Studies Undertaken Towards the Total Synthesis of Antifreeze Compounds Based on the Xylomannan Antifreeze from the Alaskan Beetle *Upis ceramboides*

by

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Abstract

Biological antifreeze substances are widely found in the tissues of cold-blooded organisms indigenous to polar environments. Prior to 2009, all these compounds were associated with protein, leading to the widespread assumption that all biological antifreeze substances must possess a protein or peptide core. This perception was dispelled by Duman and co-workers in 2009, whose discovery of a protein-free xylomannan-based antifreeze glycolipid from the Alaskan Beetle *Upis ceramboides* heralded a new class of biological antifreeze. Though the structure of the xylomannan has been known for over a decade, no one has yet to address several questions regarding the identity of lipid component, the size of the xylomannan portion and the influence of these two factors in the overall antifreeze activity. To undertake such investigations, a library of structurally well-defined glycolipid mimetics will be required, and these are typically achieved through total chemical synthesis. Each compound will differ in both the number of disaccharide repeating units (between one to five units), and three different hydrophobic aglycones selected in lieu of the unidentified lipid component. Consequently, a total of fifteen compounds will be synthesized.

A major challenge in this project is the synthesis of each β-mannosidic linkage in the xylomannan portion. Moreover, β-mannosylation as a means of glycan chain assembly remains relatively less explored. Therefore the ulosyl bromide approach was selected to investigate such a possibility. This was successfully demonstrated in the synthesis of xylomannan disaccharides; however, issues inherent to this approach led to the search for another alternative.

In the second approach, a simultaneous multiple C-2 inversion strategy was developed as a convenient way to assemble all the oligosaccharides. The strategy developed involves the use

of β-glucosylation in assembling the glycan chain, followed by simultaneous C-2 inversion to convert all the glucose residues into the β-mannosides. This was successfully demonstrated in the synthesis of all the target fifteen compounds, which will then be delivered to lab of Prof. Hubbard (Department of Chemistry, University of Alberta) for assessment of antifreeze activity.

Preface

All the synthetic work described in this thesis was done solely by me and has not been published. Mass spectroscopic data of all compounds were collected by Dr. Randy Whittal and his colleagues in the Mass spectrometric lab. Optical rotation data were recorded by Wayne Moffat and his colleagues in the Analytical Lab. NMR spectra of all my compounds were recorded personally, except for one which was done by Mark Miskolzie from the University of Alberta NMR facility.

Dedicated to all my friends and family!

Acknowledgements

First and foremost, I would like to thank my supervisor Prof. Todd L. Lowary, for allowing me the opportunity of carrying out research in his lab. I have learnt tremendously from Todd not just on science in general but also his advice on dealing with various aspects of life outside of lab. Moreover, I am deeply indebted to the extraordinary amount of trust and support he has extended to me during my graduate research. The large amount of independence that he provided, while maintaining his ability to engage into my projects, served to build my self-confidence and self-cultivation. I hope that I am able to emulate both his passion for science and ability to create a work-life balance into my future endeavors.

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One of the best things that happened to me in Edmonton was the close network of friends that I have established throughout my PhD journey. Few words could be used to describe my heartfelt appreciation towards my friends, for without them, my experience in Edmonton would be vastly different. My gratitude goes to Ms. Anik Hanning for her life advice, her unwavering support and willingness to lend an ear to my various concerns that enabled me to weather through the vicissitudes of my PhD life; to Dr. Francesco Gentile for his endless jokes and fiery passion for soccer which we shared; to Mr. Liam Heffernan for his positive outlook in life and in my opinion the best BBQ chef in town; and finally to Ms. Anne-Laure Lesoin for her intense French humor (which I have come to appreciate), her impeccable advice on everything from basic life matters to men's fashion, the delectable cuisine that she served on various occasions

and shooting the breeze together during our innumerable long walks along the river. Altogether, their ability to relate to the rigors of graduate school served to cushion me against the psychological pressure of coping with my PhD studies.

Closer to home, I would also like to take this opportunity to acknowledge the contribution of some of my closest friends, Mr. Fei-Fan Tan, Mr. Guo-Rong Tan, Mr. Chen-Long Pow and Ms. Elaine Lim. Despite the great time differences, they managed to maintain contact with me throughout the years. I am also deeply indebted to them for their efforts to re-integrate me into their lives during my brief vacations back home. I would also like to acknowledge my undergraduate advisors Prof. Shunsuke Chiba and Prof. Bengang Xing (Nanyang Technological University, Singapore) for their guidance during my undergraduate research work, and their encouragement to pursue postgraduate studies into synthetic organic chemistry.

Last, but not least, I would like to thank my family members for their unconditional love and support during my PhD studies. Their constant phone calls and delivery of my favorite food all the way from Singapore were deeply appreciated.

Table of Contents

List of Tables

List of Figures

List of Schemes

List of Abbreviations

$[\alpha]_D$	specific rotation (sodium D line)
Ac_2O	acetic anhydride
AcCl	acetyl chloride
AcOH	acetic acid
Å	angstrom
AFGL	antifreeze glycolipid
AFP	antifreeze protein
AFGP	antifreeze glycoprotein
AF(G)P	antifreeze proteins and glycoprotein
Ala	Alanine
Allyl	All
app	apparent
Ar	aromatic
BDA	benzaldehyde dimethyl acetal
$BF_3 \cdot OEt_2$	boron trifluoride etherate
Bz	benzoyl
Bn	benzyl
br s	broad singlet (NMR spectra)
BSP	1-benzenesulfinyl piperidine
calcd	calculated
CAN	cerium ammonium nitrate
COSY	correlation spectroscopy

Cp_2ZrCl_2	zirconocene dichloride
CSA	camphorsulfonic acid
d	doublet (NMR spectra)
°C	degree Celsius
D_2O	deuteriated water
DAST	diethylaminosulfur trifluoride
DBU	diazabicyclo[5.4.0]undec-7-ene
DCC	*N*,*N'*-dicyclohexylcarbodiimide
DCTB	*trans*-2-[3-(4-*tert*-butylphenyl)-2-methyl-2-propenylidene]malononitrile
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DHB	2,5-dihydroxybenzoic acid
DIPEA	*N*,*N*-diisopropylethylamine
DIS	dynamic ice shaping
DMAP	dimethylaminopyridine
DMF	dimethylformamide
DMP	Dess-Martin Periodinane
DMSO	dimethylsulfoxide
DMTST	dimethyl(methylthio)sulfonium trifluoromethanesulfonate
DTBMP	2,6-di-*tert*-butyl-4-methylpyridine
DTBS	4,6-*O*-di-*tert*-butylsilylidene
EDC·HCl	1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride
E2	elimination bimolecular

ESI	electrospray ionization
Gal	D-galactose
Gal*p*	D-galactopyranose
glc. AcOH	glacial acetic acid
Glc	D-glucose
Glc*p*	D-glucopyranose
h	hour
HAD	hydrogen-bond mediated aglycone delivery
HMBC	heteronuclear Multiple Bond Correlation
HRMS	high resolution mass spectroscopy
HSQC	heteronuclear Single Quantum Coherence
Hz	hertz
IAD	intramolecular aglycone delivery
$[Ir(COD)(PMePh_2)_2]PF_6$	(1,5-cyclooctadiene)bis(methyldiphenylphosphine)iridium(I) hexafluorophosphate
IRI	ice recrystallization inhibition
kDa	kilodalton
Lev	levulinoyl
LTBA	lithium tri-*tert*-butoxyaluminum hydride
m	multiplet (NMR spectra)
M	molar
M.S.	molecular sieves
MALDI-TOF	Matrix-Assisted Laser Desorption Ionization/Time-of-Flight

Man	D-mannose
Man*p*	D-mannopyranose
mg	milligrams
MHz	megahertz
min	minutes
mL	milliliters
mM	millimolar
mmol	millimoles
N. arctica	*Nemoura arctica*
NBS	N-bromosuccinimide
NIS	N-iodosuccinimide
NMR	nuclear magnetic resonance
PCC	pyridinium chlorochromate
$Pd(OH)_2/C$	20% palladium hydroxide on carbon
Pd/C	10% palladium on carbon
Ph	phenyl
Piv	pivalate
PMB	*para*-methoxybenzyl
PPh_3	triphenylphosphine
ppm	parts per million
Py	pyridine
q	quartet (NMR spectra)
R_f	retardation factor

rt	room temperature
R. lessonae	*Rana lessonae*
s	singlet (NMR spectra)
satd.	saturated
*sf*AFP	*snow flea* antifreeze protein
$SO_3 \cdot Py$	sulfur trioxide pyridine complex
S_N2	nucleophilic substitution bimolecular
t	triplet (NMR spectra)
TBAF	tetrabutylammonium fluoride
TMSBr	trimethylsilyl bromide
TBDMSOTf	*tert*-butyldimethylsilyl trifluoromethanesulfonate
TFA	trifluoroacetic acid
Tf_2O	trifluoromethanesulfonic anhydride
TfOH	trifluoromethanesulfonic acid
TH	thermal hysteresis
THF	tetrahydrofuran
Thr	threonine
TLC	thin layer chromatography
*tm*AFP	*Tenebrio molitor* antifreeze protein
TMSOTf	trimethylsilyl trifluoromethanesulfonate
TOF	time-of-flight
Tol	*p*-tolyl
Troc	2,2,2-trichloroethoxycarbonyl

TTBP	2,4,6-tri-*tert*-butylpyrimidine
µL	microliters
µmol	micromoles
v/v	volume/volume (concentration)
w/v	weight/volume (concentration)
Xyl	D-xylose
Xyl*p*	D-xylopyranose

Chapter 1

Biological antifreeze compounds: introduction, and research direction

1.1 Physiological adaptations to frigid climates

Environments with polar climates pose significant challenges to the survival of any organism. Despite this, many organisms have survived and even flourished in such places. For instance, warm-blooded mammals, such as the polar bears of Arctic and the penguins in Antarctica, have successfully adapted to the environment by means of developing thick layers of blubber and fur that are highly effective in trapping their internally generated heat, thus maintaining body temperature.[1] However, this adaptation cannot be applied to the cold-blooded species, due to their inability to regulate their own body temperature. Therefore, exposure of these organisms to sub-zero temperatures can be dangerous, due to the lethal formation of large ice particles within their bodies. The fact that many of these species thrive under such conditions points to the myriad of physiological adaptations by which these organisms have evolved to survive under these conditions.[2] One particular adaptation that has gathered significant attention over the past few decades is the endogenous production of large biomacromolecular compounds, collectively termed biological antifreeze compounds.

1.2 Antifreeze proteins and glycoproteins

The first biological antifreeze compound was isolated from the blood sera of Artic fishes by Arthur DeVries in the 1960s.[3,4] Consisting of a recurring Ala–Ala–Thr tripeptide sequence in which the Thr residue is glycosylated with a β-D-Gal*p*-(1→3)-α-D-Gal*p*NAc disaccharide, this glycoprotein was demonstrated by Scholander and DeVries to be the causative factor behind the large freezing point depression in the blood sera of these fish. These glycoproteins prevent ice formation within the blood, allowing these polar fishes to survive in ice-laden waters.

Since then, several more types of biological macromolecular compounds have been discovered, ranging from antifreeze proteins (AFPs) to antifreeze glycoproteins (AFGPs).[2,5,6] Although these compounds all share the same function in protecting organisms from cryodamage, their structural differences point to the different levels of cold adaptation each organism had in its own environment.[1,2,7] For example, AFPs isolated from insects like *Tenebrio molitor* are more potent than AF(G)Ps produced in polar fishes, probably due to the temperatures as low as −60 °C that can be encountered by these inland organisms. In terms of structure, AFGPs are highly conserved in the polypeptide backbone (Fig. 1-1a), but AFPs boast a huge repertoire, from the Ala-rich α-helical structures in Type I AFP (Fig. 1-1b) to tightly packed flattened coils (Fig. 1-1c) and β-solenoids (Fig. 1-1d) in *sf*AFP and *tm*AFP, respectively.

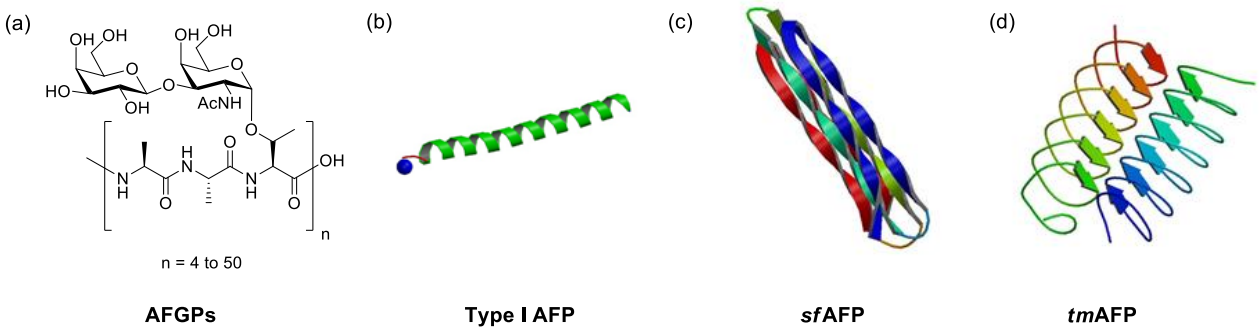


Figure 1-1: Different types of biological antifreeze agents. (a), (b) Both Type I AFPs and AGFPs are found in marine fishes. (c), (d) *sf*AFP and *tm*AFP are found in insects.[2,8]

This immense structural diversity of biological antifreeze agents posed significant challenges in developing a common, one-size-fits-all model for both the antifreeze mechanism and the structure–activity relationships. Nevertheless, some proposals have been made, which will be presented in the following subsections. Before venturing into any further discussion, it is important to understand that the term antifreeze activity is defined as an amalgamation of two main properties: Thermal Hysteresis (TH) and ice-recrystallization inhibition (IRI).

1.2.1 Thermal Hysteresis (TH)

TH is the ability of a compound to effect freezing point depression below the equilibrium melting point of water, generating a temperature difference that is known as the TH gap. The magnitude of the TH gap is a function of both the structure of the AF(G)P and its concentration at the time of measurement.[1,9] TH is widely used to identify AF(G)Ps and quantify their magnitude of antifreeze activity.[1,7,8] Solutions devoid of AF(G)Ps will freeze at the equilibrium melting/freezing points, with the ice crystals appearing as flat discs that gradually grow in size as the temperature declines. However, in the presence of an AF(G)P, ice crystals suspended within the TH gap will not experience any observable change in their sizes, giving rise to microcrystalline ice particles suspended in bulk water. These ice particles are also morphologically different than the flattened ice discs, due to the binding of AF(G)Ps to ice surfaces. This observation is termed dynamic ice shaping and it is a property in all TH-producing antifreeze compounds.[2,9]

The general accepted mechanism of action by AF(G)Ps is centralised on the concept of irreversible binding of these molecules to ice crystals. First proposed by Raymond and DeVries in 1977 as the adsorption–inhibition hypothesis,[10,11] AF(G)P molecules bind to ice surfaces, where their presence confines future ice growth into the gaps between them, forcing the ice to take on a curved form of growth (Figure 1-2). Because the addition of water molecules to a curved surface is thermodynamically unfavourable, this inhibits ice growth and leads to freezing point depression. As AF(G)Ps only disrupt ice growth, but not the melting point, this results in a TH gap.[12]

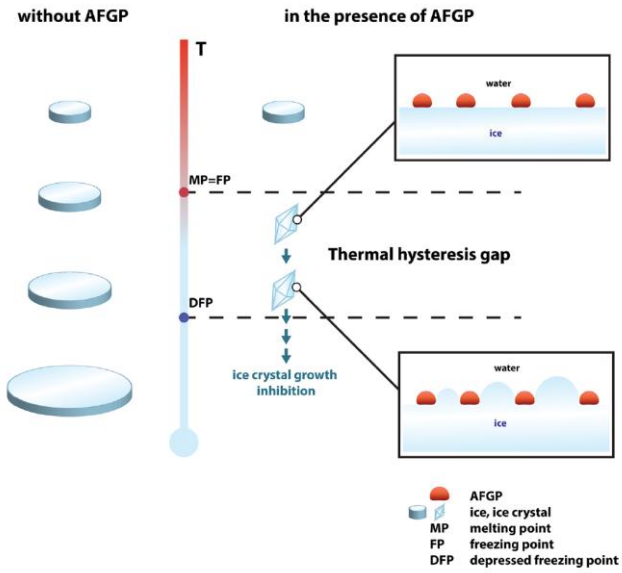


Figure 1-2: Diagram illustrating thermal hysteresis, with the red dots depicting the antifreeze substance. (Reproduced with permission from Urbańczyk, M.; Góra, J.; Latajka, R.; Sewald, N., *Amino Acids* **2017**, *49*, 209–222.)

The widely accepted method of testing TH activity is nanoliter osmometry.[9,13,14] In this process, a solution containing a known concentration of the antifreeze compound is quickly frozen to typically –40 °C, and then allowed to melt to the point where only a single ice crystal is obtained. With the melting point determined, this crystal is then cooled at a controlled rate until a sudden burst of growth is observed, marking the non-equilibrium freezing point. The disparity between the melting point and the non-equilibrium freezing point is the TH gap.

1.2.2 Ice Recrystallisation Inhibition (IRI)

Ice recrystallization is a thermodynamically-driven process that favours the formation of larger crystals over the smaller ones, and often occurs during slow thawing of an already frozen biological sample.[1,9,15] Because large ice crystals can inflict lethal damage to tissues by puncturing cellular membranes, significant efforts have been channelled into finding ways to discourage their formation.[16,17] Among these, the ability of AF(G)Ps to exhibit IRI properties has

gathered significant interest from both academia and industry.[2,9,18] Unlike TH, this property does not involve AF(G)P-mediated suppression of the freezing temperature within the organisms. As shown in Figure 1-3A, ice crystals in a completely frozen sample that is thawing/cooling tend to merge into larger ones in the absence of an antifreeze inhibitor. In contrast, introduction of an AF(G)P into the same sample prior to freezing leads to suppression of recrystallization, as evidenced by significantly smaller ice crystals (Fig. 1-3B). Because ice recrystallization is the major cause of cryodamage in frozen organs, there is significant interest in the use of AF(G)Ps with significant IRI activity as cryoprotectants.[2]

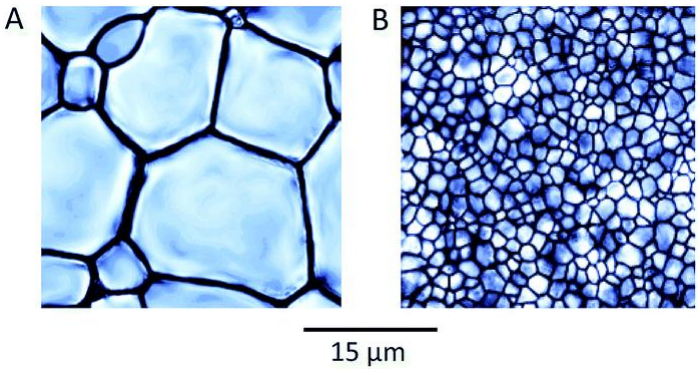


Figure 1-3: Ice Recrystallisation Inhibition via splat assay. A) Frozen sample with no AFP, B) Frozen sample with an AFP. (Reproduced with permission from Balcerzak, A. K.; Capicciotti, C. J.; Briard, J. G.; Ben, R. N. *RSC Advances* **2014**, *4*, 42682–42696)

One of the most common ways to measure the IRI activity of an AF(G)P is the 'splat' assay.[9,18-21] In this method, a thin wafer of polycrystalline ice is produced via flash-freezing of a droplet containing a buffered solution of the AF(G)P. This wafer is subsequently warmed to higher sub-zero temperatures to allow recrystallization. Growth of the ice crystals is monitored over time, by measuring either the average area or length of each crystal. Comparison of the relative mean crystal sizes between the experimental controls and the subject will determine their IRI activity.[20]

1.2.3 Structure–activity relationships of AF(G)Ps

Over four decades have passed since the first discovery of a biological antifreeze, yet the nature of how AF(G)Ps interact with the ice surfaces remains highly debatable. While most advocate irreversible binding of AF(G)Ps on the basis of the adsorption–inhibition mechanism, [10,22,23] any correlation linking AF(G)P structures to both irreversible ice binding and antifreeze activity, are difficult to generalize given the vast structural differences among AF(G)Ps.[2] Nevertheless, certain general concepts have emerged from empirical evidence. First, both hydrogen bonding[24] and hydrophobic[2,25,26] interactions are critical for irreversible binding to ice surfaces. Second, precise lattice matching between hydroxyl groups in the ice and the binding site of AFPs was implicated in irreversible binding.[27-30] Third, larger ice-binding sites can improve binding.[1] This is supported by the stronger antifreeze activity observed in larger AF(G)Ps relative to the smaller variants.[2,31,32] Fourth, facial amphiphilicity in AF(G)Ps has also been implicated in leading to both TH and IRI activity.[1] Segregation of hydrophilic and hydrophobic amino acid residues on opposite surfaces of the protein was demonstrated to be beneficial to antifreeze activity, by allowing the hydrophobic surface in AFPs to engage in ice binding while the hydrophilic surfaces inhibit ice growth over the protein by disrupting the neatly-ordered water molecules within the quasi-liquid layer.[33]

1.3 Antifreeze Glycolipids (AFGLs)

Prior to the last decade, it was believed by many that a protein is necessary for a molecule to possess antifreeze activity.[2] However, in 2009, Duman and co-workers reported the isolation of a novel antifreeze glycolipid from the freeze tolerant insect *Upis ceramboides*.[34] This compound was demonstrated to produce TH activity equivalent to some of the most potent

AF(G)Ps and this glycolipid is the first example of a biological antifreeze substance that does not rely on a protein or peptide for antifreeze activity. Subsequent structural elucidation by the combined techniques of NMR spectroscopy and MALDI-TOF mass spectrometry, as well as GC/MS analyses, led to the proposal of a [→4)-β-D-Xyl*p*-(1→4)-β-D-Man*p*-(1→] as the repeating unit of the glycan portion accompanied by a hitherto unidentified lipid component (Figure 1-4).

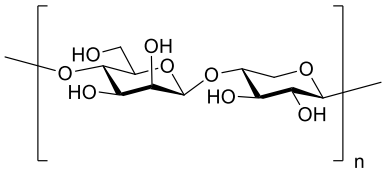


Figure 1-4: The disaccharide core of the glycan portion in a xylomannan-based antifreeze glycolipid

Since then, similar AFGLs bearing the xylomannan core were also found in other freeze-tolerant organisms, such as frogs (*Rana lessonae*), craneflies (*Tipula trivittata*), stoneflies (*Nemoura arctica*) and even the plant, bittersweet nightshades (*Solanum dulcamara*).[35] The strong sequence homology in the glycan portion of all these xylomannan-based AFGLs isolated thus far is an indication that this conserved disaccharide core may serve as the ice-binding motif essential for TH activity. IRI activity has also been reported for xylomannan-based AFGLs isolated from *R. lessonae* and *N. arctica*, pointing to an additional role for the AFGLs, which is still poorly understood.

Despite assurance in the β-(1→4)-glycosidic linkages within the xylomannan core via chemical synthesis, details on the average molecular weight of the antifreeze glycolipid and the identity of the lipid component have remained elusive. Given the large uncertainty in the average molecular weight estimation of this antifreeze glycolipid from a minimal 1kDa (defined by

MALDI) to a maximum of 30 kDa (by centrifugal filtration), no precise information has been reported on the number of disaccharide units essential to reproduce the same level of antifreeze activity as reported by Duman and coworkers.[34] As for the lipid component, its presence in the natural extracts suggested its roles as either a membrane anchor and/or modulation of antifreeze activity. The association of xylomannan AFGLs with cellular membranes implicated two possible roles: 1) controlling ice growth at the exterior cell surface as a means to prevent extracellular ice from extending into the cell interior[36-39], and 2) stabilising the membranes to maintain optimal fluidity at low temperatures, which is critical for cells to survive under these conditions.[7,35,40]

At this point, any mechanistic explanation to account for the antifreeze activity in xylomannan AFGLs remains purely conjecture. Any experiment designed to investigate these intriguing problems will require access to pure and structurally well-defined glycolipids in analytically useful quantities.[41,42] Because naturally-occurring AFGLs are often isolated in small and microheterogenous mixtures, the most pragmatic approach to obtain these compounds with the desired purity and quantity is through total chemical synthesis.[42]

1.4 Oligosaccharide assembly via chemical *O*-glycosylation

In theory, total chemical synthesis of oligosaccharides is straightforward given that monosaccharides are available from nature stereochemically well-defined and only a single bond (a glycosidic bond) has to be constructed during a chemical glycosylation.[41] However, this conceptual simplicity masks the difficulties in predicting outcomes of *O*-glycosylations, not to mention the technical challenges in protecting group manipulations and deprotection steps. Indeed, even after decades of efforts channelled into the development of new synthetic methods and strategies, to date no universal solution exists for the construction of some of the most

common glycosidic linkages found in oligosaccharides (Fig. 1-5).[43] This is because each chemical glycosylation is affected by several factors such as the steric and electronic influence of the protecting groups, solvent, temperature and activators employed, as well as the structures of the glycoside in question. Nevertheless, some reliable methods have been created, which, in combination with the development of novel convergent approaches and donor activation strategies, have overcome some of these fundamental issues, thus advancing the field of oligosaccharide synthesis.

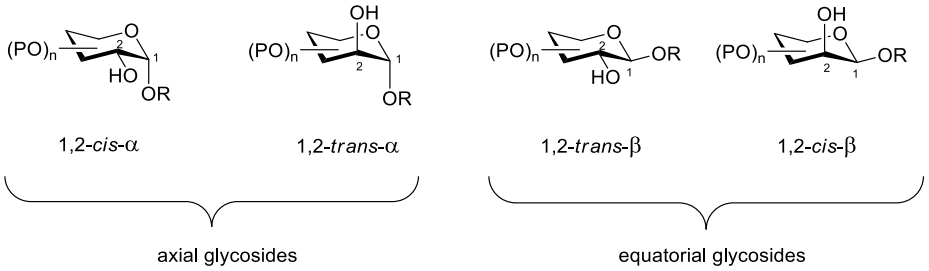


Figure 1-5: Common glycosidic linkages observed in glycosides

The chemical synthesis of each linkage featured above is widely covered in the literature. In general, equatorial glycosides in pyranosides are less thermodynamically stable in comparison to the axial glycosides.[44] This is attributed to the anomeric effect, a stereoelectronic effect that was first observed in hexopyranosides by Edward[45] and subsequently by Lemieux and Chu.[46] Nevertheless, some methods have been developed to address the problems inherent to the construction of these equatorial linkages. With the target xylomannan core of AFGLs in sight, any further discussion is solely focused on methodologies for making 1,2-*trans*- and 1,2-*cis*-equatorial glycosides.

1.4.1 Stereoselective synthesis of 1,2-*trans*-equatorial glycosides

One of the most reliable strategies employed in the synthesis of 1,2-*trans*-equatorial glycosides is the use of neighbouring group participation (Figure 1-6).[47] Activation of glycosyl donor **1.1** by a promoter, typically led to the departure of X and consequent formation of oxacarbenium ion **1.2**. A participating protecting group, typically an acyloxy group installed at the C-2 position of the glycosyl donor **1.1**, subsequently engages in an intramolecular attack on the C-1 of **1.2** to give an dioxolonium ion **1.3**, which then promotes *trans*-glycosylation by shielding one face of the donor from nucleophilic attack to give the desired equatorial glycoside **1.4**.

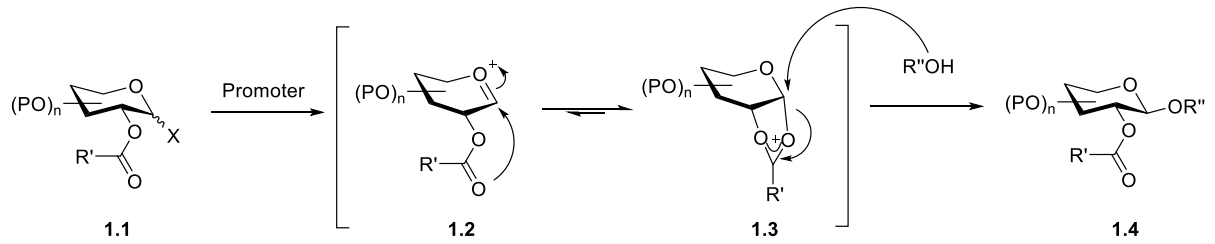


Figure 1-6: Mechanistic proposal of 1,2-*trans*-glycosylation via neighbouring group participation

Alternatively, 1,2-*trans*-equatorial glycosidic linkages can also be obtained without neighbouring group participation, by using nitrile-based solvents such as acetonitrile or propionitrile (Figure 1-7).[48] In general, these solvents interact with the oxacarbenium ions (obtained via activation of donor **1.5**) to generate axial nitrilium ions **1.6**,[49] which then engage in an S_N2-type displacement by the incoming glycosyl acceptor to yield the desired equatorial glycosides **1.7** in modest to high selectivity.

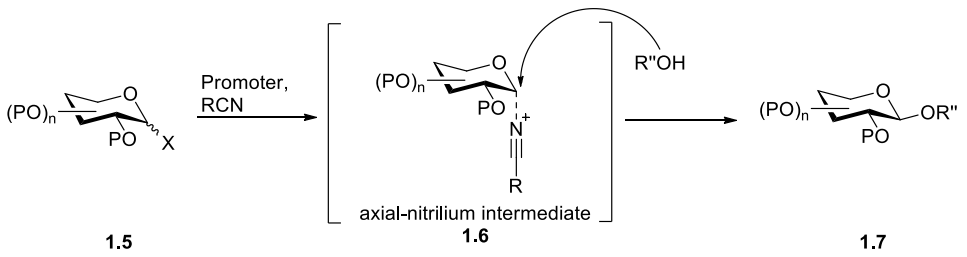


Figure 1-7: Mechanistic proposal of 1,2-*trans*-equatorial glycosylation via solvent participation

The above strategies have some disadvantages. The electron-withdrawing nature of acyl groups attenuates donor reactivity, thus leading to lower yields. In addition, orthoesters are often observed as by-products with the use of less reactive acceptors.[50] Anomeric mixtures are often observed in the case of nitrile-based solvent assistance. Recent methods have been developed to address such issues, such as the use of more electron-rich *O*-picolyl-type protecting groups,[51] as well as the 2-*O*-cyanobenzyl ethers[52] to effect highly stereoselective 1,2-*trans*-equatorial glycosylation. However, their broad applicability remains to be seen.

1.4.2 Stereoselective synthesis of 1,2-*cis*-equatorial linkages: the β-mannoside problem

Among the four linkages listed in Figure 1-5, 1,2-*cis*-equatorial (β-mannosidic) linkages are considered the most difficult to synthesize. This is due to the three factors: 1) a lack of stabilisation from the *endo*-anomeric effect, which typically favours the axial anomer, 2) steric repulsion imposed by the axial C-2 substituent, which generally discourages acceptors from approaching via the β-cis to this group, and 3) the 1,2-*cis* relative stereochemistry, which rules out neighbouring group participation.[44,47] Because these linkages are present in many biologically-relevant compounds such as *N*-linked glycoproteins[53] and structural polysaccharides,[54] new ways to construct such linkages have been developed. However, to date

there is still no universal method applicable to all β-mannosidic linkages.[55,56] In recognition of this, key approaches will be discussed in the following subsections.

1.4.2.1 The direct insoluble promoter strategy

One of the earliest approaches developed to address this β-mannosidic-linkage challenge is the use of an insoluble halophilic promoter to activate α-mannosyl halides in the presence of an acceptor. This adaptation of the traditional Koenigs–Knorr conditions is based on the ability of the promoter to bind to the α-face of the donor via the halide, thus hindering the approach of the acceptor to the same face.[57] This leaves the β-face as the sole pathway for any incoming nucleophile, leading to S_N2-type glycosylation. As an example, this approach was used by Ley and workers in their synthesis of β-mannoside **1.9** from α-mannosyl bromide **1.8**, using silver-silicate as the insoluble promoter (Figure 1-8).[58]

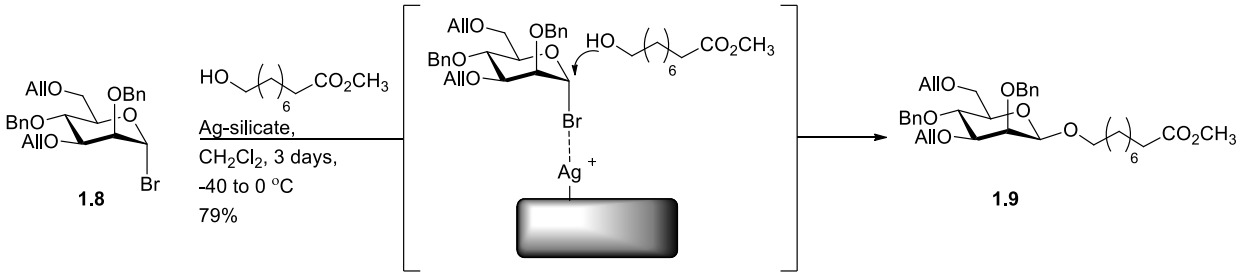


Figure 1-8: Synthesis of β-mannoside via the direct insoluble promoter strategy

Though this method can provide high β-*manno*-selectivities and good yields, its key disadvantages lie in the requirement for long reaction times, and its restricted use to only highly reactive acceptors and armed halide donors. Less reactive acceptors tend to generate anomeric mixtures and halide donors often display poor shelf stability. Consequently, many chemists have developed other approaches to solve this problem.

1.4.2.2 C-2 inversion strategy

To skirt the issue of anomeric control in direct β-mannosylation, an alternative strategy was developed that involves the straightforward construction of 1,2-*trans*-β-glucoside **1.10** through neighbouring group participation, followed by deacylation and subsequent inversion of the C-2 position in **1.12** to obtain the desired β-mannosidic-linkage. In epimerisation, two possible routes have been reported: 1) S_N2 displacement, and 2) Oxidation–reduction. The two methods are illustrated in Figure 1-9.

To effect successful S_N2 displacements at the C-2 position, a good leaving group has to be installed in β-glucoside **1.12**. Due to difficulties associated with S_N2 displacements at secondary carbons in pyranose rings,[55] triflates are most frequently employed for this purpose (as exemplified by **1.14**) and used in conjunction with either tetrabutylammonium[59-61] or cesium salts[62] of the desired nucleophiles in toluene at reflux or ultrasound promotion. This then delivers the β-mannoside **1.16**, with acyl ester at C-2. The key advantage of this method lies in its stereospecific C-2 inversion. However, potential side reactions such as ring contractions and eliminations can occur with this method, thus limiting its popularity in complex oligosaccharide synthesis.[63]

The oxidation–reduction approach is another well-established method for C-2 inversion. Various methods have been reported with regards to C-2 oxidation in β-glucoside **1.12**, including the Albright–Goldman and Swern oxidations, with subsequent reductions of uloside **1.13** accomplished using metal hydrides such as sodium or lithium borohydrides.[64,65] Bulkier reducing agents like L-Selectride[66] can be used for more challenging cases. Despite being stereoselective, only moderate β-*manno* selectivities are sometimes achieved with this approach.

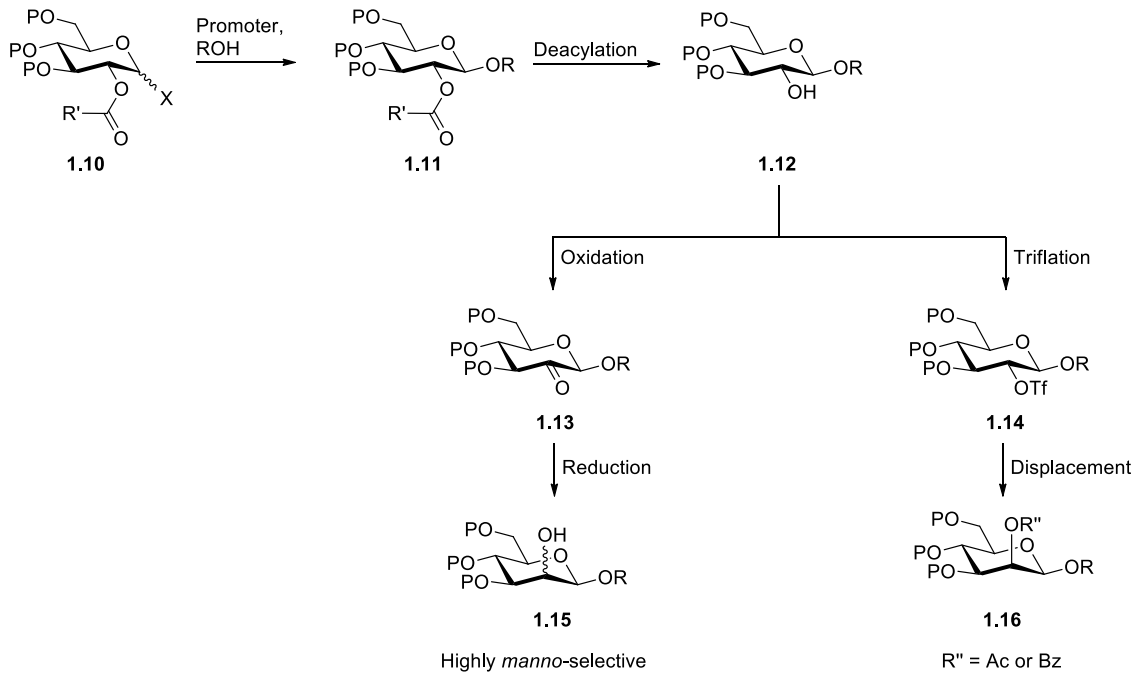


Figure 1-9: Synthesis of β-mannosides via C-2 inversion approaches

This oxidation–reduction approach has also been used in the synthesis of oligosaccharides, such as β-(1→2)-mannans reported by Sinäy and co-workers in 1996 (Figure 1-10).[67] In their work, mannoside **1.17** was glycosylated to the thioglucoside **1.18** under NIS–TfOH conditions to give disaccharide **1.19**, which was then converted to the β-mannoside **1.20** via a three-step protocol involving Zemplen deacylation, Swern oxidation and stereoselective reduction with $LiBEt_3H$. From this point, two further iterations of this glycosylation–inversion strategy are required to attain the tetrasaccharide **1.21**.

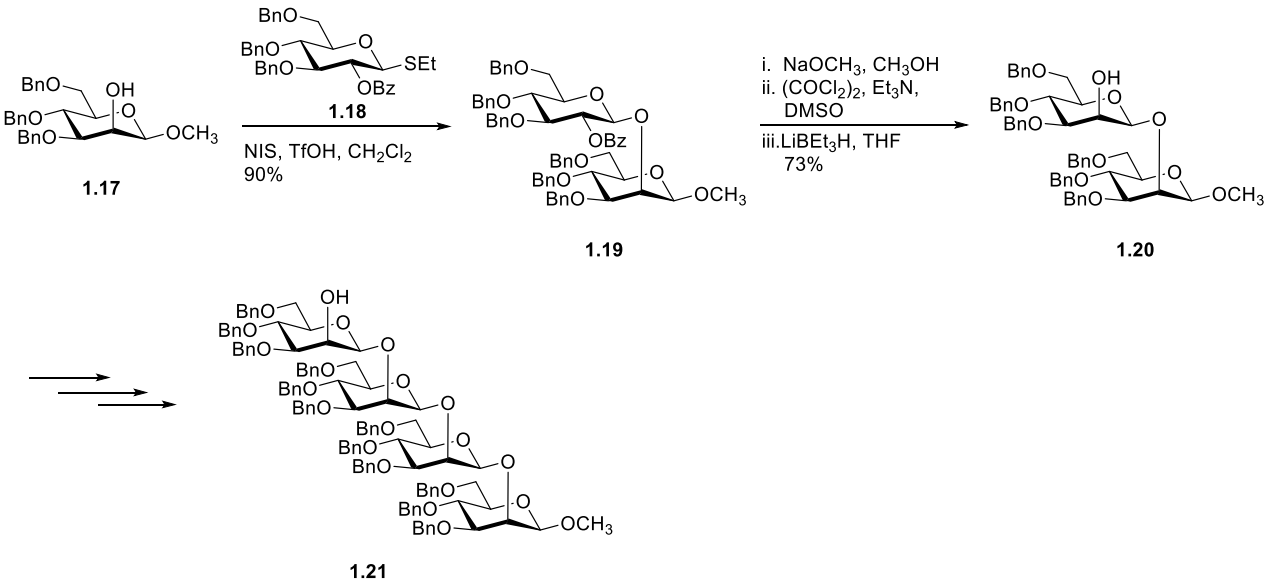


Figure 1-10: Synthesis of β-(1→2)-mannans via the oxidation–reduction approach

Despite the reliability of this approach for making β-mannosides, the numerous manipulations required to attain each individual 1,2-*cis*-equatorial linkage resulted in lower overall synthetic efficiency. Consequently, research into new ways of β-mannosylation remains a highly active field.

1.4.2.3 Ulosyl bromide approach

An interesting extension of the above C-2 inversion approach was developed in the group of Frieder W. Lichtenthaler (Figure 1-11).[68] Known as the ulosyl bromide approach, it combines the concepts of both Koenigs–Knorr glycosylations and stereoselective C-2 inversion via a highly versatile donor for indirect β-mannosylation. Placing the ketone functionality at the C-2 position of the ulosyl bromide, not only resolves the issue of steric challenge against β-attack, but also the strong electron-withdrawing characteristics of this functional group enhances the β-selectivity in the glycosylation by simultaneously accelerating the S_N2-like displacement of the bromide[69,70]

and suppressing selectivity-diminishing oxocarbenium ion formation. Moreover, these ulosyl bromides also bear the advantage of improved synthetic efficiency by eliminating the steps of deprotection–oxidation required in the classical approaches. This concept is encapsulated in the synthesis of a trisaccharide component in the glycosphingolipids from *Hyriopsis schlegelii* by Lichtenthaler *et al.*[71] Koenigs–Knorr glycosylation between ulosyl bromide **1.22** and acceptor **1.23**, followed by reduction with sodium borohydride afforded **1.24** with exclusive β-*manno* selectivity and 81% yield over two steps. The final trisaccharide **1.26** was subsequently obtained in 71% yield after silver triflate-mediated glycosylation of **1.24** with xylosyl bromide **1.25.**

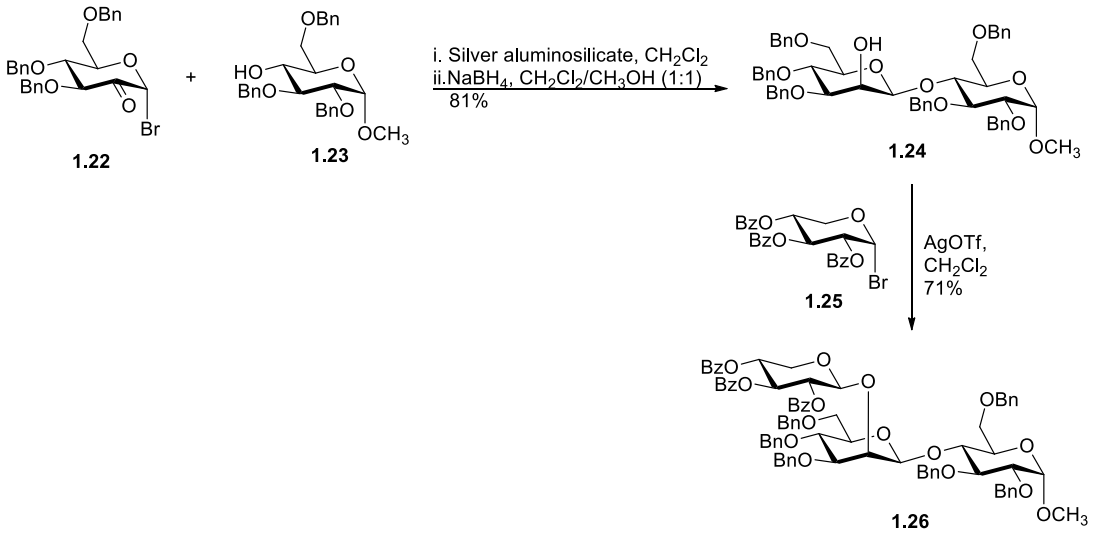


Figure 1-11: Synthesis of the trisaccharide portion of glycosphingolipids from *H. schlegelii* via the ulosyl bromide approach

Despite the apparent operational simplicity of this approach, it found limited application outside of the Lichtenthaler group due to the inherently unstable nature of the ulosyl bromides and the requirement of highly reactive acceptors for successful glycosylation.

1.4.2.4 Intramolecular Aglycone Delivery (IAD) approach

The IAD approach relies on the ability of a covalent tether (Y) on the axial C-2 position of a mannosyl donor (**1.27** or **1.28**) to direct incoming nucleophiles to attack at the β-face of the donor (Figure 1-12).[72] In this approach, the C-2 substituent on the donor is selectively converted in the presence of the acceptor ROH to forge a new mixed acetal species **1.29** such that the acceptor is situated directly above the anomeric centre of the donor. This would, in principle, lead to a highly stereocontrolled β-mannosylation to give **1.32** upon activation of the donor, assuming that the covalent tether can stabilise the positive charge generated upon departure of the acceptor and the ability of the acceptor to trap the developing oxacarbenium ion **1.30** in an S_N2-like fashion.

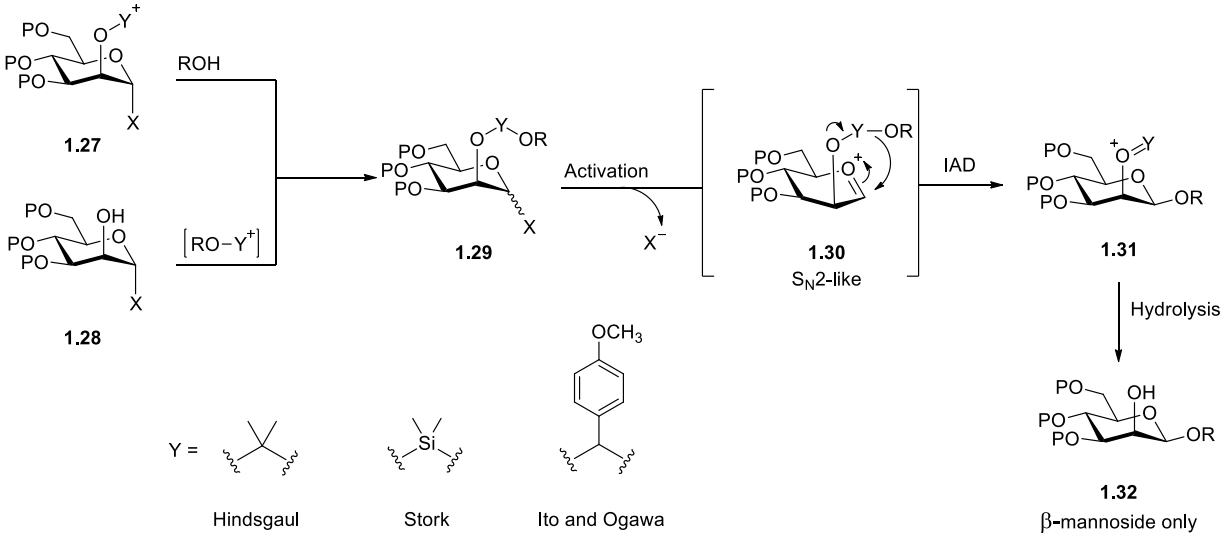


Figure 1-12: General mechanism of an IAD approach and different tethers employed

Examples of some of the tethering approaches developed over the years are shown in the above, from the pioneering isopropylidene (Hindsgaul[73]) and silylene-based tethers (Stork[74,75]) to the *p*-methoxybenzylidenes (Ito and Ogawa[76]) (Figure 1-12). *p*-Methoxybenzylidene (PMB)

ether-mediated IAD, in particular, has found broad application in the synthesis of various *N*-linked glycoproteins and other oligosaccharides containing β-mannosidic linkages. A solid-phase version of IAD based on PMB tethering was also developed.[77]

Despite these advancements, a fundamental drawback in this approach is the requirement for the formation of mixed acetals, which can be difficult due to their unstable nature. Recent efforts to explore other tether alternatives led to the development of hydrogen-bond mediated aglycone delivery (HAD) by Demchenko and co-workers[51,78] (Figure 1-13), and boron-mediated IAD with 1,2-anhydromannopyranose by Takahashi and Toshima[79,80] (Figure 1-14). Generally, HAD is facilitated by *O*-picoloyl group at either C-3 or C-6 of mannosyl donors **1.33** and **1.34**, which directs equatorial attack of the acceptor **1.35** by tethering it above the putative mannosyl carbocation via hydrogen bonding interaction. The mannosides **1.36** and **1.37** are subsequently obtained in high yields with good β-selectivities.

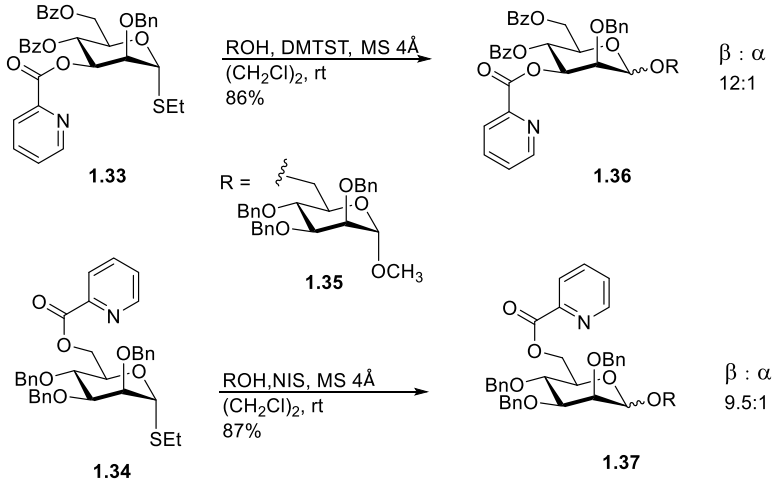


Figure 1-13: Stereoselective synthesis of β-mannosides via the HAD approach

Boron-mediated IAD, on the other hand, involves sub-stoichiometric diarylborinic acid **1.38** to activate the glycosyl acceptor **1.35**, following which the resultant complex will then react

with the donor **1.39** to give the desired β-mannoside **1.40** in quantitative yields with complete stereoselectivity.

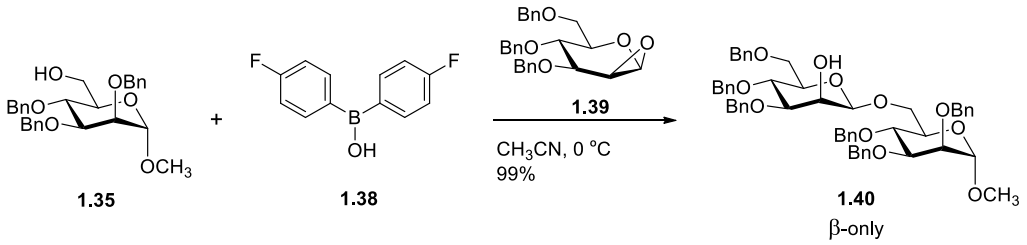


Figure 1-14: Boron-mediated IAD approach catalyzed by diarylborinic acid **1.38**

However in both cases, their widespread usage is restricted due to the requirement of highly reactive acceptors, as both methods reported decline in the β-*manno* selectivity with the use of less reactive alcohols.

1.4.2.5 Conformational restriction of donors via 4,6-*O*-tethering

In 1997, Crich *et al.*[81] disclosed a direct β-mannosylation approach, which relied on a 4,6-*O*-benzylidene acetal on the mannosyl donor to achieve high stereocontrol in excellent yields. Further mechanistic investigations revealed that the reaction proceeded initially through activation of donor **1.41** to give a stable covalent glycosyl triflate **1.42**, which then collapsed into a transient contact ion-pair (CIP) **1.43** with the triflate shielding the α-face (Figure 1-15).[82,83] At this point, introduction of the acceptor ROH into the reaction results in S_N2-like displacement of the triflate in **1.43**, leading to the formation of β-mannoside **1.44** with complete stereoselectivity. Key to the formation of this CIP intermediate is the 4,6-*O*-benzylidene acetal, which restricted further transition into the selectivity-diminishing oxacarbenium ions through a combination of torsional strain[83] and electron-withdrawing effects.[84] This approach has found broad application in the direct synthesis of β-mannans, traditionally inconvenient through indirect methods.

Automated solid-phase synthesis based on this technology has also been developed.[85] However, some problems still persisted; for instance, the reaction displayed poor selectivities with unreactive acceptors, such as the case with C4-OH of both glucose and glucosamine acceptors,[86] and tolerates neither bulky substituents at C-3 of the donor, nor use of activators other than those described in Crich's approach. The requirement for the 4,6-*O*-benzylidene acetal is also a limiting factor.

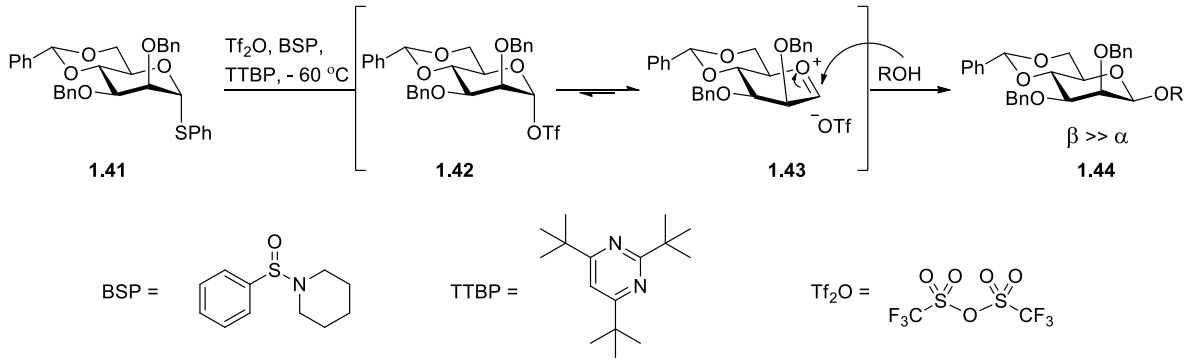


Figure 1-15: Crich's direct β-mannosylation approach

Current limitations inherent to the Crich's method led others to develop different variants. Acknowledging the critical role of 4,6-*O*-tether in stereocontrol, Bols and co-workers[86] used the di-*tert*-butylsilylene (DTBS) group in place of the benzylidene acetal to effect β-mannosylation. Their approach is advantageous given that no donor preactivation was necessary and employs standard activators: NIS and TfOH. Unfortunately, β-stereoselectivity is limited, once again, to highly reactive acceptors. Moreover, the DTBS group is much more costly to install relative to the benzylidene acetal.

Alternatively, Yu and co-workers[87] demonstrated that highly stereoselective β-mannosylation can also be achieved with 4,6-*O*-benzylidene tethered α-mannosyl *o*-

hexynylbenzoate donors **1.45** under Au(I)-catalysis instead of the more common triflate-based catalysis (Figure 1-16). Noteworthy of Yu's approach is the high tolerance towards a broad range of substrates, which included unreactive glycosyl acceptors and even bulky substituents at C-3 of the mannosyl donors. Unfortunately, this method employed expensive Au(I) salts and ligands and a generally complicated operation protocol. Moreover, to the best of my knowledge, this method has yet to be applied to the synthesis of β-mannans, which is typically seen as the ultimate testing ground for any β-mannosylation strategy.[88]

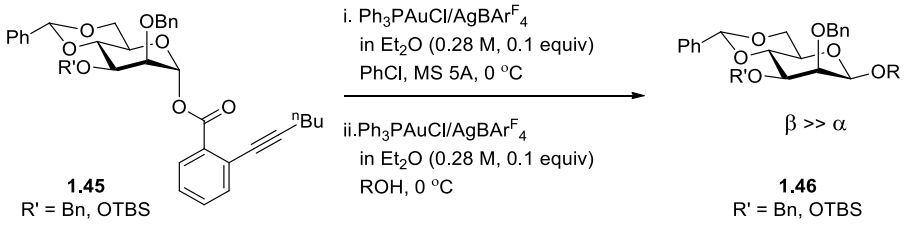
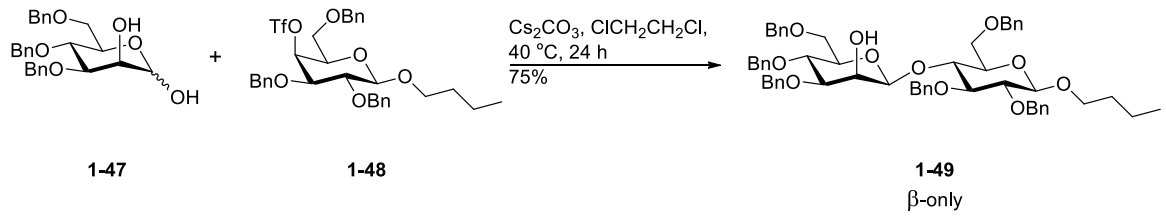


Figure 1-16: Yu's direct β-mannosylation approach using Au(I) catalysis

1.4.2.6 Alternative approaches

Other approaches have also been developed, such as the stereoselective quenching of α-anomeric radicals in α-mannosides and the anomeric *O*-alkylation approach. The former approach was demonstrated to work well only on α-mannosides with primary aglycones,[89] thus limiting its synthetic utility. Though the latter approach was initially limited to primary glycosyl triflates,[90] Zhu and co-workers[91,92] broadened its utility by using cesium salts in chelation control together with glycosyl triflates as the alkylating agent (Figure 1-17). However, none of these methods have been featured in the synthesis of β-mannans, nor widely used in synthesis of β-mannosides.



1-47 **1-48** **1-49**
β-only

Figure 1-17: Stereoselective synthesis of β-mannoside **1-49** via Cs-mediated anomeric *O*-alkylation

1.5 Overview of thesis research

As discussed in the earlier sections, numerous strategies have emerged to address the challenge of constructing β-mannosidic linkages. Such developments have allowed chemists to access complex oligosaccharides bearing these linkages and even β-mannans conveniently. These compounds not only serve as invaluable tools to elucidate the intricate biological functions of these glycans, but also bear the potential as templates for bio-inspired materials.

In the past decade, interest in developing synthetic materials to control ice formation led to the idea of using biological antifreeze compounds as templates for design.[8,9,93] Despite their well-documented antifreeze activity, use of AF(G)Ps and their mimetics have raised some concerns over potential immunogenicity and toxicity.[9,27] AFGLs on the other hand, are a potentially attractive template as glycans are, generally speaking, less immunogenic and toxic compared to proteins. Additional support for AFGL-based templates for the development of antifreeze agents comes from recent discoveries of two different antifreeze glycans[94,95] isolated from other species, as well as reports of carbohydrate-based small molecule ice recrystallization inhibitors developed by Ben and coworkers.[18] To the best of my knowledge, antifreeze activity of AFGLs has thus far only been evaluated on the xylomannan AFGLs isolated from nature. I regarded shorter and more homogenous xylomannan AFGL derivatives as interesting targets for mechanistic studies and development of novel antifreeze compounds.

Despite their apparent structural simplicity relative to other AF(G)Ps, little progress has been made in understanding how xylomannan AFGLs behave as antifreeze compounds. Moreover, the identity of the lipid component and its functional role in AFGLs remain unclear. This is in part due to technical difficulties inherent in glycolipid research in general, ranging from solubility issues to accessibility in terms of purity and quantity.[96] Unlike AFPs, which can be accessed via recombinant protein expression,[97] glycolipids can only be obtained reliably via synthesis.

I hypothesized that the antifreeze activity of xylomannan AFGLs is dependent on both the chain length of the glycan and the hydrophobicity of the lipid aglycone, with a prediction that longer glycan chains and increased hydrophobicity will afford higher antifreeze activity. Testing my hypothesis therefore requires access to a library of pure and structurally defined oligosaccharides that can mimic the native compounds, which are only accessible via chemical synthesis. This thesis is focused on the synthesis of these AFGL mimetics, with an emphasis on β-mannosylation in large glycan assembly.

Given the myriad of β-mannosylation approaches, a decision was made to settle for one that could deliver exclusive β-*manno*-selectivity reliably without the need for complicated experimental conditions or expensive reagents. To this end, I envisaged the use of indirect approaches. Consequently, in Chapter 2 the development of a ulosyl bromide coupling approach for β-mannosylation in these AFGL mimetics will be described. Limited success with this approach subsequently led to the work described in Chapter 3, in which a convergent approach via simultaneous multiple C-2 inversion will be presented. These compounds will be sent to my collaborator for evaluation of their TH and IRI activities via nanolitre osmometry and splat assay

studies respectively, the results of which may provide mechanistic insights into their antifreeze properties and facilitate development of novel antifreeze compounds for cryopreservation of cells and tissues.[9,93,98]

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Chapter 2

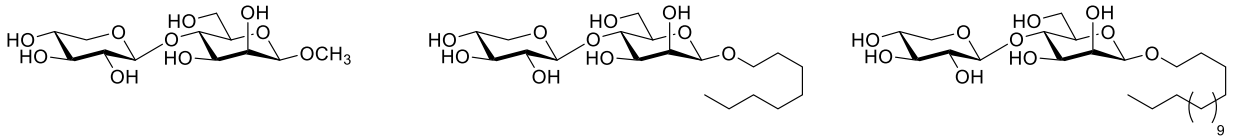
Synthetic efforts towards the synthesis of xylomannan-based AFGL mimetics via the ulosyl bromide approach

2.1 Introduction

A primary adaptation by which Alaskan beetles evolve to survive in subzero environments is the endogenous production and accumulation of xylomannan-based antifreeze glycolipids in their bodies. These antifreeze glycolipids (AFGLs) have been demonstrated by Walters *et al.*[1] to display TH activity on par with some of the most potent antifreeze proteins. Their proposal of a [→4)-β-D-Xyl*p*-(1→4)-β-D-Man*p*-(1→] fragment of the glycan portion was verified independently by two groups,[2,3] on the basis of NMR studies conducted on short synthetic models of xylomannan-based methyl glycosides. However, other crucial details such as its effective molecular weight, the type of lipid association as well as its mode of antifreeze mechanism remain to be revealed. Furthermore, apart from a tetrasaccharide model, which displayed neither TH nor IRI activity,[3] no further antifreeze assessment was conducted on these synthetic compounds.

Due to my interest in developing novel antifreeze compounds based on these naturally-occurring xylomannan AFGLs, it is imperative to understand the effect of both the glycan chain length and type of lipid component on the antifreeze activity of these glycolipids. Testing this hypothesis will therefore require access to purified, chemically well-defined xylomannan glycolipids bearing diverse hydrophobic aglycones as lipid mimetics, all of which are unavailable from natural sources. Although previous syntheses of xylomannan oligosaccharides have been reported independently by Crich,[2] Ito[3] and Serianni,[4] I am interested in the development of a new synthetic strategy based on the construction of the challenging β-mannosidic linkages as the key glycosylation step in convergent oligosaccharide assembly. This differs from previous strategies where these linkages are introduced at an earlier stage in the synthesis, prior to convergent assembly.

In this chapter, I will describe previous synthetic approaches to xylomannan glycolipids, followed by use of the ulosyl bromide approach as an indirect means to construct β-mannosidic linkages, showcased by the successful synthesis of xylomannan-based AFGL mimetics **2.1–2.3** (Scheme 2-1). Attempts made to prepare tetrasaccharides via this approach will also be presented.



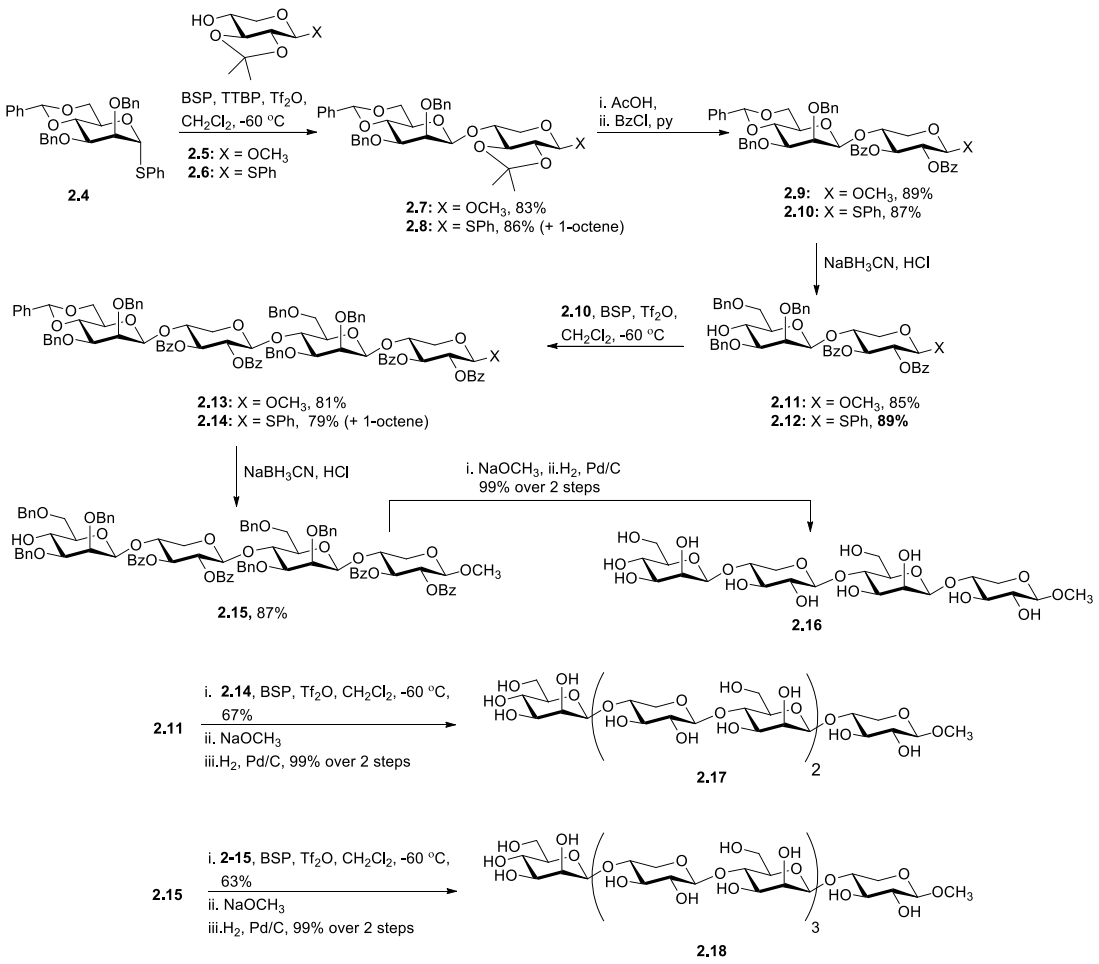
2.1 **2.2** **2.3**

Scheme 2-1: Structure of xylomannan glycolipids

2.2 Previous approaches to xylomannan antifreeze

Currently two groups have reported the synthesis of xylomannan oligosaccharides via convergent block assembly, both of which focused on the construction of β-mannosidic linkages at the disaccharide stage followed by β-xylosylation as the means to access larger oligosaccharides. Thus, in 2011, Crich *et al.*[2] harnessed his direct β-mannosylation approach (Scheme 2.2) to construct a β-D-Man*p*-(1 →4)-D-Xyl*p* disaccharide repeating donor. Subsequent β-xylosylation was used to gain access to larger oligosaccharides (tetrasaccharides to octasaccharides) via neighbouring group participation from the C-2 ester group on the xylose. This convergent strategy also employed chemoselective glycosylation at two instances. The first was between monosaccharides via preactivation of thioglycoside donor **2.4** followed by addition of thioglycoside acceptor **2.6**. The second was between disaccharides, on preactivation of thioglycoside donor **2.10** followed by introduction of acceptor **2.12**. The hexa- and octasaccharides were subsequently accessed through the use of tetrasaccharide donor **2.14** to glycoslyate acceptors **2.11** and **2.13**, respectively. Subsequent global deprotection was achieved

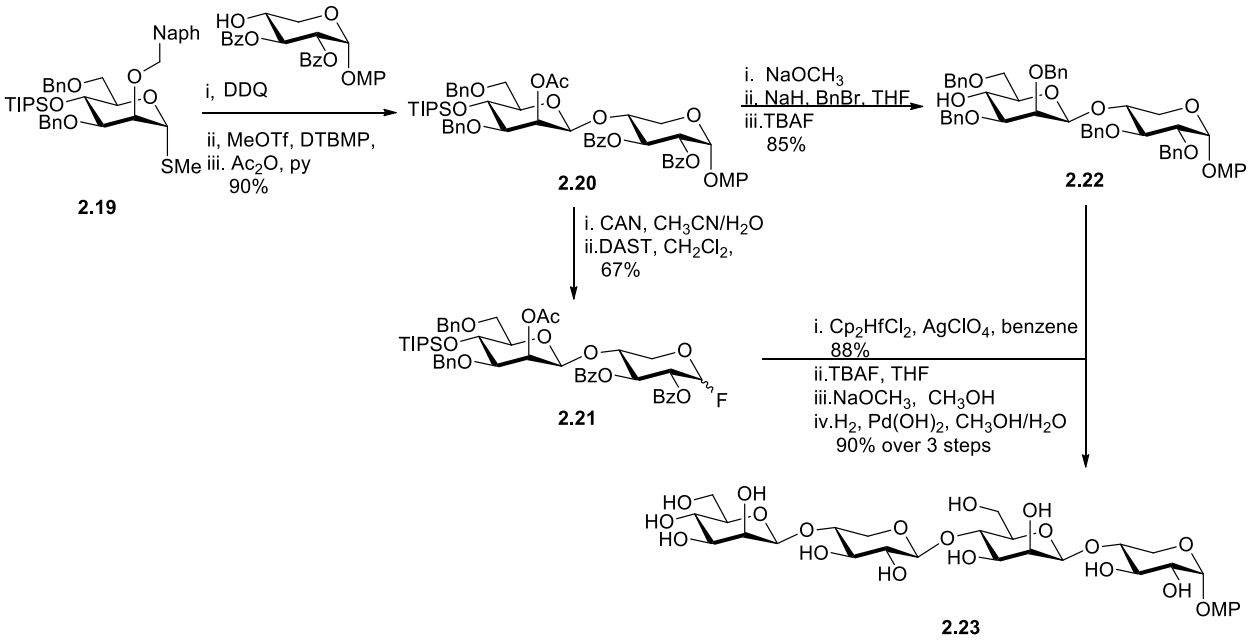
via an initial ester hydrolysis under Zemplen conditions followed by high-pressure catalytic hydrogenation in the presence of 10% palladium on charcoal. In this way, all the xylomannan tetra-, hexa- and octasaccharides could be accessed efficiently and with complete anomeric stereocontrol.



Scheme 2-2: Crich's convergent assembly of xylomannan tetra-, hexa- and octasaccharides

Ito's strategy of xylomannan synthesis (Scheme 2-3) closely resembled Crich's, with the strategic installation of the more difficult β-mannosidic linkage prior to β-xylosylation in convergent assembly.[3] The only difference was the use of the intramolecular aglycone delivery (IAD) approach for stereoselective β-mannosylation. In this approach, a naphthyl group installed

at the *O*-2 of mannose was used as a handle for the formation of a dimeric 2-naphthaldehyde bis(disaccharyl)-acetal via treatment with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ). Subsequent treatment of the mixed acetal with methyl triflate led to the desired β-mannoside. This disaccharide could then be converted into both a donor and an acceptor. The donor **2.21** was obtained via ceric ammonium nitrate (CAN)-mediated hydrolysis of the 4-methoxyphenyl glycoside followed by fluorination of the resultant lactol with diethylaminosulfur trifluoride (DAST). The acceptor **2.22** was synthesized via replacement of the acetate group followed by silyl deprotection using tetrabutylammonium fluoride (TBAF). Activation of donor **2.21** using Suzuki's Cp_2HfCl_2–$AgClO_4$ conditions[5,6] in the presence of the acceptor thus afforded the desired tetrasaccharide in high yield (88%). Subsequent silyl deprotection, ester hydrolysis and then catalytic hydrogenation with Pearlman's catalyst led to the fully deprotected xylomannan tetrasaccharide **2.23** in 90% yield over 3 steps.



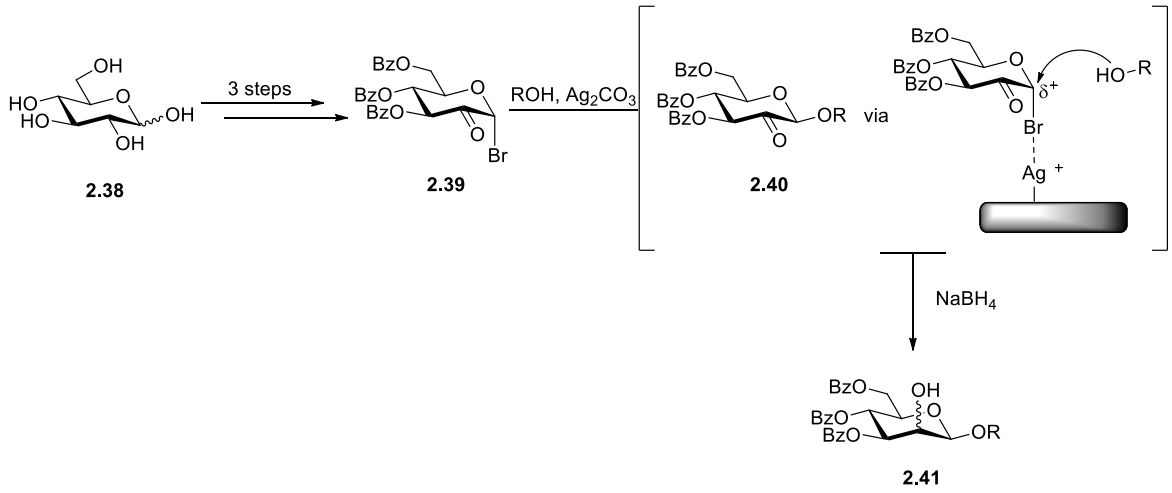
Scheme 2-3: Ito's synthesis of xylomannan tetrasaccharide

An alternative take on the chemical synthesis of xylomannan glycolipids was reported by Serianni and co-workers.[4] To elucidate the solution structure of these molecules via NMR spectroscopic studies, they prepared disaccharide and tetrasaccharide models of the xylomannan, both selectively labelled with ^{13}C (incorporated at the monosaccharide stage) at the anomeric centres. As shown in Scheme 2-4, synthesis of xylomannan disaccharide **2.28** was initiated through β-galactosylation of **2.24** with xylose acceptor **2.05**. Next, two simultaneous stereoinversions[7,8] at C-2 and C-4 of the β-Gal*p* residues in the disaccharide provided the desired **2.27**. Subsequent treatment of **2.27** with methanolic HCl and then NH_3/CH_3OH afforded methyl xylomannan disaccharide **2.28** in 73% yield. To reach the tetrasaccharide, both the donor and acceptor had to be prepared separately because only the internal residues had to be labelled with ^{13}C nuclei. Thus, acceptor **2.29** was prepared from **2.28** in just three steps, starting with a regioselective benzylidene protection of the Man*p* residue in **2.28**. Subsequent benzyl protection of the remaining hydroxyl groups and finally exposure to triethylsilane and boron trifluoride etherate effected reductive cleavage of the acetal in an overall yield of 18%. However, in the case of disaccharide donor **2.35**, the requirement of a ^{13}C-labelled xylose residue necessitated the reconstruction of the disaccharide. Consequently, β-galactosylation of ^{13}C-labelled xylose **2.30** with donor **2.24** led to the disaccharide **2.31**, which, after a series of protecting group manipulations and simultaneous inversions, yielded xylomannan **2.33**. This was then converted to the hemiacetal **2.34** via acid hydrolysis of the acetonide, followed by acetylation and removal of 4-methoxyphenyl group under oxidative conditions. After exposure to trichloroacetonitrile in the presence of DBU, the α-imidate donor **2.35** was obtained in 75% yield. Subsequent condensation of both **2.29** and **2.35** led to the tetrasaccharide **2.36** in 73% yield; finally, global deprotection produced xylomannan tetrasaccharide **2.37** in 63% yield.

Scheme 2-4: Serianni's synthesis of ^{13}C-labelled xylomannan oligosaccharides

To the best of my knowledge, no other groups have published the synthesis of xylomannan glycolipids. Though following the published strategies appeared to be an attractive option, the prerequisites for multiple benzyl protections for reactivity as well as high

stereocontrol may demand more rigorous deprotection methods through either high pressure hydrogenation[2,9] or Birch reduction.[10,11] The classic indirect β-mannosylation strategy of C-2 epimerisation of a β-glucoside, is highly reliable, but laborious due to the increase in number of synthetic manipulations and purification steps, which often results in overall decreased synthetic efficiency. Such problems will only worsen with an increase in the number of β-mannosidic linkages. On the other hand, the ulosyl bromide approach developed by Lichtenthaler[12] appeared to be an attractive option on the basis of less synthetic manipulations, higher donor reactivity and high β-*manno*-selectivity (Scheme 2-5). It was envisioned that the difficulty in constructing multiple β-mannosidic linkages in the xylomannan glycolipids could be addressed by this approach.

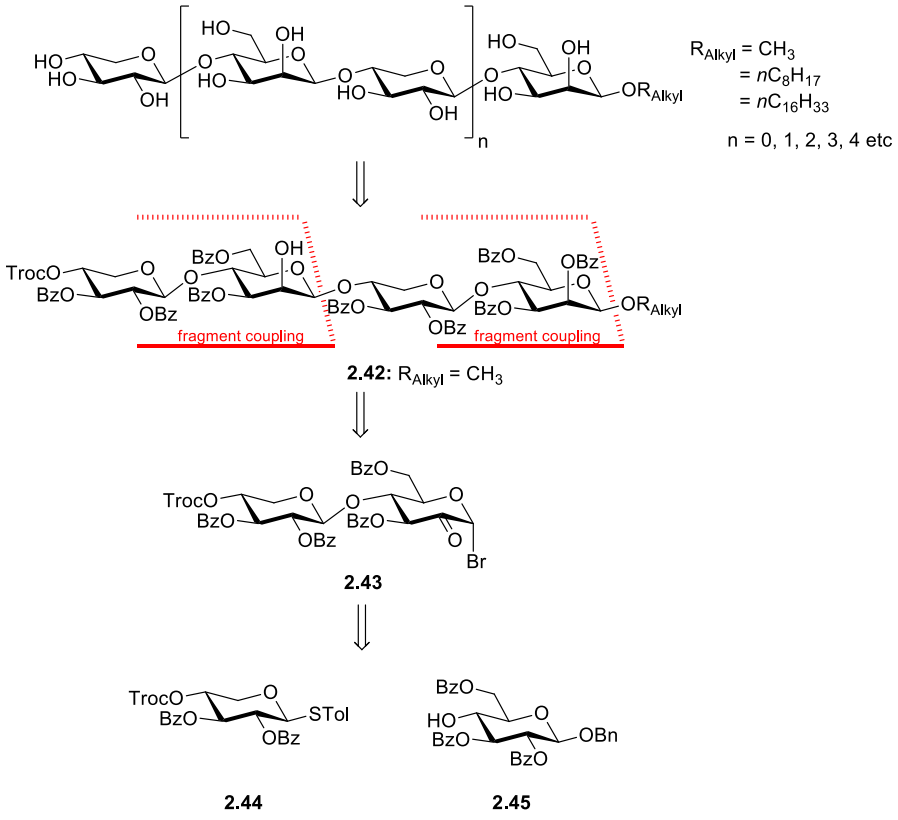


Scheme 2-5: Lichthenthaler's ulosyl bromide approach to β-mannosides

2.3 Retrosynthesis of AFGL mimetics via the ulosyl bromide approach

Taking into consideration that all these glycolipids share the same disaccharide core, a general convergent strategy to all the analogues based on a single disaccharide donor is desired. It was envisioned that all the xylomannan glycolipids could be derived from a single

disaccharide ulosyl bromide **2.43**, which, in turn, could be constructed from readily available xylose and glucose building blocks. The approach relied on the formation of the β-xylosidic linkages established early in the synthesis via neighbouring group participation. As shown in Scheme 2-6, each successful glycosylation is expected to generate a uloside, which can then be reduced in a highly stereoselective manner into the desired β-*O*-mannoside, as exemplified in the tetrasaccharide. If longer oligomers are desired, the products can be transformed into glycosyl acceptors via a two-step protocol involving protection of the C-2 hydroxyl group of each newly generated mannoside followed by Troc deprotection on the xylose residue. These glycosyl acceptors can then be coupled to the ulosyl bromide again. Finally, all the xylomannan-based AFGL mimetics can be obtained after global deprotection.



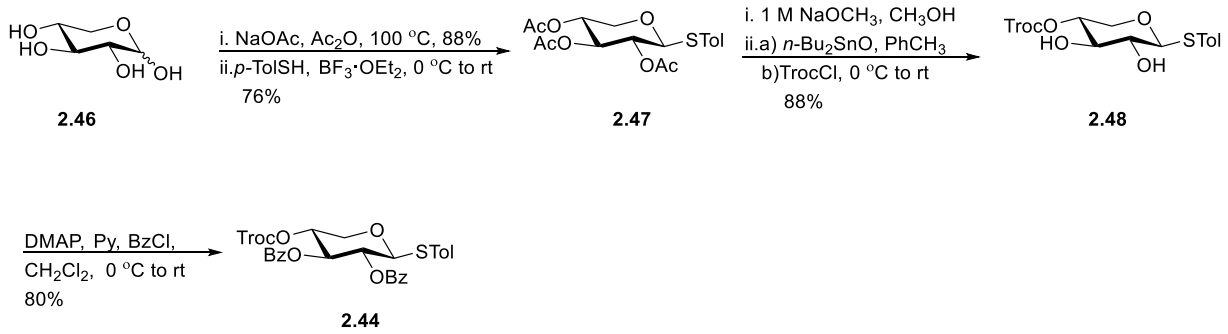
Scheme 2-6: Retrosynthesis of xylomannan-based AFGL mimetics via the ulosyl bromide approach

2.4 Results and discussion

2.4.1 Synthesis of the ulosyl bromide 2.43

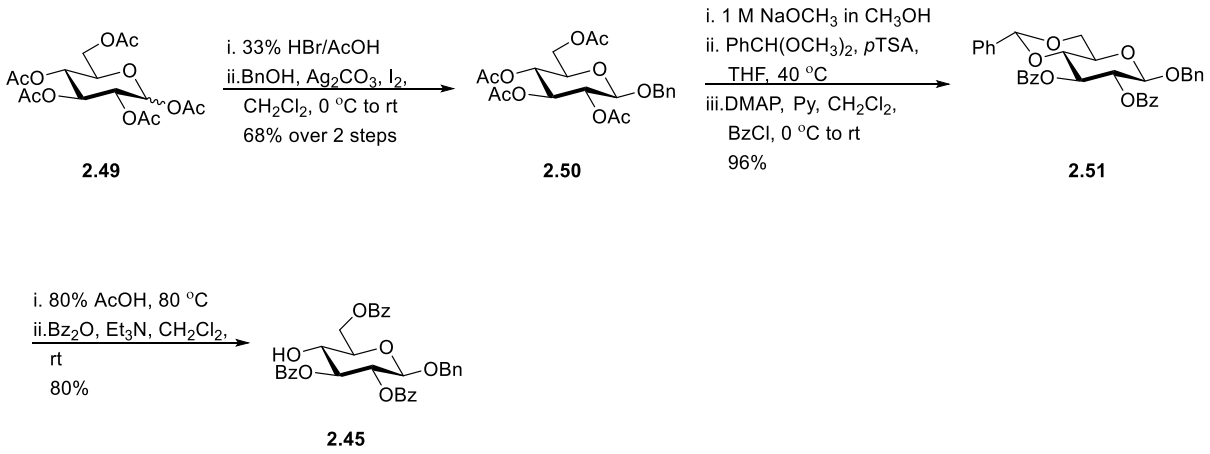
As mentioned previously, the ulosyl bromide donor could be prepared from commercially available D-xylose and D-glucose. Their syntheses are briefly discussed below.

As shown in Scheme 2-7, synthesis of thioglycoside **2.44** was achieved in five steps. First, peracetylation of D-xylose **2.46** was performed by heating with acetic anhydride at 100 °C in the presence of sodium acetate, before recrystallization in ethanol to generate the desired peracetylated xylose as the β-anomer exclusively in 88% yield.[13] Subsequent thioglycosylation with *p*-thiocresol in the presence of boron trifluoride etherate as the Lewis acid promotor gave the resultant thioxyloside **2.47**, after recrystallization, in 76% yield. Zemplen deacetylation of **2.47** followed by tin-mediated regioselective Troc protection led to the exclusive formation of diol **2.48** in 70% yield over two steps.[14] Finally, treatment of **2.48** with benzoyl chloride in the presence of pyridine and catalytic DMAP afforded the desired product **2.44** as white foamy solid in 80% yield.



Scheme 2-7: Synthesis of xylose building block **2.44**

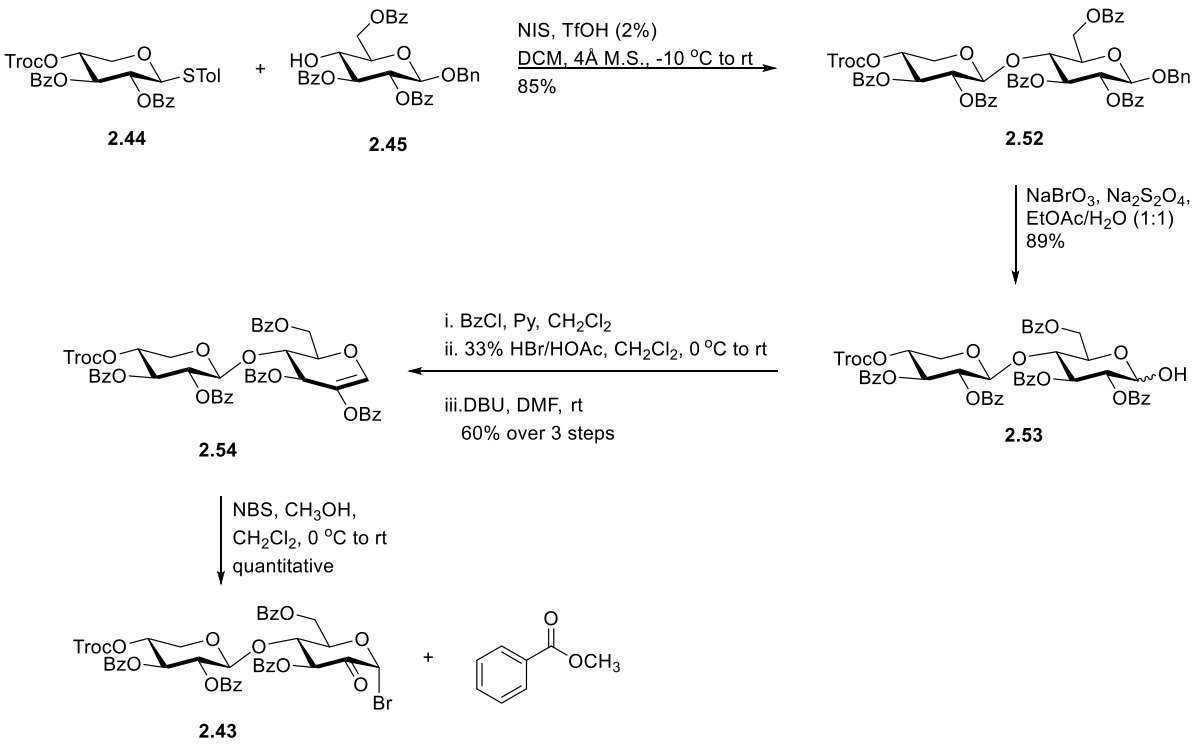
Glucose acceptor **2.45** was prepared in eight steps and required only two chromatographic purifications. This is illustrated in Scheme 2-8. Beginning with peracetylated D-glucose **2.49**, bromination with 33% HBr in AcOH led to the isolation of acetobromoglucose, which was then coupled to benzyl alcohol using the Ag_2CO_3–I_2 promoter combination to generate β-glycoside **2.50** in overall yields of 68%.[15] Subsequent Zemplen deacetylation, 4,6-*O*-benzylidene protection and then dibenzoylation furnished the product **2.51** in an overall yield of 96% after recrystallization. Removal of the benzylidene protecting group via acid hydrolysis, followed by regioselective benzoylation of the C-6 hydroxyl group led to the desired glucose acceptor **2.45** as a white solid in 80% yield.



Scheme 2-8: Synthesis of glucose building block **2.45**

With donor **2.44** and acceptor **2.45** in hand, β-xylosylation to give the desired disaccharide **2.52** was investigated (Scheme 2-9). After screening a few activation conditions, TfOH (2% v/v in CH_2Cl_2) in the presence of acceptor **2.45** gave the best yield (85%). However, the subsequent removal of benzyl protecting group proved to be a challenge. Standard hydrogenation conditions with catalytic Pd/C or $Pd(OH)_2$/C failed to yield any desired lactol **2.53**. Reduction with Raney-Ni, as reported by Marino and co-workers,[16] gave the desired lactol, but

in only 33% yield. Fortunately, it was discovered that complete anomeric deprotection could be achieved with oxidative debenzylation using a combination of $NaBrO_3$–$Na_2S_2O_4$, delivering **2.53** in 89% yield.[17,18] Benzoylation, of **2.53**, followed by bromination of the crude mixture with 33% HBr in glacial acetic acid gave the desired glycosyl bromide cleanly. This compound was then subjected to dehydrohalogenation with DBU in anhydrous DMF to afford the glycal **2.54** in 70% yield over three steps. Employing the conditions established by Lichtenthaler and co-workers,[19] reaction of **2.54** with NBS in methanol and dichloromethane yielded the desired ulosyl bromide **2.43** quantitatively, along with the stoichiometric generation of methyl benzoate as a by-product.



Scheme 2-9: Construction of the disaccharide ulosyl bromide **2.43** via Lichtenthaler's reported method

Isolation, purification and storage of ulosyl bromide **2.43** initially proved to be a challenge as it was discovered to be highly unstable, with rapid decomposition observed at room temperature (within a few hours) and immediately on exposure to silica gel. The need to remove

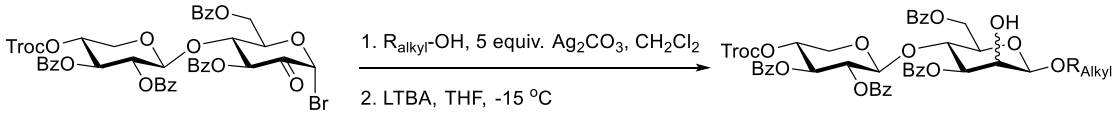
both the excess NBS and the succinimide by-product from the mixture without chromatography led me to pursue different isolation techniques. Though excess NBS could be quenched by the addition of saturated aqueous $Na_2S_2O_3$ to the crude reaction at 0 °C, succinimide proved to be more difficult to remove. Eventually, it was discovered that vigorous washing of the resultant crude product with ice water removed most, if not all, of the succinimide. Rapid in vacuo concentration at room temperature thus afforded **2.43** cleanly as off-white foam together with traces of methyl benzoate as the sole contaminant (observable in the NMR spectra of **2.43**). Verification of the ulosyl bromide was achieved by the observation of a singlet resonance at δ_H = 6.34 ppm for H-1, which was correlated with the anomeric carbon resonance at δ_C = 83.2 ppm via the HSQC spectrum. This is in good agreement with the chemical shift values reported by Lichtenthaler.[20] Further support was garnered from a correlation in the HMBC spectrum between the H-1 resonance and the ketone functionality at δ_C = 188.9 ppm. With the knowledge of instability of **2.43**, even in storage at –20 °C, the freshly prepared crude ulosyl bromide was used immediately in glycosylation reactions without further purification.

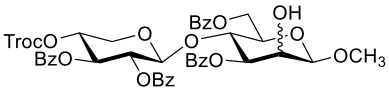
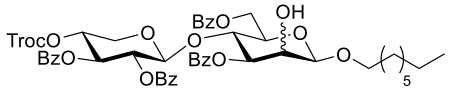
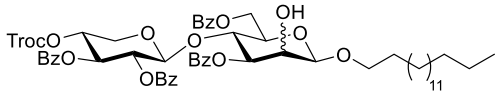
2.4.2 Evaluation of ulosyl bromide 2.43 in glycosylations

2.4.2.1 Primary alcohols as acceptors and subsequent global deprotection

Next, as part of my plan to functionalize xylomannan glycolipids with different aglycones, the applicability of **2.43** in glycosylations was interrogated with methyl (CH_3), octyl (n-C_8H_{17}) and cetyl (n-$C_{16}H_{33}$) alcohols, employing Ag_2CO_3 as the promotor to promote S_N2-type glycosylation. The results are shown in Table 2-1 where moderate coupling yields were observed in all three cases after reduction. A gradual decrease in the time taken for complete glycosylation as the hydrophobicity of the acceptor increased was observed. This could be explained through

the increase in electron donation to the hydroxyl group from the increased alkyl chain length, thus enhancing the acceptor nucleophilicity, which translated into an increased reaction rate. Due to the inherent instability of ulosides, the glycosylation products were isolated and then immediately reduced to facilitate purification and characterization.



Entry	R_{Alkyl}-OH	time (h)	Yield (%)[a]	β-*manno*/β-*gluco*
1	$HOCH_3$	8 h	 **2.55:** 60%	10:1 *1:1 with $NaBH_4$
2	HO(CH₂)₅	4 h	 **2.56:** 63%	10:1
3	HO(CH₂)₁₁	2 h	 **2.57:** 67%	10:1

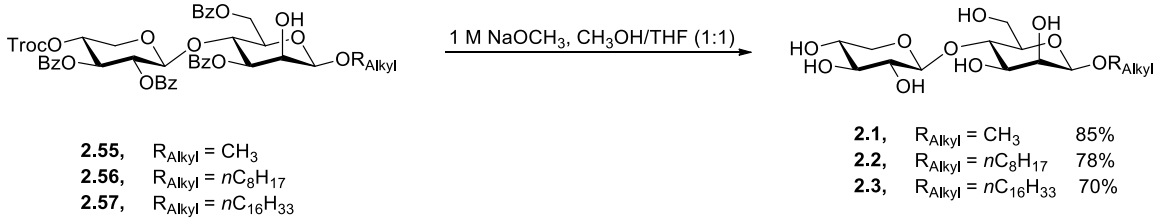
[a]Calculated over 3 steps based on the glycal **2.54**

Table 2-1: Glycosylation of ulosyl bromide **2.43** with simple alcohols and subsequent reduction

Initially, attempts to obtain high β-*manno*-selective reduction of methyl disaccharyl uloside with sodium borohydride ($NaBH_4$) led only to equimolar mixtures of the two epimers (Table 2.1, Entry 1). Use of L-Selectride led to rapid decomposition of the uloside, presumably due to the presence of base sensitive acyl groups. On the other hand, markedly improved β-*manno* selectivity (from 1:1 to 10:1) in the formation of **2.55** was observed with the use of the milder, yet bulky reducing agent lithium tri-*tert*-butoxyaluminum hydride (LTBA). The β-

anomeric configuration of each resultant glycoside after reduction was determined by the $^{1}J_{C1\text{-}H1}$ (<165 Hz), which was measured via the ^{1}H-coupled HSQC spectrum. In combination with assignments of epimers by $^{3}J_{H1\text{-}H2}$ (~8.0 Hz for β-*gluco*, <1.0 Hz for β-*manno*), the stereoselectivity of the reduction was determined based on the integration of respective anomeric proton resonances. With this information in hand, all future reductions were conducted with LTBA.

With a few milligrams of xylomannans **2.55** to **2.57** in hand, Zemplen deacetylation was conducted leading to **2.1**–**2.3**. Disaccharides **2.1** and **2.2** were purified by reversed phase (C18) chromatography, leading to high purity in almost quantitative yields. The relative insolubility of xylomannan **2.3** in water rendered it unsuitable for C18 purification. However, it was serendipitously discovered that the compound could be precipitated from a solution of H_2O–CH_3OH–THF–CH_2Cl_2 (10:1:1:2) as a method of purification. After precipitation, xylomannan **2.3** was filtered off and dried, with yields in the range of 70–85% (Scheme 2-10).



2.55, $R_{Alkyl} = CH_3$
2.56, $R_{Alkyl} = nC_8H_{17}$
2.57, $R_{Alkyl} = nC_{16}H_{33}$

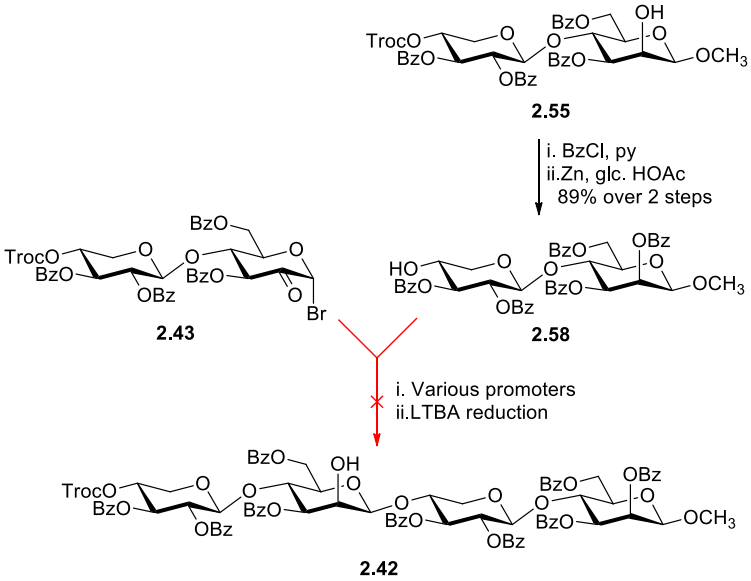
2.1, $R_{Alkyl} = CH_3$ 85%
2.2, $R_{Alkyl} = nC_8H_{17}$ 78%
2.3, $R_{Alkyl} = nC_{16}H_{33}$ 70%

Scheme 2-10: Zemplen deacetylation to effect global deprotection of **2.55**–**2.57** leading to **2.1**–**2.3**

2.4.2.2 Glycosyl acceptor and 2 + 2 glycosylation

Conversion of compound **2.55** into a glycosyl acceptor **2.58** was subsequently done by benzoylation of the C-2 hydroxyl group of the mannoside followed by liberation of the C-4 hydroxyl group of the xylose residue upon treatment with zinc in acetic acid (Scheme 2-11).

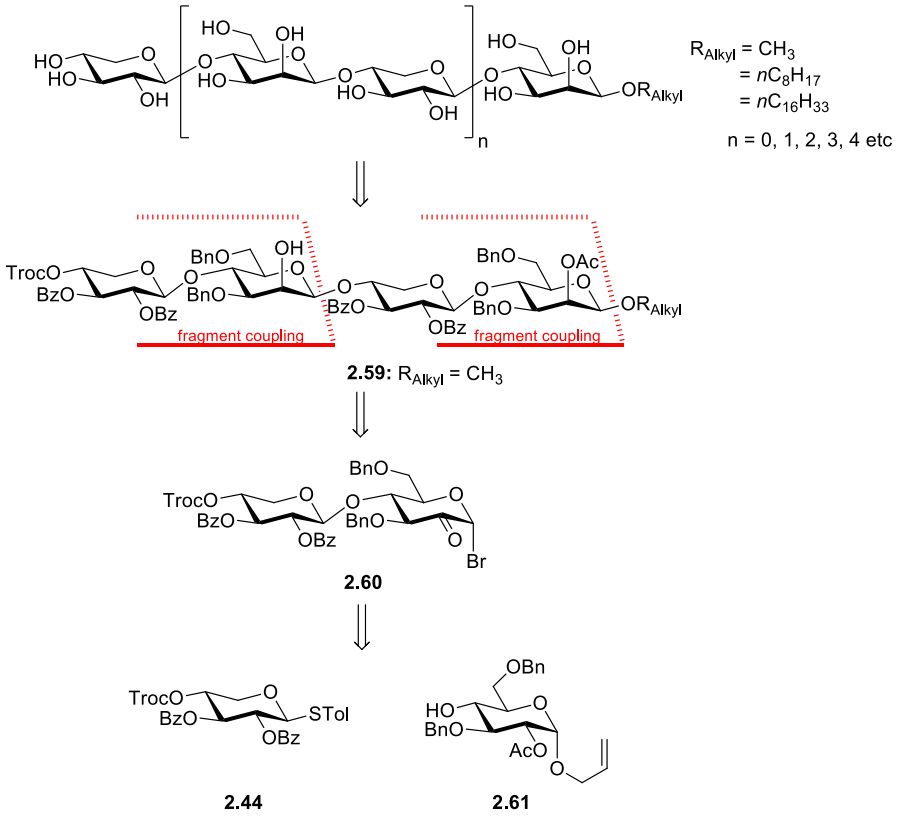
Unfortunately, exposure of ulosyl bromide **2.43** to acceptor **2.58** using Ag_2CO_3 did not lead to any profitable outcome, with the donor fully decomposing after stirring overnight. Switching to silver aluminosilicate[21] promoter led to complex reaction mixtures. Finally, attempts to activate **2.43** with AgOTf in the presence of the **2.58** in acetonitrile,[22] under both normal and inverse additions, led to complete decomposition within an hour, even at –50 °C. In all cases, complex reaction mixtures are observed, even after LTBA reduction to facilitate isolation and characterisation. Furthermore, tetrasaccharide **2.42** was not observed in any of these mixtures. The lack of progress from this approach was attributed to two factors: 1. poorer nucleophilicity of the glycosyl acceptor relative to the simple alcohols, and 2. lower anomeric reactivity of the donor as a result of having benzoyl groups on the ulosyl residue. This prompted my decision to incorporate benzyl groups into the ulosyl donors, which is described in the next section.



Scheme 2-11: Attempted 2 + 2 glycosylation between ulosyl bromide **2.43** to acceptor **2.58**

2.5 Revised ulosyl bromide approach: retrosynthesis

As mentioned in the previous section, given the lack of success with ulosyl bromide **2.43**, it was hypothesized that arming the ulosyl bromide with benzyl groups might lead to successful 2 + 2 glycosylation. Thus, with this in mind, I set out to prepare ulosyl bromide **2.60** from the xylose donor **2.44** and glucose acceptor **2.61** (Scheme 2-12). Similar to the previous approach, it was envisioned that ulosyl bromide **2.60** could be used to obtain all the desired AFGL mimetics.

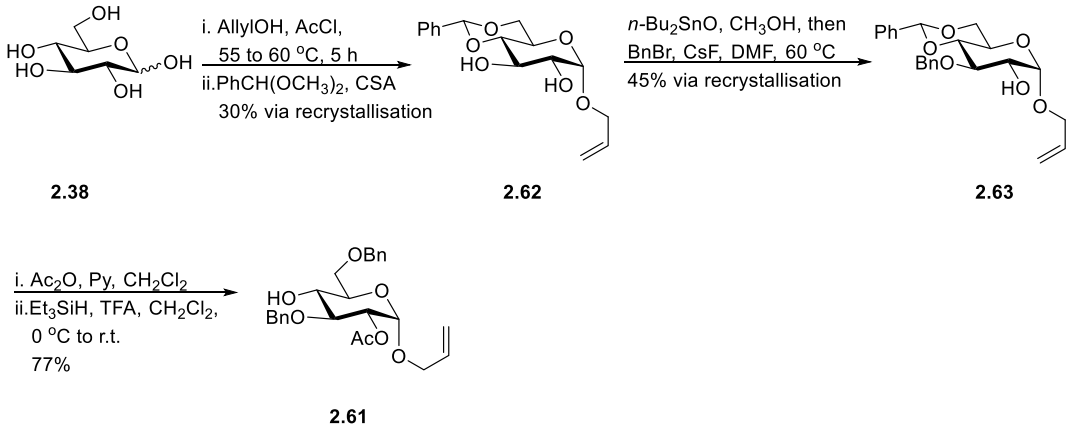


Scheme 2-12: Revised retrosynthesis of AFGL mimetics via ulosyl bromide **2.60**

2.6 Results and discussion based on the revised retrosynthesis

2.6.1 Synthesis of ulosyl bromide 2.60

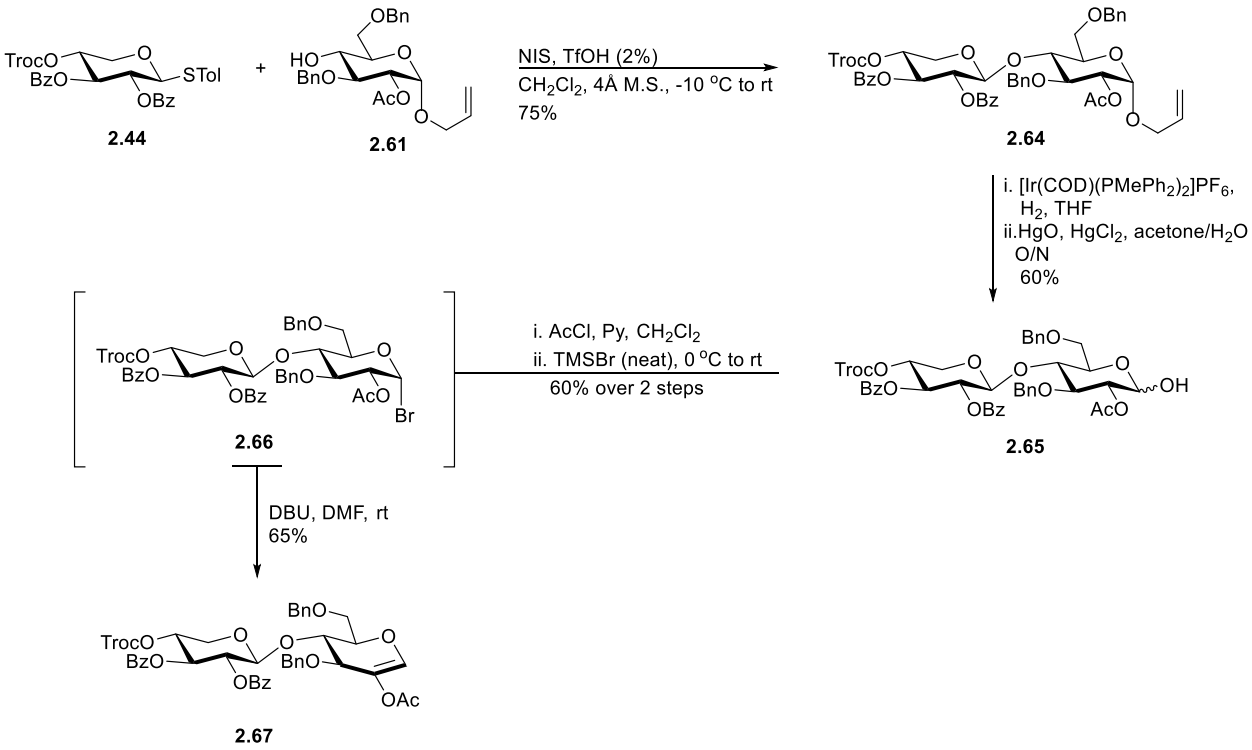
Glucose acceptor **2.61** was prepared from D-glucose **2.38** in five steps (Scheme 2-13). Allyl glucoside **2.62** was obtained in multigram quantities[23] via an initial Fischer glycosylation of **2.38** followed by 4,6-*O*-benzylidene protection. Regioselective tin-mediated benzyl protection of the C-3 hydroxyl group of **2.62** was conducted in methanol at reflux; the desired product, **2.63**, could be selectively recrystallized over the undesired regioisomer in a moderate yield of 45%.[23] Acetylation of the resultant product **2.63** under the standard pyridine–Ac_2O conditions, followed by regioselective reductive ring-opening of the benzylidene group, led to **2.61** in 77% yield over two steps.



Scheme 2-13: Synthesis of glucosyl building block **2.61**

With the glucose acceptor **2.61** in hand, I envisioned that the disaccharide glycal **2.68** could be obtained via an initial 1+1 glycosylation with xylose thioglycoside **2.44**, followed by anomeric deprotection, bromination and finally E2 elimination with DBU (Scheme 2-14). Gratifyingly, employing the same activating conditions used previously for the 1 + 1

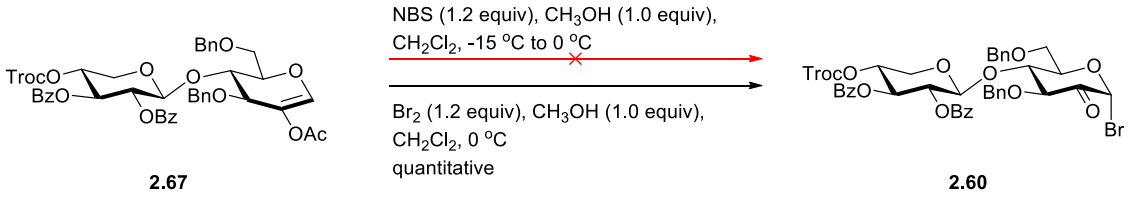
glycosylation gave disaccharide **2.64** in 75% yield. Subsequent removal of *O*-allyl anomeric protecting group via a two-step process involving an initial Ir-catalysed isomerization,[24] followed by oxymercuration–demercuration of the resultant enol ether with HgO/$HgCl_2$, gave a 60% yield of hemiacetal **2.65**. Initial attempts to obtain the glycosyl bromide **2.66** directly from hemiacetal **2.65** via exposure to oxalyl bromide yielded complex mixtures with only a detectable trace of the desired product via NMR spectroscopic and mass spectrometric analyses. Fortunately, it was found that acetylation of **2.65**, followed by exposure to neat trimethylsilyl bromide (TMSBr) for two hours at 0 °C afforded glycosyl bromide **2.66** cleanly in 70% over two steps without the need for any purification. Finally, dehydrohalogenation of the glycosyl bromide via treatment with DBU in DMF led to glycal **2.67** in 60% yield.



Scheme 2-14: Synthesis of glycal **2.67**

Guided by my experimental insights into the relative instability of ulosyl bromides, I sought to build on the success of Lichtenthaler's protocol for preparing ulosyl bromides from

glycals. Unfortunately, this method was plagued by significant decomposition of the ulosyl bromide product, in addition to contamination from succinimide. Careful NMR spectroscopic analysis of unquenched reaction aliquots attested to the complete transformation of the glycal **2.67** into the ulosyl bromide **2.60** within 15 to 30 min. However, competing decomposition of the ulosyl bromide at room temperature and hydrolysis even on brief contact with water thus led to the search for another brominating reagent. Fortunately, it was discovered that upon exposure of glycal **2.67** to stoichiometric anhydrous methanol with a slight excess of bromine, ulosyl bromide **2.60** could be obtained in quantitative yields and high purity. Notably, there was no need for any workup as both bromine and methanol could be removed via low pressure evaporation of the solvent (Scheme 2-15). This method allowed rapid and facile access to multigram quantities of ulosyl bromide **2.60**.



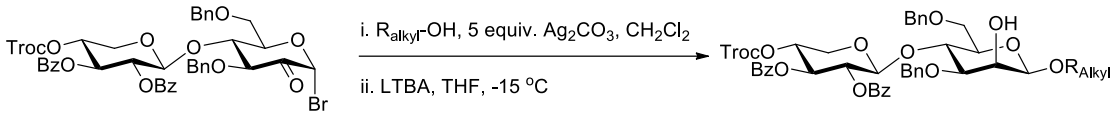
Scheme 2-15: Modified preparation of ulosyl bromide **2.60**

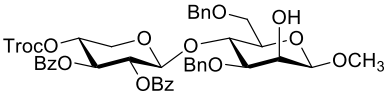
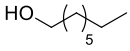
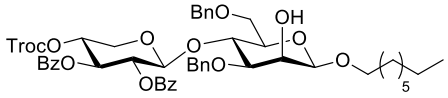
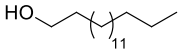
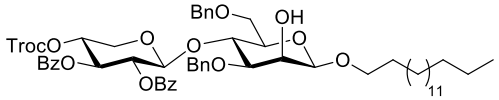
Structural verification of **2.60** was achieved on the basis of both chemical shifts and 2D NMR spectroscopic experiments. For instance, the anomeric proton of **2.60** appeared as a singlet ^{1}H resonance at δ_H = 6.35 ppm, correlated to a ^{13}C resonance at δ_C = 85.6 ppm in the HSQC spectrum. These are the expected shifts of an anomeric ^{13}C–^{1}H pair adjacent to a bromine atom. Further corroboration of the ulosyl bromide structure came from the HMBC spectrum correlation between the ketone functionality at δ_C = 193.0 ppm with the ^{1}H resonance at δ_H = 6.35 ppm.

Attempts to obtain a mass spectrum of **2.60** were unsuccessful, probably due to the inherent hydrolytic and thermal instabilities of this compound.

2.6.2 Evaluation of ulosyl bromide 2.60 as a glycosyl donor

The higher anomeric reactivity of **2.60**, already observable from the rapid hydrolysis even on brief contact with water, opened up exciting new possibilities. On exposure of **2.60** to methyl (CH_3), octyl (n-C_8H_{17}) and cetyl (n-$C_{16}H_{33}$) alcohols in the presence of Ag_2CO_3, all the glycosylations proceeded smoothly within two hours. Subsequent LTBA reduction delivered the desired β-mannosides in significantly improved yields and exquisite selectivity (Table 2-2). Once again, though L-Selectride has been demonstrated by both Bundle[22] and Lichtenthaler[25] to deliver complete β-*manno* selectivity, it was not used due to the previously observed base sensitivity of the uloside towards this reducing agent.

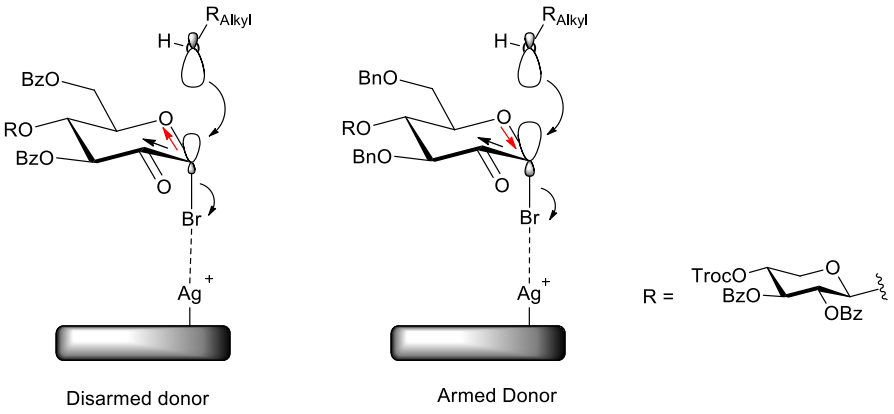


Entry	R_{Alkyl}-OH	time(h)	Yield (%)[a]	Stereochemical outcome
1	$HOCH_3$	2 h	 **2.68:** 65%	Only β-*manno*-isomer observed
2		2 h	 **2.69:** 70%	Only β-*manno*-isomer observed
3		2h	 **2.70:** 75%	Only β-m*anno*-isomer observed

[a]Yields calculated based on the glycal **2.67**

Table 2-2: Glycosylation of ulosyl bromide **2.60** with simple alcohols and subsequent reduction

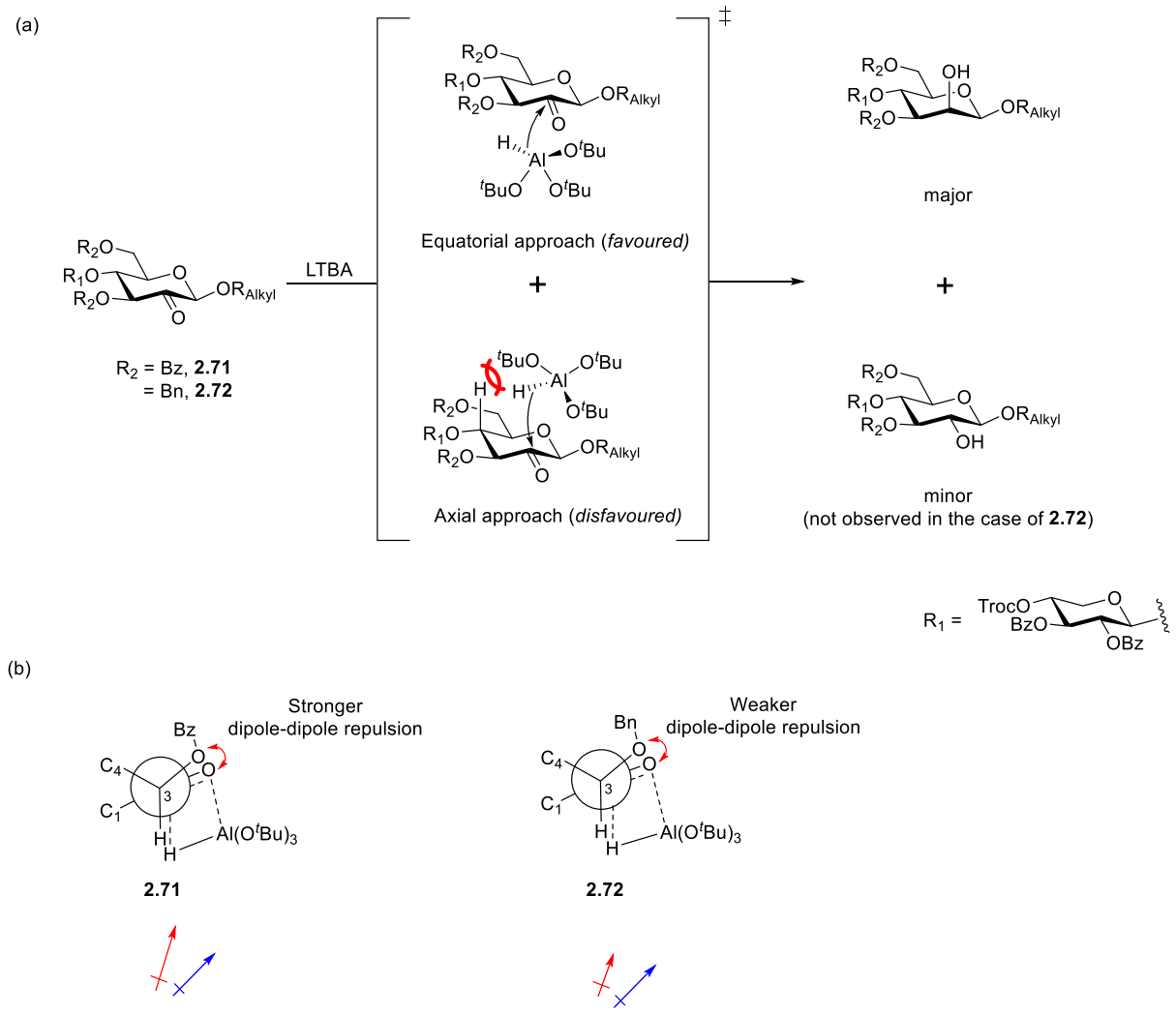
To account for the enhanced reactivity of **2.60** compared to **2.43**, an explanation can be proposed on the basis of inductive and stereoelectronic effects (Scheme 2-16). Increased electron density in the pyranose ring, as a result of replacing the electron-withdrawing benzoyl esters for the more electron-donating benzyl groups help to stabilise the transition state during the S_N2-type glycosylation, thus lowering the activation barrier of the reaction and consequently leading to rate acceleration. Moreover, the enhanced electron density could also contribute to the increased rate by weakening the anomeric C–Br bond through increased donation of n_p electrons of the pyranose oxygen atom into the C–O σ^* orbital.



Scheme 2-16: Orbital interactions that influence the relative reactivities of respective ulosyl bromides

The highly *manno*-selective LTBA reductions of all the ulosides can be rationalised from a steric perspective (Scheme 2-17a). With each uloside adopting a $^4C_1$ conformation,[25] the metal hydride will attack the ketone via an equatorial approach in preference to an approach to avoid unfavourable steric interaction from the uloside H-4. In addition, the steric bulk of LTBA enhances the stereoselectivity by overcoming the torsional strain inherent in ulosides (which would otherwise favour the *gluco* outcome).

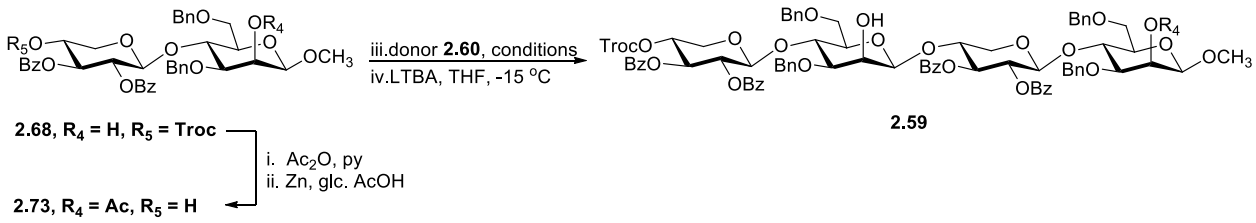
On the other hand, the reason for the difference, albeit minor, in the stereoselectivity of LTBA reduction between ulosides **2.71** and **2.72** is unclear. A possible explanation arises from the electronic nature of the polar substituents at C-3 of both **2.71** and **2.72** (Scheme 2-17b). I hypothesize that the electron-donating benzyloxy groups on C-3 of **2.72** improve the stereoselectivity by reducing the C-3–O dipole moment, which resulting in reduced dipole–dipole repulsion between the C-3–O bond and the developing negative charge on the alkoxide oxygen atom in the transition state. In contrast, placement of the electron-withdrawing benzoyloxy groups in **2.71** leads to an increased C-3–O dipole moment, resulting in increased dipole–dipole repulsion that subsequently translates into poorer selectivity.



Scheme 2-17: (a) Axial vs equatorial selectivity in the reduction of ulosides **2.71** and **2.72**. (b) Newman projections down the C-3–C-2 bond to account for the difference in the β-*manno*/β-*gluco* selectivity with C-3 different protecting groups. Red arrows denote dipole moments of the C-3–O bond, with shorter arrows an indication of lower dipole moment and blue arrows indicate the dipole moment of the developing alkoxide.

Encouraged by the improved results with the simple alcohols (Table 2.2), applicability of ulosyl bromide **2.60** for 2 + 2 glycosylation was subsequently tested using acceptor **2.73**. The results are summarized in Table 2.3. Despite the increased donor reactivity, none of the desired tetrasaccharides could be observed (via TLC or mass spectrometry) in the crude mixture upon exposure to Ag_2CO_3 and subsequent LTBA reduction. Even the introduction of silver aluminosilicate promoters did not translate to any positive outcome. Further experimentations

with AgOTf and acetonitrile as a participating solvent, as shown by Bundle and co-workers,[22] unfortunately, also failed to yield any of the desired compounds. Finally, attempts to improve the reactivity of the acceptor **2.73** via derivation with organotin compounds[26] only resulted in complex reaction mixtures upon exposure of the donor **2.60** to the organotin derivative in the presence of both soluble and insoluble promoters. In all cases, the acceptor was recovered in 55–80% yields.



Entry	Donor Equiv.	Conditions	Outcome[a]
1	1.3 to 3.0	Ag_2CO_3 (5 to 20 eq), I_2, CH_2Cl_2, rt	Donor decomp.; 80% acceptor isolated
2	1.3 to 3.0	Ag-silicate, CH_2Cl_2, rt	Donor decomp.
3	1.3 to 3.0	Ag_2O (5 to 20 eq), $SrCO_3$, CH_2Cl_2, rt	Donor decomp.
4	1.3 to 3.0	AgOTf (1.5 to 4.0 eq), DtBMP (1.6 to 5.0 eq), CH_3CN, 0 °C to rt	Donor decomp.; 55% acceptor isolated
5	1.3 to 2.0	i. $(n\text{-}Bu_3Sn)_2O$, reflux ii. Ag_2CO_3 (5 to 20 eq), I_2, CH_2Cl_2, rt	Donor decomp.; 20% acceptor isolated

[a] determined by NMR anaylsis of the crude. %recovery based on starting material

Table 2-3: Conditions explored in attempt to obtain tetrasaccharides via ulosyl bromide **2.60**

The difficulty faced in the 2 + 2 glycosylations may be attributed to the low nucleophilicity of the C-4 hydroxyl group in Xyl*p* residue of the acceptor **2.73**, as a result of the neighbouring electron-withdrawing benzoate esters at C-2 and C-3. Consequently, the inability of this hydroxyl group to displace the α-bromide or trap α-ulosyl nitrilium ions formed during activation renders the approach unviable.

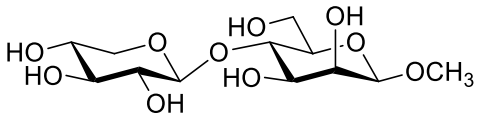
2.7 Conclusion

In summary, this chapter described the first successful application of the ulosyl bromide approach preparing xylomannan-based AFGL mimetics, via the successful synthesis of **2.1–2.3**. This approach is characterized by β-mannosylation through a disaccharide donor. The synthesis of ulosyl bromide **2.60** involved a few more steps than **2.43** and the product is also generally more difficult to handle on a multigram scale. Nevertheless, the exquisite β-*manno* selectivities that were obtained with LTBA reduction made it more synthetically appealing as this improved yields significantly and simplified the purification process. Although this approach initially appeared to be an attractive option for rapid assembly of large oligosaccharides, numerous problems faced in using this approach for 2 + 2 glycosylations in part from the instability of the ulosyl bromides **2.43** and **2.60** to the low reactivity of the glycosyl acceptors led to the search for alternative approaches. These are presented in the next chapter.

2.8 Experimental section

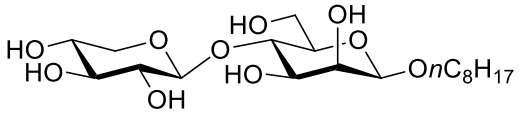
General Experimental Methods. All reagents were purchased from commercial sources and were used without further purification unless noted. Solvents used in reactions were purified by successive passage through columns of alumina and copper under argon. Both 3Å and 4Å molecular sieves were dried at 300 °C in oven. Unless stated otherwise, all reactions were carried out at room temperature and were monitored by TLC on Silica Gel G-25 F_{254} (0.25 mm). In chemical glycosylations, all the starting materials were thoroughly dried by toluene co-evaporation (3x), followed by vacuum drying over P_2O_5 overnight prior to the reaction setup. TLC spots were detected under UV light and/or by charring with a solution of *p*-anisaldehyde in ethanol, acetic acid and H_2SO_4. Column chromatography was performed on Silica Gel 60 (40–60 μm) or C18 silica gel (35−70 μm). In some cases, a dry loading technique (substrate adhered to silica, solvent removed, then loaded onto column) was used for purification. Solvents were evaporated under reduced pressure on a rotary evaporator. ^{1}H NMR spectra were recorded using 500 or 700 MHz NMR instruments and were referenced to residual proton signal of $CDCl_3$ (7.26 ppm), CD_3OD (3.30 ppm) or D_2O (4.79 ppm). ^{13}C NMR spectra were recorded using either a 125 MHz (dual cold probe) or 175 MHz (HCN cold probe) NMR instrument, and were referenced to residual ^{13}C signals of $CDCl_3$ (77.06 ppm), CD_3OD (49.0 ppm) or external acetone (31.1 ppm, D_2O). ^{1}H NMR data are reported as though they were first order, and signal assignments were made on the basis of 2D-NMR (^{1}H–^{1}H COSY, HSQC and HMBC) experiments. The stereochemistry of the anomeric centres of the pyranose rings was determined by measuring $^1J_{C1\text{-}H1}$ via coupled HSQC NMR experiments, if necessary. For ^{1}H NMR data, diastereomeric pyranoside proton signals are indicated by either a or b. In the case of methylene protons on Troc, benzyl and hydrophobic aglycones, their numbers are indicated by $n \times C\underline{H}_2$. For

example, a benzylic proton occurring at δ 4.90 ppm will be written as δ 4.92–4.88 (m, 1H, 1 × PhC<u>H</u>$_2$O). For all disaccharides, each monosaccharide residue is labelled with an increasing number of diacritical marks (` to ``) from the reducing end to the non-reducing end. For regions of the ^{13}C spectra with significant signal overlap, the number of carbons contributing to each resonance was not identified. In cases where two or more signals rounded to the nearest tenth of a decimal place, this is indicated by the number of resonances (not carbons) following the chemical shift. ESI-MS spectra (time-of-flight analyzer) were recorded on an Agilent Technologies 6220 TOF spectrometer on samples dissolved in THF, CH_3OH or CH_3CN and added NaCl. Optical rotations were measured at 22 ± 2 °C at the sodium D line (589 nm) in a microcell (10 cm, 1 mL) and are expressed in units of deg·mL(dm·g)$^{-1}$.



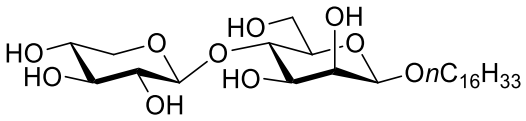
Methyl β-D-xylopyranosyl-(1→4)-β-D-mannopyranoside (2.1). To a flask containing **2.69** (69.8 mg, 76.0 μmol) in CH_3OH (5 mL) was added 0.1 M $NaOCH_3$ in CH_3OH (0.5 mL). The reaction mixture was stirred for 2 h, after which it was neutralized by the addition of Amberlite IR-120 H^+ resin. The reaction mixture was filtered, concentrated and then co-evaporated with CH_2Cl_2 (2x). The resultant crude residue was purified over by reversed phase C18 chromatography (100% H_2O to 20% CH_3OH–H_2O) and subsequently lyophilized to yield **2.1** (21.1 mg, 64.6 μmol, 85%) as a white fluffy solid. R_f = 0.24 (12:3:3:2 EtOAc–CH_3OH–AcOH–H_2O); $[\alpha]_D$ –21.5 (*c*. 0.04, CH_3OH); ^{1}H NMR (500 MHz, D_2O, δ_H) 4.62 (s, 1H, H-1`), 4.44 (d, *J* = 7.8 Hz, 1H, H-1``), 4.08–3.98 (m, 3H, H-6a`, H-2`, H-5a``), 3.85 (dd,

J = 12.2, 5.6 Hz, 1H, H-6b`), 3.81–3.73 (m, 2H, H-4`, H-3`), 3.66 (td, J = 10.0, 5.5 Hz, 1H, H-4``), 3.57 (s, 3H, $OCH_3$), 3.54 (ddd, $J$ = 8.5, 5.7, 2.2 Hz, 1H, H-5`), 3.48 (app t, $J$ = 9.4 Hz, 1H, H-3``), 3.40–3.28 (m, 2H, H-2``, H-5b``). ^{13}C NMR (125 MHz, D_2O, δ_C) 103.5 (C-1``), 100.9 (C-1`), 76.6 (C-4`), 75.7 (C-3``), 75.1 (C-5`), 73.2 (C-2``), 71.6 (C-3`), 69.9 (C-2`), 69.2 (C-4``), 65.2 (C-5``), 60.4 (C-6`), 56.9 ($O\underline{C}H_3$). HRMS (ESI) calcd for $(M + Na)^+$ $C_{12}H_{22}NaO_{10}$: 349.1105. Found: 349.1101.



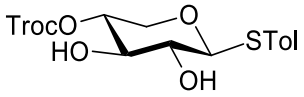
***n*-Octyl β-D-xylopyranosyl-(1→4)-β-D-mannopyranoside (2.2).** To a flask containing **2.70** (78.1 mg, 76.8 μmol) in CH_3OH (5 mL) was added 1.0 M $NaOCH_3$ in CH_3OH (0.2 mL). The reaction mixture was stirred for 2 h, before it was neutralized by the addition of Amberlite IR-120 H^+ resin. The reaction mixture was filtered and concentrated before it was co-evaporated with CH_2Cl_2 (2x). The resultant crude residue was purified by reversed phase C18 chromatography (100% H_2O to 70% CH_3OH–H_2O) and subsequently lyophilized to yield **2.2** (25.4 mg, 59.8 μmol, 78%) as a white fluffy solid. R_f = 0.49 (12:3:3:2 EtOAc–CH_3OH–AcOH–H_2O); $[\alpha]_D$ –192.0 (*c*. 0.01, CH_3OH); ^{1}H NMR (500 MHz, D_2O, δ_H) 4.70 (s, 1H, H-1`), 4.44 (d, J = 7.8 Hz, 1H, H-1``), 4.08–3.98 (m, 3H, H-6a`, H-2`, H-5a``), 3.90 (dt, J = 10.1, 6.9 Hz, 1H, 1 × $OC\underline{H}_2(CH_2)_6CH_3$), 3.85 (dd, J = 12.1, 5.4 Hz, 1H, H-6b`), 3.82–3.71 (m, 2H, H-3`, H-4`), 3.71–3.63 (m, 2H, 1 × $OC\underline{H}_2(CH_2)_6CH_3$, H-4``), 3.55–3.50 (m, 1H, H-5`), 3.48 (app t, $J$ = 9.3 Hz, 1H, H-3``), 3.40–3.28 (m, 2H, H-5b``, H-2``), 1.70–1.59 (m, 2H, $OCH_2(CH_2)_6CH_3$), 1.43–1.23 (m, 10H, $OCH_2(C\underline{H}_2)_6CH_3$), 0.96–0.84 (m, 3H, $OCH_2(CH_2)_6C\underline{H}_3$).

^{13}C NMR (125 MHz, D_2O, δ_C) 103.5 (C-1``), 99.7 (C-1`), 76.6 (C-4`), 75.7 (C-3``), 75.1 (C-5`), 73.2 (C-2``), 71.7 (C-3`), 70.3 (C-2`), 70.2 (O<u>C</u>$H_2(CH_2)_6CH_3$), 69.2 (C-4``), 65.2 (C-5``), 60.4 (C-6`), 31.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 28.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 28.5 × 2 ($OCH_2(\underline{C}H_2)_6CH_3$), 25.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.1 ($OCH_2(\underline{C}H_2)_6CH_3$), 13.5 ($OCH_2(CH_2)_6\underline{C}H_3$). HRMS (ESI) calcd for $(M + Na)^+$ $C_{19}H_{36}NaO_{10}$: 447.2201. Found 447.2196.



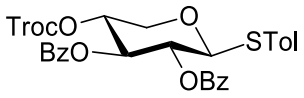
***n*-Hexadecanyl β-D-xylopyranosyl-(1→4)-β-D-mannopyranoside (2.3).** To a flask containing **2.71** (34.0 mg, 30.1 μmol) in dry CH_3OH (2.5 mL) and THF (2.5 mL) was added 1.0 M $NaOCH_3$ in CH_3OH (0.2 mL). The reaction mixture was stirred for 2 h, before it was neutralized by the addition of Amberlite IR-120 H^+ resin. The reaction mixture was filtered and concentrated, before it was co-evaporated with CH_2Cl_2 (2x). The resultant crude was triturated with hexanes and the remaining residue was re-dissolved in CH_3OH–THF–CH_2Cl_2 (2 mL, 1:1:2). To this solution was added distilled H_2O (~5 mL) and sonication was applied to ensure dissolution. White solids were observed to precipitate from the resultant mixture after slow evaporation for 4 days at room temperature. The mixture was filtered off and the residue on the filter paper was washed with distilled H_2O. The residue was then dried under vacuum to yield **2.3** (11.3 mg, 21.0 μmol, 70%) as a white powder. R_f = 0.71 (12:3:3:2 EtOAc–CH_3OH–AcOH–H_2O); ^{1}H NMR (500 MHz, 1:1 CD_3OD–$CDCl_3$, δ_H ref. to CHD_2OD) 3.73 (d, *J* = 0.9 Hz, 1H, H-1`), 3.56 (d, *J* = 7.7 Hz, 1H, H-1``), 3.25 (dd, *J* = 3.2, 0.9 Hz, 1H, H-2`), 3.20 (dd, *J* = 11.4, 5.4 Hz, 1H, H-5a``), 3.15–3.09 (m, 3H, H-6a`, H-6b`, 1 × O<u>C</u>$H_2(CH_2)_{14}CH_3$), 3.06 (app t, *J* = 9.4 Hz, 1H, H-4`),

2.86–2.72 (m, 3H, H-3`, H-4``, 1 × OC<u>H</u>$_2$(CH$_2$)$_{14}$CH$_3$), 2.64–2.56 (m, 3H, H-3`, H-3``, H-5`), 2.55–2.46 (m, 2H, H-5b``, H-2``), 0.91–0.79 (m, 2H, 2 × OCH$_2$(C<u>H</u>$_2$)$_{14}$CH$_3$), 0.65–0.41 (m, 26H, 26 × OCH$_2$(C<u>H</u>$_2$)$_{14}$CH$_3$), 0.12 (t, J = 6.9 Hz, 3H, OCH$_2$(CH$_2$)$_{14}$C<u>H</u>$_3$). ^{13}C NMR (125 MHz, 1:1 CD$_3$OD–CDCl$_3$, δ_C ref. 49.0 ppm, CD$_3$OD) 104.5 (C-1``), 100.4 (C-1`), 78.6 (C-4`), 76.9 (C-3``), 75.2 (C-5`), 73.5 (C-2``), 72.5 (C-3`), 70.4 (C-2`), 70.3 (O<u>C</u>H$_2$(CH$_2$)$_{14}$CH$_3$), 69.5 (C-4``), 66.1 (C-5``), 61.6 (C-6`), 32.1 (OCH$_2$(<u>C</u>H$_2$)$_{14}$CH$_3$), 29.8 × 5 (OCH$_2$(<u>C</u>H$_2$)$_{14}$CH$_3$), 29.7 (OCH$_2$(<u>C</u>H$_2$)$_{14}$CH$_3$), 29.6 (OCH$_2$(<u>C</u>H$_2$)$_{14}$CH$_3$), 29.5 (OCH$_2$(<u>C</u>H$_2$)$_{14}$CH$_3$), 26.1 (OCH$_2$(<u>C</u>H$_2$)$_{14}$CH$_3$), 22.8 (OCH$_2$(<u>C</u>H$_2$)$_{14}$CH$_3$), 14.1 (OCH$_2$(CH$_2$)$_{14}$<u>C</u>H$_3$). HRMS (ESI) calcd for (M + Na)$^+$ $C_{27}H_{52}NaO_{10}$: 559.3453. Found 559.3447.



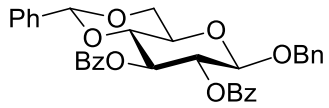
***p*-Tolyl 4-*O*-(2,2,2-trichloroethoxycarbonyl)-1-thio-β-D-xylopyranoside (2.48).** 1.0 M NaOCH$_3$ in CH$_3$OH (4.2 mL) was introduced into a solution of *p*-tolyl 2,3,4-tri-*O*-acetyl-1-thio-β-D-xylopyranoside[13] **2.47** (10.1 g, 26.3 mmol) in CH$_3$OH (50 mL). The resultant mixture was stirred for 16 h, after which the reaction was complete as determined by TLC analysis, and the solution was then neutralized with Amberlite IR-120 H$^+$ resin. Filtration of the mixture, followed by concentration of the filtrate and then co-evaporation with CH$_2$Cl$_2$ (2x) resulted in a white solid residue that was dissolved in dry toluene (250 mL). To this mixture was added *n*-Bu$_2$SnO (7.80 g, 31.3 mmol) and a Dean–Stark apparatus was subsequently fitted onto the flask. The mixture was then heated in toluene at reflux for 16 h, with azeotropic removal of water via the Dean–Stark apparatus. The resulting clear solution was cooled under argon to room temperature and then to 0 °C in an ice bath after which 2,2,2-trichloroethylchloroformate (4.0 mL, 29.1 mmol) was added

dropwise over 2 min. The resultant mixture was stirred at 0 °C for another 1 h, and then CH_3OH (1 mL) was added and subsequently warmed to room temperature. The reaction mixture was concentrated to a crude residue. To this residue was added EtOAc and the mixture was filtered through Celite, and the resultant filtrate was washed with 1 M KF solution (3x), brine and then dried over $MgSO_4$. Filtration of the mixture, followed by concentration of the filtrate, led to a crude residue that was then purified by silica gel chromatography (2:1 hexanes–EtOAc) to give **2.48** (10.0 g, 23.2 mmol, 88%) as a white solid. R_f = 0.31 (2:1 hexanes–EtOAc); $[\alpha]_D$ –31.6 (*c*. 1.1 $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.44–7.42 (m, 2H, Ar), 7.16–7.14 (m, 2H, Ar), 4.81, 4.72 (ABq, *J* = 11.8 Hz, 2H, 2 × $Cl_3CC\underline{H}_2O$), 4.72 (ddd, *J* = 10.1, 9.3, 5.4, 1H, H-4), 4.43 (d, *J* = 9.4 Hz, 1H, H-1), 4.23 (dd, *J* = 11.4, 5.4 Hz, 1H, H-5a), 3.79 (app dt, *J* = 8.9 Hz, 3.1 Hz, 1H, H-3), 3.41–3.34 (m, 2H, H-5b, H-2), 2.81 (d, *J* =3.2 Hz, 1H, O<u>H</u>), 2.67 (d, *J* = 2.6 Hz, 1H, O<u>H</u>), 2.36 (s, 3H, $ArCH_3$); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 153.5 (C=O), 139.1 (Ar), 133.9 (Ar), 130.0 (Ar), 126.9 (Ar), 94.2 ($Cl_3\underline{C}$), 88.7 (C-1), 77.1 ($Cl_3C\underline{C}H_2O$), 75.2 (C-3), 75.0 (C-4), 71.9 (C-2), 66.3 (C-5), 21.2 ($Ar\underline{C}H_3$); HRMS (ESI) calcd for $(M + NH_4)^+$ $C_{15}H_{21}NCl_3O_6S$: 448.0150. Found: 448.0144.



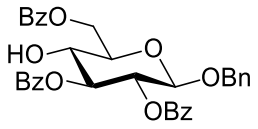
***p*-Tolyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-1-thio-β-D-xylopyranoside (2.44).** To a solution containing **2.48** (13.1 g, 30.3 mmol) in CH_2Cl_2 (250 mL), was added pyridine (70 mL) and DMAP (743 mg, 6.08 mmol). The reaction mixture was then cooled to 0 °C before benzoyl chloride (8.80 mL, 75.8 mmol) was introduced dropwise over 4 min. Upon

complete addition of benzoyl chloride, the solution was warmed to room temperature and stirred for another 8 h, at which point TLC analysis indicated reaction completion. Excess benzoyl chloride was quenched by the addition of CH_3OH (1 mL) and the mixture was then concentrated and co-evaporated with toluene (2x) to remove pyridine. The resultant thick syrup was then re-dissolved in CH_2Cl_2 (250 mL), and the resulting solution was washed with 1 M aqueous HCl, satd. aqueous $NaHCO_3$ followed by brine. The combined organic extracts were then dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a crude residue that was then purified by silica gel chromatography (10:1 hexanes–EtOAc) to afford **2.44** (14.6 g, 22.8 mmol, 87%) as a white foamy solid. R_f = 0.28 (10:1 hexanes–EtOAc); $[\alpha]_D$ –4.0 (*c*. 0.8, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.08–8.06 (m, 4H, Ar), 7.58–7.53 (m, 2H, Ar), 7.45–7.39 (m, 6H, Ar), 7.13–7.12 (m, 2H, Ar), 5.61 (app t, *J* = 6.5 Hz, 1H, H-3), 5.41 (app t, *J* = 6.0 Hz, 1H, H-2), 5.19 (d, *J* =5.5 Hz, 1H, H-1), 5.02 (app td, *J* = 6.5 Hz, 4.0 Hz, 1H, H-4), 4.73 (s, 2H, $Cl_3CC\underline{H}_2O$), 4.61 (dd, *J* = 12.8 Hz, 3.8 Hz, 1H, H-5a), 3.85 (dd, *J* = 12.8 Hz, 6.3 Hz, 1H, H-5b). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 165.1 (C=O), 165.0 (C=O), 153.3 (C=O), 138.5 (Ar), 133.7 (Ar), 133.5 (Ar), 133.2 (Ar), 130.2 (Ar), 130.1 (Ar), 129.9 (Ar), 129.3 (Ar), 129.3 (Ar), 129.2 (Ar), 128.8 (Ar), 128.6 (Ar), 128.5 (Ar), 94.1 ($Cl_3\underline{C}CH_2O$), 86.5 (C-1), 77.1 ($Cl_3C\underline{C}H_2O$), 72.1 (C-4), 69.9 (C-3), 69.6 (C-2), 62.5 (C-5), 21.2 ($Ar\underline{C}H_3$). HRMS (ESI) calcd for $(M + NH_4)^+$ $C_{29}H_{29}Cl_3NO_8S$: 656.0674. Found: 656.0671.



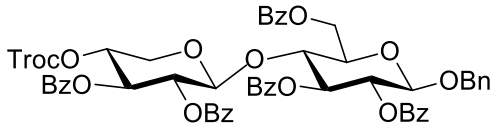
Benzyl 2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranoside (2.51). 1.0 M $NaOCH_3$ in CH_3OH (0.2 mL) was introduced into a solution of benzyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside[15] **2.50** (930 mg, 2.12 mmol) in CH_3OH (30 mL). The resultant mixture was stirred for 16 h, after which point the reaction was complete as determined by TLC analysis; the solution was then neutralized by the addition of Amberlite IR-120 H^+ resin. Filtration of the mixture, followed by concentration of the filtrate, afforded an off-white solid that was dissolved in THF (20 mL). To this solution was added CSA (98.8 mg, 0.42 mmol) followed by BDA (0.48 mL, 3.20 mmol). Reaction completion was achieved within 30 min by subjecting the resultant solution to low pressure concentration at 40 °C on a rotary evaporator. The resultant reddish residue was then diluted with CH_2Cl_2 (100 mL) and poured over satd. aqueous $NaHCO_3$. The two phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL). The organic layers were combined and then washed with brine and dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate afforded a thick oily residue that upon trituration with hexanes yielded a crude amorphous solid. To this solid was added dry CH_2Cl_2 (25 mL) and pyridine (10 mL), followed by benzoyl chloride (0.62 mL, 5.3 mmol) and DMAP (51.5 mg, 0.42 mmol). The mixture was then stirred under argon for 16 h. CH_3OH (1 mL) was added and the resultant mixture was concentrated and then co-evaporated with toluene (2x) to remove pyridine. CH_2Cl_2 (100 mL) and satd. aqueous $NaHCO_3$ were then added to the resultant mixture. The two phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL). The organic layers were combined and then washed with brine before drying over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a crude residue

that was then purified by silica gel chromatography (5:1 hexanes–EtOAc) to obtain **2.51** (1.16 g, 2.04 mmol, 96%) as a white solid. R_f = 0.20 (5:1 hexanes–EtOAc). ^{1}H NMR (500 MHz, δ_H) 7.98–7.88 (m, 4H, Ar), 7.57–7.46 (m, 2H, Ar), 7.43–7.28 (m, 9H, Ar), 7.25–7.14 (m, 5H, Ar), 5.73 (app t, *J* = 9.5 Hz, 1H, H-3), 5.58–5.51 (m, 2H, H-2, PhC<u>H</u>O$_2$), 4.91, 4.68 (ABq, *J* = 12.5 Hz, 2H, PhC<u>H</u>$_2$O), 4.83 (d, *J* = 7.8 Hz, 1H, H-1), 4.46 (dd, *J* = 10.5, 5.0 Hz, 1H, H-6a), 3.95 (app t, *J* = 9.5 Hz, 1H, H-4), 3.91 (app t, *J* = 10.3 Hz, 1H, H-6b), 3.68 (app td, *J* = 9.7, 5.0 Hz, 1H, H-5). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 165.6 (C=O), 165.2 (C=O), 136.8 (Ar), 136.6 (Ar), 133.3 (Ar), 133.1 (Ar), 129.9 (Ar), 129.8 (Ar), 129.5 (Ar), 129.4 (Ar), 129.1 (Ar), 128.4 × 2 (Ar), 128.3 × 2 (Ar), 128.0 (Ar), 127.8 (Ar), 126.2 (Ar), 101.6 (Ph<u>C</u>HO$_2$), 100.1 (C-1), 78.9 (C-4), 72.5 (C-2), 72.1 (C-3), 70.9 (Ph<u>C</u>H$_2$O), 68.7 (C-6), 66.7 (C-5). HRMS (ESI) calcd for $(M + Na)^+$ $C_{34}H_{30}NaO_8$: 589.1833. Found: 589.1836.



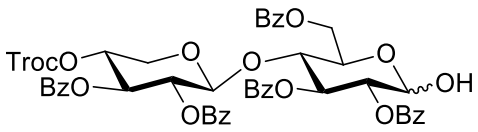
Benzyl 2,3,6-tri-*O*-benzoyl-β-D-glucopyranoside (2.45). To a flask containing **2.51** (732 mg, 1.29 mmol) was added glacial acetic acid (28 mL) and water (7 mL). The suspension was then heated to reflux, with observation of the gradual dissolution of the compound to give a colourless homogenous solution. The reaction was complete as determined by TLC analysis after 4 h. The solution was cooled to room temperature and satd. aqueous $NaHCO_3$ solution was added before CH_2Cl_2 (100 mL) was then added. The two phases were separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 50 mL) before the combined organic layers were washed with brine and dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a

crude syrup that was then triturated with hexanes. To the resultant white solid was added Bz_2O (1.30 g, 5.76 mmol), followed by CH_2Cl_2 (30 mL) and Et_3N (2.0 mL, 13 mmol) under argon. After 24 h, CH_2Cl_2 (100 mL) was added and the two phases were separated. The aqueous phase was extracted with CH_2Cl_2 (2 × 50 mL), and the combined organic phases were subsequently washed with 1.0 M aqueous HCl, followed by satd. aqueous $NaHCO_3$ and brine, before drying over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a crude residue that was then purified by silica gel chromatography (100:1 to 3:1 CH_2Cl_2–EtOAc) to afford **2.45** (535 mg, 0.92 mmol, 71% over 2 steps) as a white amorphous solid. R_f = 0.25 (3:1 CH_2Cl_2–EtOAc). ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.16–8.09 (m, 2H, Ar), 8.00–7.89 (m, 4H, Ar), 7.65–7.58 (m, 1H, Ar), 7.56–7.45 (m, 4H, Ar), 7.42–7.33 (m, 4H, Ar), 7.25–7.13 (m, 5H, Ar), 5.52 (dd, *J* = 9.7, 7.9 Hz, 1H, H-2), 5.39 (dd, *J* = 9.7, 9.1 Hz, 1H, H-3), 4.90 (d, *J* = 12.6 Hz, 1H, 1 × PhC<u>H</u>$_2$O), 4.79 (dd, *J* = 12.1, 4.6 Hz, 1H, H-6a), 4.74 (d, *J* = 9.5 Hz, 1H, H-1), 4.72–4.65 (m, 2H, H-6b, 1 × PhC<u>H</u>$_2$O), 3.93 (app t, *J* = 9.4 Hz, 1H, H-4), 3.77 (ddd, *J* = 9.7, 4.6, 2.4 Hz, 1H, H-5), 3.42 (br. s, 1H, OH). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 167.5 (C=O), 167.0 (C=O), 165.3 (C=O), 136.7 (Ar), 133.6 (Ar), 133.4 (Ar), 133.3 (Ar), 130.1 (Ar), 130.0 (Ar), 129.9 (Ar), 128.6 (Ar), 128.5 (Ar), 128.4 (Ar), 128.4 (Ar), 128.0 (Ar), 127.9 (Ar), 99.2 (C-1), 76.8 (C-3), 74.6 (C-5), 71.4 (C-2), 70.4 (C-6), 69.8 (C-4). HRMS (ESI) calcd for $(M + Na)^+$ $C_{34}H_{30}NaO_9$: 605.1782. Found: 605.1792.



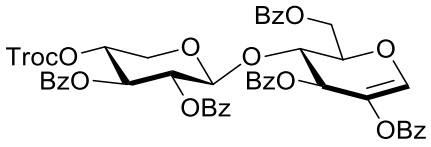
Benzyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-2,3,6-tri-*O*-benzoyl-β-D-glucopyranoside (2.52). To an oven-dried flask charged with donor **2.44** (6.15 g, 9.61 mmol) and acceptor **2.45** (3.11 g, 5.33 mmol) was added CH_2Cl_2 (60 mL) and 4 Å M.S. (8.80 g) under argon. The suspension was stirred for 30 min before it was cooled to 0 °C. The NIS (2.41 g, 10.7 mmol) was then added, followed by TfOH (2.5 mL, 1.1 mmol, 4% v/v in CH_2Cl_2). The resultant reddish-black mixture was then warmed to room temperature and stirred for an additional 3 h, before the reaction was complete as determined by TLC analysis. Then, Et_3N (1.0 mL) was added, and the mixture was filtered through Celite. The resultant filtrate was then washed with satd. aqueous $Na_2S_2O_3$ and brine before it was dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate afforded a crude residue that was then purified by silica gel chromatography (20:1 toluene–EtOAc) to give **2.43** (4.98 g, 4.53 mmol, 85%) as a white solid. R_f = 0.29 (20:1 toluene–EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.04–7.95 (m, 4H, Ar), 7.94–7.86 (m, 5H, Ar), 7.61–7.35 (m, 13H, Ar), 7.29–7.23 (m, 3H, Ar), 7.23–7.08 (m, 5H, Ar), 5.69 (app t, *J* = 9.5 Hz, 1H, H-3`), 5.49 (app t, *J* = 7.5 Hz, 1H, H-3``), 5.43 (dd, *J* = 9.6, 7.8 Hz, 1H, H-2`), 5.29 (dd, *J* = 7.7, 5.6 Hz, 1H, H-2``), 4.85 (d, *J* = 5.6 Hz, 1H, H-1``), 4.84–4.79 (m, 2H, H-4``, 1 × PhC$\underline{H}_2$O), 4.70 (d, *J* = 7.9 Hz, 1H, H-1`), 4.68–4.56 (m, 4H, H-6a`, 1 × PhC$\underline{H}_2$O, 2 × $Cl_3CC\underline{H}_2$O), 4.41 (dd, *J* = 12.1, 4.3 Hz, 1H, H-6b`), 4.17 (app t, *J* = 9.5 Hz, 1H, H-4`), 3.75 (ddd, *J* = 9.8, 4.3, 2.0 Hz, 1H, H-5`), 3.68 (dd, *J* = 12.5, 4.4 Hz, 1H, H-5a``), 3.19 (dd, *J* = 12.5, 7.1 Hz, 1H, H-5b``). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 165.8 (C=O), 165.7 (C=O), 165.3 (C=O), 165.1 (C=O), 165.0 (C=O), 153.0 (C=O), 136.57 (Ar), 133.5 (Ar), 133.4 (Ar), 133.2 × 3 (Ar), 129.9 × 3 (Ar), 129.8 × 2 (Ar), 129.7 × 2 (Ar), 129.4 (Ar), 128.8 (Ar),

128.5 × 2 (Ar), 128.4 × 4 (Ar), 128.3 (Ar), 127.9 (Ar), 127.8 (Ar), 101.1 (C-1``), 98.9 (C-1`), 94.0 ($Cl_3\underline{C}CH_2O$), 77.8 (C-4`), 76.9 ($Cl_3C\underline{C}H_2O$), 73.5 (C-3`), 73.1 (C-5`), 72.5 (C-4``), 72.1 (C-2`), 70.3 ($Ph\underline{C}H_2O$), 70.2 (C-3``), 70.1 (C-2``), 62.4 (C-6`), 60.9 (C-5``). HRMS (ESI) calcd for $(M + Na)^+$ $C_{56}H_{47}Cl_3NaO_{17}$: 1119.1771. Found: 1119.1752.



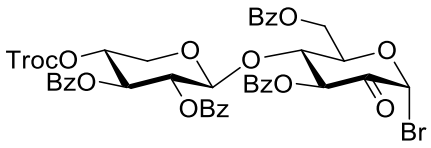
2,3-Di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-2,3,6-tri-*O*-benzoyl-D-glucopyranose (2.53). To a flask containing **2.52** (4.26 g, 3.88 mmol) in EtOAc (40 mL) was added 0.49 M aqueous $NaBrO_3$ (40 mL, 19 mmol). The resultant mixture was stirred vigorously for 10 min, after which additional 0.49 M aqueous $Na_2S_2O_4$ (40 mL, 19.4 mmol) was then introduced dropwise (2 mL/min). The biphasic mixture turned a deep orange slowly over the course of the reaction (3 h). After adding satd. aqueous $Na_2S_2O_3$ to quench the excess reagents, more EtOAc (60 mL) was added and the two phases were separated. The aqueous phase was extracted with EtOAc (2 × 50 mL) and the combined organic layers were subsequently washed with brine and dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a crude residue that was subsequently purified by silica gel chromatography (2:1 hexanes–EtOAc) to afford **2.53** as an off-white solid (3.48 g, 3.45 mmol, 89%, >10:1 α:β). R_f = 0.23 (2:1 hexanes–EtOAc); $[\alpha]_D$ +81.3 (*c*. 0.03, $CHCl_3$); ^1H NMR data of the α-isomer: ^1H NMR (500 MHz, $CDCl_3$, δ_H) 8.07–8.03 (m, 2H, Ar), 7.99–7.87 (m, 8H, Ar), 7.60–7.48 (m, 5H, Ar), 7.47–7.34 (m, 10H, Ar), 6.12 (dd, *J* = 10.2, 9.1 Hz, 1H, H-3`), 5.61 (d, *J* = 3.7 Hz, 1H, H-1`), 5.51 (app t, *J* = 6.9 Hz, 1H, H-3``), 5.31 (dd, *J* = 7.1, 5.1 Hz, 1H, H-2``),

5.18–5.11 (m, 1H, H-2`), 4.94 (d, *J* = 5.1 Hz, 1H, H-1``), 4.83 (td, *J* = 6.4, 4.0 Hz, 1H, H-4``), 4.70–4.64 (m, 3H, $Cl_3CC\underline{H}_2O$, H-6a`), 4.42 (dd, *J* = 12.3, 3.6 Hz, 1H, H-6b`), 4.34 (ddd, *J* = 10.1, 3.6, 2.0 Hz, 1H, H-5`), 4.14 (d, *J* = 10.0 Hz, 1H, H-4`), 3.82 (dd, *J* = 12.6, 4.1 Hz, 1H, H-5a``), 3.24 (dd, *J* = 12.6, 6.3 Hz, 1H, H-5b``), 2.98 (br s, 1H, O<u>H</u>). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 165.9 × 2 (C=O), 165.7 (C=O), 165.1 (C=O), 165.0 (C=O), 133.7 (Ar), 133.6 (Ar), 133.5 (Ar), 133.4 × 2 (Ar), 133.2 × 2 (Ar), 133.1 (Ar), 130.1 (Ar), 130.0 × 3 (Ar), 129.9 ×2 (Ar), 129.8 (Ar), 129.7 × 3 (Ar), 129.0 (Ar), 128.6 (Ar), 128.5 × 3 (Ar), 128.4 × 3 (Ar), 100.9 (C-1``), 94.1 ($Cl_3\underline{C}CH_2O$), 90.3 (C-1`), 78.0 (C-4`), 76.9 ($Cl_3C\underline{C}H_2O$), 72.4 × 2 (C-2`, C-4``), 70.6 (C-3`), 69.9 (C-2``), 69.6 (C-3``), 68.8 (C-5`), 62.2 (C-6`), 60.6 (C-5``). HRMS (ESI) calcd for $(M + Na)^+$ $C_{49}H_{41}Cl_3NaO_{17}$: 1029.1302. Found: 1029.1331.



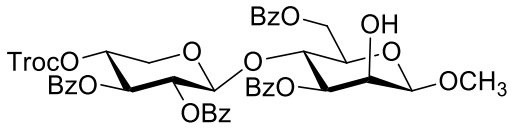
2,3-Di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-1,5-anhydro-2,3,6-tri-*O*-benzoyl-D-*arabino*-hex-1-enitol (2.54). To a flask charged with **2.53** (3.07 g, 3.05 mmol) in pyridine (5 mL) and CH_2Cl_2 (10 mL) was added Ac_2O (1 mL). The reaction mixture was stirred at room temperature for 4 h, after which point CH_3OH (1 mL) was then added. The resultant mixture was concentrated and then co-evaporated with toluene (2x) to remove pyridine before it was dried under vacuum for 1 h. To this mixture was added CH_2Cl_2 (100 mL) under argon. The reaction flask was cooled to 0 °C and then Ac_2O (1.5 mL), followed by 33% HBr–HOAc (4.1 mL, 23.4 mmol), were added. The reaction flask was brought to room temperature, after which the solution was stirred overnight. After 16 h, excess acid was quenched

by adding satd. aqueous $NaHCO_3$ at 0 °C. Upon neutralization, the two phases were separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic phases were then washed with satd. aqueous $NaHCO_3$, brine and dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a crude residue that was then placed under vacuum overnight. To this crude residue, DMF (60 mL) was added under argon. After cooling to −10 °C, DBU (550 μL, 3.68 mmol) was then added and the reaction mixture was stirred for 3 h at −10 °C, after which point the mixture was concentrated. The resultant residue was poured into a mixture of EtOAc (50 mL) and water (500 mL), and the two phases were separated. The organic phase was then washed with water (2 × 100 mL), brine and dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a crude residue that was then purified by silica gel chromatography (40:1 to 35:1 toluene–EtOAc) to afford **2.53** (2.06 g, 2.08 mmol, 60% over 3 steps) as a fluffy white solid. R_f = 0.25 (40:1 toluene–EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.08–8.03 (m, 2H, Ar), 8.03–7.94 (m, 7H, Ar), 7.93–7.87 (m, 2H, Ar), 7.58–7.50 (m, 4H, Ar), 7.50–7.29 (m, 10H, Ar), 6.85 (s, 1H, H-1`), 6.20 (d, *J* = 4.5 Hz, 1H, H-3`), 5.55 (app t, *J* = 5.6 Hz, 1H, H-3``), 5.33 (dd, *J* = 5.7, 3.8 Hz, 1H, H-2``), 5.16 (d, *J* = 3.8 Hz, 1H, H-1``), 4.97 (m, 1H, H-4``), 4.70 (d, *J* = 10.1 Hz, 3H, 2 × $Cl_3CC\underline{H}_2O$, H-6a`), 4.65 (dd, *J* = 12.1, 5.6 Hz, 1H, H-6b`), 4.55 (m, 1H, H-5`), 4.46 (dd, *J* = 6.4, 4.5 Hz, 1H, H-4`), 4.32 (dd, *J* = 13.0, 3.3 Hz, 1H, H-5a``), 3.67 (dd, *J* = 13.0, 4.9 Hz, 1H, H-5a``). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 165.9 (C=O), 165.8 (C=O), 165.2 (C=O), 165.1 (C=O), 164.9 (C=O), 153.2 (C=O), 140.0 (C-1`), 133.7 (Ar), 133.5 × 2 (Ar), 133.4 (Ar), 133.2 (Ar), 130.1 × 2 (Ar), 130.0 (Ar), 129.8 (Ar), 129.7 × 2 (Ar), 129.5 (Ar), 129.3 (Ar), 129.0 (Ar), 128.9 × 2 (Ar), 128.6 × 2 (Ar), 128.5 (Ar), 128.4 × 2 (Ar), 127.5 (C-2`), 99.7 (C-1``), 94.1 ($Cl_3\underline{C}CH_2O$), 76.8 ($Cl_3C\underline{C}H_2O$), 75.1 (C-4`), 74.82 (C-5`), 71.8 (C-4``), 68.8 × 2 (C-3`, C-2``), 68.2 (C-3``), 61.5 (C-6`), 59.9 (C-5``).



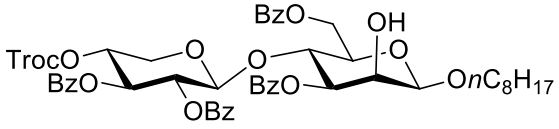
2,3-Di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzoyl-α-D-*arabino*-hexopyranos-2-ulosyl bromide (2.43). To a flask containing **2.53** (1.01 g, 1.02 mmol) and 3 Å M.S. (beads, 200 mg) was added CH_2Cl_2 (20 mL) under argon. The mixture was then stirred for 1 h before it was cooled to 0 °C before CH_3OH (50 μL, 1.24 mmol) and NBS (190 mg, 1.07 mmol) were added in this order. The reaction mixture was then brought to room temperature and stirred for 1 h before it was poured over an ice-cold satd. aqueous $Na_2S_2O_3$. To this mixture was added CH_2Cl_2 (100 mL) and the two phases were separated. The aqueous phase was then extracted with CH_2Cl_2 (2 × 20 mL) and the combined organic layers were washed thoroughly with ice-cold water, brine and dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate afforded **2.43** together with traces of methyl benzoate as off-white foam. This compound was used without further purification in the next step. ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.19–8.13 (m, 2H, Ar), 8.06–8.02 (m, 2H, Ar), 7.99–7.88 (m, 4H, Ar), 7.66–7.61 (m, 1H, Ar), 7.58–7.37 (m, 9 H, Ar), 7.31–7.27 (m, 2H, Ar), 6.38 (s, 1H, H-1`), 6.34 (d, $J$ = 9.2 Hz, 1H, H-3`), 5.53 (app t, J = 6.4 Hz, 1H, H-3``), 5.30 (dd, $J$ = 6.5, 4.5 Hz, 1H, H-2``), 5.02 (d, J = 4.5 Hz, 1H, H-1``), 4.90–4.85 (m, 1H, H-4``), 4.82 (dd, J = 12.6, 1.5 Hz, 1H, H-6a`), 4.72–4.64 (m, 2H, 2 × $Cl_3CC\underline{H}_2O$), 4.57–4.46 (m, 3H, H-6b`, H-4`, H-5`), 4.01 (dd, J = 12.8, 3.8 Hz, 1H, H-5a``), 3.38 (dd, $J$ = 12.7, 5.7 Hz, 1H, H-5b``). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 188.9 (C-2`), 165.5 (C=O), 165.1 (C=O), 165.0 (C=O), 164.9 (C=O), 153.1 (C=O), 133.9 (Ar), 133.8 (Ar), 133.6 (Ar), 133.3 (Ar), 132.9 (Ar), 130.2 (Ar), 130.0 × 2 (Ar), 129.9 × 3 (Ar), 129.7 (Ar), 129.6 (Ar), 129.3 (Ar), 128.8 (Ar), 128.7 × 2 (Ar), 128.6 × 2 (Ar), 128.5 (Ar), 128.4 × 3 (Ar), 100.1

(C-1``), 94.0 ($Cl_3\underline{C}CH_2O$), 83.2 (C-1`), 76.8 ($Cl_3C\underline{C}H_2O$), 76.5 (C-4`), 74.1 (C-3`), 73.7 (C-5`), 71.9 (C-4``), 69.2 (C-2``), 68.8 (C-3``), 61.2 (C-6`), 60.4 (C-5``).



Methyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzoyl-β-D-mannopyranoside (2.55). To a flask containing **2.43** (141 mg, 0.146 mmol) in CH_2Cl_2 (5 mL) was added 3 Å M.S. powder (40 mg) under argon. The reaction mixture was stirred for 1 h before CH_3OH (120 μL, 2.92 mmol), followed by Ag_2CO_3 (200 mg, 0.73 mmol), were introduced. The reaction mixture was then stirred in the dark for 8 h. Filtration of the mixture, followed by concentration of the filtrate, led to a crude residue that was dried via toluene co-evaporation (2x) and subsequently placed under vacuum for 1 h. The crude residue was re-dissolved in THF (5 mL) and cooled to −15 °C under argon, before adding LTBA (45.5 mg, 0.179 mmol) in two portions over 1 min. After 30 min, glacial AcOH (0.5 mL) was added, and the resultant mixture concentrated to a crude residue before EtOAc (10 mL) was added, followed by satd. aqueous $NaHCO_3$. The two phases were separated and the aqueous phase was extracted with EtOAc (2 × 10 mL). The combined organic layers were then washed with brine and dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate, led to a crude residue that was then purified by silica gel chromatography (2:1 hexanes–acetone) to yield **2.55** (80.4 mg, 0.088 mmol, 60% over 3 steps from glycal **2.54**) as a white solid. R_f = 0.28 (2:1 hexanes–acetone); $[\alpha]_D$ +14.2 (*c*. 0.1, $CHCl_3$); ^{1}H NMR (700 MHz, $CDCl_3$,, δ_H) 8.22–8.17 (m, 2H, Ar), 7.95–7.87 (m, 6H, Ar), 7.62–7.58 (m, 1H, Ar), 7.56–7.47 (m, 4H, Ar), 7.43–7.35 (m,

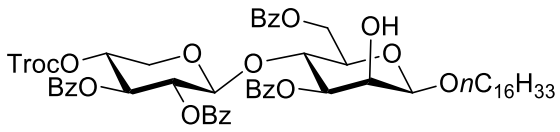
5H, Ar), 7.25 (m, 2H, Ar), 5.51 (app t, J = 7.3 Hz, 1H, H-3``), 5.32–5.26 (m, 2H, H-2``, H-3`), 4.91 (d, J = 5.5 Hz, 1H, H-1``), 4.85 (app td, $J$ = 7.2, 4.4 Hz, 1H, H-4``), 4.69–4.61 (m, 3H, 2 × $Cl_3CC\underline{H}_2O$, H-6a`), 4.54 (d, $J$ = 0.9 Hz, 1H, H-1`), 4.44 (app t, J = 9.3 Hz, 1H, H-4`), 4.40 (dd, $J$ = 11.9, 4.5 Hz, 1H, H-6b`), 4.23 (app d, J = 3.0 Hz, 1H, H-2`), 3.88 (dd, J = 12.6, 4.4 Hz, 1H, H-5a``), 3.65 (ddd, $J$ = 9.4, 4.5, 2.2 Hz, 1H, H-5`), 3.50 (s, 3H, $OCH_3$), 3.30 (dd, $J$ = 12.6, 7.2 Hz, 1H, H-5b``). ^{13}C NMR (175 MHz, $CDCl_3$, δ_C) 165.8 (C=O), 165.7 (C=O), 165.0 × 2 (C=O), 153.0 (C=O), 133.5 (Ar), 133.4 (Ar), 133.3 (Ar), 133.0 (Ar), 129.9 × 2 (Ar), 129.8 × 4 (Ar), 129.7 (Ar), 129.6 (Ar), 128.8 (Ar), 128.6 (Ar), 128.5 (Ar), 128.4 × 2 (Ar), 128.3 (Ar), 100.7 (C-1``), 100.2 (C-1`), 94.0 ($Cl_3\underline{C}CH_2O$), 76.9 ($Cl_3C\underline{C}H_2O$), 74.2 (C-4`), 74.1 (C-3`), 73.3 (C-5`), 72.5 (C-4``), 70.2 (C-2``), 70.1 (C-3``), 69.3 (C-2`), 62.7 (C-6`), 60.9 (C-5``), 57.0 ($O\underline{C}H_3$). HRMS (ESI) calcd for $(M + NH_4)^+$ $C_{43}H_{43}Cl_3NO_{16}$: 934.1642. Found: 934.1646.



***n*-Octyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzoyl-β-D-mannopyranoside (2.56).** To a flask containing **2.43** (264 mg, 0.274 mmol) in CH_2Cl_2 (10 mL) was added 3 Å M.S. powder (90 mg) under argon. The reaction mixture was stirred for 1 h before *n*-$C_8H_{17}OH$ (90 μL, 0.570 mmol), followed by Ag_2CO_3 (377 mg, 1.37 mmol) were introduced. The reaction mixture was then stirred in the dark for 4 h. Filtration of the mixture, followed by concentration of the filtrate led to a crude residue that was dried via toluene co-evaporation (2x) and subsequently placed under vacuum for 1 h. The crude residue was re-dissolved in THF (8 mL) and cooled to −15 °C under argon, before adding LTBA

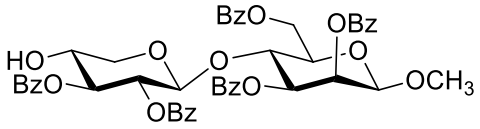
(90.6 mg, 0.356 mmol) in two portions over 1 min. After 30 min, glacial AcOH (1.0 mL) was added, and the resultant mixture concentrated to a crude residue before EtOAc (20 mL) was added, followed by satd. aqueous $NaHCO_3$. The two phases were separated and the aqueous phase was extracted with EtOAc (3 × 15 mL). The combined organic layers were then washed with brine and dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a crude residue that was purified by silica gel chromatography (7:2 to 3:1 hexanes–EtOAc) to afford **2.56** (176 mg, 0.173 mmol, 63% over 3 steps from glycal **2.54**) as a white solid. R_f = 0.33 (3:1 hexanes–EtOAc); $[\alpha]_D$ +11.4 (*c*. 0.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) δ 8.23–8.15 (m, 2H, Ar), 7.96–7.85 (m, 5H, Ar), 7.63–7.57 (m, 1H, Ar), 7.57–7.44 (m, 4H, Ar), 7.44–7.33 (m, 5H, Ar), 7.28–7.19 (m, 3H), 5.51 (app t, *J* = 7.3 Hz, 1H, H-3``), 5.31–5.24 (m, 2H, H-2``, H-3`), 4.91 (d, *J* = 5.5 Hz, 1H, H-1``), 4.85 (app td, *J* = 7.1, 4.3 Hz, 1H, H-4``), 4.70–4.59 (m, 4H, H-6a`, 2 × $Cl_3CC\underline{H}_2O$, H-1`), 4.43 (app t, *J* = 9.2 Hz, 1H, H-4`), 4.39 (dd, *J* = 12.0, 4.8 Hz, 1H, H-6b`), 4.22 (app d, *J* = 3.1 Hz, 1H, H-2`), 3.89 (dd, *J* = 12.5, 4.3 Hz, 1H, H-5a``), 3.82 (dt, *J* = 9.8, 6.7 Hz, 1H, 1 × $OC\underline{H}_2(CH_2)_6CH_3$), 3.65 (ddd, *J* = 9.6, 4.8, 2.2 Hz, 1H, H-5`), 3.49 (dt, *J* = 9.9, 6.9 Hz, 1H, 1 × $OC\underline{H}_2(CH_2)_6CH_3$), 3.31 (dd, *J* = 12.5, 7.1 Hz, 1H, H-5b``), 1.55 (app p, *J* = 7.2 Hz, 2H, 2 × $OCH_2(C\underline{H}_2)_6CH_3$), 1.34–1.15 (m, 10H, 10 × $OCH_2(C\underline{H}_2)_6CH_3$), 0.85 (t, *J* = 6.9 Hz, 3H, $OCH_2(CH_2)_6C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 165.8 × 2 (C=O), 165.0 × 2 (C=O), 153.1 (C=O), 133.5 × 2 (Ar), 133.4 (Ar), 133.0 × 2 (Ar), 129.9 × 2 (Ar), 129.8 × 2 (Ar), 129.7 (Ar), 128.8 (Ar), 128.6 × 2 (Ar), 128.5 (Ar), 128.4 (Ar), 128.3 (Ar), 100.7 (C-1``), 99.2 (C-1`), 94.1 ($Cl_3\underline{C}CH_2O$), 76.9 ($Cl_3C\underline{C}H_2O$), 74.2 × 2 (C-4`, C-3`), 73.2 (C-5`), 72.5 (C-4``), 70.2 (C-2``), 70.1 (C-3``), 69.9 ($O\underline{C}H_2(CH_2)_6CH_3$), 69.40 (C-2`), 62.8 (C-6`), 60.9 (C-5``), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 ($OCH_2(\underline{C}H_2)CH_3$), 29.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 25.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_6CH_3$),

14.1 ($OCH_2(CH_2)_6\underline{C}H_3$). HRMS (ESI) calcd for $(M + Na)^+$ $C_{50}H_{53}Cl_3NaO_{16}$: 1037.2291. Found: 1037.2305.



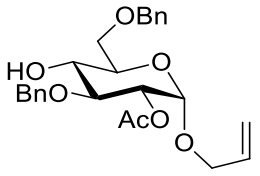
***n*-Hexadecyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzoyl-β-D-mannopyranoside (2.57).** To a flask containing **2.43** (174 mg, 0.181 mmol) in CH_2Cl_2 (10 mL) was added 3 Å M.S. powder (100 mg) under argon. The reaction mixture was stirred for 1 h before *n*-$C_{16}H_{33}OH$ (110 mg, 0.452 mmol), followed by Ag_2CO_3 (250 mg, 0.91 mmol) were introduced. The reaction mixture was then stirred in the dark for 2 h. Filtration of the mixture, followed by concentration of the filtrate led to a crude residue that was dried via toluene co-evaporation (2x) and subsequently placed on vacuum for 1 h. The crude residue was re-dissolved in THF (6 mL) and cooled to −15 °C under argon, before adding LTBA (92.3 mg, 0.360 mmol) in two portions over 1 min. After 30 min, glacial AcOH (1.0 mL) was added, and the resultant mixture was concentrated to a crude residue before EtOAc (20 mL) was added, followed by satd. aqueous $NaHCO_3$. The two phases were separated and the aqueous phase was extracted with EtOAc (2 × 10 mL). The combined organic layers were then washed with brine and dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a crude residue that was then purified by silica gel chromatography (7:2 hexanes–EtOAc) to yield **2.57** (138 mg, 0.122 mmol, 67% over 3 steps from glycal **2.54**) as a white solid. R_f = 0.29 (7:2 hexanes–EtOAc); $[\alpha]_D$ +12.0 (*c*. 0.4, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$, δ_H) 8.25–8.17 (m, 2H, Ar), 7.96–7.87 (m, 6H, Ar), 7.65–7.57 (m, 1H, Ar), 7.56–7.46 (m,

4H, Ar), 7.45–7.35 (m, 5H, Ar), 7.25–7.16 (m, 2H, Ar), 5.52 (app t, J = 7.3 Hz, 1H, H-3``), 5.32–5.26 (m, 2H, H-2``, H-3`), 4.92 (d, J = 5.5 Hz, 1H, H-1``), 4.86 (app td, $J$ = 7.1, 4.3 Hz, 1H, H-4``), 4.71–4.60 (m, 4H, H-6a`, 2 × $Cl_3CC\underline{H}_2O$, H-1`), 4.44 (app t, J = 9.3 Hz, 1H, H-4`), 4.40 (dd, $J$ = 12.0, 4.7 Hz, 1H, H-6b`), 4.23 (s, 1H, H-2`), 3.90 (dd, J = 12.5, 4.3 Hz, 1H, H-5a``), 3.83 (dt, $J$ = 9.6, 6.7 Hz, 1H, 1 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 3.65 (ddd, $J$ = 9.4, 4.6, 2.1 Hz, 1H, H-5`), 3.50 (dt, $J$ = 9.7, 6.9 Hz, 1H, 1 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 3.32 (dd, $J$ = 12.5, 7.1 Hz, 1H, H-5b``), 2.31 (d, J = 2.6 Hz, 1H, O$\underline{H}$), 1.64–1.57 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 1.35–1.19 (m, 26H, 26 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 0.89 (t, J = 6.9 Hz, 3H, $OCH_2(CH_2)_{14}C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 165.9 (C=O), 165.8 (C=O), 165.0 × 2 (C=O), 153.1 (C=O), 133.5 × 2 (Ar), 133.4 (Ar), 133.0 × 2 (Ar), 129.9 × 3 (Ar), 129.7 (Ar), 128.9 (Ar), 128.6 × 2 (Ar), 128.5 (Ar), 128.4 × 2 (Ar), 100.7 (C-1``), 99.2 (C-1`), 94.1 ($Cl_3\underline{C}CH_2O$), 77.0 ($Cl_3C\underline{C}H_2O$), 74.2 × 2 (C-4`, C-3`), 73.2 (C-5`), 72.5 (C-4``), 70.2 (C-2``), 70.1 (C-3``), 69.9 ($O\underline{C}H_2(CH_2)_{14}CH_3$), 69.4 (C-2`), 62.8 (C-6`), 60.9 (C-5``), 32.0 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.7 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.7 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.6 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.6 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 25.9 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 14.2 ($OCH_2(CH_2)_{14}\underline{C}H_3$). HRMS (ESI) calcd for $(M + Na)^+$ $C_{58}H_{69}Cl_3NaO_{16}$: 1149.3543. Found: 1149.3542.



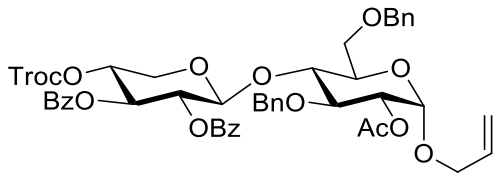
Methyl 2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2,3,6-tri-*O*-benzoyl-β-D-mannopyranoside (2.58). To a solution of **2.55** (53.3 mg, 0.058 mmol) in CH_2Cl_2 (3 mL) was added pyridine (2 mL), DMAP (14.0 mg, 0.121 mmol) and benzoyl chloride (20 μL, 0.17 mmol).

The reaction mixture was stirred overnight. Next, CH_3OH (0.5 mL) was added and the resultant mixture was concentrated and subsequently co-evaporated with toluene (2x). To the resultant crude residue was added CH_2Cl_2 (10 mL) and the solution was then washed with 1.0 M aqueous HCl, followed by satd. aqueous $NaHCO_3$ and brine, before drying over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a crude residue that was re-dissolved in glacial AcOH (1 mL) and THF (1 mL). To this solution was added freshly activated Zn powder (28.7 mg, 0.440 mmol) and the resultant mixture was then stirred for 2 h, after which point Zn powder was then filtered off by passing the mixture through a Celite bed. The resultant filtrate was concentrated and the residual AcOH was removed via toluene co-evaporation (3x). The resultant residue was then purified by silica gel chromatography (3:2 hexanes–acetone), to yield **2.58** (41.5 mg, 0.049 mmol, 89% over 2 steps) as a white fluffy solid. R_f = 0.20 (3:2 hexanes–acetone); $[\alpha]_D$ +12.8 (*c*. 0.5, $CHCl_3$); ^{1}H NMR (700 MHz, $CDCl_3$, δ_H) 8.04–7.94 (m, 6H, Ar), 7.93–7.87 (m, 4H, Ar), 7.65–7.43 (m, 6H, Ar), 7.40–7.28 (m, 7H, Ar), 7.26–7.20 (m, 2H, Ar), 5.82 (d, *J* = 3.3 Hz, 1H, H-2`), 5.52 (dd, *J* = 9.5, 3.3 Hz, 1H, H-3`), 5.34 (dd, *J* = 8.7, 6.5 Hz, 1H, H-2``), 5.12 (app t, *J* = 8.0 Hz, 1H, H-3``), 4.81 (d, *J* = 6.5 Hz, 1H, H-1``), 4.76–4.67 (m, 2H, H-1`, H-6a`), 4.50–4.37 (m, 2H, H-6b`, H-4`), 3.81–3.71 (m, 2H, H-4``, H-5`), 3.64 (dd, *J* = 12.2, 4.7 Hz, 1H, H-5a``), 3.47 (s, 3H, OC<u>H</u>$_3$), 3.06–2.94 (m, 2H, H-5b``, O<u>H</u>). ^{13}C NMR (175 MHz, $CDCl_3$, δ_C) 167.3 (C=O), 165.7 (C=O), 165.6 (C=O), 165.4 (C=O), 165.1 (C=O), 133.7 (Ar), 133.4 (Ar), 133.3 (Ar), 133.2 (Ar), 133.1 (Ar), 130.0 × 3 (Ar), 129.9 (Ar), 129.8 (Ar), 129.7 × 2 (Ar), 129.6 (Ar), 128.7 × 2 (Ar), 128.5 × 2 (Ar), 128.4 × 2 (Ar), 101.4 (C-1``), 100.0 (C-1`), 76.3 (C-3``), 74.3 (C-4`), 73.4 (C-5`), 72.3 (C-3`), 70.8 (C-2``), 69.9 (C-2`), 68.78 (C-4``), 64.8 (C-5``), 62.5 (C-6`), 57.3 (O<u>C</u>H$_3$). HRMS (ESI) calcd for $(M+NH_4)^+$ $C_{47}H_{42}NO_{15}$: 864.2862. Found: 864.2866.



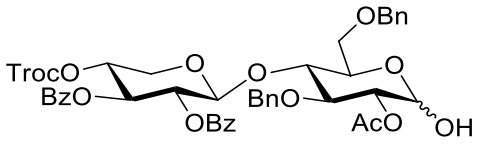
Allyl 2-*O*-acetyl-3,6-di-*O*-benzyl-α-D-glucopyranoside (2.61). To a flask charged with allyl 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside[23] **2.64** (272 mg, 0.68 mmol) was added Ac_2O (1 mL) and pyridine (5 mL). The reaction mixture was stirred at 40 °C overnight and, after cooling to room temperature, CH_3OH (1 mL) was added and the reaction mixture was then co-evaporated with toluene (2x), followed by washes with satd. aqueous $NaHCO_3$ and brine before it was dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a crude residue that was then placed under vacuum overnight. The crude residue was re-dissolved in CH_2Cl_2 (6 mL) and cooled to 0 °C before Et_3SiH (0.9 mL, 5.6 mmol) was added, followed by TFA (0.4 mL, 5.2 mmol) in dropwise over 1 min. The reaction mixture was then stirred at room temperature for 3 h before CH_2Cl_2 (10 mL) was added, followed by satd. aqueous $NaHCO_3$ and the two phases were separated. The aqueous phase was then extracted with CH_2Cl_2 (3 × 15 mL), and the combined organic layers were washed with brine dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a crude residue that was then purified by silica gel chromatography (6:1 hexanes–acetone) to obtain **2.61** as a white solid (232 mg, 0.68 mmol, 77% over 2 steps). R_f = 0.30 (6:1 hexanes–acetone); $[\alpha]_D$ +92.3 (*c*. 0.2, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.38–7.27 (m, 10H, Ar), 5.88 (dddd, *J* = 17.1, 10.3, 6.2, 5.1 Hz, 1H, H_2C=C<u>H</u>CH_2O), 5.29 (dq, *J* = 17.2, 1.7 Hz, 1H, 1 × <u>H</u>$_2$C=CHCH_2O), 5.20 (dq, *J* = 10.4, 1.4 Hz, 1H, 1 × <u>H</u>$_2$C=CHCH_2O), 5.07 (d, *J* = 3.7 Hz, 1H, H-1), 4.87–4.79 (m, 2H, 1 × PhC<u>H</u>$_2$O, H-2), 4.77–4.73 (m, 1H, 1 × PhC<u>H</u>$_2$O), 4.62, 4.56 (ABq, *J* = 12.0 Hz, 2H, 2 × PhC<u>H</u>$_2$O), 4.18 (ddt, *J* = 13.1, 5.1, 1.5 Hz, 1H, 1 × H_2C=CHC<u>H</u>$_2$O), 4.01 (ddt, *J* = 13.1, 6.2, 1.4

Hz, 1H, 1 × H_2C=CHC<u>H_2</u>O), 3.89 (dd, *J* = 10.0, 8.8 Hz, 1H, H-3), 3.82 (app dt, *J* = 9.7, 4.2 Hz, 1H, H-5), 3.77–3.67 (m, 3H, H-4, H-6a, H-6b), 2.49 (d, *J* = 2.5 Hz, 1H, O<u>H</u>), 2.06 (s, 3H, C<u>H_3</u>C(O)O). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 170.3 (C=O), 138.6 (Ar), 137.9 (Ar), 133.6 (H_2C=<u>C</u>HCH_2O), 128.6 × 2 (Ar), 128.4 (Ar), 127.8 (Ar), 127.7 × 2 (Ar), 127.6 (Ar), 117.8 (H_2<u>C</u>=CHCH_2O), 95.2 (C-1), 79.8 (C-3), 75.1 (Ph<u>C</u>H_2O), 73.7 (Ph<u>C</u>H_2O), 73.4 (C-2), 71.5 (C-4), 70.0 (C-5), 69.8 (C-6), 68.3 (H_2C=CH<u>C</u>H_2O), 21.0 (<u>C</u>H_3C(O)O). HRMS (ESI) calcd for $(M + Na)^+$ $C_{25}H_{30}NaO_7$: 465.1884. Found: 465.1885.



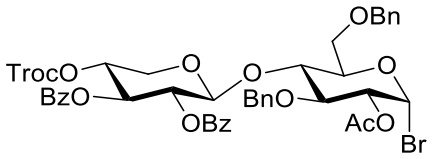
Allyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-α-D-glucopyranoside (2.64). To an oven-dried flask charged with donor **2.44** (391 mg, 0.611 mmol) and acceptor **2.61** (204 mg, 0.461 mmol) was added CH_2Cl_2 (15 mL) and 4 Å M.S. powder (100 mg) under argon. The suspension was stirred for 30 min before it was cooled to 0 °C and then NIS (187 mg, 0.83 mmol) was added, followed by TfOH (0.7 mL, 0.16 mmol, 4% v/v in CH_2Cl_2) after 5 min. The resultant reddish-black mixture was warmed to room temperature and continued to stir for an additional 2 h, after which point Et_3N (1.0 mL) was added, and the mixture was subsequently filtered through Celite. The resultant filtrate was washed with satd. aqueous $Na_2S_2O_3$, water and then brine before it was dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate afforded a crude residue that was briefly treated with PPh_3 (200 mg, 0.763 mmol) in THF–H_2O (9:1, 5 mL) for 1 h. The

resultant solution was then concentrated and re-dissolved in CH_2Cl_2 and washed with water. The two phases were separated and the organic phase was washed with brine and dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a yellow residue that was then purified by silica gel chromatography (20:1 to 16:1 toluene–EtOAc) to give **2.64** as a white solid (430 mg, 0.46 mmol, 75%). R_f = 0.28 (20:1 toluene–EtOAc); $[\alpha]_D$ +53.4 (*c*. 0.2, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.99–7.91 (m, 4H, Ar), 7.57–7.50 (m, 2H, Ar), 7.43–7.29 (m, 13H, Ar), 7.28–7.27 (m, 1H, Ar), 5.80 (dddd, *J* = 17.2, 10.4, 6.1, 5.1 Hz, 1H, H_2C=C$\underline{H}$CH_2O), 5.50 (app t, *J* = 8.1 Hz, 1H, H-3``), 5.32 (dd, *J* = 8.3, 6.4 Hz, 1H, H-2``), 5.22 (dq, *J* = 17.2, 1.6 Hz, 1H, 1 × $\underline{H}_2$C=CHCH_2O), 5.14 (dq, *J* = 10.4, 1.4 Hz, 1H, 1 × $\underline{H}_2$C=CHCH_2O), 5.04–4.96 (m, 2H, H-1`, H-4``), 4.91–4.87 (m, 1H, 1 × PhC$\underline{H}_2$O), 4.85 (dd, *J* = 9.9, 3.8 Hz, 1H, H-2`), 4.78 (d, *J* = 6.4 Hz, 1H, H-1``), 4.73–4.65 (m, 3H, 2 × Cl_3CC$\underline{H}_2$O, 1 × PhC$\underline{H}_2$O), 4.61, 4.35 (ABq, *J* = 12.0 Hz, 2H, 2 × PhC$\underline{H}_2$O), 4.17–4.11 (m, 1H, H-5a``), 4.09–4.00 (m, 2H, H-4`, 1 × $H_2$C=CHC$\underline{H}_2$O), 3.97–3.88 (m, 2H, H-3`, 1 × $H_2$C=CHC$\underline{H}_2$O), 3.68 (dd, *J* = 10.9, 3.1 Hz, 1H, H-6a`), 3.63 (app dt, *J* = 10.1, 2.3 Hz, 1H, H-5`), 3.46 (dd, *J* = 11.0, 1.8 Hz, 1H, H-6b`), 3.33 (dd, *J* = 12.2, 8.3 Hz, 1H, H-5b``), 2.00 (s, 3H, C$\underline{H}_3$C(O)O). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 170.2 (C=O), 165.3 (C=O), 165.1 (C=O), 153.3 (C=O), 138.8 (Ar), 137.9 (Ar), 133.5 (H_2C=$\underline{C}$HCH_2O), 129.9 (Ar), 129.1 (Ar), 129.0 (Ar), 128.7 (Ar), 128.5 × 2 (Ar), 128.3 (Ar), 128.1 (Ar), 128.0 (Ar), 127.6 (Ar), 127.5 (Ar), 117.8 ($H_2\underline{C}$=CHCH_2O), 100.2 (C-1``), 95.1 (C-1`), 94.1 ($Cl_3\underline{C}$C$H_2$O), 78.2 (C-3`), 77.0 ($Cl_3$C$\underline{C}H_2$O), 76.8 (C-4`), 75.2 (PhC$\underline{H}_2$O), 73.5 (Ph$\underline{C}H_2$O), 73.1 (C-2`, C-4``), 71.3 (C-3``), 71.0 (C-2``), 70.2 (C-5`), 68.4 ($H_2$C=CH$\underline{C}H_2$O), 67.6 (C-6`), 61.3 (C-5``), 20.9 ($\underline{C}H_3$C(O)O). HRMS (ESI) calcd for $(M + NH_4)^+$ $C_{47}H_{51}Cl_3NO_{15}$: 974.2319. Found: 974.2323.



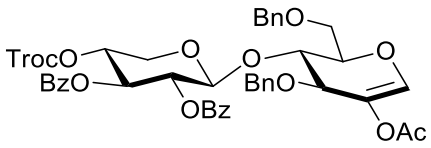
2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-D-glucopyranose (2.65). To a flask charged with **2.64** (740 mg, 0.77 mmol) in THF was added $[Ir(COD)(PMePh_2)_2]PF_6$ (4.8 mg, 5.7 μmol) under argon. The reddish solution was then degassed and flushed with H_2 gas for total of 2 minutes, during which a gradual decolourisation was observed. This purging cycle was repeated twice more with H_2 gas before replacing the reaction under argon. The reaction mixture was stirred at room temperature for 8 h, after which it was concentrated to a crude residue that was re-dissolved in acetone–H_2O (20 mL, 9:1). To this mixture was added HgO (335 mg, 1.55 mmol), followed by dropwise addition of a solution of $HgCl_2$ (418 mg, 1.54 mmol) in acetone–H_2O (5 mL, 9:1) over 5 min. The resultant yellowish suspension was then stirred at room temperature overnight. Subsequent filtration through a Celite bed afforded a yellowish filtrate that was then concentrated to a syrupy residue. This residue was re-dissolved in EtOAc (100 mL) and the resulting solution was washed with satd. aqueous KI and brine before it was dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate afforded a crude solid that was then subjected to purification by silica gel chromatography (3:1 hexanes–acetone) to yield **2.65** (529 mg, 0.57 mmol, 75%, 3:2 α:β) as a white fluffy solid. R_f = 0.35 (6:1 CH_2Cl_2–EtOAc); $[\alpha]_D$ +31.1 (*c*. 0.3, $CHCl_3$); ^{1}H NMR for α-isomer: (500 MHz, $CDCl_3$, δ_H) 7.99–7.88 (m, 4H, Ar), 7.58–7.49 (m, 2H, Ar), 7.46–7.26 (m, 14H, Ar), 5.56–5.48 (m, 1H, H-3``), 5.37 (app t, *J* = 3.2 Hz, 1H, H-1`), 5.35–5.30 (m, 1H, H-2``), 5.08–4.99 (m, 1H, H-4``), 4.93–4.88 (m, 1H, 1 × PhC$\underline{H}_2$O), 4.86 (dd, *J* = 9.6, 3.7 Hz, 1H, H-2`), 4.81–4.74 (m, 1H, H-1``), 4.74–4.62 (m, 3H, 2 × $Cl_3CC\underline{H}_2O$, 1 × PhC$\underline{H}_2$O), 4.62–4.56 (m,

1H, 1 × PhC<u>H</u>$_2$O), 4.38–4.31 (m, 1H, 1 × PhC<u>H</u>$_2$O), 4.17–4.11 (m, 1H, H-5a``), 4.03–3.93 (m, 2H, H-4`, H-3`), 3.86 (ddd, *J* = 9.5, 3.4, 1.8 Hz, 1H, H-5`), 3.71–3.61 (m, 1H, H-6a`), 3.44 (dd, *J* = 11.0, 1.8 Hz, 1H, H-6b`), 3.40–3.30 (m, 1H, H-5b``), 2.63 (br s, 1H), 1.99 (s, 3H, C<u>H</u>$_3$C(O)O). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 170.1 (C=O), 165.3 (C=O), 165.0 (C=O), 153.3 (C=O), 138.7 (Ar), 138.4 (Ar), 137.8 (Ar), 137.7 (Ar), 133.6 (Ar), 133.5 (Ar), 129.9 × 2 (Ar), 129.0 × 2 (Ar), 128.9 (Ar), 128.8 (Ar), 128.7 (Ar), 128.6 × 2 (Ar), 128.5 × 2 (Ar), 128.4 × 2 (Ar), 128.3 (Ar), 128.2 (Ar), 128.1 (Ar), 127.9 (Ar), 127.8 (Ar), 127.7 (Ar), 127.6 (Ar), 100.3 (C-1``), 94.1 ($Cl_3$<u>C</u>$CH_2O$), 90.5 (C-1`), 77.64 (C-3`), 77.0 ($Cl_3C$<u>C</u>$H_2O$), 76.9 (C-4`), 75.3 (Ph<u>C</u>$H_2O$), 73.5 (Ph<u>C</u>$H_2O$), 73.2 (C-4``), 73.1 (C-2`), 71.3 (C-3``), 71.1 (C-2``), 70.1 (C-5`), 67.7 (C-6`), 61.5 (C-5``), 20.9 (<u>C</u>$H_3C(O)O$). $^1$H NMR for β-isomer: (500 MHz, $CDCl_3$, $\delta_H$) 7.99–7.88 (m, 4H, Ar), 7.58–7.49 (m, 2H, Ar), 7.46–7.26 (m, 14H, Ar), 5.56–5.48 (m, 1H, H-3``), 5.35–5.30 (m, 1H, H-2``), 5.08–4.99 (m, 1H, H-4``), 4.93–4.88 (m, 1H, 1 × PhC<u>H</u>$_2$O), 4.81–4.74 (m, 2H, H-2`, H-1``), 4.74–4.62 (m, 3H, 2 × $Cl_3$CC<u>H</u>$_2$O, 2 × PhC<u>H</u>$_2$O), 4.48 (dd, *J* = 9.6, 8.1 Hz, 1H, H-1`), 4.38–4.31 (m, 1H, 1 × PhC<u>H</u>$_2$O), 4.17–4.11 (m, 1H, H-5a``), 4.08 (dd, *J* = 9.8, 8.9 Hz, 1H, H-4`), 3.71–3.61 (m, 2H, H-6a`, H-3`), 3.53 (dd, *J* = 11.1, 1.8 Hz, 1H, H-6b`), 3.40–3.30 (m, 2H, H-5b``, O<u>H</u>), 3.26 (m, 1H, H-5`), 1.99 (d, *J* = 0.5 Hz, 3H, C<u>H</u>$_3$C(O)O). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 171.6 (C=O), 165.3 (C=O), 165.0 (C=O), 153.3 (C=O), 138.7 (Ar), 138.4 (Ar), 137.8 (Ar), 137.7 (Ar), 133.6 (Ar), 133.5 (Ar), 129.9 × 2 (Ar), 129.0 × 2 (Ar), 128.9 (Ar), 128.8 (Ar), 128.7 (Ar), 128.6 × 2 (Ar), 128.5 × 2 (Ar), 128.4 × 2 (Ar), 128.3 (Ar), 128.2 (Ar), 128.1 (Ar), 127.9 (Ar), 127.8 (Ar), 127.7 (Ar), 127.6 (Ar), 100.4 (C-1``), 95.9 (C-1`), 94.1 ($Cl_3$<u>C</u>$CH_2O$), 80.3 (C-3`), 77.0 ($Cl_3C$<u>C</u>$H_2O$), 76.4 (C-1`), 75.5 (C-2`), 75.1 (Ph<u>C</u>$H_2O$), 74.8 (C-5`), 73.7 (Ph<u>C</u>$H_2O$), 73.2 (C-4``), 71.6 (C-3``), 71.3 (C-2``), 67.5 (C-6`), 61.8 (C-5``), 20.9 (<u>C</u>$H_3C(O)O$). HRMS (ESI) calcd for $(M + Na)^+$ $C_{44}H_{43}Cl_3NaO_{15}$: 939.1560. Found: 939.1567.



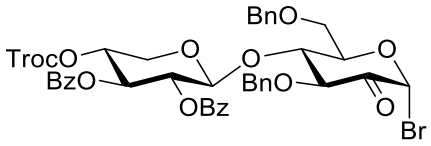
2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-α-D-glucopyranose (2.66). To a flask charged with **2.65** (1.92 g, 2.09 mmol) was added Ac_2O (10 mL) and pyridine (20 mL) and the solution was stirred at room temperature overnight before CH_3OH (10 mL) was added. The reaction mixture was concentrated and then co-evaporated with toluene (2x) to yield a crude residue that was subsequently dried under high vacuum overnight. The crude residue was re-dissolved in CH_2Cl_2 (0.5 mL) and cooled to 0 °C under argon. Then, TMSBr (5.5 mL, 42.0 mmol) was added, and the mixture was subjected to sonication for 1 min to achieve full dissolution. The reaction mixture was subsequently stirred at room temperature, with completion achieved in 3 h. The mixture was diluted with CH_2Cl_2 (50 mL) and the excess TMSBr was quenched by the addition of satd. aqueous $NaHCO_3$ at 0 °C. The two phases were separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 20 mL). The combined organic layers were subjected to additional bicarbonate washes, followed by brine and then dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate yielded **2.66** (1.70 g, 1.70 mmol, 83%) as a fluffy off-white crude that was used without further purification in the next step. R_f = 0.50 (3:1 hexanes–EtOAc). ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.01–7.91 (m, 4H, Ar), 7.58–7.51 (m, 2H, Ar), 7.46–7.27 (m, 14H), 6.59 (d, *J* = 3.9 Hz, 1H, H-1`), 5.52 (app t, *J* = 7.9 Hz, 1H, H-3``), 5.33 (dd, *J* = 8.1, 6.2 Hz, 1H, H-2``), 5.01 (app td, *J* = 8.0, 4.7 Hz, 1H, H-4``), 4.92–4.87 (m, 1H, 1 × PhC$\underline{H}_2$O), 4.83 (d, *J* = 6.3 Hz, 1H, H-1``), 4.77–4.64 (m, 4H, 2 × $Cl_3CC\underline{H}_2O$, 1 × PhC$\underline{H}_2$O, H-2`), 4.60, 4.36 (ABq, *J* = 12.0 Hz, 2H, 2 × PhC$\underline{H}_2$O), 4.20–4.12 (m, 2H, H-5a``, H-4`), 4.00 (app t, *J* = 9.4 Hz, 1H, H-3`), 3.89–3.84 (m, 1H,

H-5`), 3.74 (dd, *J* = 11.5, 2.7 Hz, 1H, H-6a`), 3.47 (dd, *J* = 11.5, 1.7 Hz, 1H, H-6b`), 3.37 (dd, *J* = 12.3, 8.1 Hz, 1H, H-5a``), 2.02 (s, 3H, $CH_3C(O)O$).



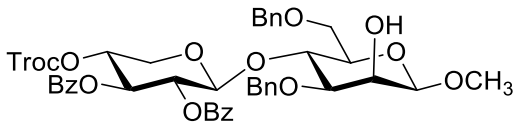
2,3-Di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-1,5-anhydro-3,6-di-*O*-benzyl-D-*arabino*-hex-1-enitol (2.67). To a flask containing crude **2.66** (1.35 g, 1.41 mmol) in DMF (6 mL) was added DBU (230 μL, 1.5 mmol) via syringe under argon and the resultant mixture was stirred for 1 h. The solution was then poured into a mixture of EtOAc (50 mL) and water (500 mL) and the two phases were separated. The organic phase was washed with water (2 × 100 mL), brine and dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a crude residue that was then purified by silica gel chromatography (20:1 toluene–EtOAc) to obtain **2.68** (760 mg, 0.85 mmol, 60%) as a white solid. R_f = 0.27 (20:1 toluene–EtOAc); $[\alpha]_D$ +15.6 (*c*. 3.9, $CHCl_3$); ^{1}H NMR (700 MHz, $CDCl_3$, δ_H) 8.09–8.00 (m, 4H, Ar), 7.58–7.54 (m, 2H, Ar), 7.44–7.40 (m, 4H, Ar), 7.35–7.26 (m, 10H, Ar), 6.60 (d, *J* = 1.0 Hz, 1H, H-1`), 5.51 (app t, *J* = 5.4 Hz, 1H, H-3``), 5.27 (dd, *J* = 5.4, 3.8 Hz, 1H, H-2``), 5.09 (d, *J* = 3.8 Hz, 1H, H-1``), 4.94 (app td, *J* = 5.1, 3.3 Hz, 1H, H-4``), 4.76, 4.75 (ABq, *J* = 1.3 Hz, 2H, $Cl_3CC\underline{H}_2O$), 4.63–4.57 (m, 3H, H-3`, 2 × $PhC\underline{H}_2O$), 4.51, 4.50 (ABq, *J* = 2.0 Hz, 2H, 2 × $PhC\underline{H}_2O$), 4.45 (dd, *J* = 13.1, 3.3 Hz, 1H, H-5a``), 4.31 (dd, *J* = 7.5, 5.5 Hz, 1H, H-4`), 4.10 (app dt, *J* = 7.8, 4.0 Hz, 1H, H-5`), 3.79 (dd, *J* = 10.9, 4.5 Hz, 1H, H-6a`), 3.68 (dd, *J* = 10.9, 3.5 Hz, 1H, H-6b`), 3.63 (dd, *J* = 13.0, 5.0, 1H, H-5b``), 2.06 (s, 3H, $CH_3C(O)O$). ^{13}C NMR (175 MHz, $CDCl_3$, δ_C) 169.4 (C=O), 165.1 (C=O), 165.0 (C=O), 153.3 (C=O), 138.9 (C-

1`), 138.1 (Ar), 137.8 (Ar), 133.6 (Ar), 133.5 (Ar), 130.1 × 2 (Ar), 129.5 (C-2`), 129.1 (Ar), 129.0 (Ar), 128.6 (Ar), 128.5 × 3 (Ar), 128.0 (Ar), 127.9 × 2 (Ar), 127.8 (Ar), 99.0 (C-1``), 94.2 ($Cl_3\underline{C}CH_2O$), 77.2 (C-5`), 77.1 ($Cl_3C\underline{C}H_2O$), 74.3 (C-3`), 73.5 ($Ph\underline{C}H_2O$), 73.0 (C-4`), 71.9 (C-4``), 70.1 ($Ph\underline{C}H_2O$), 68.8 (C-2``), 68.2 (C-3``), 67.4 (C-6`), 59.7 (C-5``), 20.7 ($\underline{C}H_3C(O)O$). HRMS (ESI) calcd for $(M + Na)^+$ $C_{44}H_{41}Cl_3NaO_{14}$: 921.1454. Found: 921.1467.



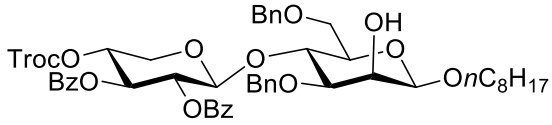
2,3-Di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-α-D-*arabino*-hexopyranos-2-ulosyl bromide (2.60). To a flask containing **2.67** (100 mg, 0.11 mmol) was added CH_2Cl_2 (5 mL) under argon. The resultant solution was then cooled to 0 °C. To this solution was added was added Br_2 (7 μL, 0.1 mmol) followed by CH_3OH (4.5 μL, 0.11 mmol). The mixture was then stirred for 20 min at 0 °C after which point it was concentrated and co-evaporated with toluene (2x) at room temperature. The resultant pale yellow syrup was then used without further purification in the next step. ^1H NMR (500 MHz, $CDCl_3$, δ_H) 8.03–7.97 (m, 4H, Ar), 7.61–7.51 (m, 2H, Ar), 7.48–7.26 (m, 12H, Ar), 7.24–7.17 (m, 2H, Ar), 6.35 (s, 1H, H-1`), 5.51 (app t, *J* = 6.5 Hz, 1H, H-3``), 5.29 (dd, *J* = 6.6, 4.8 Hz, 1H, H-2``), 5.03 (d, *J* = 10.7 Hz, 1H, 1 × $PhC\underline{H}_2O$), 4.98 (d, *J* = 4.8 Hz, 1H, H-1``), 4.94 (app td, *J* = 6.1, 3.8 Hz, 1H, H-4``), 4.83 (d, *J* = 9.9 Hz, 1H, H-3`), 4.75, 4.72 (ABq, *J* = 12 Hz, 2H, 2 × $Cl_3CC\underline{H}_2O$), 4.62 (d, *J* = 10.7 Hz, 1H, 1 × $PhC\underline{H}_2O$), 4.45, 4.40 (ABq, *J* = 12 Hz, 2H, 2 × $PhC\underline{H}_2O$), 4.34 (app t, *J* = 9.9 Hz, 1H, H-4`), 4.27 (dd, *J* = 12.8, 3.9 Hz, 1H, H-5a``), 4.19–4.13 (m, 1H, H-5`), 3.83 (dd, *J* = 11.5, 2.7 Hz, 1H, H-6a`), 3.61 (dd, *J* = 11.3, 1.8 Hz, 1H, H-6b`), 3.39 (dd, *J* = 12.8, 6.1 Hz, 1H,

H-5b``). $^{13}$C NMR (125 MHz, $CDCl_3$, $\delta_C$) 193.9 (C-2`), 165.2 (C=O), 165.0 (C=O), 153.3 (C=O), 137.3 (Ar), 137.1 (Ar), 133.7 × 2 (Ar), 130.0 (Ar), 129.9 (Ar), 129.0 (Ar), 128.9 (Ar), 128.6 × 3 (Ar), 128.5 (Ar), 128.2 × 2 (Ar), 128.0 (Ar), 127.8 (Ar), 98.9 (C-1``), 94.1 ($Cl_3\underline{C}CH_2O$), 85.6 (C-1`), 79.6 (C-3`), 76.9 ($Cl_3C\underline{C}H_2O$), 75.5 (C-4`), 75.4 (C-5`), 74.0 ($Ph\underline{C}H_2O$), 73.4 ($PhCH_2O$), 72.3 (C-4``), 69.7 (C-3``), 69.6 (C-2``), 66.7 (C-6`), 60.4 (C-5``).



Methyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranoside (2.68). To a flask containing **2.60** (134 mg, 0.143 mmol) in CH_2Cl_2 (4 mL) was added 3 Å M.S. powder (70 mg) under argon. The reaction mixture was stirred for 1 h before CH_3OH (18 μL, 0.44 mmol), followed by Ag_2CO_3 (221 mg, 0.80 mmol) were introduced. The reaction mixture was stirred for 2 h in the dark, after which point the reaction was complete as determined by TLC analysis. The mixture was then filtered through a Celite bed. Concentration of the filtrate led to a crude residue that was dried via toluene co-evaporation (2x) and subsequently placed under vacuum for 1 h. The crude residue was re-dissolved in THF (5 mL) and cooled to −15 °C under argon, before adding LTBA (45.6 mg, 0.180 mmol) in one portion. After 30 min, glacial AcOH (0.5 mL) was then added and the mixture was concentrated to a crude residue. To this crude residue was added EtOAc (15 mL) followed by satd. aqueous $NaHCO_3$. The two phases were separated and the aqueous phase was extracted with EtOAc (2 × 15 mL). The combined organic layers were then washed with brine and dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a

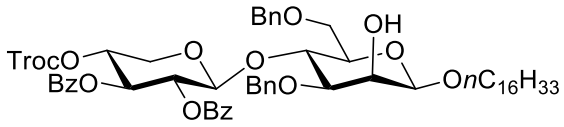
crude residue that was purified by silica gel chromatography (8:1 CH_2Cl_2–EtOAc) to yield **2.68** (82.7 mg, 0.093 mmol, 65% over 3 steps from glycal **2.67**) as a white solid. R_f = 0.24 (8:1 CH_2Cl_2–EtOAc); $[\alpha]_D$ −1.2 (*c*. 0.2, CH_2Cl_2); ^{1}H NMR (700 MHz, $CDCl_3$, δ_H) 7.97–7.92 (m, 4H, Ar), 7.55–7.50 (m, 2H, Ar), 7.42–7.32 (m, 11H, Ar), 7.32–7.27 (m, 3H), 5.53 (app t, *J* = 8.1 Hz, 1H, H-3``), 5.32 (dd, *J* = 8.2, 6.4 Hz, 1H, H-2``), 5.04 (app td, *J* = 8.2, 4.8 Hz, 1H, H-4``), 4.87 (d, *J* = 6.4 Hz, 1H, H-1``), 4.76–4.72 (m, 2H, 2 × PhC$\underline{H}_2$O), 4.71, 4.68 (ABq, *J* = 11.9 Hz, 2H, 2 × $Cl_3CC\underline{H}_2O$), 4.53, 4.33 (ABq, *J* = 12.0 Hz, 2H, 2 × PhC$\underline{H}_2$O), 4.26 (d, *J* = 1.0 Hz, 1H, H-1`), 4.23 (dd, *J* = 12.3, 4.9 Hz, 1H, H-5a``), 4.19 (app t, *J* = 9.2 Hz, 1H, H-4`), 4.06–4.03 (br s, 1H, H-2`), 3.63 (dd, *J* = 11.0, 4.3 Hz, 1H, H-6a`), 3.59 (dd, *J* = 10.9, 2.0 Hz, 1H, H-6b`), 3.51–3.46 (m, 4H, OC$\underline{H}_3$, H-3`), 3.39 (dd, *J* = 12.3, 8.3 Hz, 1H, H-5b``), 3.26 (ddd, *J* = 9.5, 4.4, 2.1 Hz, 1H, H-5`), 2.38 (br s, 1H, O$\underline{H}$). ^{13}C NMR (175 MHz, $CDCl_3$, δ_C) 165.2 (C=O), 165.1 (C=O), 153.3 (C=O), 138.2 (Ar), 138.0 (Ar), 133.5 × 2 (Ar), 129.9 × 2 (Ar), 129.1 (Ar), 128.5 × 2 (Ar), 128.0 × 2 (Ar), 127.9 (Ar), 127.8 (Ar), 100.8 (C-1``), 100.2 (C-1`), 94.1 ($Cl_3\underline{C}CH_2O$), 79.7 (C-3`), 77.0 ($Cl_3C\underline{C}H_2O$), 74.9 (C-5`), 74.1 (C-4`), 73.4 (Ph$\underline{C}H_2$O), 73.2 (C-4``), 72.4 (Ph$\underline{C}H_2$O), 71.2 (C-3``), 71.0 (C-2``), 68.5 (C-2`), 68.3 (C-6`), 61.4 (C-5``), 57.0 (O$\underline{C}H_3$). HRMS (ESI) calcd for $(M+NH_4)^+$ $C_{43}H_{47}Cl_3NO_{14}$: 906.2057. Found: 906.2063.



***n*-Octyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranoside (2.69).** To a flask containing **2.60** (103 mg, 0.11 mmol) in CH_2Cl_2 (4 mL) was added 3 Å M.S. powder (40 mg) under argon. The reaction mixture was

stirred for 1 h before *n*-$C_8H_{17}OH$ (45 μL, 0.28 mmol), followed by Ag_2CO_3 (161 mg, 0.58 mmol) were subsequently introduced. The reaction mixture was stirred for 2 h in the dark, after which point the reaction was complete as determined by TLC analysis. The mixture was then filtered through a Celite bed. Concentration of the filtrate led to a crude residue that was dried via toluene co-evaporation (2x) and subsequently placed under vacuum for 1 h. The crude residue was re-dissolved in THF (4 mL) and cooled to −15 °C under argon, before adding LTBA (35.5 mg, 0.140 mmol) in one portion. After 30 min, glacial AcOH (0.5 mL) was then added and the mixture was concentrated to a crude residue. To this crude residue was added EtOAc (15 mL) followed by satd. aqueous $NaHCO_3$. The two phases were separated and the aqueous phase was extracted with EtOAc (2 × 15 mL). The combined organic layers were then washed with brine and dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a crude residue that was then purified by silica gel chromatography (5:1 to 4:1 hexanes–acetone) to yield **2.69** (76.1 mg, 0.077 mmol, 70% over 3 steps from glycal **2.67**) as a white solid. R_f = 0.29 (4:1 hexanes–acetone); $[\alpha]_D$ −1.6 (*c*. 0.2, $CHCl_3$); ^{1}H NMR (700 MHz, $CDCl_3$, δ_H) 7.97–7.92 (m, 4H, Ar), 7.55–7.50 (m, 2H, Ar), 7.43–7.26 (m, 14H, Ar), 5.53 (app t, *J* = 8.1 Hz, 1H, H-3``), 5.32 (dd, *J* = 8.3, 6.4 Hz, 1H, H-2``) 5.04 (app td, *J* = 8.1, 4.8 Hz, 1H, H-4``), 4.87 (d, *J* = 6.4 Hz, 1H, H-1``), 4.79–4.75 (m, 1H, 1 × PhC$\underline{H}_2$O), 4.74–4.66 (m, 3H, 1 × PhC$\underline{H}_2$O, 2 × $Cl_3CC\underline{H}_2O$), 4.52, 4.32 (ABq, *J* = 12.0 Hz, 2H, 2 × PhC$\underline{H}_2$O), 4.34 (d, *J* = 1.0 Hz, 1H, H-1`), 4.23 (dd, *J* = 12.3, 4.8 Hz, 1H, H-5a``), 4.18 (app t, *J* = 9.2 Hz, 1H, H-4`), 4.06 (d, *J* = 3.2, 1H, H-2`), 3.85 (dt, *J* = 9.5, 6.7 Hz, 1H, 1 × OC$\underline{H}_2(CH_2)_6CH_3$), 3.61 (dd, *J* = 10.9, 4.3 Hz, 1H, H-6a`), 3.58 (dd, *J* = 10.9, 2.2 Hz, 1H, H-6b`), 3.49 (dd, *J* = 9.0, 3.2 Hz, 1H, H-3`), 3.45–3.36 (m, 2H, 1 × OC$\underline{H}_2(CH_2)_6CH_3$, H-5b``), 3.25 (ddd, *J* = 9.5, 4.3, 2.2 Hz, 1H, H-5`), 1.62–1.54 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_6CH_3$), 1.36–1.17 (m, 10H, 10 × $OCH_2(C\underline{H}_2)_6CH_3$), 0.87 (t, *J* = 7.0 Hz, 3H,

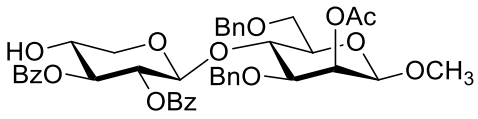
$OCH_2(CH_2)_6C\underline{H}_3$). ^{13}C NMR (175 MHz, $CDCl_3$, δ_C) 165.2 (C=O), 165.1 (C=O), 153.3 (C=O), 138.2 (Ar), 138.0 (Ar), 133.5 (Ar), 133.4 (Ar), 129.9 × 2 (Ar), 129.1 × 2 (Ar), 128.5 (Ar), 128.5 × 2 (Ar), 128.4 (Ar), 128.0 (Ar), 127.9 × 2 (Ar), 127.8 (Ar), 100.3 (C-1``), 99.8 (C-1`), 94.1 ($Cl_3\underline{C}CH_2O$), 79.8 (C-3`), 77.0 ($Cl_3C\underline{C}H_2O$), 74.9 (C-5`), 74.2 (C-4`), 73.4 ($Ph\underline{C}H_2O$), 73.2 (C-4``), 72.2 ($Ph\underline{C}H_2O$), 71.3 (C-3``), 71.1 (C-2``), 69.9 ($O\underline{C}H_2(CH_2)_6CH_3$), 68.7 (C-2`), 68.4 (C-6`), 61.4 (C-5``), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.5 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 26.0 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 14.1 ($OCH_2(CH_2)_6\underline{C}H_3$). HRMS (ESI) calcd for $(M + NH_4)^+$ $C_{50}H_{61}Cl_3NO_{14}$: 1004.3152. Found: 1004.3152.



***n*-Hexadecyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranoside (2.70).** To a flask containing **2.60** (129 mg, 0.138 mmol) in CH_2Cl_2 (5 mL) was added 4 Å M.S. powder (65 mg) under argon. The reaction mixture was stirred for 1 h before *n*-$C_{16}H_{33}OH$ (75 mg, 0.31 mmol), followed by Ag_2CO_3 (210 mg, 0.76 mmol) were introduced. The reaction mixture was stirred for 2 h in the dark, after which point the reaction was complete as determined by TLC analysis. The mixture was then filtered through a Celite bed. Concentration of the filtrate led to a crude residue that was dried via toluene co-evaporation (2x) and subsequently placed under vacuum for 1 h. The crude residue was re-dissolved in THF (5 mL) and cooled to −15 °C under argon, before adding LTBA (42.7 mg, 0.168 mmol) in one portion. After 30 min, glacial AcOH (0.5 mL) was then added and the mixture was concentrated to a crude residue. To this crude residue was added EtOAc (15 mL)

followed by satd. aqueous $NaHCO_3$. The two phases were separated and the aqueous phase was extracted with EtOAc (2 × 15 mL). The combined organic layers were then washed with brine and dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a crude residue that was then purified by silica gel chromatography using (3:1 hexanes–EtOAc) to yield **2.70** (114 mg, 0.104 mmol, 75% over 3 steps from glycal **2.67**) as a white solid. R_f = 0.29 (3:1 hexanes–EtOAc); $[\alpha]_D$ +2.0 (*c*. 0.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.95 (m, 4H, Ar), 7.56–7.48 (m, 2H, Ar), 7.43–7.27 (m, 14H, Ar), 5.53 (app t, *J* = 8.1 Hz, 1H, H-3``), 5.32 (dd, *J* = 8.2, 6.4 Hz, 1H, H-2``), 5.04 (app td, *J* = 8.1, 4.8 Hz, 1H, H-4``), 4.87 (d, *J* = 6.4 Hz, 1H, H-1``), 4.76, 4.72 (ABq, *J* = 11.0 Hz, 2H, 2 × PhC$\underline{H}_2$O), 4.71, 4.68 (ABq, *J* = 11.9 Hz, 2H, 2 × Cl_3CC$\underline{H}_2$O), 4.52, 4.32 (ABq, *J* = 12.1 Hz, 2H, 2 × PhC$\underline{H}_2$O), 4.34 (d, *J* = 1.0 Hz, 1H, H-1`), 4.23 (dd, *J* = 12.3, 4.8 Hz, 1H, H-5a``), 4.18 (app t, *J* = 9.2 Hz, 1H, H-4`), 4.06 (d, *J* = 3.0 Hz, 1H, H-2`), 3.85 (dt, *J* = 9.5, 6.8 Hz, 1H, 1 × OC$\underline{H}_2$($CH_2$)$_{14}$$CH_3$), 3.65–3.55 (m, 2H, H-6a`, H-6b`), 3.49 (dd, *J* = 9.0, 3.2 Hz, 1H, H-3`), 3.46–3.35 (m, 2H, 1 × OC$\underline{H}_2$($CH_2$)$_{14}$$CH_3$, H-5b``), 3.25 (ddd, *J* = 9.5, 4.2, 2.3 Hz, 1H, H-5`), 2.49–2.34 (br s, 1H, O$\underline{H}$), 1.63–1.53 (m, 2H, 2 × OCH_2(C$\underline{H}_2$)$_{14}$$CH_3$), 1.36–1.17 (m, 26H, 26 × OCH_2(C$\underline{H}_2$)$_{14}$$CH_3$), 0.88 (t, *J* = 6.9 Hz, 3H, OCH_2(CH_2)$_{14}$C$\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 165.2 (C=O), 165.1 (C=O), 153.3 (C=O), 138.2 (Ar), 138.0 (Ar), 133.5 (Ar), 133.4 (Ar), 129.9 × 2 (Ar), 129.1 (Ar), 128.5 × 3 (Ar), 128.4 (Ar), 128.0 × 2 (Ar), 127.9 × 2 (Ar), 127.8 (Ar), 100.2 (C-1``), 99.8 (C-1`), 94.1 ($Cl_3$$\underline{C}$$CH_2$O), 79.8 (C-3`), 77.0 ($Cl_3$$\underline{C}$$CH_2$O), 74.9 (C-5`), 74.2 (C-4`), 73.4 (Ph$\underline{C}$$H_2$O), 73.2 (C-4``), 72.2 (Ph$\underline{C}$$H_2$O), 71.3 (C-3``), 71.1 (C-2``), 69.9 (O$\underline{C}$$H_2$($CH_2$)$_{14}$$CH_3$), 68.7 (C-2`), 68.4 (C-6`), 61.4 (C-5``), 32.0 (OCH_2($\underline{C}$$H_2$)$_{14}$$CH_3$), 29.7 × 4 ($OCH_2$($\underline{C}$$H_2$)$_{14}$$CH_3$), 29.6 ($OCH_2$($\underline{C}$$H_2$)$_{14}$$CH_3$), 29.5 × 2 ($OCH_2$($\underline{C}$$H_2$)$_{14}$$CH_3$), 29.4 ($OCH_2$($\underline{C}$$H_2$)$_{14}$$CH_3$), 26.0 ($OCH_2$($\underline{C}$$H_2$)$_{14}$$CH_3$), 22.7

($OCH_2(\underline{C}H_2)_{14}CH_3$), 14.2 ($OCH_2(CH_2)_{14}\underline{C}H_3$). HRMS (ESI) calcd for $(M + NH_4)^+$ $C_{58}H_{77}Cl_3NO_{14}$: 1116.4404. Found: 1116.4411.



Methyl 2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (2.73). To a solution of **2.70** (630 mg, 0.708 mmol) in pyridine (10 mL) was added Ac_2O (2 mL) under argon. The reaction mixture was stirred at 40 °C overnight, cooled to room temperature and concentrated; then pyridine was removed via toluene co-evaporation (2x). The crude product was re-dissolved in CH_2Cl_2 and subsequently washed with 1 M aqueous HCl and brine before the organic layer was dried over Na_2SO_4. Filtration of the mixture followed by concentration of the filtrate led to a thick syrup, that was dissolved in glacial AcOH (6.4 mL). To this solution was added freshly activated Zn dust (3.80 g, 58.1 mmol) and the mixture was stirred for 2 h, before it was subsequently filtered through Celite. The resultant filtrate was concentrated and then residual AcOH was removed via toluene co-evaporation (2x). The crude residue was purified by silica gel chromatography (2:1 to 3:2 hexanes–EtOAc) to obtain **2.73** (429 mg, 0.566 mmol, 80%) as a white foamy solid. R_f = 0.20 (2:1 hexanes–EtOAc); $[\alpha]_D$ +10.6 (*c*. 0.4, $CHCl_3$); ^1H NMR (700 MHz, $CDCl_3$, δ_H) 8.00–7.95 (m, 2H, Ar), 7.93–7.88 (m, 2H, Ar), 7.56–7.49 (m, 2H, Ar), 7.42–7.33 (m, 10H, Ar), 7.33–7.27 (m, 4H, Ar), 5.58 (dd, *J* = 3.5, 1.0 Hz, 1H, H-2`), 5.33 (dd, *J* = 8.9, 7.0 Hz, 1H, H-2``), 5.08 (app t, *J* = 8.5 Hz, 1H, H-3``), 4.80–4.75 (m, 2H, H-1``, 1 × $PhC\underline{H}_2O$), 4.60–4.54 (m, 2H, 2 × $PhC\underline{H}_2O$), 4.33 (d, *J* = 0.9 Hz, 1H, H-1`), 4.30–4.27 (m, 1H, 1 × $PhC\underline{H}_2O$), 4.12–4.07 (m, 2H, H-4`, H-5a``), 3.98–3.90 (m, 1H, H-4``), 3.65 (dd, *J* = 10.9,

4.6 Hz, 1H, H-6a`), 3.62–3.55 (m, 2H, H-6b`, H-3`), 3.45 (s, 3H, OC$\underline{H}_3$), 3.30 (ddd, *J* = 9.6, 4.5, 1.9 Hz, 1H, H-5`), 3.17 (dd, *J* = 12.2, 9.0 Hz, 1H, H-5b``), 2.96 (d, *J* = 5.0 Hz, 1H, OH), 2.18 (s, 3H, C$\underline{H}_3$C(O)O). ^{13}C NMR (175 MHz, $CDCl_3$, δ_C) 170.8 (C=O), 167.6 (C=O), 165.1 (C=O), 138.3 (Ar), 137.7 (Ar), 133.7 (Ar), 133.5 (Ar), 130.0 (Ar), 129.8 (Ar), 129.2 (Ar), 128.9 (Ar), 128.6 (Ar), 128.5 (Ar), 128.4 (Ar), 128.1 (Ar), 128.0 (Ar), 127.9 (Ar), 127.8 (Ar), 100.5 (C-1``), 100.0 (C-1`), 78.3 (C-3`), 77.0 (C-3``), 75.3 (C-5`), 74.1 (C-4`), 73.4 (Ph$\underline{C}H_2$O), 72.0 (Ph$\underline{C}H_2$O), 71.4 (C-2``), 69.3 (C-4``), 68.4 (C-6`), 67.9 (C-2`), 65.2 (C-5``), 57.1 (O$\underline{C}H_3$), 21.3 ($\underline{C}H_3$C(O)O). HRMS (ESI) calcd for $(M + Na)^+$ $C_{42}H_{44}NaO_{13}$: 779.2674. Found: 779.2671.

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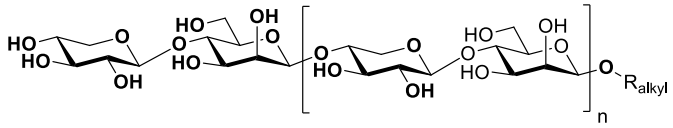
Chapter 3

Total synthesis of xylomannan-based AFGL mimetics via the oxidation–reduction approach: Development of a simultaneous multiple C-2 inversion strategy

3.1 Introduction

As mentioned in the earlier chapters, xylomannan-based AFGLs are the first biological antifreezes compounds that do not contain protein. Since their discovery from *U. ceramboides* in 2009, other freeze tolerant organisms were also reported to produce AFGLs. Reliance on a common xylomannan core in all the isolated AFGLs raises a possibility that the glycan may serve as an ice-binding motif, and is thus essential for TH activity. The function of the lipid, on the other hand, remains unknown. Thus, this makes an intriguing case for investigation into structure–activity relationships, in which synthetic mimetics of AFGLs must be used.

There have been a few reports on the chemical synthesis of AFGLs, yet no details have been disclosed on the antifreeze activity of these compounds. I believed that inclusion of a lipid mimetic would provide crucial hydrophobicity for antifreeze activity. With this in mind, octyl and cetyl lipids were installed to observe the effects of hydrophobicity with methyl glycosides as the controls. Glycan chains with a varying number of disaccharide repeating units up to decasaccharides were targeted to interrogate the effects of increased glycan length on antifreeze activity. The structures of these AFGL targets are shown in Scheme 3-1.



$R_{Alkyl} = CH_3$: **3.1,** n = 0, **3.4,** n = 1, **3.7,** n = 2, **3.10,** n = 3, **3.13,** n = 4,

$R_{Alkyl} = nC_8H_{17}$: **3.2,** n = 0, **3.5,** n = 1, **3.8,** n = 2, **3.11,** n = 3, **3.14,** n = 4,

$R_{Alkyl} = nC_{16}H_{33}$: **3.3,** n = 0, **3.6,** n = 1, **3.9,** n = 2, **3.12,** n = 3, **3.15,** n = 4,

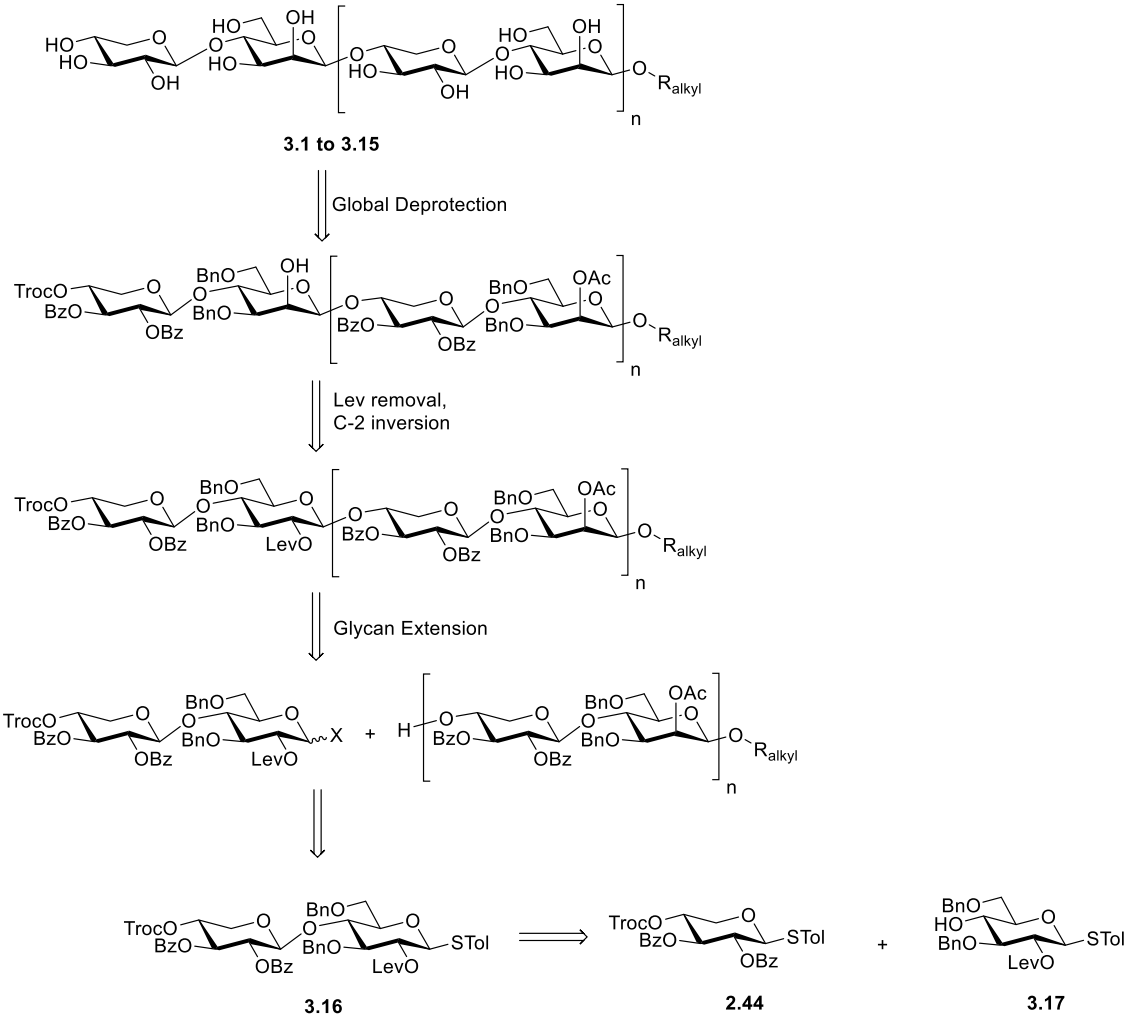
Scheme 3-1: Structures of fifteen xylomannan targets **3.1–3.15**

A major challenge in the chemical synthesis of these xylomannan glycolipids is the presence of multiple β-mannosidic linkages. In Chapter 2, I attempted to address this challenge by using the ulosyl bromide approach[1-4] to construct larger oligosaccharides. Given the numerous issues with this approach, such as the inherent instability of the ulosyl bromides, the requirement of super-stoichiometric amounts of Ag-based promoters for glycosylation and, more critically, the limitation to primary alcohols, I decided to explore alternative, more viable strategies. Inspired by the works of Sinay[5] and Nikolaev[6] on consecutive C-2 epimerisations of glucose residues to reach β-(1→2)-mannans, I decided to embark on a synthetic route that involved the initial construction of β-glucosidic linkages as the key glycan extension step, followed by C-2 inversion via an oxidation–reduction approach. The main advantage in this approach is that the challenging task of constructing β-mannosidic linkages is now broken down into two easier tasks: the first is β-stereocontrolled glucosylation via neighbouring group participation, and the second, is the intrinsic preference of an equatorial hydride approach over an axial route during the reduction of a C-2 ketone generated from the glucoside product.

3.2 Initial retrosynthetic analysis

The retrosynthetic analysis of the xylomannan glycolipids is outlined in Scheme 3-2. It was initially envisioned that all of the targets **3.1–3.15** could be assembled through a protocol involving initial β-glucosylation between a common xyloglucan donor and a xylomannan acceptor (or an aliphatic alcohol), followed by sequential deprotection, oxidation and stereoselective reduction to establish the desired β-mannoside. At this point, the xylomannan product could be transformed into an acceptor for chain extension by acetylation of the newly-formed C-2 of the β-mannoside and then Troc removal to liberate the C-4 hydroxyl group of the

terminal xylose residue. Subsequent iterations of the same glycosylation–inversion protocol would thus allow me to obtain each xylomannan glycolipid of the desired length.



Scheme 3-2: Retrosynthetic analysis of xylomannan glycolipids via consecutive C-2 inversions approach

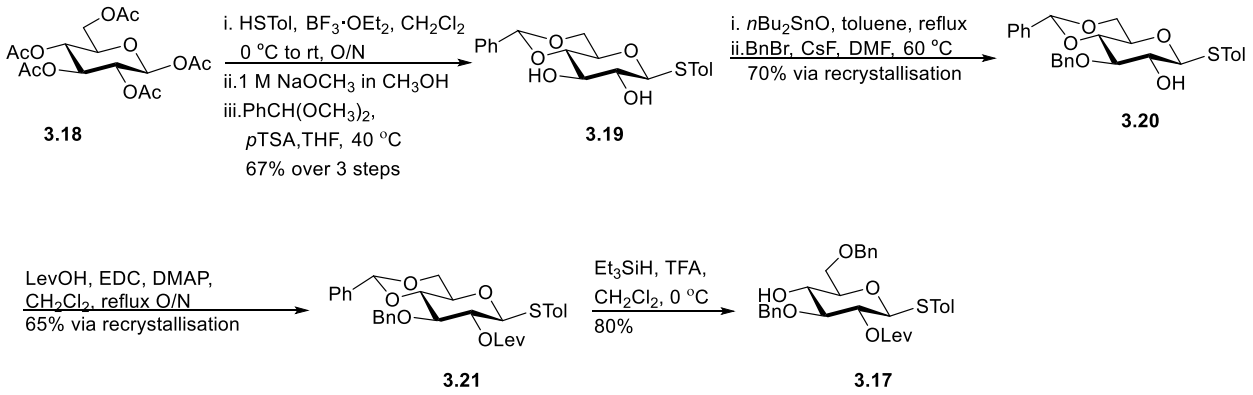
To satisfy the criteria for successful implementation of each protocol, I envisaged levulinoyl protection of the C-2 hydroxyl group of a disaccharide donor **3.16** for two reasons: first, the relative ease in both installation and subsequent selective removal in the presence of Troc and other ester protecting groups under mild conditions, and secondly, its ability to direct

β-glucosylation via neighbouring group participation. Benzyl groups were employed on the C-3 and C-6 of glucose residue to effect high *manno*-selectivity during C-2 inversions.[4,7,8]

3.3 Results and discussion on the initial synthetic route

3.3.1 Synthesis of glucose acceptor 3.17

As shown in Scheme 3-3, starting from the peracetylated β-D-glucoside **3.18**, initial thioglycosylation with *p*-thiocresol was conducted in the presence of excess $BF_3 \cdot OEt_2$, the product of which could then be titurated with hexanes to remove the remaining *p*-thiocresol. Next, protection of the C-4 and C-6 hydroxyl groups was effected by installing a 4,6-*O*-benzylidene acetal through an initial Zemplen deacetylation followed by treatment of the resultant product with benzylidene dimethyl acetal (BDA) in the presence of catalytic *p*TSA to give **3.19** in 67% yield over three steps after recrystallization. With benzylidene acetal **3.19** in hand, regioselective installation of a benzyl group on the C-3 hydroxyl group was then carried out via reaction of **3.19** with dibutyltin oxide, followed by CsF-mediated benzylation in DMF at 60 °C, thus giving the desired **3.20** in a yield of 70% after recrystallization. Initial attempts to reproduce the DCC-mediated levulinoyl protection reported by the groups of Qin[9] and Wang[10] did not proceed to completion, even after stoichiometric addition of DMAP or under reflux conditions. Following a suggestion from a colleague, levulinoyl protection using EDC and catalytic DMAP led successfully to reaction completion and furnished, following recrystallization, the desired compound **3.21** in 65% yield. Finally, regioselective ring-opening of the benzylidene acetal under Et_3SiH–TFA conditions was performed, leading to alcohol **3.17** in 80% yield.

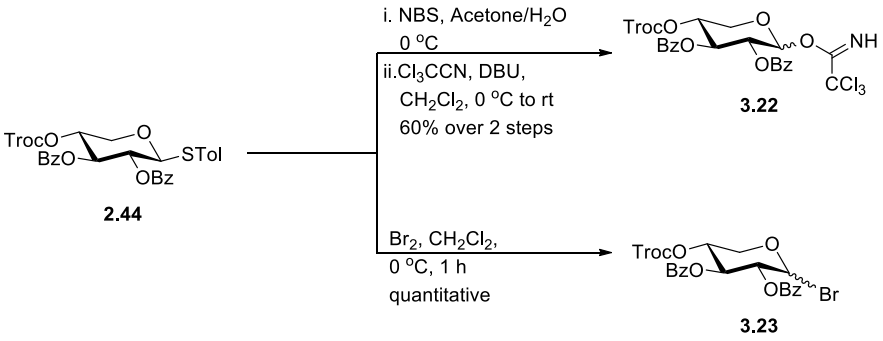


Scheme 3-3: Synthesis of glucose acceptor **3.17**

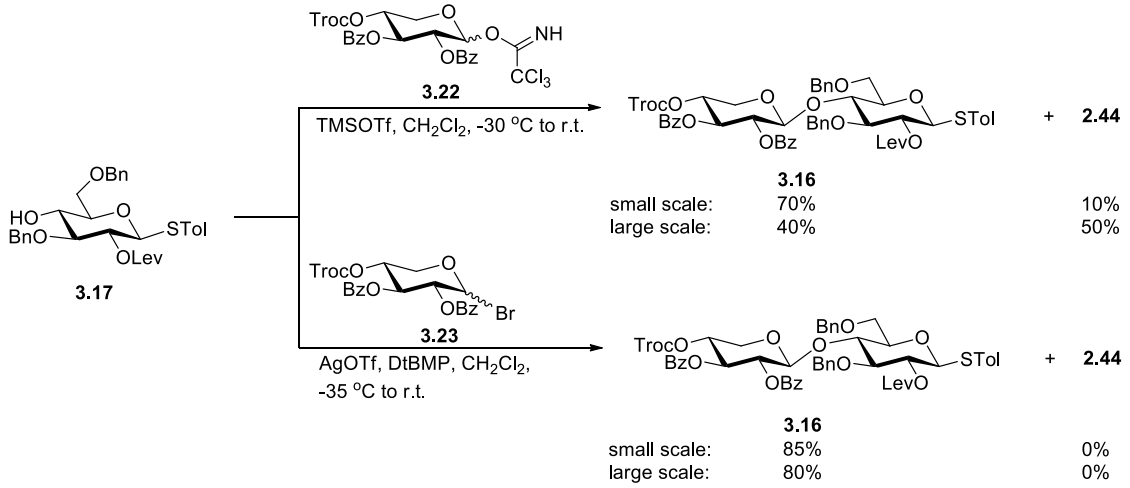
3.3.2 Synthesis of the disaccharide 3.22

With multigram quantities of glucose derivative **3.17** in hand, the 1 + 1 glycosylation was investigated (Scheme 3-5). Anticipating potential problems in the direct coupling of two thioglycosides, I explored the imidate approach through the preparation of xylosyl trichloroacetimidate donor **3.22** (Scheme 3-4). Initial reaction of **3.17** and **3.22** on milligram scale proceeded smoothly to give disaccharide **3.16** in 75% yield. However, the same success could not be reproduced in multigram scale. I encountered disappointing low yields of **3.16** (40%), along with significant formation of xylosyl thioglycoside **2.44** at 50% (relative to the starting donor) and hydrolyzed acceptors. Thioglycoside **2.44** was obtained as a result of intermolecular aglycone transfer,[11-14] a phenomenon that can be explained by the preferential reaction of the developing xylosyl oxacarbenium ion with the sulfide of acceptor **3.17**, instead of its hydroxyl group. Interestingly, these problems were not observed with the use of xylosyl bromide **3.23** as the donor in the AgOTf-mediated glycosylation of the same acceptor. As shown in Scheme 3-5, when bromide **3.23**, obtained via exposure of **2.44** to bromine at 0 °C, was

activated with AgOTf at –35 °C in the presence of **3.17**, disaccharide **3.16** was obtained in consistently high yields (80–85%).



Scheme 3-4: Derivation of xylosyl thioglycoside **2.44** into trichloroacetimidate **3.22** and bromide **3.23**

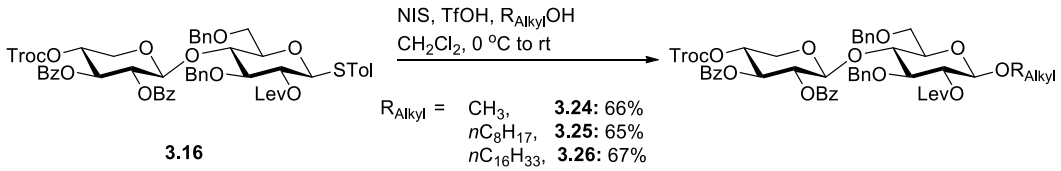


Scheme 3-5: β-Xylosylation of thioglucoside **3.17** via different donors and activation methods

The stereoselectivity of this glycosylation was directed by neighbouring group participation of the benzoyl group at the C-2 position of **3.23**. Analysis of both the 1D-TOCSY and 2D-HSQC NMR spectra of **3.16** enabled the identification of the signal for Xyl*p* anomeric proton, for which $^{3}J_{H1\text{-}H2}$ was 7.0 Hz, a value expected for a β-xylopyranoside. This was

corroborated by the signal for the Xyl*p* H-2, which appeared as a doublet of doublets ($^{3}J_{H2\text{-}H3}$ = 8.6 Hz, 6.8 Hz).

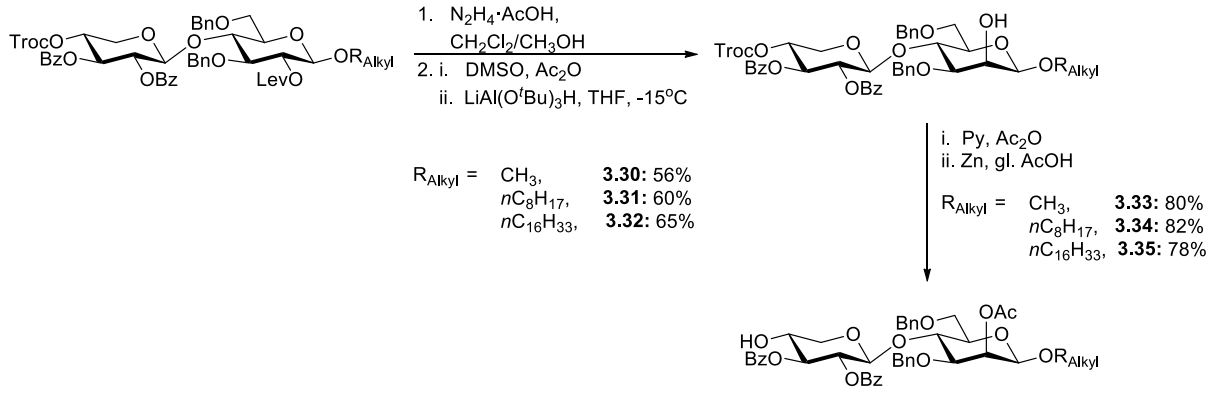
With a high yielding route to **3.16** in place, multigram quantities could be rapidly secured. This thioglycoside was then deployed as a donor for the β-glucosylation of three aliphatic alcohols: methyl (CH_3), octyl (n-C_8H_{17}) and cetyl (n-$C_{16}H_{33}$) alcohols (Scheme 3-6). Initial activation of the donor in the presence of CH_3OH via NIS–TMSOTf proceeded sluggishly even after four hours, giving complex mixtures upon the addition of more TMSOTf. Fortunately, subsequent activation with NIS–TfOH in the presence of all three alcohols proceeded smoothly to give the desired β-glycosides in yields of 65–75% with the β-linkages verified via the $^{3}J_{H1\text{-}H2}$ (7.5–8.0 Hz) and $^{1}J_{C1\text{-}H1}$ constants (158−163 Hz).



Scheme 3-6: β-Glucosylation of **3.16** with various aliphatic alcohols

Successful establishment of the desired β-glucosidic linkages in disaccharides **3.24**–**3.26** set the stage for C-2 inversion through a three-step protocol. As shown in Scheme 3-7, the first step involved the selective removal of levulinoyl ester via treatment with hydrazine acetate[15,16] to generate alcohols **3.27**–**3.29**. Following an Albright–Goldman oxidation[17,18] and stereoselective reduction of the product ketone with LTBA, the desired β-mannosides **3.30**–**3.32** were obtained in yields of ~60% over three steps. Spectroscopic evidence of the high β-*manno* selectivity in this approach was provided through the ^{1}H-coupled HSQC and 1D ^{1}H NMR spectra, which allowed the measurement of the $^{1}J_{C1\text{-}H1}$ (~156 Hz) and $^{3}J_{H1\text{-}H2}$ (<1.0 Hz) of these compounds.

To assemble larger oligosaccharides, second generation glycosyl acceptors were required. Thus, disaccharide alcohols **3.33–3.35** were derived from **3.30–3.32** via initial acetylation of the Man*p* C-2 hydroxyl group followed by Troc deprotection through the exposure of the acetylated disaccharide to freshly activated zinc dust in glacial AcOH, with yields averaging 80% over the two steps.



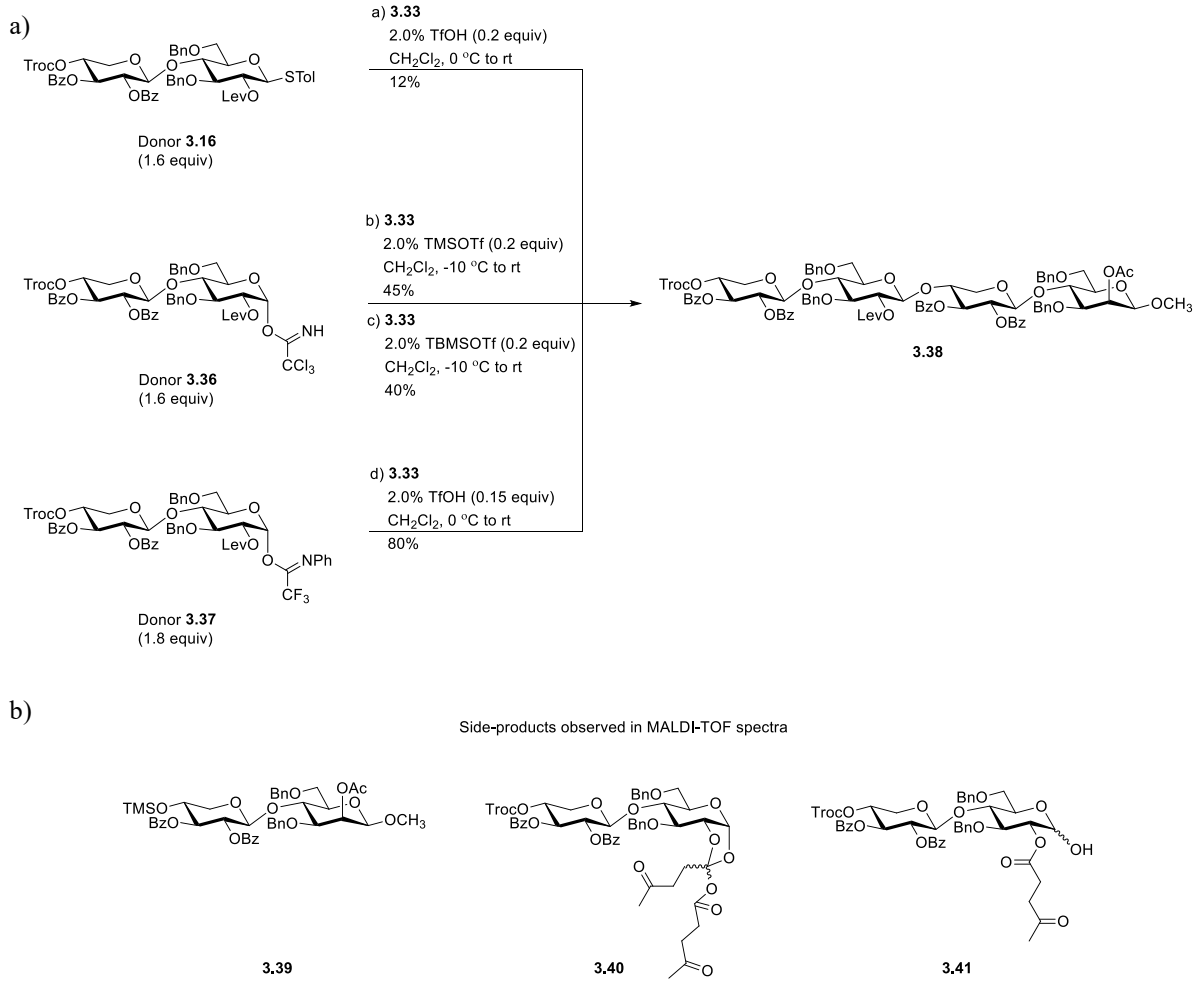
Scheme 3-7: Stereoselective C-2 inversion and subsequent derivation into second generation acceptors

3.3.3 Synthesis of methyl oligosaccharides

3.3.3.1 Methyl tetrasaccharides

With the disaccharide acceptors in hand, 2 + 2 glycosylation was investigated (Scheme 3-8a). Initial attempts to use the thioglycoside **3.16** as a donor met with little success, generating the desired tetrasaccharide **3.38** in low (12%) yields along with significant donor hydrolysis. Yields remained low using trichloroacetimidate **3.36**. MALDI mass spectrometric analysis of the side products revealed, in addition to hydrolysed donor **3.41** (M + Na: *m/z* = 995.2), both the silylated acceptor **3.39** (M + Na: *m/z* = 851.3) and levulinoyl orthoester **3.40** (M + Na: *m/z* = 1093.3) were detected as well (Scheme 3-8b). Presence of the orthoester was further supported by the diagnostic $^1J_{C1\text{-}H1}$ (179 Hz) associated with the glucose anomeric proton signal in the

NMR spectrum of the inseparable mixture. It was reasoned that acceptor silylation and orthoester formation could be avoided by using TfOH as the activator and possibly slow down donor hydrolysis with the more stable *N*-phenyl trifluoroacetimidate donor **3.37**.[19-21] Thus, I decided to activate **3.37** in the presence of acceptor **3.22** using catalytic TfOH as the activator. This approach proved to be pivotal, delivering consistently high yields of ~80%.

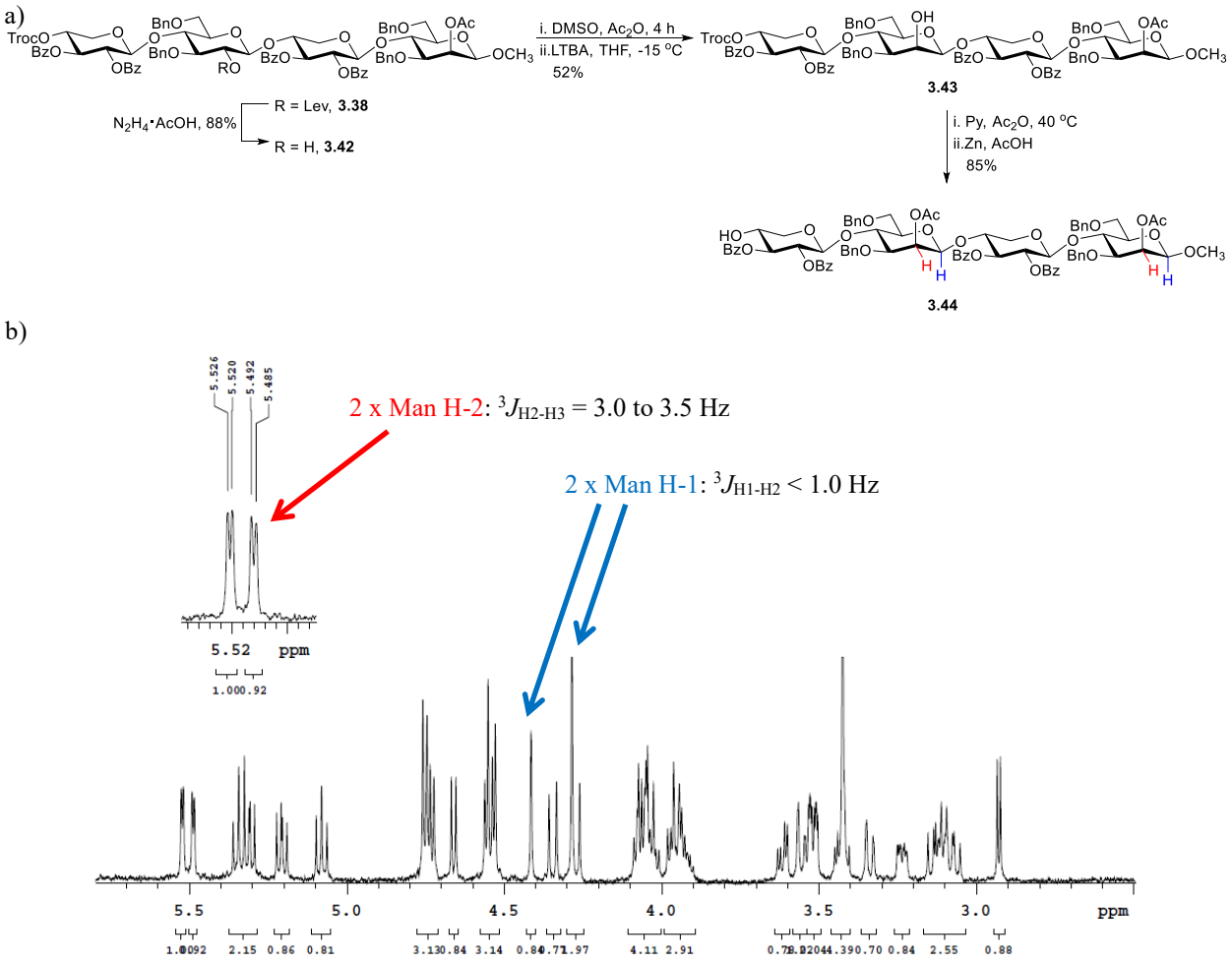


Scheme 3-8: (a) Synthesis of methyl tetrasaccharide **3.38** with different donors (b) side-products observed in the glycosylation of donor **3.36** and acceptor **3.35**

Once again, strategic placement of a levulinoyl ester at C-2 of donor **3.37** facilitated complete β-stereocontrol of the 2 + 2 glycosylation through neighbouring group participation.

Supporting evidence for the stereochemistry was garnered from analyses of the 1D ^{1}H and 2D HSQC (both proton coupled and decoupled) NMR spectra taken of **3.38**, which not only determined the newly generated H-1 signal of the glucose residue within a multiplet from δ 4.38 to 4.23, but also the anomeric configuration from the ^{13}C–^{1}H coupling constant ($^{1}J_{C1\text{-}H1}$ ~ 155 Hz), thus confirming the newly constructed glycosidic linkage to be of the β-configuration.

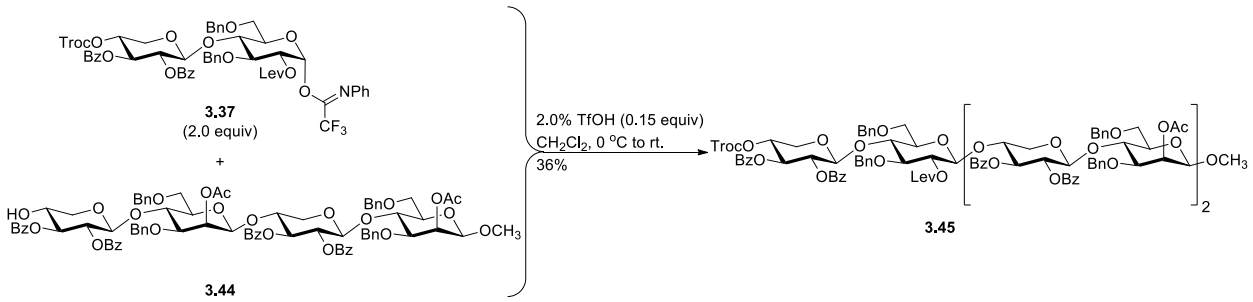
With the establishment of the β-glucosidic linkage in **3.38**, attention was then turned to C-2 stereoinversion (Scheme 3-9). The levulinoyl ester was selectively removed with hydrazine acetate, and the C-2 stereocentre in the glucoside residue in **3.42** was subsequently stereoinverted via the same oxidation–reduction sequence described previously to give tetrasaccharide **3.43** in a yield of 40% over three steps. Subsequent acetyl protection of the hydroxyl group in **3.43**, followed by Troc removal with zinc dust in glacial acetic acid, then afforded the desired xylomannan acceptor **3.44** as a white foamy solid in 85% yield. The presence of the β-mannosidic linkages was verified by both the small coupling constants ($^{3}J_{H1\text{-}H2}$ < 1.0 Hz and $^{3}J_{H2\text{-}H3}$ ~ 3.0 Hz) in the two hexopyranosides of **3.44**, as well as $^{1}J_{C1\text{-}H1}$ (<160 Hz), which was measured via an ^{1}H-coupled HSQC NMR experiment.



Scheme 3-9: (a) Conversion of tetrasaccharide **3.38** into acceptor **3.41** and b) spectral verification of β-mannosidic linkages

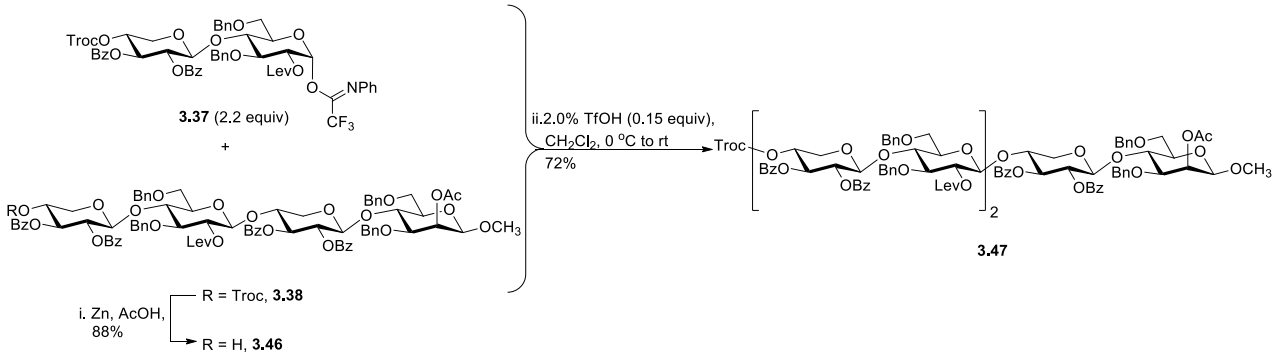
3.3.3.2 Methyl hexasaccharides

With the tetrasaccharide acceptor **3.44** in hand, I then proceeded to use the same coupling strategy for 4 + 2 glycosylation (Scheme 3-10). Though I managed to obtain hexasaccharide **3.45** successfully, the reaction was plagued by the incomplete consumption of acceptor **3.44** and the formation of numerous side-products together with donor hydrolysis. This combined to give messy product mixtures that made purification exceedingly difficult resulting in low yields (~36%) over three attempts.



Scheme 3-10: 4 + 2 glycosylation between donor **3.37** and acceptor **3.44** to reach hexasaccharide **3.45**

The difficulty in executing the 4 + 2 glycosylation with acceptor **3.44** prompted me to explore other possibilities (Scheme 3.11). In some cases, the use of an acceptor bearing a different glycosyl epimer may result in an improvement in glycosylation.[13] To this end, I synthesized acceptor **3.46**, through a Troc deprotection of tetrasaccharide **3.38** using the same general procedure described earlier. The compound differs from **3.44** in that the penultimate residue in **3.46** is of the *gluco*, instead of the *manno*, configuration. To my pleasant surprise, subsequent glycosylation between donor **3.37** and acceptor **3.46**, under essentially the same conditions used for **3.45**, led to a much-improved yield of hexasaccharide **3.47** (72%).

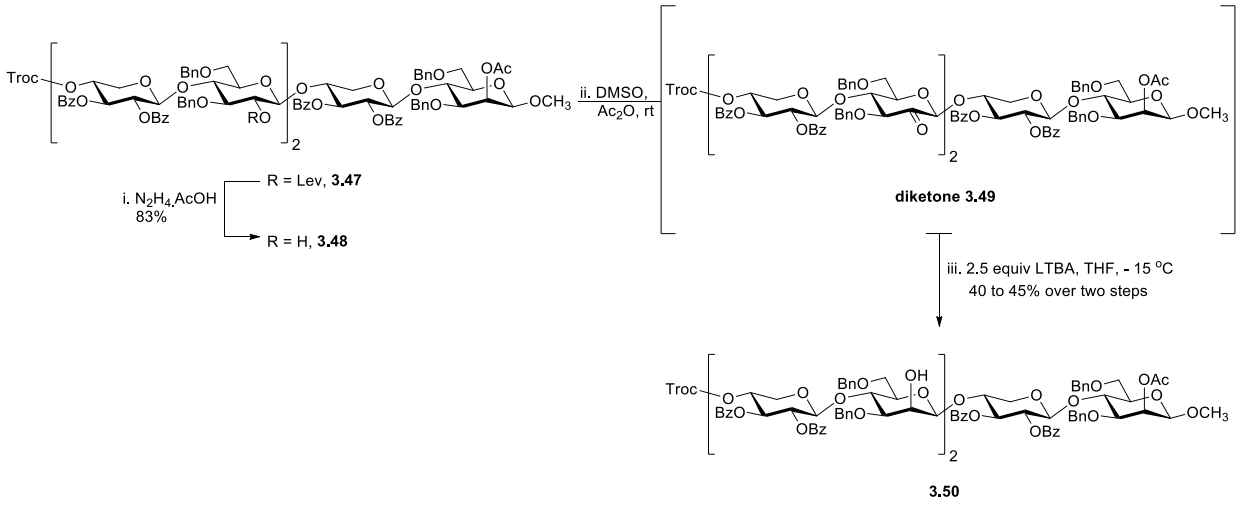


Scheme 3-11: 4 + 2 glycosylation between donor **3.37** and acceptor **3.46** to reach hexasaccharide **3.47**

Though the issue of the low yields in the 4 + 2 glycosylation was resolved through the use of acceptor **3.46**, this new route, however, set up the challenge of executing simultaneous

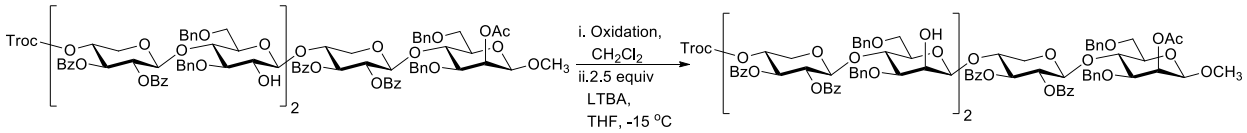
double C-2 inversions on **3.47** in high stereoselectivity to obtain β-mannose residues. I felt that this challenge could be overcome with the previously established oxidation–reduction protocol. To set the stage for the stereoinversion reactions, chemoselective hydrazinolysis of the two levulinoyl esters on the C-2 of each glucose residue was first carried out via exposure to a slight stoichiometric excess of hydrazine acetate, affording diol **3.48** in 80% yield.

With the diol **3.48** in hand, subsequent C-2 inversion was investigated. Oxidation under Albright–Goldman conditions was found to be significantly slower than on the molecules containing a single hydroxyl group (**3.27** or **3.42**) requiring overnight reaction for completion, in contrast to four hours (Scheme 3-12). Similar to the previous C-2 inversion, the diketone **3.49** was rapidly isolated via extraction and, without any further purification, taken to the next step of LTBA reduction. Gratifyingly, amid the four possible outcomes of the reduction, only diol **3.50** was isolated with the newly generated β-mannosidic linkages identified by apparent singlet peaks corresponding to the anomeric Man*p* protons in the 1D ^{1}H NMR spectrum ($^{3}J_{H1\text{-}H2} < 1.0$ Hz) and $^{1}J_{C1\text{-}H1} \sim 158$ Hz in the ^{1}H coupled HSQC spectrum.



Scheme 3-12: Simultaneous double C-2 inversion of **3.47** to provide **3.50**

Despite the initial success in employing this oxidation–reduction approach for simultaneous inversions, sluggish oxidation rates, coupled with the low overall yields of 40–45% became a concern. The Albright–Goldman oxidation, in addition to being a slower process than other methods, also can generate methylthiomethyl ethers as a side product.[18] Moreover, the use of DMSO as a solvent in this oxidation method often complicates aqueous work-up due to its water solubility, leading to yield losses. It was hypothesized that the DMSO solvent, together with the formation of this side product, may be responsible for the low yields. Consequently, I screened other oxidation conditions (Table 3-1). Of all the methods, Dess-Martin Periodinane (DMP) oxidation[18] with three equivalence of water[22] was superior in terms of overall yield (75%).



3.48 3.50

Entry	Oxidation conditions	Temp.	Time	Yield[a]
1	DMSO (10 equiv), DIPEA (6 equiv), SO_3.Py (5 equiv)	0 °C to rt	3 h	50%
2	DMSO (10 equiv) , $(COCl)_2$ (5 equiv), Et_3N (20 equiv)	-78 °C to rt	1.5 h	56%
3	PCC (5 to 10 equiv)	rt	24 h	35%
4	DMP (6 equiv)	rt	5 h	65%
5	DMP (6 equiv), H_2O (3 equiv),	rt	2 h	75%

[a] isolated yields after LTBA reduction

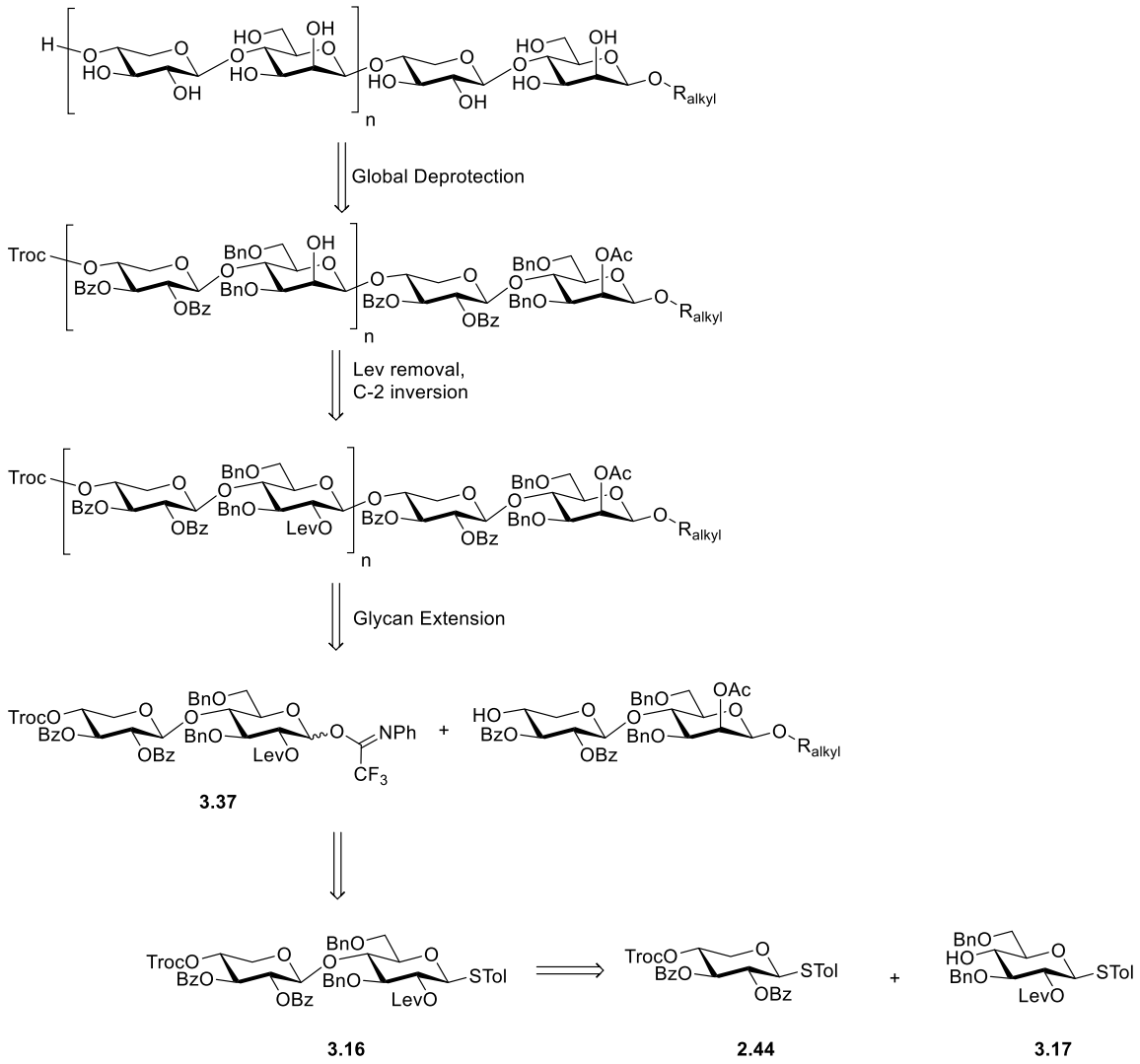
Table 3-1: Screening of different oxidation conditions, followed by stereoselective reduction with LTBA

Inspired by the above outcome and given the understanding that synthesis through the original approach – the use of acceptors with a penultimate mannose residue at the non-reducing

end and stereoinversion at one centre – would likely become even more challenging with higher oligomerization, I changed my synthetic design. Instead, I chose to use the general approach outlined in Schemes 3-11 and 3-12 – glycosylation of an acceptor with a non-reducing end glucose residue, followed by simultaneous inversions of multiple stereocentres. This approach will be discussed in the next section.

3.4 Revised retrosynthetic route based on simultaneous C-2 inversion strategy

As illustrated in Scheme 3.13, the revised route retained several key features of the previous approach to take advantage of the earlier successes, one of which was the use of donor **3.36** to facilitate glycan extension via levulinoyl-directed β-glucosylation. A second was the installation of benzyl groups on the O-3 of glucose residues, imparting greater stereochemical control during the critical stage of C-2 inversion. A third feature was the use of Troc and levulinoyl groups to protect the appropriate hydroxyl groups to allow post-glycosylation modifications, the former for further glycan elongation and the latter for implementation of simultaneous C-2 inversion. Similarities aside, the key distinction lays in the sequence of executing post-glycosylation modifications, in which all glycosylation reactions, except those leading to **3.33–3.35** (Scheme 3-7 above), were carried out prior to any C-2 epimerisation to set the stage for simultaneous multiple inversions. The advantage of this approach reduces the number of steps prior to each glycosylation and led to significant improvement in both yields and the time taken to obtain the AFGL derivatives.



Scheme 3-13: Revised retrosynthetic route to incorporate the concept of simultaneous C-2 inversions

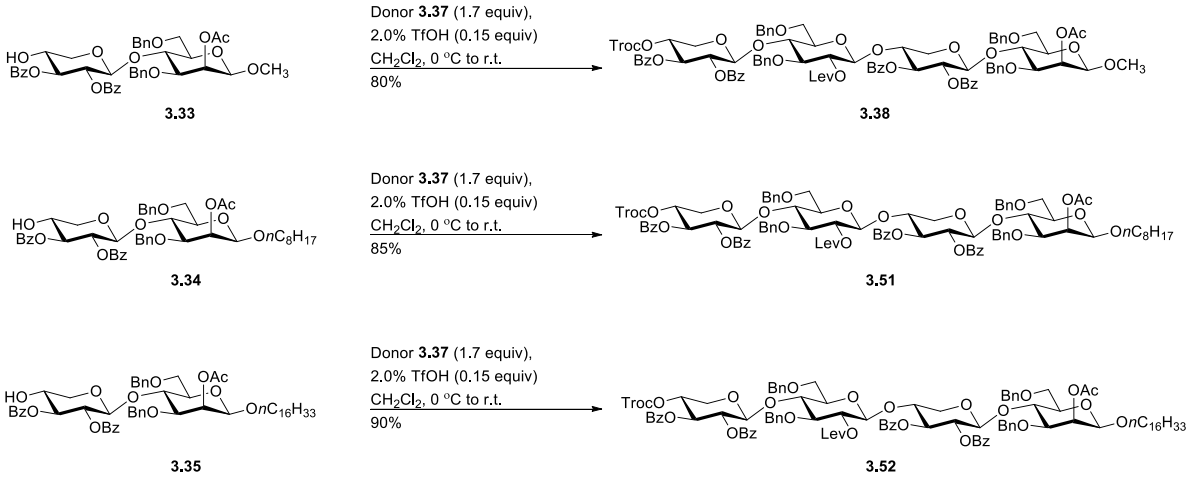
3.5 Results and discussion based on this new approach

3.5.1 Stereoselective synthesis of xylomannan tetrasaccharide derivatives

3.5.1.1 Methyl, octyl and cetyl tetrasaccharide assembly

With multigram quantities of donor **3.37** in hand, tetrasaccharide assembly began in earnest using this revised approach. Consistency in the yields based on both small and multigram

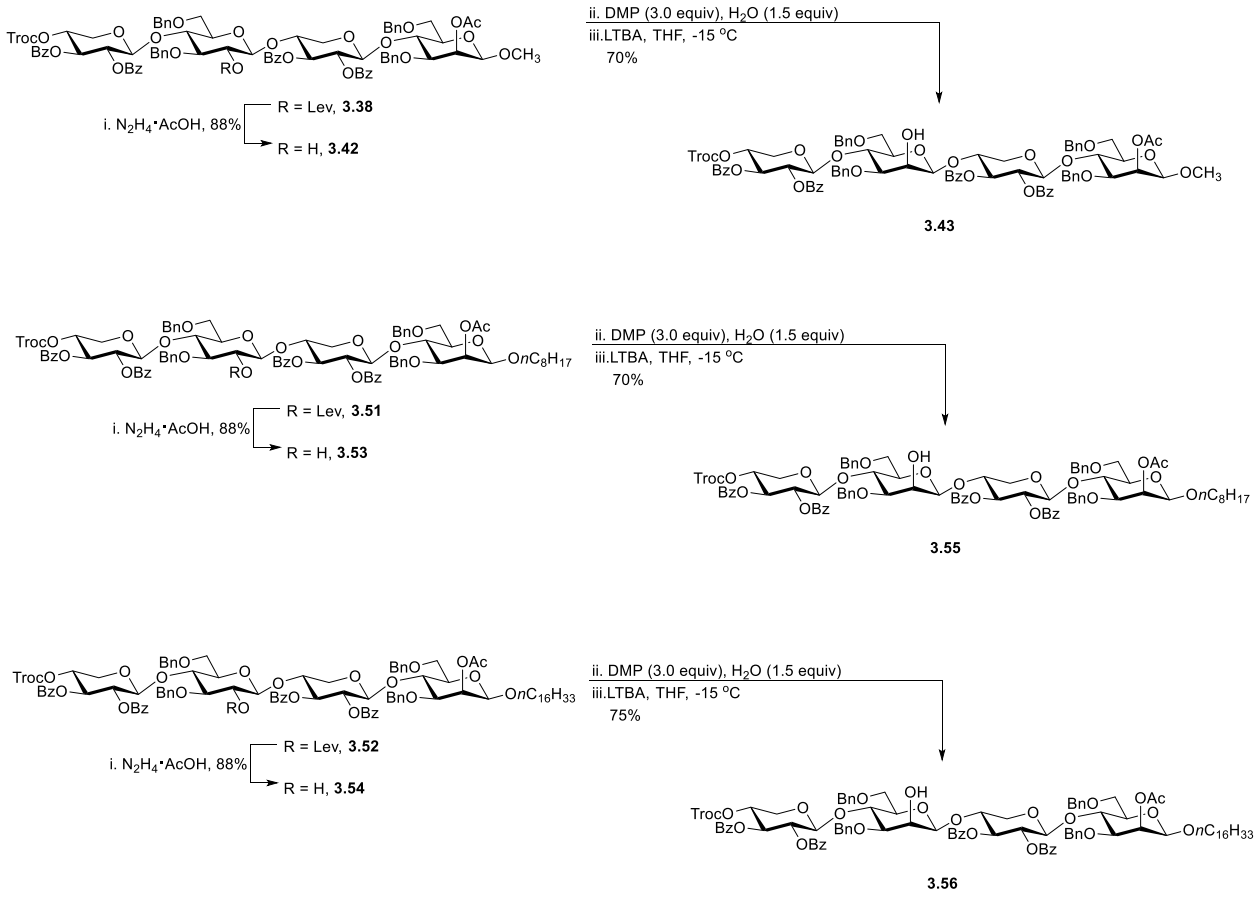
syntheses of the methyl tetrasaccharide **3.38** convinced me of the feasibility in assembling both octyl and cetyl tetrasaccharides under the same glycosylation conditions. Indeed, this was confirmed by the high respective yields (85 and 90%) obtained in experiments leading to tetrasacchrides **3.51** and **3.52** (Scheme 3-14).



Scheme 3-14: Synthesis of tetrasaccharides **3.38**, **3.51** and **3.52** via 2 + 2 glycosylation

3.5.1.2 Singular C-2 inversion

Having established a route to all the tetrasaccharides, liberation of the C-2 hydroxyl groups was then carried out via hydrazinolysis to afford **3.42**, **3.53** and **3.54** in 88% yield in all cases (Scheme 3-15). Drawing upon my experience with different oxidation methods, I oxidised the hydroxyl groups in each tetrasaccharide using DMP. With only one alcohol in the molecule, just three equivalents of DMP reagent and 1.5 equivalents of water were required to reach completion within two hours. Subsequent exposure of the crude ketones to LTBA then afforded all three xylomannan tetrasaccharides in 70–75% yield over two steps. This is in stark contrast to the moderate 52% yield achieved for **3.42** using the Albright–Goldman oxidation (Scheme 3-9 above).

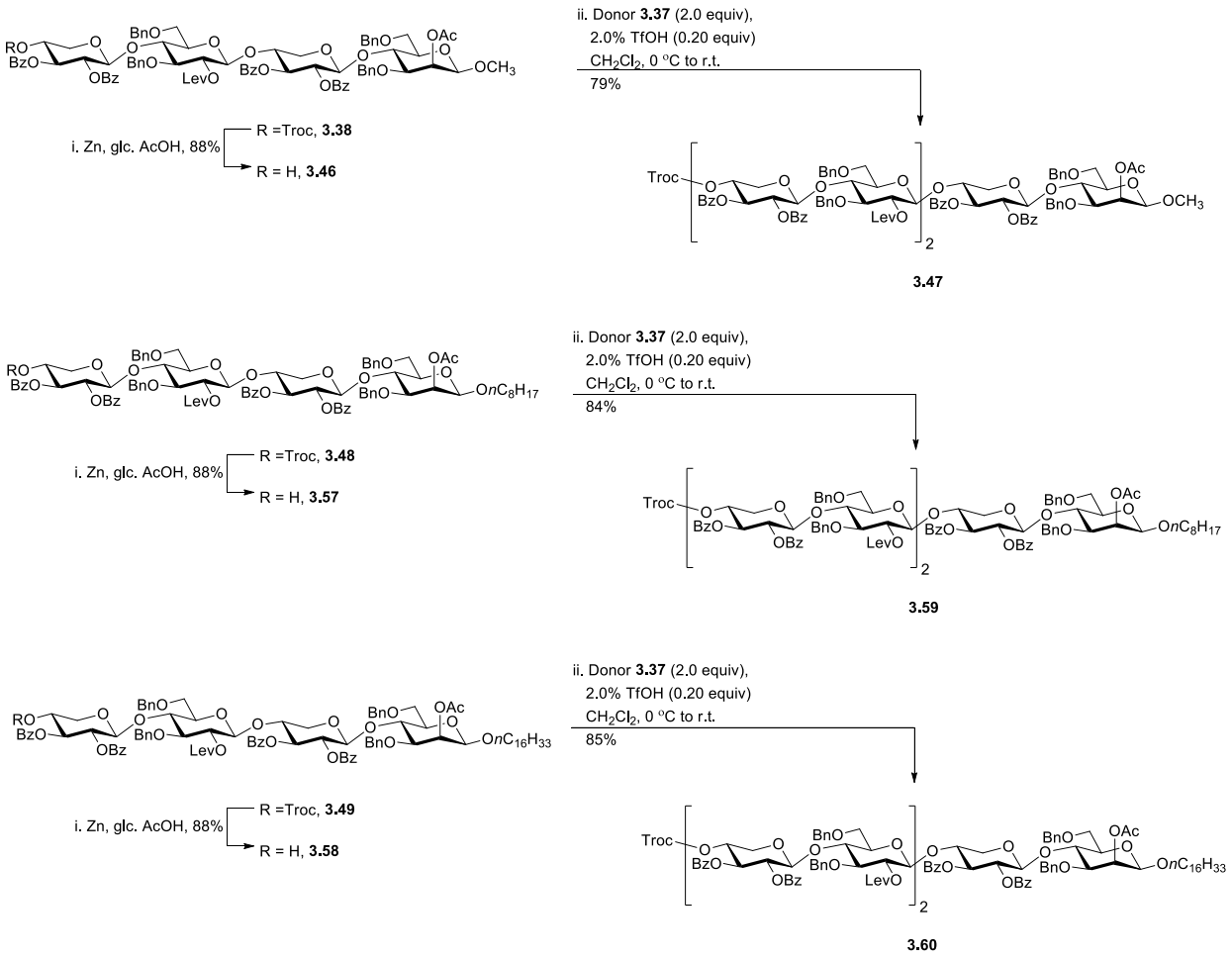


Scheme 3-15: Stereoselective C-2 inversion via a two-stage DMP oxidation and subsequent LTBA reduction

3.5.2 Stereoselective synthesis of xylomannan hexasaccharide derivatives

3.5.2.1 Hexasaccharide assembly via 4 + 2 glycosylation

Encouraged by the successful employment of donor **3.37** in the tetrasaccharide assembly, I sought to replicate the same success in the synthesis of the hexasaccharides (Scheme 3-16). Indeed, Troc deprotection of each tetrasaccharide followed by exposing the resultant acceptor **3.46**, **3.57** and **3.58** to the disaccharide donor **3.37** under increased TfOH loading, furnished all of the desired hexasaccharides in very good yields (79–85%).

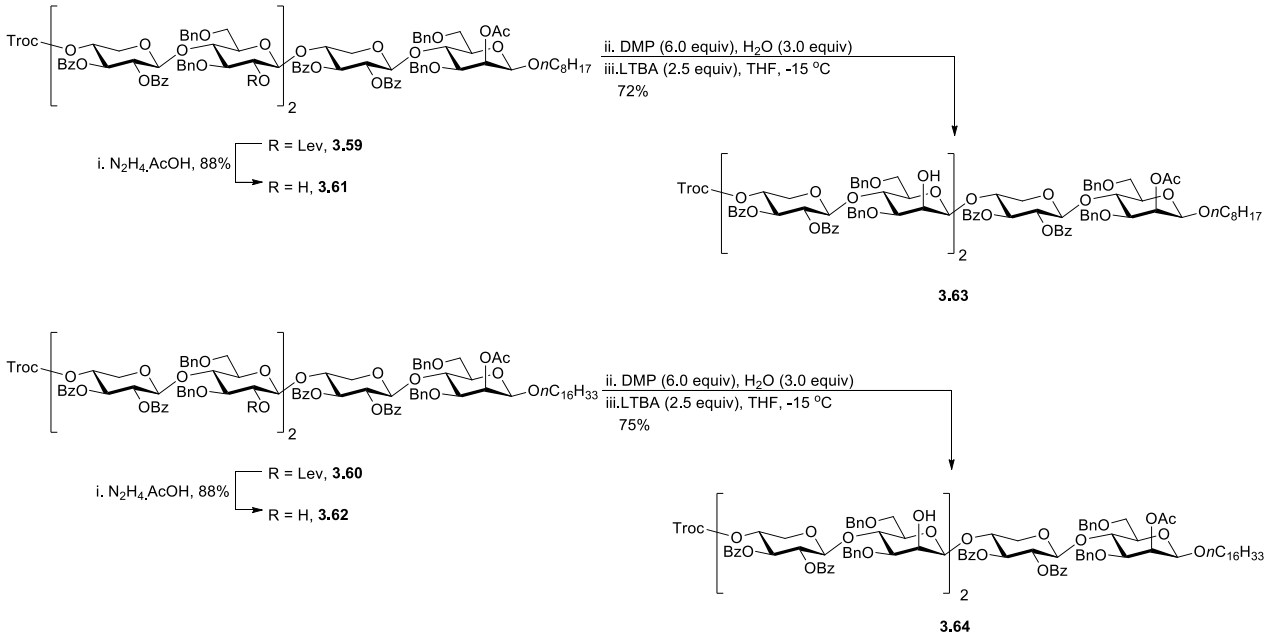


Scheme 3-16: Synthesis of hexasaccharides via 4 + 2 glycosylation

3.5.2.2 Simultaneous double C-2 inversion

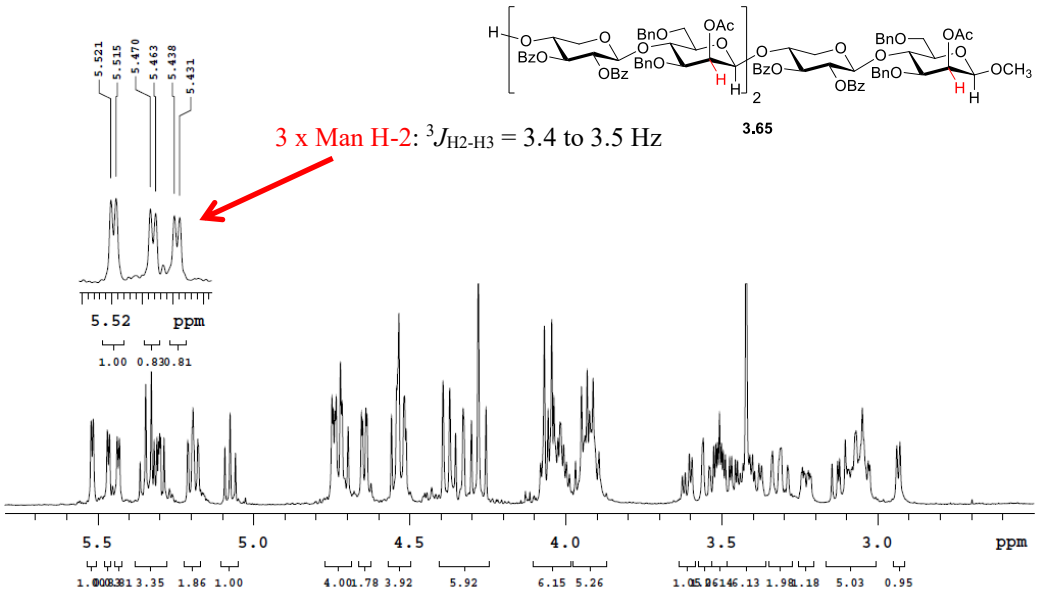
The levulinoyl groups were removed after exposing both hexasaccharides **3.59** and **3.60** to hydrazinolysis with hydrazine acetate. Leveraging on the success in executing a simultaneous double C-2 inversion on the methyl hexasaccharide **3.48** (Scheme 3-12 above), I sought to reproduce the same outcome on both hexasaccharide diols **3.61** and **3.62**, the octyl and cetyl glycoside targets, respectively. Thus, as shown in Scheme 3-17, following DMP oxidation, the crude diketones were then subjected to LTBA reduction, the molar equivalents of which were in slight excess relative to the number of free hydroxyl groups in the precursors to the oxidation.

Using this approach, both xylomannan hexasaccharides **3.63** and **3.64** were obtained as the sole diastereomers upon isolation in good overall yields of 72 and 75%, respectively. In fact, none of the undesired diastereomers were observed or isolated upon carrying out these simultaneous inversion reactions on large scale.



Scheme 3-17: Simultaneous double C-2 inversion to generate β-mannosidic linkages

Though use of 1D-TOCSY and 2D HSQC NMR experiments enabled the identification of the anomeric β-Man*p* proton signals from the overlapping benzylic methylene protons, they could not be used to resolve the anomeric Man*p* proton signals from one another. Recalling the successful verification of β-mannosidic linkages indirectly through the splitting patterns of Man*p* H-2 in tetrasaccharide **3.44** (Scheme 3-9), the same acetylation and Troc deprotection steps were then carried out with hexasaccharide **3.50** to yield **3.65**. In this way, presence of the β-mannosidic linkages was successfully verified by the $^{3}J_{H2\text{-}H3}$ constants (~ 3.0 Hz), as well as $^{1}J_{C1\text{-}H1}$ (<160 Hz) in the three hexopyranoside residues in **3.65**, evidence of which is shown in Scheme 3-18.

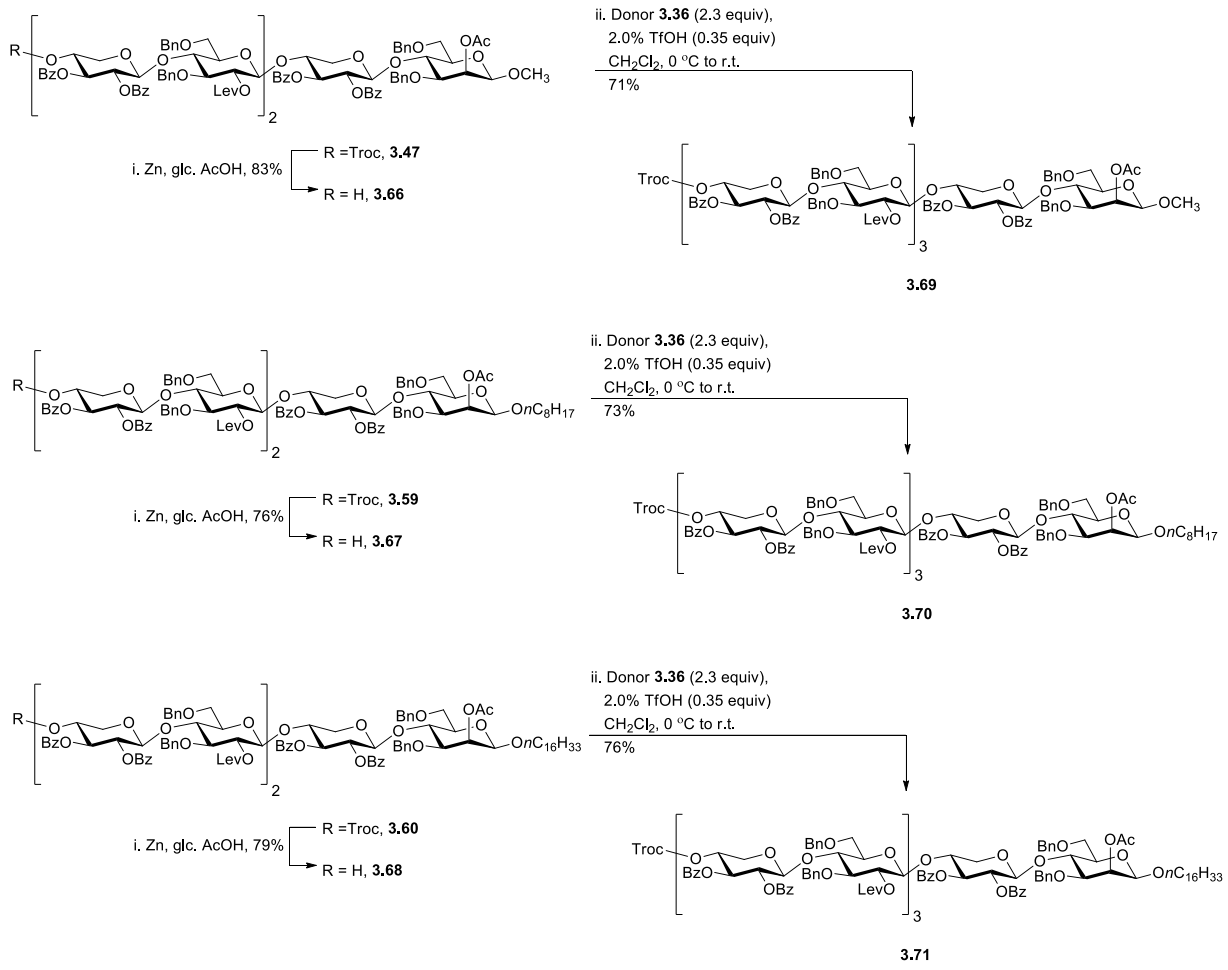


Scheme 3-18: Spectral evidence of the β-*manno* selectivity in simultaneous double C-2 inversion

3.5.3 Stereoselective synthesis of xylomannan octasaccharide derivatives

3.5.3.1 Octasaccharide assembly via 6 + 2 glycosylation

The success of the strategy just described prompted the synthesis of xylomannan octasaccharides through simultaneous triple C-2 inversions. Accordingly, liberation of the C-4 hydroxyl groups on hexasaccharides **3.47**, **3.59** and **3.60** upon treatment with zinc dust in glacial acetic acid afforded the corresponding acceptors **3.66**, **3.67** and **3.68** in yields of 73–79% (Scheme 3.19). Subsequent coupling of each acceptor with imidate donor **3.37** under catalytic TfOH conditions gave octasaccharides **3.69**, **3.70** and **3.71** in good yields of 70%, 68% and 72%, respectively.



Scheme 3-19: Octasaccharide assembly via 6 + 2 glycosylations

Though these results seemed to affirm the robustness of the newly developed glycosylation strategy, a slight decline in glycosylation yields from the tetrasaccharides to the octasaccharides was observed, along with corresponding increase in both donor usage and TfOH necessary to achieve reaction completion. This observation was not unique to the situation presented here; similar problems were encountered by Crich et al. in the synthesis of xylomannan oligosaccharides in glycosylations between two glycosyl fragments larger than disaccharides.[23] Such observations could be attributed to the nucleophilicity of the glycosyl acceptors, which may decline as a function of the size of the acceptor. Nevertheless, this

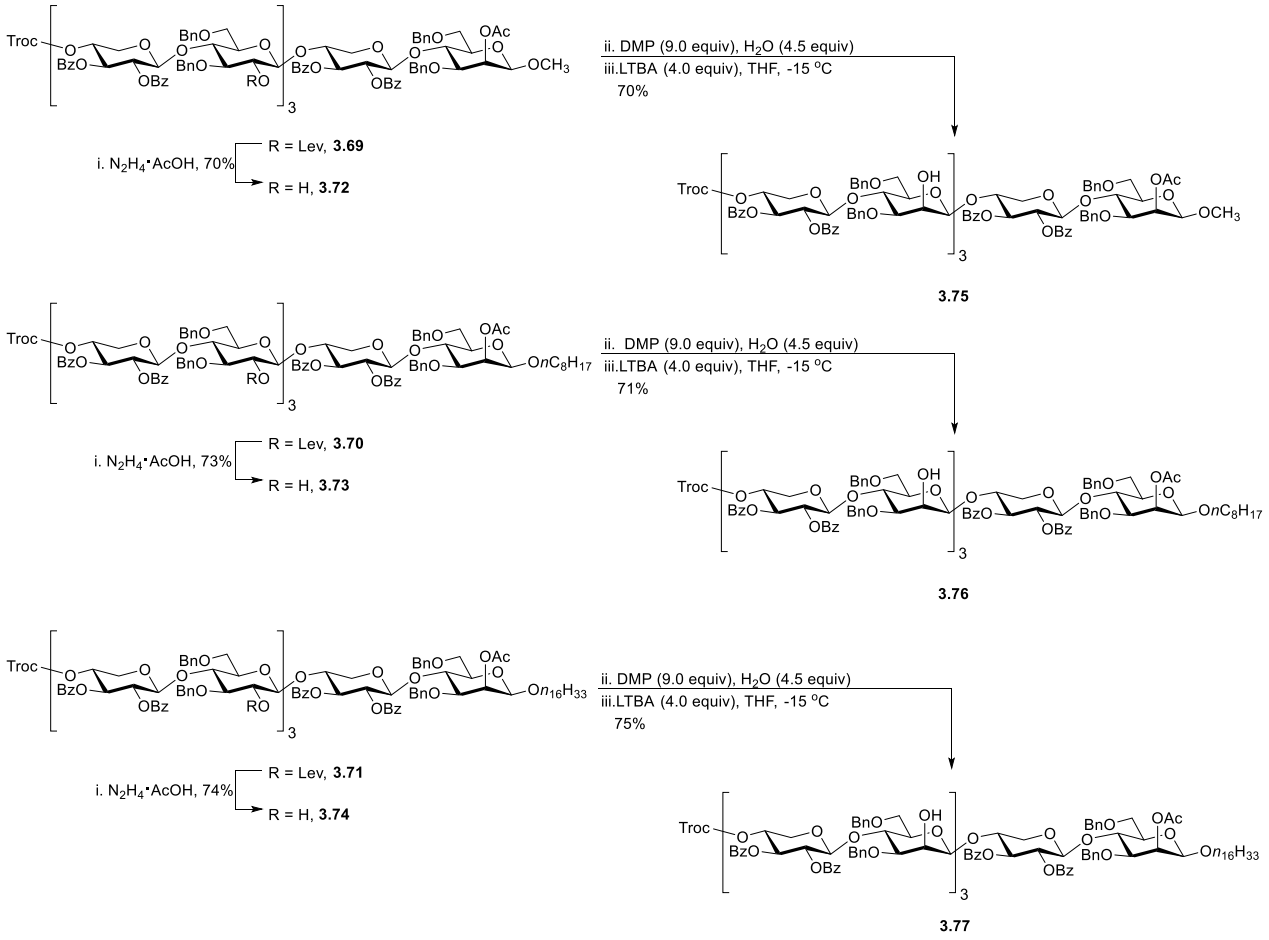
downward trend in reactivity as a function of oligosaccharide length was successfully addressed by deployment of more donors.

3.5.3.2 Simultaneous triple C-2 inversion

With the octasaccharides **3.72–3.74** in hand, care had to be taken to ensure complete removal of the three levulinoyl esters whilst avoiding any potential side reactions such as acyl deprotection. In fact, older batches of methanolic solutions of hydrazine acetate were found to proceed sluggishly, giving complex reaction mixtures from incomplete levulinoyl deprotection and the introduction of large excess of hydrazine acetate to push to completion unfortunately led to product degradation, presumably from loss of acetates. Thus, fresh batches of methanolic hydrazine acetates were always prepared prior to deprotection to ensure clean levulinoyl deprotection, with the result translated into consistently good yields (70–74%) for all three octasaccharides.

As shown in Scheme 3-20, the resultant triols were then taken to the next step – simultaneous triple inversions. Verification of the oxidation outcome was an issue due to the extensive streaking of the crude mixture on TLC plates, pointing to possible ketone hydration on exposure to silica. Thus, the reaction was brought forward to the subsequent reduction after an approximate 6 h. Judging by both the clean outcomes of LTBA reduction and the good overall yields (70 to 75%), the oxidation appeared to be complete within this timeframe. An issue encountered was the generation of 2-iodobenzoic acid upon quenching the excess DMP reagent with aqueous sodium thiosulfate. Varying traces of this acid could sometimes be found in the isolated triketone, which complicate the latter stage of reduction by quenching the reducing reagent. It was also observed that large excess of LTBA reagent relative to the starting triol

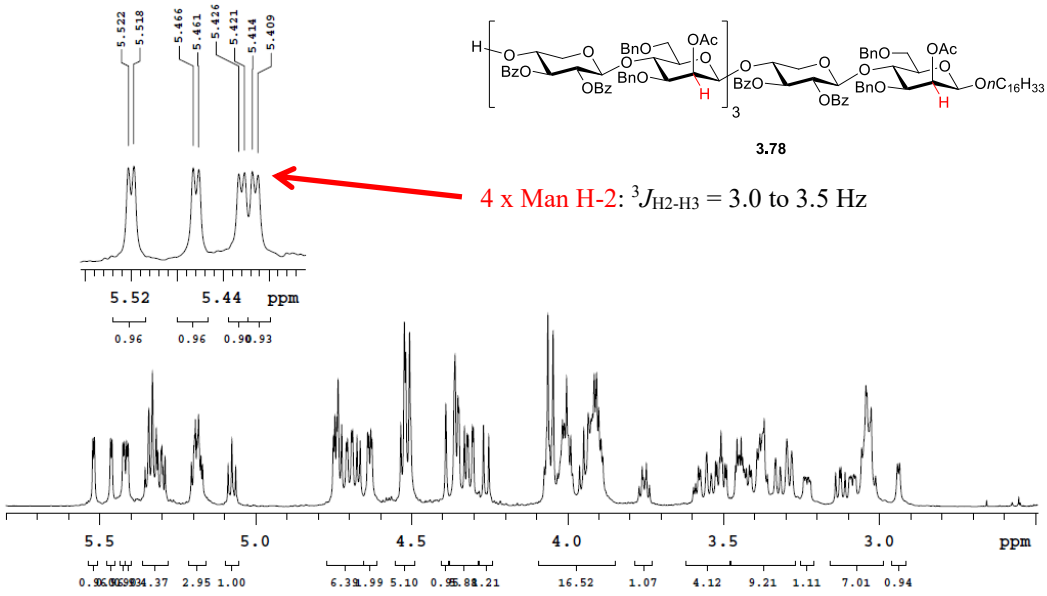
precursors often led to complex reaction mixtures. Fortunately, this was resolved by simply stirring the reaction mixture with saturated aqueous $NaHCO_3$ for an additional hour, followed by the extraction of the product and subsequent LTBA reduction into xylomannan octasaccharides **3.75–3.77**.



Scheme 3-20: Simultaneous triple C-2 inversions to generate xylomannan derivatives **3.75** to **3.77**

As done for the tetrasaccharides and hexasaccharides, proof of the β-*manno* selective reduction in **3.75–3.77** was provided by spectral data of cetyl glycoside **3.78** (Scheme 3-21). The values of the $^{3}J_{\text{H-H}}$ (2.8–3.5 Hz) of each Man H-2 proton as well as $^{1}J_{\text{C-H}}$ of each anomeric Man*p*

^{13}C–^{1}H pair (158–163 Hz) were in excellent agreement with those expected for β-mannosides and consistent with earlier observations on the smaller oligomers.



Scheme 3-21: Spectral evidence of the β-*manno* selectivity in simultaneous triple C-2 inversion

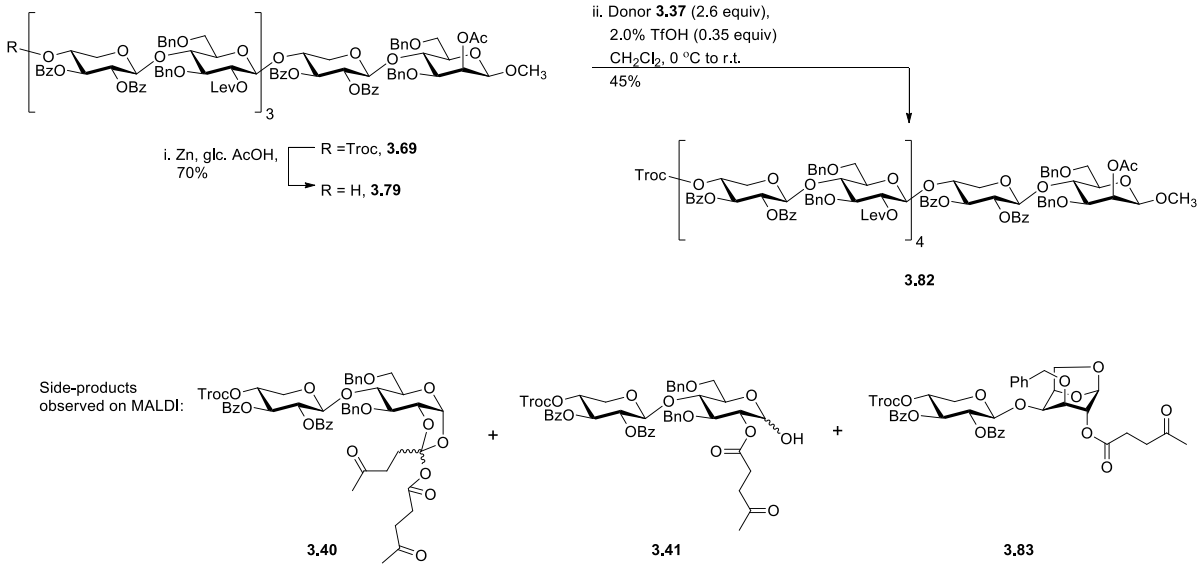
3.5.4 Stereoselective synthesis of xylomannan decasaccharide derivatives

3.5.4.1 Decasaccharide assembly via 8 + 2 glycosylation

As part of my intention to synthesize up to the xylomannan decasaccharides, I envisioned that the same glycosylation strategy could be used to reach these largest targets. Thus, Troc deprotection was accordingly performed on octasaccharides **3.69**–**3.71** to obtain the corresponding acceptors **3.79**–**3.81** in 70–80% yield.

With the octasaccharide acceptors in hand, attention was then focused on the 8 + 2 glycosylations. An initial attempt, the reaction of **3.37** and **3.79** was met with disappointing results. The desired product, decasaccharide **3.82**, was produced in only 45% yield (Scheme

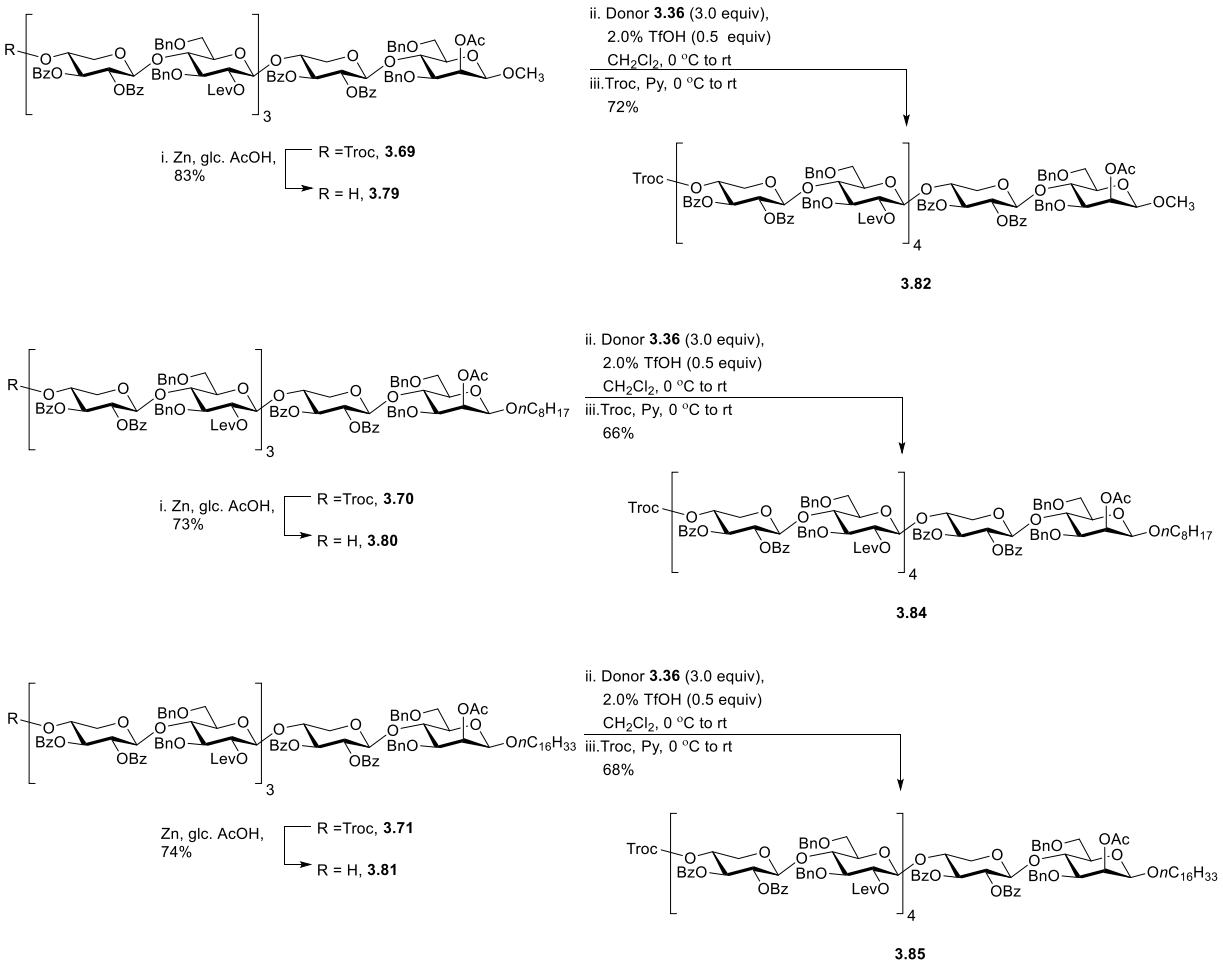
3.22), along with a 20% yield of the unreacted acceptor. MALDI-TOF analysis conducted on the side products revealed that, in addition to the hydrolysed donor **3.41**, a side product, hypothesized to be the 1,6-anhydrosugar **3.83**, was formed (M + Na: *m/z* = 887.1). Anhydrosugar **3.83** was probably formed as a result of intramolecular attack on the anomeric carbon by O-6, and subsequent loss of the benzyl group. This can occur in glycosylations that feature the use of unreactive acceptors.[13]



Scheme 3-22: Initial attempt in 8 + 2 glycosylation

One way to overcome the low yield is to use an increased number of equivalents of the donor. After a few attempts, I eventually discovered optimal conditions: use of three equivalents of donor with 0.50 equivalents of TfOH. This is demonstrated in Scheme 3-23, in which good yields (65–68%) were achieved to obtain all three decasacharides. However, purification of each compound was difficult due to traces of remaining acceptor with similar polarity to the desired product. Initial attempts to circumvent this problem by pyridine-mediated acetylation of the crude reaction mixtures were met with slow reaction rates Addition of catalytic DMAP to speed

up the reaction led only to complex reaction outcomes. This issue was finally resolved upon treatment of the crude mixtures with TrocCl in pyridine under argon at 0 °C.



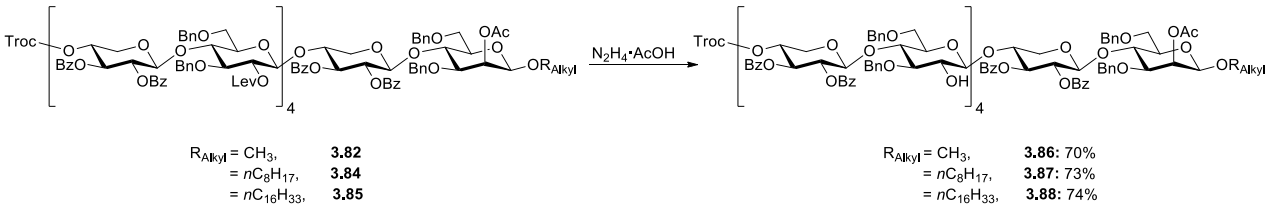
Scheme 3-23: Decasaccharide assembly via 8 + 2 glycosylation

MALDI analysis of each product after purification revealed the presence of the decasaccharide. At this point, extensive structural congruence in the glycan component of each decasaccharide resulted in significant overlapping of both anomeric ^{1}H and ^{13}C signals, making structural assignment unfeasible. Consequently, I relied on the comparison of anomeric carbon shifts to predict the anomeric configuration for each decasaccharide. Establishing the β-anomeric configuration was made with the observation that all the anomeric carbon shifts in the

decasaccharide occurred in the range expected for β-glucosides (100–102 ppm). If α-glucosylation had occurred, resonances at higher field (95–100 ppm) would be observed.

3.5.4.2 Simultaneous quadruple C-2 inversion

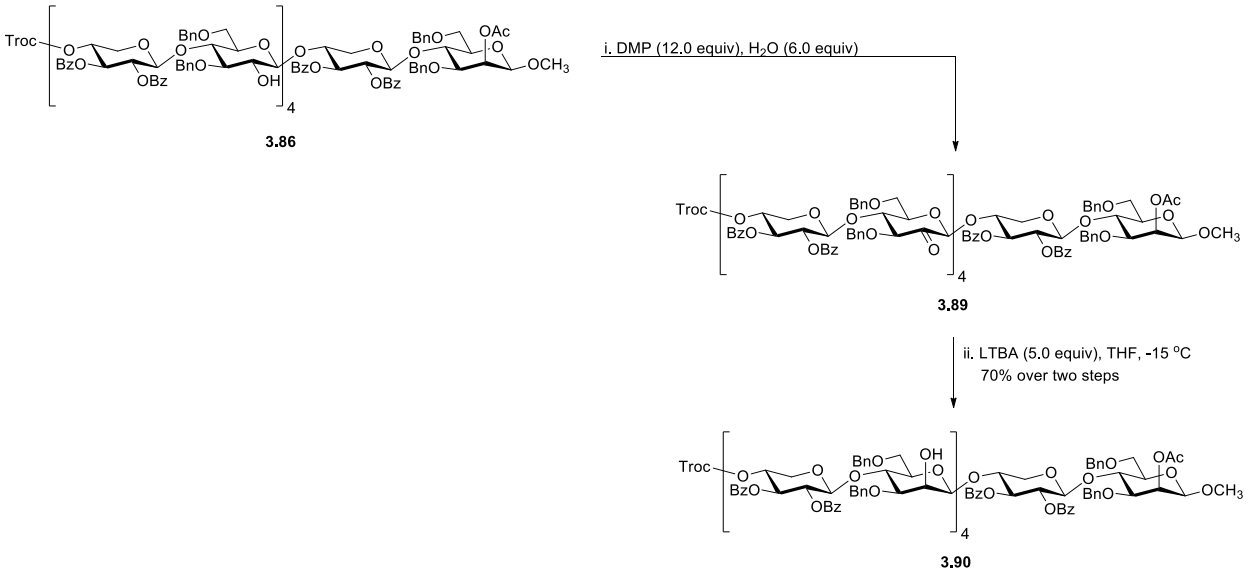
With the three decasaccharides **3.82, 3.84 and 3.85** successfully verified via both NMR spectroscopy and MALDI-TOF mass spectrometry, levulinoyl deprotection via hydrazinolysis was investigated (Scheme 3-24). Cognizant of the increasing time taken to remove multiple levulinoyl groups in larger oligosaccharides and the difficulty in monitoring of reaction progress, each deprotection was stirred overnight under argon in the presence of a five to six-fold (per oligosaccharide) excess of hydrazine acetate. Subsequent examination of the crude reaction mixture via MALDI-TOF mass spectrometric analysis revealed the improvisation to be successful in removing all the levulinoyl esters, generating only a single product, which was then purified to afford desired tetraols **3.86–3.88** in yields of 70–74%.



Scheme 3-24: Hydrazinolysis of levulinoyl esters on decasaccharides **3.82**, **3.84** and **3.85**

My approach hinged on the ability to oxidise all of the C-2 alcohols without any significant issues. In this regard, gaining access to the tetraketone derivatives became a focus. I investigated the feasibility of DMP oxidation on tetraol **3.86** (Scheme 3-25), acting on concerns regarding the possibility of ketone hydration from both the super-stoichiometric amounts of water added and the acetic acid that will be generated in the course of reaction. Previous

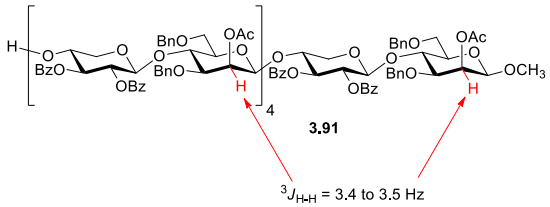
experiences with the difficulty in reaction monitoring via TLC led to the use of MALDI-TOF mass spectrometry to determine reaction completion. Any concern on complete ketone hydration during DMP oxidation was immediately dispelled with the successful detection of tetraketone **3.89** by MALDI-TOF analysis of the crude reaction (M + Na: *m/z* = 3674.2). Upon its isolation, tetraketone **3.89** was swiftly taken, without purification, to the next step. My concern in the possibility of decomposition of **3.89** or Troc degradation in the presence of large amount of LTBA was also dispelled with the successful isolation of the desired xylomannan decasaccharide **3.84** in 65% yield over two steps.



Scheme 3-25: Simultaneous quadruple C-2 inversion on tetraol **3.86**

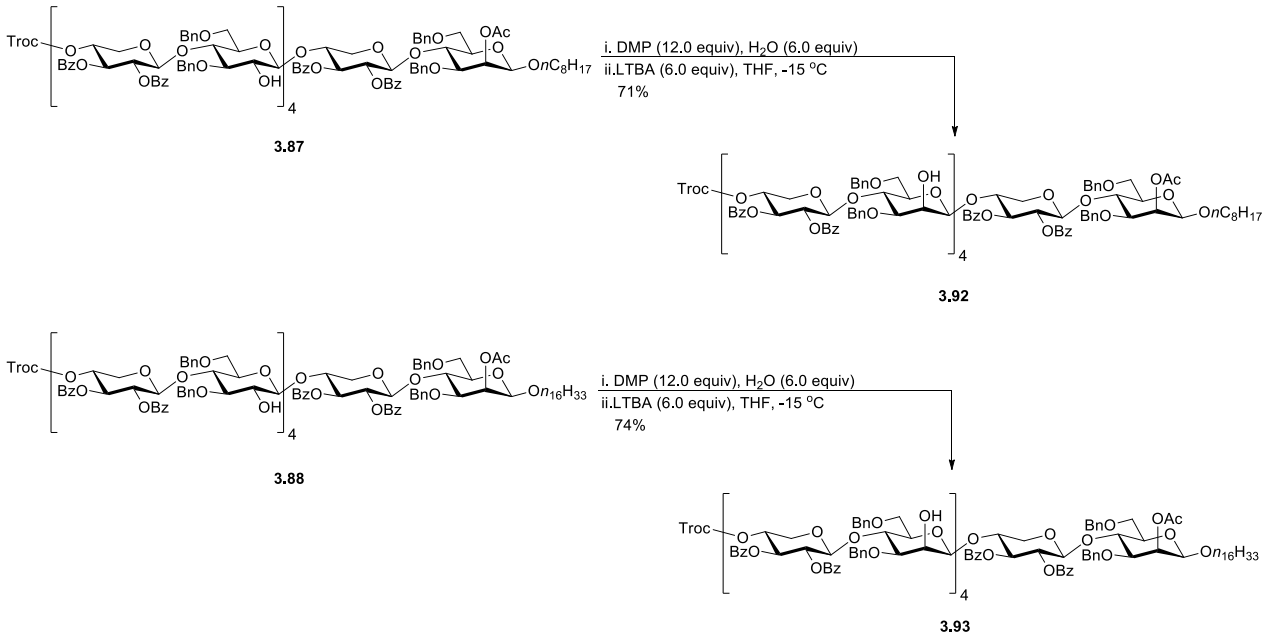
Further support for the complete *manno* selectivity in the LTBA reduction was garnered from the ^{1}H NMR spectra of **3.91**, which was obtained after acetylation of all the Man*p* C-2 hydroxyl groups and subsequent Troc removal (Scheme 3-26). Despite some degree of overlapping of the diagnostic Man*p* H-2 resonances occurring in the region δ_H 5.52–5.40 ppm, the characteristically small $^{3}J_{H\text{-}H}$ of each resonance (2.1–3.5 Hz), coupled with the diagnostic $^{1}J_{C\text{-}}$

$_H$ values in the range of 158–162 Hz, were in good agreement with the values observed in xylomannans serve as good indicators of the desired linkage.



Scheme 3-26: Indirect structural verification of the stereochemical outcome of simultaneous quadruple C-2 inversion

The reliability of this approach was demonstrated in Scheme 3-27, in which extension of this concept to the two remaining decasaccharides, **3.87** and **3.88**, led to xylomannan derivatives **3.92** and **3.93** in yields of 71% and 74%, respectively.



Scheme 3-27: Simultaneous quadruple C-2 inversion to obtain xylomannan decasaccharides **3.92** and **3.93**

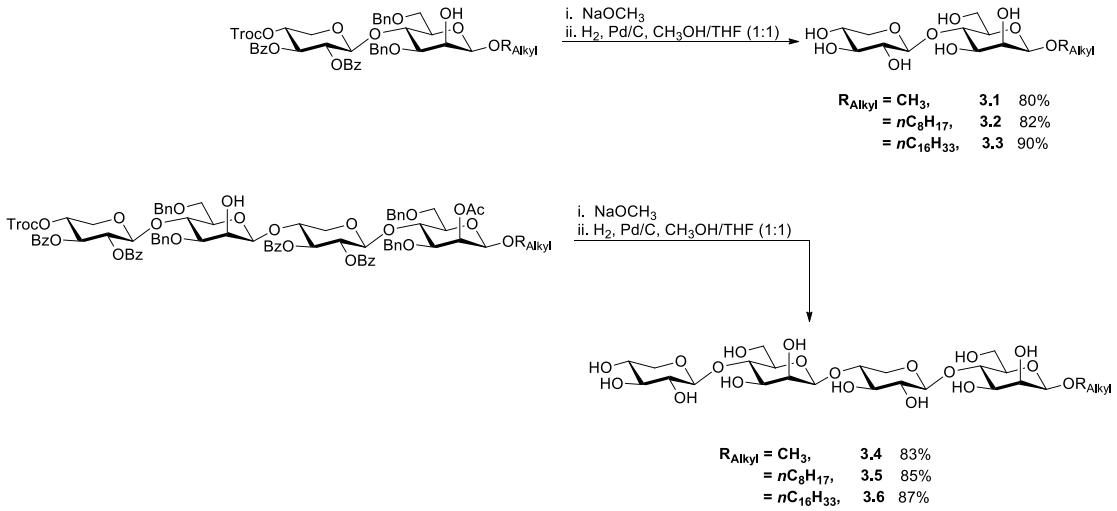
The complete *manno*-selectivity obtained in all cases after simultaneous inversion could be attributed to two main factors: 1) steric hindrance from both the bulky LTBA and uloside H-4 in overcoming local torsional strain and 2) presence of benzyloxy groups on each uloside C-3, which were crucial in delivering complete *manno*-selectivity. In addition to these, I proposed that the conformation of each oligosaccharide after C-2 oxidation may also contribute to the exquisite stereoselectivity by adopting a relatively open structure commonly observed in β-(1→4)-pyrans,[24] thus allowing the aforementioned two factors to control the stereochemistry of the reduction.

3.5.5 Global deprotection of xylomannan oligosaccharides

Having established a route to all the synthetic xylomannan derivatives, it was expected that the global deprotection of each oligosaccharide could be accomplished in a two-step procedure: an initial acyl hydrolysis under basic conditions followed by benzyl deprotection. Although it is well-known that ester deprotection can be carried out via catalytic amounts of sodium methoxide in dry methanol (i.e., Zemplen deacetylation), in my case, super-stoichiometric excess of methanolic sodium methoxide in wet methanol were required to ensure complete cleavage of the Troc carbonates and to avoid any potential side products from their partial degradation. While all the hydrolysis reactions were completed using wet methanolic sodium methoxide, caution had to be taken in quenching with the acidic ion-exchange resins to avoid over-acidification of the reaction mixture with risk of eventual product degradation. In fact, it was observed that these deacylated xylomannans undergo hydrolysis at their β-xylosidic linkages on prolonged exposure to pH lower than 1. To facilitate purification of the final compounds, each reaction mixture was subsequently subjected to three washes with *n*-hexanes to

remove all non-polar by-products. These partially deprotected compounds were then brought to the next step without any further purification.

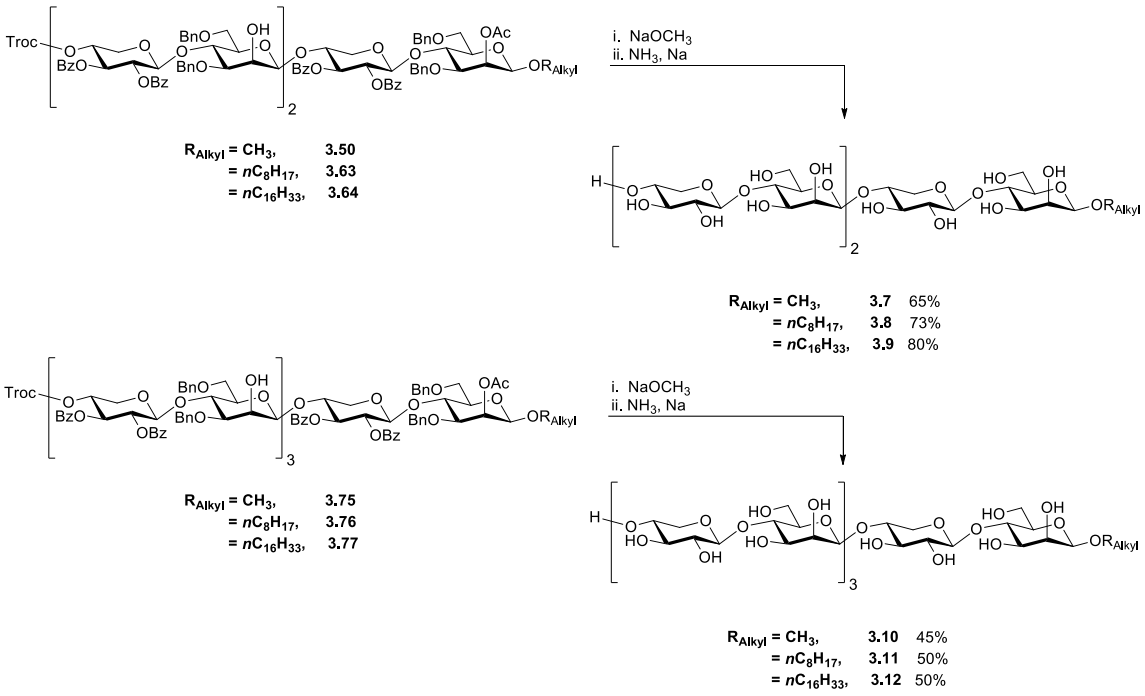
Given the number of benzyl groups in each series (in the range from two in the disaccharides to ten in the decasaccharides), it assumed that they could be efficiently removed via catalytic hydrogenation with palladium on charcoal. This idea was successfully demonstrated on the disaccharides, thus furnishing disaccharyl xylomannans **3.1–3.3** cleanly in yields of 80–90%. Similarly, catalytic hydrogenation of tetrasaccharides was also successful, producing tetrasaccharyl xylomannans **3.4–3.6** smoothly in 80–90% yields (Scheme 3-28).



Scheme 3-28: Global deprotection via methanolic $NaOCH_3$, followed by catalytic hydrogenation

Guided by my success in catalytic hydrogenation for the final benzyl ether deprotection in the di- and tetrasaccharides, I sought to replicate the same for the remaining deacylated oligosaccharides. Unfortunately, this method was plagued by incomplete debenzylation, which persisted even with a large excess of palladium on charcoal and addition of acetic acid. Prolonged stirring (beyond 64 hours) only resulted in slow decomposition of the compounds. Although complete debenzylation was achieved on overnight exposure to 20% palladium

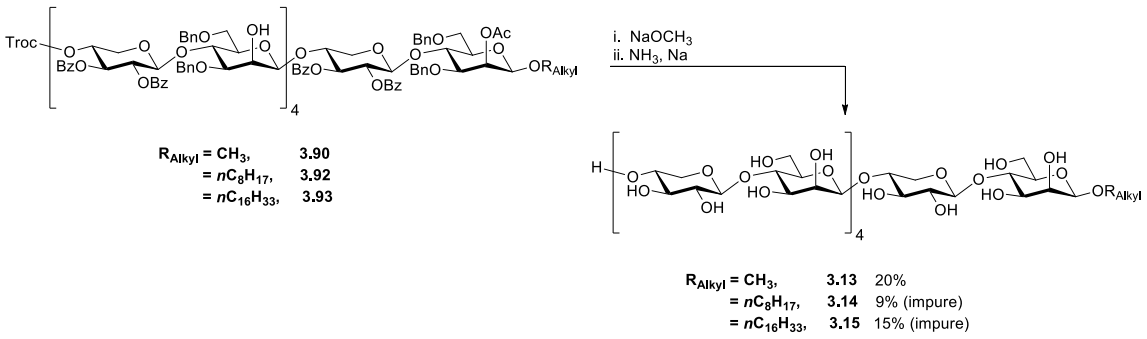
hydroxide on charcoal, observation of extensive oligosaccharide fragmentation in the crude product rendered this method undesirable. After extensive experimentation, this problem was resolved with the use of Birch reduction for debenzylation, providing hexasaccharyl xylomannans **3.7–3.9** in yields of 65–80% over two steps (Scheme 3-29). Similarly, global deprotection via acyl deprotection, followed by Birch reduction of the octasaccharides **3.75**–**3.77** furnished the octasaccharyl xylomannans **3.9–3.12**, albeit in lower yields (45–50%).



Scheme 3-29: Hexa- and octasaccharyl xylomannans via initial deacylation with $NaOCH_3$, followed by Birch reduction

The success in obtaining fully deprotected xylomannans **3.1–3.12** prompted subsequent efforts into deprotection of the decasaccharides (Scheme 3-30). Although deacylation was achieved with $NaOCH_3$, debenzylation under Birch conditions led to significant oligosaccharide breakdown in all three cases, thus necessitating two or three rounds of purification through Iatrobeads and C-18 columns to remove these fragments. Thus, decasaccharyl xylomannan **3.13**

was isolated in low yields of 20%. In the case of both xylomannans **3.14** and **3.15**, despite numerous rounds of purification, unknown greasy contaminants and traces of oligosaccharide fragments persisted, the presence of which could be detected in their NMR spectra. An acetylation–deacetylation strategy to remove all the contaminants was subsequently carried out, which succeeded in removing most of the fragments, yet the grease remained. With <1.0 mg of **3.14** and **3.15** remaining at this point, I discontinued further purification.



Scheme 3-30: Decasaccharyl xylomannans **3.13–3.15** via initial deacylation with $NaOCH_3$ followed by Birch reduction

Subsequent NMR analysis of the pure xylomannan-based AFGL mimetics revealed several similarities with the natural sample.[25] The almost identical ^1H and ^{13}C spectra observed within each series of AFGL mimetics (methyl, octyl and cetyl glycosides) arose not just due to extensive structural congruence in the xylomannan core but also reflected an open and highly regular structure that was first predicted by Ito.[26] In the case of AFGL mimetics bearing cetyl aglycones, poor solubility in polar protic solvents necessitated the use of either (1:1 CD_3OD–$CDCl_3$) systems (for **3.3** and **3.6**) or DMSO-d_6 (for **3.9, 3.12** and **3.15**) for NMR spectroscopic analysis. Although some chemical shift differences were noticed between the AFGL mimetics and the natural sample, I believed this to occur simply due to the differences in the acquisition conditions.

3.6 Conclusion

In summary, a novel convergent strategy involving a simultaneous multiple C-2 inversion approach was developed as a means to synthesize a library of structurally defined xylomannan-based antifreeze glycolipids **3.1–3.15**. This strategy bears the distinction of glycan assembly through indirect β-mannosylation, as opposed to securing these difficult linkages at the disaccharide stage prior to glycan assembly as described in earlier reports.[23,26,27] More importantly, to the best of my knowledge, this strategy showcases the first example of simultaneous multiple C-2 inversion in the synthesis of oligosaccharides containing several β-mannosidic linkages. Furthermore, only the easily accessible xylose donor **2.44** and glucose acceptor **3.17** were used to construct a common disaccharide building block **3.16**, which can be rapidly converted into other building blocks for larger glycan assembly. Each round of levulinoyl-directed β-glucosylation was followed by Troc removal of the resultant oligosaccharide to generate an acceptor, which could then undergo another round of glycosylation. In this way, oligosaccharides of any desired size can be rapidly assembled.

Although glycosylation was found to be increasingly difficult with larger acceptors, it was resolved with the use of higher donor equivalents and TfOH loading. In the case of the 8 + 2 glycosylation, difficult purifications due to traces of remaining acceptors were resolved by treatment of the crude with TrocCl and pyridine. With oligosaccharides containing various number of β-glucosides in hand, several challenging β-mannosidic linkages could then be established in just three steps via a levulinoyl deprotection followed by simultaneous multiple C-2 inversion. This led to the synthesis of all the protected xylomannan oligosaccharides in

generally good yields. Subsequent two-stage deprotection afforded the AFGL mimetics **3.1** to **3.12** in moderate to high yields.

However, there is still room for improvement in my synthetic work. Although deprotection of xylomannan oligosaccharides was successful, progressively lower yields were observed with the larger oligosaccharides. Fragmentation of the oligosaccharides is the key issue, leading to the need for extensive purifications, which contributed to diminished yields. In the case of both the octasaccharides and decasaccharides, the moderate to low yields warrant further investigation into other debenzylation strategies. Alternatively, it is possible to replace the benzyl groups on O-6 of hexopyranosides with either acetyl or benzoyl groups.[13] This may help to ameliorate the difficulties faced in both benzyl deprotection and glycosylation in larger oligomers, the former on the requirement of Birch reduction for complete deprotection and the latter was plagued by the formation of 1,6-anhydrosugars (e.g. **3.83**).

Compounds **3.1** to **3.13** will be delivered to the laboratory of my collaborator, Prof. Hubbard, in the Department of Pharmacology at University of Alberta, where they will be analysed for both TH and IRI activities. The structure-activity relationships that are subsequently obtained will allow us to gain a better understanding of the xylomannan glycolipids and their contribution to the freeze-tolerance of *Upis ceramboides.* Moreover, compounds that display promising IRI activity will be selected for further development as novel cryoprotectants for cryopreservation of cells and tissues.

3.7 Experimental Section

General Experimental Methods. All reagents were purchased from commercial sources and were used without further purification unless noted. Anhydrous solvents used in reactions were purified by successive passage through columns of alumina and copper under argon. Both 3Å and 4Å molecular sieves were dried at 300 °C in oven. Unless stated otherwise, all reactions were carried out in anhydrous solvents at room temperature and monitored by TLC on Silica Gel G-25 F_{254} (0.25 mm). In chemical glycosylations, all the starting materials were thoroughly dried under toluene co-evaporation (3x), followed by drying over P_2O_5 overnight prior to the reaction. TLC spots were detected under UV light and/or by charring with a solution of *p*-anisaldehyde in ethanol, acetic acid and H_2SO_4. Column chromatography was performed on Silica Gel 60 (40–60 μm), C18 silica gel (35−70 μm), or Iatrobeads (6RS-8060). In some cases, a dry loading technique (substrate adhered to silica, solvent removed, then loaded on column) was used for purification. Solvents were evaporated under reduced pressure on a rotary evaporator. ^{1}H NMR spectra were recorded using 400, 500 or 700 MHz NMR instruments and were referenced to residual proton signal of $CDCl_3$ (7.26 ppm), CD_3OD (3.30 ppm), DMSO-d_6 (2.50 ppm) or D_2O (4.79 ppm). ^{13}C NMR spectra were recorded using either 100 MHz, MHz (cold probe) or 175 MHz (cold probe) NMR instruments and were referenced to residual ^{13}C signals of $CDCl_3$ (77.06 ppm), CD_3OD (49.0 ppm), DMSO-d_6 (39.5 ppm) or external acetone (31.1 ppm, D_2O). ^{1}H NMR data are reported as though they were first order, and peak assignments were made on the basis of 2D-NMR (COSY, TOCSY, HSQC and HMBC) experiments. In the case where DMSO-d_6 was used, 10% D_2O was added to exchange the OH signals, and saturation frequency was applied on the resultant HOD signals. The stereochemistry of the anomeric centres of the pyranose rings was determined by measuring $^1J_{C1\text{-}H1}$ via coupled HSQC experiments, if

necessary. Starting from disaccharides to tetrasaccharides, all monosaccharide residues are labelled, when possible, by an increasing number of diacritical marks (` to ````) from the reducing end to the non-reducing end. In the case of hexasaccharides to decasaccharides, only distinguishable NMR signals were assigned and these are labelled with specified monosaccharide residue. ESI-MS spectra (time-of-flight analyzer) were recorded on an Agilent Technologies 6220 TOF spectrometer on samples dissolved in THF, CH_3OH or CH_3CN and added NaCl. MALDI-TOF mass spectrometric spectra were obtained on samples in the linear positive mode of ionization on a Bruker UltrafleXtreme MALDI-TOF/TOF mass spectrometer and Bruker 9.4T Apex-Qe FTICR using either *trans*-2-[3-(4-*tert*-Butylphenyl)-2-methyl-2-propenylidene]malononitrile (DCTB) or 2,5-Dihydroxybenzoic acid (DHB) as the matrix with NaCl added to the samples. Optical rotations were measured at 22 ± 2 °C at the sodium D line (589 nm) in a microcell (10 cm, 1 mL) and were expressed in units of $deg \cdot mL(dm \cdot g)^{-1}$.

General procedure for the removal of Levulinoyl protecting groups.

To a solution of an oligosaccharide containing *n* levulinoyl protecting groups in CH_2Cl_2–CH_3OH (9:1) was added a solution of $H_2NNH_2 \cdot HOAc$ (1.2–1.5*n* equiv) in CH_3OH. The solution was then stirred at room temperature until complete consumption of the starting materials as determined by TLC analysis. The reaction mixture was then diluted with CH_2Cl_2 and poured into satd. aqueous $NaHCO_3$. The two phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 50 mL), before the organic layers were combined and washed with H_2O, brine and dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a crude residue that was subsequently purified by silica gel chromatography using the appropriate eluent.

General procedure for the removal of Troc protecting groups.

To a solution of a Troc-protected oligosaccharide in glacial AcOH (4 mL per 100 mg oligosaccharide) was added freshly activated Zn powder, and the resultant mixture was stirred for 2 h. The Zn powder was then filtered off by passing the mixture through Celite and the resultant filtrate was concentrated to a crude residue. Residual AcOH was removed from the residue via co-evaporation with toluene (2x). The resultant residue was then purified by silica gel chromatography using the appropriate eluent.

General procedures for C-2 inversion via the oxidation–reduction approach.

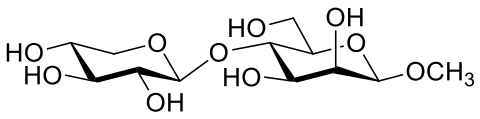
Approach A: Oxidation via Albright–Goldman conditions, followed by LTBA reduction.

To a solution of levulinoyl-deprotected oligosaccharide in anhydrous DMSO (4 mL per 100 mg oligosaccharide) was added Ac_2O (0.5 mL per 100 mg oligosaccharide) under argon. The resultant mixture was then stirred at room temperature until complete consumption of the starting materials as determined by TLC analysis. To this mixture was added CH_2Cl_2, followed by H_2O (20 mL per 1 mL DMSO). The two phases were separated and the organic layer was washed with H_2O (5x), satd. aqueous $NaHCO_3$ and brine before it was dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a crude oily residue that was co-evaporated with toluene (3x). The resultant solid residue was then placed under vacuum for 1 h. To this crude residue was added THF under argon and the reaction mixture was subsequently cooled to –15 °C. Next, LTBA (1.2 to 1.4 equiv per hydroxyl group in the precursor) was added in 2 portions over 1 min and the solution was stirred at –15 °C for 30 min before adding glacial AcOH to quench the excess LTBA reagent. The reaction mixture was concentrated and then re-dissolved in EtOAc before it was poured into satd. aqueous $NaHCO_3$. The two phases were

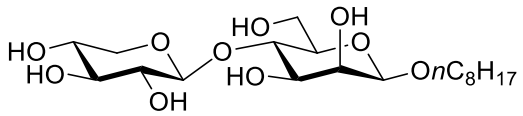
separated and the aqueous layer was extracted with EtOAc. The organic layers were then combined and washed with brine, before drying over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a crude residue that was purified by silica gel chromatography using the appropriate eluent.

Approach B: Oxidation via Dess–Martin Periodinane (DMP), followed by LTBA reduction.

To a solution of levulinoyl-deprotected oligosaccharide in CH_2Cl_2 was added DMP (3.0 equiv per hydroxyl) under argon, followed by H_2O (1.1 to 1.5 equiv per hydroxyl). The resultant mixture was then stirred at room temperature until complete consumption of the starting materials as determined by TLC analysis (typically 2–3 h for mono- or diols and 6–8 h for triols and tetraols). Excess DMP was quenched by the addition of satd. aqueous $Na_2S_2O_3$. To this mixture was added CH_2Cl_2 and the resultant mixture was then washed with H_2O (5x), satd. aqueous $NaHCO_3$ and brine before it was dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate, led to a crude residue that was co-evaporated with toluene (3x), before it was then placed under vacuum for 1 h. The crude residue was re-dissolved in THF under argon and the resultant solution was subsequently cooled to −15 °C. Next, LTBA (1.2 to 1.5 equiv per hydroxyl in the starting precursor) was added in 2 portions over 1 min and the reaction mixture was allowed to stir at −15 °C for 30 min before glacial AcOH was added to quench the excess LTBA reagent. The reaction mixture was concentrated and then re-dissolved in EtOAc before pouring into satd. aqueous $NaHCO_3$. The two phases were separated and the aqueous phase was extracted with EtOAc (3x). The combined organic phases were subsequently washed with brine and dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a crude residue that was purified by silica gel chromatography using the appropriate eluent.

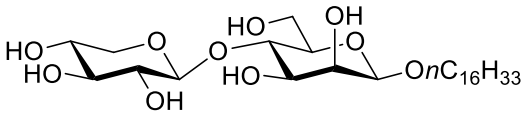


Methyl β-D-xylopyranosyl-(1→4)-β-D-mannopyranoside (3.1). To a flask containing **3.30** (138 mg, 0.155 mmol) in CH_3OH (5 mL) and CH_2Cl_2 (3 mL) was added 1.0 M $NaOCH_3$ in CH_3OH (0.3 mL). The reaction mixture was stirred for 2 h and then neutralized by the addition of Amberlite IR-120 H^+ resin. Filtration of the mixture, followed by concentration and co-evaporation of the filtrate with CH_2Cl_2 (2x) led to a residue that was triturated with hexanes. This resultant residue was re-dissolved in 1:1 THF–CH_3OH (5 mL) and then 10% Pd/C (114 mg) was added under argon. To this mixture was added glacial AcOH (1 drop) and the resultant mixture was then purged with H_2 gas before it was stirred under H_2 atmosphere overnight. The mixture was passed through Celite and the filtrate was subsequently concentrated to a crude residue that was purified by reversed phase C18 chromatography (100% H_2O to 80% H_2O–CH_3OH). Subsequent lyophilization of the product yielded **3.1** (40.5 mg, 0.124 mmol, 80%) as a white fluffy solid. R_f = 0.24 (12:3:3:2 EtOAc–CH_3OH–AcOH–H_2O); $[\alpha]_D$ –21.5 (*c*. 0.04, CH_3OH); ^1H NMR (500 MHz, D_2O, δ_H) 4.62 (s, 1H, H-1`), 4.44 (d, *J* = 7.8 Hz, 1H, H-1``), 4.08–3.98 (m, 3H, H-6a`, H-2`, H-5a``), 3.85 (dd, *J* = 12.2, 5.6 Hz, 1H, H-6b`), 3.81–3.73 (m, 2H, H-4`, H-3`), 3.66 (td, *J* = 10.0, 5.5 Hz, 1H, H-4``), 3.57 (s, 3H, $OCH_3$), 3.54 (ddd, *J* = 8.5, 5.7, 2.2 Hz, 1H, H-5`), 3.48 (app t, *J* = 9.4 Hz, 1H, H-3``), 3.40–3.28 (m, 2H, H-2``, H-5b``). ^{13}C NMR (125 MHz, D_2O, δ_C) 103.5 (C-1``), 100.9 (C-1`), 76.6 (C-4`), 75.7 (C-3``), 75.1 (C-5`), 73.2 (C-2``), 71.6 (C-3`), 69.9 (C-2`), 69.2 (C-4``), 65.2 (C-5``), 60.4 (C-6`), 56.9 ($O\underline{C}H_3$). HRMS (ESI) calcd for $(M + Na)^+$ $C_{12}H_{22}NaO_{10}$: 349.1105. Found: 349.1101.



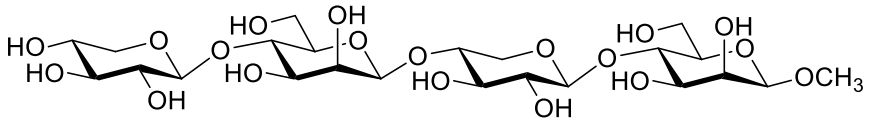
***n*-Octyl β-D-xylopyranosyl-(1→4)-β-D-mannopyranoside (3.2).** To a flask containing **3.31** (116 mg, 0.117 mmol) in CH_3OH (5 mL) and CH_2Cl_2 (3 mL) was added 1.0 M $NaOCH_3$ in CH_3OH (0.3 mL). The reaction mixture was stirred for 2 h and then neutralized with Amberlite IR-120 H^+ resin. Filtration of the mixture, followed by concentration and co-evaporation of the filtrate with CH_2Cl_2 led to a residue that was triturated with hexanes. This resultant residue was re-dissolved in 1:1 THF–CH_3OH (5 mL) and then 10% Pd/C (104 mg) was added under argon. To this mixture was added glacial AcOH (1 drop) and the resultant mixture was subsequently purged with H_2 gas before it was stirred under H_2 atmosphere overnight. The mixture was passed through Celite and the filtrate was then concentrated to a crude residue that was purified by reversed phase C18 chromatography (100% H_2O to 40% H_2O–CH_3OH). Subsequent lyophilization of the product yielded **3.2** (40.7 mg, 0.096 mmol, 82%) as a white fluffy solid. R_f = 0.49 (12:3:3:2 EtOAc–CH_3OH–AcOH–H_2O); $[\alpha]_D$ −192.0 (*c*. 0.01, CH_3OH); ^{1}H NMR (500 MHz, D_2O, δ_H) 4.70 (s, 1H, H-1`), 4.44 (d, *J* = 7.8 Hz, 1H, H-1``), 4.08–3.98 (m, 3H, H-6a`, H-2`, H-5a``), 3.90 (dt, *J* = 10.1, 6.9 Hz, 1H, 1 × OC<u>H</u>$_2$(CH$_2$)$_6$CH$_3$), 3.85 (dd, *J* = 12.1, 5.4 Hz, 1H, H-6b`), 3.82–3.71 (m, 2H, H-3`, H-4`), 3.71–3.63 (m, 2H, 1 × OC<u>H</u>$_2$(CH$_2$)$_6$CH$_3$, H-4``), 3.55–3.50 (m, 1H, H-5`), 3.48 (app t, *J* = 9.3 Hz, 1H, H-3``), 3.40–3.28 (m, 2H, H-5b``, H-2``), 1.70–1.59 (m, 2H, OCH$_2$(C<u>H</u>$_2$)$_6$CH$_3$), 1.43–1.23 (m, 10H, OCH$_2$(C<u>H</u>$_2$)$_6$CH$_3$), 0.96–0.84 (m, 3H, OCH$_2$(CH$_2$)$_6$C<u>H</u>$_3$). ^{13}C NMR (125 MHz, D_2O, δ_C) 103.5 (C-1``), 99.7 (C-1`), 76.6 (C-4`), 75.7 (C-3``), 75.1 (C-5`), 73.2 (C-2``), 71.7 (C-3`), 70.3 (C-2`), 70.2 (O<u>C</u>H$_2$(CH$_2$)$_6$CH$_3$), 69.2 (C-4``), 65.2 (C-5``), 60.4 (C-6`), 31.2 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 28.7 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 28.5 × 2

($OCH_2(\underline{C}H_2)_6CH_3$), 25.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.1 ($OCH_2(\underline{C}H_2)_6CH_3$), 13.5 ($OCH_2(CH_2)_6\underline{C}H_3$). HRMS (ESI) calcd for $(M + Na)^+$ $C_{19}H_{36}NaO_{10}$: 447.2201. Found 447.2196.



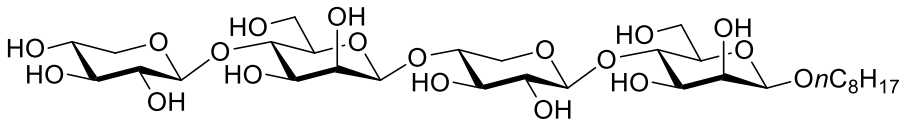
***n*-Hexadecyl β-D-xylopyranosyl-(1→4)-β-D-mannopyranoside (3.3).** To a flask containing **3.32** (67.3 mg, 61.5 μmol) in CH_3OH (1.5 mL) and THF (2.5 mL) was added 1.0 M $NaOCH_3$ in CH_3OH (0.2 mL). The reaction mixture was stirred for 2 h and then neutralized by addition of Amberlite IR-120 H^+ resin. Filtration of the mixture, followed by concentration and co-evaporation of the filtrate with CH_2Cl_2 led to a residue that was triturated with hexanes. The resultant crude residue was re-dissolved in 1:1 CH_3OH–THF (5 mL), and then 10% Pd/C (100 mg) was added under argon. To this mixture was added glacial AcOH (1 drop) and the resultant suspension was subsequently purged with H_2 gas before it was stirred under H_2 atmosphere overnight. The mixture was passed through Celite and the filtrate was then concentrated before it was co-evaporated with CH_2Cl_2. The resultant crude material was triturated with hexanes and the remaining residue was re-dissolved in CH_3OH–THF–CH_2Cl_2 (4 mL, 1:1:2). To this solution was added distilled H_2O (~5 mL) and sonication was applied to ensure dissolution. White solids were observed to precipitate from the resultant mixture after slow evaporation for 4 days at room temperature. The mixture was filtered and the residue on the filter paper was washed with distilled H_2O. The residue was then dried under vacuum to yield **3.3** (27.9 mg, 52.0 μmol, 85%) as a white powder. R_f = 0.48 (5:1 CH_2Cl_2–CH_3OH); ^{1}H NMR (500 MHz, 1:1 CD_3OD–$CDCl_3$, δ_H ref. to CHD_2OD) 3.73 (d, J = 0.9 Hz, 1H, H-1`), 3.56 (d, J = 7.7 Hz, 1H, H-1``), 3.25 (dd, J = 3.2,

0.9 Hz, 1H, H-2`), 3.20 (dd, J = 11.4, 5.4 Hz, 1H, H-5a``), 3.15–3.09 (m, 3H, H-6a`, H-6b`, 1 × OC$\underline{H}_2(CH_2)_{14}CH_3$), 3.06 (app t, $J$ = 9.4 Hz, 1H, H-4`), 2.86–2.72 (m, 3H, H-3`, H-4``, 1 × OC$\underline{H}_2(CH_2)_{14}CH_3$), 2.64–2.56 (m, 3H, H-3`, H-3``, H-5`), 2.55–2.46 (m, 2H, H-5b``, H-2``), 0.91–0.79 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 0.65–0.41 (m, 26H, 26 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 0.12 (t, $J$ = 6.9 Hz, 3H, $OCH_2(CH_2)_{14}C\underline{H}_3$). $^{13}$C NMR (125 MHz, 1:1 $CD_3OD$–$CDCl_3$, $\delta_C$ ref. 49.0 ppm, $CD_3OD$) 104.5 (C-1``), 100.4 (C-1`), 78.6 (C-4`), 76.9 (C-3``), 75.2 (C-5`), 73.5 (C-2``), 72.5 (C-3`), 70.4 (C-2`), 70.3 ($O\underline{C}H_2(CH_2)_{14}CH_3$), 69.5 (C-4``), 66.1 (C-5``), 61.6 (C-6`), 32.1 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.8 × 5 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.7 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.6 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.5 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 26.1 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 22.8 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 14.1 ($OCH_2(CH_2)_{14}\underline{C}H_3$). HRMS (ESI) calcd for $(M + Na)^+$ $C_{27}H_{52}NaO_{10}$: 559.3453. Found 559.3447.



Methyl β-D-xylopyranosyl-(1→4)-β-D-mannopyranosyl-(1→4)-β-D-xylopyranosyl-(1→4)-β-D-mannopyranoside (3.4). To a flask containing **3.43** (46.1 mg, 28.6 μmol) in 1:1 CH_2Cl_2–CH_3OH (5 mL) was added 0.1 M $NaOCH_3$ in CH_3OH (0.4 mL). The reaction mixture was stirred for 2 h and then neutralized by addition of Amberlite IR-120 H^+ resin. Filtration of the mixture, followed by concentration and then co-evaporation of the filtrate with CH_2Cl_2 led to a crude residue that was triturated with hexanes. This resultant residue was re-dissolved in 1:1 THF–CH_3OH (5 mL) and then 10% Pd/C (50 mg) was added under argon. To this mixture was added glacial AcOH (2 drops) and the resultant suspension was subsequently purged with H_2 gas

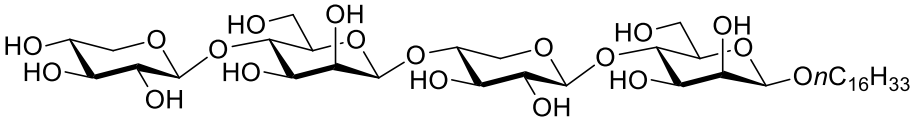
before it was stirred under H_2 atmosphere overnight. The mixture was passed through Celite and the filtrate was then concentrated to a crude residue that was purified by reversed phase C18 chromatography (100% H_2O to 80% H_2O–CH_3OH). The product was subsequently lyophilized to yield **3.4** (14.7 mg, 23.7 μmol, 83%) as a white fluffy solid. R_f = 0.12 (12:3:3:2 EtOAc–CH_3OH–AcOH–H_2O); $[\alpha]_D$ –69.7 (*c*. 0.8, H_2O); ^{1}H NMR (500 MHz, D_2O, δ_H) 4.83 (d, *J* = 1.0 Hz, 1H, H-1```), 4.62 (s, 1H, H-1`), 4.46 (d, *J* = 7.8 Hz, 1H, H-1``), 4.43 (d, *J* = 7.8 Hz, 1H, H-1````), 4.15 (dd, *J* = 11.8, 5.4 Hz, 1H, H-5a``), 4.08–3.98 (m, 5H, H-5a````, H-6a```, H-6a`, H-2```, H-2`), 3.94–3.87 (m, 1H, H-4``), 3.87–3.82 (m, 2H, H-6b`, H-6b```), 3.82–3.73 (m, 4H, H-4`, H-3`, H-3```, H-4```), 3.70–3.61 (m, 2H, H-4````, H-3``), 3.57 (s, 3H, OCH_3), 3.56–3.51 (m, 2H, H-5```, H-5`), 3.47 (app t, *J* = 9.2 Hz, 1H, H-3````), 3.44–3.27 (m, 4H, H-5b````, H-5b``, H-2````, H-2``). ^{13}C NMR (125 MHz, D_2O, δ_C) 104.4 (C-1````), 104.2 (C-1``), 101.9 (C-1`), 99.1 (C-1```), 77.4 × 2 (C-4```, C-4`), 77.1 (C-4``), 76.6 (C-3````), 76.1 (C-5```), 76.0 (C-5`), 74.8 (C-3``), 74.1 (C-2````), 73.8 (C-2``), 72.5 × 2 (C-3```, C-3`), 71.4 (C-2```), 70.9 (C-2`), 70.1 (C-4````), 66.2 (C-5````), 63.9 (C-5``), 61.3 × 2 (C-6```, C-6`), 57.8 (OCH_3). HRMS (ESI) calcd for $(M + Na)^+$ $C_{23}H_{40}NaO_{19}$: 643.2056. Found: 643.2053.



***n*-Octyl β-D-xylopyranosyl-(1→4)-β-D-mannopyranosyl-(1→4)-β-D-xylopyranosyl-(1→4)-β-D-mannopyranoside (3.5).** To a flask containing **3.55** (60.1 mg, 35.1 μmol) in 1:1 CH_2Cl_2–CH_3OH (5 mL) was added 0.1 M $NaOCH_3$ in CH_3OH (0.5 mL). The reaction mixture

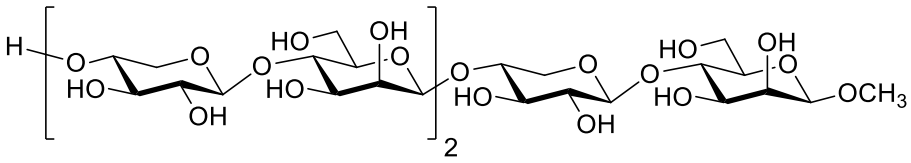
was stirred for 2 h and then neutralized by addition of Amberlite IR-120 H^+ resin. Filtration of the mixture, followed by concentration and co-evaporation of the filtrate with CH_2Cl_2 led to a residue that was triturated with hexanes. This resultant mixture was re-dissolved in 1:1 THF–CH_3OH (5 mL) and then 10% Pd/C (53 mg) was added under argon. To this mixture was added glacial AcOH (2 drops) and the resultant suspension was subsequently purged with H_2 gas before it was stirred under H_2 atmosphere overnight. overnight. The mixture was passed through Celite and the filtrate was then concentrated to a crude residue that was purified by reversed phase C18 chromatography (100% H_2O to 40% H_2O–CH_3OH). The product was subsequently lyophilized to yield **3.5** (21.4 mg, 29.8 μmol, 85%) as a white fluffy solid. R_f = 0.23 (12:3:3:2 EtOAc–CH_3OH–AcOH–H_2O); $[\alpha]_D$ –55.3 (*c*. 0.9, H_2O); ^{1}H NMR (700 MHz, D_2O, δ_H) 4.83 (s, 1H, H-1```), 4.70 (s, 1H, H-1`), 4.46 (d, *J* = 7.8 Hz, 1H, H-1``), 4.43 (d, *J* = 7.8 Hz, 1H, H-1````), 4.15 (dd, *J* = 11.8, 5.4 Hz, 1H, H-5a``), 4.07–3.98 (m, 5H, H-2```, H-5a````, H-2`, H-6a`, H-6a```), 3.93–3.87 (m, 2H, H-4``, 1 × OC<u>H</u>$_2$$(CH_2)_6CH_3$), 3.87–3.82 (m, 2H, H-6b`, H-6b```), 3.82–3.72 (m, 4H, H-3```, H-3`, H-4```, H-4`), 3.71–3.62 (m, 3H, H-3``, H-4````, 1 × OC<u>H</u>$_2$$(CH_2)_6CH_3$), 3.58–3.50 (m, 2H, H-5```, H-5`), 3.48 (app t, *J* = 9.3 Hz, 1H, H-3````), 3.41 (app t, *J* = 11.1 Hz, 1H, H-5b``), 3.38–3.29 (m, 3H, H-5b````, H-2``, H-2````), 1.68–1.60 (m, 2H, 2 × $OCH_2(C$<u>H</u>$_2)_6CH_3$), 1.41–1.25 (m, 10H, 10 × $OCH_2(C$<u>H</u>$_2)_6CH_3$), 0.89 (t, *J* = 6.8 Hz, 3H, $OCH_2(CH_2)_6C$<u>H</u>$_3$). ^{13}C NMR (175 MHz, D_2O, δ_C) 104.3 (C-1````), 104.1 (C-1``), 100.5 (C-1`), 99.0 (C-1```), 77.3 × 2 (C-4```, C-4`), 77.0 (C-4``), 76.5 (C-3````), 76.0, 75.9 (C-5```, C-5`), 74.7 (C-3``), 74.0 (C-2````), 73.7 (C-2``), 72.5, 72.3 (C-3```, C-3`), 71.2 (C-2```), 71.1 (O<u>C</u>$H_2(CH_2)_6CH_3$), 71.0 (C-2`), 70.0 (C-4````), 66.0 (C-5````), 63.8 (C-5``), 61.2 × 2 (C-6```, C-6`), 32.0 ($OCH_2($<u>C</u>$H_2)_6CH_3$), 29.5 ($OCH_2($<u>C</u>$H_2)_6CH_3$), 29.3 × 2 ($OCH_2($<u>C</u>$H_2)_6CH_3$), 26.0

($OCH_2(\underline{C}H_2)_6CH_3$), 22.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 14.3 ($OCH_2(CH_2)_6\underline{C}H_3$). HRMS (ESI) calcd for $(M + Na)^+$ $C_{30}H_{54}NaO_{19}$: 741.3152. Found: 741.3147.



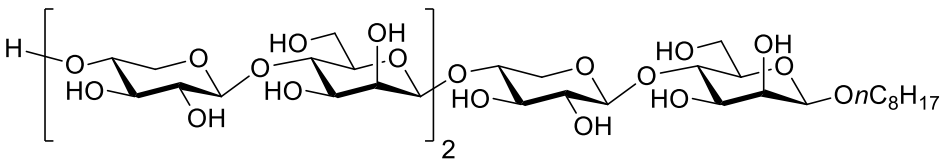
***n*-Hexadecyl β-D-xylopyranosyl-(1→4)-β-D-mannopyranosyl-(1→4)-β-D-xylopyranosyl-(1→4)-β-D-mannopyranoside (3.6).** To a flask containing **3.56** (27.8 mg, 15.6 μmol) in 1:1 CH_2Cl_2–CH_3OH (4 mL) was added 0.1 M $NaOCH_3$ in CH_3OH (0.4 mL). The reaction mixture was stirred for 2 h and then neutralized by addition of Amberlite IR-120 H^+ resin. Filtration of the mixture, followed by concentration and co-evaporation of the filtrate with CH_2Cl_2 led to a residue that was triturated with hexanes. This resultant residue was re-dissolved in 1:1 THF–CH_3OH (5 mL) and then 10% Pd/C (35 mg) was added under argon. To this mixture was added glacial AcOH (2 drops) and the resultant suspension was subsequently purged with H_2 gas before it was stirred under H_2 atmosphere overnight. The mixture was passed through Celite and the filtrate was then concentrated. The resultant crude solid was triturated with hexanes followed by distilled H_2O. The residue was then dried under vacuum to yield **3.6** (21.1 mg, 64.6 μmol, 85%) as a white powder. R_f = 0.61 (12:3:3:2 EtOAc–CH_3OH–AcOH–H_2O); $[\alpha]_D$ –47.7 (*c*. 0.6, 1:1 CD_3OD–$CDCl_3$); ^1H NMR (500 MHz, 1:1 CD_3OD–$CDCl_3$, δ_H ref. to CHD_2OD) 4.58 (s, 1H, H-1```), 4.46 (s, 1H, H-1`), 4.31 (d, *J* = 7.8 Hz, 1H, H-1``), 4.25 (d, *J* = 7.7 Hz, 1H, H-1````), 4.02 (dd, *J* = 11.5, 5.3 Hz, 1H, H-5a``), 3.96–3.69 (m, 11H, H-2```, H-2`, H-4``, H-4```, H-4`, H-5a````, H-6a```, H-6a`, H-6b```, H-6b`, 1 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 3.58–3.45 (m, 5H, H-4````, H-3``, H-3```, H-3`, 1 × $OC\underline{H}_2(CH_2)_{14}CH_3$), 3.39–3.31 (m, 3H, H-5```, H-5`, H-3`````), 3.28–3.17 (m, 4H,

H-2````, H-2``, H-5b````, H-5b``), 1.58 (p, J = 6.9 Hz, 2H, 2 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 1.35–1.15 (m, 26H, 26 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 0.84 (t, J = 6.8 Hz, 3H, $OCH_2(CH_2)_{14}C\underline{H}_3$). ^{13}C NMR (125 MHz, 1:1 CD_3OD–$CDCl_3$, δ_C ref. to CHD_2OD) 104.8 (C-1````), 104.7 (C-1``), 100.8 (C-1`), 98.6 (C-1```), 78.4 (C-4`), 78.0 (C-4```), 77.1 (C-3````), 76.1 , 76.0 (C-5```, C-4``), 75.7 (C-5`), 75.1 (C-3``), 73.9 (C-2````), 73.6 (C-2``), 72.9 (C-3```), 72.7 (C-3`), 70.8, 70.7 (C-2```, C-2`), 70.5 ($O\underline{C}H_2(CH_2)_{14}CH_3$), 70.0 (C-4````), 66.5 (C-5````), 63.7 (C-5``), 61.5 (C-6`), 61.2 (C-6```), 30.1 × 3 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 30.0 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.9 ($OCH_2(CH_2)_{14}CH_3$), 29.8 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 26.4 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 23.1 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 14.3 ($OCH_2(CH_2)_{14}\underline{C}H_3$). HRMS (ESI) calcd for $(M + Na)^+$ $C_{38}H_{70}NaO_{19}$: 853.4404. Found: 853.4398.



Methyl β-D-xylopyranosyl-(1→4)-β-D-mannopyranosyl-(1→4)-β-D-xylopyranosyl-(1→4)-β-D-mannopyranosyl-β-D-xylopyranosyl-(1→4)-β-D-mannopyranoside (3.7). To a flask containing **3.50** (32.2 mg, 14.0 μmol) in 1:1 CH_2Cl_2–CH_3OH (5 mL) was added 0.5 M $NaOCH_3$ in CH_3OH (0.4 mL). The reaction mixture was stirred for 2 h and then neutralized by addition of Amberlite IR-120 H^+ resin. Filtration of the mixture, followed by concentration and co-evaporation of the filtrate with CH_2Cl_2 led to a residue that was triturated with hexanes. This resultant residue was dried via co-evaporation with toluene (2x) and placed under vacuum overnight, after which it was then dissolved in THF (2 mL). In a separate flask containing liquid ammonia (~30 mL) at −78 °C, freshly cut sodium metal (21 mg) was added under argon. The

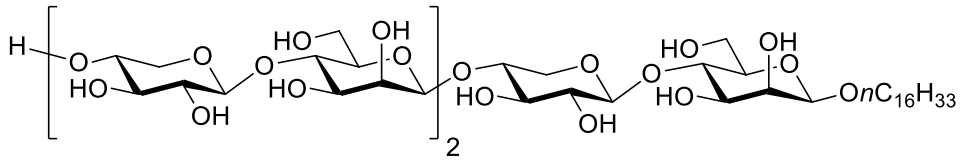
resultant blue solution was stirred for an additional 20 min, before the crude solution in THF was added dropwise over 2 min. After 1 h, CH_3OH (1 mL) was added and the mixture was evaporated to dryness. The resultant white residue was re-dissolved in CH_3OH (30 mL) and Amberlite IR-120 H^+ resin was then added. Filtration of the mixture, followed by concentration of the filtrate led to a crude residue that was purified over an Iatrobead column (12:3:3:2 to 6:3:3:2 EtOAc–CH_3OH–AcOH–H_2O). The resulting product was subsequently lyophilized to yield **3.7** (8.4 mg, 9.2 μmol, 65%) as a white fluffy solid. R_f = 0.31 (6:3:3:2 EtOAc–CH_3OH–AcOH–H_2O); $[\alpha]_D$ −56.3 (*c*. 0.8, H_2O); ^1H NMR (700 MHz, D_2O, δ_H) 4.83 (s, 2H, 2 × H-1_{Man}), 4.62 (s, 1H, H-1_{Man}), 4.48–4.42 (m, 3H, 3 × H-1_{Xyl}), 4.18–4.12 (m, 2H, 2 × H-$5a_{Xyl}$), 4.08–3.99 (m, 7H), 3.94–3.88 (m, 2H), 3.87–3.82 (m, 3H), 3.81–3.73 (m, 6H), 3.69–3.63 (m, 3H), 3.57 (s, 3H, OCH_3), 3.57–3.52 (m, 3H), 3.48 (app t, *J* = 9.2 Hz, 1H, H-3_{Xyl}), 3.44–3.39 (m, 2H, 2 × H-$5b_{Xyl}$), 3.39–3.29 (m, 4H). ^{13}C NMR (175 MHz, D_2O, δ_C) 104.3 (C-1_{Xyl}), 104.1 (C-1_{Xyl}), 101.8 (C-1_{Man}), 99.0 (C-1_{Man}), 77.3 × 2 (C), 77.2, 77.0, 76.5, 76.0 × 2 (C), 75.9, 74.7, 74.0, 73.7 × 2 (C), 72.4, 72.3 × 2 (C), 71.3 × 2 (C), 70.8, 70.0, 66.1 (C-5_{Xyl}), 63.8 (C-5_{Xyl}), 61.2 × 2 (C-6_{Man}), 57.7 (OCH_3). HRMS (ESI) calcd for $(M + Na)^+$ $C_{34}H_{58}NaO_{28}$: 937.3007. Found: 937.3008.



***n*-Octyl β-D-xylopyranosyl-(1→4)-β-D-mannopyranosyl-(1→4)-β-D-xylopyranosyl-(1→4)-β-D-mannopyranosyl-β-D-xylopyranosyl-(1→4)-β-D-mannopyranoside (3.8).** To a flask

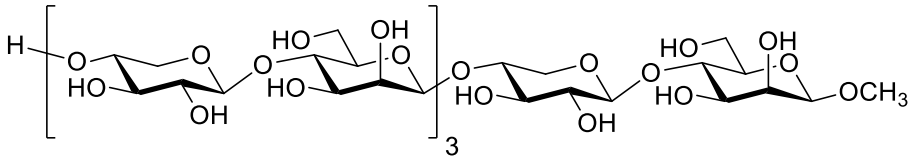
containing **3.63** (38.2 mg, 15.9 μmol) in 1:1 CH_2Cl_2–CH_3OH (5 mL) was added 0.5 M $NaOCH_3$ in CH_3OH (0.4 mL). The reaction mixture was stirred for 2 h and then neutralized by addition of Amberlite IR-120 H^+ resin. Filtration of the mixture, followed by concentration and co-evaporation of the filtrate with CH_2Cl_2 led to a residue that was triturated with hexanes. The resultant residue was dried via co-evaporation with toluene (2x) and placed under vacuum overnight, after which it was dissolved in THF (2 mL). In a separate flask containing liquid ammonia (~30 mL) at −78 °C, freshly cut sodium metal (41 mg) was added under argon. The resultant blue solution was stirred for an additional 20 min, after which the crude solution in THF was then added dropwise over 2 min. After 1 h, CH_3OH (1 mL) was added and the mixture was evaporated to dryness. The resultant white residue was dissolved in CH_3OH (30 mL) and Amberlite IR-120 H^+ resin was then added. Filtration of the mixture, followed by concentration of the filtrate led to a crude residue that was purified over an Iatrobead column (12:3:3:2 to 6:3:3:2 EtOAc–CH_3OH–AcOH–H_2O). The product was subsequently lyophilized to yield **3.8** (11.8 mg, 11.6 μmol, 73%) as a white fluffy solid. R_f = 0.51 (6:3:3:2 EtOAc–CH_3OH–AcOH–H_2O); $[\alpha]_D$ −32.2 (*c*. 0.5, H_2O); ^{1}H NMR (700 MHz, D_2O, δ_H) 4.83 (s, 2H, 2 × H-1$_{Man}$), 4.70 (s, 1H, H-1$_{Man}$), 4.49–4.41 (m, 3H, 3 × H-1$_{Xyl}$), 4.18–4.12 (m, 2H, 2 × H-5a$_{Xyl}$), 4.07–3.98 (m, 8H), 3.94–3.87 (m, 3H), 3.87–3.82 (m, 3H), 3.82–3.73 (m, 7H), 3.72–3.62 (m, 5H), 3.58–3.50 (m, 3H), 3.48 (app t, *J* = 9.3 Hz, 1H, H-3$_{xyl}$), 3.44–3.38 (m, 2H, 2 × H-5b$_{Xyl}$), 3.38–3.27 (m, 5H), 1.68–1.61 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_6CH_3$), 1.41–1.26 (m, 10H, 10 × $OCH_2(C\underline{H}_2)_6CH_3$), 0.89 (t, *J* = 6.9 Hz, 3H, $OCH_2(CH_2)_6C\underline{H}_3$). ^{13}C NMR (175 MHz, D_2O, δ_C) 104.3 (C-1$_{Xyl}$), 104.1 (C-1$_{Xyl}$), 100.6 (C-1$_{Man}$), 99.0 (C-1$_{Man}$), 77.3, 77.2, 77.0, 76.5, 76.0, 75.9, 74.7, 74.0, 73.7, 72.5, 72.3 × 2 (C), 71.3 × 2 (C), 71.1, 71.0 ($O\underline{C}H_2(CH_2)_6CH_3$), 70.0, 66.1 (C-5$_{Xyl}$), 63.8 (C-5$_{Xyl}$), 61.2 × 2 (C-6$_{Man}$), 32.0 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.5 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.3

($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 (($OCH_2(\underline{C}H_2)_6CH_3$), 26.0 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.9 (($OCH_2(\underline{C}H_2)_6CH_3$), 14.3 ($OCH_2(CH_2)_6\underline{C}H_3$). HRMS (ESI) calcd for $(M + Na)^+$ $C_{41}H_{72}NaO_{28}$: 1035.4102. Found: 1035.4091.



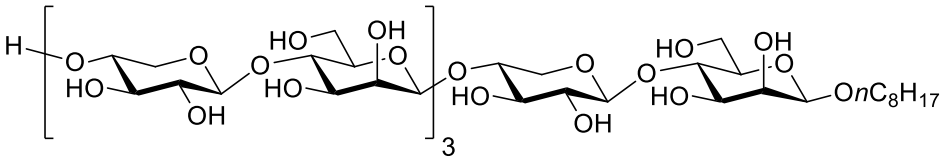
***n*-Hexadecyl β-D-xylopyranosyl-(1→4)-β-D-mannopyranosyl-(1→4)-β-D-xylopyranosyl-(1→4)-β-D-mannopyranosyl-β-D-xylopyranosyl-(1→4)-β-D-mannopyranoside (3.9).** To a flask containing **3.64** (10.6 mg, 4.23 μmol) in 1:1 CH_2Cl_2–CH_3OH (5 mL) was added 0.5 M $NaOCH_3$ in CH_3OH (0.4 mL). The reaction mixture was stirred for 2 h and then neutralized by addition of Amberlite IR-120 H^+ resin. Filtration of the mixture, followed by concentration and co-evaporation of the filtrate with CH_2Cl_2 led to a residue that was triturated with hexanes. The resultant crude material was dried via co-evaporation with toluene (2x) and placed under vacuum overnight, after which it was dissolved in THF (2 mL). In a separate flask containing liquid ammonia (~30 mL) at −78 °C, freshly cut sodium metal (23 mg) was added under argon. The resultant blue solution was stirred for an additional 20 min, after which the crude solution in THF was added dropwise over 2 min. After 1 h, CH_3OH (1 mL) was added and the mixture was evaporated to dryness. The resultant white residue was re-dissolved in CH_3OH (30 mL) and Amberlite IR-120 H^+ resin was then added. Filtration of the mixture, followed by concentration of the filtrate led to a crude residue that was purified over an Iatrobead column (12:3:3:2 to 6:3:3:2 EtOAc–CH_3OH–AcOH–H_2O) and subsequently lyophilized to yield **3.9** (3.8 mg, 3.4

μmol, 80%) as a white solid. R_f = 0.51 (6:3:3:2 EtOAc–CH_3OH–AcOH–H_2O); ^{1}H NMR (700 MHz, DMSO-d_6, δ_H) 4.61 (s, 2H, H-1_{Man}), 4.38 (s, 1H, H-1_{Man}), 4.27–4.23 (m, 2H, 2 × H-1_{Xyl}), 4.19 (d, J = 7.8 Hz, 1H, H-1_{Xyl}), 4.01–3.95 (m, 2H, 2 × H-$5a_{Xyl}$), 3.80–3.75 (m, 2H), 3.75–3.67 (m, 6H), 3.65–3.52 (m, 8H), 3.44–3.36 (m, 3H), 3.33–3.25 (m, 4H), 3.22–3.14 (m, 5H), 3.13–3.07 (m, 2H), 3.06–3.00 (m, 2H, 2 × H-$5b_{Xyl}$), 2.97 (app t, J = 8.4 Hz, 1H, H-2_{Xyl}), 1.51–1.46 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 1.28–1.20 (m, 26H, 26 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 0.85 (t, J = 7.0 Hz, 3H, $OCH_2(CH_2)_{14}C\underline{H}_3$). ^{13}C NMR (175 MHz, DMSO-d_6, δ_C) 103.8 (C-1_{Xyl}), 103.5 (C-1_{Xyl}), 100.1 (C-1_{Man}), 97.9 (C-1_{Man}), 77.3, 77.1, 76.5, 75.6 × 3 (C), 74.4, 73.3, 73.1 × 2 (C), 71.8, 71.7, 69.9 × 2 (C), 69.7, 69.3, 68.5 ($O\underline{C}H_2(CH_2)_{14}CH_3$), 65.9 (C-$5_{Xyl}$), 63.0 (C-$5_{Xyl}$), 60.4 × 2 (C-$6_{Man}$), 60.3 (C-$6_{Man}$), 31.3 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.1 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.0 (3 × $OCH_2(\underline{C}H_2)_{14}CH_3$), 28.9 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 28.7 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 25.6 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 22.1 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 13.9 ($OCH_2(CH_2)_{14}\underline{C}H_3$). HRMS (ESI) calcd for $(M + Na)^+$ $C_{49}H_{88}NaO_{28}$: 1147.5354. Found: 1147.5327.



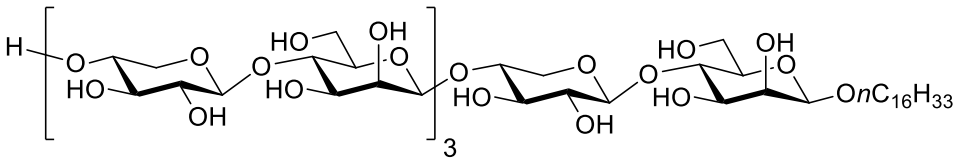
Methyl β-D-xylopyranosyl-(1→4)-β-D-mannopyranosyl-(1→4)-β-D-xylopyranosyl-(1→4)-β-D-mannopyranosyl-(1→4)-β-D-xylopyranosyl-(1→4)-β-D-mannopyranosyl-β-D-xylopyranosyl-(1→4)-β-D-mannopyranoside (3.10). To a flask containing **3.75** (4.5 mg, 1.5 μmol) in 1:1 CH_2Cl_2–CH_3OH (5 mL) was added 0.5 M $NaOCH_3$ in CH_3OH (0.4 mL). The reaction mixture was stirred for 2 h and then neutralized by addition of Amberlite IR-120 H^+

resin. Filtration of the mixture, followed by concentration and co-evaporation of the filtrate with CH_2Cl_2 led to a residue that was triturated with hexanes. The resultant crude material was dried via co-evaporation with toluene (2x) and placed under vacuum overnight, after which it was dissolved in THF (2 mL). In a separate flask containing liquid ammonia (~30 mL) at −78 °C, freshly cut sodium metal (25 mg) was added under argon. The resultant blue solution was stirred for an additional 20 min, before the crude solution in THF was added dropwise over 2 min. After 1 h, CH_3OH (1 mL) was added and the mixture was evaporated to dryness. The resultant white residue was re-dissolved in CH_3OH (30 mL) and Amberlite IR-120 H^+ resin was then added. Filtration of the mixture, followed by concentration of the filtrate led to a crude residue that was purified over an Iatrobead column (12:3:3:2 to 3:3:3:2 EtOAc–CH_3OH–AcOH–H_2O). The product was subsequently lyophilized to yield **3.10** (1.0 mg, 0.83 μmol, 55%) as a white fluffy solid. R_f = 0.20 (6:3:3:2 EtOAc–CH_3OH–AcOH–H_2O); $[\alpha]_D$ −45.0 (*c*. 0.02, H_2O); ^{1}H NMR (700 MHz, D_2O, δ_H) 4.83 (s, 3H, 3 × H-1$_{Man}$), 4.62 (s, 1H, H-1$_{Man}$), 4.49–4.40 (m, 4H, 4 × H-1$_{Xyl}$), 4.18–4.12 (m, 3H, 3 × H-5a$_{Xyl}$), 4.08–3.99 (m, 9H), 3.93–3.87 (m, 4H), 3.87–3.83 (m, 4H), 3.82–3.74 (m, 9H), 3.69–3.62 (m, 5H), 3.57 (s, 3H, OCH_3), 3.57–3.52 (m, 4H), 3.50–3.45 (m, 2H), 3.44–3.39 (m, 3H, 3 × H-5b$_{Xyl}$), 3.38–3.29 (m, 6H). ^{13}C NMR (175 MHz, D_2O, δ_C) 104.3 (C-1$_{Xyl}$), 104.1 (C-1$_{Xyl}$), 101.8 (C-1$_{Man}$), 99.0 (C-1$_{Man}$), 77.3, 77.2, 77.0, 76.5, 76.0, 75.9, 74.7, 74.0, 73.7, 72.4, 72.3, 71.3 × 2 (C), 70.8, 70.0, 66.0 (C-5$_{Xyl}$), 63.8 (C-5$_{Xyl}$), 61.2 (C-6$_{Man}$), 57.7 (OCH_3). HRMS (ESI) calcd for $(M + Na)^+$ $C_{45}H_{76}NaO_{37}$: 1231.3958. Found: 1231.3970.



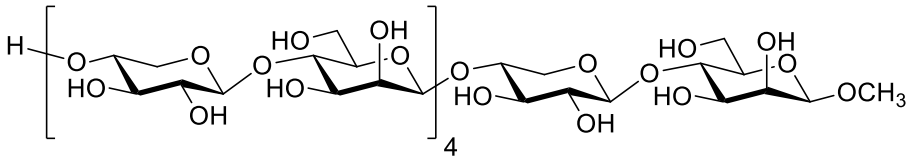
***n*-Octyl β-D-xylopyranosyl-(1→4)-β-D-mannopyranosyl-(1→4)-β-D-xylopyranosyl-(1→4)-β-D-mannopyranosyl-(1→4)-β-D-xylopyranosyl-(1→4)-β-D-mannopyranosyl-β-D-xylopyranosyl-(1→4)-β-D-mannopyranoside (3.11).** To a flask containing **3.76** (7.8 mg, 2.3 μmol) in 1:1 CH_2Cl_2–CH_3OH (5 mL) was added 0.5 M $NaOCH_3$ in CH_3OH (0.4 mL). The reaction mixture was stirred for 2 h and then neutralized by addition of Amberlite IR-120 H^+ resin. Filtration of the mixture, followed by concentration and co-evaporation of the filtrate with CH_2Cl_2 led to a residue that was triturated with hexanes. The resultant crude material was dried via co-evaporation with toluene (2x) and placed under vacuum overnight, after which it was dissolved in THF (2 mL). In a separate flask containing liquid ammonia (~30 mL) at −78 °C, freshly cut sodium metal (23 mg) was added at under argon. The resultant blue solution was stirred for an additional 20 min, before the crude solution in THF was added dropwise over 2 min. After 1 h, CH_3OH (1 mL) was added and the mixture was evaporated to dryness. The resultant white residue was re-dissolved in CH_3OH (30 mL) and Amberlite IR-120 H^+ resin was then added. Filtration of the mixture, followed by concentration led to a crude residue that was purified over an Iatrobead column (12:3:3:2 to 3:3:3:2 EtOAc–CH_3OH–AcOH–H_2O). The product was subsequently lyophilized to yield **3.11** (1.0 mg, 0.83 μmol, 55%) as a white fluffy solid. R_f = 0.30 (6:3:3:2 EtOAc–CH_3OH–AcOH–H_2O); $[\alpha]_D$ −22.0 (*c*. 0.05, H_2O); ^{1}H NMR (700 MHz, D_2O, δ_H) 4.83 (s, 3H, 3 × H-1_{Man}), 4.70 (s, 1H, H-1_{Man}), 4.50–4.41 (m, 4H, 4 × H-1_{Xyl}), 4.17–4.12 (m, 3H, 3 × H-$5a_{Xyl}$), 4.07–3.98 (m, 10H), 3.93–3.88 (m, 4H), 3.87–3.82 (m, 4H), 3.82–3.72 (m, 9H), 3.72–3.62 (m, 6H), 3.58–3.50 (m, 4H), 3.48 (app t, *J* = 9.3 Hz, 1H), 3.44–

3.38 (m, 3H, 3 × H-5b$_{Xyl}$), 3.38–3.29 (m, 6H), 1.64 (p, J = 6.9 Hz, 2H, 2 × OCH$_2$(C<u>H</u>$_2$)$_6$CH$_3$), 1.40–1.25 (m, 10H, 10 × OCH$_2$(C<u>H</u>$_2$)$_6$CH$_3$), 0.89 (t, J = 6.8 Hz, 3H, OCH$_2$(CH$_2$)$_6$C<u>H</u>$_3$). ^{13}C NMR (175 MHz, D$_2$O, δ_C) 104.3 (C-1$_{Xyl}$), 104.1 (C-1$_{Xyl}$), 100.5 (C-1$_{Man}$), 99.0 (C-1$_{Man}$), 77.3, 77.2, 77.0, 76.5, 76.0, 74.7, 74.0, 73.7, 72.5, 72.3, 71.3, 71.1, 71.0 (O<u>C</u>H$_2$(CH$_2$)$_6$CH$_3$), 70.0, 66.0 (C-5$_{Xyl}$), 63.8 (C-5$_{Xyl}$), 61.2 (C-6$_{Man}$), 31.9 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 29.5 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 29.3 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 29.2 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 25.9 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 22.9 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 14.3 (OCH$_2$(CH$_2$)$_6$<u>C</u>H$_3$). HRMS (ESI) calcd for (M + Na)$^+$ $C_{52}H_{90}NaO_{37}$: 1329.5053. Found: 1329.5049.



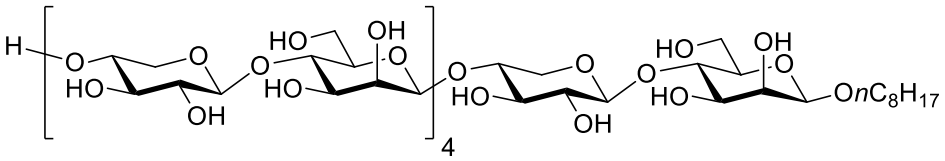
***n*-Hexadecyl β-D-xylopyranosyl-(1→4)-β-D-mannopyranosyl-(1→4)-β-D-xylopyranosyl-(1→4)-β-D-mannopyranosyl-(1→4)-β-D-xylopyranosyl-(1→4)-β-D-mannopyranosyl-β-D-xylopyranosyl-(1→4)-β-D-mannopyranoside (3.12).** To a flask containing **3.77** (7.4 mg, 2.3 μmol) in 1:1 CH_2Cl_2–CH_3OH (5 mL) was added 0.5 M $NaOCH_3$ in CH_3OH (0.4 mL). The reaction mixture was stirred for 2 h, after which it was neutralized by addition of Amberlite IR-120 H^+ resin. Filtration of the mixture, followed by concentration and co-evaporation of the filtrate with CH_2Cl_2 led to a residue that was triturated with hexanes. The resultant crude material was dried via co-evaporation with toluene (2x) and placed under vacuum overnight, after which it was dissolved in THF (2 mL). In a separate flask containing liquid ammonia (~30 mL) at –78 °C, freshly cut sodium metal (31 mg) was added under argon. The resultant blue solution

was stirred for an additional 20 min, before the crude solution in THF was added dropwise over 2 min. After 1 h, CH_3OH (1 mL) was added and the mixture was evaporated to dryness. The resultant white residue was re-dissolved in CH_3OH (30 mL) and Amberlite IR-120 H^+ resin was then added. Filtration of the mixture, followed by concentration of the filtrate led to a crude residue that was purified over an Iatrobead column (10:3:3:2 to 3:3:3:2 EtOAc–CH_3OH–AcOH–H_2O) and subsequently concentrated to yield **3.12** (1.7 mg, 1.2 μmol, 52%) as a white powder. R_f = 0.35 (6:3:3:2 EtOAc–CH_3OH–AcOH–H_2O); ^{1}H NMR (700 MHz, DMSO-d_6, δ_H) 4.60 (s, 3H, 3 × H-1_{Man}), 4.38 (s, 1H, H-1_{Man}), 4.26–4.22 (m, 3H, 3 × H-1_{Xyl}), 4.18 (d, J = 7.8 Hz, 1H, H-1_{Xyl}), 4.01–3.95 (m, 3H, 3 × H-$5a_{Xyl}$), 3.80–3.65 (m, 11H), 3.64–3.55 (m, 6H), 3.55–3.47 (m, 9H), 3.44–3.37 (m, 6H), 3.32–3.25 (m, 8H), 3.21–3.14 (m, 5H), 3.13–3.07 (m, 3H), 3.05–3.00 (m, 3H, 3 × H-$5b_{Xyl}$), 2.97 (app t, J = 8.3 Hz, 1H, H-2_{Xyl}) 1.51–1.43 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 1.28–1.17 (m, 26H, 26 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 0.83 (t, J = 6.9 Hz, 3H, $OCH_2(CH_2)_{14}C\underline{H}_3$). ^{13}C NMR (175 MHz, DMSO-d_6, δ_C) 104.0 (C-1_{Xyl}), 103.7 (C-1_{Xyl}), 100.3 (C-1_{Man}), 98.0 (C-1_{Man}), 77.4, 77.2 × 2 (C), 76.4, 75.8, 75.7 × 2 (C), 75.6, 74.4, 73.3, 73.1 × 2 (C), 73.1, 71.9, 71.7, 70.0 × 2 (C), 69.9, 69.4, 68.8 ($O\underline{C}H_2(CH_2)_{14}CH_3$), 66.0 (C-$5_{Xyl}$), 63.1 (C-$5_{Xyl}$), 60.5 (C-$6_{Man}$), 60.4 (C-$6_{Man}$), 31.5 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.3 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.2 × 3 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.1 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 28.9 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 25.7 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 22.3 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 14.2 ($OCH_2(CH_2)_{14}\underline{C}H_3$). HRMS (ESI) calcd for $(M + Na)^+$ $C_{60}H_{106}NaO_{37}$: 1441.6305. Found: 1441.6303.



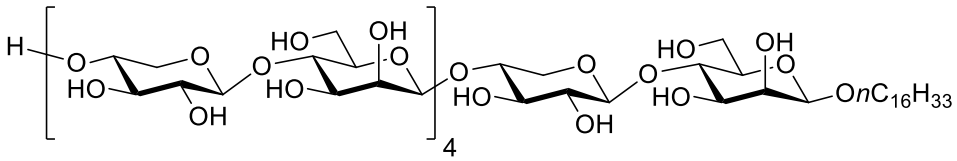
Methyl β-D-xylopyranosyl-(1→4)-β-D-mannopyranosyl-(1→4)-β-D-xylopyranosyl-(1→4)-β-D-mannopyranosyl-(1→4)-β-D-xylopyranosyl-(1→4)-β-D-mannopyranosyl-(1→4)-β-D-xylopyranosyl-(1→4)-β-D-mannopyranosyl-β-D-xylopyranosyl-(1→4)-β-D-mannopyranoside (3.13). To a flask containing **3.90** (12.2 mg, 3.33 μmol) in 1:1 CH_2Cl_2–CH_3OH (3 mL) was added 0.5 M $NaOCH_3$ in CH_3OH (0.3 mL). The reaction mixture was stirred for 2 h and then neutralized by addition of Amberlite IR-120 H^+ resin. Filtration of the mixture, followed by concentration and co-evaporation of the filtrate with CH_2Cl_2 led to a residue that was triturated with hexanes. The resultant crude material was dried via co-evaporation with toluene (2x) and placed under vacuum overnight, after which it was dissolved in THF (2 mL). In a separate flask containing liquid ammonia (~30 mL) at −78 °C, freshly cut sodium metal (26 mg) was added under argon. The resultant blue solution was stirred for an additional 20 min, before the crude solution in THF was added dropwise over 2 min. After 1 h, CH_3OH (1 mL) was added and the mixture was evaporated to dryness. The resultant white residue was re-dissolved in CH_3OH (30 mL) and Amberlite IR-120 H^+ resin was then added. Filtration of the mixture, followed by concentration of the filtrate led to a crude residue that was purified over an Iatrobead column (8:3:3:2 to 3:3:3:2 EtOAc–CH_3OH–AcOH–H_2O). The product was subsequently lyophilized to yield **3.13** (1.0 mg, 0.67 μmol, 20%) as a white fluffy solid. R_f = 0.40 (3:3:3:2 EtOAc–CH_3OH–AcOH–H_2O); $[\alpha]_D$ −12.6 (*c*. 0.10, H_2O); ^1H NMR (700 MHz, D_2O, δ_H) 4.83 (s, 4H, 4 × H-1_{Man}), 4.62 (s, 1H, H-1_{Man}), 4.49–4.41 (m, 5H, 5 × H-1_{Xyl}), 4.19–4.12 (m, 4H, 4 × H-$5a_{Xyl}$), 4.07–4.00 (m, 12H), 3.93–3.88 (m, 5H), 3.87–3.82 (m, 7H),

3.82–3.72 (m, 12H), 3.68–3.62 (m, 9H), 3.57 (s, 3H, OCH_3), 3.56–3.53 (m, 5H), 3.49–3.46 (m, 2H), 3.44–3.38 (m, 4H, 4 × H-5b$_{Xyl}$), 3.38–3.30 (m, 9H). ^{13}C NMR (175 MHz, D_2O, δ_C) 104.3 (C-1$_{Xyl}$), 104.1 (C-1$_{Xyl}$), 101.8 (C-1$_{Man}$), 99.0 (C-1$_{Man}$), 77.3, 77.0, 76.5, 76.0, 74.7, 74.0, 73.7, 72.3, 71.3, 70.8, 70.0, 66.0 (C-5$_{Xyl}$), 63.8 (C-5$_{Xyl}$), 61.2 (C-6$_{Man}$), 57.7 (OCH_3). HRMS (ESI) calcd for $(M + Na)^+$ $C_{56}H_{94}NaO_{46}$: 1525.4908. Found: 1525.4928.



***n*-Octyl β-D-xylopyranosyl-(1→4)-β-D-mannopyranosyl-(1→4)-β-D-xylopyranosyl-(1→4)-β-D-mannopyranosyl-(1→4)-β-D-xylopyranosyl-(1→4)-β-D-mannopyranosyl-(1→4)-β-D-xylopyranosyl-(1→4)-β-D-mannopyranosyl-β-D-xylopyranosyl-(1→4)-β-D-mannopyranoside (3.14).** To a flask containing **3.92** (7.8 mg, 2.1 μmol) in 1:1 CH_2Cl_2–CH_3OH (5 mL) was added 0.5 M $NaOCH_3$ in CH_3OH (0.4 mL). The reaction mixture was stirred for 2 h and then neutralized by addition of Amberlite IR-120 H^+ resin. Filtration of the mixture, followed by concentration and co-evaporation of the filtrate with CH_2Cl_2 led to a residue that was triturated with hexanes. The resultant crude material was dried via co-evaporation with toluene (2x) and placed under vacuum overnight, after which it was dissolved in THF (2 mL). In a separate flask containing liquid ammonia (~30 mL) at −78 °C, freshly cut sodium metal (23 mg) was added at under argon. The resultant blue solution was stirred for an additional 20 min, before the crude solution in THF was added dropwise over 2 min. After 1 h, CH_3OH (1 mL) was added and the mixture was evaporated to dryness. The resultant white residue was re-dissolved in

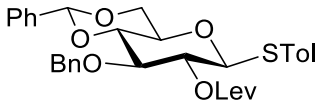
CH_3OH (30 mL) and Amberlite IR-120 H^+ resin was then added. Filtration of the mixture, followed by concentration of the filtrate led to a crude residue that was purified over an Iatrobead column (8:3:3:2 to 3:3:3:2 EtOAc–CH_3OH–AcOH–H_2O). The product was subsequently lyophilized to yield **3.14** (0.3 mg, 0.2 μmol, 9%) as a white fluffy solid. R_f = 0.51 (3:3:3:2 EtOAc–CH_3OH–AcOH–H_2O); $[\alpha]_D$ –20.7 (*c*. 0.03, H_2O); ^{1}H NMR (700 MHz, D_2O, δ_H) 4.83 (s, 4H, 4 × H-1_{Man}), 4.70 (s, 1H, H-1_{Man}), 4.47–4.41 (m, 5H, 5 × H-1_{Xyl}), 4.18–4.12 (m, 4H, 4 × H-$5a_{Xyl}$), 4.07–4.00 (m, 13H), 3.93–3.88 (m, 7H), 3.86–3.82 (m, 6H), 3.81–3.72 (m, 17H), 3.71–3.62 (m, 13H), 3.58–3.50 (m, 7H), 3.50 (m, 3H), 3.44–3.38 (m, 4H, 4 × H-$5b_{Xyl}$), 3.38–3.29 (m, 9H), 1.60–1.54 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_6CH_3$), 1.36–1.26 (m, 10H, 10 × $OCH_2(C\underline{H}_2)_6CH_3$), 0.89 (t, *J* = 6.8 Hz, 3H, $OCH_2(CH_2)_6C\underline{H}_3$). ^{13}C NMR (175 MHz, D_2O, δ_C) 104.3 (C-1_{Xyl}), 104.1 (C-1_{Xyl}), 100.6 (C-1_{Man}), 99.0 (C-1_{Man}), 77.3, 77.2, 77.0, 76.5, 76.0, 74.7, 74.0, 73.7, 72.5, 72.3, 71.3, 71.1, 71.0 ($O\underline{C}H_2(CH_2)_6CH_3$), 70.0, 66.0 (C-$5_{Xyl}$), 63.8 (C-$5_{Xyl}$), 61.2 (C-$6_{Man}$), 32.0 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 26.0 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 14.3 ($OCH_2(CH_2)_6\underline{C}H_3$). LRMS-MALDI-TOF calcd for $(M + Na)^+$ $C_{63}H_{108}NaO_{46}$: 1623.6. Found: 1623.6.



***n*-Hexadecyl β-D-xylopyranosyl-(1→4)-β-D-mannopyranosyl-(1→4)-β-D-xylopyranosyl-(1→4)-β-D-mannopyranosyl-(1→4)-β-D-xylopyranosyl-(1→4)-β-D-mannopyranosyl-(1→4)-β-D-xylopyranosyl-(1→4)-β-D-mannopyranosyl-β-D-xylopyranosyl-(1→4)-β-D-**

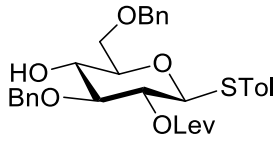
mannopyranoside (3.15). To a flask containing **3.93** (7.5 mg, 2.0 μmol) in 1:1 CH_2Cl_2–CH_3OH (5 mL) was added 0.5 M $NaOCH_3$ in CH_3OH (0.4 mL). The reaction mixture was stirred for 2 h and then neutralized by addition of Amberlite IR-120 H^+ resin. Filtration of the mixture, followed by concentration and co-evaporation of the filtrate with CH_2Cl_2 led to a residue that was triturated with hexanes. The resultant crude material was dried via co-evaporation with toluene (2x) and placed under vacuum overnight, after which it was dissolved in THF (2 mL). In a separate flask containing liquid ammonia (~30 mL) at −78 °C, freshly cut sodium metal (23 mg) was added at under argon. The resultant blue solution was stirred for an additional 20 min, before the crude solution in THF was added dropwise over 2 min. After 1 h, CH_3OH (1 mL) was added and the mixture was evaporated to dryness. The resultant white residue was re-dissolved in CH_3OH (30 mL) and Amberlite IR-120 H^+ resin was then added. Filtration of the mixture, followed by concentration of the filtrate led to a crude residue that was purified over an Iatrobead column (10:3:3:2 to 3:3:3:2 EtOAc–CH_3OH–AcOH–H_2O) and concentrated to yield **3.15** (0.5 mg, 0.3 μmol, 15%) as a white powder. R_f = 0.25 (6:3:3:2 EtOAc–CH_3OH–AcOH–H_2O); ^1H NMR (700 MHz, DMSO-d_6, δ_H) 4.61 (s, 4H, 4 × H-1_{Man}), 4.38 (s, 1H, H-1_{Man}),), 4.26–4.22 (m, 3H, 3 × H-1_{Xyl}), 4.18 (d, J = 7.7 Hz, 1H, H-1_{Xyl}), 4.01–3.94 (m, 4H, 4 × H-$5a_{Xyl}$), 3.79–3.66 (m, 15H), 3.66–3.53 (m, 19H), 3.33–3.23 (m, 13H), 3.21–3.14 (m, 7H), 3.14–3.07 (m, 4H), 3.05–3.00 (m, 4H, 4 × H-$5b_{Xyl}$), 2.97 (app t, J = 8.1 Hz, 1H, H-2_{Xyl}) 1.47–1.44 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 1.25–1.20 (m, 26H, 26 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 0.84 (t, J = 6.9 Hz, 3H, $OCH_2(CH_2)_{14}C\underline{H}_3$). ^{13}C NMR (175 MHz, DMSO-d_6, δ_C) 103.9 (C-1_{Xyl}), 103.6 (C-1_{Xyl}), 100.2 (C-1_{Man}), 98.0 (C-1_{Man}), 77.3, 77.2, 76.4, 75.8, 75.6, 74.4, 74.2, 73.2, 73.0, 71.8, 71.7, 69.9, 69.7, 69.3, 68.7 ($O\underline{C}H_2(CH_2)_{14}CH_3$), 65.9 (C-$5_{Xyl}$), 63.0 (C-$5_{Xyl}$), 60.4 (C-$6_{Man}$), 31.4 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.1 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 28.8 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 25.7

($OCH_2(\underline{C}H_2)_{14}CH_3$), 22.2 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 14.1 ($OCH_2(CH_2)_{14}\underline{C}H_3$). LRMS-MALDI-TOF calcd for $(M + Na)^+$ $C_{71}H_{124}NaO_{46}$: 1735.7. Found: 1735.6.



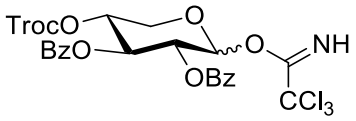
***p*-Tolyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-*O*-levulinoyl-1-thio-β-D-glucopyranoside (3.21).** To a flask containing *p*-tolyl 3-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside **3.20**[9] (27.2 g, 58.5 mmol) in CH_2Cl_2 (500 mL) was added EDC·HCl (22.6 g, 118 mmol) followed by DMAP (3.57 g, 29.3 mmol) and levulinic acid (13.6 g, 118 mmol). The resultant mixture was heated to reflux for 16 h, after which point it was cooled to room temperature and poured into satd. aqueous $NaHCO_3$. The two phases were then separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 200 mL). The combined organic phases were washed with brine and dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a reddish solid residue that was subsequently purified by recrystallization (3:1 hexanes–EtOAc), to obtain **3.21** (21.4 g, 38.0 mmol, 65%) as white crystalline solid. R_f = 0.20 (5:1 Hexanes–EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.50–7.45 (m, 2H, Ar), 7.42–7.34 (m, 5H, Ar), 7.33–7.26 (m, 5H, Ar), 7.15–7.08 (m, 2H, Ar), 5.56 (s, 1H, $PhC\underline{H}O_2$), 4.98 (dd, J = 10.1, 8.3 Hz, 1H, H-2), 4.84, 4.68 (ABq, J = 11.9 Hz, 2H, 2 × $PhC\underline{H}_2O$), 4.63 (d, J = 10.1 Hz, 1H, H-1), 4.38 (dd, J = 10.5, 5.0 Hz, 1H, H-6a), 3.79 (app t, J = 10.3 Hz, 1H, H-6b), 3.77–3.67 (m, 2H, H-3, H-4), 3.48 (ddd, J = 9.9, 8.8, 5.0 Hz, 1H, H-5), 2.80–2.72 (m, 2H, $CH_2C\underline{H}_2C(O)CH_3$), 2.67–2.48 (m, 2H, $C\underline{H}_2CH_2C(O)CH_3$), 2.34 (s, 3H, $ArC\underline{H}_3$), 2.19 (s, 3H, $CH_2CH_2C(O)C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 206.2 (C=O), 171.3 (C=O), 138.6 (Ar), 138.2 (Ar), 137.2 (Ar), 133.6 (Ar), 129.8

(Ar), 129.1 (Ar), 128.3 × 3 (Ar), 128.1 (Ar), 127.7 (Ar), 126.1 (Ar), 101.3 (Ph<u>C</u>HO$_2$), 87.1 (C-1), 81.3 (C-4), 79.8 (C-3), 74.4 (Ph<u>C</u>H$_2$O), 71.8 (C-2), 70.6 (C-5), 68.6 (C-6), 37.9 (CH$_2$<u>C</u>H$_2$C(O)CH$_3$), 30.0 (<u>C</u>H$_2$CH$_2$C(O)CH$_3$), 28.1 (CH$_2$CH$_2$C(O)<u>C</u>H$_3$), 21.2 (Ar<u>C</u>H$_3$). HRMS (ESI) calcd for (M + Na)$^+$ $C_{32}H_{34}NaO_7S$: 585.1917. Found: 585.1921.



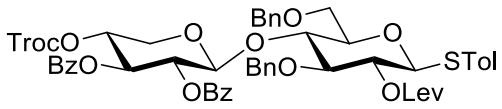
***p*-Tolyl 3,6-di-*O*-benzyl-2-*O*-levulinoyl-1-thio-β-D-glucopyranoside (3.17).** To a dual-necked round-bottomed flask mounted with a dropping funnel (50 mL) was added **3.21** (26.7 g, 47.5 mmol) under argon. Both CH_2Cl_2 (500 mL) and then Et_3SiH (78 mL, 490 mmol) were then added. The resultant mixture was stirred vigorously, with sonication, until a homogenous solution was achieved and then it was cooled to 0 °C. To this solution was added TFA (36.3 mL, 475 mmol) dropwise over 10 min via the dropping funnel. The resultant mixture was then stirred at 0 °C during which its progress was monitored by TLC analysis until complete consumption of **3.21** (typically 2 to 3 h) was observed. Satd. aqueous $NaHCO_3$ was then added to quench the excess TFA. The two phases were separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 100 mL). The combined organic phases were washed with brine and dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a thick syrup that was purified by silica gel chromatography (7:1 toluene–EtOAc), to obtain **3.17** (21.5 g, 38.0 mmol, 80 %) as a white crystalline solid. R_f = 0.24 (7:1 toluene–EtOAc); mp 105–107 °C; ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.40–7.38 (m, 2H, Ar), 7.36–7.28 (m, 10H, Ar), 7.06–7.04 (m, 2H, Ar), 4.97 (app. t, J = 9.5 Hz, 1H, H-2), 4.78, 4.70 (ABq, J = 12.0 Hz, 2H, 2 × PhC<u>H</u>$_2$O), 4.58–4.52 (m,

3H, H-1, 1 × PhC<u>H</u>$_2$O), 3.79–3.74 (m, 2H, H-6a, H-6b), 3.68 (app. td, 1H, *J* = 9.3, 2.5 Hz, H-4), 3.54 (app. t, *J* = 9.0 Hz, 1H, H-3), 3.50 (app. dt, *J* = 10.0, 5.0 Hz, 1H, H-5), 2.77 (qt, *J* = 18.5, 7.5 Hz, 2H, CH$_2$C<u>H</u>$_2$C(O)CH$_3$), 2.65–2.54 (m, 2H, C<u>H</u>$_2$CH$_2$C(O)CH$_3$), 2.30 (s, 3H, ArC<u>H</u>$_3$), 2.19 (s, 3H, C<u>H</u>$_2$CH$_2$C(O)C<u>H</u>$_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 206.2 (C=O), 171.5 (C=O), 138.3 (Ar), 138.2 (Ar), 137.9 (Ar), 133.1 (Ar), 129.7 (Ar), 129.0 (Ar), 128.6 (Ar), 128.5 (Ar), 128.0 (Ar), 127.9 (Ar), 127.8 (Ar), 127.8 (Ar), 86.6 (C-1), 83.8 (C-3), 78.3 (C-5), 74.7 (Ph<u>C</u>H$_2$O), 73.8 (Ph<u>C</u>H$_2$O), 71.9 (C-2), 71.7 (C-4), 70.4 (C-6), 37.9 (CH$_2$<u>C</u>H$_2$C(O)CH$_3$), 29.9 (CH$_2$CH$_2$C(O)<u>C</u>H$_3$), 28.2 (<u>C</u>H$_2$CH$_2$C(O)CH$_3$), 21.2 (Ar<u>C</u>H$_3$). HRMS (ESI) calcd for (M + Na)$^+$ $C_{32}H_{36}NaO_7S$: 587.2074. Found: 587.2079.



2,3-di-*O*-benzoyl-1-(trichloroacetimidoyl)-4-*O*-(2,2,2-trichloroethoxycarbonyl)-D-xylopyranose (3.22). To a solution of **2.44** (1.53 g, 2.39 mmol) in acetone (90 mL) was added H_2O (10 mL). The solution was then cooled to 0 °C. To this mixture was added NBS (2.17 g, 12.2 mmol) and the resultant solution was stirred at 0 °C for 3 h. Satd. aqueous $Na_2S_2O_3$ was then added and the resultant mixture was concentrated. The resultant residue was diluted with CH_2Cl_2 (50 mL) and poured into satd. aqueous $NaHCO_3$. The two phases were separated and the aqueous phase was then extracted with CH_2Cl_2 (3 × 25 mL). The combined organic phases were subsequently washed with satd. aqueous $NaHCO_3$ and brine before being dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a thick syrup that was then dried under vacuum overnight. This crude material was then re-dissolved in CH_2Cl_2 (100

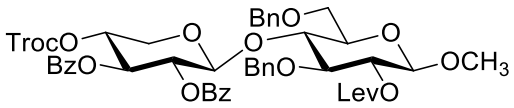
mL). To this solution was added Cs_2CO_3 (1.40 g, 4.31 mmol), followed by trichloroacetonitrile (2.15 mL, 21.4 mmol) under argon. The mixture was then stirred overnight at room temperature, after which it was concentrated to afford **3.22** (1.33 g, 1.96 mmol, 82%) as a crude foamy solid. R_f = 0.27 (6:1 hexanes–acetone); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) of the α-isomer: 8.80 (br s, 1H, NH), 7.97–7.94 (m, 4 H, Ar), 7.52–7.34 (m, 6H, Ar), 6.70 (d, *J* = 3.5 Hz, 1H, H-1), 6.14 (t, *J* = 10.0 Hz, 1H, H-3), 5.47 (dd, *J* = 10.0, 3.5 Hz, 1H, H-2), 5.32 (td, *J* = 10.0 Hz, 6.0 Hz, 1H, H-4), 4.72, 4.66 (ABq, *J* = 12.0 Hz, 2H, $Cl_3CC\underline{H}_2O$), 4.22–3.80 (m, 2H, H-5a, H-5b). ^{13}C NMR (175 MHz, $CDCl_3$, δ_C) 165.4 (C=O), 165.3 (C=O), 160.8 (C=N), 153.3 (C=O), 133.9 (Ar), 133.7 × 2 (Ar), 133.5 (Ar), 130.3 (Ar), 130.2 × 2 (Ar), 130.0 (Ar), 129.9 (Ar), 129.0 (Ar), 128.9 (Ar), 128.6 (Ar), 128.5 (Ar), 94.1 ($Cl_3\underline{C}CH_2O$), 93.2 (C-1), 77.1 ($Cl_3C\underline{C}H_2O$), 72.8 (C-4), 70.6 (C-2), 69.7 (C-3), 60.8 (C-5). LRMS-MALDI-TOF calcd for $(M + Na)^+$ $C_{24}H_{19}Cl_6NaO_9$: 697.9. Found: 697.9.



***p*-Tolyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-1-thio-β-D-glucopyranoside (3.16).** To a flask charged with **2.44** (2.02 g, 3.15 mmol) was added CH_2Cl_2 (30 mL) under argon. The solution was then cooled to 0 °C. To this solution was added Br_2 (195 μL, 3.79 mmol) dropwise over 1 min. The resultant amber solution was stirred at 0 °C until complete consumption of **2.44** (2 to 3 h) as determined by TLC analysis. The reaction mixture was brought to room temperature, concentrated and then co-evaporated with toluene (2x). To this resultant crude solid was added CH_2Cl_2 (100mL) and

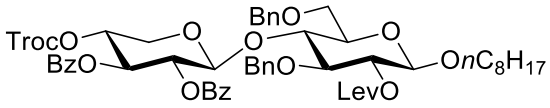
the mixture was washed thoroughly with satd. aqueous $Na_2S_2O_3$, followed by satd. aqueous $NaHCO_3$ and brine before it was dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a light yellowish syrup that was dried via co-evaporation with toluene (3x) and placed under vacuum for 1 h. The resultant light yellow foamy solid was re-dissolved in CH_2Cl_2 (30 mL) under argon and **3.17** (1.37 g, 2.43 mmol) was then added, along with 4Å M.S. powder (1.30 g) and lastly DTBMP (991 mg, 4.83 mmol) in this order. The slurry mixture was stirred at room temperature for 1 h before it was cooled to −35 °C. To this mixture was added AgOTf (1.15 g, 4.48 mmol) and the resultant mixture was then brought slowly to room temperature overnight. The reaction mixture was filtered through a Celite bed and the resulting filtrate was washed with 1.0 M aqueous HCl, followed by satd. aqueous $NaHCO_3$ and then brine before it was dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a crude yellow residue that was subsequently purified by silica gel chromatography (12:1 toluene–EtOAc), to obtain **3.16** (2.31 g, 2.14 mmol, 88%) as a white solid. R_f = 0.25 (12:1 toluene–EtOAc); $[\alpha]_D$ +97.3 (*c*. 1.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.96–7.91 (m, 4H, Ar), 7.57–7.48 (m, 2H, Ar), 7.43–7.23 (m, 16H, Ar), 7.02–6.97 (m, 2H, Ar), 5.55 (app. t, *J* = 8.6 Hz, 1H, H-3``), 5.33 (dd, *J* = 8.7, 6.8 Hz, 1H, H-2``), 5.03 (app. td, *J* = 8.7, 5.1 Hz, 1H, H-4``), 4.94 (app. t, *J* = 9.5 Hz, 1H, H-2`), 4.89–4.82 (m, 2H, H-1``, 1 × PhC$\underline{H}_2$O), 4.68 (m, 3H, 2 × $Cl_3CC\underline{H}_2O$, 1 × PhC$\underline{H}_2$O), 4.53, 4.37 (ABq, *J* = 11.8 Hz, 2H, 2 × PhC$\underline{H}_2$O), 4.44 (d, *J* = 10.0 Hz, 1H, H-1`), 4.09 (dd, *J* = 12.1, 5.1 Hz, 1H, H-5a``), 4.00 (app t, *J* = 9.4 Hz, 1H, H-4`), 3.66–3.58 (m, 2H, H-6a`, H-3`), 3.57 (dd, *J* = 11.3, 1.6 Hz, 1H, H-6b`) 3.33–3.24 (m, 2H, H-5b``, H-5`), 2.69 (m, 2H, $CH_2C\underline{H}_2C(O)CH_3$), 2.56 (dt, *J* = 17.3, 6.8 Hz, 2H, 2 × $CH_2C\underline{H}_2C(O)CH_3$), 2.45 (dt, *J* = 17.3, 7.0 Hz, 2H, 2 × $C\underline{H}_2CH_2C(O)CH_3$), 2.27 (s, 3H, Ar$C\underline{H}_3$), 2.16 (s, 3H, $CH_2CH_2C(O)C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 206.2 (C=O), 171.2 (C=O),

165.3 (C=O), 165.0 (C=O), 153.2 (C=O), 138.4 (Ar), 138.2 (Ar), 138.0 (Ar), 133.5 (Ar), 129.9 × 2 (Ar), 129.6 (Ar), 129.1 (Ar), 129.0 (Ar), 128.9 (Ar), 128.6 × 2 (Ar), 128.5 (Ar), 128.4 (Ar), 128.3 × 2 (Ar), 128.0 (Ar), 127.9 (Ar), 127.8 (Ar), 127.6 (Ar), 125.3 (Ar), 100.4 (C-1``), 94.1 ($Cl_3\underline{C}CH_2O$), 86.2 (C-1`), 82.3 (C-3`), 79.0 (C-5`), 76.9 ($Cl_3C\underline{C}H_2O$), 76.5 (C-4`), 74.9 ($Ph\underline{C}H_2O$), 73.5 ($Ph\underline{C}H_2O$), 73.2 (C-4``), 71.7 (C-2`), 71.6 (C-3``), 71.3 (C-2``), 67.9 (C-6`), 61.7 (C-5``), 38.0 ($CH_2\underline{C}H_2C(O)CH_3$), 29.8 ($CH_2CH_2C(O)\underline{C}H_3$), 28.1 ($\underline{C}H_2CH_2C(O)CH_3$), 21.2 ($Ar\underline{C}H_3$). HRMS (ESI) calcd for $(M + NH_4)^+$ $C_{54}H_{53}Cl_3NO_{15}S$: 1096.2509. Found: 1096.2511.



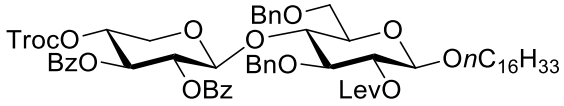
Methyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranoside (3.24). To a solution of **3.16** (277 mg, 0.255 mmol) in CH_2Cl_2 (4 mL) was added 3 Å M.S. powder (100 mg) and CH_3OH (120 μL, 2.97 mmol) under argon. The mixture was stirred for 15 min, after which it was then cooled to 0°C and NIS (75.3 mg, 0.335 mmol) was subsequently introduced. To this mixture was added TfOH (225 μL, 0.051 mmol, 2% v/v in CH_2Cl_2) dropwise over 1 min. The resultant reddish-black mixture was subsequently warmed to room temperature and stirred for an additional 2 h, before the reaction was complete as determined by TLC analysis. To this mixture was added Et_3N (100 μL) and the mixture was passed through Celite. The resultant filtrate was then washed with satd. aqueous $Na_2S_2O_3$, brine and dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a pale yellow syrup that was purified by silica gel chromatography (3:1 hexanes–acetone) to obtain **3.24** (166 mg, 0.168 mmol, 66 %) as a white

amorphous solid. R_f = 0.29 (7:2 hexanes–EtOAc); $[\alpha]_D$ +2.6 (*c*. 0.1, $CHCl_3$); ^{1}H NMR (700 MHz, $CDCl_3$, δ_H) 7.98–7.89 (m, 4H, Ar), 7.56–7.49 (m, 2H, Ar), 7.44–7.30 (m, 12H), 7.28–7.26 (m, 2H), 5.54 (app t, *J* = 8.6 Hz, 1H, H-3``), 5.34 (dd, *J* = 9.1, 6.8 Hz, 1H, H-2``), 5.04 (td, *J* = 8.6, 4.9 Hz, 1H, H-4``), 4.96 (d, *J* = 8.9 Hz, 1H, H-2`), 4.87 (d, *J* = 11.3 Hz, 1H, 1 × PhC$\underline{H}_2$O), 4.83 (d, *J* = 6.9 Hz, 1H, H-1``), 4.72–4.64 (m, 3H, 1 × PhC$\underline{H}_2$O, 2 × $Cl_3CC\underline{H}_2$O), 4.62, 4.38 (ABq, *J* = 12.0 Hz, 2H, 2 × PhC$\underline{H}_2$O), 4.20 (d, *J* = 7.9 Hz, 1H, H-1`), 4.12 (dd, *J* = 12.1, 5.0 Hz, 1H, H-5a``), 4.07 (app t, *J* = 9.3 Hz, 1H, H-4`), 3.65 (dd, *J* = 11.1, 3.5 Hz, 1H, H-6a`), 3.61 (app t, *J* = 9.2 Hz, 1H, H-3`), 3.57–3.53 (m, 1H, H-6b`), 3.40 (s, 3H, OC$\underline{H}_3$), 3.35–3.29 (m, 1H, H-5b``), 3.25 (ddd, *J* = 9.8, 3.6, 1.9 Hz, 1H, H-5`), 2.71–2.61 (m, 2H, 2 × $CH_2C\underline{H}_2C(O)CH_3$), 2.52 (dt, *J* = 17.3, 7.0 Hz, 1H, 1 × $CH_2C\underline{H}_2C(O)CH_3$), 2.42 (dt, *J* = 17.3, 7.0 Hz, 1H, 1 × $CH_2C\underline{H}_2C(O)CH_3$), 2.13 (s, 3H, $CH_2CH_2C(O)C\underline{H}_3$). ^{13}C NMR (175 MHz, $CDCl_3$, δ_C) 206.2 (C=O), 171.3 (C=O), 165.3 (C=O), 165.0 (C=O), 153.2 (C=O), 138.5 (Ar), 137.9 (Ar), 133.5 × 2 (Ar), 129.9 × 2 (Ar), 129.0 × 2 (Ar), 128.6 × 2 (Ar), 128.5 × 2 (Ar), 128.3 (Ar), 128.0 (Ar), 128.0 × 3 (Ar), 127.6 (Ar), 101.8 (C-1`), 100.3 (C-1``), 94.1 ($Cl_3\underline{C}CH_2O$), 80.9 (C-3`), 77.0 ($Cl_3C\underline{C}H_2O$), 76.6 (C-4`), 74.7 (C-5`), 74.6 (Ph$\underline{C}H_2O$), 73.5 (Ph$\underline{C}H_2O$), 73.2 (C-4``), 72.9 (C-2`), 71.6 (C-3``), 71.3 (C-2``), 67.6 (C-6`), 61.7 (C-5`), 56.7 (O$\underline{C}H_3$), 38.0 ($CH_2\underline{C}H_2C(O)CH_3$), 29.3 ($CH_2CH_2C(O)\underline{C}H_3$), 28.0 ($\underline{C}H_2CH_2C(O)CH_3$). HRMS (ESI) calcd for $(M + Na)^+$ $C_{48}H_{49}Cl_3O_{16}Na$: 1009.1978. Found: 1009.1981.



***n*-Octyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranoside (3.25).** To a solution of **3.16** (211 mg, 0.195 mmol) in CH_2Cl_2 (4 mL) was added 3 Å M.S. powder (100 mg) and *n*-$C_8H_{17}OH$ (77 μL, 0.49 mmol) under argon. The mixture was stirred for 15 min, after which point it was cooled to 0 °C and NIS (67 mg, 0.30 mmol) was subsequently introduced. To this mixture was added TfOH (172 μL, 40 μmol, 2.0% v/v in CH_2Cl_2) dropwise over 1 min. The resultant mixture was subsequently removed from the cooling bath to stir at room temperature for 2 h. To this mixture was added Et_3N (100 μL) and the mixture was passed through a bed of Celite to obtain a yellowish filtrate that was then washed with satd. aqueous $Na_2S_2O_3$, brine and dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a pale yellow syrup that was purified by silica gel chromatography (3:1 hexanes–EtOAc) to obtain **3.25** (138 mg, 0.127 mmol, 65%) as a white amorphous solid. R_f = 0.29 (3:1 hexanes–EtOAc); $[\alpha]_D$ +5.2 (*c*. 0.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.98–7.90 (m, 4H, Ar), 7.57–7.50 (m, 2H, Ar), 7.43–7.30 (m, 12H, Ar), 7.29–7.26 (m, 2H, Ar), 5.54 (app t, *J* = 8.5 Hz, 1H, H-3``), 5.34 (dd, *J* = 8.7, 6.8 Hz, 1H, H-2``), 5.03 (app td, *J* = 8.7, 5.0 Hz, 1H, H-4``), 4.95 (dd, *J* = 9.4, 7.9 Hz, 1H, H-2`), 4.86 (m, 1H, 1 × PhC$\underline{H}_2$O), 4.83 (d, *J* = 6.8 Hz, 1H, H-1``), 4.73–4.64 (m, 3H. 1 × PhC$\underline{H}_2$O, 2 × $Cl_3CC\underline{H}_2$), 4.61, 4.37 (ABq, *J* = 12.0 Hz, 2H, 2 × PhC$\underline{H}_2$O), 4.25 (d, *J* = 7.9 Hz, 1H, H-1`), 4.12 (dd, *J* = 12.1, 5.1 Hz, 1H, H-5a``), 4.05 (app t, *J* = 9.3 Hz, 1H, H-4`), 3.75 (dt, *J* = 9.6, 6.5 Hz, 1H, 1 × OC$\underline{H}_2(CH_2)_6CH_3$), 3.66–3.57 (m, 2H, H-6a`, H-3`), 3.53 (dd, *J* = 11.1, 1.8 Hz, 1H, H-6b`), 3.39–3.28 (m, 2H, H-5b``, 1 × OC$\underline{H}_2(CH_2)_6CH_3$), 3.24 (ddd, *J* = 9.7, 3.6, 1.8 Hz, 1H, H-5`), 2.65 (app t, *J* = 6.9 Hz, 2H, 2 × C$\underline{H}_2CH_2C(O)CH_3$), 2.54–2.37 (m, 2H, 2 × $CH_2C\underline{H}_2C(O)CH_3$),

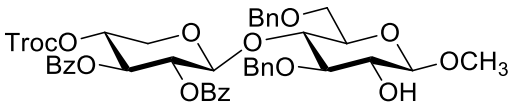
2.13 (s, 3H, $CH_2CH_2C(O)C\underline{H}_3$), 1.55–1.48 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_6CH_3$), 1.38–1.15 (m, 10H, 10 × $OCH_2(C\underline{H}_2)_6CH_3$), 0.86 (t, J = 7.0 Hz, 3H, $OCH_2(CH_2)_6C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 206.2 (C=O), 171.2 (C=O), 165.3 (C=O), 165.0 (C=O), 153.2 (C=O), 138.5 (Ar), 138.0 (Ar), 133.5 (Ar), 129.9 × 2 (Ar), 129.0 × 2 (Ar), 128.6 × 2 (Ar), 128.5 (Ar), 128.3 (Ar), 128.0 (Ar), 127.9 (Ar), 127.6 (Ar), 101.0 (C-1`), 100.3 (C-1``), 94.1 ($Cl_3\underline{C}CH_2O$), 80.9 (C-3`), 77.0 ($Cl_3C\underline{C}H_2O$), 76.6 (C-4`), 74.8 (C-5`), 74.5 ($Ph\underline{C}H_2O$), 73.5 ($Ph\underline{C}H_2O$), 73.2 (C-4``), 73.0 (C-2`), 71.6 (C-3``), 71.3 (C-2``), 69.8 ($O\underline{C}H_2(CH_2)_6CH_3$), 67.7 (C-6`), 61.7 (C-5``), 38.0 ($CH_2\underline{C}H_2C(O)CH_3$), 31.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.9 ($CH_2CH_2C(O)\underline{C}H_3$), 29.5 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 28.0 ($\underline{C}H_2CH_2C(O)CH_3$), 25.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 14.1 ($OCH_2(CH_2)_6\underline{C}H_3$). HRMS (ESI) calcd for $(M + NH_4)^+$ $C_{55}H_{67}Cl_3NO_{16}$: 1102.3520. Found: 1102.3518.



***n*-Hexadecyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranoside (3.26).** To a solution of **3.22** (624 mg, 0.577 mmol) in CH_2Cl_2 (15 mL) was added 4 Å M.S. powder (200 mg) and n-$C_{16}H_{33}OH$ (282 mg, 1.16 mmol) under argon. The mixture was stirred for 15 min, after which it was cooled to 0 °C and NIS (173 mg, 0.77 mmol) was subsequently introduced. To this mixture was added TfOH (500 μL, 0.113 mmol, 2% v/v in CH_2Cl_2) in dropwise over 1 min, and the resultant reddish black mixture was subsequently removed from the cooling bath to stir at room temperature for 2 h. To this mixture was added Et_3N (100 μL) and the mixture was passed

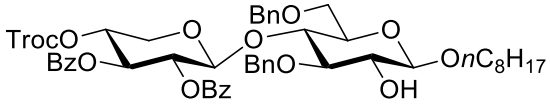
through a bed of Celite to obtain a yellowish filtrate that was then washed with satd. aqueous $Na_2S_2O_3$, brine and dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a pale yellow syrup that was purified by silica gel chromatography (7:2 hexanes–EtOAc) to obtain **3.26** (463 mg, 0.387 mmol, 67 %) as a white amorphous solid. R_f = 0.29 (7:2 hexanes–EtOAc); $[\alpha]_D$ +3.8 (*c*. 0.7, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.97–7.89 (m, 4H, Ar), 7.57–7.49 (m, 2H, Ar), 7.43–7.29 (m, 12H), 7.29–7.26 (m, 2H), 5.53 (app t, *J* = 8.5 Hz, 1H, H-3``), 5.34 (dd, *J* = 8.7, 6.8 Hz, 1H, H-2``), 5.03 (app td, *J* = 8.7, 5.1 Hz, 1H, H-4``), 4.95 (dd, *J* = 9.4, 7.9 Hz, 1H, H-2`), 4.86 (m, 1 × PhC$\underline{H}_2$O), 4.83 (d, *J* = 6.9 Hz, 1H, H-1``), 4.73–4.63 (m, 3H, 1 × PhC$\underline{H}_2$O, 2 × $Cl_3CC\underline{H}_2$), 4.61, 4.36 (ABq, *J* = 12.0 Hz, 2H, 2 × PhC$\underline{H}_2$O), 4.25 (d, *J* = 7.9 Hz, 1H, H-1`), 4.12 (dd, *J* = 12.1, 5.0 Hz, 1H, H-5a``), 4.05 (app t, *J* = 9.3 Hz, 1H, H-4`), 3.75 (dt, *J* = 9.6, 6.5 Hz, 1H, 1 × OC$\underline{H}_2(CH_2)_{14}CH_3$), 3.67–3.57 (m, 2H, H-6a`, H-3`), 3.53 (dd, *J* = 11.2, 1.8 Hz, 1H, H-6b`), 3.39–3.28 (m, 2H, H-5b``, 1 × OC$\underline{H}_2(CH_2)_{14}CH_3$), 3.24 (ddd, *J* = 9.7, 3.6, 1.8 Hz, 1H, H-5`), 2.65 (app t, *J* = 6.9 Hz, 2H, 2 × $CH_2C\underline{H}_2C(O)CH_3$), 2.54–2.38 (m, 2H, 2 × $CH_2C\underline{H}_2C(O)CH_3$), 2.13 (s, 3H, $CH_2CH_2C(O)C\underline{H}_3$), 1.53–1.42 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 1.36–1.14 (m, 26H, 26 × OC$\underline{H}_2(CH_2)_{14}CH_3$), 0.88 (t, *J* = 6.9 Hz, 3H, $OCH_2(CH_2)_{14}C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 206.2 (C=O), 171.2 (C=O), 165.3 (C=O), 165.0 (C=O), 153.2 (C=O), 138.5 (Ar), 138.0 (Ar), 133.5 (Ar), 129.9 × 2 (Ar), 129.0 × 2 (Ar), 128.6 × 2 (Ar), 128.5 (Ar), 128.3 (Ar), 128.0 (Ar), 127.9 (Ar), 127.6 (Ar), 101.0 (C-1`), 100.3 (C-1``), 94.1 ($Cl_3\underline{C}CH_2O$), 80.9 (C-3`), 77.0 ($Cl_3C\underline{C}H_2O$), 76.7 (C-4`), 74.8 (C-5`), 74.5 (Ph$\underline{C}H_2$O), 73.5 (Ph$\underline{C}H_2$O), 73.2 (C-4``), 73.0 (C-2`), 71.6 (C-3``), 71.3 (C-2``), 69.8 (O$\underline{C}H_2(CH_2)_{14}CH_3$), 67.7 (C-6`), 61.7 (C-5``), 38.0 ($CH_2\underline{C}H_2C(O)CH_3$), 32.0 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.9 ($CH_2CH_2C(O)\underline{C}H_3$), 29.7 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.5 × 2 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 28.0 ($\underline{C}H_2CH_2C(O)CH_3$), 25.9 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 22.7

($OCH_2(\underline{C}H_2)_{14}CH_3$), 14.1 ($OCH_2(CH_2)_{14}\underline{C}H_3$). HRMS (ESI) calcd for $(M + NH_4)^+$ $C_{63}H_{83}Cl_3NO_{16}$: 1214.4772. Found: 1214.4766.



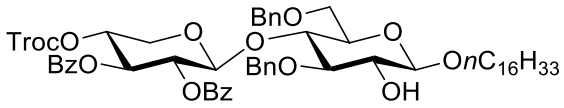
Methyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-glucopyranoside (3.27). The general procedure for levulinoyl deprotection was carried out on **3.23** (86.9 mg, 88 μmol) with H_2NNH_2·HOAc (97 μL, 110 μmol, 10% w/v in CH_3OH) in CH_2Cl_2–CH_3OH (2 mL, 10:1). The crude residue was purified by silica gel chromatography (10:1 CH_2Cl_2–EtOAc) to obtain the desired **3.26** (73.6 mg, 82.7 μmol, 94%) as a white foamy solid. R_f = 0.29 (10:1 CH_2Cl_2–EtOAc); $[\alpha]_D$ +3.8 (*c*. 0.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.00–7.88 (m, 4H, Ar), 7.57–7.49 (m, 2H, Ar), 7.45–7.27 (m, 14H), 5.53 (app t, *J* = 8.5 Hz, 1H, H-3``), 5.33 (dd, *J* = 8.6, 6.7 Hz, 1H, H-2``), 5.03 (app td, *J* = 8.5, 5.0 Hz, 1H, H-4``), 4.94 (m, 1H, 1 × PhC$\underline{H}_2$O), 4.87–4.81 (m, 2H, 1 × PhC$\underline{H}_2$O, H-1``), 4.71, 4.68 (ABq, *J* = 12.0 Hz, 2H, 2 × $Cl_3CC\underline{H}_2O$), 4.61, 4.36 (ABq, *J* = 12.0 Hz, 2H, 2 × PhC$\underline{H}_2$O), 4.17 (dd, *J* = 12.1, 5.0 Hz, 1H, H-5a``), 4.13–4.08 (m, 1H, H-1`), 4.00 (ddd, *J* = 9.3, 6.1, 3.0 Hz, 1H, H-4`), 3.65 (dd, *J* = 11.1, 3.5 Hz, 1H, H-6a`), 3.55 (dd, *J* = 11.0, 1.8 Hz, 1H, H-6b`), 3.52–3.45 (m, 5H, H-3`, H-2`, OC$\underline{H}_3$), 3.37–3.30 (m, 1H, H-5b``), 3.25 (ddd, *J* = 9.7, 3.5, 1.8 Hz, 1H, H-5`), 2.29 (s, 1H, O$\underline{H}$). $^{13}$C NMR (175 MHz, $CDCl_3$, $\delta_C$) 165.3 (C=O), 165.0 (C=O), 153.3 (C=O), 138.7 (Ar), 138.0 (Ar), 133.5 (Ar), 129.9 (Ar), 129.0 × 2 (Ar), 128.6 × 2 (Ar), 128.5 × 2 (Ar), 128.1 × 2 (Ar), 128.0 (Ar), 127.8 (Ar), 103.6 (C-1`), 100.2 (C-1``), 94.1 ($Cl_3\underline{C}CH_2O$), 82.5 (C-3`), 77.0 ($Cl_3C\underline{C}H_2O$), 76.3 (C-4`), 74.9 (Ph$\underline{C}H_2$O), 74.8 (C-5`), 74.0 (C-2`), 73.5 (Ph$\underline{C}H_2$O), 73.2 (C-4``),

71.5 (C-3``), 71.2 (C-2``), 67.8 (C-6`), 61.6 (C-5``), 57.1 (O<u>C</u>H$_3$). HRMS (ESI) calcd for (M + NH$_4$)$^+$ $C_{43}H_{47}Cl_3NO_{14}$: 906.2057. Found: 906.2054.



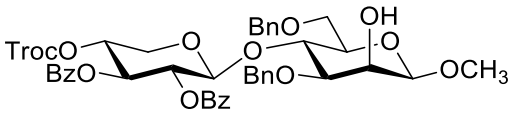
***n*-Octyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-glucopyranoside (3.28).** The general procedure for levulinoyl deprotection was carried out on **3.25** (96.6 mg, 89.0 μmol) with H_2NNH_2·HOAc (98 μL, 110 μmol, 10% w/v in CH_3OH) in CH_2Cl_2–CH_3OH (4 mL, 10:1). The crude residue was purified by silica gel chromatography (5:1 hexanes–acetone) to obtain **3.28** (74.8 mg, 75.7 μmol, 85%) as a white foamy solid. R_f = 0.23 (5:1 hexanes–acetone); $[\alpha]_D$ +6.6 (*c*. 0.4, $CHCl_3$); ^{1}H NMR (700 MHz, $CDCl_3$, δ_H) 7.97–7.91 (m, 4H, Ar), 7.55–7.50 (m, 2H, Ar), 7.39–7.27 (m, 14H, Ar), 5.52 (app t, *J* = 8.3 Hz, 1H, H-3``), 5.32 (dd, *J* = 8.5, 6.6 Hz, 1H, H-2``), 5.02 (app td, *J* = 8.4, 4.9 Hz, 1H, H-4``), 4.91, 4.88 (ABq, *J* = 11.2 Hz, 2H, 2 × PhC<u>H</u>$_2$O), 4.85 (d, *J* = 6.6 Hz, 1H, H-1``), 4.71, 4.68 (ABq, *J* = 11.9 Hz, 2H, 2 × Cl_3CC<u>H</u>$_2$O), 4.58, 4.35 (ABq, *J* = 12.0 Hz, 2H, 2 × PhC<u>H</u>$_2$O), 4.20–4.14 (m, 2H, H-5a``, H-1`), 4.00–3.94 (m, 1H, H-4`), 3.82 (dt, *J* = 9.6, 6.8 Hz, 1H, 1 × OC<u>H</u>$_2$(CH_2)$_6$$CH_3$), 3.63 (dd, *J* = 11.0, 3.7 Hz, 1H, H-6a`), 3.54 (dd, *J* = 11.0, 1.8 Hz, 1H, H-6b`), 3.52–3.48 (m, 2H, H-3`, H-2`), 3.44 (dt, *J* = 9.6, 6.9 Hz, 1H, 1 × OC<u>H</u>$_2$(CH_2)$_6$$CH_3$), 3.33 (dd, *J* = 12.3, 8.6 Hz, 1H, H-5b``), 3.25 (ddd, *J* = 9.8, 3.8, 1.8 Hz, 1H, H-5`), 2.27 (s, 1H, OH), 1.63–1.56 (m, 2H, 2 × OCH_2(C<u>H</u>$_2$)$_6$$CH_3$), 1.36–1.19 (m, 10H, 10 × OCH_2(C<u>H</u>$_2$)$_6$$CH_3$), 0.87 (t, *J* = 7.1 Hz, 3H, OCH_2(CH_2)$_6$C<u>H</u>$_3$). ^{13}C NMR (175 MHz, $CDCl_3$, δ_C) 165.3 (C=O), 165.0 (C=O), 153.3 (C=O), 138.8 (Ar), 138.0 (Ar), 133.5 × 2 (Ar), 129.9 (Ar), 129.1 (Ar), 129.0 (Ar), 128.6 × 2 (Ar),

128.5 × 2 (Ar), 128.0 × 2 (Ar), 127.9 (Ar), 127.7 × 2 (Ar), 102.7 (C-1`), 100.2 (C-1``), 94.1 ($Cl_3\underline{C}CH_2O$), 82.6 (C-3`), 77.0 ($Cl_3C\underline{C}H_2O$), 76.4 (C-4`), 74.8 × 2 ($Ph\underline{C}H_2O$, C-5`), 74.1 (C-2`), 73.5 ($Ph\underline{C}H_2O$), 73.2 (C-4``), 71.4 (C-3``), 71.1 (C-2``), 70.1 ($O\underline{C}H_2(CH_2)_6CH_3$), 67.9 (C-6`), 61.5 (C-5``), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.6 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 26.0 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 14.1 ($OCH_2(CH_2)_6\underline{C}H_3$). HRMS (ESI) calcd for $(M + NH_4)^+$ $C_{50}H_{61}Cl_3NO_{14}$: 1004.3152. Found: 1004.3149.



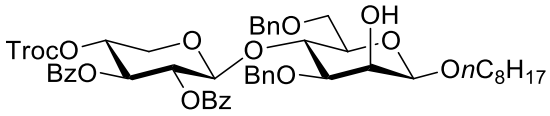
***n*-Hexadecyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-glucopyranoside (3.29).** The general procedure for levulinoyl deprotection was carried out on **3.26** (122 mg, 102 μmol) with $H_2NNH_2{\cdot}HOAc$ (121 μL, 131 μmol, 10% w/v in CH_3OH) in CH_2Cl_2–CH_3OH (5 mL, 10:1). The crude residue was purified by silica gel chromatography using (6:1 hexanes–acetone) to obtain **3.29** (104 mg, 94.5 μmol, 93%) as a white foamy solid. R_f = 0.30 (6:1 hexanes–acetone); $[\alpha]_D$ +11.0 (*c*. 0.3, $CHCl_3$); ^{1}H NMR (700 MHz, $CDCl_3$, δ_H) 7.98–7.91 (m, 4H, Ar), 7.56–7.50 (m, 2H, Ar), 7.43–7.27 (m, 14H, Ar), 5.53 (app t, *J* = 8.3 Hz, 1H, H-3``), 5.33 (dd, *J* = 8.4, 6.6 Hz, 1H, H-2``), 5.03 (app td, *J* = 8.4, 4.9 Hz, 1H, H-4``), 4.91, 4.88 (ABq, *J* = 11.2 Hz, 2H, 2 × $PhC\underline{H}_2O$), 4.85 (d, *J* = 6.6 Hz, 1H, H-1``), 4.71, 4.68 (ABq, *J* = 11.9 Hz, 2H, 2 × $Cl_3CC\underline{H}_2O$), 4.58, 4.36 (ABq, *J* = 12.0 Hz, 2H, 2 × $PhC\underline{H}_2O$), 4.20–4.15 (m, 2H, H-5a``, H-1`), 4.00–3.94 (m, 1H, H-4`), 3.82 (dt, *J* = 9.6, 6.8 Hz, 1H, 1 × $OC\underline{H}_2(CH_2)_{14}CH_3$), 3.64 (dd, *J* = 11.0, 3.7 Hz, 1H, H-6a`), 3.54 (dd, *J* = 11.0, 1.8 Hz, 1H, H-6b`), 3.53–3.48 (m, 2H, H-3`, H-2`), 3.44 (dt, *J* = 9.6, 6.9 Hz, 1H, 1 × $OC\underline{H}_2(CH_2)_{14}CH_3$),

3.34 (dd, J = 12.2, 8.6 Hz, 1H, H-5b``), 3.26 (ddd, J = 9.7, 3.7, 1.8 Hz, 1H, H-5`), 2.28 (s, 1H, OH), 1.64–1.57 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 1.35–1.19 (m, 26H, 26 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 0.88 (t, J = 7.1 Hz, 3H, $OCH_2(CH_2)_{14}C\underline{H}_3$). ^{13}C NMR (175 MHz, $CDCl_3$, δ_C) 165.3 (C=O), 165.0 (C=O), 153.3 (C=O), 138.8 (Ar), 138.0 (Ar), 133.5 × 2 (Ar), 129.9 (Ar), 129.1 (Ar), 129.0 (Ar), 128.6 (Ar), 128.5 × 3 (Ar), 128.0 × 2 (Ar), 127.9 (Ar), 127.7 (Ar), 102.7 (C-1`), 100.1 (C-1``), 94.1 ($Cl_3\underline{C}CH_2O$), 82.6 (C-3`), 77.0 ($Cl_3C\underline{C}H_2O$), 76.4 (C-4`), 74.8 × 2 ($Ph\underline{C}H_2O$, C-5`) 74.1 (C-2`), 73.5 ($Ph\underline{C}H_2O$), 73.2 (C-4``), 71.3 (C-3``), 71.1 (C-2``), 70.1 ($O\underline{C}H_2(CH_2)_{14}CH_3$), 67.9 (C-6`), 61.5 (C-5``), 32.0 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.7 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.7 × 3 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.6 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.5 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 26.0 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 14.2 ($OCH_2(CH_2)_{14}\underline{C}H_3$). HRMS (ESI) calcd for $(M + NH_4)^+$ $C_{58}H_{77}Cl_3NO_{14}$: 1116.4404. Found: 1116.4404.



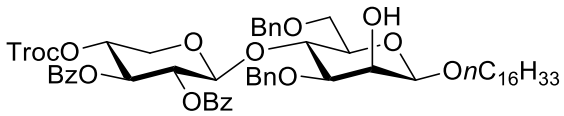
Methyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.30). Approach A for C-2 inversion was carried out on **3.27** (1.05 g, 1.18 mmol). In this approach, DMSO (42 mL) and Ac_2O (5.3 mL) were used for oxidation; subsequent reduction was conducted on the crude ketone with LTBA (390 mg, 1.53 mmol) in THF (12 mL). The resultant crude residue was purified by silica gel chromatography (6:1 hexanes–acetone) to obtain **3.30** (630 mg, 0.71 mmol, 60%) as a white solid. R_f = 0.24 (6:1 hexanes–acetone); $[\alpha]_D$ −1.2 (*c*. 0.2, CH_2Cl_2); ^{1}H NMR (700 MHz, $CDCl_3$, δ_H) 7.97–7.92 (m, 4H,

Ar), 7.55–7.50 (m, 2H, Ar), 7.42–7.32 (m, 11H, Ar), 7.32–7.27 (m, 3H), 5.53 (app t, J = 8.1 Hz, 1H, H-3``), 5.32 (dd, $J$ = 8.2, 6.4 Hz, 1H, H-2``), 5.04 (td, J = 8.2, 4.8 Hz, 1H, H-4``), 4.87 (d, $J$ = 6.4 Hz, 1H, H-1``), 4.78–4.74 (m, 2H, 2 × PhC$\underline{H}_2$O), 4.71, 4.68 (ABq, J = 11.9 Hz, 2H, 2 × $Cl_3CC\underline{H}_2O$), 4.53, 4.33 (ABq, J = 12.0 Hz, 2H, 2 × PhC$\underline{H}_2$O), 4.26 (d, J = 1.0 Hz, 1H, H-1`), 4.23 (dd, J = 12.3, 4.9 Hz, 1H, H-5a``), 4.19 (app t, $J$ = 9.2 Hz, 1H, H-4`), 4.06–4.03 (app s, 1H, H-2`), 3.63 (dd, $J$ = 11.0, 4.3 Hz, 1H, H-6a`), 3.59 (dd, $J$ = 10.9, 2.0 Hz, 1H, H-6b`), 3.51–3.46 (m, 4H, OC$\underline{H}_3$, H-3`), 3.39 (dd, $J$ = 12.3, 8.3 Hz, 1H, H-5b``), 3.26 (ddd, J = 9.5, 4.4, 2.1 Hz, 1H, H-5`), 2.38 (d, $J$ = 2.5 Hz, 1H, O$\underline{H}$). $^{13}$C NMR (175 MHz, $CDCl_3$, $\delta_C$) 165.2 (C=O), 165.1 (C=O), 153.3 (C=O), 138.2 (Ar), 138.0 (Ar), 133.5 × 2 (Ar), 129.9 × 2 (Ar), 129.1 (Ar), 128.5 × 2 (Ar), 128.0 × 2 (Ar), 127.9 (Ar), 127.8 (Ar), 100.8 (C-1`), 100.2 (C-1``), 94.1 ($Cl_3\underline{C}CH_2O$), 79.7 (C-3`), 77.0 ($Cl_3C\underline{C}H_2O$), 74.9 (C-5`), 74.1 (C-4`), 73.4 (Ph$\underline{C}H_2O$), 73.2 (C-4``), 72.4 (Ph$\underline{C}H_2O$), 71.2 (C-3``), 71.0 (C-2``), 68.5 (C-2`), 68.3 (C-6`), 61.4 (C-5``), 57.0 (O$\underline{C}H_3$). HRMS (ESI) calcd for $(M + NH_4)^+$ $C_{43}H_{47}Cl_3NO_{14}$: 906.2057. Found: 906.2063.



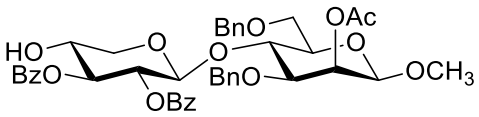
***n*-Octyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.31).** Approach A for C-2 inversion was carried out on **3.28** (1.75 g, 1.77 mmol). In this approach, DMSO (70 mL) and Ac_2O (9 mL) were used for oxidation; subsequent reduction was conducted on the crude ketone with LTBA (584 mg, 2.23 mmol) in THF (18 mL). The resultant crude residue was purified by silica gel chromatography (4:1 hexanes–acetone) to obtain **3.31** (1.22 g, 1.24 mmol, 70%) as a white solid. R_f = 0.25 (4:1

hexanes–acetone); $[\alpha]_D$ −1.6 (*c*. 0.20, $CHCl_3$); ^{1}H NMR (700 MHz, $CDCl_3$, δ_H) 7.97–7.92 (m, 4H, Ar), 7.55–7.50 (m, 2H, Ar), 7.43–7.26 (m, 14H, Ar), 5.53 (app t, *J* = 8.1 Hz, 1H, H-3``), 5.32 (dd, *J* = 8.3, 6.4 Hz, 1H, H-2``), 5.04 (app td, *J* = 8.1, 4.8 Hz, 1H, H-4``), 4.87 (d, *J* = 6.4 Hz, 1H, H-1``), 4.79–4.75 (m, 1H, 1 × PhC$\underline{H}_2$O), 4.74–4.66 (m, 3H, 1 × PhC$\underline{H}_2$O, 2 × Cl_3CC$\underline{H}_2$O), 4.52, 4.32 (ABq, *J* = 12.1 Hz, 2H, 2 × PhC$\underline{H}_2$O), 4.34 (d, *J* = 1.1 Hz, 1H, H-1`), 4.23 (dd, *J* = 12.3, 4.8 Hz, 1H, H-5a``), 4.18 (app t, *J* = 9.2 Hz, 1H, H-4`), 4.06 (d, *J* = 3.0, 1H, H-2`), 3.85 (dt, *J* = 9.5, 6.7 Hz, 1H, 1 × OC$\underline{H}_2$(CH_2)$_6$$CH_3$), 3.61 (dd, *J* = 10.9, 4.3 Hz, 1H, H-6a`), 3.58 (dd, *J* = 10.9, 2.2 Hz, 1H, H-6b`), 3.49 (dd, *J* = 9.0, 3.2 Hz, 1H, H-3`), 3.45–3.36 (m, 2H, 1 × OC$\underline{H}_2$(CH_2)$_6$$CH_3$, H-5b``), 3.25 (ddd, *J* = 9.5, 4.3, 2.2 Hz, 1H, H-5`), 1.62–1.54 (m, 2H, 2 × OCH_2(C$\underline{H}_2$)$_6$$CH_3$), 1.36–1.17 (m, 10H, 10 × OCH_2(C$\underline{H}_2$)$_6$$CH_3$), 0.87 (t, *J* = 7.1 Hz, 3H, OCH_2(CH_2)$_6$C$\underline{H}_3$). ^{13}C NMR (175 MHz, $CDCl_3$, δ_C) 165.2 (C=O), 165.1 (C=O), 153.3 (C=O), 138.2 (Ar), 138.0 (Ar), 133.5 (Ar), 133.4 (Ar), 129.9 × 2 (Ar), 129.1 × 2 (Ar), 128.5 (Ar), 128.5 × 2 (Ar), 128.4 (Ar), 128.0 (Ar), 127.9 × 2 (Ar), 127.8 (Ar), 100.3 (C-1``), 99.8 (C-1`), 94.1 ($Cl_3$C$\underline{C}H_2$O), 79.8 (C-3`), 77.0 ($Cl_3$C$\underline{C}H_2$O), 74.9 (C-5`), 74.2 (C-4`), 73.4 (PhC$\underline{H}_2$O), 73.2 (C-4``), 72.2 (PhC$\underline{H}_2$O), 71.3 (C-3``), 71.1 (C-2``), 69.9 (OC$\underline{H}_2$(CH_2)$_6$$CH_3$), 68.7 (C-2`), 68.4 (C-6`), 61.4 (C-5``), 31.8 (OCH_2(C$\underline{H}_2$)$_6$$CH_3$), 29.5 ($OCH_2$(C$\underline{H}_2$)$_6$$CH_3$), 29.4 ($OCH_2$(C$\underline{H}_2$)$_6$$CH_3$), 29.3 ($OCH_2$(C$\underline{H}_2$)$_6$$CH_3$), 26.0 ($OCH_2$(C$\underline{H}_2$)$_6$$CH_3$), 22.7 ($OCH_2$(C$\underline{H}_2$)$_6$$CH_3$), 14.1 ($OCH_2$($CH_2$)$_6C\underline{H}_3$). HRMS (ESI) calcd for $(M + NH_4)^+$ $C_{50}H_{61}Cl_3NO_{14}$: 1004.3152. Found: 1004.3152.



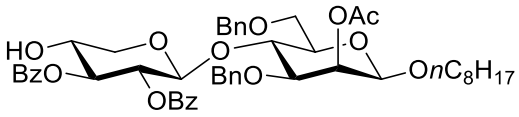
***n*-Hexadecyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.32).** Approach A to effect C-2 inversion was carried out on **3.28** (84.5 mg, 77 μmol). In this approach, DMSO (3 mL) and Ac_2O (0.5 mL) were used for oxidation; subsequent reduction was conducted on the crude ketone with LTBA (24.9 mg, 98 μmol) in THF (2 mL). The resultant crude residue was purified by silica gel chromatography (3:1 hexanes–EtOAc) to obtain **3.31** (59.3 mg, 54 μmol, 70%) as a white solid. R_f = 0.29 (3:1 hexanes–EtOAc); $[\alpha]_D$ +2.0 (*c*. 0.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.95 (m, 4H, Ar), 7.56–7.48 (m, 2H, Ar), 7.43–7.27 (m, 14H, Ar), 5.53 (app t, *J* = 8.1 Hz, 1H, H-3``), 5.32 (dd, *J* = 8.2, 6.4 Hz, 1H, H-2``), 5.04 (app td, *J* = 8.1, 4.8 Hz, 1H, H-4``), 4.87 (d, *J* = 6.4 Hz, 1H, H-1``), 4.76, 4.72 (ABq, *J* = 11.0 Hz, 2H, 2 × PhC$\underline{H}_2$O), 4.71, 4.68 (ABq, *J* = 11.9 Hz, 2H, 2 × Cl_3CC$\underline{H}_2$O), 4.52, 4.32 (ABq, *J* = 12.1 Hz, 2H, 2 × PhC$\underline{H}_2$O), 4.34 (d, *J* = 1.0 Hz, 1H, H-1`), 4.23 (dd, *J* = 12.3, 4.8 Hz, 1H, H-5a``), 4.18 (app t, *J* = 9.2 Hz, 1H, H-4`), 4.06 (d, *J* = 3.0 Hz, 1H, H-2`), 3.85 (dt, *J* = 9.5, 6.8 Hz, 1H, 1 × OC$\underline{H}_2$($CH_2$)$_{14}$$CH_3$), 3.65–3.55 (m, 2H, H-6a`, H-6b`), 3.49 (dd, *J* = 9.0, 3.2 Hz, 1H, H-3`), 3.46–3.35 (m, 2H, 1 × OC$\underline{H}_2$($CH_2$)$_{14}$$CH_3$, H-5b``), 3.25 (ddd, *J* = 9.5, 4.2, 2.3 Hz, 1H, H-5`), 2.49–2.34 (m, 1H, O$\underline{H}$), 1.63–1.53 (m, 2H, 2 × OCH_2(C$\underline{H}_2$)$_{14}$$CH_3$), 1.36–1.17 (m, 26H, 26 × OCH_2(C$\underline{H}_2$)$_{14}$$CH_3$), 0.88 (t, *J* = 6.9 Hz, 3H, OCH_2(CH_2)$_{14}$C$\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 165.2 (C=O), 165.1 (C=O), 153.3 (C=O), 138.2 (Ar), 138.0 (Ar), 133.5 (Ar), 133.4 (Ar), 129.9 × 2 (Ar), 129.1 (Ar), 128.5 × 3 (Ar), 128.4 (Ar), 128.0 × 2 (Ar), 127.9 × 2 (Ar), 127.8 (Ar), 100.2 (C-1``), 99.8 (C-1`), 94.1 ($Cl_3$$\underline{C}$$CH_2$O), 79.8 (C-3`), 77.0 ($Cl_3$C$\underline{C}$$H_2$O), 74.9 (C-5`), 74.2 (C-4`), 73.4 (Ph$\underline{C}$$H_2$O), 73.2 (C-4``), 72.2

(Ph<u>C</u>H$_2$O), 71.3 (C-3``), 71.1 (C-2``), 69.9 (O<u>C</u>H$_2$(CH$_2$)$_{14}$CH$_3$), 68.7 (C-2`), 68.4 (C-6`), 61.4 (C-5``), 32.0 (OCH$_2$(<u>C</u>H$_2$)$_{14}$CH$_3$), 29.7 × 4 (OCH$_2$(<u>C</u>H$_2$)$_{14}$CH$_3$), 29.6 (OCH$_2$(<u>C</u>H$_2$)$_{14}$CH$_3$), 29.5 × 2 (OCH$_2$(<u>C</u>H$_2$)$_{14}$CH$_3$), 29.4 (OCH$_2$(<u>C</u>H$_2$)$_{14}$CH$_3$), 26.0 (OCH$_2$(<u>C</u>H$_2$)$_{14}$CH$_3$), 22.7 (OCH$_2$(<u>C</u>H$_2$)$_{14}$CH$_3$), 14.2 (OCH$_2$(CH$_2$)$_{14}$<u>C</u>H$_3$). HRMS (ESI) calcd for $(M + NH_4)^+$ $C_{58}H_{77}Cl_3NO_{14}$: 1116.4404. Found: 1116.4411.



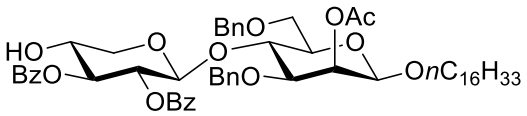
Methyl 2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.33). To a solution of **3.30** (630 mg, 0.71 mmol) in pyridine (10 mL) was added Ac_2O (2 mL) under argon. The reaction mixture was stirred at 40 °C overnight, cooled to room temperature and then CH_3OH (0.5 mL) was added. The resultant mixture was concentrated and subsequently co-evaporated with toluene (2x). The crude material was re-dissolved in CH_2Cl_2 and washed with 1 M aqueous HCl and brine before it was dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a thick syrup that was then subjected to Troc deprotection using the general procedure with Zn powder (2.31 g, 35.3 mmol) in glacial AcOH (20 mL). The crude residue was purified by silica gel chromatography (2:1 to 3:2 hexanes–EtOAc) to obtain **3.32** (429 mg, 0.566 mmol, 80 %) as a white foamy solid. R_f = 0.20 (2:1 hexanes–EtOAc); $[\alpha]_D$ +10.6 (*c*. 0.4, $CHCl_3$); ^{1}H NMR (700 MHz, $CDCl_3$, δ_H) 8.00–7.95 (m, 2H, Ar), 7.93–7.88 (m, 2H, Ar), 7.56–7.49 (m, 2H, Ar), 7.42–7.33 (m, 10H, Ar), 7.33–7.27 (m, 4H, Ar), 5.58 (dd, *J* = 3.5, 1.0 Hz, 1H, H-2`), 5.33 (dd, *J* = 8.9, 7.0 Hz, 1H, H-2``), 5.08 (app t, *J* = 8.5 Hz, 1H, H-3``), 4.80–4.75 (m, 2H, H-1``, 1 × PhC<u>H</u>$_2$O), 4.60–4.54 (m, 2H, 2 ×

PhC$\underline{H}_2$O), 4.33 (d, J = 0.9 Hz, 1H, H-1`), 4.30–4.27 (m, 1H, 1 × PhC$\underline{H}_2$O), 4.12–4.07 (m, 2H, H-4`, H-5a``), 3.94 (ddt, $J$ = 8.9, 8.0, 5.0 Hz, 1H, H-4``), 3.65 (dd, J = 10.9, 4.6 Hz, 1H, H-6a`), 3.62–3.55 (m, 2H, H-6b`, H-3`), 3.45 (s, 3H, OC$\underline{H}_3$), 3.30 (ddd, $J$ = 9.6, 4.5, 1.9 Hz, 1H, H-5`), 3.17 (dd, J = 12.2, 9.0 Hz, 1H, H-5b``), 2.96 (d, J = 5.0 Hz, 1H, OH), 2.18 (s, 3H, C$\underline{H}_3$C(O)O). ^{13}C NMR (175 MHz, $CDCl_3$, δ_C) 170.8 (C=O), 167.6 (C=O), 165.1 (C=O), 138.3 (Ar), 137.7 (Ar), 133.7 (Ar), 133.5 (Ar), 130.0 (Ar), 129.8 (Ar), 129.2 (Ar), 128.9 (Ar), 128.6 (Ar), 128.5 (Ar), 128.4 (Ar), 128.1 (Ar), 128.0 (Ar), 127.9 (Ar), 127.8 (Ar), 100.5 (C-1``), 100.0 (C-1`), 78.3 (C-3`), 77.0 (C-3``), 75.3 (C-5`), 74.1 (C-4`), 73.4 (Ph$\underline{C}$H$_2$O), 72.0 (Ph$\underline{C}$H$_2$O), 71.4 (C-2``), 69.3 (C-4``), 68.4 (C-6`), 67.9 (C-2`), 65.2 (C-5``), 57.1 (O$\underline{C}$H$_3$), 21.3 ($\underline{C}$H$_3$C(O)O). HRMS (ESI) calcd for $(M + Na)^+$ $C_{42}H_{44}NaO_{13}$: 779.2674. Found: 779.2671.



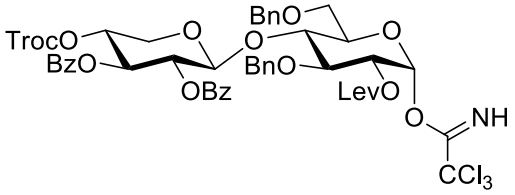
***n*-Octyl 2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.34).** To a solution of **3.31** (1.22 g, 1.24 mmol) in pyridine (20 mL) was added Ac_2O (5 mL) under argon. The reaction mixture was stirred at 40 °C overnight, cooled to room temperature and then CH_3OH (0.5 mL) was added. The resultant mixture was concentrated and subsequently co-evaporated with toluene (2x). The crude material was re-dissolved in CH_2Cl_2 and washed with 1 M aqueous HCl and brine before it was dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a thick syrup that was then subjected to Troc deprotection using the general procedure with Zn powder (4.21 g, 64.4 mmol) in glacial AcOH (20 mL). The crude residue was purified by silica gel chromatography (4:1

hexanes–acetone) to obtain **3.34** (868 mg, 1.02 mmol, 82 %) as a white foamy solid. R_f = 0.24 (4:1 hexanes–acetone); $[\alpha]_D$ +11.3 (*c*. 0.9, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.00–7.87 (m, 4H, Ar), 7.57–7.48 (m, 2H, Ar), 7.42–7.26 (m, 14H), 5.58 (d, *J* = 3.5, 1H, H-2`), 5.33 (dd, *J* = 8.9, 7.0 Hz, 1H, H-2``), 5.09 (app t, *J* = 8.5 Hz, 1H, H-3``), 4.85–4.75 (m, 2H, H-1``, 1 × PhC$\underline{H}_2$O), 4.57–4.51 (m, 2H, 2 × PhC$\underline{H}_2$O), 4.41 (d, *J* = 1.0 Hz, 1H, H-1`), 4.32–4.24 (m, 1H, 1 × PhC$\underline{H}_2$O), 4.14–4.01 (m, 2H, H-4`, H-5a``), 3.98–3.90 (m, 1H, H-4``), 3.78 (dt, *J* = 9.4, 6.8 Hz, 1H, 1 × OC$\underline{H}_2(CH_2)_6CH_3$), 3.67–3.55 (m, 3H, H-6a`, H-6b`, H-3`), 3.41 (dt, *J* = 9.4, 6.9 Hz, 1H, 1 × OC$\underline{H}_2(CH_2)_6CH_3$), 3.30 (ddd, *J* = 9.6, 4.6, 2.0 Hz, 1H, H-5`), 3.16 (dd, *J* = 12.1, 9.0 Hz, 1H, H-5b``), 2.95 (d, *J* = 5.0 Hz, 1H, OH), 2.17 (s, 3H, C$\underline{H}_3$C(O)O), 1.55–1.51 (m, 2H, $OCH_2(C\underline{H}_2)_6CH_3$), 1.33–1.17 (m, 10H, 10 × $OCH_2(C\underline{H}_2)_6CH_3$), 0.86 (t, *J* = 6.9 Hz, 3H, $OCH_2(CH_2)_6C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 170.7 (C=O), 167.5 (C=O), 165.2 (C=O), 138.3 (Ar), 137.8 (Ar), 133.7 (Ar), 133.5 (Ar), 130.0 (Ar), 129.8 (Ar), 129.2 (Ar), 128.9 (Ar), 128.5 (Ar), 128.4 × 2 (Ar), 128.0 (Ar), 127.9 (Ar), 127.8 × 2 (Ar), 100.6 (C-1``), 98.9 (C-1`), 78.5 (C-3`), 77.0 (C-3``), 75.3 (C-5`), 74.2 (C-4`), 73.4 (Ph$\underline{C}H_2$O), 71.9 (Ph$\underline{C}H_2$O), 71.4 (C-2``), 70.0 (O$\underline{C}H_2(CH_2)_6CH_3$), 69.3 (C-4``), 68.6 (C-6`), 68.1 (C-2`), 65.3 (C-5``), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 × 2 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 25.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 21.3 ($\underline{C}H_3C(O)O$), 14.13 ($OCH_2(CH_2)_6\underline{C}H_3$). HRMS (ESI) calcd for $(M + Na)^+$ $C_{49}H_{58}NaO_{13}$: 877.3770. Found: 877.3766.



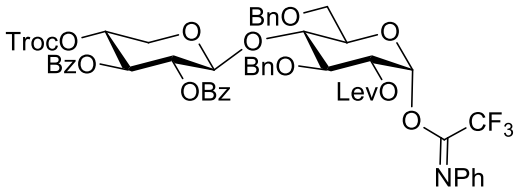
***n*-Hexadecyl 2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.35).** To a solution of **3.32** (47.4 mg, 43.0 μmol) in pyridine (2 mL) was added Ac_2O (0.4 mL) under argon. The reaction mixture was stirred at 40 °C overnight, cooled to room temperature and then CH_3OH (0.5 mL) was added. The resultant mixture was concentrated and co-evaporated with toluene (2x). The crude material was re-dissolved in CH_2Cl_2 and subsequently washed with 1 M aqueous HCl and brine before it was dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a thick syrup that was then subjected to Troc deprotection using Zn powder (155 mg, 2.37 mmol) in glacial AcOH (2 mL). The crude residue was purified by silica gel chromatography (3:1 hexanes–EtOAc) to obtain **3.35** (32.4 mg, 33.5 μmol, 78%) as a white foamy solid. R_f = 0.28 (3:1 hexanes–EtOAc); $[\alpha]_D$ −11.0 (*c*. 0.02, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.00–7.88 (m, 4H,Ar), 7.56–7.49 (m, 2H, Ar), 7.42–7.26 (m, 14H, Ar), 5.58 (d, *J* = 3.5 Hz, 1H, H-2`), 5.33 (dd, *J* = 8.9, 7.0 Hz, 1H, H-2``), 5.09 (app t, *J* = 8.5 Hz, 1H, H-3``), 4.83–4.75 (m, 2H, H-1``, 1 × PhC$\underline{H}_2$O), 4.58–4.50 (m, 2H, 2 × PhC$\underline{H}_2$O), 4.41 (d, *J* = 1.0 Hz, 1H, H-1`), 4.31–4.24 (m, 1H, 1 × PhC$\underline{H}_2$O), 4.13–4.01 (m, 2H, H-4`, H-5a``), 3.94 (td, *J* = 8.6, 5.0 Hz, 1H, H-4``), 3.78 (dt, *J* = 9.4, 6.8 Hz, 1H, 1 × OC$\underline{H}_2$(CH$_2$)$_{14}$CH$_3$), 3.67–3.55 (m, 3H, H-6a`, H-6b`, H-3`), 3.40 (dt, *J* = 9.4, 6.9 Hz, 1H, 1 × OC$\underline{H}_2$(CH$_2$)$_6$CH$_3$), 3.30 (ddd, *J* = 9.7, 4.6, 2.0 Hz, 1H, H-5`), 3.15 (dd, *J* = 12.1, 9.0 Hz, 1H, H-5b``), 2.17 (s, 3H, C$\underline{H}_3$C(O)O), 1.56–1.51 (m, 2H, 2 × OCH$_2$(C$\underline{H}_2$)$_{14}$CH$_3$), 1.33–1.20 (m, 26H, 26 × OCH$_2$(C$\underline{H}_2$)$_{14}$CH$_3$), 0.88 (t, *J* = 6.9 Hz, 3H, OCH$_2$(CH$_2$)$_{14}$C$\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 170.7 (C=O), 167.5 (C=O), 165.1 (C=O), 138.3 (Ar), 137.8 (Ar), 133.7 (Ar), 133.5 (Ar), 130.0 (Ar), 129.8 (Ar), 129.2 (Ar), 128.9 (Ar), 128.5 (Ar), 128.4 × 2 (Ar),

128.0 (Ar), 127.9 (Ar), 127.8 × 2 (Ar), 100.6 (C-1``), 98.9 (C-1`), 78.5 (C-3`), 77.0 (C-3``), 75.3 (C-5`), 74.2 (C-4`), 73.4 (Ph<u>C</u>H_2O), 71.9 (Ph<u>C</u>H_2O), 71.4 (C-2``), 70.0 (O<u>C</u>$H_2(CH_2)_{14}CH_3$), 69.3 (C-4``), 68.6 (C-6`), 68.1 (C-2`), 65.3 (C-5``), 32.0 (OCH_2(<u>C</u>$H_2)_{14}CH_3$), 29.8 (OCH_2(<u>C</u>$H_2)_{14}CH_3$), 29.7 × 3 (OCH_2(<u>C</u>$H_2)_{14}CH_3$), 29.6 (OCH_2(<u>C</u>$H_2)_{14}CH_3$), 29.4 × 2 (OCH_2(<u>C</u>$H_2)_{14}CH_3$), 25.9 (OCH_2(<u>C</u>$H_2)_{14}CH_3$), 22.7 (OCH_2(<u>C</u>$H_2)_{14}CH_3$), 21.3 (<u>C</u>H_3C(O)O), 14.12 ($OCH_2(CH_2)_{14}$<u>C</u>H_3). HRMS (ESI) calcd for $(M + Na)^+$ $C_{57}H_{74}NaO_{13}$: 989.5022. Found: 989.5017.



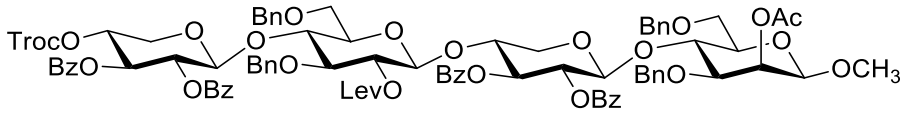
2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-1-*O*-trichloroacetimidoyl-2-*O*-levulinoyl-α-D-glucopyranoside (3.36). To a solution of **3.16** (345 mg, 0.319 mmol) in acetone (10 mL) was added H_2O (1.1 mL). The solution was then cooled to 0 °C. To this mixture was added NBS (181 mg, 1.02 mmol) and the resultant solution was stirred at 0 °C for 3 h. Satd. aqueous $Na_2S_2O_3$ solution was then added and acetone was subsequently evaporated. The resultant crude material was re-dissolved in CH_2Cl_2 (50 mL) and then poured into satd. aqueous $NaHCO_3$. The two phases were separated, and the aqueous phase was then extracted with CH_2Cl_2 (3 × 50 mL). The combined organic phases were subsequently washed with water and brine before they were dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a thick syrup that was then dried under vacuum overnight. This crude material was then re-dissolved in CH_2Cl_2 (100 mL). To this solution was added DBU (19 μL, 0.13 mmol), followed by trichloroacetonitrile (125 μL, 1.25 mmol) at room

temperature under argon. The mixture was then stirred for 2 h and then concentrated to a thick brown syrup that was subsequently purified by silica gel chromatography (3:1 hexanes–acetone, 1% Et_3N) to afford **3.36** (248 mg, 0.222 mmol, 70%) as a white foamy solid. R_f = 0.30 (3:1 hexanes–acetone); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.55 (s, 1H, NH), 8.01–7.88 (m, 4H, Ar), 7.59–7.49 (m, 2H, Ar), 7.44–7.26 (m, 14H, Ar), 6.43 (d, *J* = 3.6 Hz, 1H, H-1`), 5.50 (app t, *J* = 7.7 Hz, 1H, H-3``), 5.32 (dd, *J* = 7.9, 6.1 Hz, 1H, H-2``), 5.05 (dd, *J* = 10.0, 3.6 Hz, 1H, H-2`), 5.00 (td, *J* = 7.8, 4.6 Hz, 1H. H-4``), 4.88, 4.75 (ABq, *J* = 11.3 Hz, 2H, 2 × PhC<u>H</u>$_2$O), 4.83 (d, *J* = 6.1 Hz, 1H, H-1``), 4.73, 4.69 (ABq, *J* = 12.0 Hz, 2 × Cl_3CC<u>H</u>$_2$O), 4.61, 4.38 (ABq, *J* = 11.9 Hz, 2H, 2 × PhC<u>H</u>$_2$O), 4.22–4.14 (m, 2H, H-5a``, H-4`), 4.01 (app t, *J* = 9.6 Hz, 1H, H-3`), 3.79–3.74 (m, 1H, H-5`), 3.72 (dd, *J* = 11.2, 2.7 Hz, 1H, H-6a`), 3.49 (dd, *J* = 11.3, 1.6 Hz, 1H, H-6b`), 3.36 (dd, *J* = 12.4, 7.9 Hz, 1H, H-5b``), 2.70–2.56 (m, 2H, CH_2C<u>H</u>$_2$C(O)CH_3), 2.49–2.35 (m, 2H, C<u>H</u>$_2$$CH_2$C(O)$CH_3$), 2.12 (s, 3H, CH_2CH_2C(O)C<u>H</u>$_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 206.0 (C=O), 171.8 (C=O), 165.2 (C=O), 165.1 (C=O), 160.8 (C=N), 153.3 (C=O), 138.3 (Ar), 137.7 (Ar), 133.6 (Ar), 133.5 (Ar), 129.9 (Ar), 129.8 (Ar), 129.0 (Ar), 128.7 (Ar), 128.6 (Ar), 128.5 (Ar), 128.3 (Ar), 128.2 (Ar), 128.1 (Ar), 127.9 (Ar), 127.7 (Ar), 99.9 (C-1``), 94.1 ($Cl_3$<u>C</u>$CH_2$O), 93.7 (C-1`), 91.0 ($Cl_3$<u>C</u>C=NH), 77.5 (C-3`), 77.0 ($Cl_3$C<u>C</u>$H_2$O), 75.6 (C-4`), 75.0 (Ph<u>C</u>$H_2$O), 73.5 (Ph<u>C</u>$H_2$O), 73.1 (C-5`), 72.9 (C-4``), 72.0 (C-2`), 70.8 (C-3``), 70.6 (C-2``), 67.1 (C-6`), 61.2 (C-5``), 37.8 (CH_2<u>C</u>H_2C(O)CH_3), 29.8 (<u>C</u>H_2CH_2C(O)CH_3), 27.6 (CH_2CH_2C(O)<u>C</u>H_3).



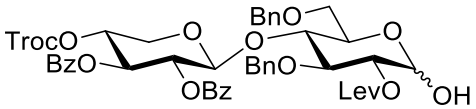
2,3-Di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-1-*O*-trifluoro(*N*-phenyl)acetimidoyl-2-*O*-levulinoyl-α-D-glucopyranoside (3.37). To a solution of **3.16** (4.88 g, 4.52 mmol) in acetone (200 mL) was added H_2O (20 mL). The solution was then cooled to 0 °C. To this solution was added NBS (2.41 g, 13.6 mmol) and the resultant yellowish mixture was stirred at 0 °C for 3 h. Satd. aqueous $Na_2S_2O_3$ was then added and acetone was subsequently evaporated. To this residue was added CH_2Cl_2 (200 mL) and the resultant solution was poured into satd. $NaHCO_3$. The two phases were separated and the aqueous phase was then extracted with CH_2Cl_2 (3 × 100 mL). The combined organic phases were thoroughly washed with water and brine before they were dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a thick syrup that was then dried under vacuum overnight. This crude material was then re-dissolved in CH_2Cl_2 (100 mL). To this solution was added DBU (0.78 mL, 5.5 mmol), followed by 2,2,2-trifluoro-*N*-phenylacetimidoyl chloride (1.43 mL, 9.09 mmol) under argon. The mixture was stirred for 2 h, after which it was concentrated to thick brown syrup that was subsequently purified by silica gel chromatography (3:1 hexanes–acetone) to afford **3.37** (3.61 g, 3.71 mmol, 82%) as a white foamy solid. R_f = 0.30 (3:1 hexanes–acetone); $[\alpha]_D$ +27.9 (*c*. 0.3, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$, δ_H, 60 °C) 8.00–7.89 (m, 4H, Ar), 7.57–7.47 (m, 2H, Ar), 7.43–7.26 (m, 14H, Ar), 7.21 (app t, *J* = 7.9 Hz, 2H, Ar), 7.02 (app t, *J* = 7.5 Hz, 1H, Ar), 6.80–6.73 (m, 2H, Ar), 5.64–5.49 (m, 2H, H-3``, H-1`), 5.32 (dd, *J* = 8.6, 6.6 Hz, 1H, H-2``), 5.20 (app t, *J* = 8.1 Hz, 1H, H-2`), 5.03 (app td, *J* = 8.4, 5.0 Hz, 1H, H-4``), 4.90–4.82 (m, 2H, 1 × PhC<u>H</u>$_2$O, H-1``), 4.74–4.65 (m, 3H, 1 × PhC<u>H</u>$_2$O, 2 ×

$Cl_3CC\underline{H}_2O$), 4.58, 4.40 (ABq, J = 12.0 Hz, 2H, 2 × $PhC\underline{H}_2O$), 4.20–4.09 (m, 2H, H-5a``, H-4`), 3.76–3.59 (m, 2H, H-3`, H-6a`), 3.57–3.48 (m, 1H, H-6b`), 3.36 (dd, $J$ = 12.2, 8.6 Hz, 1H, H-5b``), 3.32–3.20 (m, 1H, H-5`), 2.66 (app t, J = 7.1 Hz, 2H, 2 × $CH_2C\underline{H}_2C(O)CH_3$), 2.56–2.41 (m, 2H, 2 × $C\underline{H}_2CH_2C(O)CH_3$), 2.13 (s, 3H, $CH_2CH_2C(O)C\underline{H}_3$). ^{13}C NMR (100 MHz, $CDCl_3$, δ_C, 60 °C) 206.0 (C=O), 171.0 (C=O), 165.3 (C=O), 165.1 (C=O), 153.3 (C=O), 143.5 (Ar), 138.5 (Ar), 138.0 (Ar), 133.5 (Ar), 133.4 (Ar), 130.0 × 2 (Ar), 129.5 (Ar), 129.3 (Ar), 128.8 (Ar), 128.7 × 2 (Ar), 128.6 (Ar), 128.5 × 2 (Ar), 128.4 (Ar), 128.3 (Ar), 128.1 (Ar), 128.0 × 2 (Ar), 127.9 × 2 (Ar), 127.7 (Ar), 126.5 (Ar), 124.4 (Ar), 120.7 (Ar), 119.5 (Ar), 100.5 (C-1``), 95.3 (C-1`), 94.3 ($Cl_3\underline{C}CH_2O$), 80.7 (C-3`), 77.2 ($Cl_3C\underline{C}H_2O$), 76.1 (C-4`), 75.7 (C-5`), 74.4 ($Ph\underline{C}H_2O$), 73.6 ($Ph\underline{C}H_2O$), 73.4 (C-4``), 71.9 (C-2`), 71.7 (C-3``), 71.4 (C-2``), 67.6 (C-6`), 61.8 (C-5``), 38.0 ($CH_2\underline{C}H_2C(O)CH_3$), 29.6 ($CH_2CH_2C(O)\underline{C}H_3$), 28.1 ($\underline{C}H_2CH_2C(O)CH_3$). HRMS (ESI) calcd for $(M + Na)^+$ $C_{55}H_{51}Cl_3F_3NO_{16}Na$: 1166.2118. Found: 1166.2147.



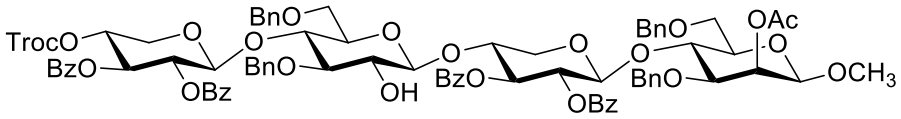
Methyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.38). To a flask containing **3.37** (4.00 g, 3.50 mmol) and **3.33** (1.61 g, 2.12 mmol) was added CH_2Cl_2 (25 mL) and 4 Å M.S. powder (1.15 g) under argon. The flask was sealed with a rubber septum connected to an argon balloon and the resultant slurry mixture was subsequently stirred for 2 h before cooling to 0 °C. The mixture was stirred for another 30 min, after which TfOH (1.77 mL, 0.40 mmol, 2% v/v in CH_2Cl_2) was added dropwise over 2 min. Upon complete addition of TfOH, the flask was then removed from the ice bath and stirred at room temperature. After 8 h, Et_3N (1 mL) was added and the mixture was passed through a bed of Celite. Concentration of the resultant filtrate led to a crude residue that was subsequently purified by silica gel chromatography (16:5 toluene–EtOAc) to obtain **3.38** (2.88 g, 1.68 mmol, 80%) as a white foamy solid. R_f = 0.28 (16:5 toluene–EtOAc); $[\alpha]_D$ +2.8 (*c*. 0.3, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.00–7.78 (m, 8H, Ar), 7.60–7.44 (m, 3H, Ar), 7.46–7.20 (m, 25H, Ar), 7.24–7.08 (m, 4H, Ar), 5.53 (d, *J* = 3.5 Hz, 1H, H-2`), 5.47 (app t, *J* = 8.7 Hz, 1H, H-3````), 5.39 (app t, *J* = 8.5 Hz, 1H, H-3``), 5.27 (dd, *J* = 8.8, 7.1 Hz, 1H, H-2````), 5.18 (dd, *J* = 8.8, 7.0 Hz, 1H, H-2``), 5.00 (app td, *J* = 8.8, 5.1 Hz, 1H, H-4````), 4.88–4.76 (m, 2H, H-2```, 1 × PhC$\underline{H}_2$O), 4.77–4.49 (m, 8H, 2 × $Cl_3CC\underline{H}_2O$, 4 × PhC$\underline{H}_2$O, H-1``, H-1````), 4.38–4.23 (m, 4H, H-1`, 2 × PhC$\underline{H}_2$O, H-1```), 4.10–3.95 (m, 4H, 1 × PhC$\underline{H}_2$O, H-5a````, H-4`, H-5a``), 3.99–3.85 (m, 2H, H-4``, H-4```), 3.61 (dd, *J* = 10.9, 4.5 Hz, 1H, H-6a`), 3.60–3.47 (m, 3H, H-3```, H-3`, H-6b`), 3.43 (s, 3H, OC$\underline{H}_3$), 3.32 (dd, *J* = 11.3, 3.3 Hz, 1H, H-6a```), 3.28–3.15 (m, 3H, H-5`, H-5b``, H-5b````), 3.04–3.00 (m, 1H, H-6b```),

3.00–2.94 (m, 1H, H-5```), 2.67–2.49 (m, 2H, 2 × $CH_2C\underline{H}_2C(O)CH_3$), 2.46–2.30 (m, 2H, 2 × $C\underline{H}_2CH_2C(O)CH_3$), 2.16 (s, 3H, $C\underline{H}_3C(O)O$), 2.10 (s, 3H, $CH_2CH_2C(O)C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 206.1 (C=O), 170.9 (C=O), 170.8 (C=O), 165.3 (C=O), 165.2 (C=O), 164.9 × 2 (C=O), 153.2 (C=O), 138.5 (Ar), 138.1 (Ar), 138.0 (Ar), 137.8 (Ar), 133.5 (Ar), 133.3 (Ar), 133.0 (Ar), 129.9 (Ar), 129.7 × 2 (Ar), 129.3 (Ar), 129.0 (Ar), 128.6 × 2 (Ar), 128.5 × 2 (Ar), 128.4 (Ar), 128.3 (Ar), 128.2 (Ar), 128.0 (Ar), 127.9 (Ar), 127.7 (Ar), 127.6 (Ar), 126.9 (Ar), 100.9 (C-1```), 100.4 (C-1``), 100.1 (C-1````), 99.9 (C-1`), 94.1 ($Cl_3\underline{C}CH_2O$), 80.6 (C-3```), 77.9 (C-3`), 76.9 ($Cl_3C\underline{C}H_2O$), 76.0 (C-4```), 75.6 (C-4``), 75.3 (C-5`), 74.9 (C-5```), 74.3 ($Ph\underline{C}H_2O$), 74.0 (C-4`), 73.4 (2 × $Ph\underline{C}H_2O$), 73.2 (C-4````), 72.9 × 2 (C-2```, C-3``), 72.0 (C-2``), 71.9 ($Ph\underline{C}H_2O$), 71.6 (C-3````), 71.3 (C-2````), 68.3 (C-6`), 68.1 (C-2`), 67.4 (C-6```), 63.0 (C-5``), 61.7 (C-5````), 57.1 ($O\underline{C}H_3$), 37.8 ($CH_2\underline{C}H_2C(O)CH_3$), 29.8 ($CH_2CH_2C(O)\underline{C}H_3$), 27.8 ($\underline{C}H_2CH_2C(O)CH_3$), 21.3 ($\underline{C}H_3C(O)O$). HRMS (ESI) calcd for $(M + NH_4)^+$ $C_{89}H_{93}Cl_3NO_{28}$: 1728.4944. Found: 1728.4945.



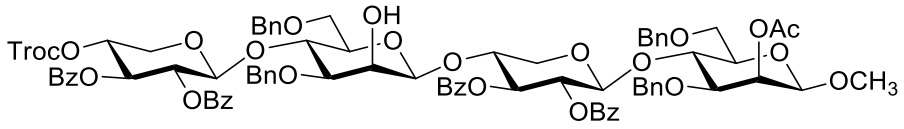
2,3-Di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-D-glucopyranose (3.41). Side-product isolated as an inseparable α/β mixture from 2+2 glcosylation between donor **3.36** and acceptor **3.35**. R_f = 0.15 (3:1 toluene–EtOAc); ^1H NMR (500 MHz, $CDCl_3$, δ_H) 7.99–7.87 (m, 4H, Ar), 7.57–7.49 (m, 2H, Ar), 7.46–7.31 (m, 12H, Ar), 7.30–7.27 (m, 2H, Ar), 5.54–5.48 (m, 2H), 5.37–5.29 (m, 4H), 5.07–4.98 (m, 3H), 4.93–4.87 (m, 2H), 4.85–4.81 (m, 1H), 4.81–4.74 (m, 4H), 4.73–4.58 (m, 10H),

4.50 (dd, J = 9.2, 8.1 Hz, 1H), 4.38–4.32 (m, 3H), 4.17–4.11 (m, 3H), 4.10–4.06 (m, 1H), 4.04–3.99 (m, 1H), 3.98–3.94 (m, 1H), 3.88–3.83 (m, 1H), 3.70–3.62 (m, 4H), 3.55–3.51 (m, 1H), 3.48–3.43 (m, 2H), 3.41–3.37 (m, 1H), 3.37–3.30 (m, 2H), 3.29–3.25 (m, 1H), 2.97 (s, 1H, OH), 2.76–2.65 (m, 4H), 2.64–2.57 (m, 2H), 2.57–2.51 (m, 2H), 2.50–2.43 (m, 1H), 2.42–2.34 (m, 2H), 2.14 (s, 3H), 2.14 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 171.9 (C=O), 165.0 (C=O), 153.3 (C=O), 138.8 (Ar), 138.4 (Ar), 137.8 (Ar), 133.6 (Ar), 133.5 × 2 (Ar), 129.9 × 3 (Ar), 129.0 (Ar), 128.9 (Ar), 128.7 × 2 (Ar), 128.6 × 2 (Ar), 128.5 × 3 (Ar), 128.4 × 2 (Ar), 128.3 × 2 (Ar), 128.2 (Ar), 128.1 (Ar), 128.0 (Ar), 127.8 (Ar), 127.7 (Ar), 127.6 (Ar), 100.3, 100.2, 95.8, 94.1, 90.1, 80.3, 77.6, 76.7, 76.3, 75.7, 75.2, 75.0, 74.8, 73.7, 73.6, 73.2 × 2 (C), 71.5, 71.3, 71.2, 71.1, 70.1, 67.7, 67.5, 61.7, 61.5, 38.1, 37.9, 29.8 × 2 (C), 28.0 × 2 (C). HRMS (ESI) calcd for $(M + NH_4)^+$ $C_{47}H_{51}Cl_3NO_{16}$: 990.2268. Found: 990.2277.



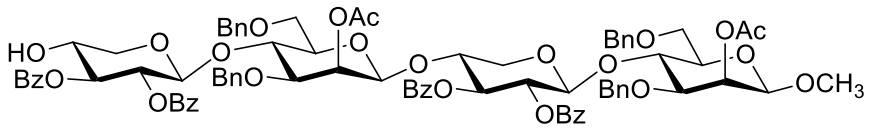
Methyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.42). The general procedure for levulinoyl deprotection was carried out on **3.38** (344 mg, 0.200 mmol) with H_2NNH_2·HOAc (226 μL, 0.24 mmol, 10% w/v in CH_3OH) in CH_2Cl_2–CH_3OH (4 mL, 10:1). The crude residue was purified by silica gel chromatography (1:1 hexanes–EtOAc) to obtain **3.42** (284 mg, 0.176 mmol, 88%) as a white foamy solid. R_f = 0.41 (1:1 hexanes–EtOAc); $[\alpha]_D$ +11.4 (*c*. 0.5, $CHCl_3$); ^{1}H NMR (500

MHz, $CDCl_3$, δ_H) 7.96–7.85 (m, 8H, Ar), 7.57–7.46 (m, 3H, Ar), 7.42–7.26 (m, 23H, Ar), 7.26–7.12 (m, 6H, Ar), 5.55 (d, *J* = 3.5 Hz, 1H, H-2`), 5.49 (app t, *J* = 8.4 Hz, 1H, H-3````), 5.42 (app t, *J* = 8.3 Hz, 1H, H-3``), 5.30–5.26 (m, 1H, H-2````), 5.22 (dd, *J* = 8.6, 6.7 Hz, 1H, H-2``), 5.00 (app td, *J* = 8.4, 4.9 Hz, 1H, H-4````), 4.90–4.84 (m, 1H, 1 × PhC$\underline{H}_2$O), 4.82–4.73 (m, 4H, H-1``, H-1````, 2 × PhC$\underline{H}_2$O), 4.69, 4.66 (ABq, *J* = 12.0 Hz, 2H, 2 × $Cl_3CC\underline{H}_2O$), 4.54–4.48 (m, 2H, 2 × PhC$\underline{H}_2$O), 4.35–4.25 (m, 3H, H-1`, 2 × PhC$\underline{H}_2$O), 4.21–4.17 (m, 1H, H-1```), 4.16–4.09 (m, 1H, H-5a````), 4.09–4.01 (m, 3H, H-5a``, H-4`, 1 × PhC$\underline{H}_2$O), 4.00–3.93 (m, 1H, H-4``), 3.86 (app t, *J* = 9.0 Hz, 1H, H-4```), 3.63–3.58 (m, 2H, H-6a`, H-6b`), 3.56 (dd, *J* = 9.2, 3.4 Hz, 1H, H-3`), 3.46–3.38 (m, 6H, OCH_3, H-3```, H-2```, H-6a```), 3.32–3.25 (m, 2H, H-5b````, H-5`), 3.20–3.13 (m, 2H, H-6b```, H-5b``), 3.07–3.02 (m, 1H, H-5```), 2.16 (s, 3H, C$\underline{H}_3$C(O)O). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 170.7 (C=O), 165.4 (C=O), 165.2 × 2 (C=O), 164.9 (C=O), 153.2 (C=O), 138.7 (Ar), 138.2 (Ar), 138.0 (Ar), 137.8 (Ar), 133.5 × 2 (Ar), 133.3 (Ar), 133.0 (Ar), 129.9 (Ar), 129.8 (Ar), 129.7 × 2 (Ar), 129.3 (Ar), 129.0 × 2 (Ar), 128.5 × 2 (Ar), 128.4 × 3 (Ar), 128.3 (Ar), 128.0 (Ar), 127.9 × 3 (Ar), 127.8 × 3 (Ar), 127.7 (Ar), 101.9 (C-1```), 100.4 (C-1``), 100.0 × 2 (C-1````, C-1`), 94.1 ($Cl_3\underline{C}CH_2O$), 82.3 (C-3```), 78.2 (C-3`), 77.0 ($Cl_3C\underline{C}H_2O$), 75.9 (C-4```), 75.3 (C-5`), 75.1 (C-5```), 74.8 (Ph$\underline{C}H_2$O), 74.3 (C-4`), 74.0 (C-4``), 73.7 (C-2```), 73.4 × 2 (Ph$\underline{C}H_2$O), 73.2 (C-4````), 72.6 (C-3``), 71.8 (Ph$\underline{C}H_2$O), 71.7 (C-2``), 71.4 (C-3````), 71.0 (C-2````), 68.5 (C-6`), 68.0 (C-2`), 67.6 (C-6```), 62.8 (C-5``), 61.5 (C-5````), 57.1 (O$\underline{C}H_3$), 21.2 ($\underline{C}H_3$C(O)O). HRMS (ESI) calcd for $(M + NH_4)^+$ $C_{84}H_{83}Cl_3NO_{26}$: 1630.4576. Found: 1630.4516.



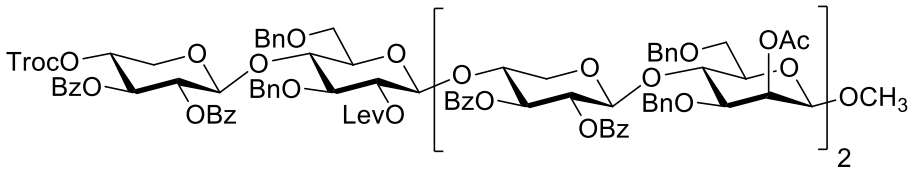
Methyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.43). Approach B for C-2 inversion was carried out on **3.42** (120 mg, 0.074 mmol). In this approach, DMP (100 mg, 0.237 mmol) and H_2O (2 μL, 0.11 mmol) in CH_2Cl_2 (2 mL) was used for oxidation; subsequent reduction was conducted on the crude ketone with LTBA (24.5 mg, 0.096 mmol) in THF (2 mL). The crude residue was purified by silica gel chromatography (6:5 hexanes–EtOAc) to afford **3.43** (83.7 mg, 0.052 mmol, 70%) as a white solid. R_f = 0.30 (6:5 hexanes–EtOAc); $[\alpha]_D$ −16.0 (*c*. 0.02, $CHCl_3$); ^{1}H NMR (700 MHz, $CDCl_3$, δ_H) 7.94–7.86 (m, 8H, Ar), 7.55–7.47 (m, 3H, Ar), 7.41–7.26 (m, 23H, Ar), 7.26–7.11 (m, 6H, Ar), 5.54 (d, *J* = 3.5 Hz, 1H, H-2`), 5.49 (app t, *J* = 8.1 Hz, 1H, H-3````), 5.34 (app t, *J* = 8.6 Hz, 1H, H-3``), 5.30 (app t, *J* = 8.0 Hz, 1H, H-2``), 5.26 (dd, *J* = 8.2, 6.4 Hz, 1H, H-2````), 5.01 (app td, *J* = 8.1, 4.9 Hz, 1H, H-4````), 4.77 (d, *J* = 6.4 Hz, 1H, H-1````), 4.76–4.72 (m, 3H, H-1``, 2 × PhC$\underline{H}_2$O), 4.71–4.65 (m, 3H, 1 × PhC$\underline{H}_2$O, 2 × $Cl_3CC\underline{H}_2$O), 4.59–4.52 (m, 2H, 2 × PhC$\underline{H}_2$O), 4.38 (s, 1H, H-1```), 4.34–4.27 (m, 2H, H-1`, 1 × PhC$\underline{H}_2$O), 4.18 (dd, *J* = 12.4, 4.8 Hz, 1H, H-5a````), 4.15–4.05 (m, 3H, 1 × PhC$\underline{H}_2$O, H-4`, H-4``), 4.02–3.94 (m, 4H, H-2```, H-4```, H-5a``, 1 × PhC$\underline{H}_2$O), 3.65 (dd, *J* = 11.0, 4.4 Hz, 1H, H-6a`), 3.57 (dd, *J* = 10.9, 1.8 Hz, 1H, H-6b`), 3.54 (dd, *J* = 9.2, 3.5 Hz, 1H, H-3`), 3.45–3.38 (m, 4H, OC$\underline{H}_3$, H-3```), 3.32 (m, 2H, H-6a```, H-5b````), 3.26 (ddd, *J* = 9.7, 4.4, 1.8 Hz, 1H, H-5`), 3.19–3.10 (m, 3H, H-5```, H-6b```, H-5b``), 2.49 (br. s, 1H, OH), 2.16 (s, 3H, C$\underline{H}_3$C(O)O). ^{13}C NMR (175 MHz, $CDCl_3$, δ_C) 170.7 (C=O), 166.3 (C=O), 165.2 (C=O), 165.1 (C=O), 165.0 (C=O), 153.3 (C=O), 138.2 (Ar),

138.2 (Ar), 138.1 (Ar), 137.8 (Ar), 133.5 (Ar), 133.4 × 2 (Ar), 133.1 (Ar), 129.9 × 2 (Ar), 129.79, 129.7 (Ar), 129.2 (Ar), 129.1 × 2 (Ar), 129.0 (Ar), 128.5 × 2 (Ar), 128.4 × 2 (Ar), 128.3 × 2 (Ar), 128.0 (Ar), 127.9 × 4 (Ar), 127.7 × 2 (Ar), 127.7 × 2 (Ar), 125.3 (Ar), 100.6 (C-1``), 100.2 (C-1````), 100.0 (C-1`), 97.2 (C-1```), 94.1 ($Cl_3\underline{C}CH_2O$), 79.5 (C-3```), 78.0 (C-3`), 77.0 ($Cl_3C\underline{C}H_2O$), 75.3 (C-5`), 75.1 (C-5```), 74.1 × 2 (C-4```, C-4`), 73.4 ($Ph\underline{C}H_2O$), 73.1 × 3 (C-4````, C-4``, $Ph\underline{C}H_2O$), 73.0 (C-3``), 72.0 ($Ph\underline{C}H_2O$), 71.9 ($Ph\underline{C}H_2O$), 71.5 (C-2``), 71.2 (C-3````), 71.0 (C-2````), 68.4 × 2 (C-2```, C-6```), 68.3 (C-6`), 68. 1 (C-2`), 62.7 (C-5``), 61.4 (C-5````), 57.1 ($O\underline{C}H_3$), 21.3 ($\underline{C}H_3C(O)O$). HRMS (ESI) calcd for $(M + NH_4)^+$ $C_{84}H_{87}Cl_3NO_{26}$: 1630.4576. Found: 1630.4571.



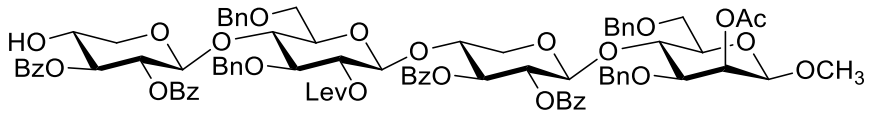
Methyl 2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.44). To a solution of **3.43** (10.3 mg, 6.38 μmol) in pyridine (2 mL) was added Ac_2O (1 mL) under argon. The reaction mixture was stirred at 40 °C overnight, cooled to room temperature and concentrated; pyridine was then removed via co-evaporation with toluene (2x). The crude material was re-dissolved in CH_2Cl_2 and subsequently washed with 1 M aqueous HCl and brine before it was dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a thick syrup that was then subjected to Troc deprotection using Zn powder (23.3 mg, 357 μmol) in glacial AcOH (3 mL). The crude residue was purified using silica gel chromatography (2:1 toluene–EtOAc) to obtain **3.44** (8.0 mg, 5.4 μmol, 84%) as

a white foamy solid. R_f = 0.23 (2:1 toluene–EtOAc); $[\alpha]_D$ +7.5 (*c*. 0.5, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$, δ_H) 7.98–7.93 (m, 2H, Ar), 7.93–7.81 (m, 6H, Ar), 7.57–7.46 (m, 3H, Ar), 7.42–7.26 (m, 24H, Ar), 7.25–7.12 (m, 5H, Ar), 5.52 (d, *J* = 3.1 Hz, 1H, H-2`), 5.49 (d, *J* = 3.5 Hz, 1H, H-2```), 5.38–5.28 (m, 2H, H-2````, H-3``), 5.21 (dd, *J* = 9.1, 7 .1 Hz, 1H, H-2``), 5.08 (app t, *J* = 8.5 Hz, 1H, H-3````), 4.78–4.71 (m, 3H, H-1````, 2 × PhC$\underline{H}_2$O), 4.66 (d, *J* = 7.1 Hz, 1H, H-1``), 4.58–4.51 (m, 3H, 3 × PhC$\underline{H}_2$O), 4.42 (s, 1H, H-1```), 4.37–4.32 (m, 1H, 1 × PhC$\underline{H}_2$O), 4.30–4.24 (m, 2H, 1 × PhC$\underline{H}_2$O, H-1`), 4.11–4.00 (m, 4H, 1 × $PhCH_2O$, H-4``, H-5a````, H-4`), 4.00–3.89 (m, 3H, H-4````, H-5a``, H-4```), 3.62 (dd, *J* = 11.0, 4.4 Hz, 1H, H-6a`), 3.58–3.54 (m, 1H, H-6b`), 3.52 (m, 2H, H-3`, H-3```), 3.47–3.40 (m, 4H, H-6a```, OC$\underline{H}_3$), 3.34 (dd, *J* = 11.3, 1.7 Hz, 1H, H-6b```), 3.24 (ddd, *J* = 9.7, 4.4, 1.8 Hz, 1H, H-5`), 3.17–3.04 (m, 3H, H-5```, H-5b``, H-5b````), 2.94 (d, *J* = 5.0 Hz, 1H, OH), 2.16 (s, 3H, C$\underline{H}_3$C(O)O), 1.94 (s, 3H, C$\underline{H}_3$C(O)O). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 170.8 (C=O), 170.5 (C=O), 167.5 (C=O), 165.5 (C=O), 165.2 (C=O), 165.1 (C=O), 138.2 (Ar), 138.1 (Ar), 137.9 (Ar), 137.7 (Ar), 133.7 (Ar), 133.5 (Ar), 133.3 (Ar), 132.9 (Ar), 130.0 (Ar), 129.9 (Ar), 129.8 (Ar), 129.7 (Ar), 129.3 (Ar), 129.2 (Ar), 128.9 (Ar), 128.6 (Ar), 128.5 × 2 (Ar), 128.4 × 2 (Ar), 128.2 × 2 (Ar), 128.0 (Ar), 128.0 (Ar), 127.9 × 2 (Ar), 127.8 (Ar), 127.7 (Ar), 100.7 (C-1``), 100.4 (C-1````), 100.0 (C-1`), 96.6 (C-1```), 78.0 (C-3`), 77.9 (C-3```), 77.0 (C-3````), 75.5 (C-5```), 75.3 (C-5`), 74.1 (C-4`), 73.8 (C-4```), 73.4 (Ph$\underline{C}H_2$O), 73.3 (Ph$\underline{C}H_2$O), 72.8 (C-4``), 72.7 (C-3``), 72.0 × 2 (C-2``, Ph$\underline{C}H_2$O), 71.3 (C-2````), 69.3 (C-4````), 68.3 × 2 (C-6```, C-6`), 68.1 (C-2`), 67.7 (C-2```), 65.2 (C-5````), 62.5 (C-5``), 57.1 (OC$\underline{H}_3$), 21.3 ($\underline{C}H_3$C(O)O), 20.8 ($\underline{C}H_3$C(O)O). HRMS (ESI) calcd for $(M + Na)^+$ $C_{83}H_{84}NaO_{25}$: 1503.5194. Found: 1503.5190.



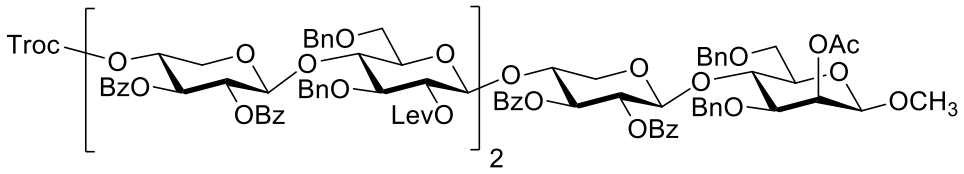
Methyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoy-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.45). To a flask containing **3.37** (124 mg, 108 μmol) and **3.44** (84.8 mg, 57 μmol) was added CH_2Cl_2 (5 mL) and 4 Å M.S. powder (42 mg) under argon. The flask was then sealed with a rubber septum connected to an argon balloon and the resultant slurry mixture was stirred for 2 h before it was cooled to 0 °C. The mixture was stirred for another 30 min, after which point TfOH (1.77 mL, 0.40 mmol, 2% v/v in CH_2Cl_2) was added dropwise over 2 min. Upon complete addition of TfOH, the flask was removed from the ice bath and stirred at room temperature. After 8 h, Et_3N (1 mL) was added and the mixture was passed through a Celite bed. Concentration of the filtrate led to a crude residue that was subsequently purified by silica gel chromatography (3:1 to 5:2 toluene–EtOAc) to obtain **3.45** (50.1 mg, 20.6 μmol, 36%) as a white foamy solid. R_f = 0.33 (5:2 toluene–EtOAc); ^{1}H NMR (700 MHz, $CDCl_3$, δ_H) 7.98–7.80 (m, 12H, Ar), 7.59–7.46 (m, 4H, Ar), 7.43–7.26 (m, 36H, Ar), 7.26–7.12 (m, 8H, Ar), 5.52 (d, J = 3.5 Hz, 1H, H-2$_{Man}$), 5.46 (app t, J = 8.7 Hz, 1H, H-3$_{Xyl}$), 5.44 (d, J = 3.5 Hz, 1H, H-2$_{Xyl}$), 5.39 (app t, J = 8.5 Hz, 1H, H-3$_{Xyl}$), 5.33 (app t, J = 8.8 Hz, 1H, H-3$_{Xyl}$), 5.26 (dd, J = 8.9, 7.0 Hz, 1H, H-2$_{Xyl}$), 5.20 (dd, J = 9.1, 7.1 Hz, 1H, H-2$_{Xyl}$), 5.16 (dd, J = 8.8, 7.0 Hz, 1H, H-2$_{Xyl}$), 4.99 (app td, J = 8.8, 5.2 Hz, 1H, H-4$_{Xyl}$), 4.85–4.79 (m, 2H, H-2$_{Glc}$, 1 × PhC$\underline{H}_2$O), 4.76–4.62 (m, 8H, 3 × H-1$_{Xyl}$, 3 × PhC$\underline{H}_2$O, 2 × $Cl_3CC\underline{H}_2O$), 4.61–4.56 (m, 1H, 1 × PhC$\underline{H}_2$O), 4.57–4.51 (m, 3H, 3 × PhC$\underline{H}_2$O), 4.38 (s, 1H, H-

1$_{Man}$), 4.33–4.24 (m, 4H, 2 × PhC$\underline{H}_2$O, H-1$_{Glc}$, H-1$_{Man}$), 4.09–3.84 (m, 10H), 3.64–3.58 (m, 1H, H-6a$_{Man}$), 3.55 (dd, *J* = 10.7, 1.7 Hz, 1H, H-6b$_{Man}$), 3.54–3.46 (m, 3H), 3.42 (s, 3H, OC$\underline{H}_3$), 3.37 (dd, *J* = 11.1, 4.5 Hz, 1H, H-6a$_{Man}$), 3.32–3.27 (m, 2H, H-6b$_{Man}$, H-6a$_{Glc}$), 3.25–3.19 (m, 2H), 3.15 (dd, *J* = 12.3, 9.1 Hz, 1H), 3.09–3.03 (m, 2H), 3.02–2.98 (m, 1H, H-6b$_{Glc}$), 2.96 (ddd, *J* = 9.6, 3.3, 1.9 Hz, 1H, H-5$_{Glc}$), 2.56 (dt, *J* = 10.4, 6.7 Hz, 2H, 2 × $CH_2C\underline{H}_2C(O)CH_3$), 2.41–2.30 (m, 2H, 2 × $C\underline{H}_2CH_2C(O)CH_3$), 2.16 (s, 3H, $CH_2CH_2C(O)C\underline{H}_3$), 2.08 (s, 3H, $C\underline{H}_3C(O)O$), 1.91 (s, 3H, $CH_3C(O)O$). ^{13}C NMR (175 MHz, $CDCl_3$, δ_C) 206.0 (C=O), 170.9 (C=O), 170.8 (C=O), 170.5 (C=O), 165.5 (C=O), 165.2 (C=O), 165.2 (C=O), 164.9 (C=O), 153.2 (C=O), 138.5 (Ar), 138.1 (Ar), 137.9 (Ar), 137.8 × 2 (Ar), 133.5 (Ar), 133.3 (Ar), 133.2 (Ar), 133.0 (Ar), 132.9 (Ar), 129.9 (Ar), 129.8 (Ar), 129.7 × 2 (Ar), 129.3 × 2 (Ar), 129.0 (Ar), 128.6 × 2 (Ar), 128.5 × 2 (Ar), 128.4 × 3 (Ar), 128.3 × 2 (Ar), 128.2 × 2 (Ar), 128.0 × 2 (Ar), 127.9 × 4 (Ar), 127.8 × 2 (Ar), 127.7 × 2 (Ar), 127.5 (Ar), 100.9 (C-1$_{Glc}$), 100.7 (C-1$_{Xyl}$), 100.3 (C-1$_{Xyl}$), 100.1 (C-1$_{Xyl}$), 100.0 (C-1$_{Man}$), 96.5 (C-1$_{Man}$), 94.1 ($Cl_3\underline{C}CH_2O$), 80.6, 77.9, 77.6, 77.0 ($Cl_3C\underline{C}H_2O$), 76.0, 75.7, 75.5, 75.3, 74.9 (C-5$_{Glc}$), 74.3 (Ph$\underline{C}H_2O$), 74.0, 73.8, 73.4 × 2 (Ph$\underline{C}H_2O$), 73.3 (Ph$\underline{C}H_2O$), 73.3 (C-4$_{Xyl}$), 72.9 × 2 (C), 72.7, 72.0, 71.9 × 2 (Ph$\underline{C}H_2O$, C-2``), 71.8 (Ph$\underline{C}H_2O$), 71.7 (C-$_{Xyl}$), 71.3 (C-2$_{Xyl}$), 68.3 (C-6$_{Man}$), 68.1 (C-2$_{Man}$), 68.1 (C-6$_{Man}$), 67.8 (C-2$_{Man}$), 67.3 (C-6$_{Glc}$), 63.0 (C-5$_{Xyl}$), 62.5 (C-5$_{Xyl}$), 61.7 (C-5$_{Xyl}$), 57.1 (O$\underline{C}H_3$), 37.8 ($CH_2\underline{C}H_2C(O)CH_3$) , 29.8 ($CH_2CH_2C(O)\underline{C}H_3$), 27.8 ($\underline{C}H_2CH_2C(O)CH_3$), 21.3 ($\underline{C}H_3C(O)O$), 20.7 ($\underline{C}H_3C(O)O$). HRMS (ESI) calcd for $(M + 2(Na))^{2+}$ $C_{130}H_{129}Cl_3Na_2O_{40}$: 1240.3455. Found: 1240.3474.



Methyl 2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.46). The general procedure for Troc deprotection was conducted on **3.38** (1.07 g, 0.622 mmol) with Zn powder (1.68 g, 25.7 mmol) in glacial AcOH (8 mL). The crude residue was purified by silica gel chromatography (4:1 to 3:1 CH_2Cl_2–EtOAc), to afford **3.46** (842 mg, 0.547 mmol, 88%) as a white fluffy solid. R_f = 0.30 (4:1 CH_2Cl_2–EtOAc); $[\alpha]_D$ +6.6 (*c*. 2.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.96–7.90 (m, 2H, Ar), 7.90–7.81 (m, 6H, Ar), 7.58–7.46 (m, 3H, Ar), 7.43–7.26 (m, 24H, Ar), 7.25–7.11 (m, 5H, Ar), 5.53 (d, *J* = 3.6 Hz, 1H, H-2`), 5.38 (app t, *J* = 8.5 Hz, 1H, H-3``), 5.29 (dd, *J* = 9.4, 7.5 Hz, 1H, H-2````), 5.18 (dd, *J* = 8.8, 6.9 Hz, 1H, H-2``), 5.05 (app t, *J* = 9.0 Hz, 1H, H-3````), 4.88–4.80 (m, 2H, H-2```, 1 × PhC$\underline{H}_2$O), 4.76–4.68 (m, 2H, H-1``, 1 × PhC$\underline{H}_2$O), 4.62 (d, *J* = 7.5 Hz, 1H, H-1````), 4.60–4.50 (m, 3H, 3 × PhC$\underline{H}_2$O), 4.37–4.24 (m, 4H, H-1```, H-1`, 2 × PhC$\underline{H}_2$O), 4.09–3.84 (m, 7H, H-4`, H-5a``, H-5a````, H-4```, H-4``, H-4````, 1 × PhC$\underline{H}_2$O), 3.64–3.47 (m, 4H, H-6a`, H-6b`, H-3`, H-3```), 3.43 (s, 3H, OC$\underline{H}_3$), 3.32 (dd, *J* = 11.2, 3.3 Hz, 1H, H-6a```), 3.24 (ddd, *J* = 9.6, 4.5, 1.9 Hz, 1H, H-5`), 3.19 (dd, *J* = 12.2, 9.0 Hz, 1H, H-5b``), 3.11 (dd, *J* = 11.9, 9.5 Hz, 1H, H-5b````), 3.01 (dd, *J* = 11.2, 1.8 Hz, 1H, H-6b```), 2.97 (ddd, *J* = 9.6, 3.3, 1.9 Hz, 1H, H-5```), 2.92 (d, *J* = 4.6 Hz, 1H, OH), 2.65–2.50 (m, 2H, 2 × $CH_2C\underline{H}_2C(O)CH_3$), 2.44–2.30 (m, 2H, 2 × $C\underline{H}_2CH_2C(O)CH_3$), 2.15 (s, 3H, $C\underline{H}_3C(O)O$), 2.09 (s, 3H, $CH_2CH_2C(O)C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 206.1 (C=O), 170.9 (C=O), 170.8 (C=O), 167.6 (C=O), 165.2 (C=O), 165.0 (C=O), 164.9 (C=O), 138.6 (Ar), 138.1 (Ar), 138.0 (Ar), 137.8 (Ar), 133.7 (Ar), 133.5 (Ar),

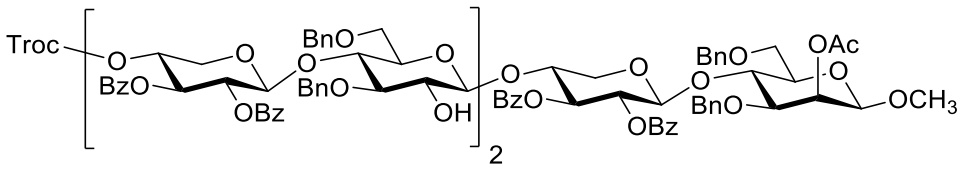
133.2 (Ar), 132.9 (Ar), 130.0 (Ar), 129.9 (Ar), 129.8 × 2 (Ar), 129.7 × 2 (Ar), 129.6 (Ar), 129.3 (Ar), 129.1 (Ar), 128.8 (Ar), 128.6 (Ar), 128.5 × 2 (Ar), 128.4 × 2 (Ar), 128.3 (Ar), 128.2 × 2 (Ar), 128.1 (Ar), 128.0 (Ar), 128.0 × 2 (Ar), 127.9 × 2 (Ar), 127.7 (Ar), 127.5 (Ar), 101.0 (C-1```), 100.4 × 2 (C-1````, C-1``), 99.9 (C-1`), 80.6 (C-3```), 77.9 (C-3`), 77.4 (C-3````), 75.9 (C-4```), 75.7 (C-4``), 75.3 (C-5`), 75.0 (C-5```), 74.5 (Ph<u>C</u>H_2O), 74.0 (C-4`), 73.5 (Ph<u>C</u>H_2O), 73.4 (Ph<u>C</u>H_2O), 72.9 × 2 (C-2```, C-3``), 72.0 (C-2``), 71.9 (Ph<u>C</u>H_2O), 71.4 (C-2````), 69.5 (C-4````), 68.3 (C-6`), 68.1 (C-2`), 67.3 (C-6```), 65.4 (C-5````), 63.0 (C-5``), 57.1 (O<u>C</u>H_3), 37.8 (CH_2<u>C</u>H_2C(O)CH_3), 29.8 (CH_2CH_2C(O)<u>C</u>H_3), 27.8 (<u>C</u>H_2CH_2C(O)CH_3), 21.2 (<u>C</u>H_3C(O)O). HRMS (ESI) calcd for $(M + NH_4)^+$ $C_{86}H_{92}NO_{26}$: 1554.5902. Found: 1554.5901.



Methyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.47). To a flask containing **3.37** (575 mg, 0.502 mmol) and **3.46** (385 mg, 0.250 mmol) was added CH_2Cl_2 (10 mL) and 4 Å M.S. powder (200 mg) under argon. The flask was then sealed with a rubber septum connected to an argon balloon and the resultant slurry mixture was stirred for 2 h before it was cooled to 0 °C. The mixture was stirred for another 30 min, after which TfOH (221 μL, 0.050 mmol, 2% v/v in CH_2Cl_2) was added dropwise over 2 min. Upon complete addition of

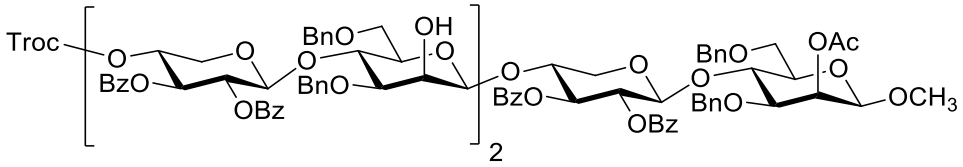
TfOH, the flask was then removed from the ice bath and stirred at room temperature. After 8 h, Et_3N (2 mL) was added and the mixture was passed through a bed of Celite. Concentration of the resultant filtrate led to a crude residue that was subsequently purified by silica gel chromatography (5:2 toluene–EtOAc) to obtain **3.47** (493 mg, 0.198 mmol, 79%) as a white foamy solid. R_f = 0.28 (5:2 toluene–EtOAc); $[\alpha]_D$ –2.2 (*c*. 0.10, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.01–7.77 (m, 12H, Ar), 7.59–7.45 (m, 4H, Ar), 7.44–7.27 (m, 36H, Ar), 7.25–7.12 (m, 8H, Ar), 5.52 (d, *J* = 3.5 Hz, 1H, H-2_{Man}), 5.46 (app t, *J* = 8.7 Hz, 1H, H-3_{Xyl}), 5.40–5.30 (m, 2H, 2 × H-3_{Xyl}), 5.25 (dd, *J* = 8.9, 7.0 Hz, 1H, H-2_{Xyl}), 5.19–5.10 (m, 2H, 2 × H-2_{Xyl}), 4.98 (app td, *J* = 8.8, 5.2 Hz, 1H, H-4_{Xyl}), 4.87–4.76 (m, 4H, 2 × PhC$\underline{H}_2$O, 2 × H-2_{Glc}), 4.75–4.47 (m, 10H, 5 × PhC$\underline{H}_2$O, 2 × $Cl_3CC\underline{H}_2O$, 3 × H-1_{Xyl}), 4.32–4.22 (m, 6H, 3 × PhC$\underline{H}_2$O, 2 × H-1_{Glc}, H-1_{Man}), 4.08–3.79 (m, 10H), 3.63–3.43 (m, 5H), 3.42 (s, 3H, OC$\underline{H}_3$), 3.30 (dd, *J* = 11.4, 3.4 Hz, 1H), 3.27–3.07 (m, 5H), 3.02–2.86 (m, 4H), 2.63–2.46 (m, 4H, 4 × $CH_2C\underline{H}_2C(O)CH_3$), 2.40–2.26 (m, 4H, 4 × $C\underline{H}_2CH_2C(O)CH_3$), 2.15 (s, 3H, $C\underline{H}_3C(O)O$), 2.08 (s, 3H, $CH_2CH_2C(O)C\underline{H}_3$), 2.082 (s, 3H, $CH_2CH_2C(O)C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 206.0 (C=O), 205.8 (C=O), 170.9 (2 × C=O), 170.8 (C=O), 165.2 × 2 (C=O), 165.0 (C=O), 164.9 × 3 (C=O), 153.2 (C=O), 138.8 (Ar), 138.4 (Ar), 138.1 (Ar), 137.9 × 2 (Ar), 137.8 (Ar), 133.5 (Ar), 133.3 (Ar), 133.2 (Ar), 132.9 (Ar), 129.9 (Ar), 129.8 (Ar), 129.7 (Ar), 129.3 (Ar), 129.2 (Ar), 129.0 (Ar), 128.7 (Ar), 128.6 × 2 (Ar), 128.5 × 3 (Ar), 128.4 × 3 (Ar), 128.3 × 2 (Ar), 128.2 × 2 (Ar), 128.1 × 2 (Ar), 128.0 (Ar), 127.9 (Ar), 127.8 (Ar), 127.7 (Ar), 127.5 (Ar), 127.4 (Ar), 100.9 (C-1_{Glc}), 100.8 (C-1_{Glc}), 100.4 × 2 (C-1_{Xyl}), 100.1 (C-1_{Xyl}), 100.0 (C-1_{Man}), 94.1 ($Cl_3\underline{C}CH_2O$), 80.5 × 2 (C), 78.0, 76.9 ($Cl_3C\underline{C}H_2O$), 76.1, 76.0, 75.9, 75.6, 75.3, 75.0, 74.9 × 2 (C), 74.4 (Ph$\underline{C}H_2$O), 74.3 (Ph$\underline{C}H_2$O), 74.0, 73.4 × 3 (Ph$\underline{C}H_2$O), 73.2 × 2 (C), 72.9 × 2 (C), 72.8, 72.2, 72.0, 71.9 (Ph$\underline{C}H_2$O), 71.6 (C-3_{Xyl}), 71.2 (C-2_{Xyl}), 68.3 (C-6_{Man}), 68.1 (C-2_{Man}), 67.4 (C-6_{Glc}), 67.2 (C-6_{Glc}), 63.3 (C-5_{Xyl}), 63.0 (C-5_{Xyl}), 61.7

(C-5$_{Xyl}$), 57.1 (O<u>C</u>H$_3$), 37.8 (CH$_2$<u>C</u>H$_2$C(O)CH$_3$), 37.7 (CH$_2$<u>C</u>H$_2$C(O)CH$_3$), 29.8 (CH$_2$CH$_2$C(O)<u>C</u>H$_3$), 29.8 (CH$_2$CH$_2$C(O)<u>C</u>H$_3$), 27.8 (<u>C</u>H$_2$CH$_2$C(O)CH$_3$), 21.3 (<u>C</u>H$_3$C(O)O). HRMS (ESI) calcd for (M + 2(NH$_4$))$^{2+}$ $C_{133}H_{141}Cl_3N_2O_{41}$: 1263.4032. Found: 1263.4040.



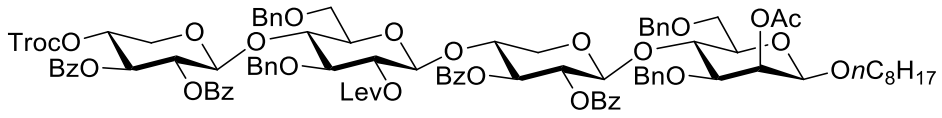
Methyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.48). The general procedure for levulinoyl deprotection was carried out on **3.47** (205 mg, 0.082 mmol) with H_2NNH_2·HOAc (196 μL, 0.21 mmol, 10% w/v in CH_3OH) in CH_2Cl_2–CH_3OH (5 mL, 10:1). The crude residue was purified by silica gel chromatography (1:1 hexanes–EtOAc) to obtain **3.48** (156 mg, 0.068 mmol, 83%) as a white foamy solid. R_f = 0.34 (1:1 hexanes–EtOAc); $[\alpha]_D$ –0.4 (*c*. 0.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.04–7.79 (m, 12H, Ar), 7.58–7.45 (m, 4H, Ar), 7.42–7.26 (m, 30H, Ar), 7.26–7.10 (m, 14H, Ar), 5.55 (d, *J* = 3.4 Hz, 1H, H-2$_{Man}$), 5.49 (app t, *J* = 8.4 Hz, 1H, H-3$_{Xyl}$), 5.44–5.39 (m, 2H, 2 × H-3$_{Xyl}$), 5.30–5.25 (m, 1H, H-2$_{Xyl}$), 5.23–5.16 (m, 2H, 2 × H-2$_{Xyl}$), 5.00 (app td, *J* = 8.5, 5.0 Hz, 1H, H-4$_{Xyl}$), 4.92–4.86 (m, 2H, 2 × PhC<u>H</u>$_2$O), 4.82–4.63 (m, 8H, 2 × Cl$_3$CC<u>H</u>$_2$O, 3 × PhC<u>H</u>$_2$O, 3 × H-1$_{Xyl}$), 4.54–4.48 (m, 2H, 2 × PhC<u>H</u>$_2$O), 4.36–4.23 (m, 4H, 3 × PhC<u>H</u>$_2$O, H-1$_{Man}$), 4.21–4.10 (m, 3H), 4.08–3.90 (m, 7H), 3.89–3.80 (m, 2H), 3.61–3.51 (m, 3H, H-6a$_{Man}$, H-6b$_{Man}$, H-3$_{Man}$), 3.44 (s, 3H, OC<u>H</u>$_3$), 3.43–3.23 (m, 9H), 3.20–3.10 (m, 4H), 3.05–3.00 (m, 2H),

2.16 (s, 3H, C<u>H</u>$_3$C(O)O), ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 170.6 (C=O), 165.4 × 2 (C=O), 165.2 × 2 (C=O), 165.1 (C=O), 164.9 (C=O), 153.2 (C=O), 138.9 (Ar), 138.7 (Ar), 138.2 (Ar), 138.0 (Ar), 137.9 (Ar), 137.8 (Ar), 133.5 × 2 (Ar), 133.3 (Ar), 133.0 (Ar), 129.9 (Ar), 129.8 × 2 (Ar), 129.7 (Ar), 129.5 (Ar), 129.3 (Ar), 129.2 (Ar), 129.0 (Ar), 128.5 × 3 (Ar), 128.4 × 3 (Ar), 128.2 × 2 (Ar), 128.0 (Ar), 127.9 × 2 (Ar), 127.8 × 3 (Ar), 127.7 × 2 (Ar), 127.6 × 2 (Ar), 101.8 × 2 (C-1_{Glc}), 100.4 × 2 (C-1_{Xyl}), 100.0 × 2 (C-1_{Xyl}, C-1_{Man}), 94.1 (Cl_3<u>C</u>CH_2O), 82.3 × 2 (C), 78.2 (C-3_{Man}), 76.9 (Cl_3C<u>C</u>H_2O), 75.9 × 2 (C), 75.3, 75.1 × 2 (C), 74.8 (Ph<u>C</u>H_2O), 74.7 (Ph<u>C</u>H_2O), 74.4, 74.2 × 2 (C), 73.6, 73.5 × 2 (C), 73.4 × 2 (Ph<u>C</u>H_2O), 73.3 (2 × Ph<u>C</u>H_2O), 73.2 (C-4_{Xyl}), 72.9, 72.7 × 2 (C), 71.8 × 2 (C), 71.7 (Ph<u>C</u>H_2O), 71.4 (C-3_{Xyl}), 71.1 (C-2_{Xyl}), 68.5 (C-6_{Man}), 67.9 (C-2_{Man}), 67.6 × 2 (C-6_{Glc}), 63.1 (C-5_{Xyl}), 62.9 (C-5_{Xyl}), 61.5 (C-5_{Xyl}), 57.1 (O<u>C</u>H_3), 21.2 (<u>C</u>H_3C(O)O). HRMS (ESI) calcd for $(M + 2(NH_4))^{2+}$ $C_{123}H_{129}Cl_3N_2O_{37}$: 1165.3664. Found: 1165.3644.



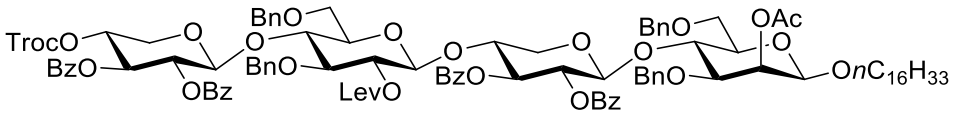
Methyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.50). Approach B for C-2 inversion was carried out on **3.48** (156 mg, 67.9 μmol). In this approach, DMP (172 mg, 406 μmol) and H_2O (3.5 μL, 190 μmol) were used for oxidation in CH_2Cl_2 (3 mL); subsequent reduction was

conducted on the crude diketone with LTBA (41.8 mg, 163 μmol) in THF (1.4 mL). The crude residue was purified by silica gel chromatography (1:2 to 2:3 hexanes–EtOAc) to afford **3.50** (117 mg, 51.0 μmol, 75%) as a white solid. R_f = 0.30 (2:3 hexanes–EtOAc); $[\alpha]_D$ +4.4 (*c*. 0.05, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.00–7.76 (m, 12H, Ar), 7.56–7.45 (m, 4H, Ar), 7.43–7.26 (m, 33H, Ar), 7.25–7.09 (m, 11H, Ar), 5.53 (d, *J* = 3.5 Hz, 1H, H-2_{Man}), 5.48 (app t, *J* = 8.1 Hz, 1H, H-3_{Xyl}), 5.37–5.22 (m, 5H), 5.00 (app td, *J* = 8.0, 4.8 Hz, 1H, H-4_{Xyl}), 4.79–4.64 (m, 10H, 2 × $Cl_3CC\underline{H}_2O$, 5 × $PhC\underline{H}_2O$, 3 × H-1_{Xyl}), 4.59–4.51 (m, 2H, 2 × $PhC\underline{H}_2O$), 4.38 (s, 2H, H-1_{Man}), 4.33 (s, 1H, H-1_{Man}), 4.32–4.26 (m, 1H, 1 × $PhC\underline{H}_2O$, H-1_{Man}), 4.17 (dd, *J* = 12.3, 4.8 Hz, 1H), 4.14–4.03 (m, 5H), 4.01–3.87 (m, 8H), 3.64 (dd, *J* = 11.0, 4.4 Hz, 1H, H-$6a_{Man}$), 3.59–3.50 (m, 2H, H-$6b_{Man}$, H-3_{Man}), 3.43 (s, 3H, OCH_3), 3.42–3.22 (m, 6H), 3.21–3.04 (m, 6H), 2.54–2.37 (m, 2H, 2 × OH), 2.16 (s, 3H, $C\underline{H}_3C(O)O$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 170.6 (C=O), 166.4 (C=O), 166.3 (C=O), 165.2 (C=O), 165.1 × 2 (C=O), 165.0 (C=O), 153.2 (C=O), 138.4 (Ar), 138.2 × 3 (Ar), 138.0 (Ar), 137.8 (Ar), 133.5 (Ar), 133.4 (Ar), 133.3 (Ar), 133.0 (Ar), 129.9 (Ar), 129.8 (Ar), 129.7 × 2 (Ar), 129.2 (Ar), 129.1 (Ar) 129.0 (Ar), 128.5 × 3 (Ar), 128.4 × 3 (Ar), 128.2 × 2 (Ar), 128.0 × 2 (Ar), 127.9 × 3 (Ar), 127.8 (Ar), 127.7 × 5 (Ar), 100.9 (C-1_{Xyl}), 100.6 (C-1_{Xyl}), 100.2 (C-1_{Xyl}), 100.0 (C-1_{Man}), 97.2 × 2 (C-1_{Man}), 94.1 ($Cl_3\underline{C}CH_2O$), 79.5, 79.2 × 2 (C), 78.0 (C-3_{Man}), 76.9 ($Cl_3C\underline{C}H_2O$), 75.3, 75.1 × 2 (C), 74.3, 74.1 × 2 (C), 73.4 ($Ph\underline{C}H_2O$), 73.3 (C-4_{Xyl}), 73.1, 72.9 × 3 (C), 72.3 ($Ph\underline{C}H_2O$), 72.0 ($Ph\underline{C}H_2O$), 71.9 ($Ph\underline{C}H_2O$), 71.6, 71.5, 71.2 (C-3_{Xyl}), 71.0 (C-2_{Xyl}), 68.8, 68.5 (C-6_{Man}), 68.4 (C-6_{Man}), 68.3 × 2 (C), 68.2 (C-2_{Man}), 62.8 (C-5_{Xyl}), 62.6 (C-5_{Xyl}), 61.3 (C-5_{Xyl}), 57.1 (OCH_3), 21.3 ($\underline{C}H_3C(O)O$). HRMS (ESI) calcd for (M + $2(NH_4)$)$^{2+}$ $C_{123}H_{129}Cl_3N_2O_{37}$: 1165.3664. Found: 1165.3666.



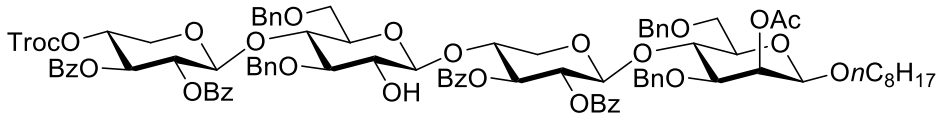
***n*-Octyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.51).** To a flask containing **3.37** (3.65 g, 3.19 mmol) and **3.34** (1.60 g, 1.87 mmol) was added CH_2Cl_2 (30 mL) and 4 Å M.S. powder (1.0 g) under argon. The flask was sealed with a rubber septum connected to an argon balloon and the resultant slurry mixture was stirred for 2 h before it was cooled to 0 °C. The mixture was stirred at 0 °C for another 30 min, after which TfOH (1.24 mL, 0.28 mmol, 2% v/v in CH_2Cl_2) was added dropwise over 2 min. Upon complete addition of TfOH, the flask was removed from the ice bath and stirred at room temperature. After 8 h, Et_3N (1.0 mL) was added and the mixture was passed through a Celite bed. Filtration of the mixture, followed by concentration of the filtrate led to a crude residue that was subsequently purified by silica gel chromatography (5:1 toluene–EtOAc) to obtain **3.51** (2.88 g, 1.59 mmol, 85%) as a white foamy solid. R_f = 0.23 (5:1 toluene–EtOAc); $[\alpha]_D$ +1.0 (*c*. 0.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.94–7.82 (m, 8H, Ar), 7.59–7.45 (m, 3H, Ar), 7.44–7.26 (m, 21H, Ar), 7.26–7.21 (m, 4H, Ar), 7.21–7.13 (m, 4H, Ar), 5.53 (d, *J* = 3.5 Hz, 1H, H-2`), 5.47 (app t, *J* = 8.7 Hz, 1H, H-3````), 5.39 (app t, *J* = 8.5 Hz, 1H, H-3``), 5.26 (dd, *J* = 8.9, 7.0 Hz, 1H, H-2````), 5.18 (dd, *J* = 8.8, 6.9 Hz, 1H, H-2``), 4.99 (app td, *J* = 8.9, 5.2 Hz, 1H, H-4````), 4.87–4.78 (m, 2H, H-2```, 1 × PhC$\underline{H}_2$O), 4.77–4.70 (m, 2H, H-1``, 1 × PhC$\underline{H}_2$O), 4.71–4.61 (m, 3H, 2 × $Cl_3CC\underline{H}_2$O, H-1````), 4.62–4.47 (m, 3H, 3 × PhC$\underline{H}_2$O), 4.37 (s, 1H, H-1`), 4.34–4.24 (m, 3H, H-1```, 2 × PhC$\underline{H}_2$O), 4.10–3.96 (m, 4H, H-5a``, H-5a````, H-4`, 1 × PhC$\underline{H}_2$O), 3.96–3.86 (m, 2H, H-4```, H-4``), 3.76 (dt, *J* = 9.4, 6.8 Hz, 1H, 1 × OC$\underline{H}_2(CH_2)_6CH_3$), 3.61–3.48 (m, 4H, H-6a`, H-6b`, H-3`, H-3```), 3.38 (dt, *J* = 9.4,

6.9 Hz, 1H, 1 × OC<u>H</u>$_2$(CH$_2$)$_6$CH$_3$), 3.31 (dd, *J* = 11.3, 3.3 Hz, 1H, H-6a```), 3.28–3.14 (m, 3H, H-5`, H-5b``, H-5b````), 3.01 (dd, *J* = 11.2, 1.7 Hz, 1H, H-6b```), 3.01–2.94 (m, 1H, H-5```), 2.64–2.54 (m, 2H, 2 × CH$_2$C<u>H</u>$_2$C(O)CH$_3$), 2.43–2.31 (m, 2H, 2 × C<u>H</u>$_2$CH$_2$C(O)CH$_3$), 2.14 (s, 3H, C<u>H</u>$_3$C(O)O), 2.10 (s, 3H, CH$_2$CH$_2$C(O)C<u>H</u>$_3$), 1.54–1.48 (m, 2H, 2 × OCH$_2$(C<u>H</u>$_2$)$_6$CH$_3$), 1.31–1.18 (m, 10H, 10 × OCH$_2$ (C<u>H</u>$_2$)$_6$CH$_3$), 0.86 (t, *J* = 6.9 Hz, 3H, OCH$_2$(CH$_2$)$_6$C<u>H</u>$_3$). ^{13}C NMR (125 MHz, CDCl$_3$, δ_C) 206.0 (C=O), 170.9 (C=O), 170.6 (C=O), 165.2 × 2 (C=O), 164.9 × 2 (C=O), 153.2 (C=O), 138.5 (Ar), 138.2 (Ar), 137.9 × 2 (Ar), 133.5 (Ar), 133.2 (Ar), 133.0 (Ar), 129.9 (Ar), 129.7 × 2 (Ar), 129.3 (Ar), 129.0 (Ar), 128.6 (Ar), 128.6 (Ar), 128.5 (Ar), 128.4 × 2 (Ar), 128.3 × 2 (Ar), 128.0 (Ar), 127.9 (Ar), 127.8 × 2 (Ar), 127.7 (Ar), 127.5 (Ar), 100.9 (C-1```), 100.4 (C-1``), 100.1 (C-1````), 98.9 (C-1`), 94.1 (Cl$_3$<u>C</u>CH$_2$O), 80.6 (C-3```), 78.1 (C-3`), 76.9 (Cl$_3$C<u>C</u>H$_2$O), 76.0 (C-4```), 75.6 (C-4``), 75.3 (C-5`), 75.0 (C-5```), 74.3 (Ph<u>C</u>H$_2$O), 74.1 (C-4`), 73.4 (Ph<u>C</u>H$_2$O), 73.3 (Ph<u>C</u>H$_2$O), 73.2 (C-4````), 72.9 × 2 (C-3``, C-2```), 72.0 (C-2``), 71.8 (Ph<u>C</u>H$_2$O), 71.6 (C-3````), 71.2 (C-2````), 69.9 (O<u>C</u>H$_2$(CH$_2$)$_6$CH$_3$), 68.5 (C-6`), 68.2 (C-2`), 67.3 (C-6```), 63.0 (C-5``), 61.7 (C-5````), 37.8 (CH$_2$<u>C</u>H$_2$C(O)CH$_3$), 31.8 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 29.8 (CH$_2$CH$_2$C(O)<u>C</u>H$_3$), 29.4 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 29.3 × 2 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 29.2 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 27.8 (<u>C</u>H$_2$CH$_2$C(O)CH$_3$), 25.9 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 22.7 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 21.3 (<u>C</u>H$_3$C(O)O), 14.1 (OCH$_2$(CH$_2$)$_6$<u>C</u>H$_3$). HRMS (ESI) calcd for (M + NH$_4$)$^+$ C$_{96}$H$_{107}$Cl$_3$NO$_{28}$: 1826.604. Found: 1826.6047.



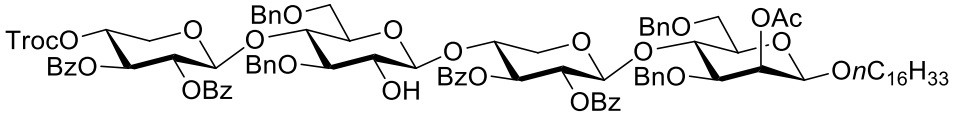
***n*-Hexadecyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.52).** To a flask containing **3.37** (0.99 g, 1.0 mmol) and **3.35** (1.93 g, 1.67 mmol) was added CH_2Cl_2 (20 mL) and 4 Å M.S. powder (0.5 g) under argon. The flask was sealed with a rubber septum connected to an argon balloon and the resultant slurry mixture was subsequently stirred for 2 h before it was cooled to 0 °C. The mixture was stirred at 0 °C for another 30 min, after which point TfOH (0.75 mL, 0.17 mmol, 2% v/v in CH_2Cl_2) was added dropwise rate over 2 min. Upon complete addition of TfOH, the flask was removed from the ice bath and stirred at room temperature. After 8 h, Et_3N (0.5 mL) was added and the mixture was passed through a Celite bed. Filtration of the mixture, followed by concentration of the filtrate led to a crude residue that was then purified by silica gel chromatography (7:1 toluene–EtOAc) to obtain **3.52** (1.77 g, 0.922 mmol, 90%) as a white foamy solid. R_f = 0.32 (7:1 toluene–EtOAc); $[\alpha]_D$ −1.7 (*c*. 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.94–7.82 (m, 8H, Ar), 7.59–7.45 (m, 3H, Ar), 7.44–7.26 (m, 21H), 7.26–7.21 (m, 4H, Ar), 7.21–7.13 (m, 4H, Ar), 5.53 (d, *J* = 3.5 Hz, 1H, H-2`), 5.47 (app t, *J* = 8.7 Hz, 1H, H-3````), 5.39 (app t, *J* = 8.5 Hz, 1H, H-3``), 5.27 (dd, *J* = 8.9, 7.0 Hz, 1H, H-2````), 5.18 (dd, *J* = 8.8, 7.0 Hz, 1H, H-2``), 4.99 (app td, *J* = 8.9, 5.2 Hz, 1H, H-4````), 4.87–4.79 (m, 2H, H-2```, 1 × PhC$\underline{H}_2$O), 4.77–4.70 (m, 2H, H-1``, 1 × PhC$\underline{H}_2$O), 4.71–4.62 (m, 3H, 2 × $Cl_3CC\underline{H}_2$O, H-1````), 4.62–4.47 (m, 3H, 3 × PhC$\underline{H}_2$O), 4.37 (s, 1H, H-1`), 4.34–4.24 (m, 3H, H-1```, 2 × PhC$\underline{H}_2$O), 4.08–3.96 (m, 4H, H-5a``, H-5a````, H-4`, 1 × PhC$\underline{H}_2$O), 3.96–3.85 (m, 2H, H-4```, H-4``), 3.76 (dt, *J* = 9.4, 6.8 Hz, 1H, 1 × OC$\underline{H}_2(CH_2)_{14}CH_3$), 3.61–3.48 (m, 4H, H-6a`, H-6b`, H-3`, H-3```),

3.38 (dt, *J* = 9.4, 6.9 Hz, 1H, 1 × OC<u>H</u>$_2$(CH$_2$)$_{14}$CH$_3$), 3.31 (dd, *J* = 11.3, 3.3 Hz, 1H, H-6a```), 3.27–3.14 (m, 3H, H-5`, H-5b``, H-5b````), 3.02 (dd, *J* = 11.2, 1.7 Hz, 1H, H-6b```), 2.99–2.95 (m, 1H, H-5```), 2.66–2.51 (m, 2H, 2 × CH$_2$C<u>H</u>$_2$C(O)CH$_3$), 2.45–2.29 (m, 2H, 2 × C<u>H</u>$_2$CH$_2$C(O)CH$_3$), 2.14 (s, 3H, C<u>H</u>$_3$C(O)O), 2.10 (s, 3H, CH$_2$CH$_2$C(O)C<u>H</u>$_3$), 1.54–1.48 (m, 2H, 2 × OCH$_2$(C<u>H</u>$_2$)$_{14}$CH$_3$), 1.35–1.15 (m, 26H, 26 × OCH$_2$ (C<u>H</u>$_2$)$_{14}$CH$_3$), 0.86 (t, *J* = 6.9 Hz, 3H, OCH$_2$(CH$_2$)$_{14}$C<u>H</u>$_3$). ^{13}C NMR (125 MHz, CDCl$_3$, δ_C) 206.0 (C=O), 170.9 (C=O), 170.6 (C=O), 165.2 × 2 (C=O), 164.9 (C=O), 164.8 (C=O), 153.1 (C=O), 138.4 (Ar), 138.1 (Ar), 137.9 (Ar), 137.8 (Ar), 133.4 (Ar), 133.2 (Ar), 132.9 (Ar), 130.0 (Ar), 129.8 (Ar), 129.7 × 2 (Ar), 129.6 (Ar), 129.2 (Ar), 128.9 (Ar), 128.5 × 2 (Ar), 128.4 × 2 (Ar), 128.3 × 2 (Ar), 128.2 × 2 (Ar), 128.0 (Ar), 127.9 × 2 (Ar), 127.8 × 2 (Ar), 127.6 (Ar), 127.5 (Ar), 100.9 (C-1```), 100.4 (C-1``), 100.1 (C-1````), 98.9 (C-1`), 94.1 (Cl$_3$<u>C</u>CH$_2$O), 80.6 (C-3```), 78.2 (C-3`), 76.9 (Cl$_3$C<u>C</u>H$_2$O), 76.0 (C-4```), 75.6 (C-4``), 75.2 (C-5`), 74.9 (C-5```), 74.2 (Ph<u>C</u>H$_2$O), 74.1 (C-4`), 73.4 (Ph<u>C</u>H$_2$O), 73.3 (Ph<u>C</u>H$_2$O), 73.2 (C-4````), 72.8 (C-3``, C-2```), 72.0 (C-2``), 71.8 (Ph<u>C</u>H$_2$O), 71.6 (C-3`````), 71.2 (C-2````), 69.9 (O<u>C</u>H$_2$(CH$_2$)$_{14}$CH$_3$), 68.5 (C-6`), 68.2 (C-2`), 67.3 (C-6```), 63.0 (C-5``), 61.7 (C-5````), 37.8 (CH$_2$<u>C</u>H$_2$C(O)CH$_3$), 31.9 (OCH$_2$(<u>C</u>H$_2$)$_{14}$CH$_3$), 29.8 (CH$_2$CH$_2$C(O)<u>C</u>H$_3$), 29.7 × 2 (OCH$_2$(<u>C</u>H$_2$)$_{14}$CH$_3$), 29.6 × 3 (OCH$_2$(<u>C</u>H$_2$)$_{14}$CH$_3$), 29.4 (OCH$_2$(<u>C</u>H$_2$)$_{14}$CH$_3$), 29.3 (OCH$_2$(<u>C</u>H$_2$)$_{14}$CH$_3$), 27.8 (<u>C</u>H$_2$CH$_2$C(O)CH$_3$), 25.9 (OCH$_2$(<u>C</u>H$_2$)$_{14}$CH$_3$), 22.7 (OCH$_2$(<u>C</u>H$_2$)$_{14}$CH$_3$), 21.2 (<u>C</u>H$_3$C(O)O), 14.1 (OCH$_2$(CH$_2$)$_{14}$<u>C</u>H$_3$). HRMS (ESI) calcd for (M + Na)$^+$ C$_{104}$H$_{119}$Cl$_3$NaO$_{28}$: 1943.6851. Found: 1943.6855.



***n*-Octyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.53).** The general procedure for levulinoyl deprotection was carried out on **3.51** (194 mg, 0.101 mmol) with H_2NNH_2·HOAc (114 μL, 0.124 mmol, 10% w/v in CH_3OH) in CH_2Cl_2–CH_3OH (4 mL, 10:1). The crude residue was purified by silica gel chromatography (2:1 hexanes–EtOAc) to obtain **3.53** (150 mg, 0.088 mmol, 88%) as a white foamy solid. R_f = 0.44 (2:1 hexanes–EtOAc); $[\alpha]_D$ +9.0 (*c*. 0.6, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.98–7.83 (m, 8H, Ar), 7.58–7.46 (m, 3H, Ar), 7.42–7.26 (m, 23H, Ar), 7.25–7.14 (m, 6H, Ar), 5.55 (d, *J* = 3.5 Hz, 1H, H-2`), 5.49 (app t, *J* = 8.3 Hz, 1H, H-3````), 5.42 (app t, *J* = 8.3 Hz, 1H, H-3``), 5.28 (dd, *J* = 8.5, 6.6 Hz, 1H, H-2````), 5.21 (dd, *J* = 8.6, 6.7 Hz, 1H, H-2``), 5.00 (app td, *J* = 8.4, 4.9 Hz, 1H H-4````), 4.89–4.84 (m, 1H, 1 × PhC$\underline{H}_2$O), 4.83–4.74 (m, 4H, H-1``, H-1````, 2 × PhC$\underline{H}_2$O), 4.69, 4.66 (ABq, *J* = 12.0 Hz, 2H, 2 × $Cl_3CC\underline{H}_2$O), 4.53–4.46 (m, 2H, 2 × PhC$\underline{H}_2$O), 4.39 (s, 1H, H-1`), 4.33–4.25 (m, 2H, 2 × PhC$\underline{H}_2$O), 4.20–4.16 (m, 1H, H-1```), 4.13 (dd, *J* = 12.2, 4.9 Hz, 1H, H-5a````), 4.09–3.93 (m, 4H, H-5a``, H-4`, 1 × PhC$\underline{H}_2$O, H-4``), 3.85 (app t, *J* = 9.2 Hz, 1H, H-4```), 3.77 (dt, *J* = 9.4, 6.8 Hz, 1H, 1 × OC$\underline{H}_2(CH_2)_6CH_3$), 3.61–3.52 (m, 3H, H-6a`, H-6b`, H-3`), 3.44–3.36 (m, 4H, H-3```, H-2```, H-6a```, OC$\underline{H}_2(CH_2)_6CH_3$), 3.32–3.24 (m, 2H, H-5b````, H-5`), 3.19–3.10 (m, 2H, H-6b```, H-5b``), 3.05 (ddd, *J* = 9.7, 3.5, 1.8 Hz, 1H, H-5```), 2.16 (s, 3H, C$\underline{H}_3$C(O)O), 1.54–1.47 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_6CH_3$), 1.33–1.15 (m, 10H, 10 × $OCH_2(C\underline{H}_2)_6CH_3$), 0.86 (t, *J* = 7.0 Hz, 4H, $OCH_2(CH_2)_6C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 170.7 (C=O), 165.4 (C=O), 165.2 × 2

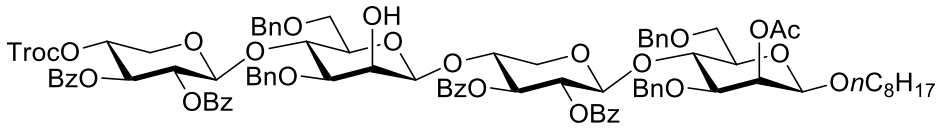
(C=O), 165.0 (C=O), 153.2 (C=O), 138.7 (Ar), 138.3 (Ar), 138.0 (Ar), 137.9 (Ar), 133.5 (Ar), 133.3 (Ar), 133.0 (Ar), 129.9 (Ar), 129.8 (Ar), 129.7 × 2 (Ar), 129.3 (Ar), 129.0 (Ar), 129.0 (Ar), 128.5 × 3 (Ar), 128.4 × 2 (Ar), 128.3 (Ar), 128.0 (Ar), 127.9 × 3 (Ar), 127.8 (Ar), 127.7 × 2 (Ar), 101.9 (C-1```), 100.4 (C-1``), 100.0 (C-1````), 98.9 (C-1`), 94.1 ($Cl_3\underline{C}CH_2O$), 82.3 (C-3```), 78.5 (C-3`), 77.0 ($Cl_3C\underline{C}H_2O$), 75.9 (C-4```), 75.3 (C-5`), 75.1 (C-5```), 74.8 ($Ph\underline{C}H_2O$), 74.3 (C-4`), 74.2 (C-4``), 73.7 (C-2```), 73.4 ($Ph\underline{C}H_2O$), 73.3 ($Ph\underline{C}H_2O$), 73.2 (C-4````), 72.7 (C-3``), 71.8 ($Ph\underline{C}H_2O$), 71.7 (C-2``), 71.4 (C-3````), 71.1 (C-2````), 69.9 ($O\underline{C}H_2(CH_2)_6CH_3$), 68.7 (C-6`), 68.1 (C-2`), 67.6 (C-6```), 62.8 (C-5``), 61.5 (C-5````), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 × 2 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 25.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 21.2 ($\underline{C}H_3C(O)O$), 14.1 ($OCH_2(CH_2)_6\underline{C}H_3$). HRMS (ESI) calcd for $(M + NH_4)^+$ $C_{91}H_{97}Cl_3NO_{26}$: 1728.5672. Found: 1728.5589.



***n*-Hexadecyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.54).** The general procedure for levulinoyl deprotection was carried out on **3.52** (25.7 mg, 13.4 μmol) with $H_2NNH_2{\cdot}HOAc$ (15.5 μL, 16.6 μmol, 10% w/v in CH_3OH) in CH_2Cl_2–CH_3OH (2 mL, 10:1). The resultant crude residue was purified by silica gel chromatography (3:2 hexanes–EtOAc) to obtain **3.54** (21.5 mg, 11.8 μmol, 88%) as a white foamy solid. R_f = 0.45 (3:2 hexanes–EtOAc); $[\alpha]_D$ −1.3 (*c*. 0.1, $CHCl_3$); ^1H NMR (500

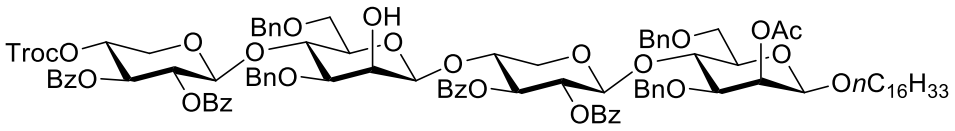
MHz, $CDCl_3$, δ_H) 8.00–7.84 (m, 8H, Ar), 7.58–7.46 (m, 3H, Ar), 7.42–7.26 (m, 23H), 7.25–7.14 (m, 6H), 5.55 (d, *J* = 3.5 Hz, 1H, H-2`), 5.49 (app t, *J* = 8.3 Hz, 1H, H-3````), 5.42 (app t, *J* = 8.3 Hz, 1H, H-3``), 5.28 (dd, *J* = 8.5, 6.6 Hz, 1H, H-2````), 5.21 (dd, *J* = 8.6, 6.7 Hz, 1H, H-2``), 5.00 (app td, *J* = 8.4, 4.9 Hz, 1H H-4````), 4.89–4.84 (m, 1H, 1 × PhC$\underline{H}_2$O), 4.83–4.74 (m, 4H, H-1``, H-1````, 2 × PhC$\underline{H}_2$O), 4.69, 4.66 (ABq, *J* = 12.0 Hz, 2H, 2 × $Cl_3CC\underline{H}_2O$), 4.53–4.46 (m, 2H, 2 × PhC$\underline{H}_2$O), 4.39 (s, 1H, H-1`), 4.33–4.25 (m, 2H, 2 × PhC$\underline{H}_2$O), 4.20–4.16 (m, 1H, H-1```), 4.13 (dd, *J* = 12.2, 4.9 Hz, 1H, H-5a````), 4.09–3.93 (m, 4H, H-5a``, H-4`, 1 × PhC$\underline{H}_2$O, H-4``), 3.85 (app t, *J* = 9.2 Hz, 1H, H-4```), 3.76 (dt, *J* = 9.4, 6.8 Hz, 1H, 1 × OC$\underline{H}_2(CH_2)_{14}CH_3$), 3.61–3.52 (m, 3H, H-6a`, H-6b`, H-3`), 3.45–3.36 (m, 4H, H-3```, H-2```, H-6a```, 1 × OC$\underline{H}_2(CH_2)_{14}CH_3$), 3.32–3.24 (m, 2H, H-5b````, H-5`), 3.19–3.10 (m, 2H, H-6b```, H-5b``), 3.05 (ddd, *J* = 9.7, 3.5, 1.8 Hz, 1H, H-5```), 2.16 (s, 3H, C$\underline{H}_3$C(O)O), 1.54–1.47 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 1.36–1.16 (m, 26H, 10 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 0.88 (t, *J* = 7.0 Hz, 4H, $OCH_2(CH_2)_{14}C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 170.7 (C=O), 165.4 (C=O), 165.2 × 2 (C=O), 165.0 (C=O), 153.2 (C=O), 138.7 (Ar), 138.3 (Ar), 138.0 (Ar), 137.9 (Ar), 133.5 (Ar), 133.3 (Ar), 133.0 (Ar), 129.9 (Ar), 129.8 (Ar), 129.7 × 2 (Ar), 129.3 (Ar), 129.0 (Ar), 129.0 (Ar), 128.5 × 3 (Ar), 128.4 × 2 (Ar), 128.3 (Ar), 128.0 (Ar), 127.9 × 3 (Ar), 127.8 (Ar), 127.7 × 2 (Ar), 101.9 (C-1```), 100.4 (C-1``), 100.0 (C-1````), 98.9 (C-1`), 94.1 ($Cl_3\underline{C}CH_2O$), 82.3 (C-3```), 78.5 (C-3`), 77.0 ($Cl_3C\underline{C}H_2O$), 75.9 (C-4```), 75.3 (C-5`), 75.1 (C-5```), 74.8 (Ph$\underline{C}H_2$O), 74.3 (C-4`), 74.2 (C-4``), 73.7 (C-2```), 73.4 (Ph$\underline{C}H_2$O), 73.3 (Ph$\underline{C}H_2$O), 73.2 (C-4````), 72.7 (C-3``), 71.8 (Ph$\underline{C}H_2$O), 71.7 (C-2``), 71.4 (C-3````), 71.1 (C-2````), 69.9 ($O\underline{C}H_2(CH_2)_{14}CH_3$), 68.8 (C-6`), 68.1 (C-2`), 67.6 (C-6```), 62.8 (C-5``), 61.5 (C-5````), 31.8 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.7 × 4 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.6 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.4 × 2 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 25.9 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 22.7

($OCH_2(\underline{C}H_2)_{14}CH_3$), 21.2 ($\underline{C}H_3C(O)O$), 14.1 ($OCH_2(CH_2)_{14}\underline{C}H_3$). HRMS (ESI) calcd for $(M + NH_4)^+$ $C_{99}H_{113}Cl_3NaO_{26}$: 1845.6478. Found: 1845.6488.



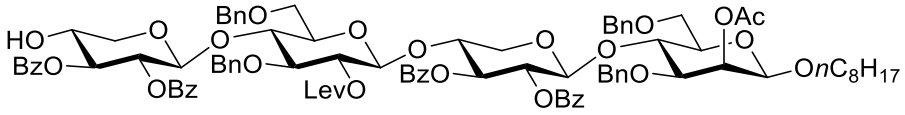
***n*-Octyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.55).** Approach B for C-2 inversion was carried out on **3.53** (95.7 mg, 55.8 μmol). In this approach, DMP (73.6 mg, 17.4 μmol) and H_2O (1.5 μL, 84 μmol) were used for oxidation in CH_2Cl_2 (3 mL); subsequent reduction was conducted on the crude ketone with LTBA (19.0 mg, 75.0 μmol) in THF (2 mL). The resultant crude residue was purified by silica gel chromatography (3:2 hexanes–EtOAc) to afford **3.55** (66.9 mg, 39.1 μmol, 70%) as a white solid. R_f = 0.34 (3:2 hexanes–EtOAc); $[\alpha]_D$ +1.9 (*c*. 0.5, $CHCl_3$); ^{1}H NMR (700 MHz, $CDCl_3$, δ_H) 7.95–7.86 (m, 8H, Ar), 7.55–7.46 (m, 3H, Ar), 7.42–7.27 (m, 23H, Ar), 7.26–7.11 (m, 6H, Ar), 5.54 (d, *J* = 3.5 Hz, 1H, H-2`), 5.49 (app t, *J* = 8.1 Hz, 1H, H-3````), 5.35 (app t, *J* = 8.5 Hz, 1H, H-3``), 5.29 (app t, *J* = 9.0, 1H, H-2``), 5.26 (dd, *J* = 8.3, 6.4 Hz, 1H, H-2````), 5.00 (app td, *J* = 8.1, 4.9 Hz, 1H, H-4````), 4.78–4.72 (m, 4H, H-1````, H-1``, 2 × PhC$\underline{H}_2$O), 4.72–4.64 (m, 3H, 1 × PhC$\underline{H}_2$O, 2 × $Cl_3CC\underline{H}_2$O), 4.56–4.51 (m, 2H, 2 × PhC$\underline{H}_2$O), 4.38 (d, *J* = 1.0 Hz, 1H, H-1`), 4.37 (d, *J* = 1.0 Hz, 1H, H-1```), 4.29 (d, *J* = 12.0 Hz, 1H, 1 × PhC$\underline{H}_2$O), 4.18 (dd, *J* = 12.4, 4.8 Hz, 1H, H-5a````), 4.13–4.08 (m, 2H, 1 × PhC$\underline{H}_2$O, H-4``), 4.05 (app t, *J* = 9.4 Hz, 1H, H-4`), 4.01–3.94 (m, 4H, H-2```, H-4```, H-5a``, 1 × PhC$\underline{H}_2$O),

3.77 (dt, J = 9.5, 6.8 Hz, 1H, 1 × OC<u>H</u>$_2$(CH$_2$)$_6$CH$_3$), 3.62 (dd, J = 11.0, 4.7 Hz, 1H, H-6a`), 3.57 (dd, $J$ = 11.0, 1.8 Hz, 1H, H-6b`), 3.54 (dd, J = 9.3, 3.5 Hz, 1H, H-3`), 3.43–3.36 (m, 2H, H-3```, 1 × OC<u>H</u>$_2$(CH$_2$)$_{14}$CH$_3$), 3.35–3.30 (m, 2H, H-6a```, H-5b````), 3.26 (ddd, J = 9.7, 4.7, 1.8 Hz, 1H, H-5`), 3.16–3.10 (m, 3H, H-5```, H-6b```, H-5b``), 2.50–2.45 (br s, 1H, OH), 2.15 (s, 3H, C<u>H</u>$_3$C(O)O), 1.55–1.49 (m, 2H, 2 × OCH$_2$(C<u>H</u>$_2$)$_6$CH$_3$), 1.33–1.19 (m, 10H, 10 × OCH$_2$(C<u>H</u>$_2$)$_6$CH$_3$), 0.86 (t, J = 7.1 Hz, 3H, OCH$_2$(CH$_2$)$_6$C<u>H</u>$_3$). ^{13}C NMR (175 MHz, CDCl$_3$, δ_C) 170.6 (C=O), 166.3 (C=O), 165.2 (C=O), 165.1 (C=O), 165.0 (C=O), 153.3 (C=O), 138.3 (Ar), 138.2 (Ar), 138.1 (Ar), 137.9 (Ar), 133.5 (Ar), 133.4 × 2 (Ar), 133.1 (Ar), 129.9 × 3 (Ar), 129.8 × 2 (Ar), 129.7 (Ar), 129.2 (Ar), 129.1 (Ar), 129.0 (Ar), 128.6 (Ar), 128.5 × 3 (Ar), 128.4 × 3 (Ar), 128.3 (Ar), 128.0 (Ar), 127.9 × 3 (Ar), 127.8 (Ar), 127.7 × 2 (Ar), 127.6 (Ar), 100.6 (C-1``), 100.2 (C-1````), 98.9 (C-1`), 97.2 (C-1```), 94.1 (Cl$_3$<u>C</u>CH$_2$O), 79.5 (C-3```), 78.2 (C-3`), 77.0 (Cl$_3$C<u>C</u>H$_2$O), 75.3 (C-5`), 75.1 (C-5```), 74.2 (C-4```), 74.1 (C-4`), 73.4 (Ph<u>C</u>H$_2$O), 73.1 × 3 (C-4````, C-4``, Ph<u>C</u>H$_2$O), 73.0 (C-3``), 72.0 (Ph<u>C</u>H$_2$O), 71.8 (Ph<u>C</u>H$_2$O), 71.6 (C-2``), 71.2 (C-3````), 71.0 (C-2````), 69.9 (O<u>C</u>H$_2$(CH$_2$)$_6$CH$_3$), 68.5 × 2 (C-2```, C-6`), 68.4 (C-6```), 68.2 (C-2`), 62.7 (C-5``), 61.4 (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 × 2 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 29.2 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 25.9 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 22.7 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 22.7 (OCH$_2$(<u>C</u>H$_2$)$_6$CH$_3$), 21.3 (<u>C</u>H$_3$C(O)O), 14.2 (OCH$_2$(CH$_2$)$_6$<u>C</u>H$_3$). HRMS (ESI) calcd for (M + Na)$^+$ C$_{91}$H$_{97}$Cl$_3$NaO$_{26}$: 1733.5226. Found: 1733.5228.



***n*-Hexadecyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl (1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.56).** Approach B for C-2 inversion was carried out on **3.54** (57.3 mg, 31.4 μmol). In this approach, DMP (41.0 mg, 96.7 μmol) and H_2O (0.80 μL, 44.0 μmol) were used for oxidation in CH_2Cl_2 (2 mL); subsequent reduction was conducted with LTBA (10.0 mg, 39.3 μmol) in THF (1 mL). The crude residue was purified by silica gel chromatography (3:2 hexanes–EtOAc) to afford **3.56** (43.0 mg, 23.6 μmol, 75%) as a white solid. R_f = 0.48 (3:2 hexanes–EtOAc); $[\alpha]_D$ +3.3 (*c*. 0.7, $CHCl_3$); ^{1}H NMR (700 MHz, $CDCl_3$, δ_H) 7.95–7.84 (m, 8H, Ar), 7.55–7.46 (m, 3H, Ar), 7.42–7.27 (m, 23H, Ar), 7.26–7.11 (m, 6H, Ar), 5.54 (d, *J* = 3.5 Hz, 1H, H-2`), 5.49 (app t, *J* = 8.1 Hz, 1H, H-3````), 5.34 (app t, *J* = 8.6 Hz, 1H, H-3``), 5.29 (dd, *J* = 9.0, 6.9 Hz, 1H, H-2``), 5.26 (dd, *J* = 8.3, 6.4 Hz, 1H, H-2````), 5.00 (app td, *J* = 8.1, 4.9 Hz, 1H, H-4````), 4.79–4.72 (m, 4H, H-1````, H-1``, 2 × PhC$\underline{H}_2$O), 4.72–4.64 (m, 3H, 1 × PhC$\underline{H}_2$O, 2 × $Cl_3CC\underline{H}_2$O), 4.56–4.51 (m, 2H, 2 × PhC$\underline{H}_2$O), 4.38 (s, 1H, H-1`), 4.37 (s, 1H, H-1```), 4.31–4.27 (m, 1H, 1 × PhC$\underline{H}_2$O), 4.18 (dd, *J* = 12.4, 4.8 Hz, 1H, H-5a````), 4.15–4.07 (m, 2H, 1 × PhC$\underline{H}_2$O, H-4``), 4.04 (app t, *J* = 9.4 Hz, 1H, H-4`), 4.01–3.94 (m, 4H, H-2```, H-4```, H-5a``, 1 × PhC$\underline{H}_2$O), 3.76 (dt, *J* = 9.5, 6.8 Hz, 1H, 1 × O$C\underline{H}_2(CH_2)_{14}CH_3$), 3.62 (dd, *J* = 11.0, 4.6 Hz, 1H, H-6a`), 3.57 (dd, *J* = 11.0, 1.8 Hz, 1H, H-6b`), 3.54 (dd, *J* = 9.3, 3.5 Hz, 1H, H-3`), 3.43–3.36 (m, 2H, H-3```, 1 × O$C\underline{H}_2(CH_2)_{14}CH_3$), 3.35–3.30 (m, 2H, H-6a```, H-5b````), 3.26 (ddd, *J* = 9.7, 4.7, 1.8 Hz, 1H, H-5`), 3.18–3.11 (m, 3H, H-5```, H-6b```, H-5b``), 2.15 (s, 3H, $C\underline{H}_3C(O)O$), 1.54–1.48 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 1.30–1.22

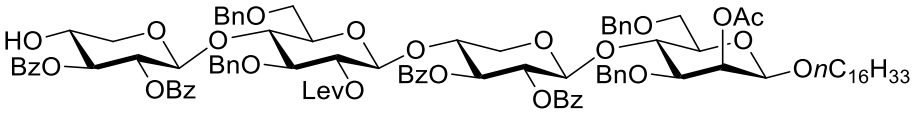
(m, 26H, 26 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 0.91–0.84 (m, 3H, $OCH_2(CH_2)_{14}C\underline{H}_3$). ^{13}C NMR (175 MHz, $CDCl_3$, δ_C) 170.6 (C=O), 166.3 (C=O), 165.1 × 2 (C=O), 165.0 (C=O), 153.2 (C=O), 138.3 (Ar), 138.2 (Ar), 138.1 (Ar), 137.9 (Ar), 133.5 × 2 (Ar), 133.4 (Ar), 133.1 (Ar), 129.9 × 2 (Ar), 129.8 (Ar), 129.7 (Ar), 129.2 (Ar), 129.1 (Ar), 129.0 (Ar), 128.5 × 3 (Ar), 128.4 × 3 (Ar), 128.3 (Ar), 128.0 (Ar), 127.9 × 2 (Ar), 127.8 (Ar), 127.7 × 3 (Ar), 100.6 (C-1``), 100.2 (C-1````), 98.9 (C-1`), 97.2 (C-1```), 94.1 ($Cl_3\underline{C}CH_2O$), 79.5 (C-3```), 78.2 (C-3`), 77.0 ($Cl_3C\underline{C}H_2O$), 75.3 (C-5`), 75.1 (C-5```), 74.2 (C-4```), 74.1 (C-4`), 73.4 ($Ph\underline{C}H_2O$), 73.1 × 3 (C-4````, C-4``, $Ph\underline{C}H_2O$), 73.0 (C-3``), 72.1 ($Ph\underline{C}H_2O$), 71.8 ($Ph\underline{C}H_2O$), 71.6 (C-2``), 71.3 (C-3````), 71.0 (C-2````), 69.9 ($O\underline{C}H_2(CH_2)_{14}CH_3$), 68.5 × 2 (C-2```, C-6`), 68.4 (C-6```), 68.2 (C-2`), 62.7 (C-5``), 61.4 (C-5````), 32.0 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.7 × 4 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.6 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.4 × 2 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 25.9 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 21.3 ($\underline{C}H_3C(O)O$), 14.2 ($OCH_2(CH_2)_{14}\underline{C}H_3$). HRMS (ESI) calcd for $(M + 2(NH_4))^{2+}$ $C_{99}H_{121}Cl_3N_2O_{26}$: 929.3631. Found: 929.3656.



***n*-Octyl 2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.57).** The general procedure for Troc deprotection was conducted on **3.51** (3.05 g, 1.68 mmol) with Zn powder (5.05 g, 77.3 mmol) in glacial AcOH (30 mL). The crude residue was purified by silica gel chromatography (1:1 hexanes–EtOAc), to afford **3.57** (2.45 g, 1.50 mmol, 89%) as a white foamy solid. R_f = 0.38 (1:1 hexanes–EtOAc);

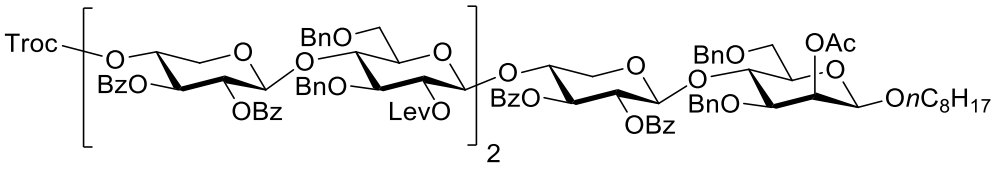
$[\alpha]_D$ +4.1 (*c*. 0.2, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.97–7.91 (m, 2H, Ar), 7.90–7.81 (m, 6H, Ar), 7.59–7.45 (m, 3H, Ar), 7.42–7.26 (m, 23H, Ar), 7.26–7.11 (m, 6H, Ar), 5.53 (d, *J* = 3.4 Hz, 1H, H-2`), 5.39 (app t, *J* = 8.5 Hz, 1H, H-3``), 5.28 (dd, *J* = 9.4, 7.5 Hz, 1H, H-2````), 5.18 (dd, *J* = 8.8, 6.9 Hz, 1H, H-2``), 5.04 (app t, *J* = 8.9 Hz, 1H, H-3````), 4.87–4.80 (m, 2H, H-2```, 1 × PhC$\underline{H}_2$O), 4.77–4.70 (m, 2H, 1 × PhC$\underline{H}_2$O, H-1``), 4.62 (d, *J* = 7.6 Hz, 1H, H-1````), 4.60–4.47 (m, 3H, 3 × PhC$\underline{H}_2$O), 4.37 (s, 1H, H-1`), 4.36–4.32 (m, 1H, 1 × PhC$\underline{H}_2$O), 4.31 (d, *J* = 7.9 Hz, 1H, H-1```), 4.29–4.25 (m, 1H, 1 × PhC$\underline{H}_2$O), 4.05–3.84 (m, 7H, 1 × PhC$\underline{H}_2$O, H-5a````, H-5a``, H-4```, H-4`, H-4````, H-4``), 3.76 (dt, *J* = 9.4, 6.8 Hz, 1H, 1 × OC$\underline{H}_2(CH_2)_6CH_3$), 3.61–3.52 (m, 3H, H-3`, H-6a`, H-6b`), 3.50 (app t, *J* = 9.1 Hz, 1H, H-3```), 3.38 (dt, *J* = 9.4, 6.9 Hz, 1H, 1 × OC$\underline{H}_2(CH_2)_6CH_3$), 3.32 (dd, *J* = 11.2, 3.3 Hz, 1H, H-6a```), 3.24 (ddd, *J* = 9.7, 4.5, 2.2 Hz, 1H, H-5`), 3.18 (dd, *J* = 12.2, 9.0 Hz, 1H, H-5b``), 3.11 (dd, *J* = 11.9, 9.5 Hz, 1H, H-5b````), 3.03–2.98 (m, 1H, H-6b```), 2.98–2.93 (m, 1H, H-5```), 2.90 (d, *J* = 4.5 Hz, 1H, O$\underline{H}$), 2.67–2.49 (m, 2H, 2 × $CH_2C\underline{H}_2C(O)CH_3$), 2.46–2.30 (m, 2H, 2 × $CH_2C\underline{H}_2C(O)CH_3$), 2.14 (s, 3H, $C\underline{H}_3C(O)O$), 2.10 (s, 3H, $CH_2CH_2C(O)\underline{C}H_3$), 1.56–1.48 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_6CH_3$), 1.33–1.17 (m, 10H, 10 × $OCH_2(C\underline{H}_2)_6CH_3$), 0.86 (t, *J* = 6.9 Hz, 3H. $OCH_2(CH_2)_6C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 206.0 (C=O), 170.9 (C=O), 170.7 (C=O), 167.6 (C=O), 165.2 (C=O), 165.0 (C=O), 164.9 (C=O), 138.6 (Ar), 138.2 (Ar), 138.0(Ar), 137.9 (Ar), 133.7 (Ar), 133.5 (Ar), 133.2 (Ar), 132.9 (Ar), 130.0 (Ar), 129.9 (Ar), 129.8 (Ar), 129.7 × 2 (Ar), 129.3 (Ar), 129.1 (Ar), 128.8 (Ar), 128.6 (Ar), 128.5 (Ar), 128.4 × 3 (Ar), 128.3 (Ar), 128.2 × 2 (Ar), 128.0 × 4 (Ar), 127.9 × 2 (Ar), 127.7 × 2 (Ar), 127.5 (Ar), 101.0 (C-1```), 100.4 × 2 (C-1``, C-1````), 98.9 (C-1`), 80.6 (C-3```), 78.2 (C-3`), 77.4 (C-3````), 75.9 (C-4```), 75.7 (C-4``), 75.3 (C-5`), 75.0 (C-5```), 74.5 (Ph$\underline{C}H_2$O), 74.2 (C-4`), 73.5 (Ph$\underline{C}H_2$O), 73.4 (Ph$\underline{C}H_2$O), 72.9 × 2 (C-2```, C-3``), 72.0 (C-2``), 71.8 (Ph$\underline{C}H_2$O), 71.4 (C-2````), 69.9 (O$\underline{C}H_2(CH_2)_6CH_3$), 69.5 (C-4````), 68.5 (C-6`), 68.2

(C-2`), 67.3 (C-6```), 65.4 (C-5````), 63.0 (C-5``), 37.8 ($CH_2\underline{C}H_2C(O)CH_3$), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.8 ($CH_2CH_2C(O)\underline{C}H_3$), 29.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 27.8 ($\underline{C}H_2CH_2C(O)CH_3$), 25.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 21.3 ($\underline{C}H_3C(O)O$), 14.1 ($OCH_2(CH_2)_6\underline{C}H_3$). HRMS (ESI) calcd for $(M + NH_4)^+$ $C_{93}H_{106}NO_{26}$: 1652.6998. Found: 1652.7011.



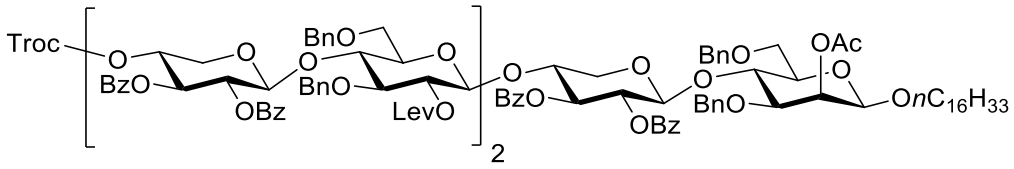
***n*-Hexadecyl 2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.58).** General procedure for Troc deprotection was conducted on **3.52** (1.09 g, 0.566 mmol). The crude residue was purified by silica gel chromatography (3:2 to 1.3:1 hexanes–EtOAc) to afford **3.58** (0.86 g, 0.49 mmol, 87%) as a white fluffy solid. R_f = 0.26 (3:2 hexanes–EtOAc); $[\alpha]_D$ +4.1 (*c*. 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.96–7.90 (m, 2H, Ar), 7.90–7.81 (m, 6H, Ar), 7.59–7.45 (m, 3H, Ar), 7.42–7.27 (m, 23H, Ar), 7.26–7.11 (m, 6H, Ar), 5.53 (d, *J* = 3.4 Hz, 1H, H-2`), 5.39 (app t, *J* = 8.5 Hz, 1H, H-3``), 5.28 (dd, *J* = 9.4, 7.5 Hz, 1H, H-2````), 5.18 (dd, *J* = 8.8, 6.9 Hz, 1H, H-2``), 5.04 (app t, *J* = 8.9 Hz, 1H, H-3````), 4.88–4.80 (m, 2H, H-2```, 1 × PhC$\underline{H}_2$O), 4.77–4.70 (m, 2H, 1 × PhC$\underline{H}_2$O, H-1``), 4.62 (d, *J* = 7.6 Hz, 1H, H-1````), 4.60–4.46 (m, 3H, 3 × PhC$\underline{H}_2$O), 4.37 (s, 1H, H-1`), 4.36–4.32 (m, 1H, 1 × PhC$\underline{H}_2$O), 4.31 (d, *J* = 7.9 Hz, 1H, H-1```), 4.29–4.25 (m, 1H, 1 × PhC$\underline{H}_2$O), 4.06–3.85 (m, 7H, 1 × PhC$\underline{H}_2$O, H-5a````, H-5a``, H-4```, H-4`, H-4````, H-4``), 3.76 (dt, *J* = 9.4, 6.8 Hz, 1H, 1 × OC$\underline{H}_2(CH_2)_{14}CH_3$), 3.62–3.52 (m, 3H, H-3`, H-6a`, H-6b`),

3.50 (app t, J = 9.1 Hz, 1H, H-3```), 3.38 (dt, J = 9.4, 6.9 Hz, 1H, 1 × OC<u>H</u>$_2$(CH$_2$)$_{14}$CH$_3$), 3.32 (dd, J = 11.2, 3.3 Hz, 1H, H-6a```), 3.24 (ddd, J = 9.7, 4.5, 2.2 Hz, 1H, H-5`), 3.18 (dd, J = 12.2, 9.0 Hz, 1H, H-5a``), 3.11 (dd, J = 11.9, 9.5 Hz, 1H, H-5b````), 3.03–2.98 (m, 1H, H-6b```), 2.98–2.93 (m, 1H, H-5```), 2.90 (d, J = 4.5 Hz, 1H, OH), 2.67–2.49 (m, 2H, 2 × CH$_2$C<u>H</u>$_2$C(O)CH$_3$), 2.46–2.30 (m, 2H, 2 × CH$_2$C<u>H</u>$_2$C(O)CH$_3$), 2.14 (s, 3H, C<u>H</u>$_3$C(O)O), 2.10 (s, 3H, CH$_2$CH$_2$C(O)<u>C</u>H$_3$), 1.57–1.46 (m, 2H, 2 × OCH$_2$(C<u>H</u>$_2$)$_{14}$CH$_3$), 1.33–1.17 (m, 10H, 26 × OCH$_2$(C<u>H</u>$_2$)$_{14}$CH$_3$), 0.88 (t, J = 6.9 Hz, 3H. OCH$_2$(CH$_2$)$_{14}$C<u>H</u>$_3$). ^{13}C NMR (125 MHz, CDCl$_3$, δ_C) 206.0 (C=O), 170.9 (C=O), 170.7 (C=O), 167.6 (C=O), 165.2 (C=O), 165.0 (C=O), 164.9 (C=O), 138.6 (Ar), 138.2 (Ar), 138.0(Ar), 137.9 (Ar), 133.7 (Ar), 133.5 (Ar), 133.2 (Ar), 132.9 (Ar), 130.0 (Ar), 129.9 (Ar), 129.8 (Ar), 129.7 × 3 (Ar), 129.3 (Ar), 129.1 (Ar), 128.8 (Ar), 128.6 (Ar), 128.5 (Ar), 128.4 × 3 (Ar), 128.3 (Ar), 128.2 × 2 (Ar), 128.0 × 4 (Ar), 127.9 × 2 (Ar), 127.7 × 2 (Ar), 127.5 (Ar), 101.0 (C-1```), 100.4 (C-1``, C-1````), 98.9 (C-1`), 80.6 (C-3```), 78.2 (C-3`), 77.4 (C-3````), 75.9 (C-4```), 75.7 (C-4``), 75.3 (C-5`), 75.0 (C-5```), 74.5 (Ph<u>C</u>H$_2$O), 74.2 (C-4`), 73.5 (Ph<u>C</u>H$_2$O), 73.4 (Ph<u>C</u>H$_2$O), 72.9 × 2 (C-2```, C-3``), 72.0 (C-2``), 71.8 (Ph<u>C</u>H$_2$O), 71.4 (C-2````), 69.9 (O<u>C</u>H$_2$(CH$_2$)$_{14}$CH$_3$), 69.5 (C-4````), 68.5 (C-6`), 68.2 (C-2`), 67.3 (C-6```), 65.4 (C-5````), 63.0 (C-5``), 37.8 (CH$_2$<u>C</u>H$_2$C(O)CH$_3$), 32.0 (OCH$_2$(<u>C</u>H$_2$)$_{14}$CH$_3$), 29.8 (CH$_2$CH$_2$C(O)<u>C</u>H$_3$), 29.7 × 4 (OCH$_2$(<u>C</u>H$_2$)$_{14}$CH$_3$), 29.6 (OCH$_2$(<u>C</u>H$_2$)$_{14}$CH$_3$), 29.4 × 2 (OCH$_2$(<u>C</u>H$_2$)$_{14}$CH$_3$), 27.8 (<u>C</u>H$_2$CH$_2$C(O)CH$_3$), 25.9 (OCH$_2$(<u>C</u>H$_2$)$_{14}$CH$_3$), 22.7 (OCH$_2$(<u>C</u>H$_2$)$_{14}$CH$_3$), 21.3 (<u>C</u>H$_3$C(O)O), 14.1 (OCH$_2$(CH$_2$)$_{14}$<u>C</u>H$_3$). LRMS-MALDI-TOF calcd for (M + Na)$^+$ C$_{101}$H$_{118}$NaO$_{26}$: 1769.8. Found: 1769.6.



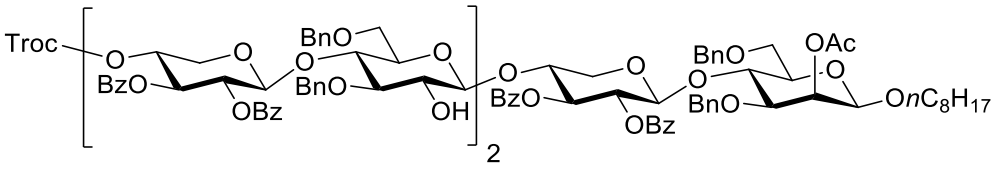
***n*-Octyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.59).** To a flask containing **3.37** (780 mg, 0.680 mmol) and **3.57** (556 mg, 0.340 mmol) was added CH_2Cl_2 (11 mL) and 4 Å M.S. powder (280 mg) under argon. The flask was then sealed with a rubber septum connected to an argon balloon and the resultant slurry mixture was stirred for 2 h before it was cooled to 0 °C. The mixture was stirred for another 30 min, after which point TfOH (300 μL, 0.068 mmol, 2% v/v in CH_2Cl_2) was added dropwise over 2 min. Upon complete addition of TfOH, the flask was removed from the ice bath and stirred at room temperature. After 8 h, Et_3N (2 mL) was added and the mixture was passed through a Celite bed. Concentration of the resultant filtrate led to a crude residue that was subsequently purified by silica gel chromatography (5:2 to 2:1 hexanes–acetone) to obtain **3.59** (739 mg, 0.285 mmol, 84%) as a white foamy solid. R_f = 0.30 (2:1 hexanes–acetone); $[\alpha]_D$ +4.8 (*c*. 0.6, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.01–7.75 (m, 12H, Ar), 7.60–7.45 (m, 4H, Ar), 7.44–7.26 (m, 36H, Ar), 7.26–7.10 (m, 8H, Ar), 5.52 (d, J = 3.6 Hz, 1H, H-2$_{Man}$), 5.45 (app t, J = 8.6 Hz, 1H, H-3$_{Xyl}$), 5.40–5.31 (m, 2H, 2 × H-3$_{Xyl}$), 5.25 (dd, J = 8.8, 7.0 Hz, 1H, H-2$_{Xyl}$), 5.19–5.10 (m, 2H, 2 × H-2$_{Xyl}$), 4.98 (app td, J = 8.9, 5.1 Hz, 1H, H-4$_{Xyl}$), 4.88–4.76 (m, 4H, 2 × PhC$\underline{H}_2$O, 2 × H-2$_{Glc}$), 4.76–4.46 (m, 10H, 5 × PhC$\underline{H}_2$O, 2 × $Cl_3CC\underline{H}_2$O, 3 × H-1$_{Xyl}$), 4.36 (s, 1H, H-1$_{Man}$), 4.32–4.23 (m, 5H, 3 ×

PhC$\underline{H}_2$O, 2 × H-1_{Glc}), 4.07–3.81 (m, 10H), 3.75 (dt, J = 9.4, 6.8 Hz, 1H, 1 × OC$\underline{H}_2(CH_2)_6CH_3$), 3.60–3.42 (m, 5H), 3.38 (dt, J = 9.3, 6.9 Hz, 1H, 1 × OC$\underline{H}_2(CH_2)_6CH_3$), 3.29 (dd, J = 11.2, 3.3 Hz, 1H), 3.27–3.07 (m, 5H), 3.01–2.85 (m, 4H), 2.61–2.46 (m, 4H, 4 × $CH_2C\underline{H}_2C(O)CH_3$), 2.41–2.24 (m, 4H, 4 × $C\underline{H}_2CH_2C(O)CH_3$), 2.14 (s, 3H, $C\underline{H}_3C(O)O$), 2.08 (s, 6H, 6 × $CH_2CH_2C(O)C\underline{H}_3$), 1.54–1.46 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_6CH_3$), 1.32–1.14 (m, 26H, 10 × $OCH_2(C\underline{H}_2)_6CH_3$), 0.86 (t, J = 6.9 Hz, 3H, $OCH_2(CH_2)_6C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 206.0 (C=O), 205.8 (C=O), 170.9 (2 × C=O), 170.7 (C=O), 165.2 (2 × C=O), 165.0 (C=O), 164.9 (2 × C=O), 164.8 (C=O), 153.2 (C=O), 138.8 (Ar), 138.4 (Ar), 138.2 (Ar), 137.9 × 2 (Ar), 133.5 (Ar), 133.2 × 2 (Ar), 132.9 (Ar), 129.9 (Ar), 129.8 (Ar), 129.7 × 3 (Ar), 129.3 (Ar), 129.2 (Ar), 120.0 (Ar), 128.6 × 3 (Ar), 128.5 × 2 (Ar), 128.4 (Ar), 128.3 × 2 (Ar), 128.2 × 2 (Ar), 128.1 (Ar), 128.0 × 3 (Ar), 127.9 × 3 (Ar), 127.7 (Ar), 127.6 (Ar), 127.4 (Ar), 100.9 (C-1_{Glc}), 100.8 (C-1_{Glc}), 100.4 × 2 (C-1_{Xyl}), 100.1 (C-1_{Xyl}), 98.9 (C-1_{Man}), 94.1 ($Cl_3\underline{C}CH_2O$), 80.5 × 2 (C), 78.1, 76.9 ($Cl_3C\underline{C}H_2O$), 76.0, 75.9 × 2 (C), 75.6, 75.3, 75.0, 74.9, 74.4 (Ph$\underline{C}H_2$O), 74.3 (Ph$\underline{C}H_2$O), 74.2, 73.4 × 3 (Ph$\underline{C}H_2$O), 73.2 × 2 (C), 72.9 × 2 (C), 72.8, 72.1, 72.0, 71.8 (Ph$\underline{C}H_2$O), 71.6 (C-3_{Xyl}), 71.2 (C-2_{Xyl}), 69.9 (O$\underline{C}H_2(CH_2)_6CH_3$), 68.5 (C-$6_{Man}$), 68.2 (C-$2_{Man}$), 67.4 (C-$6_{Glc}$), 67.2 (C-$6_{Glc}$), 63.3 (C-$5_{Xyl}$), 63.0 (C-$5_{Xyl}$), 61.7 (C-$5_{Xyl}$), 37.8 ($CH_2\underline{C}H_2C(O)CH_3$), 37.7 ($CH_2\underline{C}H_2C(O)CH_3$), 31.9 (O$\underline{C}H_2(CH_2)_6CH_3$), 29.8 × 2 ($CH_2CH_2C(O)\underline{C}H_3$), 29.4 × 2 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 27.8 ($\underline{C}H_2CH_2C(O)CH_3$), 25.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 21.3 ($\underline{C}H_3C(O)O$), 14.1 ($OCH_2(CH_2)_6\underline{C}H_3$). HRMS (ESI) calcd for $(M + 2Na)^{2+}$ $C_{140}H_{147}Cl_3Na_2O_{41}$: 1317.4134. Found: 1317.4146.



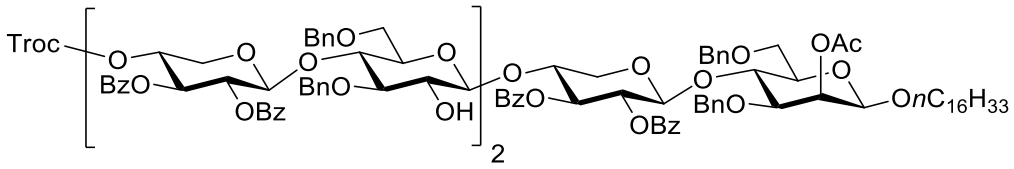
***n*-Hexadecyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.60).** To a flask containing **3.37** (1.03 g, 0.895 mmol) and **3.58** (790 mg, 0.452 mmol) was added CH_2Cl_2 (10 mL) and 4 Å M.S. powder (300 mg) under argon. The flask was then sealed with a rubber septum connected to an argon balloon and the resultant slurry mixture was stirred for 2 h before it was cooled to 0 °C. The mixture was stirred for another 30 min, after which point TfOH (400 μL, 0.090 mmol, 2% v/v in CH_2Cl_2) was added dropwise over 2 min. Upon complete addition of TfOH, the flask was then removed from the ice bath and stirred at room temperature. After 10 h, Et_3N (2 mL) was added and the mixture was passed through a Celite bed. Concentration of the resultant filtrate led to a crude residue that was subsequently purified by silica gel chromatography (8:5 to 7:5 hexanes–EtOAc) to obtain **3.60** (1.04 g, 0.384 mmol, 85%) as a white foamy solid. R_f = 0.18 (2:1 hexanes–EtOAc); $[\alpha]_D$ +1.2 (*c*. 1.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.98–7.75 (m, 12H, Ar), 7.60–7.44 (m, 4H, Ar), 7.42–7.26 (m, 36H, Ar), 7.25–7.11 (m, 8H, Ar), 5.52 (d, *J* = 3.6 Hz, 1H, H-2_{Man}), 5.46 (app t, *J* = 8.6 Hz, 1H, H-3_{Xyl}), 5.40–5.31 (m, 2H, 2 × H-3_{Xyl}), 5.25 (dd, *J* = 8.9, 7.0 Hz, 1H, H-2_{Xyl}), 5.20–5.10 (m, 2H, 2 × H-2_{Xyl}), 4.98 (app td, *J* = 8.8, 5.1 Hz, 1H, H-4_{Xyl}), 4.87–4.76 (m, 4H, 2 × PhC$\underline{H}_2$O, 2 × H-2_{Glc}), 4.76–4.46 (m, 10H, 5 × PhC$\underline{H}_2$O, 2 × $Cl_3CC\underline{H}_2$O, 3 × H-1_{Xyl}), 4.36 (s, 1H, H-1_{Man}), 4.32–4.23 (m, 5H, 3 ×

PhC$\underline{H}_2$O, 2 × H-1_{Glc}), 4.07–3.81 (m, 10H), 3.75 (dt, J = 9.4, 6.8 Hz, 1H, 1 × OC$\underline{H}_2(CH_2)_{14}CH_3$), 3.61–3.42 (m, 5H), 3.38 (dt, J = 9.3, 6.9 Hz, 1H, 1 × OC$\underline{H}_2(CH_2)_{14}CH_3$), 3.30 (dd, J = 11.2, 3.3 Hz, 1H), 3.27–3.08 (m, 5H), 3.01–2.86 (m, 4H), 2.64–2.46 (m, 4H, 4 × $CH_2C\underline{H}_2C(O)CH_3$), 2.41–2.24 (m, 4H, 4 × $C\underline{H}_2CH_2C(O)CH_3$), 2.14 (s, 3H, $C\underline{H}_3C(O)O$), 2.09 (s, 3H, $CH_2CH_2C(O)C\underline{H}_3$), 2.08 (s, 3H, $CH_2CH_2C(O)C\underline{H}_3$), 1.54–1.45 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 1.34–1.15 (m, 26H, 26 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 0.88 (t, J = 6.9 Hz, 3H, $OCH_2(CH_2)_{14}C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 206.0 (C=O), 205.8 (C=O), 170.9 (C=O), 170.8 (C=O), 170.6 (C=O), 165.2 × 2 (C=O), 165.0 (C=O), 164.9 × 2 (C=O), 164.8 (C=O), 153.2 (C=O), 138.7 (Ar), 138.4 (Ar), 138.2 (Ar), 137.9 (Ar), 137.8 (Ar), 133.4 (Ar), 133.2 × 2 (Ar), 132.9 (Ar), 129.8 × 2 (Ar), 129.7 × 2 (Ar), 129.6 (Ar), 129.3 (Ar), 129.2 (Ar), 128.9 (Ar), 128.6 × 2 (Ar), 128.5 × 2 (Ar), 128.4 × 2 (Ar), 128.3 × 2 (Ar), 128.2 × 2 (Ar), 128.1 × 2 (Ar), 128.0 (Ar), 127.9 × 3 (Ar), 127.8 (Ar), 127.6 (Ar), 127.5 (Ar), 127.4 (Ar), 100.9 (C-1_{Glc}), 100.8 (C-1_{Glc}), 100.4 × 2 (C-1_{Xyl}), 100.01 (C-1_{Xyl}), 98.9 (C-1_{Man}), 94.1 ($Cl_3\underline{C}CH_2O$), 80.5 × 2 (C), 78.1, 76.9 ($Cl_3C\underline{C}H_2O$), 76.0, 75.9 × 2 (C), 75.6, 75.2, 74.9 × 2 (C), 74.3 (Ph$\underline{C}H_2O$), 74.2 (Ph$\underline{C}H_2O$), 74.1, 73.4 × 3 (Ph$\underline{C}H_2O$), 73.2 × 2 (C), 72.9 × 2 (C), 72.8, 72.1, 72.0, 71.8 (Ph$\underline{C}H_2O$), 71.6 (C-3_{Xyl}), 71.2 (C-2_{Xyl}), 69.9 ($O\underline{C}H_2(CH_2)_{14}CH_3$), 68.5 (C-$6_{Man}$), 68.2 (C-$2_{Man}$), 67.3 (C-$6_{Glc}$), 67.2 (C-$6_{Glc}$), 63.2 (C-$5_{Xyl}$), 63.0 (C-$5_{Xyl}$), 61.7 (C-$5_{Xyl}$), 37.8 ($CH_2\underline{C}H_2C(O)CH_3$), 37.7 ($CH_2\underline{C}H_2C(O)CH_3$), 31.9 ($O\underline{C}H_2(CH_2)_{14}CH_3$), 29.8 × 2 ($CH_2CH_2C(O)\underline{C}H_3$), 29.7 × 3 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.6 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.4 × 2 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 27.8 ($\underline{C}H_2CH_2C(O)CH_3$), 25.9 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 21.2 ($\underline{C}H_3C(O)O$), 14.1 ($OCH_2(CH_2)_{14}\underline{C}H_3$). HRMS (ESI) calcd for $(M + 2Na)^{2+}$ $C_{148}H_{163}Cl_3Na_2O_{41}$: 1373.476. Found: 1373.4755.



***n*-Octyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.61).** The general procedure for levulinoyl deprotection was carried out on **3.59** (80.6 mg, 31.1 μmol) with H_2NNH_2·HOAc (80 μL, 87.0 μmol, 10% w/v in CH_3OH) in CH_2Cl_2–CH_3OH (2 mL, 10:1). The crude residue was purified by silica gel chromatography (3:2 hexanes–EtOAc) to obtain **3.61** (65.8 mg, 27.5 μmol, 88%) as a white foamy solid. R_f = 0.29 (3:2 hexanes–EtOAc); $[\alpha]_D$ +6.4 (*c*. 0.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.95–7.79 (m, 12H, Ar), 7.58–7.45 (m, 4H, Ar), 7.42–7.26 (m, 30H, Ar), 7.26–7.10 (m, 14H, Ar), 5.55 (d, *J* = 3.4 Hz, 1H, H-2_{Man}), 5.49 (app t, *J* = 8.4 Hz, 1H, H-3_{Xyl}), 5.41 (app t, *J* = 8.5 Hz, 2H, 2 × H-3_{Xyl}), 5.28 (dd, *J* = 8.6, 6.7 Hz, 1H, H-2_{Xyl}), 5.23–5.16 (m, 2H, 2 × H-2_{Xyl}), 5.00 (app td, *J* = 8.5, 5.0 Hz, 1H, H-4_{Xyl}), 4.91–4.86 (m, 2H, 2 × PhC$\underline{H}_2$O), 4.81–4.62 (m, 8H, 2 × $Cl_3CC\underline{H}_2O$, 3 × PhC$\underline{H}_2$O, 3 × H-1_{Xyl}), 4.53–4.45 (m, 2H, 2 × PhC$\underline{H}_2$O), 4.39 (s, 1H, H-1_{Man}), 4.33–4.24 (m, 3H, 3 × PhC$\underline{H}_2$O), 4.19–4.08 (m, 3H, 2 × H-1_{Glc}, H-$5a_{Xyl}$), 4.08–3.91 (m, 7H), 3.89–3.80 (m, 2H), 3.77 (dt, *J* = 9.4, 6.8 Hz, 1H, 1 × OC$\underline{H}_2(CH_2)_6CH_3$), 3.60–3.52 (m, 3H, H-$6a_{Man}$, H-$6b_{Man}$, H-$3_{Man}$), 3.43–3.32 (m, 7H), 3.31–3.24 (m, 2H, H-5_{Man}, H-$5b_{Xyl}$), 3.20–3.09 (m, 4H), 3.07–2.98 (m, 2H), 2.15 (s, 3H, $C\underline{H}_3C(O)O$), 1.56–1.47 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_6CH_3$), 1.34–1.18 (m, 10H, 10 × $OCH_2(C\underline{H}_2)_6CH_3$), 0.92–0.80 (m, 3H, $OCH_2(CH_2)_6C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 170.6 (C=O), 165.4 × 2 (C=O), 165.2 × 2 (C=O), 165.1 (C=O), 164.9

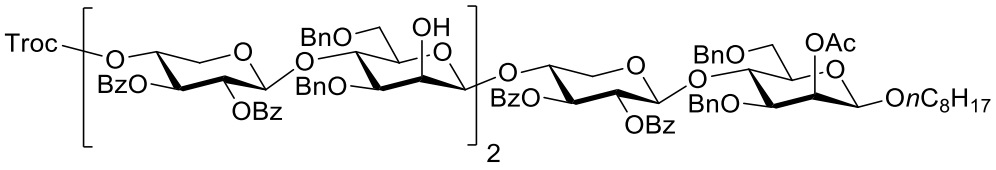
(C=O), 153.2 (C=O), 138.9 (Ar), 138.7 (Ar), 138.3 (Ar), 138.0 (Ar), 137.9 (Ar), 137.8 (Ar), 133.5 × 2 (Ar), 133.0 (Ar), 129.9 (Ar), 129.8 × 2 (Ar), 129.7 (Ar), 129.6 (Ar), 129.3 (Ar), 129.2 (Ar), 129.0 (Ar), 128.5 × 3 (Ar), 128.4 × 3 (Ar), 128.2 × 2 (Ar), 128.0 (Ar), 127.9 × 3 (Ar), 127.8 × 3 (Ar), 127.7 × 2 (Ar), 127.6 (Ar), 101.9 × 2 (C-1_{Glc}), 100.5 (C-1_{Xyl}), 100.4 (C-1_{Xyl}), 100.0 (C-1_{Xyl}), 98.9 (C-1_{Man}), 94.1 ($Cl_3\underline{C}CH_2O$), 82.3 × 2 (C), 78.4 (C-3_{Man}), 76.9 ($Cl_3C\underline{C}H_2O$), 75.9 × 2 (C), 75.3, 75.1 × 2 (C), 74.8 ($Ph\underline{C}H_2O$), 74.7 ($Ph\underline{C}H_2O$), 74.4, 74.2 × 2 (C), 73.6, 73.5 × 2 (C), 73.4 × 2 ($Ph\underline{C}H_2O$), 73.3 (2 × $Ph\underline{C}H_2O$), 73.2 (C-4_{Xyl}), 72.9, 72.7 × 2 (C), 71.8 × 2 (C), 71.7 ($Ph\underline{C}H_2O$), 71.4 (C-3_{Xyl}), 71.1 (C-2_{Xyl}), 69.9 ($O\underline{C}H_2(CH_2)_6CH_3$), 68.7 (C-$6_{Man}$), 68.1 (C-$2_{Man}$), 67.6 × 2 (C-$6_{Glc}$), 63.1 (C-$5_{Xyl}$), 62.9 (C-$5_{Xyl}$), 61.5 (C-$5_{Xyl}$), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 × 2 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 25.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 21.2 ($\underline{C}H_3C(O)O$), 14.1 ($OCH_2(CH_2)_6\underline{C}H_3$). HRMS-MALDI-TOF calcd for $(M + Na)^+$ $C_{130}H_{135}Cl_3NaO_{37}$: 2415.76400 Found: 2415.76573.



***n*--Hexadecyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.62).** The general procedure for levulinoyl deprotection was carried out on **3.60** (150 mg, 56.0 μmol) with H_2NNH_2·HOAc (151 μL, 164 μmol, 10% w/v in CH_3OH) in CH_2Cl_2–CH_3OH (3 mL, 10:1). The crude residue was

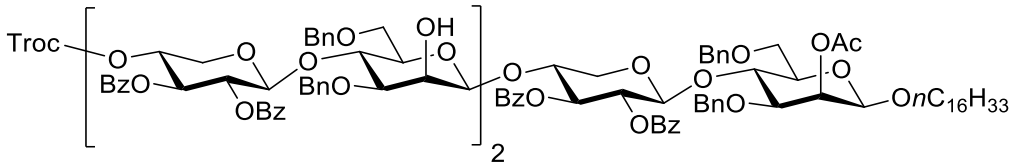
purified by silica gel chromatography (3:2 hexanes–EtOAc) to obtain **3.62** (110 mg, 44.0 μmol, 80%) as a white foamy solid. R_f = 0.41 (8:5 to 3:2 hexanes–EtOAc); $[\alpha]_D$ +15.5 (*c*. 0.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.99–7.80 (m, 12H, Ar), 7.59–7.45 (m, 4H, Ar), 7.41–7.26 (m, 30H, Ar), 7.26–7.13 (m, 14H, Ar), 5.55 (d, *J* = 3.4 Hz, 1H, H-2$_{Man}$), 5.49 (app t, *J* = 8.4 Hz, 1H, H-3$_{Xyl}$), 5.41 (app t, *J* = 8.5 Hz, 2H, 2 × H-3$_{Xyl}$), 5.28 (dd, *J* = 8.6, 6.7 Hz, 1H, H-2$_{Xyl}$), 5.24–5.15 (m, 2H, 2 × H-2$_{Xyl}$), 5.00 (app td, *J* = 8.5, 5.0 Hz, 1H, H-4$_{Xyl}$), 4.91–4.85 (m, 2H, 2 × PhC$\underline{H}_2$O), 4.82–4.63 (m, 8H, 2 × $Cl_3CC\underline{H}_2O$, 3 × PhC$\underline{H}_2$O, 3 × H-1$_{Xyl}$), 4.53–4.45 (m, 2H, 2 × PhC$\underline{H}_2$O), 4.39 (s, 1H, H-1$_{Man}$), 4.34–4.25 (m, 3H, 3 × PhC$\underline{H}_2$O), 4.20–4.09 (m, 3H, 2 × H-1, H-5a$_{Xyl}$), 4.08–3.91 (m, 7H), 3.89–3.80 (m, 2H), 3.77 (dt, *J* = 9.4, 6.8 Hz, 1H, 1 × OC$\underline{H}_2(CH_2)_{14}CH_3$), 3.62–3.52 (m, 3H, H-6a$_{Man}$, H-6b$_{Man}$, H-3$_{Man}$), 3.44–3.32 (m, 7H), 3.31–3.24 (m, 2H, H-5$_{Man}$, H-5b$_{Xyl}$), 3.20–3.09 (m, 4H), 3.06–2.99 (m, 2H), 2.20 (br s, OH), 2.16 (br s, OH), 2.15 (s, 3H, C$\underline{H}_3$C(O)O), 1.57–1.49 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 1.34–1.18 (m, 26H, 26 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 0.88 (m, 3H, *J* = 6.9 Hz, $OCH_2(CH_2)_{14}C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 170.6 (C=O), 165.4 × 2 (C=O), 165.2 × 2 (C=O), 165.1 (C=O), 164.9 (C=O), 153.2 (C=O), 138.9 (Ar), 138.7 (Ar), 138.3 (Ar), 138.0 (Ar), 137.9 (Ar), 137.8 (Ar), 133.5 × 2 (Ar), 133.0 (Ar), 129.9 (Ar), 129.8 × 2 (Ar), 129.7 (Ar), 129.6 (Ar), 129.3 (Ar), 129.2 (Ar), 129.0 (Ar), 128.5 × 3 (Ar), 128.4 × 3 (Ar), 128.2 × 2 (Ar), 128.0 (Ar), 127.9 × 4 (Ar), 127.8 × 3 (Ar), 127.7 × 2 (Ar), 127.6 (Ar), 101.9 × 2 (C-1$_{Glc}$), 100.5 (C-1$_{Xyl}$), 100.4 (C-1$_{Xyl}$), 100.0 (C-1$_{Xyl}$), 98.9 (C-1$_{Man}$), 94.1 ($Cl_3\underline{C}CH_2O$), 82.3 × 2 (C), 78.4 (C-3$_{Man}$), 76.9 ($Cl_3C\underline{C}H_2O$), 75.9 × 2 (C), 75.3, 75.1 × 2 (C), 74.8 (Ph$\underline{C}H_2O$), 74.7 (Ph$\underline{C}H_2O$), 74.4, 74.2 × 2 (C), 73.6, 73.5 × 2 (C), 73.4 × 2 (Ph$\underline{C}H_2O$), 73.3 (2 × Ph$\underline{C}H_2O$), 73.2 (C-4$_{Xyl}$), 72.9, 72.7 × 2 (C), 71.8 × 2 (C), 71.7 (Ph$\underline{C}H_2O$), 71.4 (C-3$_{Xyl}$), 71.1 (C-2$_{Xyl}$), 69.9 (O$\underline{C}H_2(CH_2)_{14}CH_3$), 68.7 (C-6$_{Man}$), 68.1 (C-2$_{Man}$), 67.6 × 2 (C-6$_{Glc}$), 63.1 (C-5$_{Xyl}$), 62.9 (C-5$_{Xyl}$), 61.5 (C-5$_{Xyl}$), 32.0 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.7 × 4 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.6 × 4

($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.4 × 2 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 25.9 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 21.2 ($\underline{C}H_3C(O)O$), 14.2 ($OCH_2(CH_2)_{14}\underline{C}H_3$). HRMS (ESI) calcd for (M + $2(NH_4)$)$^{2+}$ $C_{138}H_{151}Cl_3N_2O_{37}$: 1270.4838. Found: 1270.4831.



***n*-Octyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.63).** Approach B for C-2 inversion was carried out on **3.61** (127 mg, 52.8 μmol). In this approach, DMP (137 mg, 324 μmol) and H_2O (3.0 μL, 2 μmol) were used for oxidation in CH_2Cl_2 (2 mL); subsequent reduction was conducted on the crude diketone with LTBA (41.4 mg, 163 μmol) in THF (1 mL). The resultant crude residue was purified by silica gel chromatography (1:1 to 5:6 hexanes–EtOAc) to afford **3.63** (91.4 mg, 38.2 μmol, 72%) as a white solid. R_f = 0.20 (5:6 hexanes–EtOAc); $[\alpha]_D$ –0.1 (*c*. 0.2, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.00–7.81 (m, 12H, Ar), 7.57–7.46 (m, 4H, Ar), 7.44–7.26 (m, 33H, Ar), 7.25–7.10 (m, 11H, Ar), 5.54 (d, *J* = 3.6 Hz, 1H, H-2_{Man}), 5.49 (app t, *J* = 8.1 Hz, 1H, H-3_{Xyl}), 5.38–5.23 (m, 5H, 2 × H-3_{Xyl}, 3 × H-2_{Xyl}), 5.01 (app td, *J* = 8.0, 4.8 Hz, 1H, H-4_{Xyl}), 4.81–4.63 (m, 10H, 2 × $Cl_3CC\underline{H}_2O$, 5 × $PhC\underline{H}_2O$, 3 × H-1_{Xyl}), 4.56–4.51 (m, 2H, 2 × $PhC\underline{H}_2O$), 4.38 (s, 2H, 2 × H-1_{Man}), 4.33 (s, 1H, H-1_{Man}), 4.32–4.27 (m, 1H, 1 × $PhC\underline{H}_2O$), 4.18 (dd, *J* = 12.3, 4.8 Hz, 1H), 4.15–4.01 (m, 5H), 4.01–3.88 (m, 8H), 3.77 (dt, *J* = 9.5, 6.8 Hz, 1H, 1

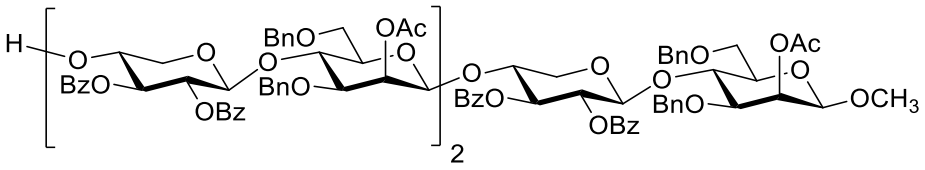
× $OC\underline{H}_2(CH_2)_6CH_3$), 3.66–3.49 (m, 3H, H-6a$_{Man}$, H-6b$_{Man}$, H-3$_{Man}$), 3.44–3.35 (m, 3H), 3.35–3.22 (m, 4H), 3.21–3.05 (m, 6H), 2.51–2.43 (m, 2H, 2 × OH), 2.16 (s, 3H, $C\underline{H}_3C(O)O$), 1.57–1.49 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_6CH_3$), 1.32–1.20 (m, 10H, 10 × $OCH_2(C\underline{H}_2)_6CH_3$), 0.87 (t, J = 6.9 Hz, 3H, $OCH_2(CH_2)_6C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 170.6 (C=O), 166.4 (C=O), 166.3 (C=O), 165.2 (C=O), 165.1 × 2 (C=O), 165.0 (C=O), 153.2 (C=O), 138.3 (Ar), 138.2 × 3 (Ar), 138.0 (Ar), 137.9 (Ar), 133.4 × 2 (Ar), 133.3 (Ar), 133.0 (Ar), 129.9 × 2 (Ar), 129.8 (Ar), 129.7 × 2 (Ar), 129.2 × 2 (Ar), 129.0 × 2 (Ar), 128.5 × 2 (Ar), 128.4 × 3 (Ar), 128.3 (Ar), 128.2 × 2 (Ar), 128.0 (Ar), 127.9 × 2 (Ar), 127.8 × 2 (Ar), 127.7 × 3 (Ar), 127.6 × 2 (Ar), 127.5 (Ar), 100.8 (C-1$_{Xyl}$), 100.6 (C-1$_{Xyl}$), 100.1 (C-1$_{Xyl}$), 98.9 (C-1$_{Man}$), 97.2 × 2 (C-1$_{Man}$), 94.1 ($Cl_3\underline{C}CH_2O$), 79.5, 79.2 × 2 (C), 78.2 (C-3$_{Man}$), 76.9 ($Cl_3C\underline{C}H_2O$), 75.2, 75.1, 74.3, 74.2, 74.1, 73.4 ($Ph\underline{C}H_2O$), 73.3 (C-4$_{Xyl}$), 73.1, 72.9 × 3 (C), 72.3 ($Ph\underline{C}H_2O$), 72.0 ($Ph\underline{C}H_2O$), 71.8 ($Ph\underline{C}H_2O$), 71.6 × 2 (C), 71.2 (C-3$_{Xyl}$), 70.9 (C-2$_{Xyl}$), 69.9 ($O\underline{C}H_2(CH_2)_6CH_3$), 68.8, 68.5 (C-6$_{Man}$), 68.4 (C-6$_{Man}$), 68.3 × 2 (C), 68.2 (C-2$_{Man}$), 62.8 (C-5$_{Xyl}$), 62.6 (C-5$_{Xyl}$), 61.3 (C-5$_{Xyl}$), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 25.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 21.2 ($CH_3C(O)O$), 14.1 ($OCH_2(CH_2)_6\underline{C}H_3$). HRMS-MALDI-TOF calcd for $(M + Na)^+$ $C_{130}H_{135}Cl_3NaO_{37}$: 2415.76400. Found: 2415.76573.



***n*-Hexadecyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-**

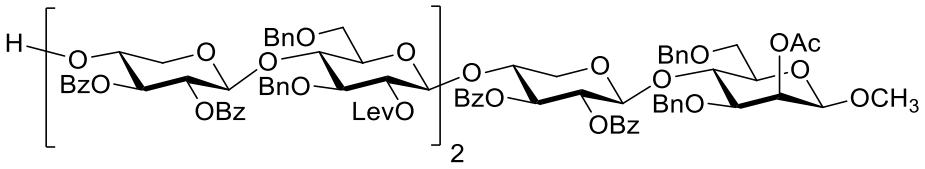
(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.64). Approach B for C-2 inversion was carried out on **3.62** (105 mg, 41.9 μmol). In this approach, DMP (110 mg, 260 μmol) and H_2O (2 μL, 100 μmol) were used for oxidation in CH_2Cl_2 (2 mL); subsequent reduction was conducted on the crude diketone with LTBA (26.9 mg, 106 μmol) in THF (1 mL). The resultant crude residue was purified by silica gel chromatography (1:1 hexanes–EtOAc) to afford **3.64** (78.8 mg, 31.0 μmol, 75%) as a white amorphous solid. R_f = 0.31 (1:1 hexanes–EtOAc); $[\alpha]_D$ +4.9 (*c*. 0.2, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.00–7.80 (m, 12H, Ar), 7.55–7.46 (m, 4H, Ar), 7.44–7.26 (m, 33H, Ar), 7.25–7.10 (m, 11H, Ar), 5.54 (d, *J* = 3.5 Hz, 1H, H-2_{Man}), 5.49 (app t, *J* = 8.1 Hz, 1H, H-3_{Xyl}), 5.38–5.23 (m, 5H, 2× H-3_{Xyl}, 3 × H-2_{Xyl}), 5.01 (app td, *J* = 8.0, 4.8 Hz, 1H, H-4_{Xyl}), 4.80–4.63 (m, 10H, 2 × $Cl_3CC\underline{H}_2O$, 5 × $PhC\underline{H}_2O$, 3 × H-1_{Xyl}), 4.56–4.49 (m, 2H, 2 × $PhC\underline{H}_2O$), 4.38 (s, 2H, 2 × H-1_{Man}), 4.33 (s, 1H, H-1_{Man}), 4.31–4.27 (m, 1H, 1 × $PhC\underline{H}_2O$), 4.18 (dd, *J* = 12.3, 4.8 Hz, 1H), 4.15–4.01 (m, 5H), 4.01–3.87 (m, 8H), 3.76 (dt, *J* = 9.5, 6.8 Hz, 1H, 1 × $OC\underline{H}_2(CH_2)_{14}CH_3$), 3.65–3.49 (m, 3H, H-$6a_{Man}$, H-$6b_{Man}$, H-$3_{Man}$), 3.44–3.35 (m, 3H), 3.35–3.22 (m, 4H), 3.21–3.05 (m, 6H), 2.53–2.40 (m, 2H, 2 × OH), 2.16 (s, 3H, $C\underline{H}_3C(O)O$), 1.56–1.48 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 1.35–1.18 (m, 26H, 26 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 0.88 (t, *J* = 6.9 Hz, 3H, $OCH_2(CH_2)_{14}C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 170.6 (C=O), 166.4 (C=O), 166.3 (C=O), 165.2 (C=O), 165.1 × 2 (C=O), 165.0 (C=O), 153.2 (C=O), 138.3 (Ar), 138.2 × 3 (Ar), 138.0 (Ar), 137.9 (Ar), 133.5 (Ar), 133.4 (Ar), 133.3 (Ar), 133.0 (Ar), 129.9 × 2 (Ar), 129.8 (Ar), 129.7 × 2 (Ar), 129.2 × 2 (Ar), 129.1 (Ar), 129.0 (Ar), 128.5 × 2 (Ar), 128.4 × 3 (Ar), 128.3 (Ar), 128.2 (Ar), 128.0 (Ar), 127.9 × 3 (Ar), 127.8 × 2 (Ar), 127.7 × 3 (Ar), 127.6 × 2 (Ar), 100.8 (C-1_{Xyl}), 100.6 (C-1_{Xyl}), 100.2 (C-1_{Xyl}), 98.9 (C-1_{Man}), 97.2 × 2 (C-1_{Man}), 94.1 ($Cl_3\underline{C}CH_2O$), 79.5, 79.2 × 2 (C), 78.2 (C-3_{Man}), 76.9 ($Cl_3C\underline{C}H_2O$), 75.3, 75.1 ×

2 (C), 74.3, 74.2, 74.1 × 2 (C), 73.4 (Ph<u>C</u>H_2O), 73.3 (C-4_{Xyl}), 73.1, 72.9 × 3 (C), 72.3 (Ph<u>C</u>H_2O), 72.0 (Ph<u>C</u>H_2O), 71.8 (Ph<u>C</u>H_2O), 71.6 × 2 (C), 71.2 (C-3_{Xyl}), 70.9 (C-2_{Xyl}), 69.9 (O<u>C</u>H_2(CH_2)$_{14}$$CH_3$), 68.8, 68.5 (C-$6_{Man}$), 68.4 (C-$6_{Man}$), 68.3 × 2 (C), 68.2 (C-2_{Man}), 62.8 (C-5_{Xyl}), 62.6 (C-5_{Xyl}), 61.3 (C-5_{Xyl}), 32.0 (OCH_2(<u>C</u>H_2)$_{14}$$CH_3$), 29.7 × 3 (OC$H_2$(<u>C</u>$H_2$)$_{14}$$CH_3$), 29.6 × 2 (OC$H_2$(<u>C</u>$H_2$)$_{14}$$CH_3$), 29.4 × 2 (OC$H_2$(<u>C</u>$H_2$)$_{14}$$CH_3$), 25.9 (OC$H_2$(<u>C</u>$H_2$)$_{14}$$CH_3$), 22.7 (OC$H_2$(<u>C</u>$H_2$)$_{14}$$CH_3$), 21.3 (<u>C</u>$H_3$C(O)O), 14.2 (OC$H_2$($CH_2$)$_{14}$<u>C</u>$H_3$). HRMS (ESI) calcd for (M + 2(NH_4))$^{2+}$ $C_{138}H_{151}Cl_3N_2O_{37}$: 1270.4838. Found: 1270.4831.



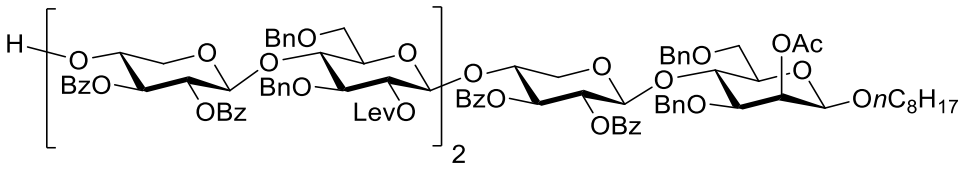
Methyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.65). To a solution of **3.50** (12.5 mg, 5.44 μmol) in pyridine (2 mL) was added Ac_2O (0.40 mL) and DMAP (1 mg, 8.0 μmol) under argon. The reaction mixture was stirred at 40 °C overnight and cooled to room temperature; pyridine was then removed via co-evaporation with toluene (2x). The crude material was re-dissolved in CH_2Cl_2 and subsequently washed with 1 M aqueous HCl and brine before it was dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a crude syrup that was then subjected to Troc deprotection using the general procedure with Zn powder (17.8 mg, 272 μmol) in glacial AcOH (2 mL). The crude residue was

purified by silica gel chromatography (1:1 to 5:6 hexanes–EtOAc) to obtain **3.65** (9.8 mg, 4.4 μmol, 82%) as a white foamy solid. R_f = 0.21 (1:1 hexanes–EtOAc); $[\alpha]_D$ +3.0 (*c*. 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.99–7.93 (m, 2H, Ar), 7.92–7.82 (m, 10H, Ar), 7.58–7.45 (m, 4H, Ar), 7.41–7.27 (m, 32H, Ar), 7.25–7.11 (m, 12H, Ar), 5.52 (d, *J* = 3.5 Hz, 1H, H-2$_{Man}$), 5.47 (d, *J* = 3.3 Hz, 1H, H-2$_{Man}$), 5.43 (d, *J* = 3.4 Hz, 1H, H-2$_{Man}$), 5.37–5.28 (m, 3H), 5.23–5.17 (m, 2H), 5.08 (app t, *J* = 8.5 Hz, 1H), 4.77–4.68 (m, 4H, 3 × PhC$\underline{H}_2$O, H-1$_{Xyl}$), 4.67–4.62 (m, 2H, 2 × H-1$_{Xyl}$), 4.58–4.49 (m, 4H, 4 × PhC$\underline{H}_2$O), 4.39 (s, 1H, H-1$_{Man}$), 4.37 (s, 1H, H-1$_{Man}$), 4.36–4.23 (m, 4H, 1 × PhC$\underline{H}_2$O, H-1$_{Man}$), 4.09–3.88 (m, 11H), 3.61 (dd, *J* = 11.0, 4.5 Hz, 1H, H-6a$_{Man}$), 3.58–3.53 (m, 1H, H-6b$_{Man}$), 3.53–3.27 (m, 10H), 3.25–3.19 (m, 1H, H-5$_{Man}$), 3.17–3.00 (m, 5H), 2.94 (br s, 1H, OH), 2.93 (br s, 1H, OH), 2.16 (s, 3H, C$\underline{H}_3$C(O)O), 1.92 (s, 3H, C$\underline{H}_3$C(O)O), 1.91 (s, 3H, C$\underline{H}_3$C(O)O). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 170.8 (C=O), 170.5 (C=O), 167.5 (C=O), 165.4 × 2 (C=O), 165.2 (C=O), 165.1 × 2 (C=O), 138.2 (Ar), 138.1 (Ar), 137.8 × 2 (Ar), 137.7 (Ar), 133.7 (Ar), 133.5 (Ar), 133.3 (Ar), 132.9 (Ar), 130.0 (Ar), 129.9 × 2 (Ar), 129.8 × 2 (Ar), 129.7 (Ar), 129.3 × 2 (Ar), 129.2 × 2 (Ar), 128.9 (Ar), 128.6 (Ar), 128.5 × 2 (Ar), 128.4 × 3 (Ar), 128.2 × 2 (Ar), 128.0 (Ar), 127.9 × 2 (Ar), 127.8 × 3 (Ar), 127.7 × 2 (Ar), 100.7 (C-1$_{Xyl}$), 100.6 (C-1$_{Xyl}$), 100.4 (C-1$_{Xyl}$), 100.0 (C-1$_{Man}$), 96.5 × 2 (C-1$_{Man}$), 78.0 , 77.9, 77.6, 77.0 (C-3$_{Xyl}$), 75.5 × 2 (C), 75.3 (C-5$_{Man}$), 74.0, 73.8, 73.7, 73.4 (Ph$\underline{C}H_2$O), 73.3 × 2 (Ph$\underline{C}H_2$O), 72.8, 72.7, 72.0 × 3 (C), 71.9 (Ph$\underline{C}H_2$O), 71.3, 69.3, 68.3 (C-6$_{Man}$), 68.1 (C-2$_{Man}$), 68.0 × 2 (C-6$_{Man}$), 67.9 (C-2$_{Man}$), 67.7 (C-2$_{Man}$), 65.2 (C-5$_{Xyl}$), 62.5 × 2 (C-5$_{Xyl}$), 57.1 (OCH_3), 21.3 ($\underline{C}H_3$C(O)O), 20.8 × 2 ($\underline{C}H_3$C(O)O). LRMS-MALDI-TOF calcd for $(M + Na)^+$ $C_{124}H_{124}NaO_{37}$: 2227.8. Found: 2227.4.



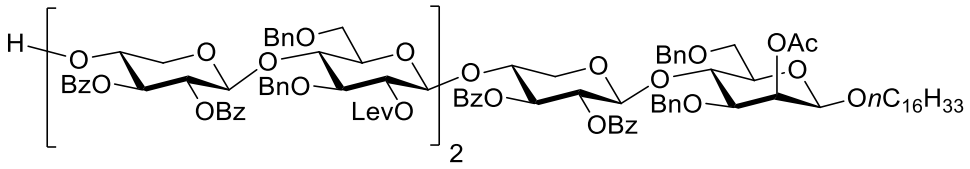
Methyl 2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.66). The general procedure for Troc deprotection was conducted on **3.47** (365 mg, 0.146 mmol) using Zn powder (449 mg, 6.86 mmol) in glacial AcOH (10 mL). The crude residue was purified by silica gel chromatography (5:6 to 5:7 hexanes–EtOAc), to afford **3.66** (282 mg, 0.121 mmol, 83%) as a white fluffy solid. R_f = 0.25 (5:7 hexanes–EtOAc); $[\alpha]_D$ +4.4 (*c*. 0.8, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.96–7.89 (m, 2H, Ar), 7.90–7.75 (m, 10H, Ar), 7.58–7.44 (m, 4H, Ar), 7.41–7.26 (m, 33H, Ar), 7.26–7.10 (m, 11H, Ar), 5.52 (d, *J* = 3.5 Hz, 1H, H-2_{Man}), 5.39–5.31 (m, 2H, 2 × H-3_{Xyl}), 5.27 (dd, *J* = 9.3, 7.5 Hz, 1H, H-2_{Xyl}), 5.19–5.10 (m, 2H, 2 × H-2_{Xyl}), 5.03 (app t, *J* = 8.6 Hz, 1H, H-3_{Xyl}), 4.90–4.76 (m, 4H, 2 × H-2_{Glc}, 2 × PhC$\underline{H}_2$O), 4.75–4.66 (m, 2H, 2 × PhC$\underline{H}_2$O), 4.60 (d, *J* = 7.5 Hz, 1H, H-1_{Xyl}), 4.59–4.49 (m, 5H), 4.33–4.23 (m, 6H, H-1_{Man}, 2 × H-1_{Glc}, 3 × PhC$\underline{H}_2$O), 4.07–3.79 (m, 12H), 3.59 (dd, *J* = 10.9, 4.4 Hz, 1H, H-$6a_{Man}$), 3.57–3.43 (m, 4H), 3.42 (s, 3H, OCH_3), 3.33–3.27 (m, 1H), 3.27–3.20 (m, 2H), 3.19–3.04 (m, 3H), 3.00–2.85 (m, 5H), 2.63–2.44 (m, 4H, 4 × $CH_2C\underline{H}_2C(O)CH_3$), 2.42–2.23 (m, 4H, 4 × $C\underline{H}_2CH_2C(O)CH_3$), 2.15 (s, 3H, $C\underline{H}_3C(O)O$), 2.08 (s, 6H, $CH_2CH_2C(O)C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 206.1 (C=O), 205.9 (C=O), 170.9 (C=O), 170.8 (C=O), 167.6 (C=O), 165.2 (C=O), 165.1 (C=O), 165.0 (C=O), 164.9 × 2 (C=O), 138.8, 138.5, 138.1, 138.0, 137.9, 137.8, 133.7, 133.4, 133.3 × 2 (Ar), 132.9, 130.0, 129.9, 129.8, 129.7 × 2 (Ar), 129.3, 129.2, 129.1, 128.8, 128.6 × 2 (Ar), 128.5 × 3 (Ar),

128.4 × 2 (Ar), 128.2 × 3 (Ar), 128.1, 128.0 × 2 (Ar), 127.9, 127.7, 127.5, 127.4, 100.9 × 2 (C-1_{Glc}), 100.4 × 2 (C-1_{Xyl}), 100.0 (C-1_{Man}), 80.5 × 2 (C), 77.9, 77.4 (H-3_{Xyl}), 76.0, 75.9, 75.6, 75.3, 75.0 × 2 (C), 74.5, 74.3, 74.0, 73.4 × 2 (C), 73.2, 72.9 × 2 (C), 72.8, 72.2, 72.0, 71.9, 71.4 (C-2_{Xyl}), 69.5, 68.3 (C-6_{Man}), 68.1 (C-2_{Man}), 67.3 (C-6_{Glc}), 67.2 (C-6_{Glc}), 65.4 (C-5_{Xyl}), 63.3 (C-5_{Xyl}), 63.0 (C-5_{Xyl}), 57.1 (OCH_3), 37.8 ($CH_2\underline{C}H_2C(O)CH_3$), 37.7 ($CH_2\underline{C}H_2C(O)CH_3$), 29.8 ($CH_2CH_2C(O)\underline{C}H_3$), 29.8 ($CH_2CH_2C(O)\underline{C}H_3$), 27.8 × 2 ($\underline{C}H_2CH_2C(O)CH_3$), 21.2 ($\underline{C}H_3C(O)O$). HRMS (ESI) calcd for $(M+2(NH_4))^{2+}$ $C_{130}H_{140}N_2O_{39}$: 1176.4511. Found: 1176.4519.



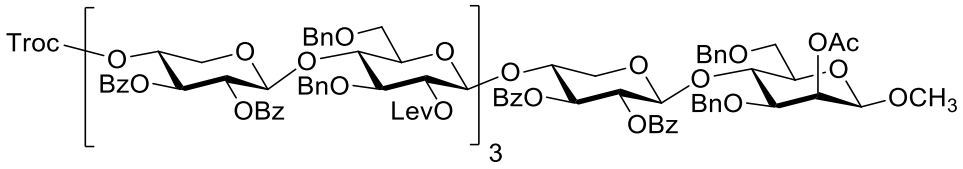
***n*-Octyl 2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.67).** The general procedure for Troc deprotection was conducted on **3.59** (326 mg, 126 μmol) using Zn powder (352 mg, 5.38 mmol) in glacial AcOH (10 mL). The crude residue was purified by silica gel chromatography (6:5 hexanes–EtOAc), to afford **3.67** (254 mg, 105 μmol, 83%) as a white fluffy solid. R_f = 0.30 (6:5 hexanes–EtOAc); $[\alpha]_D$ +2.8 (*c*. 0.2, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$, δ_H) 7.96–7.90 (m, 2H, Ar), 7.90–7.78 (m, 10H, Ar), 7.58–7.45 (m, 4H, Ar), 7.41–7.27 (m, 33H, Ar), 7.24–7.11 (m, 11H, Ar), 5.52 (d, *J* = 3.5 Hz, 1H, H-2_{Man}), 5.41–5.31 (m, 2H, 2 × H-3_{Xyl}), 5.27 (dd, *J* = 9.3, 7.5 Hz, 1H, H-2_{Xyl}), 5.20–5.10 (m, 2H, 2 × H-2_{Xyl}), 5.03 (app t, *J* = 8.6 Hz, 1H, H-3_{Xyl}), 4.89–4.76 (m,

4H, 2 × H-2$_{Glc}$, 2 × PhC$\underline{H}_2$O), 4.76–4.68 (m, 2H, 2 × PhC$\underline{H}_2$O), 4.61 (d, J = 7.5 Hz, 1H, H-1$_{Xyl}$), 4.59–4.47 (m, 5H), 4.36 (s, 1H, H-1$_{Man}$), 4.33–4.23 (m, 5H, 2 × H-1$_{Glc}$, 3 × PhC$\underline{H}_2$O), 4.04–3.80 (m, 12H), 3.76 (dt, J = 9.3, 6.8 Hz, 1H, 1 × OC$\underline{H}_2$(CH$_2$)$_6$CH$_3$), 3.61–3.42 (m, 5H), 3.38 (dt, J = 9.3, 6.9 Hz, 1H, 1 × OC$\underline{H}_2$(CH$_2$)$_6$CH$_3$), 3.33–3.27 (m, 1H), 3.27–3.20 (m, 2H), 3.20–3.06 (m, 3H), 3.00–2.86 (m, 5H), 2.62–2.47 (m, 4H, 4 × CH$_2$C$\underline{H}_2$C(O)CH$_3$), 2.41–2.25 (m, 4H, 4 × C$\underline{H}_2$CH$_2$C(O)CH$_3$), 2.14 (s, 3H, C$\underline{H}_3$C(O)O), 2.08 (s, 6H, CH$_2$CH$_2$C(O)C$\underline{H}_3$), 1.53–1.47 (m, 2H, 2 × OCH$_2$(C$\underline{H}_2$)$_6$CH$_3$), 1.34–1.23 (m, 10H, 10 × OCH$_2$(C$\underline{H}_2$)$_6$CH$_3$), 0.86 (t, J = 6.9 Hz, 4H, OCH$_2$(CH$_2$)$_6$C$\underline{H}_3$). ^{13}C NMR (125 MHz, CDCl$_3$, δ_C) 206.0 (C=O), 205.9 (C=O), 170.9 × 2 (C=O), 170.7 (C=O), 167.6 (C=O), 165.2 (C=O), 165.0 (2 × C=O), 164.9 × 2 (C=O), 138.8, 138.5, 138.2, 138.0, 137.9, 133.7, 133.4, 133.3, 133.2, 132.9 × 2 (Ar), 130.0, 129.9, 129.8, 129.7 × 2 (Ar), 129.3, 129.2, 129.1, 128.8, 128.6, 128.5 × 3 (Ar), 128.4 × 2 (Ar), 128.3, 128.2 × 4 (Ar), 128.1, 128.0, 127.9 × 2 (Ar), 127.8, 127.7 × 2 (Ar), 127.5, 127.4, 100.8 × 2 (C-1$_{Glc}$), 100.4 × 2 (C-1$_{Xyl}$), 98.9 (C-1$_{Man}$), 80.5 × 2 (C), 78.1, 77.4 (C-3$_{Xyl}$), 76.0, 75.9, 75.6, 75.3, 74.9 × 2 (C), 74.4, 74.3, 74.1, 73.4 × 3 (C), 73.2, 72.9 × 2 (C), 72.8, 72.2, 72.0, 71.8, 71.4 (C-2$_{Xyl}$), 69.9 (O$\underline{C}$H$_2$(CH$_2$)$_6$CH$_3$) 69.5, 68.5 (C-6$_{Man}$), 68.2 (C-2$_{Man}$), 67.3 (C-6$_{Glc}$), 67.2 (C-6$_{Glc}$), 65.4 (C-5$_{Xyl}$), 63.3 (C-5$_{Xyl}$), 63.0 (C-5$_{Xyl}$), 37.8 (CH$_2$$\underline{C}H_2$C(O)CH$_3$), 37.7 (CH$_2$$\underline{C}H_2$C(O)CH$_3$), 31.8 (OCH$_2$($\underline{C}H_2$)$_6CH_3$), 29.8 (CH$_2CH_2$C(O)$\underline{C}H_3$), 29.4 (OCH$_2$($\underline{C}H_2$)$_6CH_3$), 29.3 (OCH$_2$($\underline{C}H_2$)$_6CH_3$), 29.2 (OCH$_2$($\underline{C}H_2$)$_6CH_3$), 27.8 × 2 ($\underline{C}H_2CH_2$C(O)CH$_3$), 25.9 (OCH$_2$($\underline{C}H_2$)$_6CH_3$), 22.7 (OCH$_2$($\underline{C}H_2$)$_6CH_3$), 21.2 (CH$_3$C(O)O), 14.1 (OCH$_2$(CH$_2$)$_6$$\underline{C}H_3$). HRMS-MALDI-TOF calcd for (M + Na)$^+$ C$_{137}$H$_{146}$NaO$_{39}$: 2437.93335. Found: 2437.92958.



***n*-Hexadecyl 2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.68).** The general procedure for Troc deprotection was conducted on **3.60** (716 mg, 0.265 mmol) using Zn powder (922 mg, 14.1 mmol) in glacial AcOH (20 mL). The crude residue was purified by silica gel chromatography (6:5 to 1:1 hexanes–EtOAc), to afford **3.68** (529 mg, 0.209 mmol, 88%) as a white fluffy solid. R_f = 0.30 (6:5 hexanes–EtOAc); $[\alpha]_D$ +3.2 (*c*. 1.4, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$, δ_H) 7.96–7.91 (m, 2H, Ar), 7.90–7.75 (m, 10H, Ar), 7.58–7.45 (m, 4H, Ar), 7.41–7.27 (m, 33H, Ar), 7.24–7.11 (m, 11H, Ar), 5.52 (d, *J* = 3.5 Hz, 1H, H-2_{Man}), 5.39–5.31 (m, 2H, 2 × H-3_{Xyl}), 5.27 (dd, *J* = 9.3, 7.5 Hz, 1H, H-2_{Xyl}), 5.20–5.10 (m, 2H, 2 × H-2_{Xyl}), 5.03 (app t, *J* = 8.6 Hz, 1H, H-3_{Xyl}), 4.88–4.76 (m, 4H, 2 × H-2_{Glc}, 2 × PhC$\underline{H}_2$O), 4.76–4.68 (m, 2H, 2 × PhC$\underline{H}_2$O), 4.60 (d, *J* = 7.5 Hz, 1H, H-1_{Xyl}), 4.59–4.47 (m, 5H), 4.36 (s, 1H, H-1_{Man}), 4.33–4.23 (m, 5H, 2 × H-1_{Glc}, 3 × PhC$\underline{H}_2$O), 4.03–3.80 (m, 12H), 3.75 (dt, *J* = 9.3, 6.8 Hz, 1H, 1 × OC$\underline{H}_2(CH_2)_{14}CH_3$), 3.59–3.41 (m, 5H), 3.38 (dt, *J* = 9.3, 6.9 Hz, 1H, 1 × OC$\underline{H}_2(CH_2)_{14}CH_3$), 3.33–3.27 (m, 1H), 3.27–3.20 (m, 2H), 3.17–3.05 (m, 3H), 3.00–2.85 (m, 5H), 2.62–2.45 (m, 4H, 4 × $CH_2C\underline{H}_2C(O)CH_3$), 2.41–2.24 (m, 4H, 4 × $C\underline{H}_2CH_2C(O)CH_3$), 2.14 (s, 3H, $C\underline{H}_3C(O)O$), 2.08 (s, 6H, $CH_2CH_2C(O)C\underline{H}_3$), 1.53–1.46 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 1.32–1.15 (m, 26H, 26 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 0.88 (t, *J* = 6.9 Hz, 3H, $OCH_2(CH_2)_{14}C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 206.1 (C=O), 205.9 (C=O),

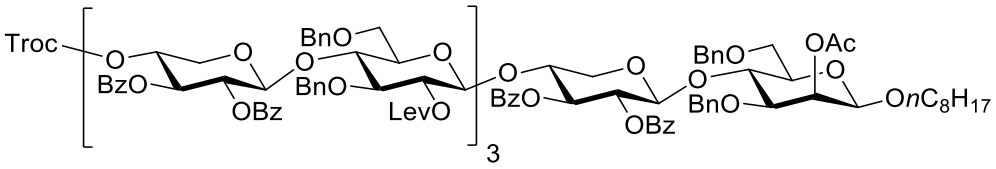
170.9 × 2 (C=O), 170.7 (C=O), 167.6 (C=O), 165.2 (C=O), 165.1 (C=O), 165.0 (C=O), 164.9 × 2 (C=O), 138.8, 138.5, 138.2, 138.0, 137.9, 133.7, 133.4, 133.3, 133.2, 132.9 × 2 (Ar), 130.0, 129.9, 129.8, 129.7 × 2 (Ar), 129.3, 129.2, 129.1, 128.8, 128.6 × 2 (Ar), 128.5 × 3 (Ar), 128.4 × 2 (Ar), 128.3, 128.2 × 4 (Ar), 128.1, 128.0 × 2 (Ar), 127.9, 127.7, 127.5, 127.4, 100.9 (C-1_{Glc}), 100.4 × 2 (C-1_{Xyl}), 98.9 (C-1_{Man}), 80.5 × 2 (C), 78.2, 77.4 (C-3_{Xyl}), 76.0, 75.9, 75.6, 75.3, 75.0 × 2 (C), 74.5, 74.3, 74.2, 74.0, 73.4 × 3 (C), 73.2, 72.9 × 2 (C), 72.8, 72.2, 72.0, 71.8, 71.4 (C-2_{Xyl}), 69.9 (O<u>C</u>$H_2(CH_2)_{14}CH_3$) 69.5, 68.5 (C-6_{Man}), 68.2 (C-2_{Man}), 67.3 (C-6_{Glc}), 67.2 (C-6_{Glc}), 65.4 (C-5_{Xyl}), 63.3 (C-5_{Xyl}), 63.0 (C-5_{Xyl}), 37.8 (CH_2<u>C</u>H_2C(O)CH_3), 37.7 (CH_2<u>C</u>H_2C(O)CH_3), 32.0 (OCH_2(<u>C</u>H_2)$_{14}CH_3$), 29.8 × 2 (CH_2CH_2C(O)<u>C</u>H_3), 29.7 × 4 (OCH_2(<u>C</u>H_2)$_{14}CH_3$), 29.6 (OCH_2(<u>C</u>H_2)$_{14}CH_3$), 29.4 × 2 (OCH_2(<u>C</u>H_2)$_{14}CH_3$), 27.8 × 2 (<u>C</u>H_2CH_2C(O)CH_3), 25.9 (OCH_2(<u>C</u>H_2)$_{14}CH_3$), 22.7 (OCH_2(<u>C</u>H_2)$_{14}CH_3$), 21.3 (<u>C</u>H_3C(O)O), 14.2 (O$CH_2(CH_2)_{14}$<u>C</u>H_3). HRMS (ESI) calcd for $(M + Na)^+$ $C_{145}H_{162}NaO_{39}$: 2550.0585. Found: 2550.0604.



Methyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.69). To a flask containing **3.37** (373 mg, 0.326 mmol) and **3.66** (350 mg,

0.151 mmol) was added CH_2Cl_2 (7.4 mL) and 4 Å M.S. powder (163 mg) under argon. The flask was then sealed with a rubber septum connected to an argon balloon and the resultant slurry mixture was stirred for 3 h before it was cooled to 0 °C. The mixture was stirred for another 30 min, after which point TfOH (230 μL, 0.052 mmol, 2% v/v in CH_2Cl_2) was added dropwise over 2 min. Upon complete addition of TfOH, the flask was then removed from the ice bath and stirred at room temperature. After 10 h, Et_3N (2 mL) was added and the mixture was passed through a Celite bed. Concentration of the resultant filtrate led to a crude residue that was subsequently purified by silica gel chromatography (1:1 to 5:6 hexanes–EtOAc) to obtain **3.69** (351 mg, 0.107 mmol, 71%) as a white foamy solid. R_f = 0.28 (5:6 hexanes–EtOAc); $[\alpha]_D$ –4.0 (*c*. 0.4, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.93–7.76 (m, 16H, Ar), 7.57–7.45 (m, 5H, Ar), 7.42–7.26 (m, 46H, Ar), 7.25–7.09 (m, 13H, Ar), 5.52 (d, *J* = 3.6 Hz, 1H, H-2$_{Man}$), 5.46 (app t, *J* = 8.6 Hz, 1H, H-3$_{Xyl}$), 5.40–5.29 (m, 3H, 3 × H-3$_{Xyl}$), 5.25 (dd, *J* = 8.8, 7.0 Hz, 1H, H-2$_{Xyl}$), 5.20–5.09 (m, 3H, 3 × H-2$_{Xyl}$), 4.98 (app td, *J* = 8.8, 5.2 Hz, 1H, H-4$_{Xyl}$), 4.87–4.48 (m, 19H), 4.33–4.20 (m, 8H), 4.09–3.78 (m, 15H), 3.60 (dd, *J* = 10.9, 4.4 Hz, 1H, H-6a$_{Man}$), 3.57–3.40 (m, 8H), 3.33–3.06 (m, 8H), 2.99–2.85 (m, 6H), 2.64–2.47 (m, 6H, 6 × $CH_2C\underline{H}_2C(O)CH_3$), 2.40–2.25 (m, 6H, 6 × $C\underline{H}_2CH_2C(O)CH_3$), 2.15 (s, 3H, $C\underline{H}_3C(O)O$), 2.08 (s, 6H, $CH_2CH_2C(O)C\underline{H}_3$), 2.07 (s, 3H, $CH_2CH_2C(O)C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 206.0 (C=O), 205.9 (C=O), 205.8 (C=O), 170.9 × 2 (C=O), 170.7 (C=O), 165.2 × 2 (C=O), 165.0 (C=O), 164.9 × 2 (C=O), 153.2 (C=O), 138.7 × 2 (Ar), 138.4, 138.1, 137.9, 137.8 × 3 (Ar), 133.4, 133.2, 132.9, 129.8 × 2 (Ar), 129.7 × 2 (Ar), 129.6 × 2 (Ar), 129.3, 129.1, 128.9, 128.6, 128.5 × 3 (Ar), 128.4, 128.3, 128.2 × 2 (Ar), 128.1 × 2 (Ar), 128.0, 127.8, 127.7, 127.5, 127.4, 100.8 × 2 (C), 100.4 × 2 (C), 100.1 (C-1$_{Xyl}$), 99.9 (C-1$_{Man}$), 94.1 ($Cl_3\underline{C}CH_2O$), 80.5, 80.4, 77.9, 76.9 ($Cl_3\underline{C}CH_2O$), 76.0, 75.9 × 2 (C), 75.6, 75.2, 74.9, 74.3, 74.2, 74.0, 73.4, 73.2, 73.1, 72.9, 72.8, 72.1, 72.0, 71.9, 71.6, 71.2,

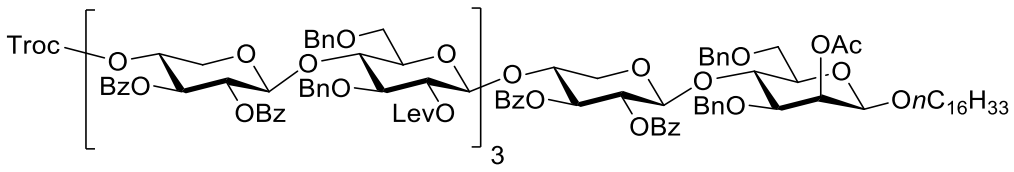
68.3 (C-6_{Man}), 68.1 (C-2_{Man}), 67.4 (C-6_{Glc}), 67.2 (C-6_{Glc}), 63.2 × 2 (C-5_{Xyl}), 63.0 (C-5_{Xyl}), 61.7 (C-5_{Xyl}), 57.1 (O<u>C</u>H_3), 37.7 × 2 (CH_2<u>C</u>H_2C(O)CH_3), 29.8 × 2 (CH_2CH_2C(O)<u>C</u>H_3), 27.8 × 2 (<u>C</u>H_2CH_2C(O)CH_3), 21.2 (<u>C</u>H_3C(O)O). HRMS-MALDI-TOF calcd for $(M + Na)^+$ $C_{177}H_{177}Cl_3NaO_{54}$: 3294.00620. Found: 3293.00492.



***n*-Octyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.70).** To a flask containing **3.37** (279 mg, 0.244 mmol) and **3.67** (254 mg, 0.105 mmol) was added CH_2Cl_2 (5.4 mL) and 4 Å M.S. powder (130 mg) under argon. The flask was then sealed with a rubber septum connected to an argon balloon and the resultant slurry mixture was stirred for 3 h before it was cooled to 0 °C. The mixture was stirred for another 30 min, after which point TfOH (160 μL, 0.037 mmol, 2% v/v in CH_2Cl_2) was added dropwise over 2 min. Upon complete addition of TfOH, the flask was then removed from the ice bath and stirred at room temperature. After 10 h, Et_3N (2 mL) was added and the mixture was passed through a Celite bed. Concentration of the resultant filtrate led to a crude residue that was subsequently purified by silica gel chromatography (7:5 to 1:1 hexanes–EtOAc) to obtain **3.70**

(257 mg, 0.076 mmol, 73%) as a white foamy solid. R_f = 0.21 (7:5 hexanes–EtOAc); $[\alpha]_D$ –0.9 (*c*. 0.3, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.01–7.72 (m, 16H, Ar), 7.59–7.45 (m, 5H, Ar), 7.43–7.27 (m, 39H, Ar), 7.22–7.04 (m, 20H, Ar), 5.52 (d, *J* = 3.5 Hz, 1H, H-2_{Man}), 5.45 (app t, *J* = 8.7 Hz, 1H, H-3_{Xyl}), 5.40–5.28 (m, 3H, 3 × H-3_{Xyl}), 5.25 (dd, *J* = 8.8, 7.0 Hz, 1H, H-2_{Xyl}), 5.20–5.08 (m, 3H, 3 × H-2_{Xyl}), 4.98 (app td, *J* = 8.8, 5.2 Hz, 1H, H-4_{Xyl}), 4.86–4.47 (m, 19H), 4.36 (s, 1H, H-1_{Man}), 4.31–4.20 (m, 7H), 4.10–3.79 (m, 14H), 3.76 (dt, *J* = 9.3, 6.7 Hz, 1H, 1 × $OC\underline{H}_2(CH_2)_6CH_3$), 3.60–3.41 (m, 6H), 3.38 (dt, *J* = 9.3, 6.8 Hz, 1H, 1 × $OC\underline{H}_2(CH_2)_6CH_3$), 3.29 (dd, *J* = 11.3, 3.3 Hz, 1H), 3.26–3.05 (m, 7H), 3.01–2.83 (m, 6H), 2.61–2.47 (m, 6H, 6 × $CH_2C\underline{H}_2C(O)CH_3$), 2.41–2.24 (m, 6H, 6 × $C\underline{H}_2CH_2C(O)CH_3$), 2.14 (s, 3H, $C\underline{H}_3C(O)O$), 2.08 (s, 6H, $CH_2CH_2C(O)C\underline{H}_3$), 2.07 (s, 3H, $CH_2CH_2C(O)C\underline{H}_3$), 1.55–1.48 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_6CH_3$), 1.33–1.17 (m, 10H, 10 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 0.88 (t, *J* = 6.9 Hz, 3H, $OCH_2(CH_2)_6C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 206.0 (C=O), 205.9 (C=O), 205.8 (C=O), 170.9 × 2 (C=O), 170.7 × 2 (C=O), 165.2 × 2 (C=O), 165.0 × 2 (C=O), 164.9 × 4 (C=O), 153.2 (C=O), 138.8, 138.7, 138.4, 138.2, 137.9 × 2 (Ar), 133.5, 133.3, 132.9 × 2 (Ar), 129.8, 129.7 × 2 (Ar), 129.3, 129.2, 129.0, 128.6 × 2 (Ar), 128.5, 128.4, 128.3 × 3 (Ar), 128.2 × 2 (Ar), 128.1 × 2 (Ar), 128.0, 127.9 × 2 (Ar), 127.8, 127.7, 127.5, 127.4, 100.9, 100.8 × 2 (C), 100.4 × 3 (C), 100.1 (C-1_{Xyl}), 98.9 (C-1_{Man}), 94.1 ($Cl_3\underline{C}CH_2O$), 80.5, 80.4, 78.1 (C-3_{Man}), 76.9 ($Cl_3\underline{C}CH_2O$), 76.0 × 2 (C), 75.9, 75.6, 75.3, 74.9, 74.3 × 2 (C), 74.2, 73.4 × 2 (C), 73.2 × 2 (C), 72.9, 72.8, 72.1, 72.0, 71.8, 71.6, 71.2, 69.9 ($O\underline{C}H_2(CH_2)_6CH_3$), 68.5 (C-$6_{Man}$), 68.2 (C-$2_{Man}$), 67.4 (C-$6_{Glc}$), 67.2 (C-$6_{Glc}$), 63.3 (C-$5_{Xyl}$), 63.0 (C-$5_{Xyl}$), 61.7 (C-$5_{Xyl}$), 37.8 × 2 ($CH_2\underline{C}H_2C(O)CH_3$), 37.7 ($CH_2\underline{C}H_2C(O)CH_3$), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.8 × 2 ($CH_2CH_2C(O)\underline{C}H_3$), 29.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 27.8 × 2

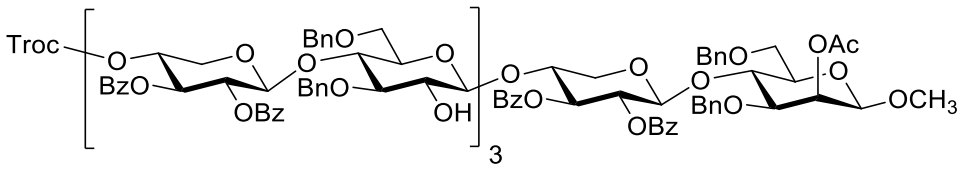
($\underline{C}H_2CH_2C(O)CH_3$), 25.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 21.3 ($\underline{C}H_3C(O)O$), 14.2 ($OCH_2(CH_2)_6\underline{C}H_3$). HRMS-MALDI-TOF calcd for $(M + Na)^+$ $C_{184}H_{191}Cl_3NaO_{54}$: 3392.11575. Found: 3392.11668.



***n*-Hexadecyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.71).** To a flask containing **3.37** (236 mg, 0.206 mmol) and **3.68** (247 mg, 0.098 mmol) was added CH_2Cl_2 (7.4 mL) and 4 Å M.S. powder (163 mg) under argon. The flask was then sealed with a rubber septum connected to an argon balloon and the resultant slurry mixture was stirred for 3 h before it was cooled to 0 °C. The mixture was stirred for another 30 min, after which point TfOH (155 μL, 0.035 mmol, 2% v/v in CH_2Cl_2) was added dropwise over 2 min. Upon complete addition of TfOH, the flask was then removed from the ice bath and stirred at room temperature. After 10 h, Et_3N (1 mL) was added and the mixture was passed through a Celite bed. Concentration of the resultant filtrate led to a crude residue that was subsequently purified by silica gel chromatography (6:5 to 1:1 hexanes–EtOAc) to obtain **3.71** (259 mg, 0.074 mmol, 76%) as a white foamy solid. R_f = 0.34 (6:5 hexanes–EtOAc); $[\alpha]_D$ +1.3

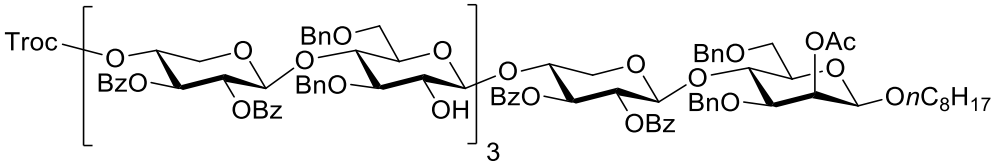
(*c*. 1.6, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.94–7.72 (m, 16H, Ar), 7.58–7.45 (m, 5H, Ar), 7.41–7.27 (m, 39H, Ar), 7.25–7.11 (m, 20H, Ar), 5.52 (d, J = 3.5 Hz, 1H, H-2_{Man}), 5.45 (app t, J = 8.7 Hz, 1H, H-3_{Xyl}), 5.39–5.29 (m, 3H, 3 × H-3_{Xyl}), 5.25 (dd, J = 8.8, 7.0 Hz, 1H, H-2_{Xyl}), 5.19–5.09 (m, 3H, 3 × H-2_{Xyl}), 4.98 (app td, J = 8.8, 5.2 Hz, 1H, H-4_{Xyl}), 4.86–4.46 (m, 19H), 4.36 (s, 1H, H-1_{Man}), 4.32–4.19 (m, 7H), 4.07–3.78 (m, 14H), 3.75 (dt, J = 9.3, 6.7 Hz, 1H, 1 × $OC\underline{H}_2(CH_2)_{14}CH_3$), 3.61–3.41 (m, 6H), 3.38 (dt, J = 9.3, 6.8 Hz, 1H, 1 × $OC\underline{H}_2(CH_2)_{14}CH_3$), 3.29 (dd, J = 11.3, 3.3 Hz, 1H), 3.26–3.05 (m, 7H), 3.00–2.83 (m, 6H), 2.62–2.45 (m, 6H, 6 × $CH_2C\underline{H}_2C(O)CH_3$), 2.41–2.24 (m, 6H, 6 × $C\underline{H}_2CH_2C(O)CH_3$), 2.14 (s, 3H, $C\underline{H}_3C(O)O$), 2.08 (s, 6H, $CH_2CH_2C(O)C\underline{H}_3$), 2.07 (s, 3H, $CH_2CH_2C(O)C\underline{H}_3$), 1.55–1.48 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 1.32–1.17 (m, 26H, 26 × $OC\underline{H}_2(CH_2)_{14}CH_3$), 0.88 (t, J = 6.9 Hz, 3H, 3 × $OCH_2(CH_2)_{14}C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 206.0 (C=O), 205.9 (C=O), 205.8 (C=O), 170.9 × 3 (C=O), 170.7 (C=O), 165.2 × 2 (C=O), 165.0 (C=O), 164.9 × 4 (C=O), 153.2 (C=O), 138.8, 138.7, 138.4, 138.2, 137.9 × 2 (Ar), 133.5, 133.3, 132.9 × 2 (Ar), 129.8, 129.7 × 2 (Ar), 129.3, 129.2, 129.0, 128.6 × 2 (Ar), 128.5, 128.4 × 2 (Ar), 128.3 × 2 (Ar), 128.2 × 2 (Ar), 128.1, 128.0 × 2 (Ar), 127.9 × 2 (Ar), 127.7, 127.5, 127.4, 100.9, 100.8, 100.4 × 3 (C), 100.1 (C-1_{Xyl}), 98.9 (C-1_{Man}), 94.1 ($Cl_3\underline{C}CH_2O$), 80.5, 80.4, 78.1 (C-3_{Man}), 76.9 ($Cl_3\underline{C}CH_2O$), 76.0 × 2 (C), 75.9, 75.6, 75.3, 74.9, 74.3 × 2 (C), 74.2, 73.4 × 2 (C), 73.2 × 2 (C), 72.9, 72.8, 72.1, 72.0, 71.8, 71.6, 71.2, 69.9 ($O\underline{C}H_2(CH_2)_{14}CH_3$), 68.5 (C-$6_{Man}$), 68.2 (C-$2_{Man}$), 67.4 (C-$6_{Glc}$), 67.2 (C-$6_{Glc}$), 63.3 (C-$5_{Xyl}$), 63.0 (C-$5_{Xyl}$), 61.7 (C-$5_{Xyl}$), 37.8 × 2 ($CH_2\underline{C}H_2C(O)CH_3$), 37.7 ($CH_2\underline{C}H_2C(O)CH_3$), 32.0 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.8 × 2 ($CH_2CH_2C(O)\underline{C}H_3$), 29.7 × 3 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.6 × 2 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.4 × 2 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 27.8 × 2 ($\underline{C}H_2CH_2C(O)CH_3$), 25.9

($OCH_2(\underline{C}H_2)_{14}CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 21.3 ($\underline{C}H_3C(O)O$), 14.2 ($OCH_2(\underline{C}H_2)_{14}CH_3$). HRMS-MALDI-TOF calcd for $(M + Na)^+$ $C_{192}H_{207}Cl_3NaO_{54}$: 3504.24095. Found: 3504.224359.



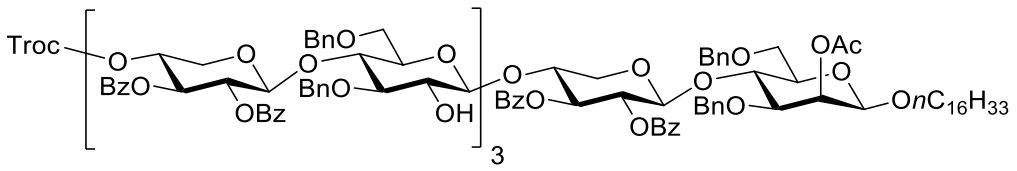
Methyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.72). The general procedure for levulinoyl deprotection was carried out on **3.69** (106 mg, 32.0 μmol) with H_2NNH_2·HOAc (250 μL, 140 μmol, 5% w/v in CH_3OH) in CH_2Cl_2–CH_3OH (5 mL, 10:1). The crude residue was purified by silica gel chromatography (3:2 hexanes–EtOAc) to obtain **3.72** (67.1 mg, 22.5 μmol, 70%) as a white foamy solid. R_f = 0.38 (1:1 hexanes–EtOAc); $[\alpha]_D$ +14.6 (*c*. 0.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.96–7.79 (m, 16H, Ar), 7.58–7.45 (m, 5H, Ar), 7.42–7.27 (m, 40H, Ar), 7.26–7.12 (m, 19H), 5.54 (d, *J* = 3.4 Hz, 1H, H-2_{Man}), 5.48 (app t, *J* = 8.4 Hz, 1H, H-3_{Xyl}), 5.44–5.37 (m, 3H, 3 × H-3_{Xyl}), 5.27 (dd, *J* = 8.6, 6.7 Hz, 1H, H-2_{Xyl}), 5.23–5.15 (m, 3H, 3 × H-2_{Xyl}), 5.00 (app td, *J* = 8.5, 5.0 Hz, 1H, H-4_{Xyl}), 4.93–4.85 (m, 3H), 4.82–4.62 (m, 10H), 4.54–4.48 (m, 2H), 4.34–4.23 (m, 5H), 4.20–4.08 (m, 5H), 4.08–3.91 (m, 10H), 3.88–3.76 (m, 3H), 3.65–3.57 (m, 2H, H-$6a_{Man}$, H-$6b_{Man}$), 3.55 (dd, *J* = 9.2, 3.5 Hz, 1H, H-3_{Man}), 3.44 (s, 3H, OCH_3), 3.43–3.24 (m, 12H), 3.20–3.05 (m, 6H), 3.05–2.95 (m, 3H), 2.20 (br s, 1H, OH), 2.18–2.13 (m, 5H, 2 × O$\underline{H}$,

C<u>H</u>$_3$C(O)O). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 170.7 (C=O), 165.4 × 4 (C=O), 165.2 × 2 (C=O), 165.1 (C=O), 164.9 (C=O), 153.2 (C=O), 138.9, 138.8, 138.7, 138.2, 138.0 × 2 (Ar), 137.9, 137.8, 133.5 × 2 (Ar), 133.3, 133.0, 129.9, 129.8 × 2 (Ar), 129.7, 129.6, 129.3, 129.2 × 2 (Ar), 129.0, 128.5 × 3 (Ar), 128.4 × 3 (Ar), 128.2, 128.0, 127.9 × 4 (Ar), 127.8 × 3 (Ar), 127.7, 127.6 × 2 (Ar), 101.8 × 2 (C-1_{Glc}), 100.4 × 3 (C), 100.0 × 2 (C-1_{Xyl}, C-1_{Man}), 94.1 ($Cl_3C\underline{C}H_2O$), 82.3, 78.2 (C-3_{Man}), 76.9 ($Cl_3C\underline{C}H_2O$), 75.9 × 2 (C), 75.3, 75.1 × 2 (C), 74.8, 74.7, 74.4 × 2 (C), 74.2, 74.0, 73.6, 73.5, 73.4 × 2 (C), 73.2, 73.0, 72.7, 71.8 × 2 (C), 71.4 (C-3_{Xyl}), 71.1 (C-2_{Xyl}), 68.5 (C-6_{Man}), 68.0 (C-2_{Man}), 67.6 (C-6_{Glc}), 63.1 × 2 (C-5_{Xyl}), 62.9 (C-5_{Xyl}), 61.5 (C-5_{Xyl}), 57.1 (OCH_3), 21.2 ($\underline{C}H_3C(O)O$). HRMS-MALDI-TOF calcd for $(M + Na)^+$ $C_{162}H_{159}Cl_3NaO_{48}$: 2999.89586. Found: 2999.89538.



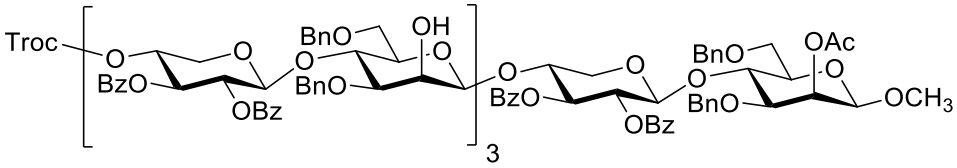
***n*-Octyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.73).** The general procedure for levulinoyl deprotection was carried out on **3.70** (159 mg, 47.1 μmol) with H_2NNH_2·HOAc (400 μL, 220 μmol, 5% w/v in CH_3OH) CH_2Cl_2–CH_3OH (5 mL, 10:1). The crude residue was purified by silica gel chromatography (1:1 hexanes–EtOAc) to obtain **3.73** (106 mg, 34.5 μmol, 73%) as a

white foamy solid. R_f = 0.26 (1:1 hexanes–EtOAc); $[\alpha]_D$ –3.0 (*c*. 0.04, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$, δ_H) 7.97–7.78 (m, 16H, Ar), 7.58–7.45 (m, 5H, Ar), 7.42–7.27 (m, 40H, Ar), 7.25–7.12 (m, 19H, Ar), 5.55 (d, *J* = 3.6 Hz, 1H, H-2_{Man}), 5.48 (app t, *J* = 8.4 Hz, 1H, H-3_{Xyl}), 5.43–5.36 (m, 3H, 3 × H-3_{Xyl}), 5.27 (dd, *J* = 8.5, 6.7 Hz, 1H, H-2_{Xyl}), 5.23–5.15 (m, 3H, 3 × H-2_{Xyl}), 4.99 (app td, *J* = 8.5, 5.0 Hz, 1H, H-4_{Xyl}), 4.91–4.83 (m, 3H), 4.81–4.62 (m, 10H), 4.53–4.45 (m, 2H), 4.39 (s, 1H, H-1_{Man}), 4.33–4.23 (m, 4H), 4.19– 4.09 (m, 4H), 4.08–3.91 (m, 10H), 3.89–3.73 (m, 4H), 3.61–3.50 (m, 3H, H-$6a_{Man}$, H-$6b_{Man}$, H-3_{Man}), 3.44–3.23 (m, 12H), 3.21–3.06 (m, 6H), 3.05–2.96 (m, 3H), 2.22 (br s, 1H, O$\underline{H}$), 2.18 (br s, 2H, 2 × O$\underline{H}$), 2.15 (s, 3H, C$\underline{H}_3$C(O)O), 1.56–1.50 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_6CH_3$), 1.34–1.19 (m, 10H, 10 × $OCH_2(C\underline{H}_2)_6CH_3$), 0.86 (t, *J* = 6.9 Hz, 3H, $OCH_2(CH_2)_6C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 170.7 (C=O), 165.4 × 3 (C=O), 165.2 × 2 (C=O), 165.1 (C=O), 164.9 (C=O), 153.2 (C=O), 138.9, 138.8, 138.7, 138.3, 138.0 × 2 (Ar), 137.9, 137.8, 133.5, 133.3, 133.0, 129.9, 129.8 × 2 (Ar), 129.7, 129.3, 129.2, 129.0, 128.5 × 3 (Ar), 128.4 × 3 (Ar), 128.2 , 128.0 × 2 (Ar), 127.9 × 3 (Ar), 127.8 × 3 (Ar), 127.7, 127.6 × 2 (Ar), 101.9 × 2 (C-1_{Glc}), 100.5, 100.4 × 2 (C), 100.0 (C-1_{Xyl}), 98.9 (C-1_{Man}), 94.1 ($Cl_3\underline{C}CH_2O$), 82.3, 78.4 (C-3_{Man}), 77.0 ($Cl_3C\underline{C}H_2O$), 75.9, 75.3, 75.1, 74.8, 74.7, 74.4 × 2 (C), 74.2, 73.6, 73.5 × 2 (C), 73.4 × 2 (C), 73.3, 73.2, 73.0, 72.7, 71.8 × 2 (C), 71.4 (C-3_{Xyl}), 71.1 (C-2_{Xyl}), 69.9 ($O\underline{C}H_2(CH_2)_6CH_3$), 68.7 (C-$6_{Man}$), 68.1 (C-$2_{Man}$), 67.6 (C-$6_{Glc}$), 63.1 (C-$5_{Xyl}$), 62.9 (C-$5_{Xyl}$), 61.5 (C-$5_{Xyl}$), 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 ($OCH_2(\underline{C}H_2)_6CH_3$), 25.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 21.2 ($\underline{C}H_3C(O)O$), 14.1 ($OCH_2(CH_2)_6\underline{C}H_3$). HRMS-MALDI-TOF calcd for $(M + Na)^+$ $C_{169}H_{173}Cl_3NaO_{48}$: 3098.00541. Found: 3098.00752.



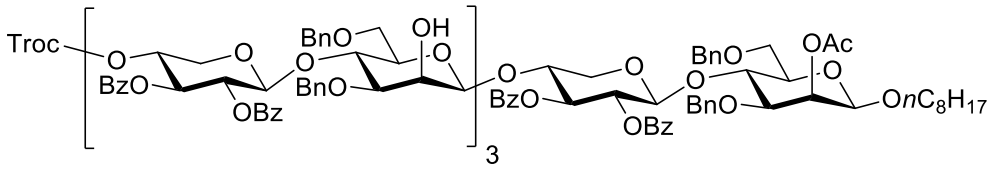
***n*-Hexadecyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.74).** The general procedure for levulinoyl deprotection was carried out on **3.71** (259 mg, 74.4 μmol) with H_2NNH_2·HOAc (600 μL, 330 μmol, 5% w/v in CH_3OH) in CH_2Cl_2–CH_3OH (10 mL, 10:1). The crude residue was purified by silica gel chromatography (6:5 hexanes–EtOAc) to obtain **3.74** (190 mg, 60.0 μmol, 80%) as a white foamy solid. R_f = 0.35 (6:5 hexanes–EtOAc); $[\alpha]_D$ +13.4 (*c*. 0.3, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.98–7.77 (m, 16H, Ar), 7.57–7.44 (m, 5H, Ar), 7.42–7.26 (m, 40H, Ar), 7.25–7.11 (m, 19H, Ar), 5.55 (d, *J* = 3.6 Hz, 1H, H-2_{Man}), 5.48 (app t, *J* = 8.4 Hz, 1H, H-3_{Xyl}), 5.45–5.37 (m, 3H, 3 × H-3_{Xyl}), 5.27 (dd, *J* = 8.5, 6.7 Hz, 1H, H-2_{Xyl}), 5.23–5.15 (m, 3H, 3 × H-2_{Xyl}), 5.00 (app td, *J* = 8.5, 5.0 Hz, 1H, H-4_{Xyl}), 4.92–4.85 (m, 3H), 4.81–4.63 (m, 10H), 4.53–4.45 (m, 2H), 4.39 (s, 1H, H-1_{Man}), 4.33–4.25 (m, 4H), 4.20–4.09 (m, 4H), 4.08–3.92 (m, 10H), 3.88–3.72 (m, 4H), 3.61–3.51 (m, 3H, H-$6a_{Man}$, H-$6b_{Man}$, H-3_{Man}), 3.44–3.23 (m, 12H), 3.20–3.05 (m, 6H), 3.05–2.96 (m, 3H), 2.19 (br s, 1H, O<u>H</u>), 2.18–2.12 (m, 5H, C<u>H</u>$_3$C(O)O, 2 × O<u>H</u>), 1.56–1.50 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 1.33–1.18 (m, 26H, 26 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 0.88 (t, *J* = 7.0 Hz, 3H, $OCH_2(CH_2)_{14}C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 170.7 (C=O), 165.4 × 3 (C=O), 165.2 × 2 (C=O), 165.1 (C=O), 164.9 (C=O), 153.2 (C=O), 138.9, 138.8, 138.7,

138.3, 138.0 × 2 (Ar), 137.9, 137.8, 133.5, 133.3, 133.0, 129.9, 129.8 × 2 (Ar), 129.7, 129.3, 129.2, 129.0, 128.5 × 3 (Ar), 128.4 × 3 (Ar), 128.2 , 128.0 × 2 (Ar), 127.9 × 3 (Ar), 127.8 × 2 (Ar), 127.7, 127.6 × 2 (Ar), 101.9 × 2 (C-1_{Glc}), 100.5, 100.4 × 2 (C), 100.0 (C-1_{Xyl}), 98.9 (C-1_{Man}), 94.1 ($Cl_3\underline{C}CH_2O$), 82.3, 78.4 (C-3_{Man}), 77.0 ($Cl_3C\underline{C}H_2O$), 75.9 × 2 (C), 75.3, 75.1, 74.8, 74.7, 74.4 × 2 (C), 74.2, 73.6, 73.5, 73.4 × 3 (C), 73.3, 73.2, 73.0, 72.7, 71.8 × 2 (C), 71.4 (C-3_{Xyl}), 71.1 (C-2_{Xyl}), 69.9 ($O\underline{C}H_2(CH_2)_{14}CH_3$), 68.7 (C-$6_{Man}$), 68.1 (C-$2_{Man}$), 67.6 (C-$6_{Glc}$), 63.1 × 2 (C-$5_{Xyl}$), 62.9 (C-$5_{Xyl}$), 61.5 (C-$5_{Xyl}$), 32.0 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.7 × 3 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.6 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.4 × 2 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 25.9 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 21.2 ($\underline{C}H_3C(O)O$), 14.2 ($OCH_2(CH_2)_{14}\underline{C}H_3$). HRMS-MALDI-TOF calcd for $(M + Na)^+$ $C_{177}H_{189}Cl_3NaO_{48}$: 3210.13061. Found: 3210.13157.



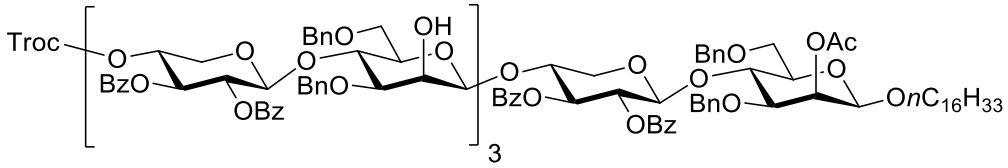
Methyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.75). Approach B for C-2 inversion was carried out on **3.72** (91.1 mg, 30.6 μmol). In this approach, DMP (119 mg, 281 μmol) and H_2O (2.5 μL, 140 μmol) were used for oxidation in CH_2Cl_2 (2 mL); subsequent reduction of the crude triketone was conducted with LTBA (28.6 mg, 113 μmol) in THF (1.5 mL). The resultant crude

residue was purified by silica gel chromatography (1:1 to 1:2 hexanes–acetone) to afford **3.75** (68.2 mg, 22.9 μmol, 75%) as a white solid. R_f = 0.25 (5:6 hexanes–acetone); $[\alpha]_D$ +21.2 (*c*. 0.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.97–7.79 (m, 16H, Ar), 7.57–7.45 (m, 5H, Ar), 7.43–7.27 (m, 40H, Ar), 7.26–7.09 (m, 19H, Ar), 5.53 (d, *J* = 3.5 Hz, 1H, H-2_{Man}), 5.49 (app t, *J* = 8.0 Hz, 1H, H-3_{Xyl}), 5.38–5.22 (m, 7H), 5.00 (app td, *J* = 8.0, 4.8 Hz, 1H, H-4_{Xyl}), 4.81–4.62 (m, 13H), 4.59–4.51 (m, 2H), 4.38 (s, 1H, H-1_{Man}), 4.36–4.32 (m, 2H, 2 × H-1_{Man}), 4.32–4.27 (m, 2H, 1 × PhC$\underline{H}_2$O, H-1_{Man}), 4.18 (dd, *J* = 12.4, 4.8 Hz, 1H), 4.14–4.03 (m, 7H), 4.02–3.87 (m, 12H), 3.64 (dd, *J* = 11.0, 4.3 Hz, 1H, H-6a_{Man}), 3.60–3.51 (m, 2H, H-6b_{Man}, H-3_{Man}), 3.43 (s, 3H, OC$\underline{H}_3$), 3.42–3.21 (m, 8H), 3.20–3.03 (m, 9H), 2.53–2.40 (m, 3H, 3 × OH), 2.16 (s, 3H, C$\underline{H}_3$C(O)O). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 170.7 (C=O), 166.4 × 2 (C=O), 166.3 (C=O), 165.2 (C=O), 165.1 × 2 (C=O), 165.0 (C=O), 153.2 (C=O), 138.3, 138.2 × 2 (Ar), 138.0, 137.8, 133.5, 133.4, 133.3, 133.0, 129.9, 129.8, 129.7, 129.7, 129.2, 129.1, 129.0, 1285, 128.5, 128.4 × 3 (Ar), 128.3, 128.2 × 2 (Ar), 128.0, 127.9 × 3 (Ar), 127.8, 127.7 × 3 (Ar), 127.6, 100.8 × 2 (C-1_{Xyl}), 100.5 (C-1_{Xyl}), 100.1 (C-1_{Xyl}), 100.0 (C-1_{Man}), 97.2 (C-1_{Man}), 94.1 ($Cl_3\underline{C}CH_2O$), 79.5, 79.2, 78.0 (C-3_{Man}), 76.9 ($Cl_3C\underline{C}H_2O$), 75.3, 75.1 × 2 (C), 74.3, 74.1, 73.4, 73.3, 73.1, 72.9, 72.3, 72.0, 71.9, 71.6, 71.2, 70.9, 68.8, 68.3 (C-6_{Man}), 68.1 (C-2_{Man}), 62.8 × 2 (C-5_{Xyl}), 62.7 (C-5_{Xyl}), 61.3 (C-5_{Xyl}), 57.1 (OCH_3), 21.2 ($\underline{C}H_3C(O)O$). HRMS-MALDI-TOF calcd for $(M + Na)^+$ $C_{162}H_{159}Cl_3NaO_{48}$: 2999.89586. Found: 2999.89414.



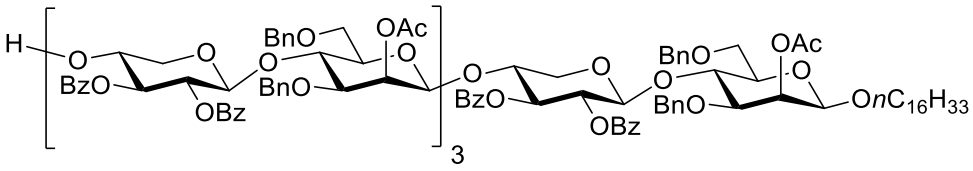
***n*-Octyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.76).** Approach B for C-2 inversion was carried out on **3.73** (20.5 mg, 6.67 μmol). In this approach, DMP (25.9 mg, 61.1 μmol) and H_2O (0.6 μL, 30.0 μmol) were used for oxidation in CH_2Cl_2 (2 mL); subsequent reduction of the crude triketone was conducted with LTBA (6.3 mg, 24.8 μmol) in THF (1 mL). The resultant crude residue was purified by silica gel chromatography (5:6 to 1:2 hexanes–EtOAc) to afford **3.76** (15.1 mg, 4.90 μmol, 73%) as a white solid. R_f = 0.36 (5:7 hexanes–EtOAc); $[\alpha]_D$ +3.5 (*c*. 0.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.97–7.79 (m, 16H, Ar), 7.56–7.45 (m, 5H, Ar), 7.44–7.26 (m, 40H, Ar), 7.26–7.06 (m, 19H, Ar), 5.53 (d, *J* = 3.5 Hz, 1H, H-2_{Man}), 5.48 (app t, *J* = 8.1 Hz, 1H, H-3_{Xyl}), 5.38–5.22 (m, 7H), 5.00 (app td, *J* = 8.1, 4.8 Hz, 1H, H-4_{Xyl}), 4.81–4.61 (m, 13H), 4.56–4.49 (m, 2H), 4.38 (s, 2H, 2 × H-1_{Man}), 4.33 (s, 1H, H-1_{Man}), 4.32 (s, 1H, H-1_{Man}), 4.31–4.26 (m, 1H, 1 × PhC$\underline{H}_2$O), 4.17 (dd, *J* = 12.4, 4.7 Hz, 1H), 4.14–4.00 (m, 7H), 4.00–3.85 (m, 12H), 3.76 (dt, *J* = 9.1, 6.8 Hz, 1H, 1 × OC$\underline{H}_2(CH_2)_6CH_3$), 3.66–3.50 (m, 3H, H-$6a_{Man}$, H-$6b_{Man}$, H-$3_{Man}$), 3.43–3.21 (m, 8H), 3.20–3.06 (m, 9H), 2.15 (s, 3H, C$\underline{H}_3$C(O)O), 1.56–1.51 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_6CH_3$), 1.33–1.19 (m, 10H, 10 × $OCH_2(C\underline{H}_2)_6CH_3$), 0.86 (t, *J* = 6.9 Hz, 3H, $OCH_2(CH_2)_{14}C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 170.6 (C=O), 166.4 × 2 (C=O), 166.3

(C=O), 165.2 (C=O), 165.1 × 2 (C=O), 165.0 (C=O), 153.2 (C=O), 138.3, 138.2 × 2 (Ar), 138.0, 137.9, 133.5, 133.4, 133.3, 133.0, 129.9, 129.8, 129.2, 129.1, 129.0, 128.5 × 2 (Ar), 128.4 × 2 (Ar), 128.3, 128.2 × 2 (Ar), 128.0, 127.9 × 3 (Ar), 127.8, 127.7 × 3 (Ar), 127.6, 100.8 × 2 (C-1_{Xyl}), 100.6 (C-1_{Xyl}), 100.1 (C-1_{Xyl}), 98.9 (C-1_{Man}), 97.2 (C-1_{Man}), 94.1 ($Cl_3\underline{C}CH_2O$), 79.5, 79.2, 78.2 (C-3_{Man}), 76.9 ($Cl_3C\underline{C}H_2O$), 75.3, 75.1, 74.3, 74.2, 74.1, 73.4, 73.3, 73.1 × 3 (C), 73.0, 72.3, 72.0, 71.8, 71.6, 71.2, 70.9, 69.9 ($O\underline{C}H_2(CH_2)_6CH_3$), 68.8 × 2 (C), 68.5 (C-6_{Man}), 68.4 (C-6_{Man}), 68.3 × 2 (C), 68.2 (C-2_{Man}), 62.8 × 2 (C-5_{Xyl}), 62.7 (C-5_{Xyl}), 61.3 (C-5_{Xyl}), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 25.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 21.3 ($\underline{C}H_3C(O)O$), 14.3 ($OCH_2(CH_2)_6\underline{C}H_3$). HRMS-MALDI-TOF calcd for $(M + Na)^+$ $C_{169}H_{173}Cl_3NaO_{48}$: 3098.00541. Found: 3098.00723.



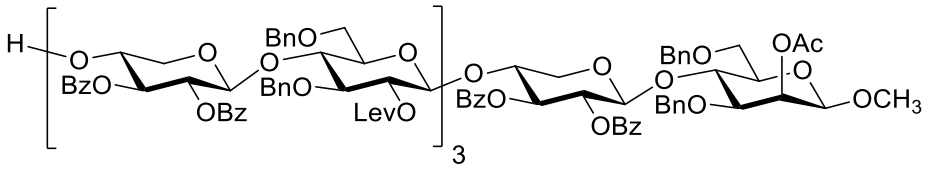
***n*-Hexadecyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.77).** Approach B for C-2 inversion was carried out on 3.74 (42.3 mg, 13.3 μmol). In this approach, DMP (51.2 mg, 121 μmol) and H_2O (1.0 μL, 55.6 μmol) were used for oxidation in CH_2Cl_2 (2 mL); subsequent reduction on the crude triketone was conducted with LTBA (13.3 mg, 51.2 μmol) in THF (1 mL).

The resultant crude residue was purified by silica gel chromatography (9:5 to 1:1 hexanes–acetone) to afford **3.77** (30.1 mg, 9.43 μmol, 71%) as a white solid. R_f = 0.34 (9:5 hexanes–acetone); $[\alpha]_D$ +4.2 (*c*. 0.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.97–7.79 (m, 16H, Ar), 7.56–7.45 (m, 5H, Ar), 7.44–7.26 (m, 41H, Ar), 7.25–7.09 (m, 18H, Ar), 5.54 (d, *J* = 3.5 Hz, 1H, H-2_{Man}), 5.49 (app t, *J* = 8.1 Hz, 1H, H-3_{Xyl}), 5.38–5.22 (m, 7H), 5.00 (td, *J* = 8.1, 4.8 Hz, 1H, H-4_{Xyl}), 4.79–4.62 (m, 13H), 4.57–4.48 (m, 2H), 4.38 (s, 2H, 2 × H-1_{Man}), 4.34 (s, 1H, H-1_{Man}), 4.32 (s, 1H, H-1_{Man}), 4.31–4.26 (m, 1H, 1 × PhC$\underline{H}_2$O), 4.18 (dd, *J* = 12.3, 4.8 Hz, 1H), 4.13–4.00 (m, 7H), 4.00–3.86 (m, 12H), 3.76 (dt, *J* = 9.1, 6.8 Hz, 1H, 1 × OC$\underline{H}_2(CH_2)_{14}CH_3$), 3.65–3.51 (m, 3H, H-$6a_{Man}$, H-$6b_{Man}$, H-$3_{Man}$), 3.44–3.22 (m, 9H), 3.20–3.03 (m, 9H), 2.15 (s, 3H, C$\underline{H}_3$C(O)O), 1.56–1.50 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 1.33–1.19 (m, 26H, 26 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 0.88 (t, *J* = 6.9 Hz, 3H, $OCH_2(CH_2)_{14}C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 170.6 (C=O), 166.4 × 2 (C=O), 166.3 (C=O), 165.2 (C=O), 165.1 × 2 (C=O), 165.0 (C=O), 153.2 (C=O), 138.3, 138.2 × 2 (Ar), 138.0, 137.9, 133.5, 133.4, 133.3, 133.1, 129.9, 129.8, 129.7 × 2 (Ar), 129.2 × 2 (Ar), 129.1, 129.0, 128.5 × 2 (Ar), 128.4 × 3 (Ar), 128.3, 128.2 × 2 (Ar), 128.0, 127.9 × 2 (Ar), 127.8 × 2 (Ar), 127.7 × 3 (Ar), 127.6, 100.8 × 2 (C-1_{Xyl}), 100.6 (C-1_{Xyl}), 100.1 (C-1_{Xyl}), 98.9 (C-1_{Man}), 97.2 (C-1_{Man}), 94.1 ($Cl_3\underline{C}CH_2O$), 79.5, 79.2, 78.2 (C-3_{Man}), 76.9 ($Cl_3C\underline{C}H_2O$), 75.3, 75.1, 74.3, 74.2, 74.1, 73.4, 73.3, 73.1, 72.9, 72.3, 72.0, 71.8, 71.6, 71.2, 70.9, 69.9 ($O\underline{C}H_2(CH_2)_{14}CH_3$), 68.8 × 2 (C), 68.5 (C-6_{Man}), 68.4 (C-6_{Man}), 68.3 × 2 (C), 68.2 (C-2_{Man}), 62.8 × 2 (C-5_{Xyl}), 62.7 (C-5_{Xyl}), 61.3 (C-5_{Xyl}), 32.0 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.7 × 3 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.6 × 2 ($OCH_2(CH_2)_{14}CH_3$), 29.4 × 2 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 25.9 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 21.3 ($\underline{C}H_3C(O)O$), 14.2 ($OCH_2(\underline{C}H_2)_{14}CH_3$). HRMS-MALDI-TOF calcd for $(M + Na)^+$ $C_{177}H_{189}Cl_3NaO_{48}$: 3210.13061. Found: 3210.13276.



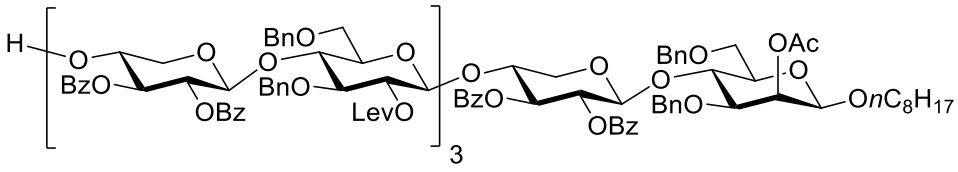
***n*-Hexadecyl 2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.78).** To a solution of **3.77** (30.0 mg, 9.40 μmol) in pyridine (2 mL) was added Ac_2O (0.50 mL) and DMAP (1.0 mg, 8.0 μmol) under argon. The reaction mixture was stirred at 40 °C overnight, cooled to room temperature and concentrated; pyridine was then removed via co-evaporation with toluene (2x). The crude material was re-dissolved in CH_2Cl_2 and subsequently washed with 1 M aqueous HCl and brine before it was dried over Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a crude syrup, that was then subjected to Troc deprotection using the general procedure with Zn powder (31.9 mg, 0.488 mmol) in glacial AcOH (1 mL). The crude residue was purified by silica gel chromatography (12:9 to 11:10 hexanes–EtOAc) to obtain **3.78** (21.0 mg, 6.7 μmol, 71%) as a white foamy solid. R_f = 0.26 (12:9 hexanes–EtOAc); $[\alpha]_D$ +13.9 (*c*. 0.7, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.97–7.93 (m, 2H, Ar), 7.92–7.82 (m, 14H, Ar), 7.57–7.45 (m, 5H, Ar), 7.41–7.26 (m, 39H, Ar), 7.26–7.10 (m, 20H, Ar), 5.52 (d, *J* = 3.4 Hz, 1H, H-2_{Man}), 5.46 (d, *J* = 3.5 Hz, 1H, H-2_{Man}), 5.42 (d, *J* = 3.5 Hz, 1H, H-2_{Man}), 5.41 (d, *J* = 3.5 Hz, 1H, H-2_{Man}), 5.37–5.28 (m, 4H), 5.22–5.15 (m, 3H), 5.08 (app t, *J* = 8.5 Hz, 1H, H-3_{Xyl}), 4.77–4.68 (m, 5H), 4.67 (d, *J* = 7.1 Hz, 1H, H-1_{Xyl}), 4.65–4.61 (m, 2H, 2 × H-1_{Xyl}), 4.55–4.48 (m, 5H), 4.39 (s, 1H, H-1_{Man}), 4.38–4.29 (m, 6H, 4 × H-1_{Man}, 2 × PhC$\underline{H}_2$O), 4.28–4.24 (m, 1H, 1 × PhC$\underline{H}_2$O),

4.09–3.97 (m, 8H), 3.96–3.86 (m, 7H), 3.75 (dt, J = 9.5, 6.8 Hz, 1H, 1 × OC<u>H</u>$_2$(CH$_2$)$_{14}$CH$_3$), 3.59 (dd, J = 10.9, 4.6 Hz, 1H, H-6a$_{Man}$), 3.57–3.53 (m, 1H, H-6b$_{Man}$), 3.53–3.48 (m, 2H, 2 × H-3$_{Man}$), 3.47–3.40 (m, 3H, 3 × H-3$_{Man}$), 3.40–3.35 (m, 3H), 3.34–3.31 (m, 1H), 3.31–3.26 (m, 2H), 3.23 (ddd, J = 9.7, 4.6, 2.0 Hz, 1H, H-5$_{Man}$), 3.13 (dd, J = 12.2, 9.0 Hz, 1H), 3.09 (ddd, J = 9.7, 4.4, 1.8 Hz, 1H), 3.07–3.00 (m, 5H), 2.94 (d, J = 5.0 Hz, 1H, OH), 2.15 (s, 3H, C<u>H</u>$_3$C(O)O), 1.95–1.85 (m, 9H, 9 × C<u>H</u>$_3$C(O)O), 1.54–1.49 (m, 2H, 2 × OCH$_2$(C<u>H</u>$_2$)$_{14}$CH$_3$), 1.32–1.19 (m, 26H, 26 × OCH$_2$(C<u>H</u>$_2$)$_{14}$CH$_3$), 0.88 (t, J = 7.1 Hz, 4H, OCH$_2$(CH$_2$)$_{14}$C<u>H</u>$_3$). ^{13}C NMR (125 MHz, CDCl$_3$, δ_C) 170.7 (C=O), 170.5 (C=O), 167.5 (C=O), 165.5 × 2 (C=O), 165.2 (C=O), 165.1 × 3 (C=O), 138.2 × 2 (Ar), 138.1 × 2 (Ar), 137.9, 137.8, 137.7 × 2 (Ar), 133.5, 133.3, 132.9, 130.0, 129.9, 129.8, 129.7 × 2 (Ar), 129.3 × 2 (Ar), 129.2, 128.9 × 2 (Ar), 128.5 × 3 (Ar), 128.4 × 2 (Ar), 128.3, 128.2 × 2 (Ar), 128.0, 127.9 × 2 (Ar), 127.8 × 3 (Ar), 127.7, 127.6, 100.7 (C-1$_{Xyl}$), 100.6 (C-1$_{Xyl}$), 100.4 (C-1$_{Xyl}$), 98.9 (C-1$_{Man}$), 96.6 × 3 (C-1$_{Man}$), 78.2 (C-3$_{Man}$), 77.9 (C-3$_{Man}$), 77.6 (C-3$_{Man}$), 77.0 (C-3$_{Xyl}$), 75.5, 75.3 (C-5$_{Man}$), 74.2, 73.8, 73.4, 73.3 × 2 (C), 72.7, 72.0, 71.9 × 2 (C), 71.8, 71.3, 69.9 (O<u>C</u>H$_2$(CH$_2$)$_{14}$CH$_3$), 69.3, 68.5 (C-6$_{Man}$), 68.3 (C-2$_{Man}$), 68.1, 68.0, 67.9 × 2 (C), 67.7, 65.2 (C-5$_{Xyl}$), 62.5 (C-5$_{Xyl}$), 32.0 (OCH$_2$(<u>C</u>H$_2$)$_{14}$CH$_3$), 29.7 × 4 (OCH$_2$(<u>C</u>H$_2$)$_{14}$CH$_3$), 29.6 (OCH$_2$(<u>C</u>H$_2$)$_{14}$CH$_3$), 29.4 × 2 (OCH$_2$(<u>C</u>H$_2$)$_{14}$CH$_3$), 25.9 (OCH$_2$(<u>C</u>H$_2$)$_{14}$CH$_3$), 22.7 (OCH$_2$(<u>C</u>H$_2$)$_{14}$CH$_3$), 21.3 (<u>C</u>H$_3$C(O)O), 20.8 (<u>C</u>H$_3$C(O)O), 20.7 (<u>C</u>H$_3$C(O)O), 14.2 (OCH$_2$(CH$_2$)$_{14}$<u>C</u>H$_3$). HRMS-MALDI-TOF calcd for (M + Na)$^+$ C$_{180}$H$_{194}$NaO$_{49}$: 3162.25809. Found: 3162.25633.



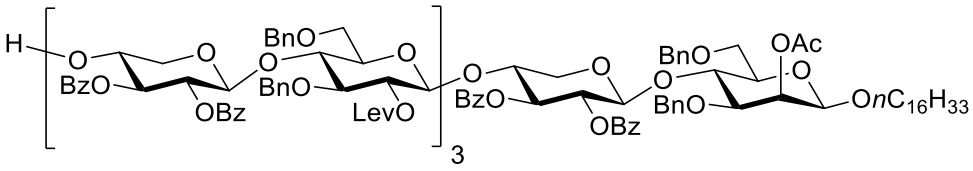
Methyl 2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.79). The general procedure for Troc deprotection was conducted on **3.69** (294 mg, 89.6 μmol) using Zn powder (252 mg, 3.85 mmol) in glacial AcOH (30 mL). The crude residue was purified by silica gel chromatography (1:1 to 2:3 hexanes–EtOAc), to afford **3.79** (231 mg, 74.2 μmol, 83%) as a white fluffy solid. R_f = 0.31 (2:3 hexanes–EtOAc); $[\alpha]_D$ −17.6 (*c*. 0.05, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.95–7.90 (m, 2H, Ar), 7.89–7.74 (m, 14H, Ar), 7.58–7.45 (m, 5H, Ar), 7.41–7.26 (m, 37H, Ar), 7.26–7.06 (m, 22H, Ar), 5.52 (d, *J* = 3.5 Hz, 1H, H-2_{Man}), 5.39–5.29 (m, 3H), 5.27 (dd, *J* = 9.3, 7.5 Hz, 1H, H-2_{Xyl}), 5.19–5.08 (m, 3H), 5.03 (app t, *J* = 9.0 Hz, 1H, H-3_{Xyl}), 4.87–4.67 (m, 8H), 4.60 (d, *J* = 7.5 Hz, 1H, H-1_{Xyl}), 4.58–4.48 (m, 7H), 4.34–4.19 (m, 8H), 4.06–3.77 (m, 16H), 3.59 (dd, *J* = 10.9, 4.4 Hz, 1H), 3.57–3.43 (m, 5H), 3.42 (s, 3H, OCH_3), 3.33–3.27 (m, 1H), 3.26–3.19 (m, 3H), 3.19–3.06 (m, 4H), 2.99–2.83 (m, 7H), 2.64–2.46 (m, 6H, 6 × $CH_2C\underline{H}_2C(O)CH_3$), 2.41–2.23 (m, 6H, 6 × $C\underline{H}_2CH_2C(O)CH_3$), 2.15 (s, 3H, $C\underline{H}_3C(O)O$), 2.10–2.04 (m, 9H, 9 × $CH_2CH_2C(O)C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 206.1 (C=O), 205.9 (C=O), 170.9 (C=O), 170.7 (C=O), 167.6 (C=O), 165.2 (C=O), 165.0 × 2 (C=O), 164.9 × 3 (C=O), 138.8, 138.7, 138.5, 138.1, 138.0, 137.9, 137.8 × 2 (Ar), 133.7, 133.4, 133.2, 132.9, 132.9, 130.0, 129.9, 129.8, 129.7 × 2 (Ar), 129.3, 129.2, 129.1, 128.6, 128.5 × 4 (Ar), 128.4 × 2 (Ar) 128.2 × 3 (Ar), 128.1 × 2

(Ar), 128.0 × 2 (Ar), 127.9, 127.7, 127.5, 127.4, 100.8 × 2 (C), 100.4 × 3 (C), 99.9 (C-1_{Man}), 80.5 × 2 (C), 80.4, 77.9 (C-3_{Man}), 77.4 (C-3_{Xyl}), 76.0 × 2 (C), 75.9 × 2 (C), 75.6, 75.3, 74.9 × 2 (C), 74.4, 74.3 × 2 (C), 74.0, 73.4 (3 × C), 73.2, 72.9 × 2 (C), 72.8, 72.1, 72.0, 71.9, 71.4 (C-2_{Xyl}), 69.5, 68.3 (C-6_{Man}), 68.1 (C-2_{Man}), 67.3 (C-6_{Glc}), 67.2 × 2 (C-6_{Glc}), 65.4 (C-5_{Xyl}), 63.3 (C-5_{Xyl}), 63.2 (C-5_{Xyl}), 63.0 (C-5_{Xyl}), 57.1 (O<u>C</u>H_3), 37.8 (CH_2<u>C</u>H_2C(O)CH_3), 37.7 (CH_2<u>C</u>H_2C(O)CH_3), 29.8 × 2 (CH_2CH_2C(O)<u>C</u>H_3), 29.7 (CH_2CH_2C(O)<u>C</u>H_3), 27.8 × 2 (<u>C</u>H_2CH_2C(O)CH_3), 21.2 (<u>C</u>H_3C(O)O). HRMS (ESI) calcd for $(M + 2(NH_4))^{2+}$ $C_{174}H_{184}N_2O_{52}$: 1566.5902. Found: 1566.5905.



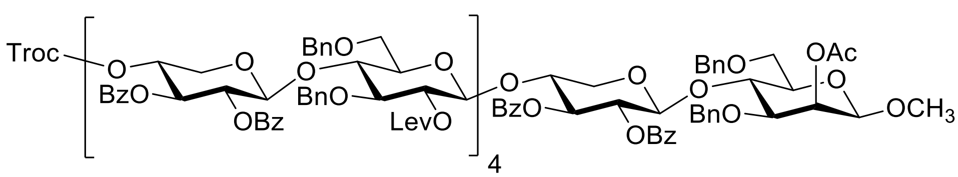
***n*-Octyl 2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.80).** The general procedure for Troc deprotection was conducted on **3.70** (257 mg, 76.2 μmol) using Zn powder (279 mg, 4.27 mmol) in glacial AcOH (25 mL). The crude residue was purified by silica gel chromatography (1:1 to 5:6 hexanes–EtOAc), to afford **3.80** (181 mg, 56.6 μmol, 74%) as a white fluffy solid. R_f = 0.40 (5:6 hexanes–EtOAc); $[\alpha]_D$ +5.3 (*c*. 0.03, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.95–7.91 (m, 2H, Ar), 7.89–7.74 (m, 14H, Ar), 7.58–7.45 (m, 5H, Ar), 7.42–7.26 (m, 37H, Ar), 7.25–

7.06 (m, 22H, Ar), 5.52 (d, J = 3.5 Hz, 1H, H-2_{Man}), 5.40–5.30 (m, 3H), 5.27 (dd, J = 9.4, 7.5 Hz, 1H, H-2_{Xyl}), 5.19–5.08 (m, 3H), 5.03 (app t, J = 8.9 Hz, 1H, H-3_{Xyl}), 4.86–4.69 (m, 8H), 4.60 (d, J = 7.5 Hz, 1H, H-1_{Xyl}), 4.59–4.45 (m, 7H), 4.36 (s, 1H, H-1_{Man}), 4.34–4.19 (m, 7H), 4.03–3.79 (m, 16H), 3.76 (dt, J = 9.4, 6.8 Hz, 1H, $OC\underline{H}_2(CH_2)_6CH_3$), 3.60–3.41 (m, 6H), 3.38 (dt, J = 9.4, 6.9 Hz, 1H, $OC\underline{H}_2(CH_2)_6CH_3$), 3.33–3.28 (m, 1H), 3.26–3.18 (m, 3H), 3.18–3.05 (m, 4H), 3.00–2.84 (m, 7H), 2.60–2.48 (m, 6H, 6 × $CH_2C\underline{H}_2C(O)CH_3$), 2.36–2.26 (m, 6H, 6 × $C\underline{H}_2CH_2C(O)CH_3$), 2.14 (s, 3H, $C\underline{H}_3C(O)O$), 2.11–2.05 (m, 9H, 9 × $CH_2CH_2C(O)C\underline{H}_3$), 1.55–1.48 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_6CH_3$), 1.35–1.16 (m, 10H, 10 × $OCH_2(C\underline{H}_2)_6CH_3$), 0.86 (t, J = 6.9 Hz, 3H, $OCH_2(CH_2)_6C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 206.0 (C=O), 205.9 (C=O), 170.9 (C=O), 170.7 (C=O), 167.6 (C=O), 165.2 (C=O), 165.0 × 2 (C=O), 164.9 × 2 (C=O), 138.7 × 2 (Ar), 138.5, 138.2, 138.0, 137.9, 137.8, 133.7, 133.4, 133.3, 133.2, 133.0, 132.9, 132.9, 130.0, 129.9, 129.8, 129.7 × 3 (Ar), 129.3, 129.2, 129.1 × 2 (Ar), 128.8, 128.6, 128.5 × 3 (Ar), 128.5 × 2 (Ar) 128.4 × 2 (Ar), 128.3 × 2 (Ar), 128.2 × 2 (Ar), 128.1 × 2 (Ar), 128.0 × 3 (Ar), 127.9 × 3 (Ar), 127.7, 127.5, 127.4, 125.3, 100.8 × 2 (C), 100.4, 98.9 (C-1_{Man}), 80.5 × 2 (C), 80.4, 78.1 (C-3_{Man}), 77.4 (C-3_{Xyl}), 76.0 × 2 (C), 75.9 × 2 (C), 75.6, 75.3, 74.9 × 2 (C), 74.4, 74.3 × 2 (C), 74.1, 73.4 × 3 (C), 73.2, 72.9 × 2 (C), 72.8, 72.1 × 2 (C), 72.0, 71.8, 71.4 (C-2_{Xyl}), 69.9 ($O\underline{C}H_2(CH_2)_6CH_3$), 69.5 × 2 (C), 68.5 (C-6_{Man}), 68.2 (C-2_{Man}), 67.3 (C-6_{Glc}), 67.2 × 2 (C-6_{Glc}), 65.4 (C-5_{Xyl}), 63.3 (C-5_{Xyl}), 63.2 (C-5_{Xyl}), 63.0 (C-5_{Xyl}), 37.8 ($CH_2\underline{C}H_2C(O)CH_3$), 37.7 ($CH_2\underline{C}H_2C(O)CH_3$), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.8 ($CH_2CH_2C(O)\underline{C}H_3$), 29.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 27.8 × 2 ($\underline{C}H_2CH_2C(O)CH_3$) , 25.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 21.2 ($\underline{C}H_3C(O)O$), 14.1 ($OCH_2(CH_2)_6\underline{C}H_3$). HRMS-MALDI-TOF calcd for $(M + Na)^+$ $C_{181}H_{190}NaO_{52}$: 3218.21154. Found: 3218.21424.



***n*-Hexadecyl 2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.81).** The general procedure for Troc deprotection was conducted on **3.71** (231 mg, 66.4 μmmol) using Zn powder (221 mg, 3.39 mmol) in glacial AcOH (30 mL). The crude residue was purified by gel chromatography (1:1 to 5:6 hexanes–EtOAc), to afford **3.81** (166 mg, 50.0 mol, 75%) as a white fluffy solid. R_f = 0.31 (10:11 hexanes–EtOAc); $[\alpha]_D$ +2.7 (*c*. 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.95–7.91 (m, 2H, Ar), 7.89–7.75 (m, 14H, Ar), 7.58–7.44 (m, 5H, Ar), 7.42–7.27 (m, 37H, Ar), 7.26–7.06 (m, 22H, Ar), 5.52 (d, *J* = 3.5 Hz, 1H, H-2_{Man}), 5.39–5.29 (m, 3H), 5.27 (dd, *J* = 9.4, 7.5 Hz, 1H, H-2_{Xyl}), 5.19–5.08 (m, 3H), 5.02 (app t, *J* = 8.9 Hz, 1H, H-3_{Xyl}), 4.87–4.67 (m, 8H), 4.60 (d, *J* = 7.5 Hz, 1H, H-1_{Xyl}), 4.58–4.46 (m, 7H), 4.36 (s, 1H, H-1_{Man}), 4.33–4.19 (m, 7H), 4.03–3.78 (m, 16H), 3.75 (dt, *J* = 9.3, 6.7 Hz, 1H, OC$\underline{H}_2(CH_2)_{14}CH_3$), 3.60–3.41 (m, 6H), 3.37 (dt, *J* = 9.4, 6.9 Hz, 1H, OC$\underline{H}_2(CH_2)_{14}CH_3$), 3.33–3.27 (m, 1H), 3.26–3.19 (m, 3H), 3.18–3.05 (m, 4H), 2.99–2.85 (m, 7H), 2.62–2.44 (m, 6H, 6 × $CH_2C\underline{H}_2C(O)CH_3$), 2.41–2.23 (m, 6H, 6 × $C\underline{H}_2CH_2C(O)CH_3$), 2.14 (s, 3H, $C\underline{H}_3C(O)O$), 2.11–2.05 (m, 9H, 9 × $CH_2CH_2C(O)C\underline{H}_3$), 1.53–1.46 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 1.32–1.18 (m, 26H, 26 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 0.88 (t, *J* = 6.9 Hz, 3H, $OCH_2(CH_2)_{14}C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 206.0 (C=O), 205.9 (C=O), 170.9 (C=O), 170.7 (C=O), 167.6 (C=O), 165.2 (C=O), 165.0 × 2 (C=O), 164.9 (C=O), 138.8,

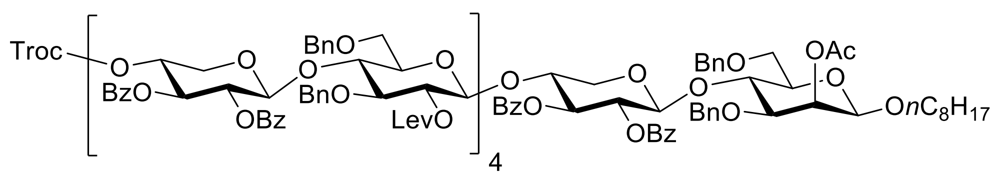
138.7, 138.5, 138.2, 138.0, 137.9, 137.8, 133.7, 133.4, 133.3, 133.2, 132.9, 133.0, 132.9, 130.0, 129.9, 129.8, 129.7 × 2 (Ar), 129.3, 129.2, 129.1, 128.8, 128.6, 128.5 × 2 (Ar), 128.4, 128.3, 128.2 × 3 (Ar), 128.1, 128.0 × 4 (Ar), 127.9 × 2 (Ar), 127.7, 127.5, 127.4, 100.8, 100.7, 100.4 × 2 (C), 98.9 ($C\text{-}1_{Man}$), 80.5 × 2 (C), 80.4 (C), 78.1 ($C\text{-}3_{Man}$), 77.4 ($C\text{-}3_{Xyl}$), 76.0 × 2 (C), 75.9 × 2 (C), 75.6, 75.3, 75.0, 74.9, 74.4 × 2 (C), 74.3, 74.2, 73.4 × 2 (C), 73.2, 72.9, 72.8, 72.1, 72.0, 71.8, 71.4 ($C\text{-}2_{Xyl}$), 69.9 ($O\underline{C}H_2(CH_2)_{14}CH_3$), 69.5 × 2 (C), 68.5 ($C\text{-}6_{Man}$), 68.2 ($C\text{-}2_{Man}$), 67.3 ($C\text{-}6_{Glc}$), 67.2 × 2 ($C\text{-}6_{Glc}$), 65.4 ($C\text{-}5_{Xyl}$), 63.3 × 2 ($C\text{-}5_{Xyl}$), 63.0 ($C\text{-}5_{Xyl}$), 37.8 ($CH_2\underline{C}H_2C(O)CH_3$), 37.7 ($CH_2\underline{C}H_2C(O)CH_3$), 32.0 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.8 × 2 ($CH_2CH_2C(O)\underline{C}H_3$), 29.7 × 4 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.6 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.4 × 2 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 27.8 × 2 ($CH_2\underline{C}H_2C(O)CH_3$), 25.9 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 21.3 ($\underline{C}H_3C(O)O$), 14.2 ($OCH_2(CH_2)_{14}\underline{C}H_3$). HRMS-MALDI-TOF calcd for $(M + Na)^+$ $C_{189}H_{206}NaO_{52}$: 3330.33674. Found: 3330.33840.



Methyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-

benzyl-β-D-mannopyranoside (3.82). To a flask containing **3.37** (112 mg, 98.0 μmol) and **3.79** (105 mg, 33.8 μmol) was added CH_2Cl_2 (2.5 mL) and 4 Å M.S. powder (90 mg) under argon. The flask was then sealed with a rubber septum connected to an argon balloon and the resultant slurry mixture was stirred for 4 h before it was cooled to 0 °C. The mixture was stirred for another 30 min, after which point TfOH (67 μL, 15.0 mmol, 2% v/v in CH_2Cl_2) was added over 2 min. Upon complete addition of TfOH, the flask was then removed from the ice bath and stirred at room temperature. After 10 h, the mixture was cooled to 0 °C and Et_3N (1.0 mL) was added. To this mixture was added DMAP (5 mg), followed by TrocCl (50 μL) and the resultant mixture was then stirred at room temperature. After 1 h, CH_3OH (1 mL) was added and the mixture was filtered through a Celite bed. The resultant filtrate was concentrated to a crude residue that was subsequently purified by silica gel chromatography (5:6 to 5:8 hexanes–EtOAc) to obtain **3.82** (100 mg, 24.5 μmol, 72%) as a white amorphous solid. R_f = 0.23 (5:6 hexanes–EtOAc); $[\alpha]_D$ +1.9 (*c*. 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.93–7.88 (m, 2H, Ar), 7.88–7.73 (m, 18H, Ar), 7.58–7.45 (m, 7H, Ar), 7.43–7.27 (m, 44H, Ar), 7.25–7.07 (m, 29H, Ar), 5.52 (d, *J* = 3.5 Hz, 1H, H-2_{Man}), 5.45 (app t, *J* = 8.7 Hz, 1H, H-3_{Xyl}), 5.39–5.28 (m, 4H), 5.25 (dd, *J* = 8.9, 7.0 Hz, 1H, H-2_{Xyl}), 5.19–5.07 (m, 4H), 4.98 (app td, *J* = 8.8, 5.2 Hz, 1H, H-4_{Xyl}), 4.88–4.46 (m, 23H), 4.33–4.18 (m, 10H), 4.10–3.74 (m, 19H), 3.59 (dd, *J* = 10.9, 4.4 Hz, 1H), 3.56–3.43 (m, 6H), 3.42 (s, 3H, OC$\underline{H}_3$), 3.32–3.26 (m, 1H), 3.26–3.04 (m, 9H), 3.00–2.80 (m, 8H), 2.64–2.44 (m, 8H, 8 × $CH_2C\underline{H}_2C(O)CH_3$), 2.40–2.24 (m, 8H, 8 × $C\underline{H}_2CH_2C(O)CH_3$), 2.15 (s, 3H, $C\underline{H}_3C(O)O$), 2.11–2.02 (m, 12H, $CH_2CH_2C(O)C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 206.0 (C=O), 205.9 (C=O), 205.8 (C=O), 170.9 × 2 (C=O), 170.7 (C=O), 165.2 × 2 (C=O), 165.0 × 2 (C=O), 164.9 × 2 (C=O), 153.2 (C=O), 138.7 × 2 (Ar), 138.4, 138.1, 137.9, 137.8 × 2 (Ar), 133.5, 133.2, 132.9 × 2 (Ar), 129.8, 129.7, 129.6, 129.3, 129.2, 128.9, 128.6 × 2 (Ar),

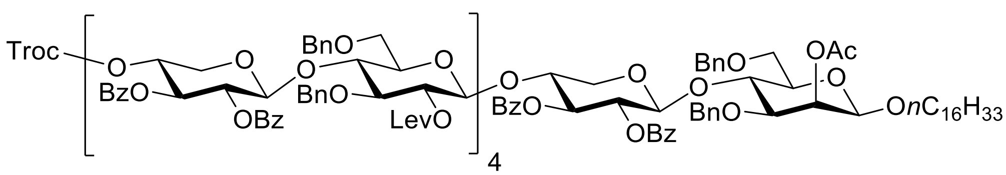
128.5 × 2 (Ar), 128.4, 128.3 × 2 (Ar), 128.2 × 2 (Ar), 128.1 × 2 (Ar), 128.0, 127.9 × 2 (Ar), 127.7, 127.5, 127.4, 100.9, 100.8, 100.4 × 2 (C), 100.1, 99.9, 94.1 ($Cl_3\underline{C}CH_2O$), 80.5 × 2 (C), 80.4, 77.9 (C-3_{Man}), 76.9 ($Cl_3C\underline{C}H_2O$), 76.0 × 2 (C), 75.9, 75.6, 75.3, 74.9, 74.3 × 2 (C), 74.0 × 2 (C), 73.2, 73.1, 72.9 × 2 (C), 72.1, 72.0, 71.9, 71.6 (C-3_{Xyl}), 71.2 (C-2_{Xyl}), 68.3 (C-6_{Man}), 68.1 (C-2_{Man}), 67.4 (C-6_{Glc}), 67.2 (C-6_{Glc}), 63.2 × 2 (C-5_{Xyl}), 63.0 (C-5_{Xyl}), 61.7 (C-5_{Xyl}), 57.1 (OCH_3), 37.8 × 2 ($CH_2\underline{C}H_2C(O)CH_3$), 37.7 ($CH_2\underline{C}H_2C(O)CH_3$), 29.8 × 2 ($CH_2CH_2C(O)\underline{C}H_3$), 27.8 × 2 ($\underline{C}H_2CH_2C(O)CH_3$), 21.2 ($\underline{C}H_3C(O)O$). HRMS-MALDI-TOF calcd for $(M + Na)^+$ $C_{221}H_{221}Cl_3NaO_{67}$: 4074.28439. Found: 4074.28203.



***n*-Octyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.84).** To a flask containing **3.37** (179 mg, 157 μmol) and **3.80** (165 mg, 51.6 μmol) was added CH_2Cl_2 (2.5 mL) and 4 Å M.S. powder (90 mg) under argon. The flask was then sealed with a rubber septum connected to an argon balloon and the resultant slurry mixture was stirred for 4 h before cooling it to 0 °C. The mixture was stirred for another

30 min, after which point TfOH (114 μL, 26.0 μmol, 2% v/v in CH_2Cl_2) was added dropwise over 2 min. Upon complete addition of TfOH, the flask was then removed from the ice bath and stirred at room temperature. After 10 h, the mixture was cooled to 0 °C and Et_3N (1.0 mL) was added. To this mixture was added DMAP (5 mg), followed by TrocCl (50 μL) and the mixture was then stirred at room temperature. After 1 h, CH_3OH (1 mL) was added and the mixture was filtered through a Celite bed. The resultant filtrate was concentrated to a crude residue that was subsequently purified by silica gel chromatography (5:2 toluene–EtOAc) to obtain **3.84** (153 mg, 36.7 μmol, 71%) as a white foamy solid. R_f = 0.23 (5:6 hexanes–EtOAc); $[\alpha]_D$ +1.9 (*c*. 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.92–7.88 (m, 2H, Ar), 7.88–7.76 (m, 18H, Ar), 7.58–7.44 (m, 7H, Ar), 7.41–7.26 (m, 44H, Ar), 7.25–7.08 (m, 29H, Ar), 5.52 (d, *J* = 3.5 Hz, 1H, H-2_{Man}), 5.45 (app t, *J* = 8.6 Hz, 1H, H-3_{Xyl}), 5.40–5.28 (m, 4H), 5.25 (dd, *J* = 8.8, 7.0 Hz, 1H, H-2_{Xyl}), 5.19–5.07 (m, 4H), 4.98 (app td, *J* = 8.7, 5.2 Hz, 1H, H-4_{Xyl}), 4.86–4.45 (m, 24H), 4.36 (s, 1H, H-1_{Man}), 4.32–4.19 (m, 9H), 4.07–3.78 (m, 18H), 3.75 (dt, *J* = 9.4, 6.8 Hz, 1H, 1 × $OC\underline{H}_2(CH_2)_6CH_3$), 3.60–3.40 (m, 8H), 3.38 (dt, *J* = 9.4, 6.9 Hz, 1H, 1 × $OC\underline{H}_2(CH_2)_6CH_3$), 3.31–3.26 (m, 1H), 3.26–3.04 (m, 9H), 3.01–2.81 (m, 8H), 2.59–2.47 (m, 8H, 8 × $CH_2C\underline{H}_2C(O)CH_3$), 2.38–2.25 (m, 8H, 8 × $C\underline{H}_2CH_2C(O)CH_3$), 2.14 (s, 3H, $C\underline{H}_3C(O)O$), 2.11–2.02 (m, 12H, $CH_2CH_2C(O)C\underline{H}_3$), 1.54–1.50 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_6CH_3$), 1.32–1.24 (m, 10H, 10 × $OCH_2(C\underline{H}_2)_6CH_3$), 0.92–0.83 (m, 3H, $OCH_2(CH_2)_6C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 206.0 (C=O), 205.9 (C=O), 205.8 (C=O), 170.9 × 2 (C=O), 170.7 (C=O), 165.2 × 2 (C=O), 165.0 (C=O), 164.9 × 3 (C=O), 153.2 (C=O), 138.8, 138.7, 138.4, 138.2, 137.9 × 2 (Ar), 133.5, 133.3, 132.9 × 2 (Ar), 129.8, 129.7 × 2 (Ar), 129.3, 129.2, 129.0, 128.6 × 2 (Ar), 128.5, 128.4, 128.3 × 3 (Ar), 128.2 × 2 (Ar), 128.1, 128.0 × 2 (Ar), 127.9 × 2 (Ar), 127.8, 127.7, 127.5, 127.4, 100.9, 100.8, 100.4 × 2 (C), 100.1 (C-1_{Xy}), 98.9 (C-1_{Man}), 94.1 ($Cl_3\underline{C}CH_2O$), 80.5, 80.4, 78.1 (C-3_{Man}),

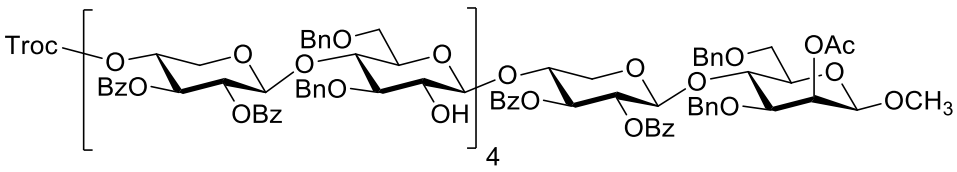
76.9 ($Cl_3C\underline{C}H_2O$), 76.0 × 2 (C), 75.9, 75.6, 75.3, 74.9 × 2 (C), 74.3 × 2 (C), 74.2, 73.4 × 2 (C), 73.2 × 2 (C), 72.9, 72.8, 72.1 × 3 (C), 72.0, 71.8, 71.6 (C-3_{Xyl}), 71.2 (C-2_{Xyl}), 69.9 ($O\underline{C}H_2(CH_2)_6CH_3$), 68.5 (C-$6_{Man}$), 68.2 (C-$2_{Man}$), 67.4 (C-$6_{Glc}$), 67.2 (C-$6_{Glc}$), 63.2 × 2 (C-$5_{Xyl}$), 63.0 (C-$5_{Xyl}$), 61.7 (C-$5_{Xyl}$), 37.8 ($CH_2\underline{C}H_2C(O)CH_3$), 37.7 ($CH_2\underline{C}H_2C(O)CH_3$), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.8 × 2 ($CH_2CH_2C(O)\underline{C}H_3$), 29.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 27.8 × 2 ($\underline{C}H_2CH_2C(O)CH_3$), 25.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 21.3 ($\underline{C}H_3C(O)O$), 14.2 ($OCH_2(CH_2)_6\underline{C}H_3$). HRMS-MALDI-TOF calcd for $(M + Na)^+$ $C_{228}H_{235}Cl_3NaO_{67}$: 4172.39394. Found: 4172.39567.



***n*-Hexadecyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.85).** To a flask containing **3.37** (156 mg, 136 μmol) and **3.81** (152 mg, 45.8 μmol) was added CH_2Cl_2 (2.5 mL) and 4 Å M.S. powder (75 mg) under argon. The flask was then sealed with a rubber septum connected to an argon balloon and the resultant slurry mixture was stirred for 4 h before it was cooled to 0 °C. The mixture was stirred for

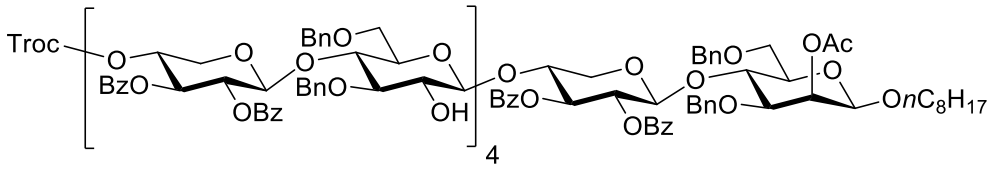
another 30 min, after which point TfOH (96 μL, 21.7 μmol, 2% v/v in CH_2Cl_2) was added dropwise rate over 2 min. Upon complete addition of TfOH, the flask was then removed from the ice bath and stirred at room temperature. After 10 h, the mixture was cooled to 0 °C and Et_3N (1.0 mL) was added. To this mixture was added DMAP (5 mg), followed by TrocCl (50 μL) and the mixture was then stirred at room temperature. After 1 h, the mixture was filtered through a Celite bed. The resultant filtrate was concentrated to a crude residue that was subsequently purified by silica gel chromatography (5:2 toluene–EtOAc) to obtain **3.85** (135 mg, 31.6 μmol, 68%) as a white foamy solid. R_f = 0.23 (5:6 hexanes–EtOAc); $[\alpha]_D$ +1.4 (*c*. 0.7, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.93–7.88 (m, 2H, Ar), 7.88–7.76 (m, 18H, Ar), 7.57–7.45 (m, 7H, Ar), 7.41–7.27 (m, 44H, Ar), 7.26–7.10 (m, 29H, Ar), 5.52 (d, J = 3.5 Hz, 1H, H-2_{Man}), 5.45 (app t, J = 8.7 Hz, 1H, H-3_{Xyl}), 5.39–5.27 (m, 4H), 5.25 (dd, J = 8.9, 7.0 Hz, 1H, H-2_{Xyl}), 5.19–5.07 (m, 4H), 4.98 (app td, J = 8.7, 5.2 Hz, 1H, H-4_{Xyl}), 4.88–4.46 (m, 23H), 4.36 (s, 1H, H-1_{Man}), 4.31–4.19 (m, 9H), 4.07–3.78 (m, 19H), 3.75 (dt, J = 9.4, 6.8 Hz, 1H, 1 × $OC\underline{H}_2(CH_2)_{14}CH_3$), 3.60–3.40 (m, 7H), 3.38 (dt, J = 9.3, 6.9 Hz, 1H, 1 × $OC\underline{H}_2(CH_2)_{14}CH_3$), 3.32–3.26 (m, 1H), 3.26–3.05 (m, 9H), 3.01–2.81 (m, 8H), 2.63–2.45 (m, 8H, 8 × $CH_2C\underline{H}_2C(O)CH_3$), 2.41–2.24 (m, 8H, 8 × $C\underline{H}_2CH_2C(O)CH_3$), 2.14 (s, 3H, $C\underline{H}_3C(O)O$), 2.11–2.04 (m, 12H, $CH_2CH_2C(O)C\underline{H}_3$), 1.56–1.48 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 1.35–1.16 (m, 26H, 26 × $OCH_2(CH_2)_{14}CH_3$), 0.88 (t, J = 6.9 Hz, 4H, $OCH_2(CH_2)_{14}C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 206.0 (C=O), 205.9 (C=O), 205.8 (C=O), 170.9 × 2 (C=O), 170.7 (C=O), 165.2 × 2 (C=O), 165.0 × 2 (C=O), 164.9 × 2 (C=O), 153.2 (C=O), 138.7 × 2 (Ar), 138.4, 138.2, 137.9 × 2 (Ar), 137.8, 133.5, 133.2, 132.9, 129.9, 129.8, 129.7 × 2 (Ar), 129.3, 129.2, 128.9, 128.6 × 2 (Ar), 128.5, 128.4, 128.3 × 2 (Ar), 128.2, 128.1 × 2 (Ar), 128.0, 127.9 × 3 (Ar), 127.7, 127.5, 127.4, 100.8 × 2 (C), 100.4 × 2 (C), 100.1 (C-1_{Xyl}), 98.9 (C-1_{Man}), 94.1 ($Cl_3\underline{C}CH_2O$), 80.5, 80.4, 78.1 (C-3_{Man}), 76.9 ($Cl_3C\underline{C}H_2O$),

76.0, 75.9, 75.6, 75.3, 74.9, 74.3 × 2 (C), 74.2, 73.4 × 2 (C), 73.2, 73.1, 72.9, 72.8, 72.1, 72.0, 71.8, 71.6 (C-3_{Xyl}), 71.2 (C-2_{Xyl}), 69.9 (O<u>C</u>$H_2(CH_2)_{14}CH_3$), 68.5 (C-6_{Man}), 68.2 (C-2_{Man}), 67.4 (C-6_{Glc}), 67.2 (C-6_{Glc}), 63.2 × 2 (C-5_{Xyl}), 63.0 (C-5_{Xyl}), 61.7 (C-5_{Xyl}), 37.8 (CH_2<u>C</u>H_2C(O)CH_3), 37.7 (CH_2<u>C</u>H_2C(O)CH_3), 32.0 (OCH_2(<u>C</u>H_2)$_{14}CH_3$), 29.8 × 2 (CH_2CH_2C(O)<u>C</u>H_3), 29.7 × 3 (OCH_2(<u>C</u>H_2)$_{14}CH_3$), 29.6 × 2 (OCH_2(<u>C</u>H_2)$_{14}CH_3$), 29.4 × 2 (OCH_2(<u>C</u>H_2)$_{14}CH_3$), 27.8 × 2 (<u>C</u>H_2CH_2C(O)CH_3), 25.9 (OCH_2(<u>C</u>H_2)$_{14}CH_3$), 22.7 (OCH_2(<u>C</u>H_2)$_{14}CH_3$), 21.3 (<u>C</u>H_3C(O)O), 14.2 ($OCH_2(CH_2)_{14}$<u>C</u>H_3). HRMS-MALDI-TOF calcd for $(M + Na)^+$ $C_{236}H_{251}Cl_3NaO_{67}$: 4284.51914. Found: 4284.52029.



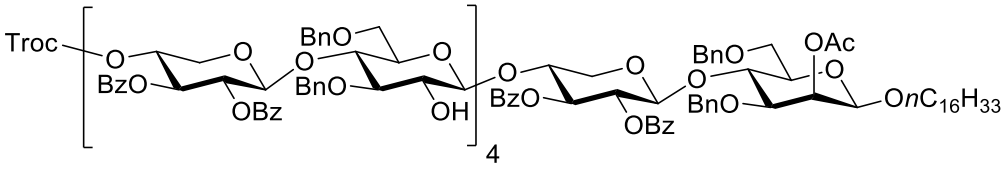
Methyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.86). The general procedure for levulinoyl deprotection was carried out on **3.82** (102 mg, 25.1 μmol) with H_2NNH_2·HOAc (240 μL, 130 μmol, 5% w/v in CH_3OH) in CH_2Cl_2–CH_3OH (4 mL, 10:1). The crude residue was purified by silica gel chromatography (5:6 hexanes–EtOAc) to obtain **3.86** (71.7 mg, 19.6 μmol, 80%) as a foamy white solid. R_f = 0.35 (1:1 hexanes–EtOAc); $[\alpha]_D$ +13.6 (*c*. 0.2, $CHCl_3$); ^{1}H NMR (500

MHz, $CDCl_3$, δ_H) 7.94–7.91 (m, 2H, Ar), 7.90–7.78 (m, 18H, Ar), 7.57–7.45 (m, 7H, Ar), 7.41–7.27 (m, 52H, Ar), 7.26–7.13 (m, 21H, Ar), 5.55 (d, J = 3.5 Hz, 1H, H-2_{Man}), 5.49 (app t, J = 8.4 Hz, 1H, H-3_{Xyl}), 5.44–5.36 (m, 4H), 5.28 (dd, J = 8.6, 6.7 Hz, 1H, H-2_{Xyl}), 5.23–5.15 (m, 4H), 5.00 (app td, J = 8.5, 5.0 Hz, 1H, H-4_{Xyl}), 4.91–4.85 (m, 4H), 4.81–4.62 (m, 12H), 4.54–4.48 (m, 2H), 4.33–4.25 (m, 6H), 4.19–4.10 (m, 5H), 4.08–3.91 (m, 14H), 3.88–3.77 (m, 6H), 3.63–3.58 (m, 2H, H-$6a_{Man}$, H-$6b_{Man}$), 3.58–3.53 (m, 1H, H-3_{Man}), 3.44 (s, 3H, OCH_3), 3.42–3.24 (m, 15H), 3.20–3.05 (m, 8H), 3.05–2.95 (m, 4H), 2.21 (s, 1H, OH), 2.19–2.12 (m, 6H, $C\underline{H}_3C(O)O$, 3 × OH). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 170.7 (C=O), 165.4 × 3 (C=O), 165.2 × 2 (C=O), 165.1 × 2 (C=O), 164.9 (C=O), 153.2 (C=O), 138.8 × 2 (Ar), 138.6, 138.3, 138.2, 138.0 × 2 (Ar), 137.9, 137.8, 133.5 × 2 (C), 133.3, 133.0, 129.9, 129.8 × 2 (Ar), 129.7 × 2 (Ar), 129.6 × 2 (C), 129.3, 129.2, 129.0, 128.5 × 3 (Ar), 128.4 × 3 (Ar), 128.2 × 2 (Ar), 128.0 × 2 (Ar), 127.9 × 5 (Ar), 127.8 × 2 (Ar), 127.7 × 2 (C), 127.6 × 2 (Ar), 101.8 × 3 (C-1_{Glc}), 100.4 × 3 (C-1_{Xyl}), 100.0 × 2 (C-1_{Xyl}, C-1_{Man}), 94.1 ($Cl_3\underline{C}CH_2O$), 82.3, 78.2 (C-3_{Man}), 76.9 ($Cl_3C\underline{C}H_2O$), 75.9 × 3 (C), 75.3, 75.1, 74.8, 74.7, 74.4 × 2 (C), 74.2, 74.0, 73.6, 73.5, 73.4, 73.3, 73.2, 73.0, 71.9, 71.8 × 2 (C), 71.4 (C-3_{Xyl}), 71.1 (C-2_{Xyl}), 68.5 (C-6_{Man}), 68.0 (C-2_{Man}), 67.6 (C-6_{Glc}), 63.1 × 2 (C-5_{Xyl}), 62.9 (C-5_{Xyl}), 61.5 (C-5_{Xyl}), 57.1 (OCH_3), 21.2 ($\underline{C}H_3C(O)O$). HRMS-MALDI-TOF calcd for $(M + Na)^+$ $C_{201}H_{197}Cl_3NaO_{59}$: 3682.13727. Found: 3682.13373.



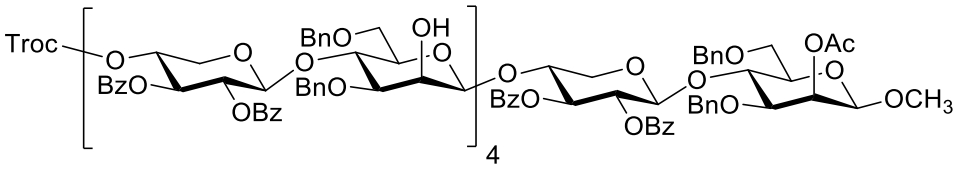
***n*-Octyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.87).** The general procedure for levulinoyl deprotection was carried out on **3.84** (67.7 mg, 16.3 μmol) with H_2NNH_2·HOAc (186 μL, 101 μmol, 5% w/v in CH_3OH) in CH_2Cl_2–CH_3OH (2 mL, 10:1). The crude residue was purified by silica gel chromatography (3:2 hexanes–EtOAc) to obtain **3.87** (45.7 mg, 12.2 μmol, 76%) as a foamy white solid. R_f = 0.50 (1:1 hexanes–EtOAc); $[\alpha]_D$ +16.0 (*c*. 0.03, $CHCl_3$); ^{1}H NMR (700 MHz, $CDCl_3$, δ_H) 7.95–7.90 (m, 2H, Ar), 7.90–7.79 (m, 18H, Ar), 7.58–7.44 (m, 7H, Ar), 7.41–7.26 (m, 52H, Ar), 7.26–7.11 (m, 21H, Ar), 5.55 (d, *J* = 3.6 Hz, 1H, H-2_{Man}), 5.48 (app t, *J* = 8.4 Hz, 1H, H-3_{Xyl}), 5.44–5.35 (m, 4H), 5.27 (dd, *J* = 8.6, 6.7 Hz, 1H, H-2_{Xyl}), 5.23–5.15 (m, 4H), 4.99 (app td, *J* = 8.4, 5.0 Hz, 1H, H-4_{Xyl}), 4.91–4.83 (m, 4H), 4.81–4.62 (m, 12H), 4.52–4.45 (m, 2H), 4.39 (s, 1H, H-1_{Man}), 4.32–4.24 (m, 5H), 4.20–4.09 (m, 5H), 4.08–3.90 (m, 14H), 3.88–3.73 (m, 6H), 3.61–3.51 (m, 3H, H-$6a_{Man}$, H-$6b_{Man}$, H-3_{Man}), 3.44–3.24 (m, 15H), 3.20–3.05 (m, 8H), 3.05–2.95 (m, 4H), 2.20 (s, 1H, OH), 2.18–2.12 (m, 6H, $C\underline{H}_3C(O)O$, 3 × OH), 1.56–1.50 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_6CH_3$), 1.29–1.20 (m, 10H, 10 × $OCH_2(C\underline{H}_2)_6CH_3$), 0.86 (t, *J* = 6.9 Hz, 3H, $OCH_2(CH_2)_6C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 170.7 (C=O), 165.4 × 3 (C=O), 165.2 × 2

(C=O), 165.1 × 2 (C=O), 164.9 (C=O), 153.2 (C=O), 138.9, 138.8, 138.7, 138.3, 138.0 × 2 (Ar), 137.9, 137.8, 133.5, 133.3, 133.0, 129.9, 129.8 × 2 (Ar), 129.7 × 2 (Ar), 129.3, 129.2, 129.0, 128.5 × 3 (Ar), 128.4 × 3 (Ar), 128.2 × 2 (Ar), 128.0 × 2 (Ar), 127.9 × 3 (Ar), 127.8 × 2 (Ar), 127.7, 127.6 × 2 (Ar), 101.8 × 3 (C-1_{Glc}), 100.5 (C-1_{Xyl}), 100.4 × 2 (C-1_{Xyl}), 100.0 (C-1_{Xyl}), 98.9 (C-1_{Man}), 94.1 ($Cl_3\underline{C}CH_2O$), 82.3, 78.4 (C-3_{Man}), 76.9 ($Cl_3C\underline{C}H_2O$), 75.9, 75.3, 75.1, 74.8, 74.7, 74.4 × 2 (C), 74.2, 73.6, 73.4 × 2 (C), 73.3, 73.2, 73.0, 72.7, 71.9, 71.8 × 2 (C), 71.4 (C-3_{Xyl}), 71.1 (C-2_{Xyl}), 69.9 ($O\underline{C}H_2(CH_2)_6CH_3$), 68.7 (C-$6_{Man}$), 68.1 (C-$2_{Man}$), 67.6 (C-$6_{Glc}$), 63.1 × 2 (C-$5_{Xyl}$), 62.9 (C-$5_{Xyl}$), 61.6 (C-$5_{Xyl}$), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 × 2 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 25.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 21.2 ($\underline{C}H_3C(O)O$), 14.3 ($OCH_2(CH_2)_6\underline{C}H_3$). HRMS-MALDI-TOF calcd for $(M + Na)^+$ $C_{208}H_{211}Cl_3NaO_{59}$: 3780.24682. Found: 3780.24635.



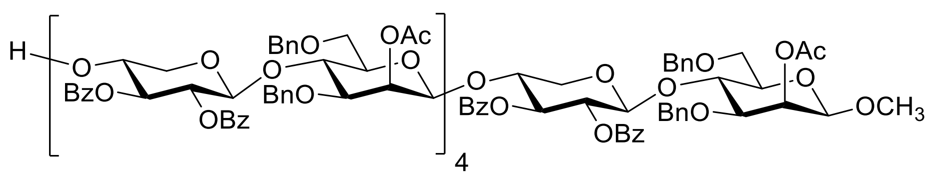
***n*-Hexadecyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.88).** The general procedure for levulinoyl deprotection was carried out on **3.85** (125 mg, 29.3 μmol) with H_2NNH_2·HOAc (320

μL, 174 μmol, 5% w/v in CH_3OH) in CH_2Cl_2–CH_3OH (4 mL, 10:1). The crude residue was purified by silica gel chromatography (1:1 hexanes–EtOAc) to obtain **3.88** (83.5 mg, 21.5 μmol, 74%) as a foamy white solid. R_f = 0.52 (1:1 hexanes–EtOAc); $[\alpha]_D$ +10.5 (*c*. 0.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.94–7.90 (m, 2H, Ar), 7.90–7.79 (m, 18H, Ar), 7.58–7.45 (m, 7H, Ar), 7.41–7.27 (m, 52H, Ar), 7.26–7.12 (m, 21H, Ar), 5.55 (d, *J* = 3.5 Hz, 1H, H-2_{Man}), 5.48 (app t, *J* = 8.4 Hz, 1H, H-3_{Xyl}), 5.44–5.35 (m, 4H), 5.28 (dd, *J* = 8.6, 6.7 Hz, 1H, H-2_{Xyl}), 5.23–5.15 (m, 4H), 5.00 (app td, *J* = 8.4, 5.0 Hz, 1H, H-4_{Xyl}), 4.91–4.85 (m, 4H), 4.82–4.63 (m, 12H), 4.52–4.46 (m, 2H), 4.39 (s, 1H, H-1_{Man}), 4.33–4.24 (m, 5H), 4.20–4.09 (m, 5H), 4.07–3.90 (m, 14H), 3.88–3.73 (m, 6H), 3.61–3.53 (m, 3H), 3.44–3.23 (m, 16H), 3.21–3.05 (m, 8H), 3.04–2.95 (m, 4H), 2.20 (s, 1H, OH), 2.19–2.13 (m, 6H, $C\underline{H}_3C(O)O$, 3 × OH), 1.56–1.50 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 1.29–1.20 (m, 26H, 26 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 0.86 (t, *J* = 6.9 Hz, 3H, $OCH_2(CH_2)_{14}C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 170.7 (C=O), 165.4 × 3 (C=O), 165.2 × 2 (C=O), 165.1 (C=O), 164.9 (C=O), 153.2 (C=O), 138.9, 138.8, 138.7, 138.3, 138.0 × 2 (Ar), 137.9, 137.8, 133.5, 133.3, 133.0, 129.9, 129.8 × 2 (Ar), 129.7 × 2 (Ar), 129.6, 129.3, 129.2, 129.0, 128.5 × 3 (Ar), 128.4 × 3 (Ar), 128.2 × 2 (Ar), 128.0 × 2 (Ar), 127.9 × 4 (Ar), 127.8 × 2 (Ar), 127.7 × 2 (Ar), 127.6 × 2 (Ar), 101.8 × 2 (C-1_{Glc}), 100.5 (C-1_{Xyl}), 100.4 × 2 (C-1_{Xyl}), 100.0 (C-1_{Xyl}), 98.9 (C-1_{Man}), 94.1 ($Cl_3\underline{C}CH_2O$), 82.3, 78.4 (C-3_{Man}), 76.9 ($Cl_3C\underline{C}H_2O$), 75.9, 75.3, 75.1, 74.8, 74.7, 74.4 × 2 (C), 74.2, 73.6, 73.5, 73.4, 73.3 × 2 (C), 73.2, 73.0, 72.7, 71.9, 71.8, 71.4 (C-3_{Xyl}), 71.1 (C-2_{Xyl}), 69.9 ($O\underline{C}H_2(CH_2)_{14}CH_3$), 68.7 (C-$6_{Man}$), 68.1 (C-$2_{Man}$), 67.6 × 2 (C-$6_{Glc}$), 63.1 × 2 (C-$5_{Xyl}$), 62.9 (C-$5_{Xyl}$), 61.5 (C-$5_{Xyl}$), 32.0 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.7 × 3 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.6 × 2 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.4 × 2 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 25.9 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 21.2 ($\underline{C}H_3C(O)O$), 14.2 ($OCH_2(CH_2)_{14}\underline{C}H_3$). HRMS-MALDI-TOF calcd for $(M + Na)^+$ $C_{216}H_{227}Cl_3NaO_{59}$: 3892.37202. Found: 3892.37399.



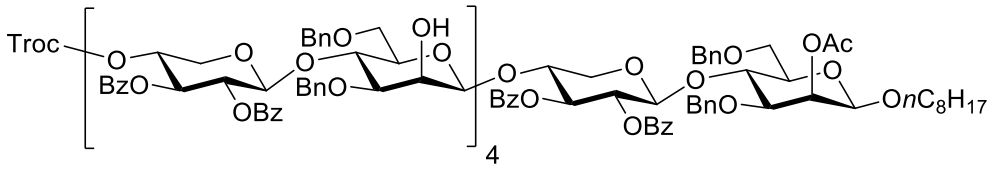
Methyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.90). Approach B for C-2 inversion was carried out on **3.86** (71.1 mg, 19.6 μmol). In this approach, DMP (101 mg, 239 μmol) and H_2O (2.0 μL, 111 μmol) were used for oxidation in CH_2Cl_2 (2 mL); subsequent reduction was conducted on the crude tetraketone with LTBA (31.0 mg, 120 μmol) in THF (1.5 mL). The resultant crude residue was purified by silica gel chromatography (6:5 to 1:1 hexanes–acetone) to afford **3.90** (50.1 mg, 13.7 μmol, 70%) as a white solid. R_f = 0.24 (6:5 hexanes–acetone); $[\alpha]_D$ +1.3 (*c*. 0.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.95–7.76 (m, 20H, Ar), 7.55–7.45 (m, 7H, Ar), 7.43–7.27 (m, 52H, Ar), 7.25–7.09 (m, 21H, Ar), 5.53 (d, *J* = 3.5 Hz, 1H, H-2$_{Man}$), 5.48 (app t, *J* = 8.1 Hz, 1H, H-3$_{Xyl}$), 5.37–5.21 (m, 9H), 5.00 (app td, *J* = 8.0, 4.8 Hz, 1H, H-4$_{Xyl}$), 4.79–4.62 (m, 17H), 4.59–4.51 (m, 3H), 4.37 (s, 1H, H-1$_{Man}$), 4.33 (s, 3H, 3 × H-1$_{Man}$), 4.31–4.27 (m, 2H, H-1$_{Man,}$ 1 × PhC$\underline{H}_2$O), 4.17 (dd, *J* = 12.3, 4.8 Hz, 1H, H-5a$_{Xyl}$), 4.14–4.03 (m, 10H), 4.01–3.86 (m, 17H), 3.64 (dd, *J* = 11.0, 4.3 Hz, 1H, H-6a$_{Man}$), 3.59–3.51 (m, 2H, H-3$_{Man}$, H-6b$_{Man}$), 3.43 (s, 3H, OCH_3), 3.42–3.38 (m, 2H), 3.38–3.22 (m, 10H), 3.20–3.03 (m, 12H), 2.45 (s, 3H, 3 × OH), 2.16 (s, 3H, C$\underline{H}_3$C(O)O). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 170.7 (C=O), 166.4 × 2

(C=O), 166.3 (C=O), 165.2 (C=O), 165.1 × 2 (C=O), 165.0 (C=O), 153.2 (C=O), 138.3, 138.2 (2 × Ar), 138.0, 137.8, 133.5, 133.4, 133.3, 133.0, 129.9, 129.8, 129.7 (2 × Ar), 129.2, 129.1, 129.0, 128.5, 128.4 × 4 (Ar), 128.2 × 2 (Ar), 128.0, 127.9 × 3 (Ar), 127.8, 127.7 × 3 (Ar), 127.6, 100.8 × 2 (C-1_{Xyl}), 100.6 (C-1_{Xyl}), 100.2 (C-1_{Xyl}), 100.0 (C-1_{Man}), 97.2 (C-1_{Man}), 94.1 ($Cl_3\underline{C}CH_2O$), 79.5, 79.2, 78.0 (C-3_{Man}), 76.9 ($Cl_3C\underline{C}H_2O$), 75.3, 75.1 × 3 (C), 74.3, 74.1, 73.4, 73.3, 73.1, 73.0, 72.3, 72.0, 71.9, 71.6, 71.2, 70.9, 68.8, 68.4 (C-6_{Man}), 68.3 (C-6_{Man}), 68.1 (C-2_{Man}), 62.8 (C-5_{Xyl}), 62.7 (C-5_{Xyl}), 61.3 (C-5_{Xyl}), 57.1 (OCH_3), 21.2 ($\underline{C}H_3C(O)O$). HRMS-MALDI-TOF calcd for $(M + Na)^+$ $C_{201}H_{197}Cl_3NaO_{59}$: 3682.13727. Found: 3682.13384.



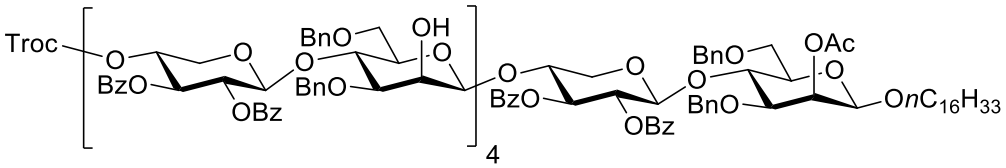
Methyl 2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.91). To a solution of **3.89** (10.0 mg, 2.7 μmol) in pyridine (2 mL) was added Ac_2O (0.50 mL) and DMAP (1.0 mg, 8.0 μmol) under argon. The reaction mixture was stirred at 40 °C overnight and cooled to room temperature; pyridine was then removed via co-evaporation with toluene (2x). The crude residue was re-dissolved in CH_2Cl_2 and washed with 1 M aqueous HCl and brine before it was dried over

Na_2SO_4. Filtration of the mixture, followed by concentration of the filtrate led to a crude syrup, that was then subjected to Troc deprotection using the general procedure with Zn powder (10.7 mg, 164 μmol) in glacial AcOH (3 mL). The resultant crude residue was purified by silica gel chromatography (57% hexanes–EtOAc) to obtain **3.91** (7.0 mg, 1.9 μmol, 70%) as a white foamy solid. R_f = 0.29 (57% hexanes–EtOAc); $[\alpha]_D$ +11.2 (*c*. 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.97–7.92 (m, 2H, Ar), 7.92–7.74 (m, 18H, Ar), 7.57–7.44 (m, 7H, Ar), 7.42–7.27 (m, 48H, Ar), 7.24–7.03 (m, 25H, Ar), 5.52 (d, *J* = 3.4 Hz, 1H, H-2_{Man}), 5.46 (d, *J* = 3.4 Hz, 1H, H-2_{Man}), 5.43 (d, *J* = 3.5 Hz, 1H, H-2_{Man}), 5.41 (d, *J* = 3.1 Hz, 2H, 2 × H-2_{Man}), 5.37–5.25 (m, 5H), 5.22–5.13 (m, 4H), 5.07 (app t, *J* = 8.5 Hz, 1H, H-3_{Xyl}), 4.75–4.66 (m, 6H), 4.66–4.59 (m, 4H), 4.58–4.46 (m, 7H), 4.39 (s, 1H, H-1_{Man}), 4.37 (s, 1H, H-1_{Man}), 4.35 (s, 2H, 2 × H-1_{Man}), 4.33–4.23 (m, 6H, H-1_{Man}, 5 × PhC$\underline{H}_2$O), 4.13–3.83 (m, 20H), 3.61 (dd, *J* = 10.9, 4.4 Hz, 1H, H-$6a_{Man}$), 3.58–3.53 (m, 1H, H-$6b_{Man}$), 3.53–3.48 (m, 2H, 2 × H-3_{Man}), 3.48–3.43 (m, 3H), 3.42 (s, 3H, OCH_3), 3.41–3.19 (m, 9H), 3.16–2.97 (m, 9H), 2.16 (s, 3H, C$\underline{H}_3$C(O)O), 1.96–1.82 (m, 12H, C$\underline{H}_3$C(O)O). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 170.8 (C=O), 170.5 (C=O), 167.5 × 2 (C=O), 165.2 (C=O), 165.1 × 2 (C=O), 138.2, 138.1 × 2 (Ar), 137.8, 137.7, 133.7, 133.5, 133.3, 132.9, 130.0, 129.9, 129.8, 129.7 × 2 (Ar), 129.3 × 2 (Ar), 129.2, 128.9, 128.5 × 2 (Ar), 128.4 × 2 (Ar), 128.2, 128.0, 127.9, 127.8 × 2 (Ar), 127.7, 100.7 (C-1_{Xyl}), 100.6 × 2 (C-1_{Xyl}), 100.4 (C-1_{Xyl}), 100.0 (C-1_{Man}), 96.5 × 3 (C-1_{Man}), 77.9 × 2 (C-3_{Man}), 77.6 (C-3_{Man}), 77.0 (C-3_{Xyl}), 75.5 × 2 (C), 75.3, 74.0, 73.8, 73.4, 73.3, 72.7, 71.9 × 2 (C), 71.3, 68.3, 68.1, 68.0, 67.9, 65.2 (C-5_{Xyl}), 62.5 (C-5_{Xyl}), 57.1 (OCH_3), 21.3 ($\underline{C}H_3C(O)O$), 20.8 ($\underline{C}H_3C(O)O$), 20.7 ($\underline{C}H_3C(O)O$). HRMS-MALDI-TOF calcd for $(M + Na)^+$ $C_{206}H_{204}NaO_{61}$: 3676.27532. Found: 3676.27221.



***n*-Octyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.92).** Approach B for C-2 inversion was carried out on **3.87** (45.7 mg, 12.6 μmol). In this approach, DMP (62.8 mg, 148 μmol) and H_2O (1.5 μL, 83.3 μmol) were used for oxidation in CH_2Cl_2 (2 mL); subsequent reduction was conducted on the crude tetraketone with LTBA (18.5 mg, 72.8 μmol) in THF (2 mL). The resultant crude residue was purified by silica gel chromatography (7:5 to 2:3 hexanes–acetone) to afford **3.92** (32.4 mg, 8.61 μmol, 71%) as a white solid. R_f = 0.29 (7:5 hexanes–acetone); $[\alpha]_D$ +8.0 (*c*. 0.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.95–7.81 (m, 20H, Ar), 7.56–7.45 (m, 7H, Ar), 7.43–7.27 (m, 52H, Ar), 7.25–7.08 (m, 21H, Ar), 5.54 (d, *J* = 3.5 Hz, 1H, H-2$_{Man}$), 5.48 (app t, *J* = 8.1 Hz, 1H, H-3$_{Xyl}$), 5.37–5.22 (m, 9H), 5.00 (app td, *J* = 8.0, 4.8 Hz, 1H, H-4$_{Xyl}$), 4.80–4.62 (m, 17H), 4.57–4.49 (m, 2H), 4.37 (s, 2H, 2 × H-1$_{Man}$), 4.35–4.31 (m, 3H, 3 × H-1$_{Man}$), 4.31–4.26 (m, 1H, 1 × PhC$\underline{H}_2$O), 4.18 (dd, *J* = 12.3, 4.8 Hz, 1H), 4.14–4.01 (m, 9H), 4.01–3.85 (m, 15H), 3.76 (dt, *J* = 9.5, 6.8 Hz, 1H, 1 × OC$\underline{H}_2$(CH$_2$)$_6$CH$_3$), 3.62 (dd, *J* = 11.0, 4.5 Hz, 1H, H-6a$_{Man}$), 3.59–3.50 (m, 2H, H-6b$_{Man}$, H-3$_{Man}$), 3.43–3.22 (m, 12H), 3.19–3.03 (m, 11H), 2.45 (s, 3H, 3 × OH), 2.15 (s, 3H, C$\underline{H}_3$C(O)O), 1.56–1.50 (m, 2H, 2 × OCH$_2$(C$\underline{H}_2$)$_6$CH$_3$), 1.31–1.19 (m,

10H, 10 × $OCH_2(C\underline{H}_2)_6CH_3$), 0.86 (t, J = 6.9 Hz, 3H, $OCH_2(CH_2)_6C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 170.6 (C=O), 166.4 × 2 (C=O), 166.3 (C=O), 166.2 (C=O), 165.1 × 2 (C=O), 165.0 (C=O), 153.2 (C=O), 138.3, 138.2 × 2 (Ar), 138.1, 138.0, 137.9, 133.4 × 2 (Ar), 133.3, 133.0, 129.9, 129.8, 129.7 × 2 (Ar), 129.2 × 2 (Ar), 129.0 × 2 (Ar), 128.5, 128.4 × 4 (Ar), 128.3, 128.2 × 2 (Ar), 128.0, 127.9 × 2 (Ar), 127.8 × 3 (Ar), 127.7 × 3 (Ar), 127.6, 100.8 × 2 (C-1_{Xyl}), 100.6 (C-1_{Xyl}), 100.1 (C-1_{Xyl}), 98.9 (C-1_{Man}), 97.1 (C-1_{Man}), 94.1 ($Cl_3\underline{C}CH_2O$), 79.5, 79.2, 78.2 (C-3_{Man}), 76.9 ($Cl_3C\underline{C}H_2O$), 75.2, 75.0, 74.3, 74.2, 74.1, 73.4, 73.3, 73.1, 72.9, 72.3, 72.0, 71.8, 71.6, 71.2, 70.9, 69.9 ($O\underline{C}H_2(CH_2)_6CH_3$), 68.7 × 2 (C), 68.5 (C-6_{Man}), 68.4 (C-6_{Man}), 68.3 × 2 (C-6_{Man}), 68.2 (C-2_{Man}), 62.8 × 2 (C-5_{Xyl}), 62.6 (C-5_{Xyl}), 61.3 (C-5_{Xyl}), 31.8 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.4 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.3 ($OCH_2(\underline{C}H_2)_6CH_3$), 29.2 ($OCH_2(\underline{C}H_2)_6CH_3$), 25.9 ($OCH_2(\underline{C}H_2)_6CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_6CH_3$), 21.2 ($\underline{C}H_3C(O)O$), 14.1 ($OCH_2(CH_2)_6\underline{C}H_3$). HRMS-MALDI-TOF calcd for $(M + Na)^+$ $C_{208}H_{211}Cl_3NaO_{59}$: 3780.24682. Found: 3780.24603.



***n*-Hexadecyl 2,3-di-*O*-benzoyl-4-*O*-(2,2,2-trichloroethoxycarbonyl)-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (3.93).** Approach B for C-2

inversion was carried out on **3.88** (68.1 mg, 19.6 μmol) for C-2 inversion. In this approach, DMP (97.8 mg, 231 μmol) and H_2O (2.0 μL, 111 μmol) were used for oxidation in CH_2Cl_2 (3 mL); subsequent reduction was conducted on the crude tetraketone with LTBA (30.3 mg, 119 μmol) in THF (2 mL). The resultant crude residue was purified by silica gel chromatography (3:2 to 1:1 hexanes–acetone) to afford **3.93** (48.5 mg, 12.5 μmol, 74%) as a white solid. R_f = 0.33 (3:2 hexanes–acetone); $[\alpha]_D$ +5.9 (*c*. 0.2, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.95–7.74 (m, 20H, Ar), 7.56–7.44 (m, 6H, Ar), 7.44–7.27 (m, 52H, Ar), 7.25–7.05 (m, 22H, Ar), 5.54 (d, *J* = 3.6 Hz, 1H, H-2_{Man}), 5.48 (app t, *J* = 8.1 Hz, 1H, H-3_{Xyl}), 5.38–5.20 (m, 9H), 5.00 (app td, *J* = 8.0, 4.8 Hz, 1H, H-4_{Xyl}), 4.83–4.61 (m, 17H), 4.56–4.49 (m, 2H), 4.37 (s, 2H, 2 × H-1_{Man}), 4.35–4.30 (m, 3H, 3 × H-1_{Man}), 4.30–4.26 (m, 1H, 1 × PhC$\underline{H}_2$O), 4.18 (dd, *J* = 12.3, 4.8 Hz, 1H), 4.15–3.88 (m, 24H), 3.76 (dt, *J* = 9.5, 6.8 Hz, 1H, 1 × OC$\underline{H}_2(CH_2)_{14}CH_3$), 3.61 (dd, *J* = 11.0, 4.5 Hz, 1H, H-$6a_{Man}$), 3.59–3.51 (m, 2H, H-$6b_{Man}$, H-3_{Man}), 3.44–3.21 (m, 11H), 3.20–3.00 (m, 12H), 2.45 (br s, 3H, 3 × OH), 2.15 (s, 3H, C$\underline{H}_3$C(O)O), 1.57–1.49 (m, 2H, 2 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 1.33–1.18 (m, 26H, 26 × $OCH_2(C\underline{H}_2)_{14}CH_3$), 0.88 (t, *J* = 6.9 Hz, 3H, $OCH_2(CH_2)_{14}C\underline{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 170.6 (C=O), 166.4 × 2 (C=O), 166.3 (C=O), 166.2 (C=O), 165.1 × 2 (C=O), 165.0 (C=O), 153.2 (C=O), 138.3, 138.2 × 3 (Ar), 138.0, 137.9, 133.5, 133.4, 133.3, 133.0, 129.9, 129.8, 129.7 × 2 (Ar), 129.2 × 2 (Ar), 129.1, 129.0, 128.5, 128.4 × 3 (Ar), 128.3, 128.2 × 2 (Ar), 128.0, 127.9 × 3 (Ar), 127.8, 127.7 × 3 (Ar), 127.6, 100.8 × 2 (C-1_{Xyl}), 100.6 (C-1_{Xyl}), 100.1 (C-1_{Xyl}), 98.9 (C-1_{Man}), 97.2 (C-1_{Man}), 94.1 ($Cl_3\underline{C}CH_2O$), 79.5, 79.2, 78.2 (C-3_{Man}), 76.9 ($Cl_3C\underline{C}H_2O$), 75.3, 75.1 × 2 (C), 74.3, 74.2, 74.1, 73.4, 73.3, 73.1, 73.0, 72.3, 72.0, 71.8, 71.6, 71.2, 70.9, 69.9 ($O\underline{C}H_2(CH_2)_{14}CH_3$), 68.8 × 2 (C), 68.5 (C-6_{Man}), 68.4 (C-6_{Man}), 68.3 × 2 (C-6_{Man}), 68.2 (C-2_{Man}), 62.8 (C-5_{Xyl}), 62.7 (C-5_{Xyl}), 61.3 (C-5_{Xyl}), 32.0 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.7 × 3 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.6 × 2 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.4 × 2 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 29.3

($OCH_2(\underline{C}H_2)_{14}CH_3$), 25.9 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 22.7 ($OCH_2(\underline{C}H_2)_{14}CH_3$), 21.3 ($\underline{C}H_3C(O)O$), 14.2 ($OCH_2(CH_2)_{14}\underline{C}H_3$). HRMS-MALDI-TOF calcd for $(M + Na)^+$ $C_{216}H_{227}Cl_3NaO_{59}$: 3892.37202. Found: 3893.37354.

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Chapter 4

Summary and future research direction

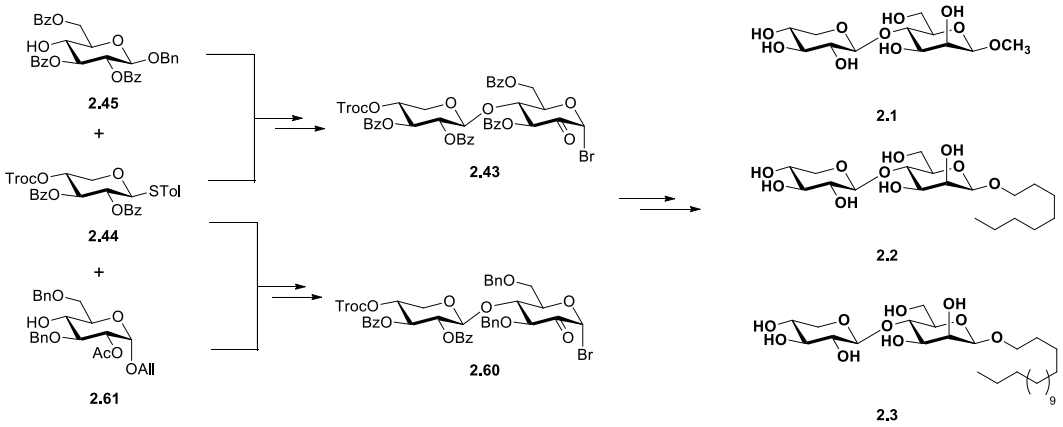
4.1 Thesis overview

This thesis described the total synthesis of xylomannan AFGL mimetics by using two different β-mannosylation approaches: the ulosyl bromide approach and a simultaneous multiple C-2 inversion strategy. Unlike previous syntheses, which focused on the conventional approach of constructing the difficult β-mannosides followed by the readily accessible β-xylosylation for glycan chain extension, our route bears the distinction of using β-mannosylation as a means of large glycan assembly.

4.2 Summary

4.2.1 Ulosyl bromide approach

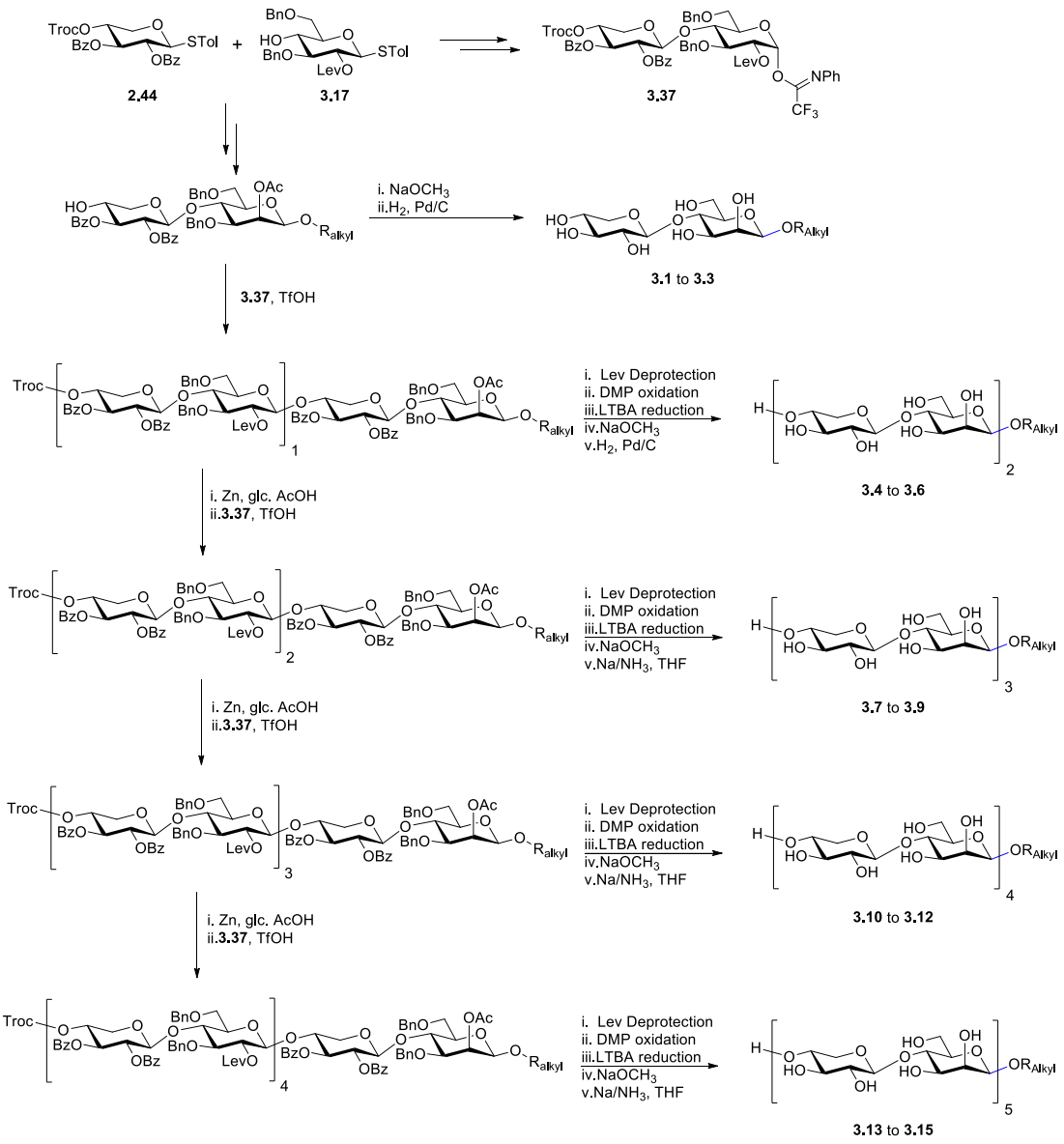
In Chapter 2, we explored the use of ulosyl bromides to construct the β-mannosidic linkages in AFGL mimetics. Key features of our synthetic route included the synthesis of ulosyl bromides from the monosaccharide building blocks, glycosylations followed by stereoselective reduction and subsequent deprotection steps. This approach was found to be effective on primary aliphatic alcohols with yields of 60 to 65% after reduction, and this led to the synthesis of targets **2.1–2.3** (Scheme 4-1). However, attempts to extend this approach to carbohydrate acceptors did not work as planned.



Scheme 4-1: Ulosyl bromide approach to AFGL mimetics **2.1**–**2.3**

4.2.2 Simultaneous multiple C-2 inversion strategy

In Chapter 3, we disclosed the synthesis of AFGL mimetics via a simultaneous multiple C-2 inversion strategy (Scheme 4-2). This strategy is an extension of the oxidation–reduction strategy, which builds upon the preference of equatorial attack by the incoming hydride on 2-ulosides to deliver β-mannosides. Critical to the success of this approach is the use of *N*-phenyltrifluoroacetimidate donors in glycosylations, and the DMP oxidation reagent as well as mild, yet highly selective LTBA reagent to effect stereoselective C-2 inversion. This allowed not only rapid assembly of glycan chain via β-glucosylation, but also exclusive β-*manno*-selectivity upon simultaneous multiple C-2 inversion, which is the hallmark of this approach. After C-2 inversion, global deprotection steps were then carried out via ester hydrolysis followed by removal of benzyl groups.



Scheme 4-2: Synthesis of AFGL mimetics via a simultaneous multiple C-2 inversion strategy

In principle, removal of the benzyl groups can be achieved by catalytic hydrogenation. However, we discovered that this method did not work well on xylomannan oligomers beyond tetrasaccharides. Though this was resolved with Birch reduction, oligosaccharide breakdown became increasingly common with larger oligosaccharides. This was reflected in the gradual decline in the yields of the deprotection steps, from 80% in hexasaccharides to 50% in octasaccharides. Unfortunately for decasaccharides, almost complete breakdown was observed in

all the cases under Birch reduction, losing most of the precious compounds in the process. Despite this setback, we managed to obtain pure methyl decasaccharide **3.13**, albeit in low yield of 20%.

4.3 Future Work

Despite the success of the simultaneous C-2 inversion strategy, poor deprotection yields in the cases of the decasaccharides warrant further investigation into other deprotection methods. One of these alternatives is the oxidative debenzylation in the presence of $NaBrO_3$ and $Na_2S_2O_3$[1,2], which was used to achieve anomeric deprotection in Chapter 2. Problems encountered in 8 + 2 glycosylation also remain to be addressed. One possible solution is to replace the C-6 benzyloxy group in the disaccharide donor with non-ether protecting groups such as *p*-toluoyl or *p*-methoxybenzoyl esters to avoid the cyclisation side-product. Another alternative is to enhance the reactivity of the acceptor by replacing the acyl groups with electron-donating groups such as benzyl or silyl groups.[3,4]

Gaining structural insights into these AFGL mimetics is an important step towards understanding their antifreeze activity. Though analysis of Molecular Dynamics (MD) simulations of large xylomannan oligomers based on synthetic tetrasaccharides suggested that these molecules may adopt a possible helical conformation[3,4], this observation has yet to be experimentally verified. We believe that verification can be achieved by obtaining X-ray crystallographic data of the xylomannan oligomers. Since all our AFGL mimetics share identical xylomannan cores and bear the appearance as solids, it may be possible to obtain crystals of these mimetics suitable for X-ray diffraction analysis.

From a broader perspective, we hypothesize that our simultaneous C-2 inversion strategy may be applicable in the synthesis of other oligosaccharides bearing multiple β-mannosidic linkages, such as β-(1→3)- and β-(1→4)-mannans. Another possibility is the use of our strategy to construct multiple *N*-acetyl-β-mannosaminic (β-ManNAc) linkages found in the cell walls of certain pathogenic bacteria, such as *Streptococcus pneumoniae*[5] and *Pseudomonas aeruginosa* respectively[6]. This can be achieved using β-glucosylation to secure the *trans*-equatorial linkages at an early stage, followed by simultaneous C-2 manipulation of these β-glucosyl residues into the β-ManNAc linkages via a five stage sequence[7]: deacylation, oxidation, oxime formation, stereoselective reduction[6] and lastly, *N*-acetylation.

Finally, as part of a collaboration, compounds **3.1–3.13** will be delivered to the lab of Prof. Hubbard in the Department of Pharmacology at the University for Alberta for evaluation of their TH and IRI activities. We hope these compounds will be able to reveal the structure–activity relationships of xylomannan AFGLs and also serve as novel antifreeze compounds for commercial applications.

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