline{H}_2$(CH$_2$)$_6$CH$_3$), 3.42 (app t, 1H, J = 9.1 Hz, Xyl-H-3), 3.38 (ddd, 1H, J = 9.9, 3.7, 1.8 Hz, Glc-H-5), 3.05 (dd, 1H, J = 9.1, 8.0 Hz, Xyl-H-2), 2.97 (app t, 1H, J = 10.9 Hz, Xyl-H-5b), 2.07 (s, 3H, COC$\underline{H}_3$), 1.94 (s, 3H, COC$\underline{H}_3$), 1.60 – 1.54 (m, 2H, OCH$_2$C$\underline{H}_2$(CH$_2$)$_5$CH$_3$), 1.33 – 1.15 (m, 10H, OCH$_2$CH$_2$(C$\underline{H}_2$)$_5$CH$_3$), 1.06 (d, 3H, J = 6.6 Hz, Fuc-H-6), 0.85 (t, 3H, J = 7.2 Hz, O(CH$_2$)$_7$C$\underline{H}_3$); ^{13}C NMR (176 MHz; CDCl$_3$): δ 170.6 (C$\underline{O}$CH$_3$), 169.7 (C$\underline{O}$CH$_3$), 159.1 (Ar), 138.9 (Ar), 138.7(3) (Ar), 138.7 (Ar), 138.4 (Ar), 138.2 (Ar), 130.1 (Ar), 129.6 (Ar), 128.4 (Ar), 128.3 (Ar), 128.2(8) (Ar), 128.2(6) (Ar), 128.0(4) (Ar), 128.0(2) (Ar), 127.8 (Ar), 127.7 (Ar), 127.6 (Ar), 127.5(6) (Ar), 127.5(1) (Ar), 127.5 (Ar), 127.1 (Ar), 126.7 (Ar), 113.5 (Ar), 103.6, 103.4 (Xyl-C-1 & Glc-C-1), 96.8 (Fuc-C-1, J_{C-H} = 174.9 Hz), 83.8 (Xyl-C-3), 83.1 (Glc-C-2), 82.6 (Xyl-C-2), 78.4 (Xyl-C-4), 75.7 (Ar$\underline{C}$H$_2$), 75.2(3) (Glc-C-5), 75.2 (Ar$\underline{C}$H$_2$), 74.9 (Glc-C-4), 74.3 (Glc-C-3), 73.7 (Ar$\underline{C}$H$_2$), 73.3 (Ar$\underline{C}$H$_2$), 72.8 (Ar$\underline{C}$H$_2$), 72.4 (Fuc-C-4), 72.0 (Ar$\underline{C}$H$_2$), 71.9 (Fuc-C-2), 70.3 (Fuc-C-3), 70.2 (O$\underline{C}$H$_2$(CH$_2$)$_6$CH$_3$), 67.8 (Glc-C-6), 63.8 (Xyl-C-5), 63.6 (Fuc-C-5), 55.2 (ArO$\underline{C}$H$_3$), 31.8 (OCH$_2$(C$\underline{H}_2$)$_6$CH$_3$), 29.6 (OCH$_2$(C$\underline{H}_2$)$_6$CH$_3$), 29.4 (OCH$_2$(C$\underline{H}_2$)$_6$CH$_3$), 29.2

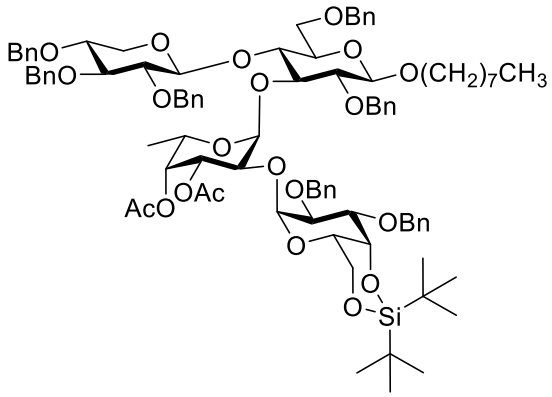
($OCH_2(\underline{C}H_2)_6CH_3$), 26.1 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 21.0 ($CO\underline{C}H_3$), 20.7 ($CO\underline{C}H_3$), 15.8 (Fuc-C-6), 14.1 ($O(CH_2)_7\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{72}H_{88}NaO_{17}$: 1247.5914; Found 1247.5914.



Octyl 3,4-di-*O*-acetyl-α-L-fucopyranosyl-(1→3)-[2,3,4-tri-*O*-benzyl-β-D-xylopyranosyl-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranoside (2.36)

To a stirred solution of **2.10** (153.6 mg, 125.3 μmol) in dry CH_2Cl_2 (10.0 mL) was added trifluoroacetic acid (0.10 mL) drop-wise at 0 ˚C, under an Ar atmosphere. The reaction mixture was slowly warmed to room temperature and stirred for 5 h and then was chilled to 0 ˚C and triethylamine added. The solvent was evaporated and the resulting residue was purified via flash chromatography (3:1 hexanes─ EtOAc) to give **2.36** (121.9 mg, 88%) as a colourless film. R_f 0.37 (3:1 hexanes─ EtOAc); $[\alpha]_D$ ─ 44.1 (*c* 1.7, $CHCl_3$); ^1H NMR (700 MHz; $CDCl_3$): δ 7.39 – 7.23 (m, 25H, Ar), 5.62 (d, 1H, *J* = 3.8 Hz, Fuc-H-1), 5.30 (dd, 1H, *J* = 10.4, 3.2 Hz, Fuc-H-3), 5.15 (dd, 1H, *J* = 3.3, 1.3 Hz, Fuc-H-4), 4.94 (d, 1H, *J* = 10.4 Hz, $ArC\underline{H}_2$), 4.86 (app q, 1H, *J* = 6.6 Hz, Fuc-H-5), 4.86 (d, 1H, *J* = 10.9 Hz, $ArC\underline{H}_2$), 4.90, 4.78 (d, 1H, *J* = 11.0 Hz, $ArC\underline{H}_2$), 4.75 – 4.71 (m, 3H, $ArC\underline{H}_2$), 4.68 (d, 1H, *J* = 11.1 Hz, $ArC\underline{H}_2$), 4.63 (d, 1H, *J* = 10.3 Hz,

ArC$\underline{H}_2$), 4.61 (d, 1H, J = 12.2 Hz, ArC$\underline{H}_2$), 4.43 (d, 1H, J = 12.0 Hz, ArC$\underline{H}_2$), 4.39 (d, 1H, J = 7.9 Hz, Xyl-H-1), 4.38 (d, 1H, J = 7.8 Hz, Glc-H-1), 4.31 (dd, 1H, J = 11.4, 5.3 Hz, Xyl-H-5a), 3.93 (dt, 1H, J = 8.5, 6.0 Hz, OC$\underline{H}_2(CH_2)_6CH_3$), 3.92 – 3.83 (m, 4H, Fuc-H-2, Glc-H-3, Glc-H-4, Glc-H-6a), 3.65 (dd, 1H, J = 10.9, 1.8 Hz, Glc-H-6b), 3.59 (ddd, 1H, J = 10.6, 9.0, 5.3 Hz, Xyl-H-4), 3.50 (dt, 1H, J = 9.6, 6.9 Hz, OC$\underline{H}_2(CH_2)_6CH_3$), 3.42 (dd, 1H, J = 9.0, 7.7 Hz, Glc-H-2), 3.41 (app t, 1H, J = 9.1 Hz, Xyl-H-3), 3.33 (ddd, 1H, J = 9.3, 3.5, 1.8 Hz, Glc-H-5), 3.06 (dd, 1H, J = 9.1, 7.9 Hz, Xyl-H-2), 3.00 (app t, 1H, J = 11.1 Hz, Xyl-H-5b), 2.14 (s, 3H, COC$\underline{H}_3$), 2.04 (s, 3H, COC$\underline{H}_3$), 1.69 – 1.59 (m, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.43 – 1.21 (m, 10H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 1.05 (d, 3H, J = 6.7 Hz, Fuc-H-6), 0.87 (t, 3H, J = 7.0 Hz, $O(CH_2)_7C\underline{H}_3$); ^{13}C NMR (176 MHz; $CDCl_3$): δ 170.7 ($\underline{C}OCH_3$), 170.4 ($\underline{C}OCH_3$), 138.7 (Ar), 138.5 (Ar), 138.3 (Ar), 138.1 (Ar), 137.9 (Ar), 128.5 (Ar), 128.4 (Ar), 128.3(6) (Ar), 128.3 (Ar), 128.0 (Ar), 127.9(8) (Ar), 127.9 (Ar), 127.7(3) (Ar), 127.7 (Ar), 127.6(7) (Ar), 127.6(3) (Ar), 127.6 (Ar), 127.5 (Ar), 103.5, 103.3 (Xyl-C-1 & Glc-C-1), 97.8 (Fuc-C-1), 83.8 (Xyl-C-3), 82.7, 82.4 (Xyl-C-2 & Glc-C-2), 78.3 (Xyl-C-4), 75.6 (Ar$\underline{C}H_2$), 75.2 (Ar$\underline{C}H_2$), 75.0, 74.9(8), 74.7 (Glc-C-3 & Glc-C-4 & Glc-C-5), 74.6 (Ar$\underline{C}H_2$), 73.3 (Ar$\underline{C}H_2$), 72.9 (Ar$\underline{C}H_2$), 71.0 (Fuc-C-4), 71.2 (Fuc-C-3), 70.1 (O$\underline{C}H_2(CH_2)_6CH_3$), 67.6 (Glc-C-6), 67.0 (Fuc-C-2), 64.3 (Fuc-C-5), 63.6 (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 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 26.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 21.0 ($CO\underline{C}H_3$), 20.7 ($CO\underline{C}H_3$), 15.9 (Fuc-C-6), 14.1 ($O(CH_2)_7\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{64}H_{80}NaO_{16}$: 1127.5339; Found 1127.5340.

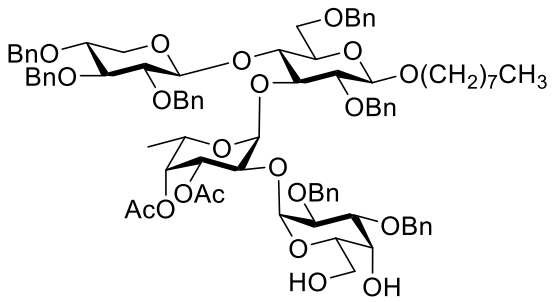


Octyl 2,3-di-*O*-benzy-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranosyl-(1→2)-3,4-di-*O*-acetyl-α-L-fucopyranosyl-(1→3)-[2,3,4-tri-*O*-benzyl-β-D-xylopyranosyl-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranoside (2.37)

To a stirred solution of acceptor **2.36** (56.1 mg, 50.8 μmol) and donor **2.18** (62.5 mg, 103 μmol) in dry Et_2O (7.0 mL) was added oven-dried molecular sieves (0.7 g, 4Å, powder) under an Ar atmosphere. After stirring at room temperature for 1 h, methyl trifluoromethanesulfonate (0.04 mL, 366 μmol) was added drop-wise at room temperature. The reaction mixture was stirred at room temperature for 51 h before triethylamine was added. The solution was filtered through Celite and the filtrate was concentrated. The crude residue was purified via flash chromatography (6:1 hexanes─ EtOAc) to give **2.37** (57.4 mg, 71%) as a colourless film. R_f 0.62 (3:1 hexanes─ EtOAc); $[\alpha]_D$ ─ 1.74 (*c* 5.1, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.51 – 7.47 (m, 2H, Ar), 7.42 – 7.16 (m, 31H, Ar), 6.98 – 6.95 (m, 2H, Ar), 5.65 (dd, 1H, J = 10.6, 3.3 Hz, Fuc-H-3), 5.53 (d, 1H, J = 3.5 Hz, Fuc-H-1), 5.24 – 5.21 (m, 2H, Fuc-H-4, Gal-H-1), 5.07 (qd, 1H, J = 6.6, 1.5 Hz, Fuc-H-5), 4.94 (d, 1H, J = 13.1 Hz, ArC$\underline{H}_2$), 4.86 (d, 1H, J = 10.9 Hz, ArC$\underline{H}_2$), 4.81 (d, 1H, J = 12.5 Hz, ArC$\underline{H}_2$), 4.80 – 4.77 (m, 2H, ArC$\underline{H}_2$), 4.77 (d, 1H, J = 10.9 Hz, ArC$\underline{H}_2$), 4.74 (d, 1H, J = 11.6 Hz, ArC$\underline{H}_2$), 4.74 (d, 1H, J = 11.4 Hz, ArC$\underline{H}_2$), 4.72 (d, 1H, J = 12.8 Hz, ArC$\underline{H}_2$),

4.68 (d, 1H, J = 11.1 Hz, ArC$\underline{H}_2$), 4.65 (d, 1H, J = 11.7 Hz, ArC$\underline{H}_2$), 4.62 (d, 1H, J = 12.1 Hz, ArC$\underline{H}_2$), 4.48 – 4.45 (m, 2H, Xyl-H-5a, ArC$\underline{H}_2$), 4.42 (d, 1H, J = 8.0 Hz, Xyl-H-1), 4.34 (d, 1H, J = 7.8 Hz, Glc-H-1), 4.13 (dd, 1H, J = 10.5, 3.6 Hz, Fuc-H-2), 4.11 (d, 1H, J = 13.3 Hz, ArC$\underline{H}_2$), 4.02 – 3.96 (m, 3H, Glc-H-4, Gal-H-4, Gal-H-2), 3.94 (app t, 1H, J = 9.1 Hz, Glc-H-3), 3.89 (dt, 1H, J = 9.6, 6.3 Hz, OC$\underline{H}_2(CH_2)_6CH_3$), 3.87 (dd, 1H, J = 10.9, 3.8 Hz, Glc-H-6a), 3.79 (dd, 1H, J = 10.1, 2.9 Hz, Gal-H-3), 3.72 – 3.67 (m, 2H, Xyl-H-4, Glc-H-6b), 3.50 (dd, 1H, J = 12.7, 1.7 Hz, Gal-H-6a), 3.43 (app t, 1H, J = 9.1 Hz, Xyl-H-3), 3.40 (dd, 1H, J = 8.9, 7.8 Hz, Glc-H-2), 3.39 – 3.34 (m, 2H, OC$\underline{H}_2(CH_2)_6CH_3$, Glc-H-5), 3.07 – 3.04 (m, 2H, Xyl-H-2, Gal-H-5), 3.01 (app t, 1H, J = 10.9 Hz, Xyl-H-5b), 2.80 (dd, 1H, J = 12.8, 2.2 Hz, Gal-H-6b), 2.17 (s, 3H, COC$\underline{H}_3$), 1.83 (s, 3H, COC$\underline{H}_3$), 1.58 – 1.49 (m, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.27 – 1.07 (m, 10H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 1.10 (d, 3H, J = 6.7 Hz, Fuc-H-6), 0.97 (s, 9H, $C(C\underline{H}_3)_3$), 0.95 (s, 9H, $C(C\underline{H}_3)_3$), 0.84 (t, 3H, J = 7.3 Hz, $O(CH_2)_7C\underline{H}_3$); ^{13}C NMR (176 MHz; $CDCl_3$): δ 170.8 ($\underline{C}OCH_3$), 169.5 ($\underline{C}OCH_3$), 139.1 (Ar), 138.8 (Ar), 138.7 (Ar), 138.6(8) (Ar), 138.4 (Ar), 138.1 (Ar), 128.6 (Ar), 128.5 (Ar), 128.4 (Ar), 128.3 (Ar), 128.2(7) (Ar), 128.2 (Ar), 128.1 (Ar), 128.0 (Ar), 128.1 (Ar), 127.9 (Ar), 127.7 (Ar), 127.6(9) (Ar), 127.6(3) (Ar), 127.5(5) (Ar), 127.5 (Ar), 127.4(6) (Ar), 127.4 (Ar), 126.8 (Ar), 124.7 (Ar), 103.6 (Glc-C-1), 103.4 (Xyl-C-1), 97.6 (Gal-C-1, $J_{C\text{-}H}$ = 174.9 Hz), 97.2 (Fuc-C-1), 83.9 (Xyl-C-3), 82.6, 82.5 (Glc-C-2 & Xyl-C-2), 78.4 (Xyl-C-4), 76.5 (Gal-C-3), 75.7 (Ar$\underline{C}H_2$), 75.2 (Ar$\underline{C}H_2$), 75.1, 74.9 (Glc-C-5 & Glc-C-4), 74.4 (Gal-C-2), 73.9 (Glc-C-3), 73.4 (Ar$\underline{C}H_2$), 72.9 (Ar$\underline{C}H_2$), 72.4 (Ar$\underline{C}H_2$), 72.2 (Fuc-C-4), 72.0 (Ar$\underline{C}H_2$), 71.5 (Gal-C-4), 71.4(7) (Ar$\underline{C}H_2$), 71.4 (Fuc-C-3), 70.0 (O$\underline{C}H_2(CH_2)_6CH_3$), 68.9 (Fuc-C-2), 67.7 (Glc-C-6), 67.4 (Gal-C-5), 66.1 (Gal-C-6), 63.7 (Fuc-C-5), 63.7 (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 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 27.8 ($C(\underline{C}H_3)_3$), 27.3 ($C(\underline{C}H_3)_3$), 26.1 ($OCH_2(\underline{C}H_2)_6CH_3$), 23.1 ($\underline{C}(CH_3)_3$), 22.6

($OCH_2(\underline{C}H_2)_6CH_3$), 21.1 ($CO\underline{C}H_3$), 21.0 ($CO\underline{C}H_3$), 20.5 ($\underline{C}(CH_3)_3$), 15.7 (Fuc-C-6), 14.1 ($O(CH_2)_7\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{92}H_{118}NaO_{21}Si$: 1909.7827; Found 1609.7824.

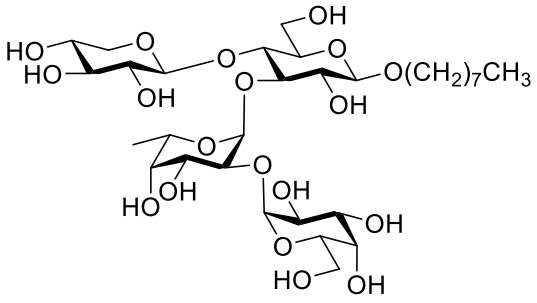


Octyl 2,3-di-*O*-benzy-α-D-galactopyranosyl-(1→2)-3,4-di-*O*-acetyl-α-L-fucopyranosyl-(1→3)-[2,3,4-tri-*O*-benzyl-β-D-xylopyranosyl-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranoside (2.38)

To a stirred solution of **2.37** (58.1 mg, 36.6 μmol) in THF─ pyridine (1:1, 2.0 mL THF, 2.0 mL pyridine) under an Ar atmosphere was added HF·pyridine (0.5 mL, hydrogen fluoride ~70%, pyridine ~30%) at 0 ˚C. The reaction mixture was stirred at 0 ˚C for 2 h and then was diluted with EtOAc (15 mL) and poured into saturated $NaHCO_3$ (aq). The aqueous layer was extracted with EtOAc (10 mL × 3) and the combined organic layers were dried over Na_2SO_4, filtere and then the filtrate was concentrated. The crude residue was purified via flash chromatography (2:1 hexanes─ EtOAc then 2:1 EtOAc─ hexanes) to give **2.38** (44.4 mg, 84%) as a colourless film. R_f 0.10 (2:1 hexanes─ EtOAc); $[\alpha]_D$ ─ 14.3 (*c* 0.8, $CHCl_3$); ^1H NMR (700 MHz; $CDCl_3$): δ 7.44 –

7.37 (m, 6H, Ar), 7.36 – 7.20 (m, 27H, Ar), 7.07 – 7.03 (m, 2H, Ar), 5.66 (dd, 1H, *J* = 10.6, 3.3 Hz, Fuc-H-3), 5.60 (d, 1H, *J* = 3.5 Hz, Fuc-H-1), 5.42 (d, 1H, *J* = 3.5 Hz, Gal-H-1), 5.22 (dd, 1H, *J* = 3.3, 1.5 Hz, Fuc-H-4), 5.04 (app q, 1H, *J* = 6.3 Hz, Fuc-H-5), 4.96 (d, 1H, *J* = 12.8 Hz, ArC$\underline{H}_2$), 4.87 (d, 1H, *J* = 10.9 Hz, ArC$\underline{H}_2$), 4.83 (d, 1H, *J* = 12.0 Hz, ArC$\underline{H}_2$), 4.78 (d, 1H, *J* = 10.9 Hz, ArC$\underline{H}_2$), 4.77, 4.74 (ABq, 2H, J_{AB} = 11.6 Hz, ArC$\underline{H}_2$), 4.74 (d, 1H, *J* = 11.6 Hz, ArC$\underline{H}_2$), 4.70 (d, 1H, *J* = 12.0 Hz, ArC$\underline{H}_2$), 4.69 (d, 1H, *J* = 11.1 Hz, ArC$\underline{H}_2$), 4.64, 4.63 (ABq, 2H, *J* = 11.6 Hz, ArC$\underline{H}_2$), 4.62 (d, 1H, *J* = 12.1 Hz, ArC$\underline{H}_2$), 4.47 (d, 1H, *J* = 12.1 Hz, ArC$\underline{H}_2$), 4.45 (dd, 1H, *J* = 11.2, 5.3 Hz, Xyl-H-5a), 4.43 (d, 1H, *J* = 7.9 Hz, Xyl-H-1), 4.38 (d, 1H, *J* = 7.8 Hz, Glc-H-1), 4.20 (d, 1H, *J* = 11.6 Hz, ArC$\underline{H}_2$), 4.18 (dd, 1H, *J* = 10.6, 3.5 Hz, Fuc-H-2), 4.02 (app t, 1H, *J* = 9.4 Hz, Glc-H-4), 3.98 (app t, 1H, *J* = 8.9 Hz, Glc-H-3), 3.90 (dt, 1H, *J* = 9.6, 6.4 Hz, OC$\underline{H}_2(CH_2)_6CH_3$), 3.88 (dd, 1H, *J* = 10.7, 3.6 Hz, Glc-H-6a), 3.86 (dd, 1H, *J* = 9.8, 3.4 Hz, Gal-H-2), 3.81 (dd, 1H, *J* = 9.9, 3.2 Hz, Gal-H-3), 3.73 – 3.66 (m, 2H, Xyl-H-4, Glc-H-6b), 3.58 (dd, 1H, *J* = 3.3, 1.5 Hz, Gal-H-4), 3.46 (app t, 1H, *J* = 8.2 Hz, Glc-H-2), 3.44 (app t, 1H, *J* = 9.1 Hz, Xyl-H-3), 3.42 – 3.36 (m, 2H, OC$\underline{H}_2(CH_2)_6CH_3$, Glc-H-5), 3.21 – 3.17 (m, 1H, Gal-H-5), 3.15 (dd, 1H, *J* = 12.2, 4.4 Hz, Gal-H-6a), 3.07 (dd, 1H, *J* = 9.1, 8.0 Hz, Xyl-H-2), 3.04 (app t, 1H, *J* = 10.9 Hz, Xyl-H-5b), 3.01 (dd, 1H, *J* = 11.4, 3.8 Hz, Gal-H-6b), 2.14 (s, 3H, COC$\underline{H}_3$), 1.82 (s, 3H, COC$\underline{H}_3$), 1.61 – 1.51 (m, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.31 – 1.07 (m, 10H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 1.11 (d, 3H, *J* = 6.6 Hz, Fuc-H-6), 0.84 (t, 3H, *J* = 7.3 Hz, $O(CH_2)_7C\underline{H}_3$); ^{13}C NMR (176 MHz; $CDCl_3$): δ 170.8 ($\underline{C}OCH_3$), 169.4 ($\underline{C}OCH_3$), 138.8 (Ar), 138.7 (Ar), 138.6(7) (Ar), 138.4 (Ar), 138.3 (Ar), 138.2 (Ar), 138.1 (Ar), 128.8 (Ar), 128.5 (Ar), 128.4 (Ar), 128.3(7) (Ar), 128.3(4) (Ar), 128.3 (Ar), 128.2 (Ar), 128.1 (Ar), 128.0(7) (Ar), 128.0 (Ar), 127.7 (Ar), 127.6(9) (Ar), 127.6(5) (Ar), 127.6 (Ar), 127.5(9) (Ar), 127.5(7) (Ar), 127.4 (Ar), 127.2 (Ar), 125.1 (Ar), 103.4, 103.3(8) (Xyl-C-1 & Glc-C-1), 97.1 (Fuc-C-1), 96.9 (Gal-C-1), 83.9

(Xyl-C-3), 82.6, 82.5 (Xyl-C-2 & Glc-C-2), 78.4 (Xyl-C-4), 75.7 (Ar$\underline{C}H_2$), 75.5 (Gal-C-3), 75.4 (Gal-C-2), 75.2 (Ar$\underline{C}H_2$), 75.1 (Glc-C-5), 74.9 (Glc-C-4), 73.9 (Glc-C-3), 73.4 (Ar$\underline{C}H_2$), 72.9 (Ar$\underline{C}H_2$), 72.8(9) (Ar$\underline{C}H_2$), 72.2 (Ar$\underline{C}H_2$), 72.1 (Fuc-C-4), 72.0 (Ar$\underline{C}H_2$), 71.5 (Fuc-C-3), 70.4 (Gal-C-4), 70.0 (O$\underline{C}H_2(CH_2)_6CH_3$), 69.1 (Fuc-C-2), 68.7 (Gal-C-5), 67.8 (Glc-C-6), 63.8 (Fuc-C-5), 63.7 (Xyl-C-5), 62.8 (Gal-C-6), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 26.1 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 21.1 (CO$\underline{C}H_3$), 20.8 (CO$\underline{C}H_3$), 15.7 (Fuc-C-6), 14.1 ($O(CH_2)_7\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{84}H_{102}NaO_{21}$: 1469.6806; Found 1469.6805.

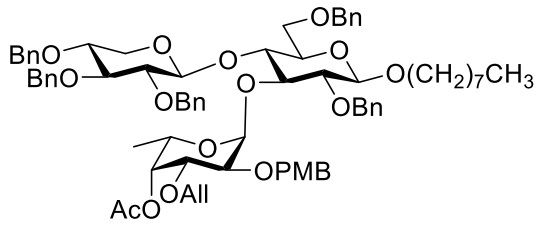


Octyl α-D-galactopyranosyl-(1→2)-α-L-fucopyranosyl-(1→3)-[β-D-xylopyranosyl-(1→4)]-β-D-glucopyranoside (2.4)

To a stirred solution of **2.38** (79.6 mg, 55.0 μmol) in CH_3OH (3.0 mL) was added $NaOCH_3$ in CH_3OH (2.0 mL, 0.6 M). The reaction mixture was stirred at room temperature for 24 h. Amberlite® IR-120 (H^+) cation exchange resin was added, the mixture filtered and then the filtrate was concentrated. The crude residue was purified via flash chromatography (3:2 EtOAc─

hexanes →EtOAc). The residue was dissolved in THF─ H_2O (1:1, 3.0 mL THF, 3.0 mL H_2O) and 20% $Pd(OH)_2/C$ (41.1 mg) was added under Ar atmosphere. The reaction mixture was stirred at room temperature, under a H_2 atmosphere, for 48 h and was then filtered and the filtrate wad concentrated. The crude residue was purified via Iatrobead chromatography (CH_2Cl_2:CH_3OH→CH_3OH, 10% stepwise gradient) to give **2.4** as a white film (32.6 mg, 54%). R_f 0.15 (2:2:1 EtOAc─ acetone─ H_2O); $[\alpha]_D$ ─ 23.8 (*c* 0.9, CH_3OH); ^{1}H NMR (700 MHz; D_2O): δ 5.62 (d, 1H, *J* = 3.9 Hz, Fuc-H-1), 5.27 (d, 1H, *J* = 4.0 Hz, Gal-H-1), 4.73 (app q, 1H, *J* = 6.4 Hz, Fuc-H-5), 4.45 (d, 1H, *J* = 8.0 Hz, Glc-H-1), 4.42 (d, 1H, *J* = 7.8 Hz, Xyl-H-1), 4.15 (dd, 1H, *J* = 10.4, 3.4 Hz, Fuc-H-3), 4.07 (app t, 1H, *J* = 6.3 Hz, Gal-H-5), 4.03 (app d, 1H, *J* = 3.3 Hz, Gal-H-4), 3.99 (dd, 1H, *J* = 12.4, 2.2 Hz, Glc-H-6a), 3.96 – 3.89 (m, 4H, Gal-H-3, Xyl-H-5a, Fuc-H-2, $OC\underline{H}_2(CH_2)_6CH_3$), 3.86 (app t, 1H, *J* = 9.3 Hz, Glc-H-3), 3.85 – 3.80 (m, 2H, Gal-H-2, Glc-H-6b), 3.78 (app d, 1H, *J* = 3.0 Hz, Fuc-H-4), 3.77 – 3.70 (m, 3H, Gal-H-6a, Gal-H-6b, Glc-H-4), 3.68 (dt, 1H, *J* = 9.9, 6.8 Hz, $OC\underline{H}_2(CH_2)_6CH_3$), 3.58 (ddd, 1H, *J* = 9.9, 4.7, 2.3 Hz, Glc-H-5), 3.54 – 3.48 (m, 1H, Xyl-H-4), 3.45 (dd, 1H, *J* = 10.3, 7.1 Hz, Glc-H-2), 3.44 (app t, 1H, *J* = 8.2 Hz, Xyl-H-3), 3.27 (app t, 1H, *J* = 11.1 Hz, Xyl-H-5b), 3.15 (dd, 1H, *J* = 9.3, 7.9 Hz, Xyl-H-2), 1.62 (app p, 2H, *J* = 6.9 Hz, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.38 – 1.24 (m, 10H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 1.21 (d, 3H, *J* = 6.6 Hz, Fuc-H-6), 0.87 (t, 3H, *J* = 6.8 Hz, $O(CH_2)_7C\underline{H}_3$); ^{13}C NMR (176 MHz; D_2O): δ 103.4 (Xyl-C-1), 103.2 (Glc-C-1), 101.0 (Gal-C-1), 98.2 (Fuc-C-1, $J_{C\text{-}H}$ = 177.8 Hz), 76.5, 76.2, 75.9(4), 75.9 (Xyl-C-3 & Glc-C-3 & Glc-C-5 & Glc-C-2), 74.8 (Fuc-C-2), 74.7, 74.6 (Glc-C-4 & Xyl-C-2), 73.3 (Fuc-C-4), 72.2 (Gal-C-5), 71.8 ($O\underline{C}H_2(CH_2)_6CH_3$), 70.5 (Xyl-C-4), 70.3 (Gal-C-3), 70.0 (Gal-C-4, Fuc-C-3), 69.6 (Gal-C-2), 67.2 (Fuc-C-5), 65.9 (Xyl-C-5), 61.9 (Gal-C-6), 60.5 (Glc-C-6), 31.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 25.9 ($OCH_2(\underline{C}H_2)_6CH_3$),

22.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 15.9 (Fuc-C-6), 14.3 ($O(CH_2)_7\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{31}H_{56}NaO_{19}$: 755.3308; Found 755.3307.



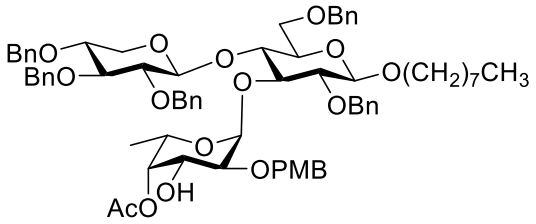
Octyl 2,3,4-tri-*O*-benzyl-β-D-xylopyranosyl-(1→4)-[4-*O*-acetyl-3-*O*-allyl-2-*O*-(4-methoxybenzyl)-α-L-fucopyranosyl-(1→3)]-2,6-di-*O*-benzyl-β-D-glucopyranoside (2.11)

To a stirred solution of acceptor **2.12** (193.7 mg, 221.3 μmol) and donor **2.14** (206.5 mg, 436.9 μmol) in dry Et_2O (8.0 mL) was added oven-dried molecular sieves (0.8 g, 4Å, powder) under an Ar atmosphere. After stirring at room temperature for 45 min, methyl trifluoromethanesulfonate (0.10 mL, 914 μmol) was added drop-wise at room temperature. The reaction mixture was stirred at room temperature for 19 h before triethylamine was added. The solution was filtered through Celite and the filtrate was concentrated. The crude residue was purified via flash chromatography (5:1 hexanes─ EtOAc) to give **2.11** (238.5 mg, 88%) as a colourless syrup. R_f 0.63 (2.5:1 hexanes─ EtOAc); $[\alpha]_D$ ─ 4.8 (*c* 2.1, $CHCl_3$); ^1H NMR (700 MHz; $CDCl_3$): δ 7.36 – 7.20 (m, 25H, Ar), 7.08 – 7.04 (m, 2H, Ar), 6.67 – 6.62 (m, 2H, Ar), 5.89 (ddt, 1H, *J* = 17.2, 10.5, 5.3 Hz, $OCH_2C\underline{H}=CH_2$), 5.63 (d, 1H, *J* = 3.7 Hz, Fuc-H-1), 5.28 (app dq, 1H, *J* = 17.3, 1.8 Hz, $OCH_2CH=C\underline{H}_2$), 5.14 (app d, 1H, *J* = 2.5 Hz, Fuc-H-4), 5.12 (app dq, 1H, *J* = 10.4, 1.6 Hz,

$OCH_2CH=C\underline{H}_2$), 4.99 (d, 1H, J = 11.6 Hz, $ArC\underline{H}_2$), 4.87 (app q, 1H, J = 6.7 Hz, Fuc-H-5), 4.84, 4.82 (ABq, 2H, J_{AB} = 11.0 Hz, $ArC\underline{H}_2$), 4.76 (d, 1H, J = 11.1 Hz, $ArC\underline{H}_2$), 4.73 (d, 1H, J = 11.7 Hz, $ArC\underline{H}_2$), 4.67 (d, 1H, J = 11.5 Hz, $ArC\underline{H}_2$), 4.67 (d, 1H, J = 11.2 Hz, $ArC\underline{H}_2$), 4.63 (d, 1H, J = 12.0 Hz, $ArC\underline{H}_2$), 4.58 (d, 1H, J = 11.7 Hz, $ArC\underline{H}_2$), 4.58, 4.56 (ABq, 2H, J_{AB} = 11.8 Hz, $ArC\underline{H}_2$), 4.41 (d, 1H, J = 12.0 Hz, $ArC\underline{H}_2$), 4.39 (d, 1H, J = 8.0 Hz, Xyl-H-1), 4.35 (d, 1H, J = 7.8 Hz, Glc-H-1), 4.08 (app ddt, 1H, J = 10.8, 5.4, 1.9 Hz, $OC\underline{H}_2CH=CH_2$), 4.02 (app t, 1H, J = 9.6 Hz, Glc-H-4), 4.00 (dd, 1H, J = 11.5, 3.5 Hz, Fuc-H-3), 3.93 (app ddt, 1H, J = 12.3, 4.9, 1.6 Hz, $OC\underline{H}_2CH=CH_2$), 3.92 – 3.84 (m, 3H, Glc-H6a, Glc-H-3, $OC\underline{H}_2(CH_2)_6CH_3$), 3.79 (dd, 1H, J = 11.7, 5.6 Hz, Xyl-H-5a), 3.72 (s, 3H, $ArOC\underline{H}_3$), 3.67 (dd, 1H, J = 10.1, 3.7 Hz, Fuc-H-2), 3.64 (dd, 1H, J = 11.1, 1.8 Hz, Glc-H-6b), 3.51 (dd, 1H, J = 9.1, 7.9 Hz, Glc-H-2), 3.46 (ddd, 1H, J = 10.6, 9.0, 5.5 Hz, Xyl-H-4), 3.42 (dt, 1H, J = 9.8, 7.0 Hz, $OC\underline{H}_2(CH_2)_6CH_3$), 3.39 (app t, 1H, J = 9.1 Hz, Xyl-H-3), 3.32 (ddd, 1H, J = 9.8, 3.4, 1.8 Hz, Glc-H-5), 3.06 (app t, 1H, J = 8.6 Hz, Xyl-H-2), 2.95 (app t, 1H, J = 11.2 Hz, Xyl-H-5b), 2.11 (s, 3H, $COC\underline{H}_3$), 1.60 – 1.50 (m, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.33 – 1.14 (m, 10H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 1.06 (d, 3H, J = 6.6 Hz, Fuc-H-6), 0.85 (t, 3H, J = 7.3 Hz, $O(CH_2)_7C\underline{H}_3$); ^{13}C NMR (176 MHz; $CDCl_3$): δ 170.8 ($\underline{C}OCH_3$), 158.9 (Ar), 138.9 (Ar), 138.5 (Ar), 138.2 (Ar), 138.1(7) (Ar), 138.1(6) (Ar) 135.2 ($OCH_2\underline{C}H=CH_2$), 130.6 (Ar), 129.6 (Ar), 128.5 (Ar), 128.4 (Ar), 128.3(4) (Ar), 128.3 (Ar), 128.2 (Ar), 128.0 (Ar), 127.9 (Ar), 127.8 (Ar), 127.6(4) (Ar), 127.6(3) (Ar), 127.6 (Ar), 127.1 (Ar), 126.7 (Ar), 116.1 ($OCH_2CH=\underline{C}H_2$), 113.5 (Ar), 103.7 (Glc-C-1), 103.2 (Xyl-C-1), 97.3 (Fuc-C-1), 84.0 (Xyl-C-3), 83.0 (Glc-C-2), 82.5 (Xyl-C-2), 78.4 (Xyl-C-4), 76.2 (Fuc-C-3), 75.8 ($Ar\underline{C}H_2$), 75.2 (Glc-C-5), 75.1(7) ($Ar\underline{C}H_2$), 74.8, 74.6 (Glc-C-3 & Glc-C-4), 73.9 (Fuc-C-2), 73.6 ($Ar\underline{C}H_2$), 73.5 ($Ar\underline{C}H_2$), 73.3 ($Ar\underline{C}H_2$), 72.8 ($Ar\underline{C}H_2$), 71.6 (Fuc-C-4), 70.4 ($O\underline{C}H_2CH=CH_2$), 70.2 ($O\underline{C}H_2(CH_2)_6CH_3$), 67.7 (Glc-C-6), 64.1 (Xyl-C-5), 64.0 (Fuc-C-5), 55.2 ($ArO\underline{C}H_3$), 31.8

($OCH_2(\underline{C}H_2)_6CH_3$), 29.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 26.1 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 20.9 ($CO\underline{C}H_3$), 16.1 (Fuc-C-6), 14.1 ($O(CH_2)_7\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{73}H_{90}NaO_{16}$: 1245.6121; Found 1245.6120.

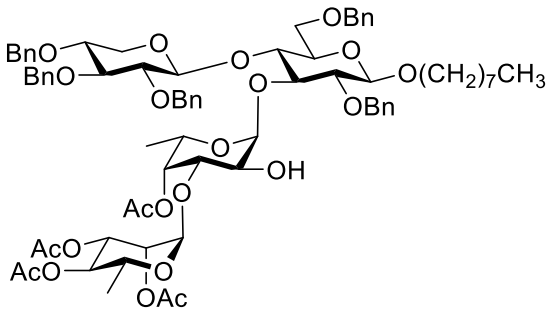
From iodohydrin (2.11a and 2.11b): To a stirred solution of iodohydrin isomeric mixture **2.11a** and **2.11b** (1.031 g, 0.7537 mmol) in toluene (30.0 mL) was added triphenylphosphine (0.793 g, 3.02 mmol) and imidazole (0.206 g, 3.03 mmol). The reaction mixture was heated to 100 °C and iodine (0.385 g, 1.51 mmol) was added. The mixture was stirred at reflux for 40 min, cooled to room temperature and then concentrated. The residue was diluted with EtOAc (100 mL) and washed with saturated $Na_2S_2O_3$ (aq) and water. The aqueous layers were extracted with EtOAc (130 mL) and the combined organic layers were dried over Na_2SO_4, filtered and then the filtrate was concentrated. The crude residue was purified via flash chromatography (4:1 hexanes─EtOAc) to give **2.11** (0.865 g, 94%) as a colourless syrup.



Octyl 2,3,4-tri-*O*-benzyl-β-D-xylopyranosyl-(1→4)-[4-*O*-acetyl-2-*O*-(4-methoxybenzyl)-α-L-fucopyranosyl-(1→3)]-2,6-di-*O*-benzyl-β-D-glucopyranoside (2.36)

A solution of **2.11** (148.0 mg, 121.0 μmol) in dry THF (4.0 mL) was degassed via vacuum and (1,5-Cyclooctadiene)bis(methyldiphenylphosphine)iridium(I) hexafluorophosphate (6.2 mg, 7.3 μmol) was added under an Ar atmosphere. The resulting mixture was stirred at 0 ˚C for 20 min before the catalyst was activated with hydrogen (stirring for 2 min under a hydrogen atmosphere). Excess hydrogen was removed by three cycles of vacuum purging with Ar. The reaction mixture was stirred at room temperature for 2.5 h under an Ar atmosphere and then concentrated. The residue was dissolved in acetone─ water (10:1, 4.0 mL) and HgO (44.5 mg, 170 μmol) and $HgCl_2$ (40.6 mg, 150 μmol) were added. The reaction mixture was stirred at room temperature for 2 h and then concentrated. The residue was diluted with EtOAc (80 mL) and was washed with 10% KI (aq), 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 then the filtrate was concentrated. The crude residue was purified via flash chromatography (3:1 hexanes─ EtOAc) to give **2.36** (127.7 mg, 89%) as a syrup. R_f 0.30 (3:1 hexanes─ EtOAc); $[\alpha]_D$ ─ 39.9 (*c* 2.0, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.37 – 7.22 (m, 25H, Ar), 7.04 – 7.00 (m, 2H, Ar), 6.79 – 6.74 (m, 2H, Ar), 5.74 (d, 1H, J = 3.5 Hz, Fuc-H-1), 5.16 (d, 1H, J = 11.9 Hz, ArC$\underline{H}_2$), 5.08 (dd, 1H, J = 3.6, 1.4 Hz, Fuc-H-4), 4.90 (app q, 1H, J = 6.3 Hz, Fuc-H-5), 4.83, 4.80 (ABq, 2H, J_{AB} = 11.0 Hz, ArC$\underline{H}_2$) , 4.76 (d, 1H, J = 11.1 Hz, ArC$\underline{H}_2$), 4.73 (d, 1H, J = 11.5 Hz, ArC$\underline{H}_2$), 4.67 (d, 1H, J = 11.1 Hz, ArC$\underline{H}_2$), 4.62 (d, 1H, J = 11.9 Hz, ArC$\underline{H}_2$), 4.60 (d, 1H, J = 11.9 Hz, ArC$\underline{H}_2$), 4.59 (d, 1H, J = 11.5 Hz, ArC$\underline{H}_2$), 4.55 (d, 1H, J = 11.8 Hz, ArC$\underline{H}_2$), 4.40 (d, 1H, J = 11.9 Hz, ArC$\underline{H}_2$), 4.39 (d, 1H, J = 7.8 Hz, Glc-H-1), 4.38 (d, 1H, J = 8.0 Hz, Xyl-H-1), 4.22 (app dt, 1H, J = 10.2, 3.0 Hz, Fuc-H-3), 4.13 (d, 1H, J = 11.8 Hz, ArC$\underline{H}_2$), 4.01 (app t, 1H, J = 9.5 Hz, Glc-H-4), 3.94 (app t, 1H, J = 9.2 Hz, Glc-H-3), 3.91 (dd, 1H, J = 11.0, 3.3 Hz, Glc-H-6a), 3.89 (dt, 1H, J = 9.6, 6.5 Hz, OC$\underline{H}_2$(CH_2)$_6$$CH_3$), 3.76 (s, 3H, ArOC$\underline{H}_3$), 3.78 – 3.72 (m, 1H,

Xyl-H-5a), 3.64 (dd, 1H, *J* = 10.9, 1.9 Hz, Glc-H-6b), 3.54 (dd, 1H, *J* = 10.2, 3.5 Hz, Fuc-H-2), 3.52 (dd, 1H, *J* = 9.1, 7.8 Hz, Glc-H-2), 3.49 – 3.42 (m, 2H, Xyl-H-4, $OC\underline{H}_2(CH_2)_6CH_3$), 3.37 (app t, 1H, *J* = 9.1 Hz, Xyl-H-3), 3.34 (ddd, 1H, *J* = 9.7, 3.6, 2.1 Hz, Glc-H-5), 3.06 (app t, 1H, *J* = 8.6 Hz, Xyl-H-2), 2.93 (app t, 1H, *J* = 11.2 Hz, Xyl-H-5b), 2.08 (s, 3H, $COC\underline{H}_3$), 1.92 (d, 1H, *J* = 2.7 Hz, Fuc-3-O<u>H</u>), 1.59 – 1.51 (m, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.33 – 1.14 (m, 10H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 1.08 (d, 3H, *J* = 6.6 Hz, Fuc-H-6), 0.84 (t, 3H, *J* = 7.2 Hz, $O(CH_2)_7C\underline{H}_3$); ^{13}C NMR (176 MHz; $CDCl_3$): δ 171.0 ($\underline{C}OCH_3$), 159.3 (Ar), 138.9 (Ar), 138.5 (Ar), 138.3 (Ar), 138.2 (Ar), 138.1 (Ar), 129.9 (Ar), 129.5 (Ar), 128.5 (Ar), 128.4 (Ar), 128.3(3) (Ar), 128.3 (Ar), 128.2(9) (Ar), 128.0 (Ar), 127.9 (Ar), 127.8 (Ar), 127.7 (Ar), 127.6(2) (Ar), 127.6 (Ar), 127.1 (Ar), 126.4 (Ar), 113.8 (Ar), 103.6, 103.2 (Glc-C-1 & Xyl-C-1), 96.2 (Fuc-C-1), 83.9 (Xyl-C-3), 83.1 (Glc-C-2), 82.4 (Xyl-C-2), 78.5 (Xyl-C-4), 75.7 ($Ar\underline{C}H_2$), 75.3, 75.2 (Fuc-C-2 & Glc-C-5), 75.1(7) ($Ar\underline{C}H_2$), 74.9 (Glc-C-3, Glc-C-4), 73.6 ($Ar\underline{C}H_2$), 73.5(9) (Fuc-C-4), 73.5(5) ($Ar\underline{C}H_2$), 73.3 ($Ar\underline{C}H_2$), 71.4 ($Ar\underline{C}H_2$), 70.1 ($O\underline{C}H_2(CH_2)_6CH_3$), 67.6 (Glc-C-6), 67.2 (Fuc-C-3), 64.2 (Fuc-C-5), 64.1 (Xyl-C-5), 55.2 ($ArO\underline{C}H_3$), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 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 ($OCH_2(\underline{C}H_2)_6CH_3$), 20.9 ($CO\underline{C}H_3$), 16.1 (Fuc-C-6), 14.1 ($O(CH_2)_7\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{70}H_{86}NaO_{16}$: 1205.5808; Found 1205.5808.

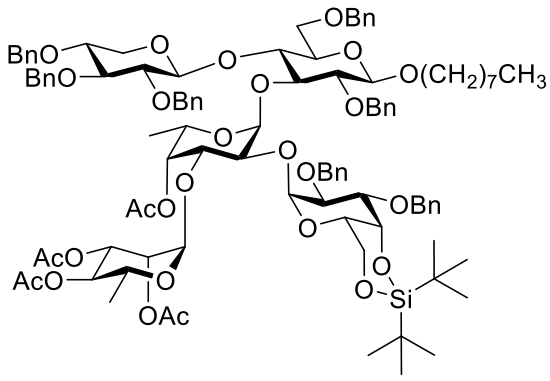


Octyl 2,3,4-tri-*O*-acetyl-α-D-rhamnopyranosyl-(1→3)-4-*O*-acetyl-α-L-fucopyranosyl-(1→3)-[2,3,4-tri-*O*-benzyl-β-D-xylopyranosyl-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranoside (2.40)

To a stirred solution of acceptor **2.39** (68.8 mg, 58.1 μmol) and donor **2.17** (46.4 mg, 117 μmol) in dry CH_2Cl_2 (5.0 mL) was added oven-dried molecular sieves (0.5 g, 4Å, powder) under an Ar atmosphere. After stirring at room temperature for 50 min, *N*-iodosuccinimide (26.2 mg, 116 μmol) and trifluoromethanesulfonic acid (1.5μL, 17 μmol) were added successively at room temperature. The reaction mixture was stirred at room temperature for 50 min before triethylamine was added. The solution was diluted with CH_2Cl_2 (15 mL) and filtered through Celite. The filtrate was washed with saturated $Na_2S_2O_3$ (aq) and saturated $NaHCO_3$ (aq). The combined aqueous layers were extracted with CH_2Cl_2 (3 × 15 mL), dried over Na_2SO_4, filtered, and the filtrate was concentrated. The crude residue was passed through a silica column (2.5:1 hexanes─ EtOAc). The resulting product was dissolved in dry CH_2Cl_2 (10.0 mL) and then trifluoroacetic acid (0.10 mL) was added drop-wise at 0 ˚C, under Ar atmosphere. The reaction mixture was slowly warmed to room temperature and stirred for 5 h and then was chilled to 0 ˚C and triethylamine added. The solution was concentrated and the resulting residue was purified via flash chromatography (3:1 hexanes─ EtOAc) to give **2.40** (49.5 mg, 64%) as a colourless syrup. R_f 0.57 (3:1 hexanes─ EtOAc); $[\alpha]_D$ ─ 21.3 (*c* 1.0, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$):

δ 7.36 – 7.22 (m, 25H, Ar), 5.53 (d, 1H, *J* = 4.0 Hz, Fuc-H-1), 5.35 (dd, 1H, *J* = 3.4, 1.8 Hz, Rha-H-2), 5.17 (dd, 1H, *J* = 10.2, 3.4 Hz, Rha-H-3), 5.13 (d, 1H, *J* = 1.8 Hz, Rha-H-1), 5.08 (dd, 1H, *J* = 3.6, 1.3 Hz, Fuc-H-4), 5.04 (app t, 1H, *J* = 10.0 Hz, Rha-H-4), 4.92 (d, 1H, *J* = 10.4 Hz, ArC$\underline{H}_2$), 4.80 (ABq, 2H, J_{AB} = 11.5 Hz, ArC$\underline{H}_2$), 4.77 (app q, 1H, *J* = 7.3 Hz, Fuc-H-5), 4.74 (d, 1H, *J* = 11.3 Hz, ArC$\underline{H}_2$), 4.71 (d, 1H, *J* = 11.2 Hz, ArC$\underline{H}_2$), 4.66 (d, 1H, *J* = 11.1 Hz, ArC$\underline{H}_2$), 4.63 (d, 1H, *J* = 12.0 Hz, ArC$\underline{H}_2$), 4.61 (d, 1H, *J* = 10.4 Hz, ArC$\underline{H}_2$), 4.58 (d, 1H, *J* = 11.2 Hz, ArC$\underline{H}_2$), 4.42 (d, 1H, *J* = 12.0 Hz, ArC$\underline{H}_2$), 4.38 (d, 1H, *J* = 8.0 Hz, Xyl-H-1), 4.35 (d, 1H, *J* = 7.7 Hz, Glc-H-1), 4.06 (dd, 1H, *J* = 9.9, 3.5 Hz, Fuc-H-3), 4.00 (dq, 1H, *J* = 9.8, 6.2 Hz, Rha-H-5), 3.94 (dd, 1H, *J* = 11.7, 5.6 Hz, Xyl-H-5a), 3.92 – 3.85 (m, 3H, OC$\underline{H}_2(CH_2)_6CH_3$, Glc-H-6a, Fuc-H-2), 3.87 (app t, 1H, *J* = 9.5 Hz, Glc-H-4), 3.81 (app t, 1H, *J* = 9.3 Hz, Glc-H-3), 3.62 (dd, 1H, *J* = 11.0, 1.9 Hz, Glc-H-6b), 3.51 (ddd, 1H, *J* = 10.6, 8.8, 5.6 Hz, Xyl-H-4), 3.47 (dt, 1H, *J* = 9.5, 6.9 Hz, OC$\underline{H}_2(CH_2)_6CH_3$), 3.41 (dd, 1H, *J* = 9.6, 8.2 Hz, Glc-H-2), 3.38 (app t, 1H, *J* = 9.4 Hz, Xyl-H-3), 3.28 (ddd, 1H, *J* = 9.6, 3.2, 1.8 Hz, Glc-H-5), 3.08 (dd, 1H, *J* = 9.1, 8.0 Hz, Xyl-H-2), 3.01 (app t, 1H, *J* = 11.4 Hz, Xyl-H-5b), 2.19 (s, 3H, COC$\underline{H}_3$), 2.11 (s, 3H, COC$\underline{H}_3$), 2.04 (s, 3H, COC$\underline{H}_3$), 1.96 (s, 3H, COC$\underline{H}_3$), 1.67 – 1.59 (m, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.40 – 1.16 (m, 10H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 1.19 (d, 3H, *J* = 6.3 Hz, Rha-H-6), 1.04 (d, 3H, *J* = 6.6 Hz, Fuc-H-6), 0.86 (t, 3H, *J* = 7.1 Hz, $O(CH_2)_7C\underline{H}_3$); ^{13}C NMR (176 MHz; $CDCl_3$): δ 171.2 ($\underline{C}OCH_3$), 170.2 ($\underline{C}OCH_3$), 170.0 ($\underline{C}OCH_3$), 169.9(5) ($\underline{C}OCH_3$), 138.4 (Ar), 138.2 (Ar), 138.1(5) (Ar), 138.0 (Ar), 137.9 (Ar), 128.5 (Ar), 128.4 (Ar), 128.3(8) (Ar), 128.3(4) (Ar), 128.3 (Ar), 127.9 (Ar), 127.8(9) (Ar), 127.8 (Ar), 127.7(5) (Ar), 127.7 (Ar), 127.6(4) (Ar), 127.6(2) (Ar), 127.4 (Ar), 103.5 (Glc-C-1), 103.2 (Xyl-C-1), 99.2 (Rha-C-1, $J_{C\text{-}H}$ = 177.4 Hz), 98.1 (Fuc-C-1), 84.0 (Xyl-C-3), 82.6 (Glc-C-2), 82.3 (Xyl-C-2), 78.5 (Xyl-C-4), 75.7 (Ar$\underline{C}H_2$), 75.6 (Glc-C-3), 75.4 (Fuc-C-3), 75.1 (Ar$\underline{C}H_2$), 75.0, 74.8 (Glc-C-4 & Glc-C-5), 74.5 (Ar$\underline{C}H_2$), 73.4 (Ar$\underline{C}H_2$ × 2, Fuc-

C-4), 70.8 (Rha-C-4), 70.2 (O<u>C</u>H$_2$(CH$_2$)$_6$CH$_3$), 69.9 (Rha-C-2), 69.2 (Fuc-C-2), 69.0 (Rha-C-3), 67.6 (Glc-C-6), 66.8 (Rha-C-5), 64.6 (Fuc-C-5), 64.0 (Xyl-C-5), 31.8 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 29.7 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 29.4 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 29.2 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 26.2 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 22.6 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 20.9 (CO<u>C</u>H$_3$), 20.8(8) (CO<u>C</u>H$_3$), 20.8 (CO<u>C</u>H$_3$), 20.7 (CO<u>C</u>H$_3$), 17.8 (Rha-C-6), 16.0 (Fuc-C-6), 14.1 (O(CH$_2$)$_7$<u>C</u>H$_3$); HRMS (ESI) Calc. for [M + Na]$^+$ $C_{74}H_{98}NaO_{22}$: 1357.6129; Found 1357.6142.

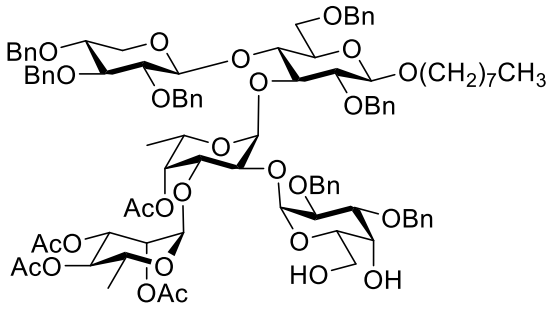


Octyl 2,3,4-tri-*O*-acetyl-α-D-rhamnopyranosyl-(1→3)-[2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranosyl-(1→2)]-4-*O*-acetyl-α-L-fucopyranosyl-(1→3)-[2,3,4-tri-*O*-benzyl-β-D-xylopyranosyl-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranoside (2.42)

To a stirred solution of acceptor **2.40** (49.0 mg, 36.7 μmol) and donor **2.18** (44.1 mg, 72.6 μmol) in dry Et$_2$O (5.0 mL) was added oven-dried molecular sieves (0.7 g, 4Å, powder) under an Ar atmosphere. After stirring at room temperature for 40 min, methyl trifluoromethanesulfonate (0.05 mL, 442 μmol) was added drop-wise at room temperature. The reaction mixture was stirred at room temperature for 52 h before triethylamine was added. The solution was filtered through

Celite and the filtrate was concentrated. The crude residue was purified via flash chromatography (3:1 hexanes─ EtOAc) to give **2.42** (54.8 mg, 82%) as a colourless film. R_f 0.34 (3:1 hexanes─ EtOAc); [α]ᴅ ─ 1.42 (*c* 1.3, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.39 – 7.16 (m, 33H, Ar), 7.05 – 7.01 (m, 2H, Ar), 5.48 (d, 1H, *J* = 3.5 Hz, Fuc-H-1), 5.31 (dd, 1H, *J* = 3.1, 1.9 Hz, Rha-H-2), 5.17 (d, 1H, *J* = 3.6 Hz, Gal-H-1), 5.12 – 5.10 (m, 1H, Fuc-H-4), 5.11 (dd, 1H, *J* = 9.9, 3.1 Hz, Rha-H-3), 5.02 (d, 1H, *J* = 1.9 Hz, Rha-H-1), 4.97 (d, 1H, *J* = 12.5 Hz, ArC$\underline{H}_2$), 4.92 (d, 1H, *J* = 12.7 Hz, ArC$\underline{H}_2$), 4.92 (app t, 1H, *J* = 9.9 Hz, Rha-H-4), 4.87 (app q, 1H, *J* = 6.8 Hz, Fuc-H-5), 4.83, 4.81 (ABq, 2H, J_{AB} = 10.9 Hz, ArC$\underline{H}_2$), 4.76 (d, 1H, *J* = 11.1 Hz, ArC$\underline{H}_2$), 4.69 (d, 1H, *J* = 11.3 Hz, ArC$\underline{H}_2$), 4.68 (d, 1H, *J*=11.0 Hz, ArC$\underline{H}_2$), 4.65 (d, 1H, *J* = 11.9 Hz, ArC$\underline{H}_2$), 4.62 (d, 1H, *J* = 12.3 Hz, ArC$\underline{H}_2$), 4.62 (d, 1H, *J* = 12.2 Hz, ArC$\underline{H}_2$), 4.58 (d, 1H, *J* = 11.3 Hz, ArC$\underline{H}_2$), 4.55 (dd, 1H, *J* = 10.2, 3.4 Hz, Fuc-H-3), 4.47 (d, 1H, *J* = 11.9 Hz, ArC$\underline{H}_2$), 4.47 (d, 1H, *J* = 8.0 Hz, Xyl-H-1), 4.45 (d, 1H, *J* = 11.4 Hz, ArC$\underline{H}_2$), 4.35 (d, 1H, *J* = 7.6 Hz, Glc-H-1), 4.23 (d, 1H, *J* = 12.6 Hz, ArC$\underline{H}_2$), 4.15 – 4.05 (m, 3H, Gal-H-4, Fuc-H-2, Xyl-H-5a), 4.02 (dd, 1H, *J* = 10.0, 3.4 Hz, Gal-H-2), 3.99 (app t, 1H, *J* = 9.3 Hz, Glc-H-4), 3.94 – 3.84 (m, 4H, Glc-H-6a, Glc-H-3, OC$\underline{H}_2(CH_2)_6CH_3$, Rha-H-5), 3.83 (dd, 1H, *J* = 10.1, 3.0 Hz, Gal-H-3), 3.69 – 3.63 (m, 3H, Gal-H-6a, Glc-H-6b, Xyl-H-4), 3.44 (app t, 2H, *J* = 9.0 Hz, Xyl-H-3), 3.39 – 3.32 (m, 3H, OC$\underline{H}_2(CH_2)_6CH_3$, Glc-H-5, Glc-H-2), 3.20 (app s, 1H, Gal-H-5), 3.16 – 3.09 (m, 3H, Xyl-H-5b, Gal-H-6b, Xyl-H-2), 2.25 (s, 3H, COC$\underline{H}_3$), 2.00 (s, 3H, COC$\underline{H}_3$), 1.86 (s, 3H, COC$\underline{H}_3$), 1.63 (s, 3H, COC$\underline{H}_3$), 1.56 – 1.49 (m, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.28 – 1.06 (m, 10H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 1.16 (d, 3H, *J* = 6.2 Hz, Rha-H-6), 1.08 (d, 3H, *J* = 6.7 Hz, Fuc-H-6), 0.98 (s, 9H, C(C$\underline{H}_3)_3$), 0.97 (s, 9H, C(C$\underline{H}_3)_3$), 0.83 (t, 3H, *J* = 7.3 Hz, $O(CH_2)_7C\underline{H}_3$); ^{13}C NMR (176 MHz; $CDCl_3$): δ 171.3 ($\underline{C}OCH_3$), 170.1 ($\underline{C}OCH_3$), 169.6 ($\underline{C}OCH_3$), 169.4 ($\underline{C}OCH_3$), 139.7 (Ar), 139.0 (Ar), 138.6 (Ar), 138.5 (Ar), 138.3 (Ar), 138.2 (Ar), 138.1 (Ar), 128.5 (Ar), 128.4(5)

(Ar), 128.3(3) (Ar), 128.3 (Ar), 128.1 (Ar), 128.0 (Ar), 127.9(4) (Ar), 127.9 (Ar), 127.7(2) (Ar), 127.7(1) (Ar), 127.7 (Ar), 127.6(2) (Ar), 127.6 (Ar), 127.4 (Ar), 127.3(9) (Ar), 127.0 (Ar), 126.9 (Ar), 126.8 (Ar), 125.2 (Ar), 103.5, 103.4 (Glc-C-1 & Xyl-C-1), 100.4 (Rha-C-1), 98.4 (Gal-C-1), 96.7 (Fuc-C-1), 84.0 (Xyl-C-3), 82.4, 82.3 (Glc-C-2 & Xyl-C-2), 78.7 (Xyl-C-4), 77.4 (Gal-C-3), 76.9 (Fuc-C-3), 75.7 (Ar$\underline{C}H_2$), 75.2(3) (Ar$\underline{C}H_2$), 75.2 (Glc-C-4), 75.0 (Glc-C-5), 74.7 (Fuc-C-4), 73.9 (Gal-C-2), 73.7 (Glc-C-3), 73.4 (Ar$\underline{C}H_2$), 73.3 (Ar$\underline{C}H_2$), 72.3 (Ar$\underline{C}H_2$), 72.2 (Ar$\underline{C}H_2$), 71.3, 71.1 (Gal-C-4 & Fuc-C-2), 70.8 (Ar$\underline{C}H_2$), 70.7 (Rha-C-4), 69.9 (O$\underline{C}H_2(CH_2)_6CH_3$), 69.5, 69.4(7) (Rha-C-2 & Rha-C-3), 67.7 (Glc-C-6), 67.5 (Gal-C-5), 67.0 (Rha-C-5), 66.5 (Gal-C-6), 64.6 (Fuc-C-5), 64.0 (Xyl-C-5), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 28.0 ($C(\underline{C}H_3)_3$), 27.8 ($C(\underline{C}H_3)_3$), 27.63 ($C(\underline{C}H_3)_3$), 27.3 ($C(\underline{C}H_3)_3$), 26.1 ($OCH_2(\underline{C}H_2)_6CH_3$), 23.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 21.2 ($CO\underline{C}H_3$), 20.9 ($CO\underline{C}H_3$), 20.6 ($CO\underline{C}H_3$), 20.5(6) ($\underline{C}(CH_3)_3$), 20.4 ($CO\underline{C}H_3$), 19.7 ($\underline{C}(CH_3)_3$), 17.9 (Rha-C-6), 16.2 (Fuc-C-6), 14.1 ($(CH_2)_7\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{102}H_{132}NaO_{27}Si$: 1839.8617; Found 1839.8635.

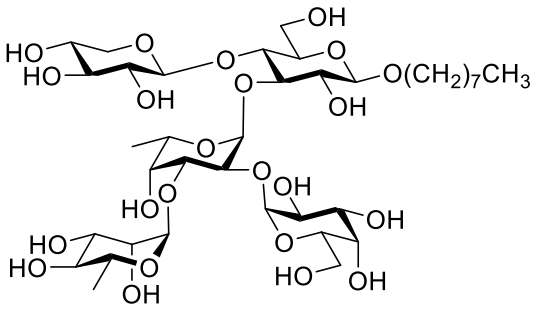


Octyl 2,3,4-tri-*O*-acetyl-α-D-rhamnopyranosyl-(1→3)-[2,3-di-*O*-benzyl-α-D-galactopyranosyl-(1→2)]-4-*O*-acetyl-α-L-fucopyranosyl-(1→3)-[2,3,4-tri-*O*-benzyl-β-D-xylopyranosyl-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranoside (2.43)

To a stirred solution of **2.42** (56.2 mg, 30.9 μmol) in THF─ pyridine (1:1, 3.2 mL THF, 3.2 mL pyridine) under an Ar atmosphere was added HF·pyridine (0.8 mL, hydrogen fluoride ~70%, pyridine ~30%) at 0 ˚C. The reaction mixture was slowly warmed to room temperature and stirred for a total of 20 h. The reaction mixture was diluted with EtOAc (15 mL) and poured into a saturated solution of $NaHCO_3$ (aq). The aqueous layer was extracted with EtOAc (10 mL × 3) and the combined organic layers were dried over Na_2SO_4, filtered and then the filtrate was concentrated. The crude residue was purified via flash chromatography (3:2 EtOAc─ hexanes) to give **2.43** (40.2 mg, 78%) as a colourless film. R_f 0.36 (3:2 EtOAc─ hexanes); $[\alpha]_D$ ─ 8.6 (*c* 2.6, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.37 – 7.18 (m, 33H, Ar), 7.17 – 7.13 (m, 2H, Ar), 5.54 (d, 1H, *J* = 3.5 Hz, Fuc-H-1), 5.31 (dd, 1H, *J* = 3.2, 1.8 Hz, Rha-H-2), 5.21 (d, 1H, *J* = 2.7 Hz, Gal-H-1), 5.11 (app d, 1H, *J* = 3.2 Hz, Fuc-H-4), 5.10 (dd, 1H, *J* = 10.1, 3.2 Hz, Rha-H-3), 5.01 (d, 1H, *J* = 1.8 Hz, Rha-H-1), 4.95 (d, 1H, *J* = 12.4 Hz, ArC$\underline{H}_2$), 4.95 (app t, 1H, *J* = 10.1 Hz, Rha-H-4), 4.86 – 4.80 (m, 3H, ArC$\underline{H}_2$, Fuc-H-5), 4.80 (d, 1H, *J* = 12.6 Hz, ArC$\underline{H}_2$), 4.77 (d, 1H, *J* = 11.1 Hz, ArC$\underline{H}_2$), 4.70 (d, 1H, *J* = 11.3 Hz, ArC$\underline{H}_2$), 4.69 (d, 1H, *J* = 11.2 Hz, ArC$\underline{H}_2$), 4.65 (d, 1H, *J* = 12.0 Hz, ArC$\underline{H}_2$), 4.62 (d, 1H, *J* = 11.7 Hz, ArC$\underline{H}_2$), 4.59 (d, 1H, *J* = 11.3 Hz,

ArC$\underline{H}_2$), 4.57 – 4.52 (m, 3H, ArC$\underline{H}_2$, Fuc-H-3), 4.48 (d, 1H, J = 12.3 Hz, ArC$\underline{H}_2$), 4.47 (d, 1H, J = 7.8 Hz, Xyl-H-1), 4.40 (d, 1H, J = 7.6 Hz, Glc-H-1), 4.34 (d, 1H, J = 12.4 Hz, ArC$\underline{H}_2$), 4.14 (dd, 1H, J = 10.1, 3.6 Hz, Fuc-H-2), 4.08 (dd, 1H, J = 11.5, 5.6 Hz, Xyl-H-5a), 4.02 (app t, 1H, J = 9.1 Hz, Glc-H-4), 3.96 (app t, 1H, J = 8.6 Hz, Glc-H-3), 3.94 – 3.80 (m, 5H, Glc-H-6a, Rha-H-5, OC$\underline{H}_2(CH_2)_6CH_3$, Gal-H-2, Gal-H-3), 3.76 (app br s, 1H, Gal-H-4), 3.69 – 3.63 (m, 2H, Xyl-H-4, Glc-H-6b), 3.47 – 3.42 (m, 3H, Gal-H-5, Xyl-H-3, Glc-H-2), 3.42 – 3.35 (m, 2H, OC$\underline{H}_2(CH_2)_6CH_3$, Glc-H-5), 3.34 – 3.29 (m, 2H, Gal-H-6a, Gal-H-6b), 3.13 (app t, 1H, J = 8.3 Hz, Xyl-H-2), 3.13 (d, 1H, J = 9.1 Hz, Xyl-H-5b), 2.21 (s, 3H, COC$\underline{H}_3$), 2.01 (s, 3H, COC$\underline{H}_3$), 1.87 (s, 3H, COC$\underline{H}_3$), 1.69 (s, 3H, COC$\underline{H}_3$), 1.58 – 1.52 (m, 2H, OCH$_2$C$\underline{H}_2(CH_2)_5CH_3$), 1.30 – 1.13 (m, 10H, OCH$_2$CH$_2$(C$\underline{H}_2)_5CH_3$), 1.18 (d, 3H, J = 6.2 Hz, Rha-H-6), 1.08 (d, 3H, J = 6.6 Hz, Fuc-H-6), 0.84 (t, 3H, J = 7.3 Hz, O(CH$_2)_7$C$\underline{H}_3$); ^{13}C NMR (176 MHz; CDCl$_3$): δ 171.3 ($\underline{C}OCH_3$), 170.1 ($\underline{C}OCH_3$), 169.9 ($\underline{C}OCH_3$), 169.6 ($\underline{C}OCH_3$), 139.3 (Ar), 138.6 (Ar), 138.5 (Ar), 138.3 (Ar), 138.2(7) (Ar), 138.0 (Ar), 128.6 (Ar), 128.5 (Ar), 128.4(8) (Ar), 128.4 (Ar), 128.3(7) (Ar), 128.3 (Ar), 128.2 (Ar), 128.1 (Ar), 128.0(4) (Ar), 128.0 (Ar), 127.9 (Ar), 127.8 (Ar), 127.7 (Ar), 127.6 (Ar), 127.4 (Ar), 127.2 (Ar), 127.1 (Ar), 126.8 (Ar), 125.7(8) (Ar), 103.4 (Xyl-C-1), 103.2 (Glc-C-1), 100.3 (Rha-C-1), 97.6 (Gal-C-1), 96.3 (Fuc-C-1), 84.0 (Xyl-C-3), 82.4 (Xyl-C-2), 82.2 (Glc-C-2), 78.7 (Xyl-C-4), 76.9 (Gal-C-3), 76.7 (Fuc-C-3), 75.6 (Ar$\underline{C}H_2$), 75.3 (Glc-C-4, Gal-C-2), 75.2 (Ar$\underline{C}H_2$), 75.0 (Glc-C-5), 74.6 (Fuc-C-4), 73.9 (Glc-C-3), 73.4 (Ar$\underline{C}H_2$), 73.3 (Ar$\underline{C}H_2$), 72.6 (Ar$\underline{C}H_2$), 72.4 (Ar$\underline{C}H_2$), 72.3 (Ar$\underline{C}H_2$), 71.8 (Fuc-C-2), 70.6 Rha-C-4), 69.9 (O$\underline{C}H_2(CH_2)_6CH_3$), 69.6, 69.5, 69.4, 69.2 (Gal-C-5 & Rha-C-2 & Rha-C-3 & Gal-C-4), 67.8 (Glc-C-6), 67.0 (Rha-C-5), 64.6 (Fuc-C-5), 64.1 (Xyl-C-5), 62.6 (Gal-C-6), 31.8 (OCH$_2$($\underline{C}H_2)_6CH_3$), 29.7 (OCH$_2$($\underline{C}H_2)_6CH_3$), 29.4 (OCH$_2$($\underline{C}H_2)_6CH_3$), 29.2 (OCH$_2$($\underline{C}H_2)_6CH_3$), 26.1 (OCH$_2$($\underline{C}H_2)_6CH_3$), 22.6 (OCH$_2$($\underline{C}H_2)_6CH_3$), 21.0 (CO$\underline{C}H_3$), 20.9 (CO$\underline{C}H_3$), 20.7 (CO$\underline{C}H_3$),

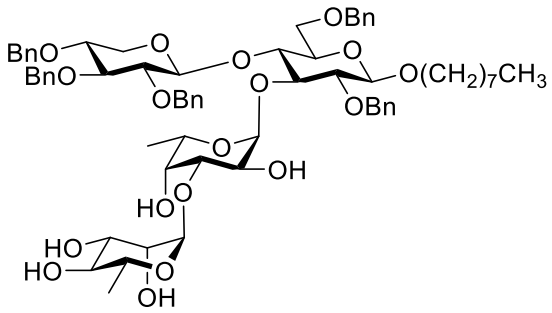
20.5 ($CO\underline{C}H_3$), 17.9 (Rha-C-6), 16.2 (Fuc-C-6), 14.1($O(CH_2)_7\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{94}H_{116}NaO_{27}$: 1699.7596; Found 1699.7607.



Octyl α-D-rhamnopyranosyl-(1→3)-[α-D-galactopyranosyl-(1→2)]-α-L-fucopyranosyl-(1→3)-[β-D-xylopyranosyl-(1→4)]-β-D-glucopyranoside (2.5)

To a stirred solution of **2.43** (61.8 mg, 36.8 μmol) in CH_3OH (6.0 mL) was added NaOH (48.1 mg, 1.20 mmol). The reaction mixture was stirred at room temperature for 24 h. Amberlite® IR-120 (H^+) cation exchange resin was added, the mixture filtered and then the filtrate was concentrated. The crude residue was purified via flash chromatography (12:1 CH_2Cl_2─ CH_3OH). The product was dissolved in THF─ H_2O (1:1, 2.5 mL THF, 2.5 mL H_2O) and 20% $Pd(OH)_2/C$ (13.2 mg) was added under an Ar atmosphere. The reaction mixture was stirred at room temperature, under a H_2 atmosphere, for 23 h and was then filtered and concentrated. The crude residue was purified via Iatrobead chromatography (CH_2Cl_2:CH_3OH→CH_3OH, 10% stepwise gradient) to give **2.5** as a white film (4.5 mg, 14%). R_f 0.54 (4:1:1:1 EtOAc─ CH_3OH─ H_2O─ AcOH); $[\alpha]_D$ ─ 6.1 (*c* 0.2, CH_3OH); ^1H NMR (700 MHz; D_2O): δ 5.63 (d, 1H, *J* = 3.9 Hz, Fuc-

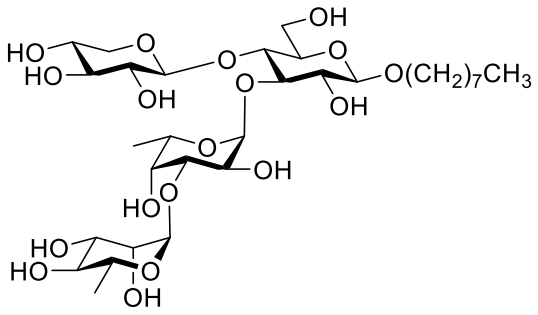
H-1), 5.22 (d, 1H, J = 4.0 Hz, Gal-H-1), 4.99 (d, 1H, J = 1.6 Hz, Rha-H-1), 4.77 – 4.71 (m, 1H, Fuc-H-5), 4.46 (d, 1H, J = 8.0 Hz, Glc-H-1), 4.43 (d, 1H, J = 7.9 Hz, Xyl-H-1), 4.22 (dd, 1H, J = 10.5, 3.2 Hz, Fuc-H-3), 4.10 (dd, 1H, J = 3.5, 1.6 Hz, Rha-H-2), 4.07 – 4.02 (m, 3H, Fuc-H-2, Gal-H-4, Gal-H-5), 4.01 – 3.95 (m, 2H, Glc-H-6a, Xyl-H-5a), 3.91 (dt, 1H, J = 10.1, 6.8 Hz, $OC\underline{H}_2(CH_2)_6CH_3$), 3.91 – 3.76 (m, 7H, Glc-H-3, Gal-H-3, Rha-H-3, Gal-H-2, Glc-H-6b, Rha-H-5, Fuc-H-4), 3.74 – 3.73 (m, 2H, Gal-H-6a, Gal-H-6b), 3.71 (app t, 1H, J = 9.6 Hz, Glc-H-4), 3.68 (dt, 1H, J = 10.1, 6.5 Hz, $OC\underline{H}_2(CH_2)_6CH_3$), 3.62 – 3.55 (m, 2H, Glc-H-5, Xyl-H-4), 3.49 (app t, 1H, J = 9.7 Hz, Rha-H-4), 3.45 (dd, 1H, J = 9.3, 8.0 Hz, Xyl-H-3), 3.45 (app t, 1H, J = 9.2 Hz, Glc-H-2), 3.29 (app t, 1H, J = 11.1 Hz, Xyl-H-5b), 3.15 (dd, 1H, J = 9.4, 7.9 Hz, Xyl-H-2), 1.63 (app pent, 2H, J = 6.9 Hz, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.40 – 1.27 (m, 10H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 1.30 (d, 3H, J = 6.3 Hz, Rha-H-6), 1.20 (d, 3H, J = 6.7 Hz, Fuc-H-6), 0.87 (t, 3H, J = 6.8 Hz, $O(CH_2)_7C\underline{H}_3$); ^{13}C NMR (176 MHz; D_2O): δ 104.1 (Rha-C-1), 103.5 (Xyl-C-1), 103.2 (Glc-C-1), 100.3 (Gal-C-1, $J_{C\text{-}H}$ = 176.8 Hz), 98.1 (Fuc-C-1), 79.2 (Fuc-C-3), 76.5 (Xyl-C-3), 76.0, 75.9 (Glc-C-2 & Glc-C-5), 75.7 (Glc-C-3), 74.8 (Glc-C-4), 74.6 (Xyl-C-2), 73.3 (Fuc-C-4), 72.9 (Rha-C-4), 72.0 (Gal-C-5), 71.8 ($O\underline{C}H_2(CH_2)_6CH_3$), 71.5 (Fuc-C-2), 71.1 (Rha-C-3), 71.0 (Rha-C-2), 70.6, 70.5 (Xyl-C-4 & Gal-C-3), 69.9 (Gal-C-4), 69.8 (Rha-C-5), 69.3 (Gal-C-2), 67.2 (Fuc-C-5), 65.7 (Xyl-C-5), 61.8 (Gal-C-6), 60.4 (Glc-C-6), 31.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 25.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 17.5 (Rha-C-6), 15.7 (Fuc-C-6), 14.2 ($O(CH_2)_7\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{37}H_{66}NaO_{23}$: 901.3887; Found 901.3881.



Octyl α-D-rhamnopyranosyl-(1→3)-α-L-fucopyranosyl-(1→3)-[2,3,4-tri-*O*-benzyl-β-D-xylopyranosyl-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranoside (2.41)

To a stirred solution of **2.40** (20.5 mg, 15.3 μmol) in CH_3OH (5.0 mL) was added NaOH (86.0 mg, 2.15 mmol). The reaction mixture was stirred at room temperature for 16 h. Amberlite® IR-120 (H^+) cation exchange resin was added, the mixture filtered and then the filtrate was concentrated. The crude residue was purified via flash chromatography (10:1 CH_2Cl_2─ CH_3OH) to give **2.41** (16.6 mg, 93%) as a colourless film. R_f 0.45 (10:1 CH_2Cl_2─ CH_3OH); $[\alpha]_D$ ─ 22.3 (*c* 1.4, $CHCl_3$); ^1H NMR (700 MHz; $CDCl_3$): δ 7.33 – 7.16 (m, 25H, Ar), 5.51 (d, 1H, J = 3.7 Hz, Fuc-H-1), 5.09 (app s, 1H, Rha-H-1), 4.88 (d, 1H, J = 10.4 Hz, ArC$\underline{H}_2$), 4.81, 4.79 (ABq, 2H, J_{AB} = 11.1 Hz, ArC$\underline{H}_2$), 4.74 (d, 1H, J = 11.2 Hz, ArC$\underline{H}_2$), 4.69 – 4.63 (m, 3H, ArC$\underline{H}_2$, Fuc-H-5), 4.61 (d, 1H, J = 10.5 Hz, ArC$\underline{H}_2$), 4.61 (d, 1H, J = 12.1 Hz, ArC$\underline{H}_2$), 4.58 (d, 1H, J = 11.4 Hz, ArC$\underline{H}_2$), 4.40 (d, 1H, J = 12.0 Hz, ArC$\underline{H}_2$), 4.36 (d, 1H, J = 7.9 Hz, Xyl-H-1), 4.33 (d, 1H, J = 7.7 Hz, Glc-H-1), 4.08 (app s, 1H, Rha-H-2), 3.97 (dd, 1H, J = 11.6, 5.5 Hz, Xyl-H-5a), 3.95 (dd, 1H, J = 9.9, 3.0 Hz, Fuc-H-3), 3.93 – 3.84 (m, 5H, Fuc-H-2, OC$\underline{H}_2(CH_2)_6CH_3$, Rha-H-3, Glc-H-4, Glc-H-6a), 3.83 (app t, 1H, J = 9.1 Hz, Glc-H-3), 3.77 (dq, 1H, J = 12.9, 6.8 Hz, Rha-H-5), 3.66 (app d, 1H, J = 3.5 Hz, Fuc-H-4), 3.61 (dd, 1H, J = 11.1, 1.9 Hz, Glc-H-6b), 3.52 – 3.42 (m, 3H, Xyl-H-4, Rha-H-4, OC$\underline{H}_2(CH_2)_6CH_3$), 3.40 (app t, 1H, J = 8.3 Hz, Glc-H-2), 3.37

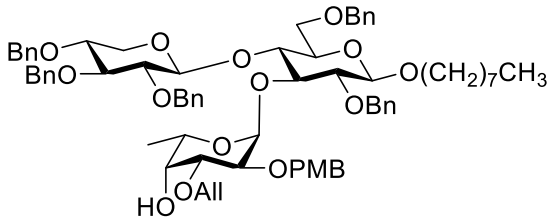
(app t, 1H, J = 9.0 Hz, Xyl-H-3), 3.28 (app dt, 1H, J = 9.2, 2.6 Hz, Glc-H-5), 3.08 (app t, 1H, J = 8.6 Hz, Xyl-H-2), 2.99 (app t, 1H, J = 11.1 Hz, Xyl-H-5b), 1.65 – 1.55 (m, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.38 – 1.20 (m, 10H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 1.26 (d, 3H, J = 6.5 Hz, Rha-H-6), 1.17 (d, 3H, J = 6.6 Hz, Fuc-H-6), 0.85 (t, 3H, J = 7.1 Hz, $O(CH_2)_7C\underline{H}_3$); ^{13}C NMR (176 MHz; $CDCl_3$): δ 138.6 (Ar), 138.3 (Ar), 138.2(9) (Ar), 138.0 (Ar), 137.9(8) (Ar), 128.4 (Ar), 128.3(9) (Ar), 128.4 (Ar), 128.3 (Ar), 127.9(3) (Ar), 127.9(2) (Ar), 127.7 (Ar), 127.6(5) (Ar), 127.6(1) (Ar), 127.6 (Ar), 127.5 (Ar), 103.5 (Glc-C-1), 103.1 (Xyl-C-1), 102.4 (Rha-C-1), 98.0 (Fuc-C-1), 83.9 (Xyl-C-3), 82.5 (Glc-C-2), 82.4 (Xyl-C-2), 78.9 (Fuc-C-3), 78.7 (Xyl-C-4), 75.6 ($Ar\underline{C}H_2$), 75.2 (Glc-C-3), 75.1 ($Ar\underline{C}H_2$), 75.0 (Glc-C-5), 74.7 (Glc-C-4), 74.4 ($Ar\underline{C}H_2$), 73.3 ($Ar\underline{C}H_2$), 73.2(8) ($Ar\underline{C}H_2$), 73.0 (Rha-C-4), 72.9 (Fuc-C-4), 71.6 (Rha-C-3), 70.8 (Rha-C-2), 70.2 ($O\underline{C}H_2(CH_2)_6CH_3$), 68.6 (Rha-C-5), 68.2 (Fuc-C-2), 67.6 (Glc-C-6), 65.4 (Fuc-C-5), 63.9 (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 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 26.1 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 18.1 (Rha-C-6), 16.1 (Fuc-C-6), 14.1 ($O(CH_2)_7\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{66}H_{86}NaO_{18}$: 1189.5706; Found 1189.5709.



Octyl α-D-rhamnopyranosyl-(1→3)-α-L-fucopyranosyl-(1→3)-[β-D-xylopyranosyl-(1→4)]-β-D-glucopyranoside (2.7)

To a stirred solution of **2.41** (46.8 mg, 40.1 μmol) in THF─ H_2O (1:1, 2.0 mL THF, 2.0 mL H_2O) was added 20% $Pd(OH)_2/C$ (17.0 mg) under an Ar atmosphere. The reaction mixture was stirred at room temperature, under a H_2 atmosphere, for 24 h and was then filtered and concentrated. The crude residue was purified via Iatrobead chromatography (CH_2Cl_2:CH_3OH→CH_3OH, 10% stepwise gradient) to give **2.7** as a white film (20.3 mg, 71%). R_f 0.64 (4:1:1:1 EtOAc─ CH_3OH─ H_2O─ AcOH); [α]D ─ 60.0 (*c* 0.4, CH_3OH); ^{1}H NMR (700 MHz; D_2O): δ 5.53 (d, 1H, *J* = 3.9 Hz, Fuc-H-1), 4.97 (d, 1H, *J* = 1.7 Hz, Rha-H-1), 4.69 (app q, 1H, *J* = 6.7 Hz, Fuc-H-5), 4.47 (d, 1H, *J* = 8.1 Hz, Glc-H-1), 4.44 (d, 1H, *J* = 7.9 Hz, Xyl-H-1), 4.10 (dd, 1H, *J* = 3.4, 1.7 Hz, Rha-H-2), 4.04 (dd, 1H, *J* = 10.4, 3.2 Hz, Fuc-H-3), 3.99 (dd, 1H, *J* = 12.3, 2.2 Hz, Glc-H-6a), 3.95 (dd, 1H, *J* = 11.5, 5.4 Hz, Xyl-H-5a), 3.92 (dt, 1H, *J* = 10.0, 6.6 Hz, $OC\underline{H}_2(CH_2)_6CH_3$), 3.89 (dd, 1H, *J* = 10.3, 3.7 Hz, Fuc-H-2), 3.86 (dd, 1H, *J* = 9.9, 3.5 Hz, Rha-H-3), 3.85 – 3.77 (m, 4H, Glc-H-6b, Rha-H-5, Glc-H-3, Fuc-H-4), 3.75 (app t, 1H, *J* = 9.6 Hz, Glc-H-4), 3.68 (dt, 1H, *J* = 10.0, 6.9 Hz, $OC\underline{H}_2(CH_2)_6CH_3$), 3.62 – 3.56 (m, 2H, Glc-H-5, Xyl-H-4), 3.50 (dd, 1H, *J* = 9.1, 8.1 Hz, Glc-H-2), 3.48 (app t, 1H, *J* = 9.7 Hz, Rha-H-4), 3.45 (app t, 1H, *J* = 9.2 Hz, Xyl-H-3), 3.29 (app t, 1H, *J* = 11.1 Hz, Xyl-H-5b), 3.17 (dd, 1H, *J* = 9.4,

7.9 Hz, Xyl-H-2), 1.63 (app pent, 2H, J = 6.9 Hz, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.40 – 1.26 (m, 10H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 1.30 (d, 3H, J = 6.3 Hz, Rha-H-6), 1.19 (d, 3H, J = 6.7 Hz, Fuc-H-6), 0.87 (t, 3H, J = 6.9 Hz, $O(CH_2)_7C\underline{H}_3$); ^{13}C NMR (176 MHz; D_2O): δ 103.8 (Rha-C-1), 103.4 (Xyl-C-1), 102.9 (Glc-C-1), 98.8 (Fuc-C-1), 78.7 (Fuc-C-3), 77.0 (Glc-C-3), 76.5 (Xyl-C-3), 76.0 (Glc-C-5), 75.6 (Glc-C-2), 74.6, 74.5(7) (Glc-C-4 & Xyl-C-2), 73.0 (Fuc-C-4), 72.9 (Rha-H-4), 71.7 ($O\underline{C}H_2(CH_2)_6CH_3$), 71.1 (Rha-C-3), 70.9(6) (Rha-C-2), 70.5 (Xyl-C-4), 69.7 (Rha-C-5), 68.1 (Fuc-C-2), 67.2 (Fuc-C-5), 65.7 (Xyl-C-5), 60.5 (Glc-C-6), 31.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 25.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 17.5 (Rha-C-6), 15.9 (Fuc-C-6), 14.3 ($O(CH_2)_7\underline{C}H_3$);HRMS (ESI) Calc. for $[M + Na]^+$ $C_{31}H_{56}NaO_{18}$: 739.3359; Found 739.3354.

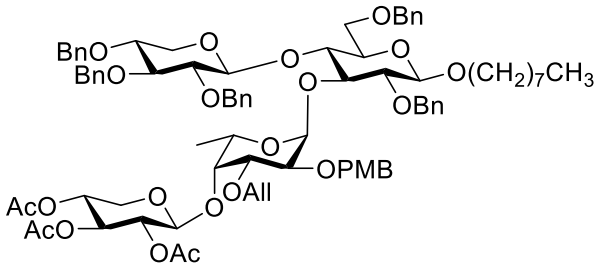


Octyl 2,3,4-tri-*O*-benzyl-β-D-xylopyranosyl-(1→4)-[3-*O*-allyl-2-*O*-(4-methoxybenzyl)-α-L-fucopyranosyl-(1→3)]-2,6-di-*O*-benzyl-β-D-glucopyranoside (2.44)

To a stirred solution of **2.11** (254.5 mg, 208.0 μmol) in CH_3OH (4.0 mL) was added NaOH (105.2 mg, 2.630 mmol). The reaction mixture was stirred at room temperature for 28 h.

Amberlite® IR-120 (H^+) cation exchange resin was added, the mixture filtered and then the filtrate was concentrated. The crude residue was purified via flash chromatography (3:1 hexanes─ EtOAc) to give **2.44** (210.9 mg, 86%) as a colourless syrup. R_f 0.40 (3:1 hexanes─ EtOAc); [α]ᴅ ─ 13.7 (*c* 7.8, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.37 – 7.21 (m, 25H, Ar), 7.06 – 7.01 (m, 2H, Ar), 6.69 – 6.64 (m, 2H, Ar), 5.94 (ddt, 1H, *J* = 17.2, 10.6, 5.4 Hz, $OCH_2C\underline{H}=CH_2$), 5.67 (d, 1H, *J* = 3.7 Hz, Fuc-H-1), 5.29 (app dq, 1H, *J* = 17.2, 1.7 Hz, $OCH_2CH=C\underline{H}_2$), 5.16 (app dq, 1H, *J* = 10.5, 1.5 Hz, $OCH_2CH=C\underline{H}_2$), 5.06 (d, 1H, *J* = 11.5 Hz, $ArC\underline{H}_2$), 4.87 – 4.81 (m, 2H, $ArC\underline{H}_2$), 4.80 (d, 1H, *J* = 11.1 Hz, $ArC\underline{H}_2$), 4.77 (app q, 1H, *J* = 3.7 Hz, Fuc-H-5), 4.72 (d, 1H, *J* = 11.8 Hz, $ArC\underline{H}_2$), 4.69 (d, 1H, *J* = 11.1 Hz, $ArC\underline{H}_2$), 4.65 (d, 1H, *J* = 11.6 Hz, $ArC\underline{H}_2$) 4.65 (d, 1H, *J* = 12.0 Hz, $ArC\underline{H}_2$), 4.58 (d, 1H, *J* = 11.8 Hz, $ArC\underline{H}_2$), 4.54 (d, 1H, *J* = 11.9 Hz, $ArC\underline{H}_2$), 4.45 (d, 1H, *J* = 11.9 Hz, $ArC\underline{H}_2$), 4.42 (d, 1H, *J* = 11.6 Hz, $ArC\underline{H}_2$), 4.40 (d, 1H, *J* = 8.0 Hz, Xyl-H-1), 4.37 (d, 1H, *J* = 7.8 Hz, Glc-H-1), 4.15 – 4.12 (m, 1H, $OC\underline{H}_2CH=CH_2$), 4.08 (app ddt, 1H, *J* = 12.8, 5.7, 1.5 Hz, $OC\underline{H}_2CH=CH_2$), 4.04 (app t, 1H, *J* = 9.6 Hz, Glc-H-4), 3.97 (app t, 1H, *J* = 9.3 Hz, Glc-H-3), 3.94 – 3.87 (m, 3H, Fuc-H-3, Glc-H-6a, $OC\underline{H}_2(CH_2)_6CH_3$), 3.77 (dd, 1H, *J* = 4.9, 11.7 Hz, Xyl-H-5a), 3.72 (s, 3H, $ArOC\underline{H}_3$), 3.68 (dd, 1H, *J* = 9.9, 3.7 Hz, Fuc-H-2), 3.67 – 3.64 (m, 2H, Fuc-H-4, Glc-H-6b), 3.54 (dd, 1H, *J* = 9.2, 7.8 Hz, Glc-H-2), 3.46 – 3.37 (m, 3H, $OC\underline{H}_2(CH_2)_6CH_3$, Xyl-H-3, Xyl-H-4), 3.34 (ddd, 1H, *J* = 9.8, 3.4, 1.8 Hz, Glc-H-5), 3.09 (app t, 1H, *J* = 8.3 Hz, Xyl-H-2), 2.97 (dd, 1H, *J* = 11.8, 10.0 Hz, Xyl-H-5b), 1.62 – 1.53 (m, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.24 (d, 3H, *J* = 6.7 Hz, Fuc-H-6), 1.35 – 1.16 (m, 10H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 0.86 (t, 3H, *J* = 7.2 Hz, $O(CH_2)_7C\underline{H}_3$); ^{13}C NMR (176 MHz; $CDCl_3$): δ 159.0 (Ar), 138.8 (Ar), 138.5(Ar), 138.3 (Ar), 138.2(3) (Ar), 138.2(2) (Ar), 135.2 ($OCH_2\underline{C}H=CH_2$), 130.5 (Ar), 129.5 (Ar), 128.5 (Ar), 128.42 (Ar × 2), 128.4 (Ar), 128.3 (Ar), 128.0 (Ar), 127.9 (Ar), 127.8(9) (Ar), 127.7 (Ar), 127.6(6) (Ar), 127.6(4) (Ar), 127.6

(Ar), 127.1 (Ar), 126.6 (Ar), 116.4 ($OCH_2CH=\underline{C}H_2$), 113.6 (Ar), 103.7 (Glc-C-1), 103.2 (Xyl-C-1), 96.8 (Fuc-C-1), 84.1 (Xyl-C-3), 83.1 (Glc-C-2), 82.7 (Xyl-C-2), 78.3 (Xyl-C-4), 77.8 (Fuc-C-3), 75.8 ($Ar\underline{C}H_2$), 75.3 (Glc-C-5), 75.2 ($Ar\underline{C}H_2$), 74.7 (Glc-C-4), 74.3 (Glc-C-3), 74.1 (Fuc-C-2), 73.6 ($Ar\underline{C}H_2$), 73.4 ($Ar\underline{C}H_2$), 73.3 ($Ar\underline{C}H_2$), 72.4 ($Ar\underline{C}H_2$), 71.1 ($O\underline{C}H_2CH=CH_2$), 70.7 (Fuc-C-4), 70.2 ($O\underline{C}H_2(CH_2)_6CH_3$), 67.8 (Glc-C-6), 64.5 (Fuc-C-5), 64.0 (Xyl-C-5), 55.2 ($ArO\underline{C}H_3$), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 26.1 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 16.2 (Fuc-C-6), 14.1 ($O(CH_2)_7\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{71}H_{88}NaO_{15}$: 1203.6015; Found 1203.6015.

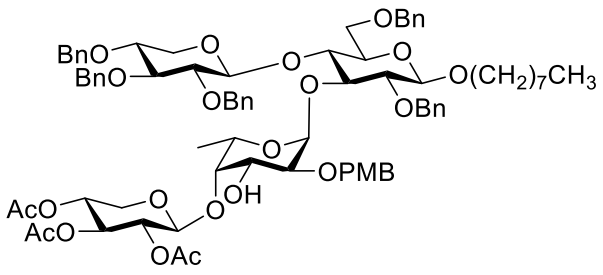


Octyl 2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl-(1→4)-3-*O*-allyl-2-*O*-(4-methoxybenzyl)-α-L-fucopyranosyl-(1→3)-[2,3,4-tri-*O*-benzyl-β-D-xylopyranosyl-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranoside (2.45)

To a stirred solution of acceptor **2.44** (146.0 mg, 123.6 μmol) and donor **2.19** (83.8 mg, 187 μmol) in dry CH_2Cl_2 (4.0 mL) was added oven-dried molecular sieves (0.4 g, 4Å, powder) under

an Ar atmosphere. After stirring at room temperature for 30 min, the solution was chilled to ─ 30 ˚C and trifluoromethanesulfonic acid (0.110 μL, 1.25 μmol) was added drop-wise. The resulting solution was stirred for 1 h at ─ 30 ˚C before triethylamine was added. The solution was filtered through Celite and the filtrate was concentrated. The crude residue was purified via flash chromatography (3:1:1 hexanes─ EtOAc─ CH_2Cl_2) to give **2.45** (145.9 mg, 82%) as a colourless syrup. R_f 0.56 (2.5:1:1 hexanes─ EtOAc─ CH_2Cl_2); $[\alpha]_D$ ─ 34.1 (*c* 2.5, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.38 – 7.21 (m, 25H, Ar), 7.21 – 7.18 (m, 2H, Ar), 7.09 – 7.01 (m, 2H, Ar), 6.65 – 6.61 (m, 2H, Ar), 5.94 (dddd, 1H, *J* = 17.3, 10.5, 5.6, 4.9 Hz, $OCH_2C\underline{H}=CH_2$), 5.55 (d, 1H, *J* = 3.7 Hz, Fuc-H-1), 5.31 (app dq, 1H, *J* = 17.3, 1.8 Hz, $OCH_2CH=C\underline{H}_2$), 5.13 (app dq, 1H, *J* = 10.5, 1.5 Hz, $OCH_2CH=C\underline{H}_2$), 5.01 (app t, 1H, *J* = 6.0 Hz, Xyl'-H-3), 4.98 (d, 1H, *J* = 11.5 Hz, $ArC\underline{H}_2$), 4.95 (dd, 1H, *J* = 6.1, 4.4 Hz, Xyl'-H-2), 4.84 – 4.80 (m, 3H, $ArC\underline{H}_2$, Xyl'-H-4), 4.78 (d, 1H, *J* = 11.1 Hz, $ArC\underline{H}_2$), 4.69 (d, 1H, *J* = 11.8 Hz, $ArC\underline{H}_2$), 4.67 – 4.62 (m, 4H, $ArC\underline{H}_2$, Fuc-H-5), 4.63 (d, 1H, *J* = 7.6 Hz, Xyl'-H-1), 4.59 – 4.54 (m, 3H, $ArC\underline{H}_2$), 4.40 (d, 1H, *J* = 12.3 Hz, $ArC\underline{H}_2$), 4.38 (d, 1H, *J* = 8.0 Hz, Xyl-H-1), 4.34 (dd, 1H, *J* = 12.7, 3.8 Hz, Xyl'-H-5a), 4.33 (d, 1H, *J* = 7.9 Hz, Glc-H-1), 4.11 (app ddt, 1H, *J* = 12.4, 5.6, 1.4 Hz, $OC\underline{H}_2CH=CH_2$), 4.02 (app t, 1H, *J* = 9.6 Hz, Glc-H-4), 3.97 (app ddt, 1H, *J* = 12.4, 4.9, 1.6 Hz, $OC\underline{H}_2CH=CH_2$), 3.93 (dd, 1H, *J* = 10.3, 2.8 Hz, Fuc-H-3), 3.89 (app t, 1H, *J* = 9.3 Hz, Glc-H-3), 3.90 – 3.83 (m, 2H, $OC\underline{H}_2(CH_2)_6CH_3$, Glc-H-6a), 3.80 (dd, 1H, *J* = 11.5, 4.5 Hz, Xyl-H-5a), 3.75 (dd, 1H, *J* = 10.2, 3.7 Hz, Fuc-H-2), 3.69 (s, 3H, $ArOC\underline{H}_3$), 3.66 – 3.61 (m, 2H, Fuc-H-4, Glc-H-6b), 3.49 (dd, 1H, *J* = 9.2, 7.8 Hz, Glc-H-2), 3.44 – 3.37 (m, 4H, $OC\underline{H}_2(CH_2)_6CH_3$, Xyl'-H-5b, Xyl-H-3, Xyl-H-4), 3.30 (ddd, 1H, *J* = 9.8, 3.4, 1.9 Hz, Glc-H-5), 3.05 (dd, 1H, *J* = 9.0, 7.9 Hz, Xyl-H-2), 2.94 (dd, 1H, *J* = 11.8, 10.3 Hz, Xyl-H-5b), 2.08 (s, 3H, $COC\underline{H}_3$), 2.06 (s, 3H, $COC\underline{H}_3$), 1.85 (s, 3H, $COC\underline{H}_3$), 1.59 – 1.50 (m, 2H, , $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.33 – 1.15 (m, 10H,

$OCH_2CH_2(C\underline{H}_2)_5CH_3$), 1.13 (d, 3H, J = 6.6 Hz, Fuc-H-6), 0.85 (t, 3H, J = 7.2 Hz, $O(CH_2)_7C\underline{H}_3$); ^{13}C NMR (176 MHz; $CDCl_3$): δ 169.9 ($\underline{C}OCH_3$), 169.8 ($\underline{C}OCH_3$), 169.4 ($\underline{C}OCH_3$), 158.9 (Ar), 138.8 (Ar), 138.4 (Ar), 138.2 (Ar), 138.1(7) (Ar), 138.1(6) (Ar), 135.4 ($OCH_2\underline{C}H=CH_2$), 130.7 (Ar), 129.4 (Ar), 128.5 (Ar), 128.4 (Ar), 128.3(8) (Ar), 128.3(5) (Ar), 128.2 (Ar), 128.1 (Ar), 127.9 (Ar), 127.8 (Ar), 127.7(6) (Ar), 127.7 (Ar), 127.6(3) (Ar), 127.6(1) (Ar), 127.5(8) (Ar), 127.5(6) (Ar), 127.5(1) (Ar), 127.1 (Ar), 126.7 (Ar), 116.09 ($OCH_2CH=\underline{C}H_2$), 113.5 (Ar), 103.7 (Glc-C-1), 103.1 (Xyl-C-1), 100.0 (Xyl'-C-1, $J_{C\text{-}H}$ = 166.9 Hz), 97.1 (Fuc-C-1), 84.0 (Xyl-C-3), 83.0 (Glc-C-2), 82.6 (Xyl-C-2), 79.2 (Fuc-C-4), 78.3 (Xyl-C-4), 77.8 (Fuc-C-3), 75.9 ($Ar\underline{C}H_2$), 75.2 (Glc-C-5), 75.1 ($Ar\underline{C}H_2$), 74.6 (Glc-C-4), 74.3 (Glc-C-3), 73.9 (Fuc-C-2), 73.6 ($Ar\underline{C}H_2$), 73.3 ($Ar\underline{C}H_2$), 73.2 ($Ar\underline{C}H_2$), 72.7 ($Ar\underline{C}H_2$), 70.8 ($O\underline{C}H_2CH=CH_2$), 70.2 ($O\underline{C}H_2(CH_2)_6CH_3$), 69.2 (Xyl'-C-3), 69.1 (Xyl'-C-2), 68.2 (Xyl'-C-4), 67.8 (Glc-C-6), 65.2 (Fuc-C-5), 63.9 (Xyl-C-5), 60.6 (Xyl'-C-5), 55.1 ($ArOCH_3$), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 26.1 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 20.9 ($CO\underline{C}H_3$), 20.8(5) ($CO\underline{C}H_3$), 20.5 ($CO\underline{C}H_3$), 16.4 (Fuc-C-6), 14.1 ($O(CH_2)_7\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{82}H_{102}NaO_{22}$: 1461.6755; Found 1461.6765.

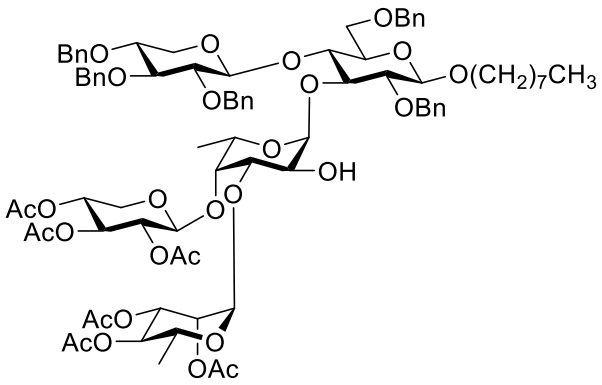


Octyl 2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl-(1→4)-2-*O*-(4-methoxybenzyl)-α-L-fucopyranosyl-(1→3)-[2,3,4-tri-*O*-benzyl-β-D-xylopyranosyl-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranoside (2.46)

A solution of **2.45** (84.1 mg, 58.4 μmol) in dry THF (3.0 mL) was degassed via vacuum and (1,5-Cyclooctadiene)bis(methyldiphenylphosphine)iridium(I) hexafluorophosphate (7.9 mg, 9.3 μmol) was added under an Ar atmosphere. The resulting mixture was stirred at 0 ˚C for 15 min before the catalyst was activated with hydrogen (stirring for 2 min under a hydrogen atmosphere). Excess hydrogen was removed by three cycles of vacuum purging with Ar. The reaction mixture was stirred at room temperature for 22 h under an Ar atmosphere and then concentrated. The residue was dissolved in acetone─ water (10:1, 2.5 mL) and HgO (21.6 mg, 82.6 μmol) and $HgCl_2$ (19.2 mg, 70.7 μmol) were added. The reaction mixture was stirred at room temperature for 2.5 h and then concentrated. The residue was diluted with EtOAc (40 mL) and was washed with 10% KI (aq), saturated $Na_2S_2O_3$ (aq), and water. The aqueous layers were extracted with EtOAc (80 mL) and the combined organic layers were dried over Na_2SO_4, filtered and then the filtrate was concentrated. The crude residue was purified via flash chromatography (2:1 hexanes─ EtOAc→1:1 hexanes─ EtOAc) to give **2.46** (64.5 mg, 79%) as a syrup. R_f 0.60 (1:1 hexanes─ EtOAc); $[\alpha]_D$ ─ 55.4 (*c* 1.1, $CHCl_3$); ^1H NMR (700 MHz; $CDCl_3$): δ 7.37 – 7.23 (m, 23H, Ar), 7.23 – 7.19 (m, 2H, Ar), 7.12 – 7.08 (m, 2H, Ar), 6.75 – 6.70 (m, 2H, Ar), 5.60 (d,

1H, *J* = 3.6 Hz, Fuc-H-1), 5.15 (app t, 1H, *J* = 9.1 Hz, Xyl'-H-3), 5.00 (d, 1H, *J* = 11.5 Hz, ArC$\underline{H}_2$), 4.97 (dd, 1H, *J* = 9.2, 7.4 Hz, Xyl'-H-2), 4.95 (app td, 1H, *J* = 9.3, 5.4 Hz, Xyl'-H-4), 4.82 – 4.75 (m, 4H, ArC$\underline{H}_2$, Fuc-H-5), 4.67 (d, 1H, *J* = 11.5 Hz, ArC$\underline{H}_2$), 4.67 (d, 1H, *J* = 11.2 Hz, ArC$\underline{H}_2$), 4.64 – 4.60 (m, 3H, ArC$\underline{H}_2$), 4.56 (d, 1H, *J* = 11.8 Hz, ArC$\underline{H}_2$), 4.46 (d, 1H, *J* = 7.4 Hz, Xyl'-H-1), 4.41 – 4.37 (m, 3H, ArC$\underline{H}_2$, Xyl-H-1), 4.34 (d, 1H, *J* = 7.7 Hz, Glc-H-1), 4.12 (app td, 1H, *J* = 9.9, 3.1 Hz, Fuc-H-3), 4.05 (dd, 1H, *J* = 11.7, 5.4 Hz, Xyl'-H-5a), 4.01 (app t, 1H, *J* = 9.6 Hz, Glc-H-4), 3.93 (dd, 1H, *J* = 11.7, 5.2 Hz, Xyl-H-5a), 3.90 – 3.83 (m, 3H, Glc-H-3, OC$\underline{H}_2(CH_2)_6CH_3$, Glc-H-6a), 3.74 (s, 3H, ArOC$\underline{H}_3$), 3.63 (dd, 1H, *J* = 11.0, 1.8 Hz, Glc-H-6b), 3.56 (dd, 1H, *J* = 3.2, 1.3 Hz, Fuc-H-4), 3.52 – 3.46 (m, 2H, Fuc-H-2, Glc-H-2), 3.44 – 3.39 (m, 2H, OC$\underline{H}_2(CH_2)_6CH_3$, Xyl-H-4), 3.38 (app t, 1H, *J* = 8.8 Hz, Xyl-H-3), 3.31 (ddd, *J* = 9.8, 3.4, 1.9 Hz, 1H, Glc-H-5), 3.28 (dd, 1H, *J* = 11.8, 9.5 Hz, Xyl'-H-5b), 3.05 (app t, 1H, *J* = 8.4 Hz, Xyl-H-2), 3.00 – 2.93 (m, 2H, Xyl-H-5b, Fuc-3-O$\underline{H}$), 2.03 (s, 3H, COC$\underline{H}_3$), 2.03 (s, 3H, COC$\underline{H}_3$), 2.01 (s, 3H, COC$\underline{H}_3$), 1.57 – 1.49 (m, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.31 – 1.13 (m, 10H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 1.10 (d, 3H, *J* = 6.7 Hz, Fuc-H-6), 0.84 (t, 3H, *J* = 7.2 Hz, $O(CH_2)_7C\underline{H}_3$); ^{13}C NMR (176 MHz; $CDCl_3$): δ 170.2 ($\underline{C}OCH_3$), 169.7 ($\underline{C}OCH_3$), 169.3 ($\underline{C}OCH_3$), 159.0 (Ar), 138.9 (Ar), 138.4 (Ar), 138.3 (Ar), 138.2 (Ar), 138.1 (Ar), 130.5 (Ar), 129.7 (Ar), 128.5 (Ar), 128.4 (Ar), 128.3(9) (Ar), 128.3 (Ar), 128.2 (Ar), 128.1 (Ar), 127.8 (Ar), 127.7(6) (Ar), 127.6(4) (Ar), 127.6 (Ar), 127.5 (Ar), 127.1 (Ar), 126.6(6) (Ar), 113.5 (Ar), 103.7 (Glc-C-1), 103.2 (Xyl-C-1), 102.3 (Xyl'-C-1), 97.0 (Fuc-C-1), 84.8 (Fuc-C-4), 84.0 (Xyl-C-3), 83.0 (Glc-C-2), 82.5 (Xyl-C-2), 78.5 (Xyl-C-4), 76.0 (Ar$\underline{C}H_2$), 75.7 (Fuc-C-2), 75.2 (Glc-C-5), 75.1 (Ar$\underline{C}H_2$), 74.8 (Glc-C-4), 74.7 (Glc-C-3), 73.6(7) (Ar$\underline{C}H_2$), 73.3 (Ar$\underline{C}H_2$), 73.2 (Ar$\underline{C}H_2$), 72.4 (Ar$\underline{C}H_2$), 72.0 (Xyl'-C-3), 71.5 (Xyl'-C-2), 70.1 (O$\underline{C}H_2(CH_2)_6CH_3$), 68.5(9), 68.5(6) (Xyl'-C-4 & Fuc-C-3), 67.7 (Glc-C-6), 64.9 (Fuc-C-5), 64.0 (Xyl-C-5), 62.4 (Xyl'-C-5), 55.2 (ArO$\underline{C}H_3$), 31.8

($OCH_2(\underline{C}H_2)_6CH_3$), 29.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 26.1 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 20.8 ($CO\underline{C}H_3$), 20.7 ($CO\underline{C}H_3$), 20.6(5) ($CO\underline{C}H_3$), 16.2 (Fuc-C-6), 14.1 ($O(CH_2)_7\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{79}H_{98}NaO_{22}$: 1421.6442; Found 1421.6439.

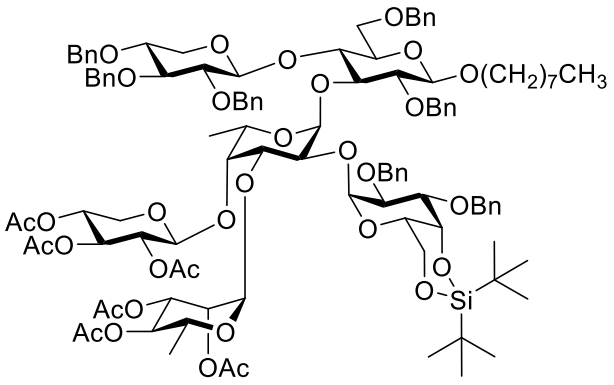


Octyl 2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl-(1→4)-[2,3,4-tri-*O*-acetyl-α-D-rhamnopyranosyl-(1→3)]-α-L-fucopyranosyl-(1→3)-[2,3,4-tri-*O*-benzyl-β-D-xylopyranosyl-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranoside (2.49)

To a stirred solution of acceptor **2.46** (66.4 mg, 47.4 μmol) and donor **2.17** (37.6 mg, 94.8 μmol) in dry CH_2Cl_2 (3.0 mL) was added oven-dried molecular sieves (0.3 g, 4Å, powder) under an Ar atmosphere. After stirring at room temperature for 30 min, the solution was chilled to ─ 30 ˚C and *N*-iodosuccinimide (21.4 mg, 95.1 μmol) and trifluoromethanesulfonic acid (1.24 μL, 14.1 μmol) were added successively. The resulting solution was stirred at ─ 30 ˚C before for 50 min before triethylamine was added. The solution was filtered through Celite and the filtrate was

concentrated. The crude residue was passed through a silica column (3:2 hexanes─ EtOAc). The resulting product was dissolved in dry CH_2Cl_2 (5.0 mL) and then trifluoroacetic acid (0.05 mL) was added drop-wise at 0 ˚C, under an Ar atmosphere. The reaction mixture was slowly warmed to room temperature and stirred for 5 h and was then chilled to 0 ˚C and triethylamine added. The solution was concentrated and the resulting residue was purified via flash chromatography (2:1 hexanes─ EtOAc→3:2 hexanes─ EtOAc) to give **2.49** (52.1 mg, 71%) as a colourless film. R_f 0.44 (3:2 EtOAc─ hexanes); [α]D ─ 40.25 (*c* 2.2, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.36 – 7.22 (m, 25H, Ar), 5.46 (d, 1H, *J* = 4.0 Hz, Fuc-H-1), 5.44 (dd, 1H, *J* = 3.5, 1.8 Hz, Rha-H-2), 5.38 (dd, 1H, *J* = 10.1, 3.4 Hz, Rha-H-3), 5.15 (d, 1H, *J* = 1.8 Hz, Rha-H-1), 5.08 (app t, 1H, *J* = 6.3 Hz, Xyl'-H-3), 5.05 (app t, 1H, *J* = 9.9 Hz, Rha-H-4), 4.96 (dd, 1H, *J* = 6.4, 4.6 Hz, Xyl'-H-2), 4.92 – 4.87 (m, 2H, Ar$\underline{C}H_2$, Xyl'-H-4), 4.81, 4.78 (ABq, 2H, J_{AB} = 11.0 Hz, Ar$\underline{C}H_2$), 4.76 (d, 1H, *J* = 11.2 Hz, Ar$\underline{C}H_2$), 4.70 (d, 1H, *J* = 11.3 Hz, Ar$\underline{C}H_2$), 4.68 – 4.55 (m, 5H, Ar$\underline{C}H_2$, Xyl'-H-1), 4.56 (app q, 1H, *J* = 7.0 Hz, Fuc-H-5), 4.46 (dd, 1H, *J* = 12.4, 3.9 Hz, Xyl'-H-5a), 4.42 (d, 1H, *J* = 12.0 Hz, Ar$\underline{C}H_2$), 4.37 (d, 1H, *J* = 8.0 Hz, Xyl-H-1), 4.33 (d, 1H, *J* = 7.7 Hz, Glc-H-1), 4.17 (dq, 1H, *J* = 9.8, 6.3 Hz, Rha-H-5), 3.97 (dd, 1H, *J* = 10.1, 2.9 Hz, Fuc-H-3), 3.95 (dd, 1H, *J* = 11.4, 5.4 Hz, Xyl-H-5a), 3.93 – 3.86 (m, 3H, OC$\underline{H}_2(CH_2)_6CH_3$, Fuc-H-2, Glc-H-6a), 3.85 (app t, 1H, *J* = 9.5 Hz, Glc-H-4), 3.81 (app t, 1H, *J* = 9.3 Hz, Glc-H-3), 3.65 – 3.59 (m, 2H, Glc-H-6b, Xyl'-H-5b), 3.54 (app d, 1H, *J* = 2.9 Hz, Fuc-H-4), 3.52 – 3.44 (m, 2H, OC$\underline{H}_2(CH_2)_6CH_3$, Xyl-H-4), 3.39 (dd, 1H, *J* = 9.5, 7.3 Hz, Glc-H-2), 3.38 (app t, 1H, *J* = 8.0 Hz, Xyl-H-3), 3.28 (ddd, 1H, *J* = 9.5, 3.3, 1.8 Hz, Glc-H-5), 3.07 (dd, 1H, *J* = 9.1, 8.1 Hz, Xyl-H-2), 3.00 (app t, 1H, *J* = 11.1 Hz, Xyl-H-5b), 2.13 (s, 3H, COC$\underline{H}_3$), 2.07 (s, 3H, COC$\underline{H}_3$), 2.05 (s, 3H, COC$\underline{H}_3$), 2.03 (s, 3H, COC$\underline{H}_3$), 1.97 (s, 3H, COC$\underline{H}_3$), 1.97 (s, 3H, COC$\underline{H}_3$), 1.68 – 1.56 (m, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.41 – 1.20 (m, 10H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 1.17 (d, 3H, *J* = 6.3 Hz,

Rha-H-6), 1.14 (d, 3H, J = 6.7 Hz, Fuc-H-6), 0.86 (t, 3H, J = 7.0 Hz, $O(CH_2)_7C\underline{H}_3$); ^{13}C NMR (176 MHz; $CDCl_3$): δ 170.1 ($\underline{C}OCH_3$), 169.9 ($\underline{C}OCH_3$ × 2), 169.8 ($\underline{C}OCH_3$), 169.7 ($\underline{C}OCH_3$), 169.3 ($\underline{C}OCH_3$), 138.3 (Ar), 138.2 (Ar), 138.1 (Ar), 137.9 (Ar), 128.4(5) (Ar), 128.4(3) (Ar), 128.4(1) (Ar), 128.3(8) (Ar), 128.3(7) (Ar), 128.3(4) (Ar), 128.0 (Ar), 127.9 (Ar), 127.7(7) (Ar), 127.7(6) (Ar), 127.7(3) (Ar), 127.7 (Ar), 127.6 (Ar), 127.5(5) (Ar), 127.3 (Ar), 103.5 (Glc-C-1), 103.2 (Xyl-C-1), 100.1 (Xyl'-C-1), 99.4 (Rha-C-1, $J_{C\text{-}H}$ = 175.5 Hz), 97.8 (Fuc-C-1), 84.1 (Xyl-C-3), 82.7 (Glc-C-2), 82.4 (Xyl-C-2), 81.1 (Fuc-C-4), 78.5 (Xyl-C-4), 76.9 (Fuc-C-3), 75.8 ($Ar\underline{C}H_2$), 75.1 ($Ar\underline{C}H_2$), 75.0(7), 74.9(6) (Glc-C-5 & Glc-C-3), 74.7 (Glc-C-4), 74.6 ($Ar\underline{C}H_2$), 73.4 ($Ar\underline{C}H_2$), 73.2 ($Ar\underline{C}H_2$), 71.3 (Rha-C-4), 70.2 ($O\underline{C}H_2(CH_2)_6CH_3$), 70.0 (Rha-C-2), 69.4 (Xyl'-C-2), 69.2 (Xyl'-C-3), 69.0 (Rha-C-3), 68.7 (Fuc-C-2), 68.4 (Xyl'-C-4), 67.6 (Glc-C-6), 66.4 (Rha-C-5), 66.0 (Fuc-C-5), 64.0 (Xyl-C-5), 60.5 (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 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 26.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 20.9 ($CO\underline{C}H_3$), 20.8(8) ($CO\underline{C}H_3$), 20.8(2) ($CO\underline{C}H_3$), 20.8(1) ($CO\underline{C}H_3$), 20.7 ($CO\underline{C}H_3$), 20.6(9) ($CO\underline{C}H_3$), 17.9 (Rha-C-6), 16.4 (Fuc-C-6), 14.1 ($O(CH_2)_7\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{83}H_{106}Na_2O_{28}$: 798.3328; Found 798.3334.

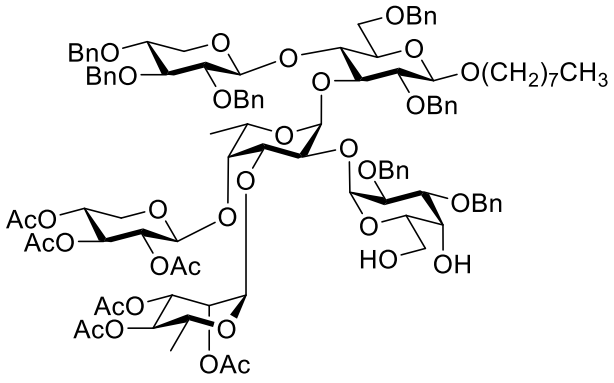


Octyl 2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl-(1→4)-[2,3,4-tri-*O*-acetyl-α-D-rhamnopyranosyl-(1→3)]-[2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranosyl-(1→2)]-α-L-fucopyranosyl-(1→3)-[2,3,4-tri-*O*-benzyl-β-D-xylopyranosyl-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranoside (2.50)

To a stirred solution of acceptor **2.49** (49.8 mg, 32.1 μmol) and donor **2.18** (38.5 mg, 63.4 μmol) in dry Et_2O (4.0 mL) was added oven-dried molecular sieves (0.4 g, 4Å, powder) under an Ar atmosphere. After stirring at room temperature for 30 min, methyl trifluoromethanesulfonate (0.03 mL, 265 μmol) was added drop-wise at room temperature. The reaction mixture was stirred at room temperature for 26 h before triethylamine was added. The solution was filtered through Celite and the filtrate was concentrated. The crude residue was purified via flash chromatography (2:1:1 hexanes─ EtOAc─ CH_2Cl_2) to give **2.50** (44.7 mg, 69%) as a colourless film. R_f 0.56 (3:1 hexanes─ EtOAc); [α]D ─ 20.1 (*c* 3.7, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.40 – 7.18 (m, 33H, Ar), 7.12 – 7.08 (m, 2H, Ar), 5.44 (dd, 1H, *J* = 3.2, 1.8 Hz, Rha-H-2), 5.38 (d, 1H, *J* = 3.4 Hz, Fuc-H-1), 5.37 (dd, 1H, *J* = 6.0, 3.2 Hz, Rha-H-3), 5.13 (app t, 1H, *J* = 6.7 Hz, Xyl'-H-3), 5.10 – 5.08 (m, 1H, Xyl'-H-2), 5.08 (d, 1H, *J* = 1.8 Hz, Rha-H-1), 4.97 (app t, 1H, *J* = 9.8 Hz, Rha- H-4), 4.97 (d, 1H, *J* = 3.3 Hz, Gal-H-1), 4.95 – 4.91 (m, 2H, Xyl'-H-4, ArC$\underline{H}_2$), 4.88 (d, 1H, *J* = 12.3 Hz, ArC$\underline{H}_2$), 4.82 (ABq, 2H, J_{AB} = 10.9 Hz, ArC$\underline{H}_2$), 4.78 (d, 1H, *J* = 11.2 Hz,

ArC$\underline{H}_2$), 4.71 – 4.68 (m, 2H, ArC$\underline{H}_2$, Xyl'-H-1), 4.67 (d, 1H, *J* = 11.2 Hz, ArC$\underline{H}_2$), 4.64 (d, 1H, *J* = 12.2 Hz, ArC$\underline{H}_2$), 4.62 (d, 1H, *J* = 12.4 Hz, ArC$\underline{H}_2$), 4.61 – 4.57 (m, 3H, ArC$\underline{H}_2$), 4.55 (app q, 1H, *J* = 6.8 Hz, Fuc-H-5), 4.47 (d, 1H, *J* = 12.0 Hz, ArC$\underline{H}_2$), 4.43 (d, 1H, *J* = 8.0 Hz, Xyl-H-1), 4.42 – 4.38 (m, 2H, Xyl'-H-5a, Fuc-H-3), 4.37 (d, 1H, *J* = 7.4 Hz, Glc-H-1), 4.32 (d, 1H, *J* = 12.7 Hz, ArC$\underline{H}_2$), 4.30 (dq, 1H, *J* = 9.8, 6.3 Hz, Rha-H-5), 4.21 (app d, 1H, *J* = 2.9 Hz, Gal-H-4), 4.08 (dd, 1H, *J* = 11.6, 5.7 Hz, Xyl-H-5a), 4.03 (dd, 1H, *J* = 10.2, 3.6 Hz, Fuc-H-2), 3.98 (dd, 1H, *J* = 10.0, 3.6 Hz, Gal-H-2), 3.96 (app t, 1H, *J* = 9.2 Hz, Glc-4), 3.90 (app t, 1H, *J* = 8.4 Hz, Glc-H-3), 3.89 (dd, 1H, *J* = 10.8, 3.3 Hz, Glc-H-6a), 3.86 (dt, 1H, *J* = 9.6, 6.5 Hz, OC$\underline{H}_2(CH_2)_6CH_3$), 3.81 (dd, 1H, *J* = 10.1, 2.9 Hz, Gal-H-3), 3.73 (dd, 1H, *J* = 13.0, 2.0 Hz, Gal-H-6a), 3.69 (ddd, 1H, *J* = 10.4, 8.8, 5.7 Hz, Xyl-H-4), 3.65 (dd, 1H, *J* = 10.9, 2.1 Hz, Glc-H-6b), 3.62 (app d, 1H, *J* = 3.0 Hz, Fuc-H-4), 3.57 (dd, 1H, *J* = 12.1, 6.4 Hz, Xyl'-H-5b), 3.44 (app t, 1H, *J* = 8.9 Hz, Xyl-H-3), 3.40 – 3.31 (m, 5H, OC$\underline{H}_2(CH_2)_6CH_3$, Glc-H-5, Glc-H-2, Gal-H-6b, Gal-H-5), 3.10 (app t, 1H, *J* = 11.0 Hz, Xyl-H-5b), 3.09 (app t, 1H, *J* = 8.4 Hz, Xyl-H-2), 2.08 (s, 3H, COC$\underline{H}_3$), 2.06 (s, 3H, COC$\underline{H}_3$), 2.01 (s, 3H, COC$\underline{H}_3$), 2.01 (s, 3H, COC$\underline{H}_3$), 1.88 (s, 3H, COC$\underline{H}_3$), 1.67 (s, 3H, COC$\underline{H}_3$), 1.58 – 1.51 (m, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.21 (d, 3H, *J* = 6.8 Hz, Fuc-H-6), 1.28 – 1.16 (m, 10H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 1.16 (d, 3H, *J* = 6.4 Hz, Rha-H-6), 0.97 (s, 9H, C(C$\underline{H}_3)_3$), 0.94 (s, 9H, C(C$\underline{H}_3)_3$), 0.84 (t, 3H, *J* = 7.3 Hz, $O(CH_2)_7C\underline{H}_3$); ^{13}C NMR (176 MHz; $CDCl_3$): δ 170.1 ($\underline{C}OCH_3$), 170.0(8) ($\underline{C}OCH_3$), 169.7 ($\underline{C}OCH_3$), 169.6 ($\underline{C}OCH_3$), 169.4 ($\underline{C}OCH_3$), 169.1 ($\underline{C}OCH_3$), 139.6 (Ar), 139.1 (Ar), 138.6 (Ar), 138.5(5) (Ar), 138.4 (Ar), 138.3 (Ar), 138.1 (Ar), 128.7 (Ar), 128.5 (Ar), 128.4(6) (Ar), 128.4(4) (Ar), 128.4(2) (Ar), 128.3(8) (Ar), 128.3(5) (Ar), 128.3(4), 128.3(3) (Ar), 128.2(2) (Ar), 128.2(1) (Ar), 128.1(5) (Ar), 128.0 (Ar), 127.9 (Ar), 127.8(9) (Ar), 127.8(5) (Ar), 127.7(3) (Ar), 127.7 (Ar), 127.6(5) (Ar), 127.6(2) (Ar), 127.6 (Ar), 127.5(7) (Ar), 127.5 (Ar), 127.3(4) (Ar), 127.3 (Ar), 127.2 (Ar), 127.0

(Ar), 126.9 (Ar), 125.8 (Ar), 103.3 (Xyl-C-1), 103.1 (Glc-C-1), 100.3 (Rha-C-1), 100.2 (Xyl'-C-1), 99.1 (Gal-C-1, $J_{C\text{-}H}$ = 172.6 Hz), 95.9 (Fuc-C-1), 84.0 (Xyl-C-3), 82.5 (Xyl-C-2), 82.1 (Glc-C-2), 81.2 (Fuc-C-4), 78.6 (Xyl-C-4), 77.3 (Gal-C-3), 76.7 (Fuc-C-3), 75.7 (Ar$\underline{C}H_2$), 75.1 (Ar$\underline{C}H_2$), 75.0, 74.9 (Glc-C-5 & Glc-C-4), 73.7 (Gal-C-2), 73.4 (Ar$\underline{C}H_2$), 73.3(6) (Glc-C-3), 73.0 (Ar$\underline{C}H_2$), 72.9 (Fuc-C-2), 72.4 (Ar$\underline{C}H_2$), 72.2 (Ar$\underline{C}H_2$), 71.4 (Rha-C-4), 71.2 (Gal-C-4), 70.7 (Ar$\underline{C}H_2$), 69.9, 69.8 (Xyl'-C-2 & Rha-C-2), 69.7(5) (O$\underline{C}H_2(CH_2)_6CH_3$), 69.6 (Xyl'-C-3), 69.4 (Rha-C-3), 68.6 (Xyl'-C-4), 67.8 (Glc-C-6), 67.6 (Gal-C-5), 66.6 (Gal-C-6), 66.4 (Rha-C-5), 65.6 (Fuc-C-5), 64.0 (Xyl-C-5), 60.6 (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 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 28.0 ($C(\underline{C}H_3)_3$), 27.7 ($C(\underline{C}H_3)_3$), 27.6 ($C(\underline{C}H_3)_3$), 27.3 ($C(\underline{C}H_3)_3$), 26.1 ($OCH_2(\underline{C}H_2)_6CH_3$), 23.2 ($\underline{C}(CH_3)_3$), 22.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 20.8 ($CO\underline{C}H_3$), 20.8(3) ($CO\underline{C}H_3$ × 2), 20.8 ($CO\underline{C}H_3$), 20.6(4) ($CO\underline{C}H_3$), 20.6 ($\underline{C}(CH_3)_3$), 20.5 ($CO\underline{C}H_3$), 18.1 (Rha-C-6), 16.6 (Fuc-C-6), 14.1 ($O(CH_2)_7\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{111}H_{144}Na_2O_{33}Si$: 1039.4572; Found 1039.4621.

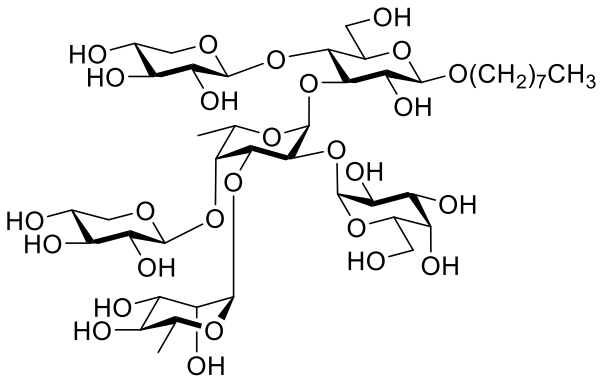


Octyl 2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl-(1→4)-[2,3,4-tri-*O*-acetyl-α-D-rhamnopyranosyl-(1→3)]-[2,3-di-*O*-benzyl-α-D-galactopyranosyl-(1→2)]-α-L-fucopyranosyl-(1→3)-[2,3,4-tri-*O*-benzyl-β-D-xylopyranosyl-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranoside (2.51)

To a stirred solution of **2.50** (62.6 mg, 30.8 μmol) in THF─ pyridine (3.75:1, 3.75 mL THF, 1.00 mL pyridine) under an Ar atmosphere was added HF·pyridine (0.20 mL, hydrogen fluoride ~70%, pyridine ~30%) at 0 ˚C. The reaction mixture was slowly warmed to room temperature and stirred for a total of 24.5 h. The reaction mixture was diluted with EtOAc (15 mL) and poured into a saturated solution of $NaHCO_3$ (aq). The aqueous layer was extracted with EtOAc (10 mL × 3) and the combined organic layers were dried over Na_2SO_4, filtered and then the filtrate was concentrated. The crude residue was purified via flash chromatography (1:1 EtOAc─ hexanes→19:1 EtOAc─ CH_3OH) to give **2.51** (42.5 mg, 73%) as a colourless film. Due to time constraints, the compound was not fully characterized (missing mass spectrum and optical rotation). R_f 0.26 (1:2:1 EtOAc─ hexanes─ acetone); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.37 – 7.16 (m, 40H, Ar), 5.48 (d, 1H, J = 3.5 Hz, Fuc-H-1), 5.38 (dd, 1H, J = 3.2, 1.7 Hz, Rha-H-2), 5.35 (dd, 1H, J = 10.0, 3.2 Hz, Rha-H-3), 5.21 (app t, 1H, J = 8.3 Hz, Xyl'-H-3), 5.19 (d, 1H, J = 3.2 Hz, Gal-H-1), 5.13 (dd, 1H, J = 8.6, 6.3 Hz, Xyl'-H-2), 5.02 (d, 1H, J = 1.8 Hz, Rha-H-1), 4.96 (app t, 1H, J = 9.9 Hz, Rha-H-4), 4.94 (app dt, 1H, J = 8.1, 4.1 Hz, Xyl'-H-4), 4.89 (d, 1H, J =

12.0 Hz, ArC$\underline{H}_2$), 4.83, 4.82 (ABq, 2H, J_{AB} = 10.7 Hz, ArC$\underline{H}_2$), 4.79 (d, 1H, J = 12.2 Hz, ArC$\underline{H}_2$), 4.79 (d, 1H, J = 10.6 Hz, ArC$\underline{H}_2$), 4.69 (d, 1H, J = 11.3 Hz, ArC$\underline{H}_2$), 4.68 (d, 1H, J = 11.2 Hz, ArC$\underline{H}_2$), 4.65 (d, 1H, J = 10.9 Hz, ArC$\underline{H}_2$), 4.64 (d, 1H, J = 10.9 Hz, ArC$\underline{H}_2$), 4.63 (d, 1H, J = 8.1 Hz, Xyl'-H-1), 4.62 – 4.56 (m, 3H, ArC$\underline{H}_2$, Fuc-H-5), 4.53 (d, 1H, J = 11.7 Hz, ArC$\underline{H}_2$), 4.47 (d, 1H, J = 12.0 Hz, ArC$\underline{H}_2$), 4.46 (d, 1H, J = 8.0 Hz, Xyl-H-1), 4.43 (dd, 1H, J = 10.3, 2.7 Hz, Fuc-H-3), 4.38 (d, 1H, J = 7.5 Hz, Glc-H-1), 4.37 (d, 1H, J = 12.0 Hz, ArC$\underline{H}_2$), 4.36 (dt, 1H, J = 9.9, 6.4 Hz, Rha-H-5), 4.30 (dd, 1H, J = 11.8, 4.9 Hz, Xyl'-H-5a), 4.17 (dd, 1H, J = 10.3, 3.5 Hz, Fuc-H-2), 4.08 (dd, 1H, J = 11.5, 5.6 Hz, Xyl-H-5a), 4.01 (app t, 1H, J = 9.1 Hz, Glc-H-4), 3.95 (app t, 1H, J = 8.5 Hz, Glc-H-3), 3.90 (dd, 1H, J = 10.8, 3.4 Hz, Glc-H-6a), 3.87 (dt, 1H, J = 9.6, 6.5 Hz, OC$\underline{H}_2(CH_2)_6CH_3$), 3.84 (dd, 1H, J = 9.7, 3.3 Hz, Gal-H-2), 3.81 (dd, 1H, J = 9.8, 3.0 Hz, Gal-H-3), 3.70 – 3.62 (m, 4H, Fuc-H-4, Xyl-H-4, Glc-H-6b, Gal-H-4), 3.49 (m, 2H, Gal-H-6a, Gal-H-5), 3.47 – 3.43 (m, 2H, Glc-H-2, Xyl-H-3), 3.42 – 3.35 (m, 3H, Xyl'-H-5b, OC$\underline{H}_2(CH_2)_6CH_3$, Glc-H-5), 3.17 – 3.08 (m, 3H, Gal-H-6b, Xyl-H-5b, Xyl-H-2), 2.09 (s, 3H, COC$\underline{H}_3$), 2.03 (s, 3H, COC$\underline{H}_3$), 2.02 (s, 3H, COC$\underline{H}_3$), 2.02 (s, 3H, COC$\underline{H}_3$), 1.89 (s, 3H, COC$\underline{H}_3$), 1.65 (s, 3H, COC$\underline{H}_3$), 1.59 – 1.52 (m, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.22 (d, 3H, J = 6.8 Hz, Fuc-H-6), 1.31 – 1.15 (m, 10H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 1.14 (d, 3H, J = 6.3 Hz, Rha-H-6), 0.84 (t, 3H, J = 7.2 Hz, $O(CH_2)_7C\underline{H}_3$); ^{13}C NMR (176 MHz; $CDCl_3$): δ 170.2 ($\underline{C}OCH_3$), 170.1 ($\underline{C}OCH_3$), 170.0 ($\underline{C}OCH_3$), 169.7 ($\underline{C}OCH_3$), 169.6 ($\underline{C}OCH_3$), 169.4 ($\underline{C}OCH_3$), 139.4 (Ar), 138.5 (Ar), 138.3 (Ar), 138.2(7) (Ar), 138.0(7) (Ar), 138.0 (Ar), 128.5 (Ar), 128.4(7) (Ar), 128.4 (Ar), 128.3(6) (Ar), 128.3(5) (Ar), 128.2 (Ar), 128.0(2) (Ar), 128.0 (Ar), 127.9(8) (Ar), 127.9 (Ar), 127.7(4) (Ar), 127.7 (Ar), 127.6(9) (Ar), 127.6(5) (Ar), 127.6 (Ar), 127.3 (Ar), 127.0 (Ar), 126.9 (Ar), 126.2 (Ar), 103.3 (Xyl-C-1), 103.2 (Glc-C-1), 100.7 (Xyl'-C-1), 100.2 (Rha-C-1), 97.8 (Gal-C-1), 96.3 (Fuc-H-1), 84.0 (Xyl-C-3), 82.5 (Xyl-C-2), 82.0 (Glc-C-2), 80.1 (Fuc-C-4), 78.6

(Xyl-C-4), 77.1 (Gal-C-3), 76.9 (Fuc-C-3), 75.8 (Ar$\underline{C}H_2$), 75.1 (Ar$\underline{C}H_2$), 75.0(8) × 2, 74.9(8) (Glc-C-4 & Gal-C-2 & Glc-C-5), 73.6 (Glc-C-3), 73.4 (Ar$\underline{C}H_2$), 73.0 (Ar$\underline{C}H_2$), 72.4 (Ar$\underline{C}H_2$), 72.3 (Ar$\underline{C}H_2$), 72.2 (Ar$\underline{C}H_2$), 71.3, 71.2 (Rha-C-4 & Fuc-C-2), 70.9 (Xyl'-C-2), 70.5 (Xyl'-C-3, Gal-C-5), 69.9 (O$\underline{C}H_2(CH_2)_6CH_3$), 69.8 (Rha-C-2), 69.4, 69.3 (Xyl'-C-4 & Rha-C-3), 68.7 (Gal-C-4), 67.8 (Glc-C-6), 66.4 (Rha-C-5), 65.6 (Fuc-C-5), 64.0 (Xyl-C-5), 62.3 (Gal-C-6), 61.5 (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 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 26.1 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 20.8 ($CO\underline{C}H_3$), 20.7(6) ($CO\underline{C}H_3$), 20.7(5) ($CO\underline{C}H_3$), 20.7 ($CO\underline{C}H_3$), 20.6 ($CO\underline{C}H_3$), 20.4 ($CO\underline{C}H_3$), 18.0 (Rha-C-6), 16.9 (Fuc-C-6), 14.1 ($O(CH_2)_7\underline{C}H_3$).

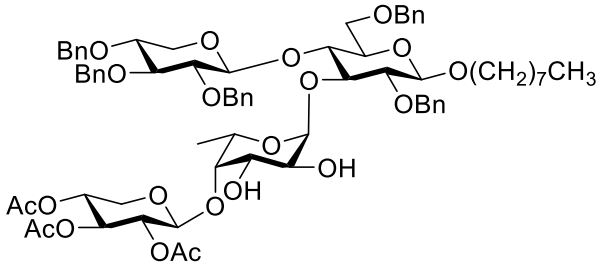


Octyl β-D-xylopyranosyl-(1→4)-[α-D-rhamnopyranosyl-(1→3)]-[α-D-galactopyranosyl-(1→2)]-α-L-fucopyranosyl-(1→3)-[β-D-xylopyranosyl-(1→4)]-β-D-glucopyranoside (2.6)

To a stirred solution of **2.51** (42.4 mg, 22.4 μmol) in CH_3OH (6.0 mL) was added NaOH (56.6 mg, 1.42 mmol). The reaction mixture was stirred at room temperature for 17.5 h. Amberlite®

IR-120 (H^+) cation exchange resin was added, the mixture filtered and then the filtrate was concentrated. The crude residue was purified via flash chromatography (7:1 EtOAc─CH_3OH). The residue was dissolved in THF─ H_2O (1:1, 2.0 mL THF, 2.0 mL H_2O) and 20% $Pd(OH)_2/C$ (12.2 mg) was added under an Ar atmosphere. The reaction mixture was stirred at room temperature, under a H_2 atmosphere, for 38 h and was then filtered and the filtrate concentrated. The residue was dissolved in pyridine (2.0 mL) and acetic anhydride (1.0 mL) was added at 0 ˚C. The reaction mixture was warmed to room temperature and stirred for 20 h and then concentrated. The crude residue was passed through a silica column (3:2 hexanes─ EtOAc). The crude product was dissolved in CH_3OH (6.0 mL) and NaOH (56.4 mg, 1.41 mmol) was added. The reaction mixture was stirred at room temperature for 18 h. Amberlite® IR-120 (H^+) cation exchange resin was added, the mixture filtered and then the filtrate was concentrated. The crude product was purified via Iatrobead chromatography (CH_2Cl_2:CH_3OH→CH_3OH, 10% stepwise gradient) to give **2.6** as a white film (tentative 13.4 mg, 59%). R_f 0.26 (4:1:1:1 EtOAc─ CH_3OH─ H_2O─ AcOH); $[\alpha]_D$ ─ 19.4 (*c* 0.5, $CHCl_3$); ^{1}H NMR (700 MHz; D_2O): δ 5.64 (d, 1H *J* = 3.9 Hz, Fuc-H-1), 5.23 (d, 1H, *J* = 4.0 Hz, Gal-H-1), 5.05 (app s, 1H, Rha-H-1), 4.78 – 4.74 (m, 1H, Fuc-H-5), 4.47 (d, 1H, *J* = 7.7 Hz, Xyl'-H-1), 4.45 (d, 1H, *J* = 8.0 Hz, Glc-H-1), 4.42 (d, 1H, *J* = 7.9 Hz, Xyl-H-1), 4.22 (dd, 1H, *J* = 10.6, 2.8 Hz, Fuc-H-3), 4.15 (dd, 1H, *J* = 10.6, 3.9 Hz, Fuc-H-2), 4.11 (dt, 1H, *J* = 12.8, 6.3 Hz, Rha-H-5), 4.08 – 3.97 (m, 6H, Gal-H-5, Rha-H-2, Xyl'-H-5a, Gal-H-4, Xyl-H-5a, Glc-H-6a), 3.93 – 3.79 (m, 6H, $OC\underline{H}_2(CH_2)_6CH_3$, Glc-H-3, Fuc-H-4, Gal-H-3, Glc-H-6b, Gal-H-2), 3.78 – 3.64 (m, 6H, Rha-H-3, Gal-H-6a, Gal-H-6b, $OC\underline{H}_2(CH_2)_6CH_3$, Glc-H-4, Xyl'-H-4), 3.63 – 3.55 (m, 2H, Xyl-H-4, Glc-H-5), 3.50 (app t, 1H, *J* = 9.6 Hz, Rha-H-4), 3.48 – 3.43 (m, 3H, Xyl-H-3, Xyl'-H-3, Glc-H-2), 3.39 (app t, 1H, *J* = 8.6 Hz, Xyl'-H-2), 3.28 (app t, 1H, *J* = 11.1 Hz, Xyl-H-5b), 3.24 (app t, 1H, *J* = 11.2 Hz, Xyl'-H-

5b), 3.15 (app t, 1H, J = 8.6 Hz, Xyl-H-2), 1.63 (app pent, J = 7.0 Hz, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.39 – 1.25 (m, 10H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 1.31 (d, 3H, J = 6.9 Hz, Fuc-H-6), 1.29 (d, 3H, J = 6.4 Hz, Rha-H-6), 0.87 (t, 3H, J = 6.7 Hz, $O(CH_2)_7C\underline{H}_3$); ^{13}C NMR (176 MHz; D_2O): δ 105.1 (Xyl'C-1), 103.7, 103.6 (Rha-C-1 & Xyl-C-1), 103.2 (Glc-C-1), 99.8 (Gal-C-1), 98.1 (Fuc-C-1), 82.0 (Fuc-C-4), 76.7, 76.6, 76.5 (Fuc-C-3 & Xyl-C-3 & Xyl'-C-3), 76.0, 75.9, 75.8 (Glc-C-2 & Glc-C-3 & Glc-C-5), 74.9 (Glc-C-4), 74.5, 74.4 (Xyl-C-2 & Xyl'C-2), 72.8 (Rha-C-4), 72.1 (Gal-C-5), 71.8 ($O\underline{C}H_2(CH_2)_6CH_3$), 71.6 (Fuc-C-2), 71.1, 71.0 (Rha-C-2 & Rha-C-3), 70.6, 70.5 (Xyl-C-4 & Gal-C-3), 70.2 (Xyl'-C-4), 70.0 (Gal-C-4), 69.7 (Rha-C-5), 69.2 (Gal-C-2), 68.0 (Fuc-C-5), 65.7 × 2 (Xyl-C-5, Xyl'-C-5), 61.9 (Gal-C-6), 60.4 (Glc-C-6), 31.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 25.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 17.5 (Rha-C-6), 15.7 (Fuc-C-6), 14.2 ($O(CH_2)_7\underline{C}H_3$).

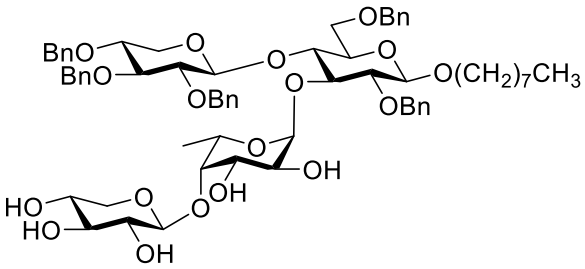


Octyl 2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl-(1→4)-α-L-fucopyranosyl-(1→3)-[2,3,4-tri-*O*-benzyl-β-D-xylopyranosyl-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranoside (2.47)

To a stirred solution of **2.46** (29.0 mg, 20.7 μmol) in dry CH_2Cl_2 (5.0 mL) was added trifluoroacetic acid (0.05 mL) drop wise at 0 ˚C, under an Ar atmosphere. The reaction mixture

was slowly warmed to room temperature and stirred for 4 h and was then chilled to 0 ˚C and triethylamine added. The solution was concentrated and the resulting residue was purified via flash chromatography (1:1 hexanes─ EtOAc→3:2 EtOAc─ hexanes) to give **2.47** (23.1 mg, 87%) as a colourless film. R_f 0.45 (3:2 EtOAc─ hexanes); [α]D ─ 45.9 (*c* 1.3, $CHCl_3$); ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.39 – 7.23 (m, 25H, Ar), 5.48 (d, 1H, *J* = 3.9 Hz, Fuc-H-1), 5.19 (app t, 1H, *J* = 9.2 Hz, Xyl'-H-3), 5.03 – 4.96 (m, 2H, Xyl'-H-4, Xyl'-H-2), 4.88 (d, 1H, *J* = 10.2 Hz, ArC$\underline{H}_2$), 4.81 (ABq, 2H, J_{AB} = 11.1 Hz, ArC$\underline{H}_2$), 4.76 (d, 1H, *J* = 11.1 Hz, ArC$\underline{H}_2$), 4.69 (d, 1H, *J* = 11.5 Hz, ArC$\underline{H}_2$), 4.69, 4.62 (ABq, 2H, J_{AB} = 11.5 Hz, ArC$\underline{H}_2$), 4.66 (d, 1H, *J* = 11.3 Hz, ArC$\underline{H}_2$), 4.68 – 4.63 (m, 1H, Fuc-H-5), 4.63 (d, 1H, *J* = 12.1 Hz, ArC$\underline{H}_2$), 4.47 (d, 1H, *J* = 7.6 Hz, Xyl'-H-1), 4.41 (d, 1H, *J* = 12.0 Hz, ArC$\underline{H}_2$), 4.37 (d, 1H, *J* = 8.0 Hz, Xyl-H-1), 4.33 (d, 1H, *J* = 7.7 Hz, Glc-H-1), 4.18 (dd, 1H, *J* = 11.7, 5.5 Hz, Xyl'-H-5a), 3.93 – 3.84 (m, 4H, OC$\underline{H}_2$(CH_2)$_6$$CH_3$, Xyl-H-5a, Glc-H-4, Glc-H-6a), 3.82 (dd, 1H, *J* = 10.1, 3.0 Hz, Fuc-H-3), 3.79 (app t, 1H, *J* = 9.3 Hz, Glc-H-3), 3.65 – 3.60 (m, 2H, Fuc-H-2, Glc-H-6b), 3.57 (dd, 1H, *J* = 3.2, 1.2 Hz, Fuc-H-4), 3.47 (dt, 1H, *J* = 9.5, 6.8 Hz, OC$\underline{H}_2$(CH_2)$_6$$CH_3$), 3.44 – 3.34 (m, 4H, Xyl-H-4, Glc-H-2, Xyl-H-3, Xyl'-H-5b), 3.28 (ddd, 1H, *J* = 9.7, 3.3, 1.9 Hz, Glc-H-5), 3.06 (app t, 1H, *J* = 8.3 Hz, Xyl-H-2), 2.98 (dd, 1H, *J* = 11.7, 10.1 Hz, Xyl-H-5b), 2.03 (s, 3H, COC$\underline{H}_3$), 2.02 (s, 3H, COC$\underline{H}_3$), 2.02 (s, 3H, COC$\underline{H}_3$), 1.67 – 1.57 (m, 2H, OCH_2C$\underline{H}_2$(CH_2)$_5$$CH_3$), 1.41 – 1.19 (m, 10H, , OCH_2CH_2(C$\underline{H}_2$)$_5$$CH_3$), 1.09 (d, 3H, *J* = 6.6 Hz, Fuc-H-6), 0.86 (t, 3H, *J* = 7.1 Hz, O(CH_2)$_7$C$\underline{H}_3$); ^{13}C NMR (176 MHz; $CDCl_3$): δ 170.2 (C$\underline{O}$$COCH_3$), 169.7 (C$\underline{O}$$COCH_3$), 169.2 (C$\underline{O}$$COCH_3$), 138.4 (Ar), 138.3 (Ar), 138.1 (Ar), 138.0 (Ar), 128.5 (Ar), 128.4(7) (Ar), 128.4 (Ar), 128.3(5) (Ar), 128.3 (Ar), 128.1 (Ar), 127.9 (Ar), 127.8 (Ar), 127.7(6) (Ar), 127.7(2) (Ar), 127.7 (Ar), 127.6 (Ar), 127.5(6) (Ar), 103.6 (Glc-C-1), 103.0 (Xyl-C-1), 102.4 (Xyl'-C-1), 98.2 (Fuc-C-1), 84.2 (Fuc-C-4), 83.9 (Xyl-C-3), 82.5, 82.4(5) (Glc-C-2 & Xyl-C-2), 78.3 (Xyl-C-4), 75.9

(Ar<u>C</u>H$_2$), 75.6 (Glc-C-3), 75.1 (Ar<u>C</u>H$_2$), 75.0(8) (Glc-C-5), 74.5 (Ar<u>C</u>H$_2$), 74.4(9) (Glc-C-4), 73.4 (Ar<u>C</u>H$_2$), 73.2 (Ar<u>C</u>H$_2$), 72.0 (Xyl'-C-3), 71.5 (Xyl'-C-2), 70.1 (O<u>C</u>H$_2$(CH$_2$)$_6$CH$_3$), 69.9 (Fuc-C-2), 69.7 (Fuc-C-3), 68.6 (Xyl'-C-4), 67.7 (Glc-C-6), 65.3 (Fuc-C-5), 63.9 (Xyl-C-5), 62.6 (Xyl'-C-5), 31.8 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 29.7 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 29.4 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 29.2 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 26.2 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 22.6 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 20.7 (CO<u>C</u>H$_3$), 20.6(6) (CO<u>C</u>H$_3$ × 2), 16.2 (Fuc-C-6), 14.1 (O(CH$_2$)$_7$<u>C</u>H$_3$); HRMS (ESI) Calc. for [M + Na]$^+$ C$_{71}$H$_{90}$NaO$_{21}$: 1301.5867; Found 1301.5856.

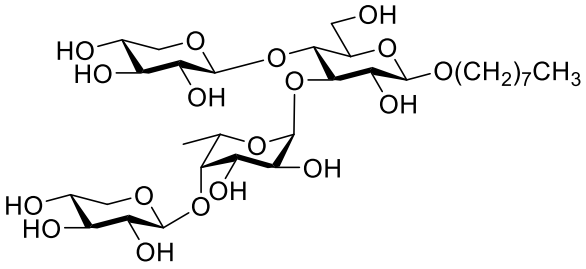


Octyl β-D-xylopyranosyl-(1→4)-α-L-fucopyranosyl-(1→3)-[2,3,4-tri-*O*-benzyl-β-D-xylopyranosyl-(1→4)]-2,6-di-*O*-benzyl-β-D-glucopyranoside (2.48)

To a stirred solution of **2.47** (76.6 mg, 59.9 μmol) in CH$_3$OH (6.0 mL) was added NaOH (48.8 mg, 1.22 mmol). The reaction mixture was stirred at room temperature for 16 h. Amberlite® IR-120 (H$^+$) cation exchange resin was added, the mixture filtered and then the filtrate was concentrated. The crude residue was purified via flash chromatography (10:1 CH$_2$Cl$_2$─ CH$_3$OH) to give **2.48** (60.1 mg, 87%) as a colourless film. R_f 0.29 (10:1 CH$_2$Cl$_2$─ CH$_3$OH); [α]$_D$ ─ 45.9 (*c* 3.3, CHCl$_3$); ^{1}H NMR (700 MHz; CDCl$_3$): δ 7.42 – 7.38 (m, 2H, Ar), 7.37 – 7.22 (m, 23H, Ar),

5.59 (d, 1H, J = 4.0 Hz, Fuc-H-1), 4.91 (d, 1H, J = 10.0 Hz, ArC$\underline{H}_2$), 4.80 (ABq, 2H, J_{AB} = 11.3 Hz, ArC$\underline{H}_2$), 4.74 (d, 1H, J = 11.1 Hz, ArC$\underline{H}_2$), 4.69 (app q, 1H, J = 5.9 Hz, Fuc-H-5), 4.67, 4.61 (ABq, 2H, J_{AB} = 11.5 Hz, ArC$\underline{H}_2$), 4.66 (d, 1H, J = 9.5, ArC$\underline{H}_2$), 4.64 (d, 1H, J = 11.3 Hz, ArC$\underline{H}_2$), 4.63 (d, 1H, J = 12.6 Hz, ArC$\underline{H}_2$), 4.41 (d, 1H, J = 12.0 Hz, ArC$\underline{H}_2$), 4.36 (d, 1H, J = 7.9 Hz, Xyl-H-1), 4.33 (d, 1H, J = 7.7 Hz, Glc-H-1), 4.08 (d, 1H, J = 6.9 Hz, Xyl'-H-1), 3.94 – 3.84 (m, 4H, OC$\underline{H}_2(CH_2)_6CH_3$, Glc-H-4, Xyl-H-5a, Glc-H-6a), 3.81 (dd, 1H, J = 10.0, 2.9 Hz, Fuc-H-3), 3.79 (app t, 1H, J = 9.3 Hz, Glc-H-3), 3.71 (dd, 1H, J = 10.1, 4.2 Hz, Fuc-H-2), 3.71 – 3.67 (m, 1H, Xyl'-H-5a), 3.61 (dd, 1H, J = 11.1, 1.8 Hz, Glc-H-6b), 3.59 (app d, 1H, J = 3.0 Hz, Fuc-H-4), 3.48 (dt, 1H, J = 9.5, 6.9 Hz, OC$\underline{H}_2(CH_2)_6CH_3$), 3.45 (dd, 1H, J = 9.2, 7.7 Hz, Glc-H-2), 3.43 – 3.34 (m, 4H, Xyl-H-3, Xyl-H-4, Xyl'-H-2, Xyl'-H-3), 3.29 (app dt, 1H, J = 9.6, 2.6 Hz, Glc-H-5), 3.26 – 3.20 (m, 1H, Xyl'-H-4), 3.10 (app t, 1H, J = 10.9 Hz, Xyl'-H-5b), 3.05 (app t, 1H, J = 8.3 Hz, Xyl-H-2), 2.98 (app t, 1H, J = 10.2 Hz, Xyl-H-5b), 1.68 – 1.58 (m, 2H, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.43 – 1.21 (m, 10H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 1.19 (d, 3H, J = 6.7 Hz, Fuc-H-6), 0.86 (t, 3H, J = 7.0 Hz, $O(CH_2)_7C\underline{H}_3$); ^{13}C NMR (176 MHz; $CDCl_3$): δ 138.4 (Ar), 138.2 (Ar), 138.1 (Ar), 138.0 (Ar), 137.9(8) (Ar), 128.9 (Ar), 128.5 (Ar), 128.4(6) (Ar), 128.4 (Ar), 128.3(6) (Ar), 128.3 (Ar), 128.1 (Ar), 128.0 (Ar), 127.9 (Ar), 127.8 (Ar), 127.7 (Ar), 127.6(3) (Ar), 127.6 (Ar), 127.5(8) (Ar), 104.3 (Xyl'-C-1), 103.4 (Glc-C-1), 103.1 (Xyl-C-1), 97.7 (Fuc-C-1), 83.9 (Xyl-C-3), 82.9 (Glc-C-2), 82.4 (Xyl-C-2), 81.8 (Fuc-C-4), 78.2 (Xyl-C-4), 76.0 (Xyl'-C-3), 75.8 (Ar$\underline{C}H_2$), 75.4 (Glc-C-3), 75.1 (Ar$\underline{C}H_2$), 75.0 (Glc-C-5), 74.7 (Ar$\underline{C}H_2$), 74.5 (Glc-C-4), 73.4 (Ar$\underline{C}H_2$), 73.2 (Ar$\underline{C}H_2$), 73.0 (Xyl'-C-2), 70.2 (Fuc-C-2), 70.1 (O$\underline{C}H_2(CH_2)_6CH_3$), 69.6 (Xyl'-C-4), 69.5 (Fuc-C-3), 67.6 (Glc-C-6), 66.0 (Fuc-C-5), 65.8 (Xyl'-C-5), 63.9 (Xyl-C-5), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_6CH_3$),

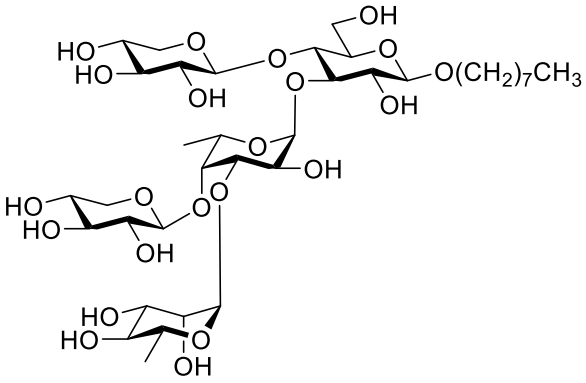
29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 26.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 16.1 (Fuc-C-6), 14.1 ($O(CH_2)_7\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{65}H_{84}NaO_{18}$: 1175.5550; Found 1175.5547.



Octyl β-D-xylopyranosyl-(1→4)-α-L-fucopyranosyl-(1→3)-[β-D-xylopyranosyl-(1→4)]-β-D-glucopyranoside (2.8)

To a stirred solution of **2.48** (59.5 mg, 51.6 μmol) in THF─ H_2O (1:1, 2.0 mL THF, 2.0 mL H_2O) was added 20% $Pd(OH)_2/C$ (21.2 mg) under an Ar atmosphere. The reaction mixture was stirred at room temperature, under a H_2 atmosphere, for 20 h and was then filtered and the filtrate concentrated. The crude residue was purified via C_{18} chromatography (H_2O:CH_3OH→CH_3OH, 10% stepwise gradient) to give **2.8** as a white film (26.8 mg, 74%). R_f 0.67 (4:1:1:1 EtOAc─ CH_3OH─ H_2O─ AcOH); $[\alpha]_D$ ─ 99.8 (*c* 0.6, CH_3OH); ^1H NMR (700 MHz; D_2O): δ 5.49 (d, 1H, *J* = 4.0 Hz, Fuc-H-1), 4.71 (app q, 1H, *J* = 6.7 Hz, Fuc-H-5), 4.45 (d, 1H, *J* = 8.1 Hz, Glc-H-1), 4.44 (d, 1H, *J* = 7.8 Hz, Xyl-H-1), 4.40 (d, 1H, *J* = 7.7 Hz, Xyl'-H-1), 4.02 – 3.96 (m, 2H, Xyl'-H-5a, Glc-H-6a), 3.96 – 3.88 (m, 4H, Fuc-H-3, Fuc-H-4, Xyl-H-5a, $OC\underline{H}_2(CH_2)_6CH_3$), 3.84 (dd, 1H, *J* = 12.3, 4.6 Hz, Glc-H-6b), 3.80 (app t, 1H, *J* = 9.1 Hz, Glc-H-3), 3.78 (dd, 1H, *J* = 9.4, 3.9 Hz, Fuc-H-2), 3.75 (app t, 1H, *J* = 9.4 Hz, Glc-H-4), 3.70 – 3.63 (m, 2H, Xyl'-H-4, $OC\underline{H}_2(CH_2)_6CH_3$), 3.56 (app dt, 1H, *J* = 9.0, 2.7 Hz, Glc-H-5), 3.53 (app dt, 2H, *J* = 10.1, 4.8 Hz, Xyl-H-4), 3.50 (app t, 1H, *J* = 8.4 Hz, Glc-H-2), 3.46 (app t, 1H, *J* = 9.2 Hz, Xyl'-H-3), 3.46 (app t, 1H, *J* = 9.3 Hz, Xyl-H-3), 3.40 (dd, 1H, *J* = 9.5, 7.6 Hz, Xyl'-H-2), 3.30 (app t, 1H, *J* =

11.1 Hz, Xyl'-H-5b), 3.27 (app t, 1H, *J* = 11.1 Hz, Xyl-H-5b), 3.18 (app t, 1H, *J* = 8.6 Hz, Xyl-H-2), 1.63 (app pent, 2H, *J* = 6.9 Hz, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.38 – 1.27 (m, 10H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 1.30 (d, 3H, *J* = 6.6 Hz, Fuc-H-6), 0.87 (t, 3H, *J* = 6.8 Hz, $O(CH_2)_7C\underline{H}_3$); ^{13}C NMR (176 MHz; D_2O): δ 104.7 (Xyl'-C-1), 103.3 (Xyl-C-1), 102.9 (Glc-C-1), 99.3 (Fuc-C-1), 81.6 (Fuc-C-4), 78.2 (Glc-C-3), 76.5 (Xyl'-C-3, Xyl-C-3), 76.0 (Glc-C-5), 75.4 (Glc-C-2), 74.5(4), 74.5(2) (Glc-C-4 & Xyl-C-2), 74.3 (Xyl'-C-2), 71.7 ($O\underline{C}H_2(CH_2)_6CH_3$), 70.4 (Xyl-C-4), 70.1 (Xyl'-C-4), 69.8 (Fuc-C-2), 69.3 (Fuc-C-3), 67.5 (Fuc-C-5), 66.0 (Xyl'-C-5), 65.9 (Xyl-C-5), 60.5 (Glc-C-6), 32.0 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 26.0 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 16.0 (Fuc-C-6), 14.3 ($O(CH_2)_7\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{30}H_{54}NaO_{18}$: 725.3202; Found 725.3202.



Octyl β-D-xylopyranosyl-(1→4)-[α-D-rhamnopyranosyl-(1→3)]-α-L-fucopyranosyl-(1→3)-[β-D-xylopyranosyl-(1→4)]-β-D-glucopyranoside (2.9)

To a stirred solution of **2.49** (52.3 mg, 33.7 μmol) in CH_3OH (5.0 mL) was added NaOH (58.9 mg, 1.47 mmol). The reaction mixture was stirred at room temperature for 18.5 h. Amberlite®

IR-120 (H^+) cation exchange resin was added, the mixture filtered and then the filtrate was concentrated. The crude residue was passed through a silica column (6:1 CH_2Cl_2─ CH_3OH). The residue was dissolved in THF─ H_2O (1:1, 2.0 mL THF, 2.0 mL H_2O) and 20% $Pd(OH)_2/C$ (19.1 mg) was added under an Ar atmosphere. The reaction mixture was stirred at room temperature, under a H_2 atmosphere, for 26 h and was then filtered and the filtrate was concentrated. The crude residue was purified via Iatrobead chromatography (CH_2Cl_2:CH_3OH→CH_3OH, 10% stepwise gradient) to give **2.9** as a white film (16.3 mg, 57%). R_f 0.70 (4:1:1:1 EtOAc─ CH_3OH─ H_2O─ AcOH); $[\alpha]_D$ ─ 69.9 (*c* 0.5, CH_3OH); ^{1}H NMR (700 MHz; D_2O): δ 5.56 (d, 1H, *J* = 4.0 Hz, Fuc-H-1), 4.99 (d, 1H, *J* = 1.7 Hz, Rha-H-1), 4.70 (app q, 1H, *J* = 6.8 Hz, Fuc-H-5), 4.46 (d, 1H, *J* = 8.3 Hz, Glc-H-1), 4.44 (d, 1H, *J* = 8.0 Hz, Xyl'-H-1), 4.43 (d, 1H, *J* = 7.9 Hz, Xyl-H-1), 4.06 (dd, 1H, *J* = 3.5, 1.7 Hz, Rha-H-2), 4.06 – 3.97 (m, 5H, Rha-H-5, Fuc-H-3, Xyl-H-5a, Glc-H-6a, Xyl'-H-5a), 3.95 – 3.90 (m, 2H, $OC\underline{H}_2(CH_2)_6CH_3$, Fuc-H-2), 3.89 (app d, 1H, *J* = 3.0 Hz, Fuc-H-4), 3.83 (app t, 1H, *J* = 9.3 Hz, Glc-H-4), 3.85 – 3.80 (m, 1H, Glc-H-6b), 3.80 (dd, 1H, *J* = 9.7, 3.4 Hz, Rha-H-3), 3.75 (app t, 1H, *J* = 9.6 Hz, Glc-H-3), 3.68 (dt, 1H, *J* = 10.1, 6.8 Hz, $OC\underline{H}_2(CH_2)_6CH_3$), 3.65 (ddd, 1H, *J* = 10.6, 9.0, 5.5 Hz, Xyl-H-4), 3.61 (ddd, 1H, *J* = 10.9, 9.2, 5.6 Hz, Xyl'-H-4), 3.58 (ddd, 1H, *J* = 9.9, 4.8, 2.0 Hz, Glc-H-5), 3.51 (dd, 1H, *J* = 9.2, 8.1 Hz, Glc-H-2), 3.50 (app t, 1H, *J* = 9.6 Hz, Rha-H-4), 3.46 (app t, 1H, *J* = 9.2 Hz, Xyl-H-3), 3.45 (app t, 1H, *J* = 9.2 Hz, Xyl'-H-3), 3.38 (dd, 1H, *J* = 9.4, 7.7 Hz, Xyl'-H-2), 3.29 (app t, 1H, *J* = 11.1 Hz, Xyl'-H-5b), 3.25 (dd, 1H, *J* = 11.7, 10.6 Hz, Xyl-H-5b), 3.17 (dd, 1H, *J* = 9.4, 7.9 Hz, Xyl-H-2), 1.62 (app pent, 2H, *J* = 6.9 Hz, $OCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.38 – 1.25 (m, 10H, $OCH_2CH_2(C\underline{H}_2)_5CH_3$), 1.30 (d, 3H, *J* = 6.5 Hz, Fuc-H-6), 1.29 (d, 3H, *J* = 6.3 Hz, Rha-H-6), 0.87 (t, 3H, *J* = 6.9 Hz, $O(CH_2)_7C\underline{H}_3$); ^{13}C NMR (176 MHz; D_2O): δ 105.2 (Xyl'-C-1), 103.5 (Rha-C-1), 103.3 (Xyl-C-1), 103.0 (Glc-C-1), 98.8 (Fuc-C-1), 81.8 (Fuc-C-4), 76.9 (Glc-C-4),

76.7, 76.5 (Xyl-C-3 & Xyl'-C-3), 75.9 (Fuc-C-3, Glc-C-5), 75.5 (Glc-C-2), 74.7 (Glc-C-3), 74.5 (Xyl-C-2, Xyl'-C-2), 72.9 (Rha-C-4), 71.7 ($O\underline{C}H_2(CH_2)_6CH_3$), 71.0 (Rha-C-2, Rha-C-3), 70.5 (Xyl'-C-4), 70.2 (Xyl-C-4), 69.7 (Rha-C-5), 69.0 (Fuc-C-2), 67.9 (Fuc-C-5), 65.8 (Xyl-C-5), 65.7 (Xyl'-C-5), 60.5 (Glc-C-6), 31.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 25.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 17.6 (Rha-C-6), 15.9 (Fuc-C-6), 14.3 ($O(CH_2)_7\underline{C}H_3$); HRMS (ESI) Calc. for $[M + Na]^+$ $C_{36}H_{64}NaO_{22}$: 871.3781; Found 871.3782.

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Chapter 3

Summary and Future Work

3.1 Summary and future work

Detailed in this thesis is the synthesis of six structural analogs of the chlorovirus PBCV-1 MCP *N*-glycan (**Figure 3-1)**. This included three oligosaccharides based on truncated *N*-glycans expressed by antigenic PBCV-1 mutants (**3.1**, **3.2**, and **3.3**) and three possible biosynthetic intermediates (**3.4**, **3.5**, and **3.6**). The six targets were derived from the central α-L-Fuc*p*-(1→3)-[β-D-Xyl*p*- (1→4)]-β-D-Glc*p* core. The trisaccharide core was further elaborated to generate branched products. The use of orthogonal protecting groups on the fucose residue allowed for selective access to the desired glycosylation sites.

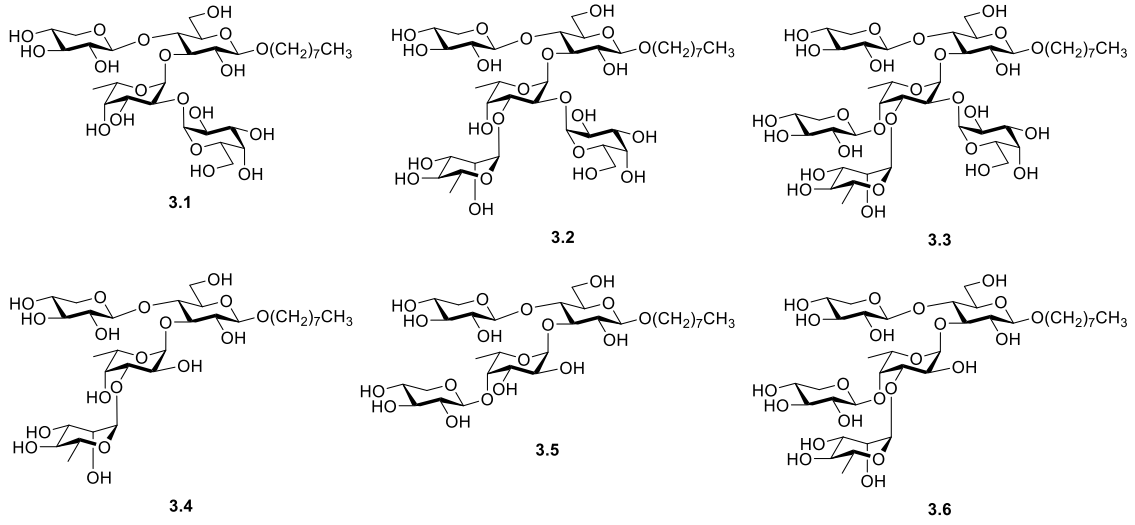

Figure 3-1: Structures of synthesised target analogs of the major MCP *N*-glycan of chlorovirus PBCV-1.

In a recent study conducted by the group of Dr. Cristina De Castro, genetic and glycan structural evidence were used to infer the protein function of several previously annotated PBCV-1 putative GT genes.[1] Thus, the next step for these compounds is for their use in biochemical assays, aimed at studying the activities of the previously described A111/114R, A075L, and A071R glycosyltransferases. The study will be conducted through an ongoing collaborative project with Dr. Cristina De Castro at the University of Napoli in Italy.

Furthermore, a current biological assay study has been finalized, looking to probe the viral *N*-glycan biosynthetic pathway. A colleague, Dr. Sicheng Lin, had synthesised several *N*-glycan fragments from PBCV-1 to serve as probes (**3.7–3.10**) in the investigation of the A064R GT (**Figure 3-2**). The results of the study have been published, confirming the initial predicted functions of the multi-domain A064R GT.[2]

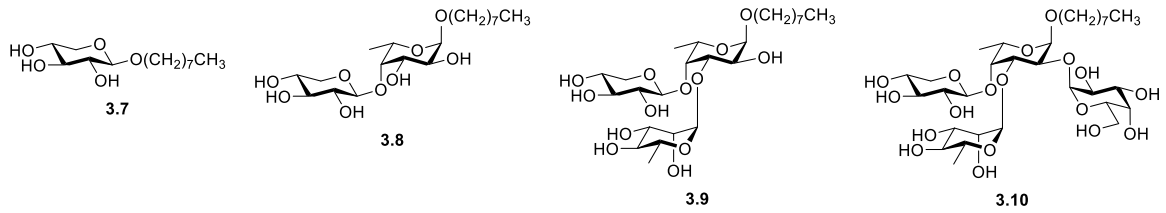

Figure 3-2: Structures of PBCV-1 *N*-glycan fragments as synthetic probes for A064R GT.[2, 3]

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