DEVELOPMENT OF SECOND GENERATION SYNTHESES OF LEGIONAMINIC ACID AND PSEUDAMINIC ACID DONORS;

SIDE CHAIN CONFORMATION AND ITS INFLUENCE ON GLYCOSYLATION SELECTIVITY IN HEXO- AND HIGHER CARBON FURANOSIDES

by

SAMEERA SIYABALAPITIYA ARACHCHIGE

(Under the Direction of David Crich)

ABSTRACT

Sialic acids are nine carbon keto sugar acids that are essential in human pathology. The most common sialic acid, *N*-acetylneuraminic acid (NeuAc), is the parent sialic acid in the family. Legionaminic acid (Leg) and pseudaminic acid (Pse) are 9-deoxy analogues of NeuAc that are rare but essential. Gram-negative pathogenic bacteria contain legionaminic acid and pseudaminic acid glycosides, which are important in their pathogenic processes. Chapter one describes the biology and chemistry of legionaminic acid and pseudaminic acid including their previously reported syntheses.

The development of improved syntheses of legionaminic acid (Leg) and pseudaminic acid (Pse) donors is described in chapter two. Cleavage of the *N*-acetylneuraminic acid side chain at C7 gives the corresponding aldehyde, which, after conversion to the Ellman *S* or *R* sulfinimines, was coupled with acetaldehyde in a samarium iodide-mediated process to install the new side chains

stereoselectively. This side chain exchange strategy afforded legionaminic acid, 8-*epi*-legionaminic acid, acetaminic acid, and 8-*epi*-acetaminic acid donors in 12 steps, along with a pseudaminic acid donor in 15 steps from *N*-acetylneuraminic acid.

These conformationally constrained donors showed different reactivities and selectivities in glycosylation reactions compared to their mono cyclic donors. Therefore, side chain conformation was identified as an important factor, which influences reactivity and selectivity in the glycosylation reactions.

Chapter three reviews, influence of side chain conformations in various glycosyl donors on glycosylation reactivity and selectivity.

Chapter four describes the syntheses of four hexofuranosyl thiglycoside donors, analysis of their side chain conformations, and their glycosylation reactions. A L-idofuranosyl donor and a D-altrofuranosyl donor with predominant *gt* conformation and a L-galactofuranosyl donor with the *gg* conformation showed 1,2-*cis*-selectivity in their glycosylations. In contrast, a D-glucofuranosyl donor with the most electron withdrawing *tg* conformation was 1,2-*trans*-selective. Low temperature NMR studies revealed the formation of configuration dependent complex mixtures from the activated D-glucofuranosyl and L-idofuranosyl donors, which were interpreted as indicative of the formation of bridged bicyclic oxonium ions by participation of various benzyl ethers.

INDEX WORDS: Sialic acid, legionaminic acid, pseudaminic acid, acetaminic acid, Ellmann sulfinyl imines, aza-pinacol cross coupling, side chain conformation, ions, mixtures, furanoside glycosylation and selectivity, VT-NMR, benzyl ether participation.

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The University of Georgia
May 2022

DEDICATION

I dedicate my PhD work to the five most important people in my life for their unflinching support and endless love – my parents, Mr. Jones Siyabalapitiya Arachachige, Mrs. Ranjini Kalansooriya Arachchige, my wife, Mrs. Dinusha De Alwis, my two daughters, Diana Siyabalapitiya Arachchige and Dinara Siyabalapitiya Arachchige.

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LIST OF ABBREVIATIONS

Ac	Acetyl
Ada	Adamantyl
AIBN	Azobisisobutyronitrile
Ar	Aryl
Ax	Axial
Bn	Benzyl
Boc	*tert*-Butoxycarbonyl
Bz	Benzoyl
Calcd	Calculated
CAN	Ceric ammonium nitrate
Cbz	Benzyloxycarbonyl
CIP	Contact Ion Pair
CMP	Cytidine-5-monophosphate
CSA	Camphorsulfonic acid
DBU	1,8-Diazabicyclo(5.4.0)undec-7-ene

DCM	Dichloromethane
DDQ	2,3-Dichloro-5,6-dicyano-1,4-benzoquinone
DEAD	Diethyl azodicarboxylate
DIAD	Diisopropyl azodicarboxylate
DIBAL-H	Diisobutylaluminium hydride
DIPEA	Diisopropylethylamine
DMAC	Dimethylacetamide
DMAP	4-(Dimethylamino)-pyridine
DMF	Dimethyl formamide
DMP	Dess-Martin periodinane
DMSO	Dimethyl sulfoxide
DPPA	Diphenylphosphoryl azide
ESI	Electrospray Ionization
Et	Ethyl
EtOAc	Ethyl Acetate
Eq	Equatorial
Equiv	Equivalent
Gal	Galactose

GalNAc	N-Acetyl galactosamine
GDP	Guanosine diphosphate
GlcN	Glucosamine
gg	gauche-gauche
gt	gauche-trans
h	Hour
HATU	*O*-(7-Azabenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate
HRMS	High Resolution Mass Spectrometry
Hz	Hertz
iPr	Isopropyl
Im	Imidazole
KDN	Keto deoxy nonulosonic acid
KDO	Keto deoxy octulosonic acid
Leg	Legionaminic acid
LPS	Lipopolysaccharide
m-CPBA	*meta*-Chloroperoxybenzoic acid
Me	Methyl
mmol	Millimole

MS	Molecular sieves
Nap	Naphthyl
NAD	Nicotinamide adenine dinucleotide
NDP	Nicotinamid diphosphate
NeuAc	5-*N*-Acetylneuraminic acid
Neu5Gc	5-*N*-Glycolylneuraminic acid
NIS	*N*-Iodosuccinimide
NMR	Nuclear magnetic resonance
NOE	Nuclear overhauser effect spectroscopy
NulO	Nonulosonate
Ph	Phenyl
Piv	Pivoloyl
Pse	Pseudaminic acid
Pyr	Pyridine
rt	Room temperature
Sia	Sialic acid
Siglec	Sialic acid-binding immunoglobin-like lectin
sTn	Sialyl Tn antigen

TBDPS	*tert*-Butyldiphenylsilyl
TBS	*tert*-Butyldimethylsilyl
Tf	Trifluoromethanesulfonyl
TFA	Trifluoroacetic acid
tg	trans-gauche
THF	Tetrahydrofuran
TLC	Thin layer chromatography
Ts	*p*-Toluenesulfonyl
Tol	Toluenyl
VT	variable temperature

CHAPTER ONE

BIOLOGY AND CHEMISTRY OF LEGIONAMINIC ACID AND PSEUDAMINIC ACID

1.1 Sialic Acids

Sialic acids have been identified as biologically essential 9-carbon keto sugar acids categorized under the family of nonulosonic acids synthesized in animals.[1, 2] They exist at the non-reducing end of various *N*-linked and *O*-linked glycoproteins and glycolipids and are involved in a wide range of biological processes.[1] Sialic acids are synthesized inside the cell by some bacterial species, while other bacterial species acquire them from a host, as part of the host-parasite interactions.[3] To date, over 50 derivatives of sialic acids have been discovered from cellular organisms, which are widely spread throughout nature, and *N*-acetylneuraminic acid is found to be the most common.[1] Therefore, *N*-acetylneuraminic acid is considered the parent sialic acid, and the other family members are treated as its derivatives.[4] The most critical derivatives in the family of bacterial sialic acids are legionaminic acid and pseudaminic acid, which are common in human pathogens.[5]

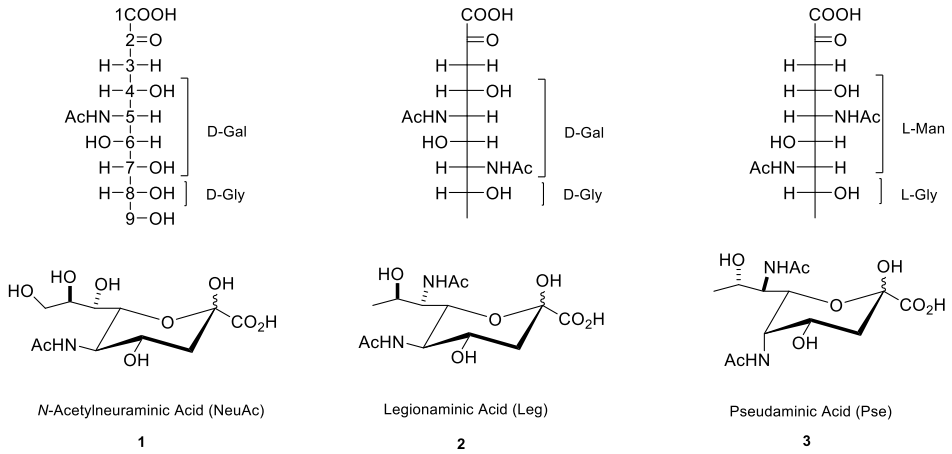


Figure 1. Structures of *N*-acetylneuraminic acid (NeuAc), legionaminic acid (Leg) and pseudaminic acid (Pse).

1.2 Biological role of Sialic Acids

Sialic acids have been found in glycoconjugates of some bacteria, viruses, protozoa, fungi, and animals of the deuterostome lineage, testifying to their widespread nature.[6-8] In mammals and lower vertebrates, sialic acids are present in the form of glycoproteins, and glycolipid-like gangliosides and glycosaminoglycans, which act as ligands or receptors for cell-cell communication or host-parasite interaction.[6, 9, 10] The parent sialic acid *N*-acetylneuraminic acid has been reported in cicada of *Philaenus spumarius (P. spumarius)* and mollusca of both *Arion lusitanicus (A. lusitanicus)* and *Arion rufus (A. rufus)*.[11, 12] The human gangliosides have sialylated glycolipids that function as a receptor for pathogenic bacterial infection on the gut epithelial cells.[6, 13]

The unique nature of sialic acids affects the function and structure of their glycoconjugates and produces many roles in biological systems. Specifically, these glycoconjugates act as ligands for lectins, antibodies, and enzymes to promote cell-cell recognition, communication, aggregation, development, carbohydrate-protein interactions. They also have significant activities in

immunology where they control the lifetimes of glycoconjugates in organisms and so mediate bacterial and viral infections, tumor growth and metastasis, microbiome, cell signaling, reproduction, and nervous system biology.

The molecular structure of the sialic acids contains a carboxylic function such that they can acquire negative charge and become a hydrophilic molecule according to the conditions. This unique structure enables sialic acids to change physical properties in glycoconjugates involved in neural plasticity, glomerular filtration, or blood cell charge repulsion.[9] Sialic acids are present in the binding sites of receptors for multiple pathogens and toxins. These receptors are classified as two types: extrinsic receptors and intrinsic receptors. The extrinsic receptors known, as pathogen-binding protein receptors, identify sialic acid structures by specific linkages in a defined underlying sugar chain.[9] The intrinsic receptors enable 'molecular mimicry', whereby microbial pathogens synthesize host sialic acids, and therefore can escape from the host immune response.[9]

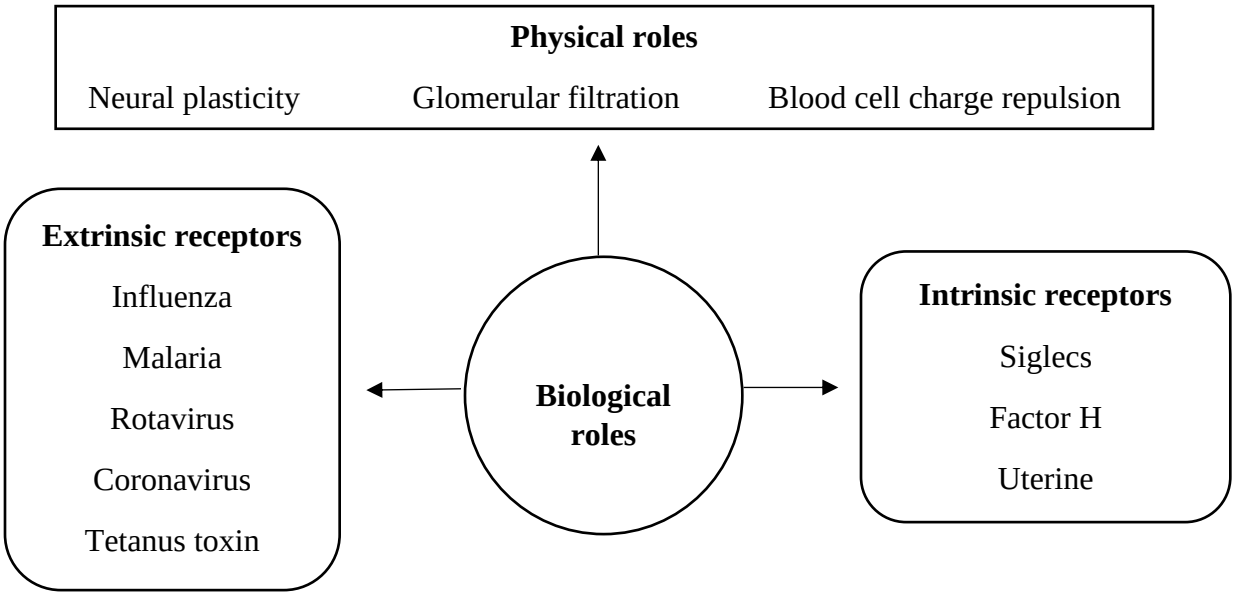


Figure 2. Biological and pathological roles of sialic acids.

1.2.1 Sialic acid and human disease

With the predominant existence of sialic acids on eukaryotic cell surfaces, pathogens are adopt the properties of sialic acids and mimic host sialic acids to bypass the host immune responses.[14] Bacteria can mimic them by either *de novo* biosynthesis or acquiring sialic acids from their environment and transporting them to the cell surface, where they are included in the host-parasite interaction.[14] This interaction can be employed by bacteria to metabolize and use sialic acid to colonize and express their disease-causing properties (Table 1).[14] All these interactions depend on the substitutions at carbon 5 of the sialic acid, or on covalent modifications of its 4,7,8,9-hydroxyl groups.

Table 1. Diseases expressed by pathogenic bacteria.

Pathogen	Major disease
Sialic acid synthesized by pathogen	
Neisseria meningitidis B	Meningitis
Escherichia coli K1	Neonatal meningitis
Group B Streptococcus	Neonate and infant infections
Campylobacter jejuni	Enteritis, Guillian-Barré syndrome
Host sialic acid taken up by pathogen	
Hemophilus influenza	Respiratory infections
Hemophilus ducreyi	Chancroid
Host sialic acid transferred by trans-sialidase	
Trypanosoma cruzi	Chagas disease
Corynebacterium diphtheria	Diphtheria
Host CMP-sialic acid used by sialyltransferase	
Neisseria gonorrhoea	Gonorrhoea

Neisseria meningitides group A	Meningitis
Source of sialic acid unknown	
Sporotrichium schenkii	Skin infection
Aspergillus fumigates	Opportunistic infections

The pathological significance of sialic acids is described by the following three examples.

1. The equatorial (2→3) linked glycoconjugate chain is preferentially recognized by *influenza* viruses, but fortunately humans have equatorial (2→6) linked sialic acids in their airways. Therefore, humans have resistant to such *influenza* viruses, which must undergo mutation to change the linkage type and infect humans. Animals who are devoid of equatorial linked sialic acids in their airways like chimpanzees are resistant to human *influenza* A.[15]
2. The only Gram-positive bacteria that produces a sialic acid containing capsule is *Streptococcus agalactiae (S agalactiae),* which causes serious infections in newborns.[14] It produces this sialic acid containing capsule using a sialyltransferase to install a terminal equatorial (2→3) linked NeuAc to galactose in the capsule's oligosaccharide repeat.[16]
3. The significance of 9-*O*-acetylated sialic acids have two contradictory effect as this modification can block the binding of the *influenza* A virus, while this is required for binding of common cold viruses like *influenza* C and certain coronaviruses.[17, 18] This difference enables the detection of *influenza* C by screening for 9-*O*-acetylated sialic acid.[17, 19]

Some examples of the naturally occurring sialic acid glycosides with various linkages are shown here (Figure 3).

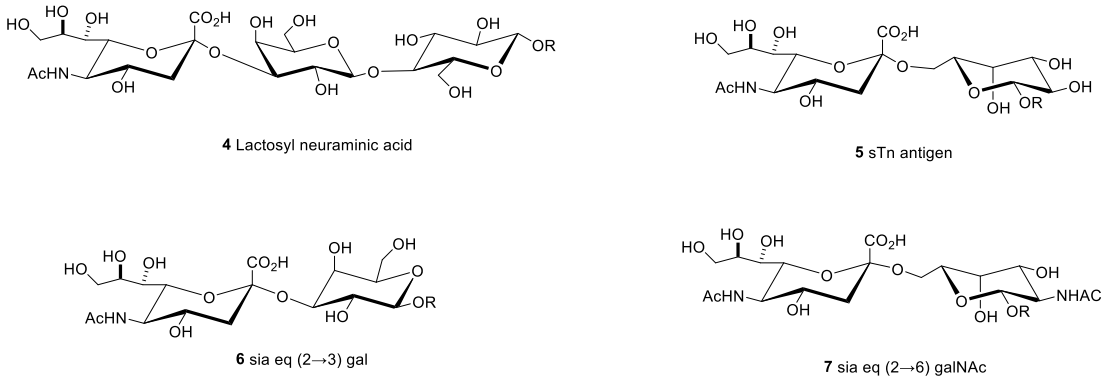


Figure 3. Naturally occurring sialic acid linkages.

1.3 Legionaminic acid and pseudaminic acid

The legionaminic acid and pseudaminic acids belong to the growing family of bacterial nonulosonate sugars that resemble the parent sialic acid *N*-acetylneuraminic acid in being 9-carbon acids, but differ in that they are deoxy at C9.[20] This family currently includes six known members including 4-*epi*-legionaminic acid, 8-*epi*-legionaminic, acinetaminic acid, and fusaminic acid.[21-27] Furthermore, all of these bacterial sialic acids have acylamino substituents at C7 instead of the more typical hydroxy group except for fusaminic acid. They also have more diversity in their C5 *N*-acyl substituents compared to other sialic acids.[20] Although legionaminic acid is 9-deoxy and 7-amido, it is the only member of the group that has the same absolute and relative configuration as *N*-acetylneuraminic acid.[20] Gram-negative bacteria such as *Pseudomonas aeruginosa*, *Legionella pneumophila* serogroup 1, *Camphylobacter jejuni*, and *Camphylobacter coli* contain legionaminic acid and pseudaminic acid glycosides in their lipopolysaccharides and glycoproteins.[26-28]

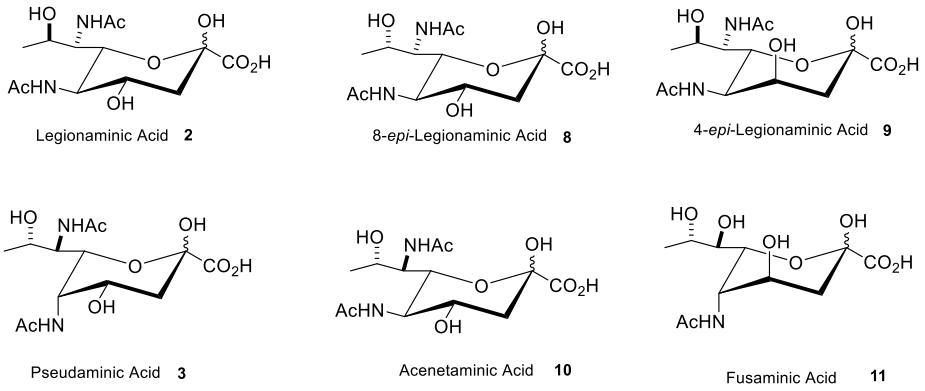


Figure 4. Family of natural bacterial nonulosonate (NulO) sugars.

Based on the Rosanoff nomenclature convention,[29] the equatorial glycosides of NeuAc and Leg are α-glycosides, whereas the equatorial glycosides of Pse are β-glycosides. Therefore, to avoid any confusion in the description of their glycosides, in this thesis all glycosides will be simply classified as equatorial or axial glycosides.

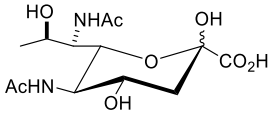
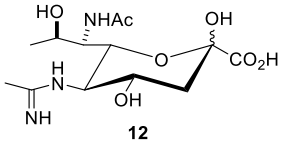
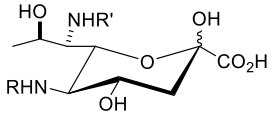
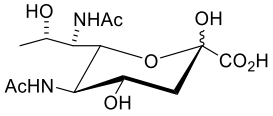
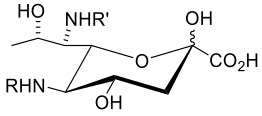
1.3.1 Legionaminic acid and its role in biological systems

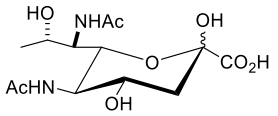
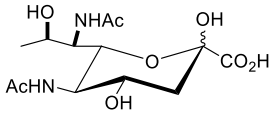
In 1994 Knirel and coworkers characterized legionaminic acid by isolating it from the lipopolysaccharide (LPS) 1 *O*-chain of *Legionella pneumophila*, a Gram-negative bacterium that is responsible for the Legionnaires' disease, where it incoperates legionaminic acid as a 5-*N*-acetimidoyl-7-*N*-acetyl-legionaminic acid homopolymer with equatorial-2→4-linkages.[21] Legionnaire's disease is caused by breathing the mist from water that contains the *Legionella pneumophila* bacteria, typically from hot tubs, showers, or air-conditioning units of large buildings. This is a type of pneumonia that is often fatal because *Legionella pneumophila* replicates within the alveolar macrophages of the human lung tissues.[30] In addition, legionaminic acid has been reported in various bacterial glycoconjugates incorporated in the repeating unit of heteropolymeric LPS,[31] capsular polysaccharides,[32, 33] and *O*-linked monosaccharide modifications on the flagellae of *Campylobacter jejuni*[34].

The nature of the host-pathogen interaction with legionaminic acid is largely unknown although Leg is structurally homologous to NeuAc, but it is established that the interaction depends upon features of the glycerol and exocyclic moiety, as replacing Leg by NeuAc can affect pathogen interactions.[20] In 2011 Watson and coworkers discovered the biological activity of NeuAc interacting molecules could be influenced by the presence of sialic acid analogues in Siglecs (sialic acid-binding lectins).[35] The same group in 2015 further showed the importance of the glycerol or exocyclic moiety on the biological properties of nonulosonates by synthesizing GD1a with a terminal Leg.[36] In 2015 the Seeberger group used remodeled antibodies to Leg to enhance the half-life of serum and explained the importance of the C7–C9 exocyclic moiety in a biological context.[37] This was further studied by Gulati and coworkers in 2015, who found that Leg can counteract the serum protection afforded to *Neisseria gonorrhoeae* by NeuAc.[38] *Neisseria gonorrhoeae* utilizes CMP-NeuAc from the host cell and modifies its cell surface molecules with NeuAc, and as a consequence it can survive in the host by complement-mediated killing. However, with the introduction of CMP-Leg to these cells**,** the surface is modified Leg and they become sensitive to complement-mediated killing themselves.[20] Therefore, CMP-Leg is identified and is being evaluated as a potential treatment or prevention of *N. gonorrhoeae* infections.[38]

The various derivatives of legionaminic acid which have been identified including 8-*epi*-legionaminic acid are summarized in Table 2.

Table 2. Legionaminic acid derivatives found in bacteria.

Legionaminic acid derivative	Bacterial source	Reference
legionaminic acid (D-*glycero*-D-*galacto*)		
 **2**	*Vibrio alginolyticus* 945-80 *Acinetobacter baumannii* O24 *Vibrio parahaemolyticus* O2 *Campylobacter jejuni* 11168 *Escherichia coli* O161	39, 40 39, 41 42, 43 44 45
 **12**	*Legionella pneumophila* serogroup 1 *Pseudomonas fluorescens* ATCC 49271 *Vibrio salmonicida* NCMB 2262 *Campylobacter coli* VC167 *Campylobacter jejuni* 11168	21, 39 39, 46 39, 43 47 44
 **13-16** R = C(=O)$CH_2CH(OH)CH_3$; R' = Ac R = Ac; R' = C(=O)CH(NHAc)CH_3 R' = $CH(NHCH_3)CH_3$; R" = Ac R' = (=O)$CH_2CH_2CH(CO_2H)NHCH_3$; R" = Ac	*Acinetobacter baumannii* O24 *Vibrio parahaemolyticus* KX-V212 *Escherichia coli* O161 *Campylobacter coli* VC167 *Campylobacter jejuni* 11168 *Clostridium botulinum*	39, 41 42, 45 47 44 48
8-*epi*-legionminic acid (L-*glycero*-D-*galacto*)		
 **8**	*Pseudomonas aeruginosa* O12 *Providencia stuartii* O20 *Escherichia coli* O108	49 50 51
 **17-21** R = C(=NH)CH_3; R' = Ac R = Ac; R' = C(=NH)CH_3 R = Ac; R' = C(=O)CH(NHAc)CH_3 R = C(=O)$CH_2CH(OH)CH_3$; R' = Ac R = C(=O)$CH_2CH_2CH_2OH$; R' = Ac	*Morganella morganii* KF 1676 *Shewanella putrefaciens* A6 *Escherichia coli* O108 *Salmonella arizonae* O61 *Yersinia ruckeri* O1	52 53 54 55 56
Acinetaminic acid derivative		
Acinetaminic acid (L-*glycero*-L-*altro*)		

 **10**	*Acinetobacter baumannii* isolate D36	25, 57
8-*epi*-Acinetaminic acid (D-*glycero*-L-*altro*)		
 **22**	*Acinetobacter baumannii* K7L3	58

1.3.2 Pseudaminic acid and its role in biological systems

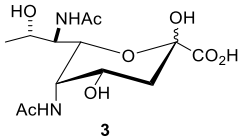
Pseudaminic acid was first reported by Knirel and co-workers in 1984, who isolated it from the lipopolysaccharides of *Pseudomonas aeruginosa* O7/O9 and *Shigella* bodyii type 7.[4] Although this substance was identified as 5,7-diacetamido-3,5,7,9-tetradeoxy-L-glycero-L-manno-non-2-ulosonic acid, it is not a direct derivative of neuraminic acid,[1] as compared to the parent sialic acid NeuAc, it is 9-deoxy and 7-amido and has the opposite configuration at C5, C7 and C8. There have been discovered several naturally occurring Pse derivatives from a growing number of bacterial species (Table 3) proving it to be widespread within biological systems. All of these acids have the L-*glycero*-L-*manno* configuration but differ in the type of *N*-acyl substitution at C5 and C7.

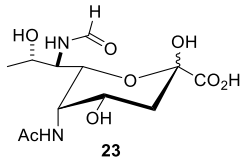
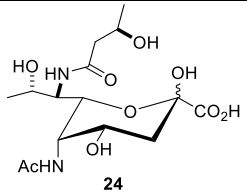
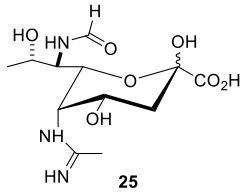
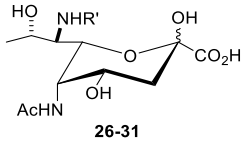
Pseudaminic acid and its derivatives are unique among the bacterial sialic acids because they are found as components of important cell surface glycans including oligosaccharides (lipopolysaccharide *O*-antigens[22] and capsular polysaccharides[59]) and glycoproteins (pilins[60] and flagellins[61, 62]). These glycans are the important structural features for bacterial virulence and Pse is found in both equatorial and axial linked forms and is less common at the terminal end. Although in humans both cystic fibrosis and various gastrointestinal diseases are caused by virulence behaviour of *Pseudomonas aeruginosa*,[63] the exact biological role of Pse is still understudied, due

to the inaccessible of its derivatives. Therefore, the studies of its biological roles and development of therapeutic and diagnostic vaccines will benefit from the efficient synthesis of Pse and its derivatives.

Werz and coworkers have synthesized azidoacetamide-functionalized Pse substrates and transferred them onto bacterial flagellin (*B. thuringiensis* and *C. Jejuni*), and studied them by an immunoblotting assay.[64] They found their constructs to be useful biochemical and diagnostic molecular tools for detection of virulence in Pse-expressing bacteria and for identification of anti-virulence agents. Immunological destruction of bacteria that contain pseudaminic acid has been promoted by Kaewsapsak utilizing azide-labelled glycosylated proteins in *H. pylori* to ligate immune stimulants.[65] In addition, the three small molecules were reported by Menard *et al*., which can penetrate to the cell membrane of Gram-negative bacteria and inhibit the enzyme PseB by preventing the formation of flagella.[66]

Table 3. Pseudaminic acid derivatives found in various bacteria.

Pseudaminic acid	Bacterial source	Reference
 **3**	*Escherichia coli* O136	67
	Proteus vulgaris O39	68
	Campylobacter jejuni 81-176	62, 69
	Campylobacter jejuni 11168	44
	Campylobacter coli VC167	70
	Pseudoateromonas atlantica T9	22
	Helicobacter pylori 1061	61, 69
	Pseudoalteromonas atlantica IAM 14165	71
	Aeromonas caviae UU51	69
	Rhizobium sp. NGR234	72
	Sinorhizobium meliloti Rm1021	73, 74
	Cellulophaga fucicola	75
	Vibrio vulnificus 27562	76
	Piscirickettsia salmonis	77

 **23**	*Pseudomonas aeruginosa* O7a, 7b, 7d and O7a, 7d *Pseudoalteromonas distincta* KMM 638	78, 79 80
 **24**	*Pseudomonas aeruginosa* O10a *Shigella* boydii type 7 *Pseudomonas aeruginosa* O9a, 9b *Sinorhizobium fredii* HH103 *Kribbella spp*. VKM *Actinoplanes utahensis* VKM Ac-674	4 4, 81, 82 49, 81 83 84, 85 84, 86
 **25**	*Vibrio cholera* O:2 *Campylobacter jejuni* 81-176 *Campylobacter coli* VC167	87 62, 69 70
 **26-31**		
R = Ac; R’ = glycate	*Vibrio vulnificus* 27562	76
R = (=O)$CH_2CH(OH)CH_2$; R’ = C(=O)H	*Pseudamonas aeruginosa* O7a, 7b, 7c	79
R = R’ = C(=O)$CH(OH)CH_2OH$	*Campylobacter jejuni* 81-176	62
R = Ac; R’ = $C(=NH)CH_3$	*Campylobacter jejuni* 11168	44
R = $C(=O)CH(OCH_3)CH_2OCH_3$; R’ = $C(=NH)CH_3$	*Campylobacter jejuni* 11168	44
R = $C(=O)CH(OCH_3)CH_2OCH_3$; R’ = Ac	*Campylobacter jejuni* 11168	44

1.3.3 Linkages of legionaminic and pseudaminic acid present in biological systems

In biological systems Leg and Pse are bound by a diverse array of linkages. In *Legionella pneumophila*, a Gram-negative bacterium, Leg is found in the form of an equatorially linked homopolymer **32** in its *O*-chain lipopolysaccharide.[21] A 5-*N*-formyl derivative of legionaminic acid was discovered by Kandiba *et al*. from the glycan of a haloarchaeal pleomorphic virus (HRPV-1) **33** in 2012.[88] This pentasaccharide glycan includes a terminal 5-*N*-formyl-legionaminic acid residue alongside glucose, glucuronic acid, mannose, and sulphated glucuronic acid.

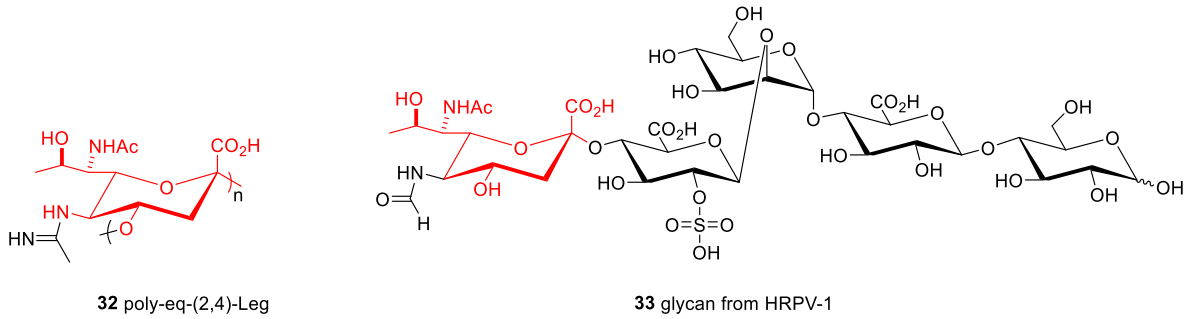


Figure 5. Examples of Leg linkages.

Pse is found in *Pseudamonas aeruginosa* O10 linked equatorially in the lipopolysaccharide, and some Pse derivatives have been established to be linked via their C5 or C7 amines, such as a C7 linked derivative found in *Kribella spp.*[49] In addition, Pse units that are attached via both equatorial and axial glycosidic linkages to other sugars and alcohol functionalities of serine and threonine, have been also characterized (Figure 6).

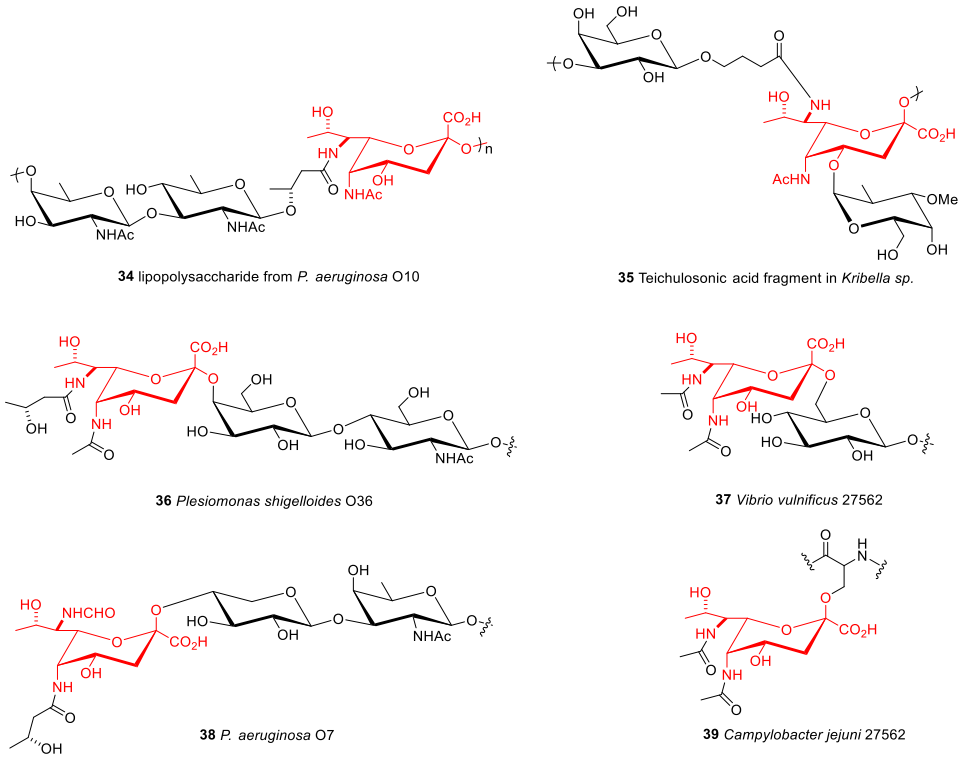
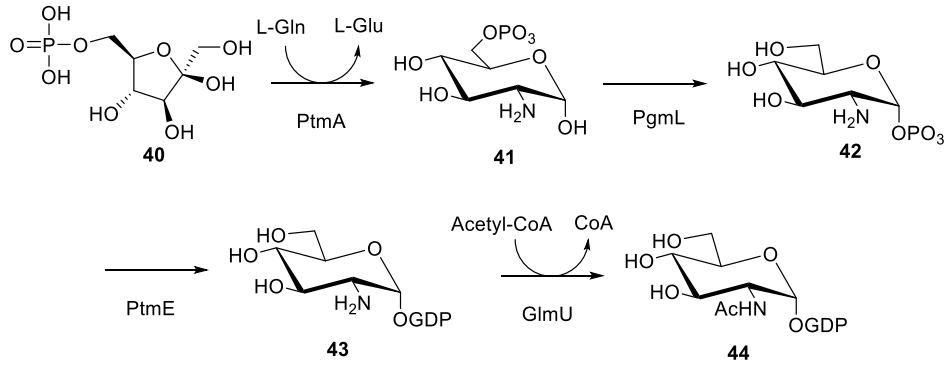


Figure 6. Examples of Pse linkages.

1.4 Biosynthesis of legionaminic acid and pseudaminic acid

The biosynthetic pathway for CMP-Leg in *Campylobacter jejuni* was elucidated in 2009 by Logan and coworkers.[89] It is similar to the biosynthesis of NeuAc and involves two segments. The first segment of the biosynthesis is production of the GDP-sugar building block from fructose-6-phosphate while the second segment converts this GDP-sugar building block to the final CMP-Leg.[89]

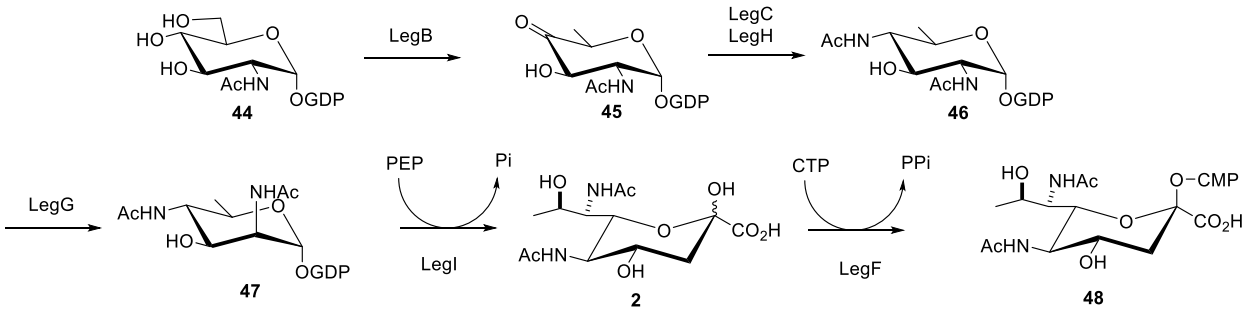
In the first segment of biosynthesis of legionaminic acid, the glutaminase (PtmA) coverts fructose-6-phosphate **40** into glucosamine-6-P **41** in presence of L-glutamine. Then conversion of **41** to glucosamine-1-P **42** is triggered by phosphoglucosamine mutase (PgmL), and next the phosphate group at O1 in **42** is replaced by a GDP-group with the help of guanylyltransferase (PtmE) to give the common intermediate GDP- glucosamine **43**. Finally, an *N*-acetyltransferase (GlmU) catalyzes acetylation of the C2 amine to give the intermediate GDP-acetyl-glucosamine **44**, which is a common precursor for both Leg and Pse biosynthesis.



Scheme 1. The first segment of the biosynthetic pathway of Leg and Pse.

The common precursor **44** undergoes elimination of a water molecule from C4 and C6 with help of LegB, an NAD-dependent 4,6-dehydratase to give the GDP-2-acetamido-2,6-dideoxy-alpha-D-xylo-hexos-4-ulose **45**. Conversion of the 4-ketone to an amine in compound **45** is

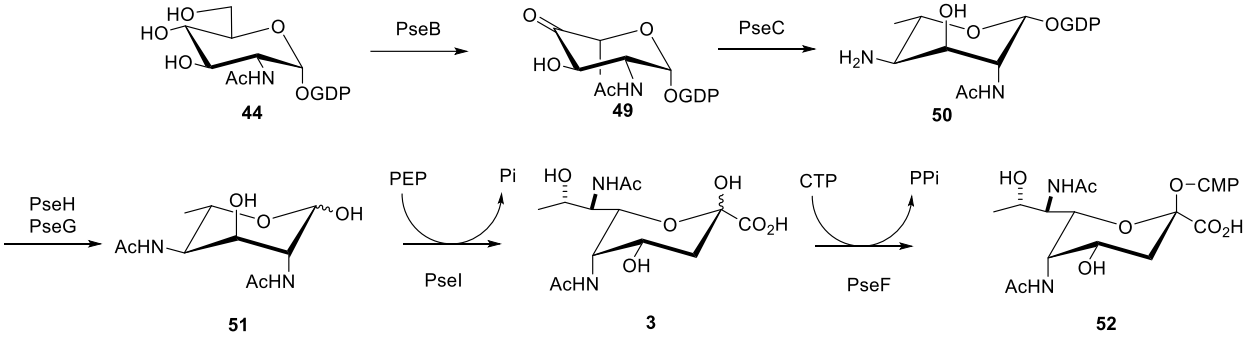
catalyzed by LegC, a PLP-dependent aminotransferase. The newly formed 4-amino group is further acetylated to give GDP-2,4-diacetamido-2,4,6-trideoxy-α-D-glucopyranose **46** by an enzyme known as LegH, an *N*-acetyltransferase. The enzyme LegG, acts as an NDP-sugar hydrolase and 2-epimerase, which catalyzes epimerization as well as cleavage of the GDP-glycosidic linkage in **46** and provides 6-deoxy-mannose derivative, 2,4-diacetamido-2,4,6-trideoxy-D-mannopyranose **47**. Legionaminic acid synthase (LegI) catalyzes the conversion of compound **47** to legionaminic acid **2** via an aldol condensation. For the resulting 9 carbon α-keto sugars to be incorporated into glycans, they must be nucleotide-activated as the CMP derivative.[90, 91] Therefore, the enzyme LegF, a CMP-Leg synthetase (LegF) activates the Leg to give CMP-Leg **48**.



Scheme 2. The second segment of the biosynthetic pathway of Leg.

The biosynthesis of Pse, which also uses the GDP-acetyl-glucosamine **44** as precursor, was also elucidated in *Campylobacter jejuni*.[47, 90, 92, 93] This five-step pathway starts with dehydration and was followed by epimerization at C5 to provide keto derivative **49** with the help of a dual functionality enzyme (PseB), which acts as both an NAD(P)-dependant dehydratase and a C-5 epimerase.[90, 91, 94, 95] The intermediate L-sugar **49** is then converted into UDP-4-amino-4,6-dideoxy-β-L-AltNac **50**, by enzyme PseC.[90, 93, 96] Next, the two enzymes PseH and PseG convert intermediate **50** to a 2,4-diacetamido-2,4,6-trideoxy-β-L-altropyranose **51**, which then undergoes

aldol condensation with phosphoenolpyruvate (PEP) in the presence of the enzyme PseI, giving pseudaminic acid **3**.[67, 90, 91, 97, 98] Similarly to Leg synthesis, Pse **3** is converted to its CMP-derivative **52** by a CMP-Pse synthetase enzyme PseF,.[90, 91]



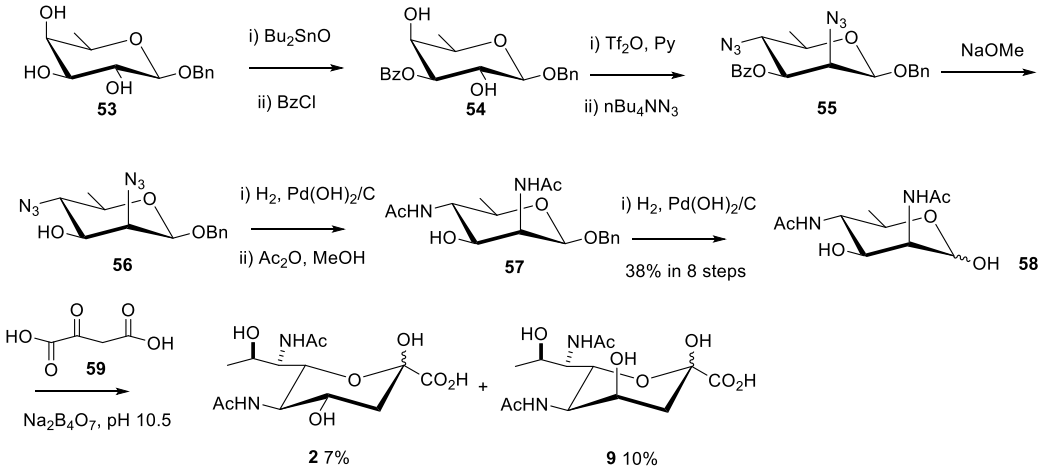
Scheme 3. Second segment of the biosynthetic pathway of Pse.

1.5 Synthesis of legionaminic acid

1.5.1 Tsvetkov's synthesis of legionaminic acid

The first chemical synthesis of legionaminic acid was reported by Tsvetkov and cowerkers in 2007.[39] Their synthesis was performed starting from benzyl β-D-fucopyranoside **53** that was first converted to the 3-*O*-benzoyl derivative **54** via a Bu_2SnO-mediated selective benzoylation. Triflation of the remaining secondary alcohols provided the corresponding 2,4-di-*O*-triflate, which then gave diazide **55** with the manno configuration, by bis-azidation with Bu_4NN_3. After the removal of the benzoyl groups in diazide **55**, selective hydrogenolysis was performed to reduce the azido groups without effecting the anomeric benzyl glycoside, and further acetylation of the intermediate amine provided the acetamide **57**. Compound **58**, which is the precursor for legionaminic acid synthesis, was obtained after removal of anomeric benzyl group in 38% overall yield. Finally, precursor **58** was condensed with oxalacetic acid in the presence of sodium tetraborate while maintaining the pH at 10.5 to obtain legionaminic acid **2** in 7% yield and it's C4

epimer **9** in 10% yield. Tsvetkov's synthesis of legionaminic acid enabled the configuration of both legionaminic acid and 4-*epi*- legionaminic acid to be defined, paving the way for further work in the field.

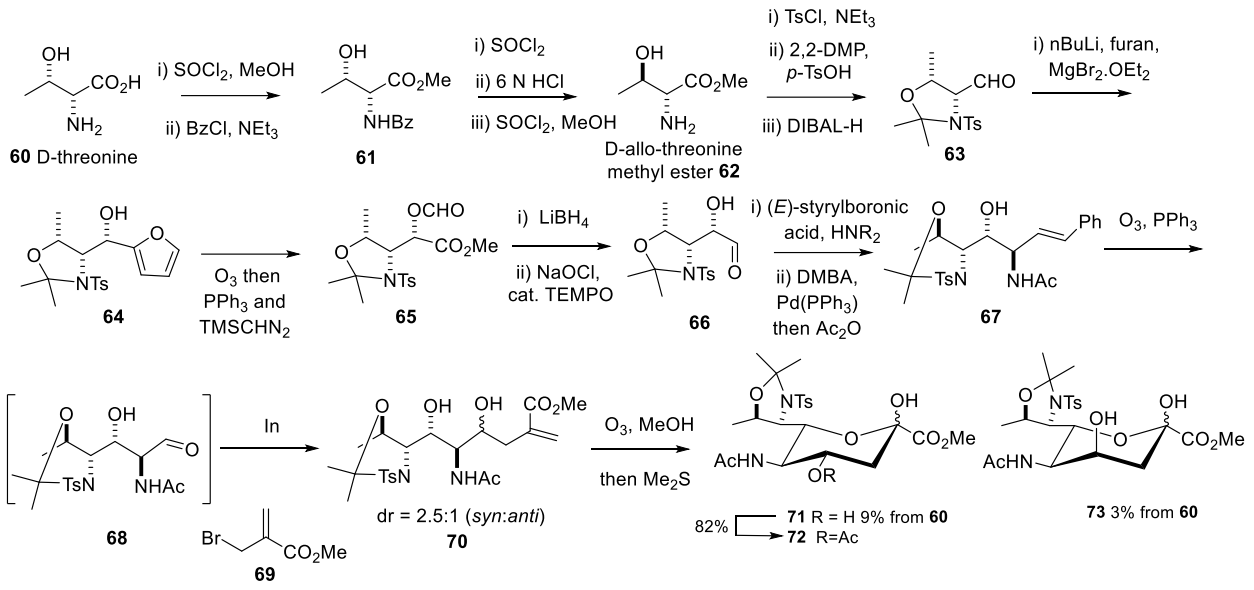


Scheme 4. Tsvetkov's synthesis of legionaminic acid.

1.5.2 Seeberger's synthesis of a legionaminic acid donor

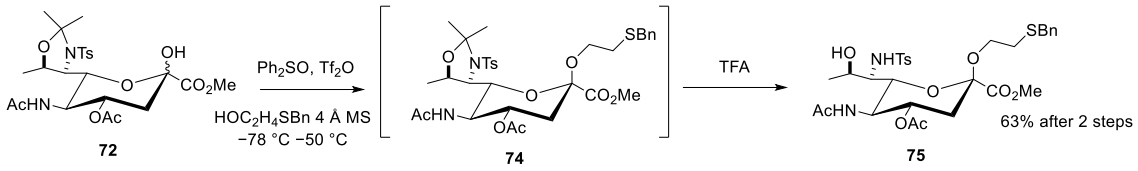
Seeberger and coworkers have synthesized a donor of legionaminic acid **71** for serological studies starting from D-threonine **60**.[37] First, D-threonine was converted to intermediate **61** via methyl ester formation and *N*-benzoylation. The D-allo-threonine **62** was obtained using thionyl chloride-induced cyclization followed by acidic hydrolysis of the intermediate oxazoline, and esterification. Then D-allo-threonine was transformed into the corresponding *N*-toluenesulfonamide which was subjected to acetalization followed by DIBAL-H reduction of the intermediate ester to give D-allo-threoninal **63**. This aldehyde was reacted with 2-lithiofuran and provided the *syn*-configured alcohol **64**. Next, the oxidation of **64** using ozone gave methyl ester **65**, and the key α-hydroxy aldehyde intermediate **66** was obtained from methyl ester **65** via reduction followed by selective TEMPO oxidation. The α-hydroxy aldehyde was used as a

precursor to introduce a protected amine via a Petasis borono−Mannich reaction, which gave the desired anti-diastereomer, of a monoallyl amine intermediate with a d.r. > 19:1. This allylic amine intermediate into *N*-acetate **67** was achieved by Pd (0) catalyzed dealkylation followed by chemoselective *N*-acetylation. Oxidative cleavage of the double bond in **67** resulted in aldehyde **68**, to which a masked pyruvate unit was introduced by indium-mediated allylation giving adduct **70** with the *syn*-configuration. Ozonolytic cleavage of the alkene moiety in **70** followed by reductive workup provided legionaminic acid derivative **71** in 9% yield and the 4-*epi*-legionaminic acid derivative **73** in 3% yield after 17 steps. The so-synthesized legionaminic acid derivative was to the acetylated derivative **72** to access a donor for glycosylation.



Scheme 5. Seeberger's synthesis of a legionaminic acid donor **72**.

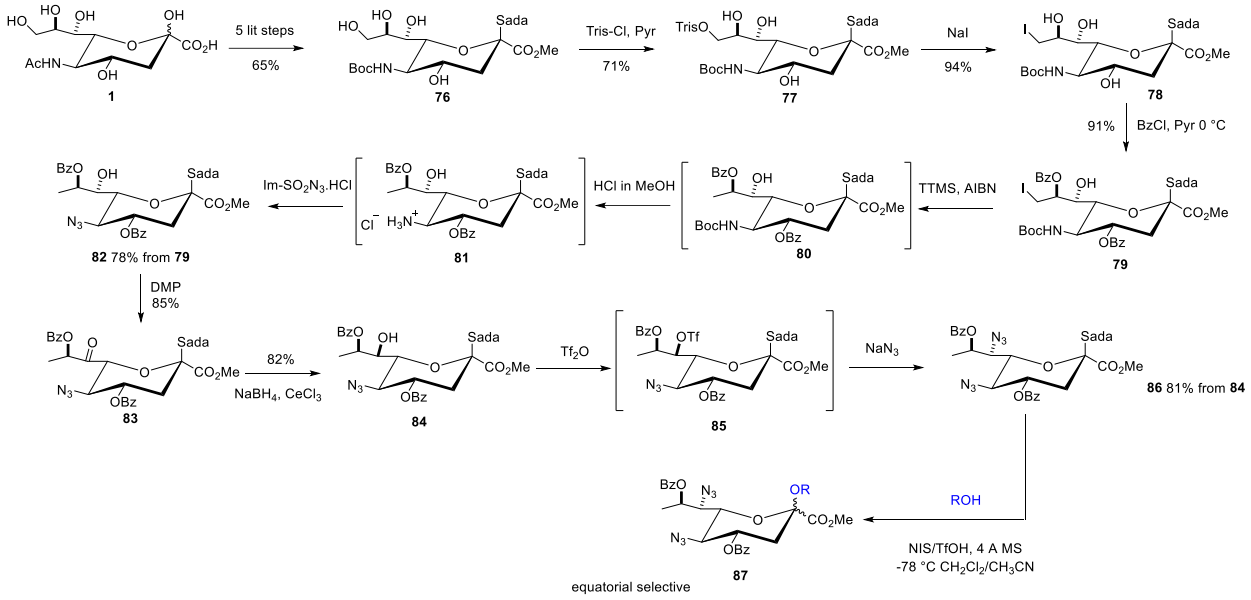
Coupling to a simple primary alcohol by the Gin dehydrative method gave the axial glycoside **75** in 63% yield, after removal of the acetonide. It was reported that the equatorial glycoside was also observed, but it was not quantified as the authors were not able to isolate it in pure form.



Scheme 6. Seeberger's Gin dehydrative glycosylation.

1.5.3 Crich's synthesis of a legionaminic acid donor

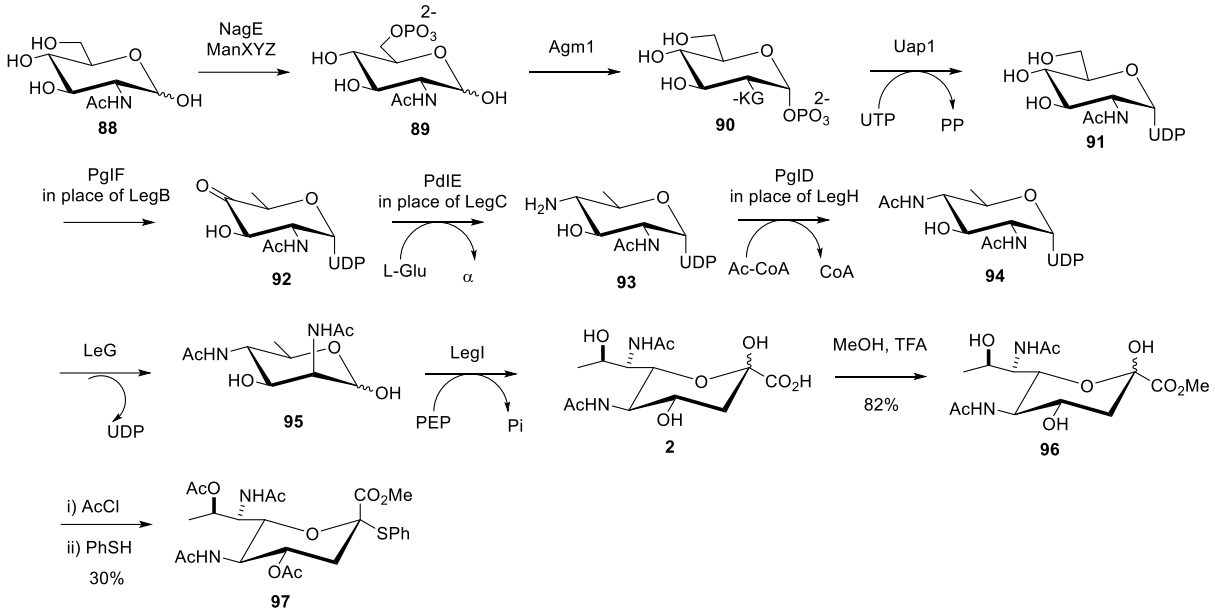
More recently, Crich and coworkers developed a method to obtain a legionaminic acid glycosyl donor **86** from commercially available *N*-acetylneuraminic acid **1** in 15 steps and 17% overall yield.[99] In this study (Scheme 7), the *N*-Boc adamantanyl thioglycoside **76** was first synthesized from the *N*-acetylneuraminic acid by 5 literature steps.[100, 101] With a view to removing the primary alcohol group, an iodo derivative **78** was synthesized from **77**, which was obtained by selective sulfonylation of **76**. Selective benzoyl protection of **78** gave the 4,8-di-*O*-benzoate derivative **79** and was followed by a radical reaction to give deiodinated product **80**. The removal of the Boc group was achieved under acidic conditions to give corresponding amine as the hydrochloride salt **81**, which was converted to the azide derivative **82** using Stick's reagent. Introduction of the C-N bond at the 7-position, was achieved by conversion of the 7-hydroxyl group to an azide in 4 straightforward steps, to obtain the donor **86** in 17% overall yield. The glycosylation of various acceptors by the donor, gave excellent yields and good to excellent equatorial selectivities.



Scheme 7. Crich's synthesis of a legionaminic acid donor **86** and subsequence glycosylation.

1.5.4 Schoenhofen's chemoenzymatic synthesis of legionaminic acid

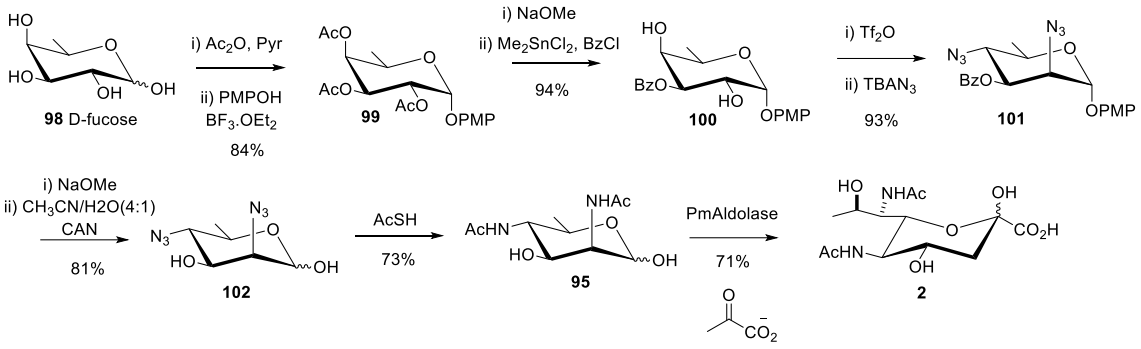
The first total *de novo* biosynthetic pathway of legionaminic acid was described by Schoenhofen and coworkers in 2016, and combined various metabolic modules from three different bacterial sources (*Saccharomyces cerevisiae*, *C. jejuni*, and *L. pneumophila*).[102] After the purification of Leg from the culture broth, it was activated in the form of CMP-Leg. The activated Leg was converted into its methyl ester, which was acetylated followed by thioglycosylation to generate an equatorial phenyl thioglycoside donor **97** for chemical glycosylation reactions. Although Schoenhofen *et al*. did not report any glycosylation reactions, this method provided a donor for possible future chemical glycosylation reactions.



Scheme 8. Schoenhofen's biosynthetic synthesis of Leg and of a functionalized donor.

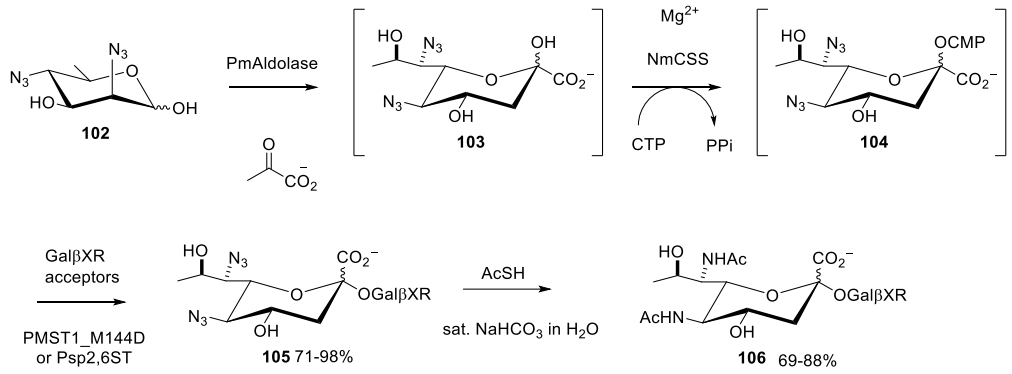
1.5.5 Chen's chemoenzymatic synthesis of Leg and its glycosides

Chen's approach includes a 9 step chemical synthesis, which started from D-fucose **98**, and a one-pot multienzyme cascade to synthesize legionaminic acid and its glycosides.[103] In the 9-step chemical synthesis, first the derivative **99** was obtained by acetylation of D-fucose, followed by $BF_3.OEt_2$-mediated glycosylation of *p*-methoxyphenol. After deacetylation of **99**, tin-mediated selective benzoylation at C3 provided intermediate **100**. Introduction of C-N bonds to C2 and C3 was achieved by displacement of a ditriflate with tetrabutyl ammonium azide and gave diazido compound **101**. Debenzylation followed by cleavage of the *p*-methoxyphenyl glycoside gave **102**, which subjected to thioacetic acid reduction to provide the acetamido sugar **95**. The legionaminic acid **2** was then obtained in 31% overall yield by coupling to pyruvic acid using PmAldolase.



Scheme 9. Chen's chemoenzymatic approach to legionaminic acid.

Chen and coworkers enzymatically converted the precursor **102** to a functionalized Leg donor in order to enzymatically glycosylate with three different acceptors. These glycosylation reactions provided the equatorial (2,3/6) glycosides depending upon the type of the enzymes employed. In their multienzyme cascade the diazido precursor was chemoenzymatically transformed to form the diazido derivative of Leg (**103**, Leg-5,7-di-N_3) by PmAldolase, and this diazido derivative was then reacted with cytidine 5'-triphosphate (CTP) in the presence of *Neisseria meningitidis* CMP-sialic acid synthetase (NmCSS) to form CMP-Leg-5,7-di-N_3 **104** in situ. Sialyltransferase PsP2 6ST catalyzed the subsequence conversion to equatorial (2,3/6) linked Leg-5,7-di-N_3-containing glycosides, while PmST1_M144D sialytransferase catalyzed conversion to equatorial (2,3) linked Leg-5,7-di-N_3-containing glycosides in the yields of 71-98%. Thioacetic acid-mediated azide to acetamide conversion then delivered the final Leg containing glycosides **104** in 69-88% yield (Scheme 10).



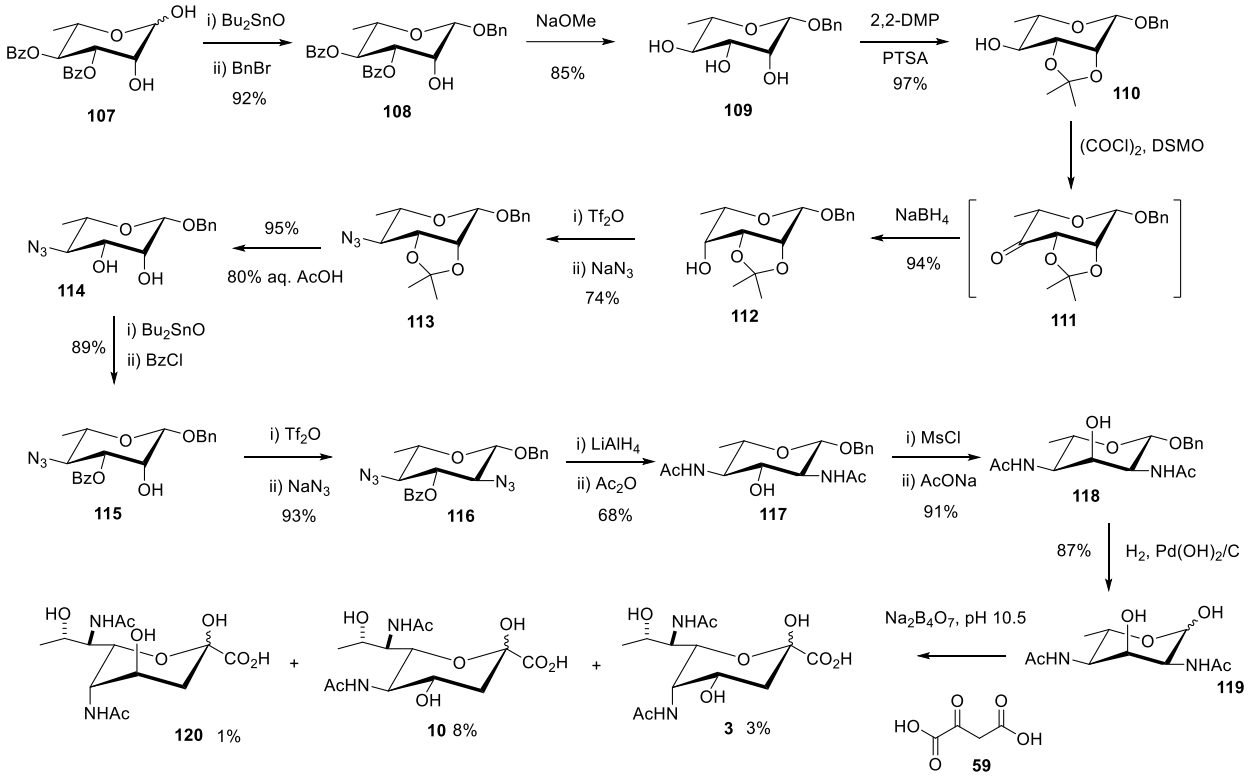
Scheme 10. Chemoenzymatic synthesis of Leg-5,7-di-N_3 followed by glycosylations and deprotections.

1.6 Synthesis of pseudaminic acid

1.6.1 Tsvetkov's synthesis of pseudaminic acid

The different classes of 5,7-diamino-3,5,7,9-tetradeoxynon-2-ulosonic acids have been synthesized in 2001 by Tsvetkov and coworkers using 2,3-di-*O*-benzoyl β-L-rhamnopyranose **107** as the precursor of choice.[104] First, **107** was transformed in to its benzyl glycoside **108**, which was then debenzylated to provide intermediate **109**. After introduction of an acetonide to protect the 2,3-diol, the equatorial alcohol at C4 was converted to inverted via Swern oxidation followed by sodium borohydride reduction. The equatorial C-N bond at C4 was then introduced via displacement of a triflate by tetrabutyl ammonium azide to give azido compound **113**. The cleavage of acetonide resulted in the corresponding diol **114**, equatorial alcohol was selectively benzoylated to give intermediate **115**. Another displacement of a triflate by azide at C2 provided the diazido compound **116**, which was then subjected to a reduction followed by acetylation to give acetamido intermediate **117**. After epimerization of the C3 alcohol in **117**, hydrogenation over $Pd(OH)_2/C$ converted acetamido **118** to the precursor **119** that was reacted with oxalacetic acid **59** to provide pseudaminic acid **3** in 3% yield along with 4-*epi*- pseudaminic acid **120** and

acinetaminic acid **10**. Although this method only provided small quantities of pseudaminic acid, it was the first total synthesis of Pse and enabled confirmation of the definitive structures and configuration of the bacterial nonulosonates paving the way for further work in the field.

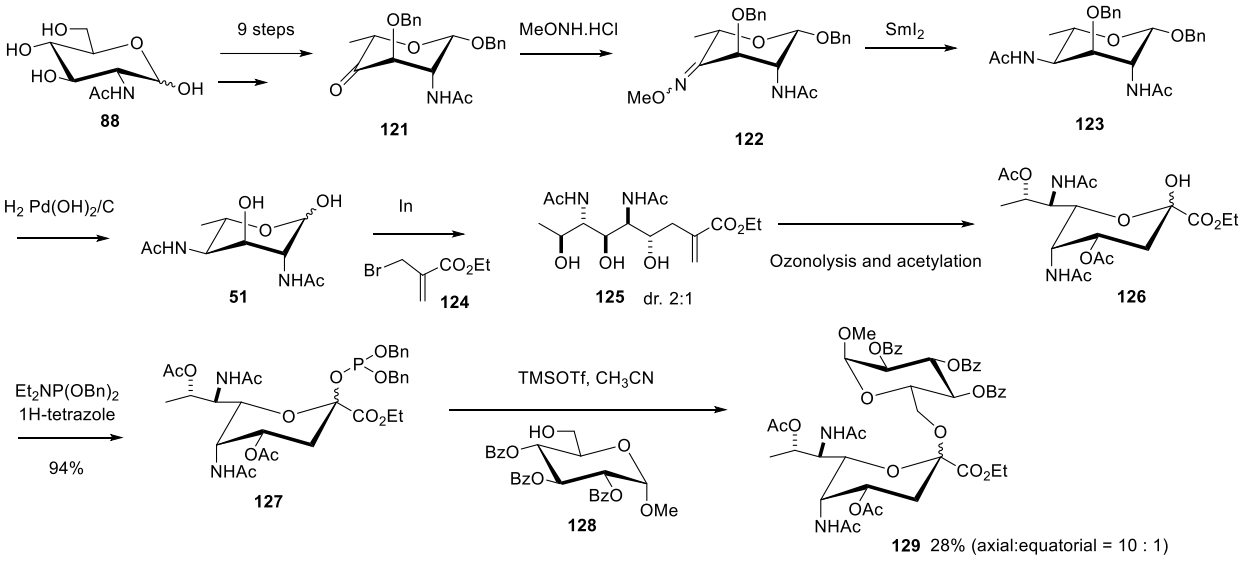


Scheme 11. Tsvetkov's approach to the synthesize of Pse.

1.6.2 Ito's synthesis of pseudaminic acid and one of its glycosides

Ito and coworkers developed a synthesis of a Pse donor starting from *N*-acetylglucosamine (Scheme 12). They were able to synthesis key intermediate **121** from *N*-acetylglucosamine **88** by using 9 straightforward steps including deoxygenation and oxidation. Reaction of ketone **121** with *O*-methylhydroxylamine hydrochloride afforded the oxime which was subjected to SmI_2 reduction and then acetylation to give a diacetamido compound **123** as a single isomer. Hydrogenolysis of benzyl ethers provided the 6-deoxy-AltdiNAc **51**. The In-mediated allylation of this precursor **51**

with a bromomethacrylate ester followed by ozonolysis and hydrolysis gave the Pse ethyl ester **126**. This Pse derivative was transformed to the dibenzyl phospite donor **127** in order to perform glycosylation reactions. The glycosylation of this donor with the primary acceptor **128** in acetonitrile afforded the disaccharide **129** in 28% yield with 10:1 axial to equatorial anomeric selectivity (Scheme 12).

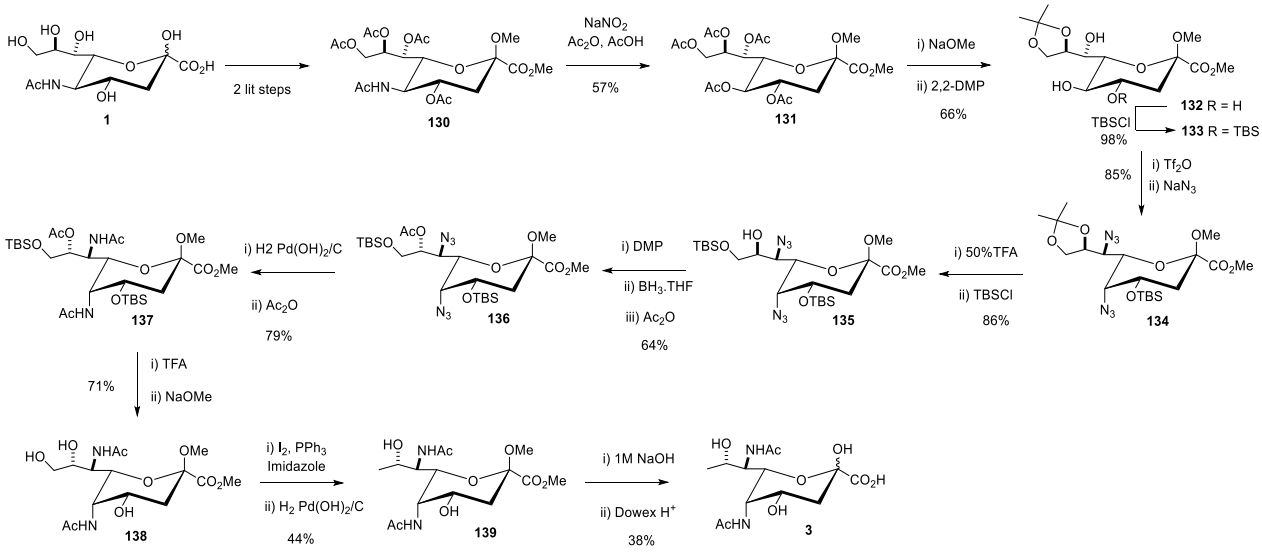


Scheme 12. Ito's synthesis of a Pse donor and a glycoside.

1.6.3 Kiefel's synthesis of pseudaminic acid

In 2016 Kiefel and coworkers reported a synthesis of Pse starting from the *N*-acetylneuraminic acid **1**.[105] The NeuAc was converted into its acetylated methyl glycoside **130**. Oxidative deamination of 5-*N*-acetamido compound using acetic acid as nucleophile then provided **131** in the form of the pentaacetate (Scheme 13). After deacetylation followed by introduction of an acetonide to protect the 8,9-diol, selective silylation with TBSCl gave intermediate **133**. Displacement of the ditriflate derivative converted **133** into diazido compound **134**, and the acetonide was then cleaved, followed by selective silylation with TBS to give the disilylated

compound **135**. Inversion of configuration at C8 was achieved via Dess-Martin oxidation followed by BH_3.THF-mediated reduction and acetylation of the remaining alcohol to give **136**, which was subjected to reduction of the two azides followed by acetylation providing the diacetamido compound **137**. Deprotection of both the acetate and TBS groups resulted in a tetraol **138**, which was converted to iodo derivative for deoxygenation at C9, which was achieved hydrogenolysis and provided the Pse methyl ester **139**. Finally, cleavage of the methyl ester and methyl glycoside in **139** afforded Pse. The concept used by Kiefel and coworkers to obtain Pse from inexpensive NeuAc is attractive, but the protocol does not provide a Pse donor with which to carry out conduct chemical glycosylation reactions.



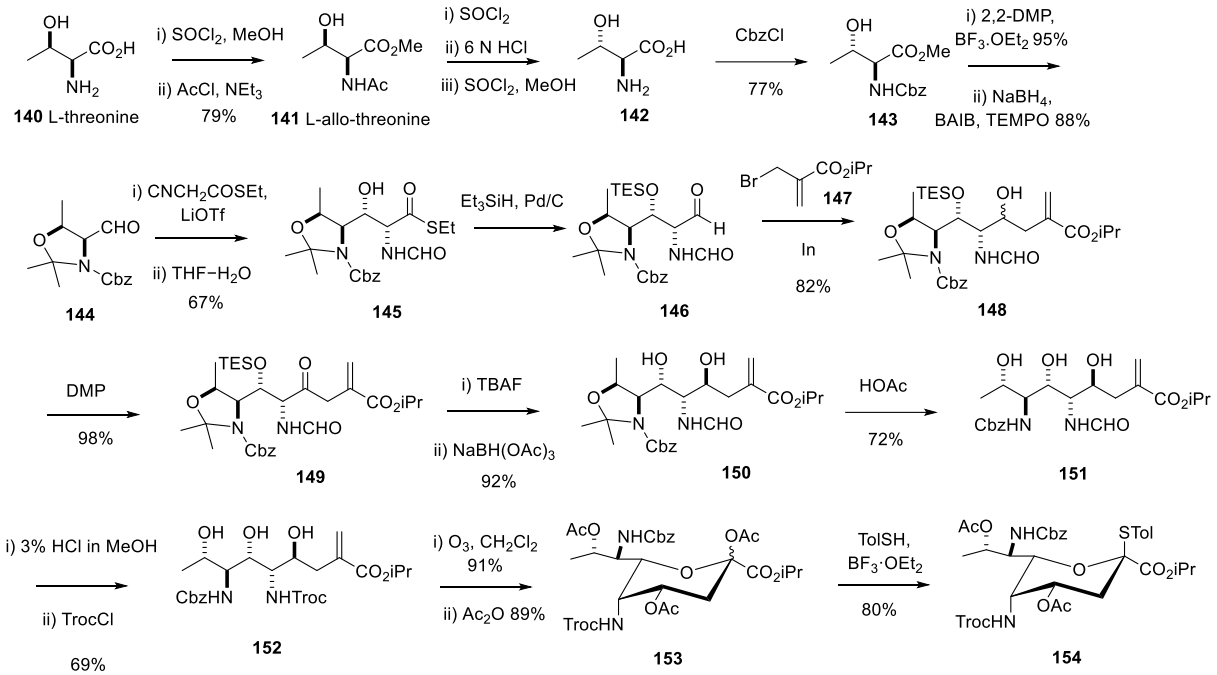
Scheme 13. Kiefel's synthesis of pseudaminic acid starting from NeuAc.

1.6.4 Liu's synthesis of pseudaminic acid and its glycosides

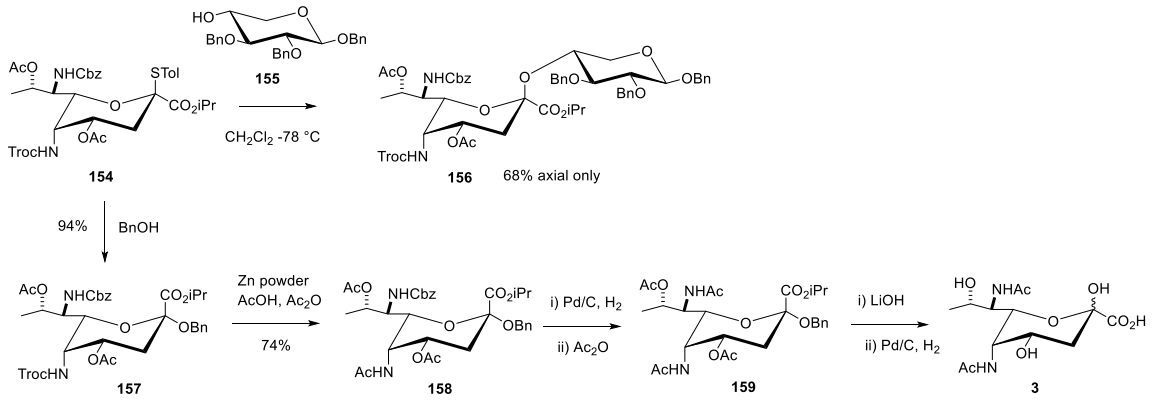
In 2017 Liu and coworkers developed a synthesis of Pse and its functionalized derivatives from easily available Cbz-L-allo-threonine methyl ester in 16 steps with 11% yield (Scheme 14).[106] The strategy employed was similar to the Seeberger's approach to legeionaminic acid synthesis

(Scheme 5). Aldol-type addition of an isonitrilo thioester to Garner-type aldehyde **144** followed by hydrolysis provided desired 5.0:1 ratio favoring diastereomer **145** in the first chain elongation step. In the second chain elongation step, the thioester **145** was transformed into the aldehyde **146** via Fukuyama reduction. The Barbier adduct **148** was afforded by indium mediated Barbier reaction of the aldehyde **146** as a 3:1−5:1 mixture of diastereomers. The undesired *syn*-adduct with the *R*-configuration was the major product, therefore, the configuration was adjusted via an oxidation/desilylation/1,3-induced diastereoselective reduction, and provided desired product **150**. After cleavage of the acetonide group and hydrolysis of the formamide, the liberated amino group was reprotected as a Troc group, giving the complete 1,3-anti-diamino skeleton with the correct configuration in **152**. Ozonolysis and subsequent acetylation then gave the cyclic Pse derivative **153**. In order to perform glycosylation reactions, the acetyl glycoside was transformed into thioglycoside **154** (Scheme 14).

All the glycosylation reactions conducted with donor **154** showed axial selectivity in good yields (Scheme 15). Finally, the authors also synthesized Pse **3** itself by converting Pse donor **154** to the benzyl glycoside, followed by hydrogenolysis and hydrolysis (Scheme 15).



Scheme 14. Li's synthesis of a pseudaminic acid donor **154**.

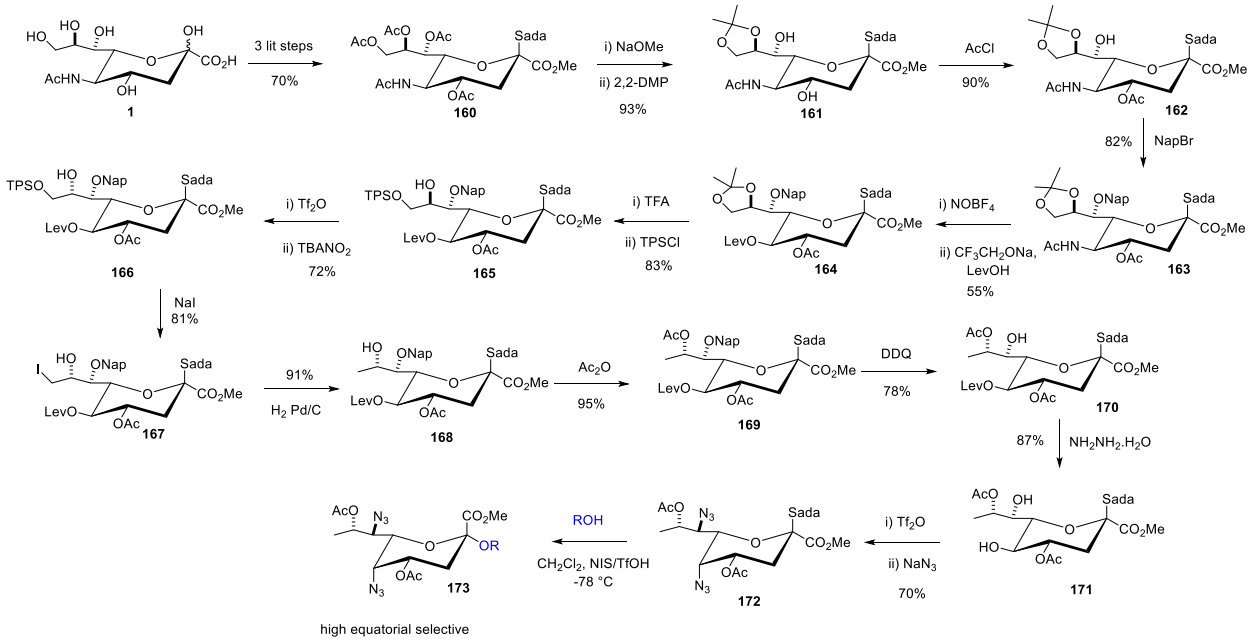


Scheme 15. Glycosylation and deprotection of the Pse glycoside **158** giving Pse.

1.6.5 Crich's synthesis of pseudaminic acid and its glycosides

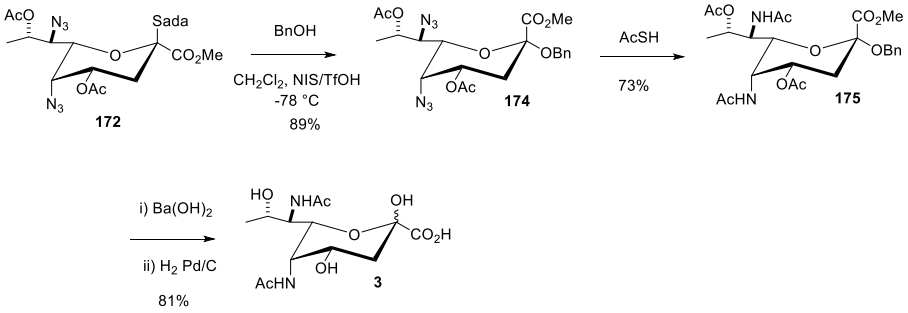
In 2018 Crich and Dhakal reported a synthesis of a novel Pse donor **172** from *N*-acetylneuraminic acid **1** in 20 steps with 5% overall yield (Scheme 16). In this protocol, first *N*-acetylneuraminic acid was transformed to tetraacetate acetamido thioglycoside **160** according to a

literature procedure.[107, 108] After deacetylation an acetonide group was introduced to protect the 8,9-diol, and was followed by selective acetylation to provide intermediate **162** before the remaining alcohol was protected as naphthalenyl methyl ether. An oxidative deamination protocol developed in Crich lab employing levulinic acid nucleophile afforded deaminated product **164**. Cleavage of the acetonide followed by selective introduction of a trisyl group to the primary alcohol provided compound **165**. The configuration of **165** at C8 was then inverted via displacement of the triflate with a nitrite followed by hydrolysis to give the 8-*epi*-isomer **166**. In order to deoxygenate C9, the trisyl group was displaced by iodide which provided compound **167**. Hydrogenolysis of over palladium on carbon afforded then dehalogenated product **168**. After acetylation of the remaining alcohol in **168**, the naphthalenyl methyl ether and levulinate ester were removed sequentially with DDQ and hydrazine hydrate giving **171**. Finally, straightforward triflation of the diol followed by reaction with sodium azide gave desired Pse donor **172**. The glycosylation of this novel donor gave excellent yields and exquisite equatorial selectivity (Scheme 16).[109]



Scheme 16. Crich's synthesis of a Pse donor **172** and its glycosylation reactions.

Crich and Dhakal also developed and implemented conditions for the regioselective release of the two amines from the corresponding azides as a required for the preparation of the lipopolysaccharides. In contrast to other syntheses of Pse this protocol paved the way to the synthesis and study of pseudaminic acid based bacterial lipopolysaccharides. Alter conversion of donor to the benzyl glycoside, the authors have performed global deprotection and synthesized Pse **3** from their novel donor (Scheme 17).

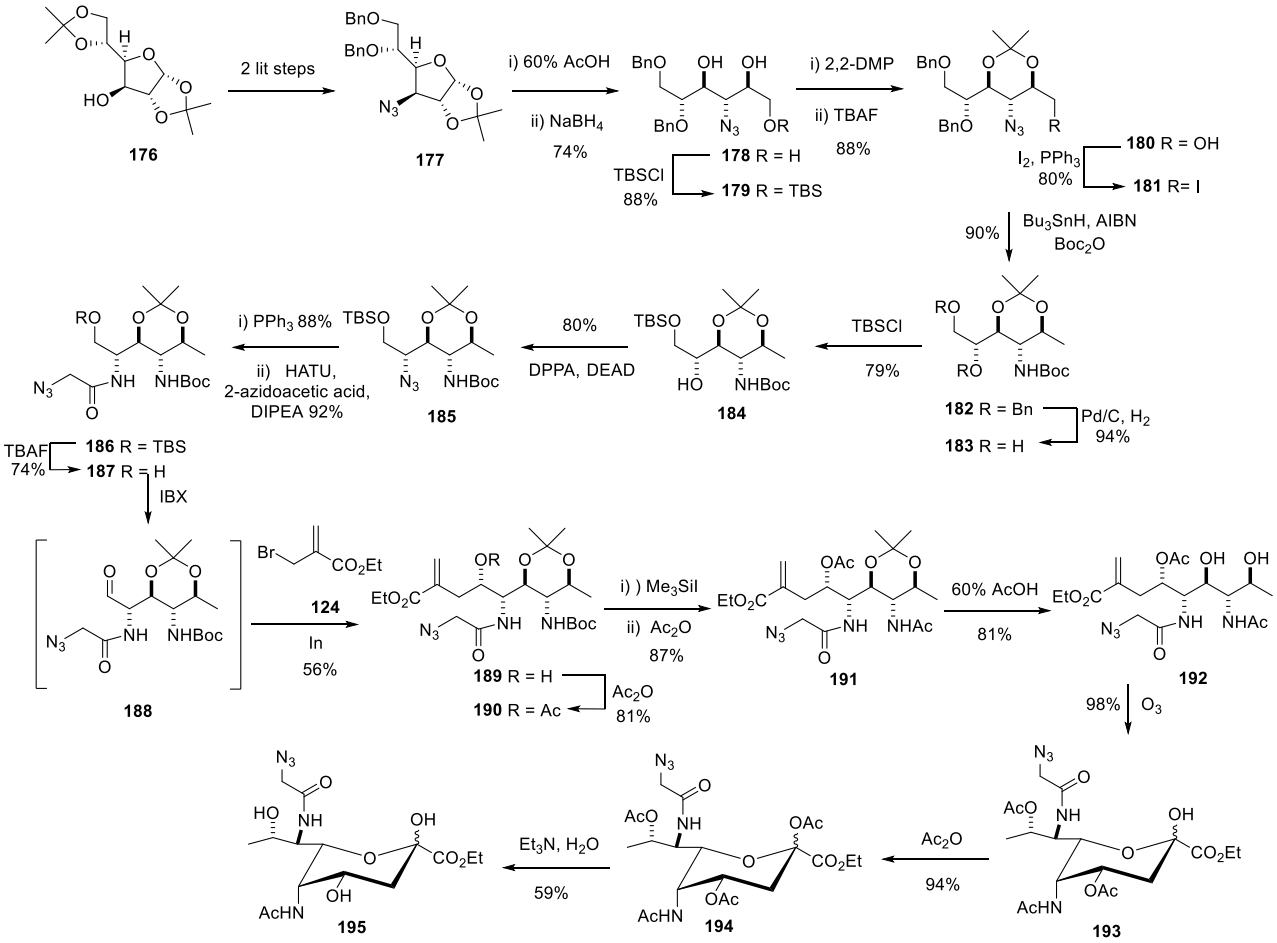


Scheme 17. Synthesis of Pse by Crich and Dhakal.

1.6.6 Fridman and Werz synthesis of a pseudaminic acid derivative

More recently, Werz and coworkers have reported the synthesis of azidoacetamido-functionalized Pse derivatives for use as metabolic labeling reagents (Scheme 18).[64] In this synthesis, D-glucose **176** was used as a cost-effective chiral pool starting material and was transformed to 5-azido bis-benzyl ether **177** by four literature steps.[110] After cleaving the remaining acetonide of **177** under vigorous acidic conditions, the resulting furanose was reduced by sodium borohydride to obtain open chain triol **178**, whose primary alcohol was then selectively silylated with TBS. The introduction of an acetonide protected the remaining two secondary alcohols of **179** and provided a fully protected intermediate, which was then converted to precursor **180** by removing the TBS ether. To achieve deoxygenation at the eventual C9 of Pse, the free alcohol of **180** was converted to the corresponding iodide using the Appel reaction. Dehalogenation using stannane and AIBN as catalyst in the presence of Boc anhydride provided the fully protected compound **182**. In **182**, the two adjacent benzyl ethers were cleaved employing Pearlman's catalyst and affording the diol **183**, whose more accessible primary alcohol was then protected by TBS to yield **184**. Installation of the C-N bond at C2 was achieved by the Mitsunobu reaction with azide as a nucleophile to furnish azido compound **185**. Next, the so-introduced azido group was reduced, and the resulting amine was coupled with 2-azidoacetic acid in the presence of HATU to give azidoacetamide **186**. In order to elongate the C6 chain by three carbon atoms, a primary alcohol was liberated from its TBS ether and oxidized to the corresponding aldehyde **188**. Chain elongation was accomplished via the In-mediated Barbier reaction with 2-bromomethyl ethyl acrylate to afford desired *anti*-configured coupled product **189** with a ratio of 3:1. After separating the two diastereoisomers, the newly generated alcohol group was acetylated to give **190**, whose Boc group was cleaved with trimethylsilyl iodide, and the freed amine was acetylated.

The removal of the acetonide from **191** afforded the diol **192**, which was subjected to ozonolysis to give the Pse derivative **193**. Acetylation of derivative **193** gave the fully protected, azido labeled Pse derivative **194**. Finally, in order to obtain native azido acetamido Pse derivative **195**, **194** was deacetylated with triethylamine to afford the target compound as its triethylammonium salt. This protocol included 21 steps with 2% overall yield to reach the azido acetamido Pse derivative.

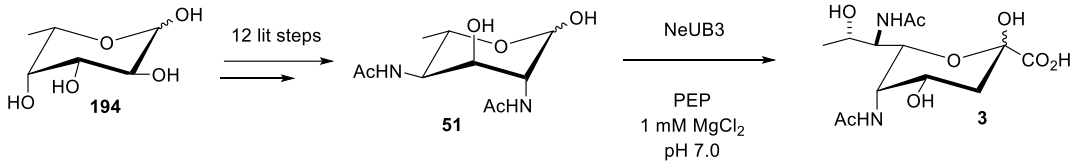


Scheme 18. Fridman and Werz synthesis of an azidoacetamido-equipped Pse derivative **195**.

1.6.7 Chou's chemoenzymatic synthesis of pseudaminic acid

In 2005 Chou and coworkers synthesized 2,4-diacetamido-2,4,6-trideoxy-β-L-altropyranose (6-deoxy-AltdiNAc) in 12 known literature steps from L-fucose **194** and used it as

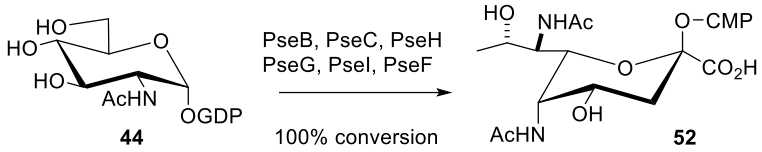
a precursor for a chemoenzymatic approach to Pse.[111] The condensation of 6-deoxy-AltdiNAc **51** with phosphoenol pyruvate (PEP) in the presence of an enzyme obtained from *Campylobacter jejuni*, pseudaminic acid synthase homolog (NeuB3), provided Pse **3** (Scheme 19).



Scheme 19. Chou's chemoenzymatic synthesis of Pse.

1.6.8 Schoenhofen's chemoenzymatic synthesis of Pse

Schoenhofen and coworkers in 2006 achived the first chemoenzymatic synthesis of CMP-Pse **52** from the natural precursor UDP-GlcNAc **44** (Scheme 20).[90] They combined all six of the biosynthetic enzymes from *H. pylori* in one-pot and monitored the conversion by proton NMR.

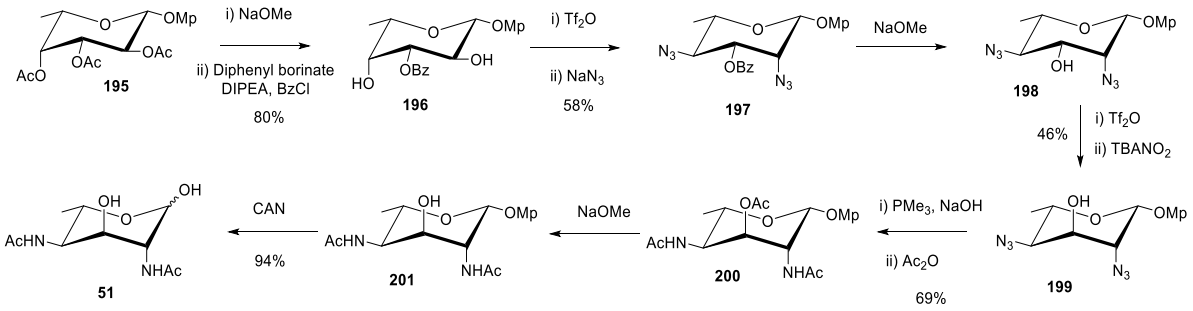


Scheme 20. Schoenhofen's one-pot enzymatic synthesis of CMP-Pse **52**.

1.6.9 Fascione's chemoenzymatic synthesis of Pse

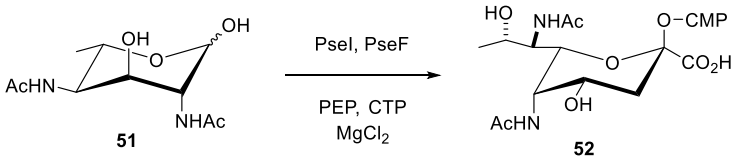
Recently, Fascione and coworkers reported the biocatalytic transfer of an activated Pse donor **52**, which enabled the enzymatic synthesis of Pse-containing glycosides.[112] This chemoenzymatic process included chemical synthesis a late-stage Pse biosynthetic intermediate 6-deoxy-L-AltdiNAc **51** and a one-pot two-enzyme process, which converted **51** into CMP-glycosyl donor **52** using the biosynthetic enzymes. The authors have established an efficient chemical pathway to obtain 6-deoxy-L-AltdiNAc precursor **51** from readily synthezied L-fucoside

195. This chemical synthesis consisted of a straightforward triple inversion of stereochemistry at the 2, 3, and 4 positions including introduction of the C-N bonds at the 2- and 4- positions as azides. Reduction of the azides followed by acetylation provided the acetamido functionality which is required in the target precursor. Finally, the removal of the anomeric methoxyphenyl group yielded the desired 6-deoxy-AltdiNAc reducing sugar **51** in an 11% overall yield (Scheme 21).



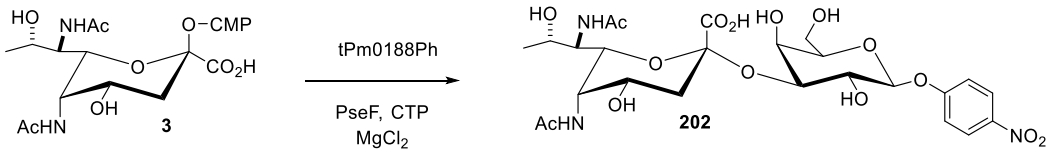
Scheme 21. Chemical synthesis of 6-Deoxy-L-AltdiNAc **51**.

The desired CMP-Pse nucleotide donor **52** was synthesized utilizing the final two enzymes (PseI and PseF) from the biosynthetic pathway in *C. jejuni*. This enzymatic reaction required excess CTP and $MgCl_2$ to afford the conversion along with the two enzymes (Scheme 22).



Scheme 22. Enzymatic production of CMP-Pse **52**.

Furthure the authors reported syntheis of equatorial Pse glycosides utilizing the *P. multocida*, pseudo-pseudaminyltransferase (tPm0188Ph) enzyme from CMP-Pse donor **52** using unprotected galactose-based acceptors in good yields (Scheme 23).



Scheme 23. tPm0188Ph-Catalyzed synthesis of Pseβ-2,3-Galβ-pNP2.

1.7 Goals

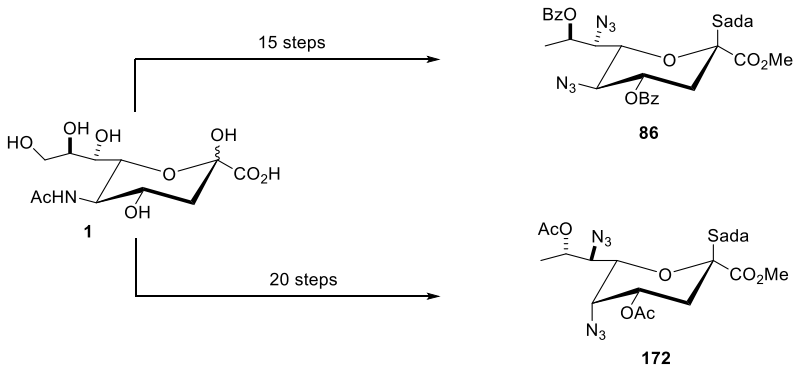
Crich's Leg and Pse donors **86** and **172** (Schemes 7 and 16) are the only chemical approached so far to enable stereoselective construction of the equatorial glycosides. The synthesis of these two donors, however, used to 15 and 20 steps, respectively from NeuAc making them impractical and in accessible to other groups. The goal of this project was to set out to develop improved, shorter, and more practical syntheses of Crich's Leg and Pse donors from a readily available cost-effective starting material.

CHAPTER TWO

DEVELOPMENT OF SECOND GERNERATION SYNTHESES OF LEGIONAMINIC ACID AND PSEUDAMINIC ACID DONORS

2.1 Background

The two best-known members of the bacterial acids, legionaminic acid and pseudaminic acid, and their glycosides are important synthetic targets so as to enable the study of their function and for application in potential therapeutic vaccines. The Crich lab, developed two successful synthetic pathways of legionaminic acid donor **86** and pseudaminic acid donor **172** starting from readily available *N*-acetylneuraminic acid **1** (Scheme 24) and showed them to provide biologically important equatorial glycosides in excellent yield and selectivity.[99, 109] While providing sufficient material to study glycosylation selectivity, their syntheses suffered from overly long step counts and perhaps also a lack of elegance.



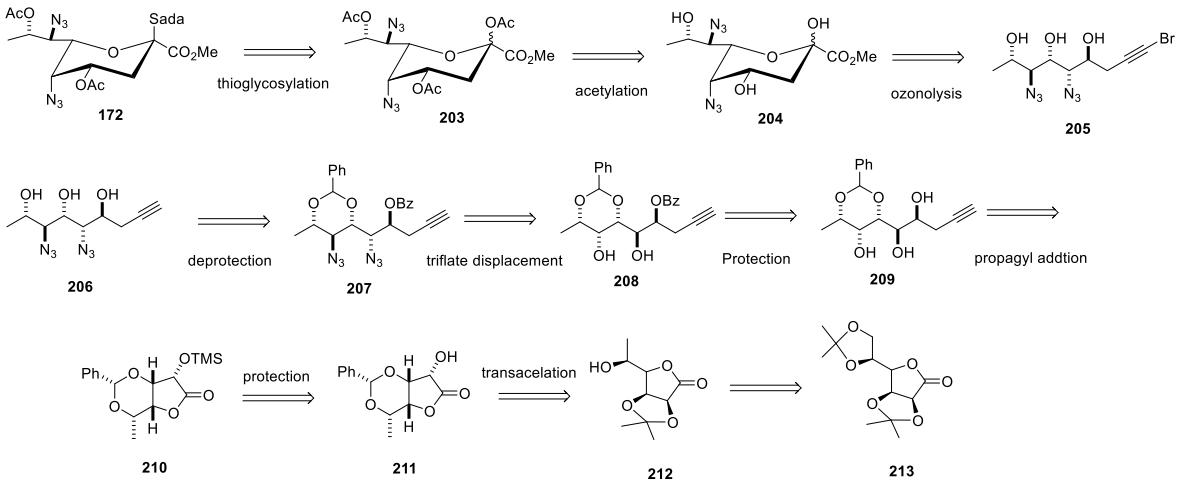
Scheme 24. Step counts for previous Crich group synthesis of Pse and Leg donors from commercial NeuAc **1**.

The aim of the research described in this chapter was to design and implement improved trimmed synthesizes of these donors with increased practicality and reduced step counts. The successful development of shortened syntheses would facilitate access to both Leg and Pse and their glycosides for future biomedical and medicinal research.

2.2 Results and discussions

2.2.1 Disconnection of the Pse donor to L-gulonic acid

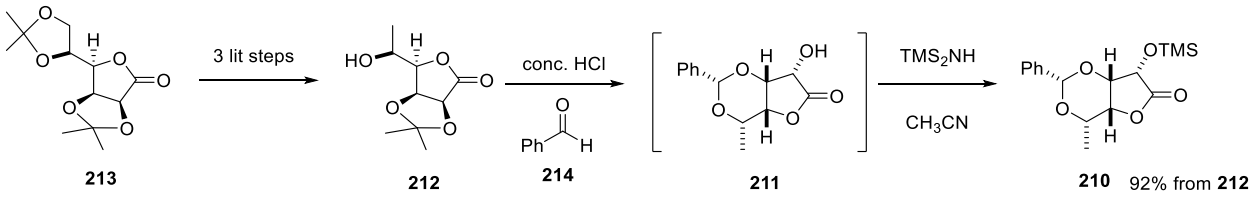
Recently the Crich lab has developed a simple synthetic path to access 2-keto-3-deoxy-D-glycero-D-galactononulosonic Acid (KDN) from 2,3;5,6-di-*O*-isopropylidene-D-mannonolactone beginning with reaction with propargyl magnesium bromide.[113] Building on this precedent a synthesis of Pse donor **172** was planned from L-gulonic acid **213,** which is a cost-effective chiral pool starting material. The thioadamantanyl group in the target donor can be introduced from the anomeric acetate **203**, which should be available after the ozonolysis of the bromoalkyne **205** followed by acetylation of intermediate **204**. Protection of O4, O6, and O8 is necessary to introduce the two azide groups at C5 and C7, and straightforward S_N2 triflate displacement by azide of protected intermediate **208** would give the diazido intermediate. The introduction of the C3 unit to the hexose intermediate can be accomplished by the addition of propargyl magnesium bromide to the fully protected lactone intermediate **210**. Transacelation would transform the acetonide-protected lactone **212** to the corresponding 3,5-*O*-benzylidene protected lactone **211**. Finally, lactone **212** can be synthesized from starting L-gulonic acid **213** using the literature protocol.[114] This planned synthesis would deliver the target Pse donor in 12 steps starting from commercial L-gulonic acid (Scheme 25).



Scheme 25. Disconnection of Pse donor **172** to L-gulonic acid **213**.

2.2.1.1 Synthesis of a 3,5-*O*-benzylidene protected lactone

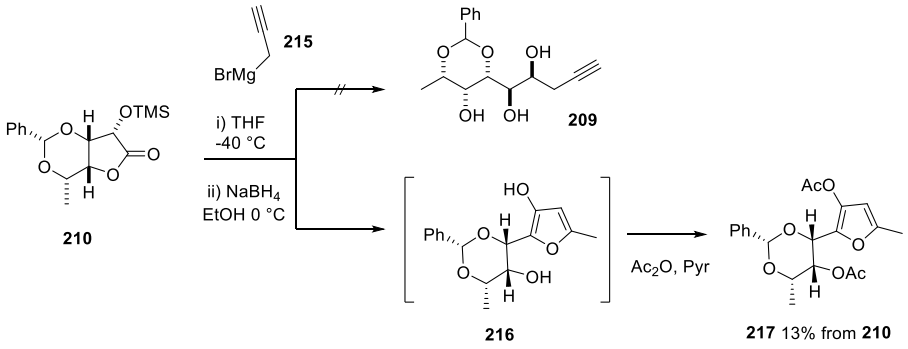
Commercial L-gulonic acid **213** was first converted to 6-deoxy-3,4-*O*-isopropylidene-L-gulonolactone **212** by three known straightforward literature steps.[114] Acid-mediated transacelation converted intermediate **212** to the corresponding benzylidene protected lactone **211**,[115] whose remaining secondary alcohol was then protected with a labile TMS group with bis(trimethylsilyl)amine affording fully protected L-gulonolactone **210** in 92% yield from **212** (Scheme 26).



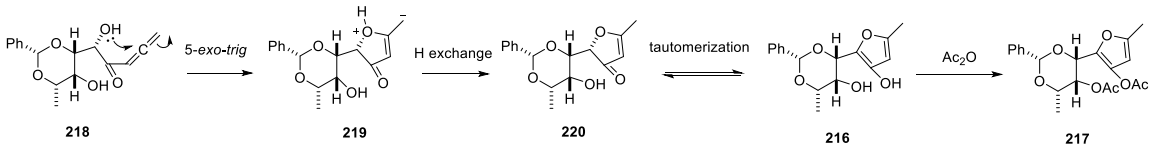
Scheme 26. Synthesis of 3,5-*O*-benzylidene-protected lactone **210**.

2.2.1.2 Addition of propargyl magnesium bromide to the lactone

In order to carry out the chain elongation by three carbons, the hexonolactone **210** was treated with propargyl magnesium bromide, which was prepared *in situ*, to give a nine-carbon addition product, which was then reduced with sodium borohydride with the goal of obtaining triol **209**. This sequence, however, gave an unpredicted product **216,** which could not be isolated (Scheme 27). Therefore, the crude reaction mixture was subjected to acetylation resulting in this isolation of **217**. Surprisingly, this substance was found to be a furan derivative that didn't include a propargyl group. It was reasoned that, during the basic reduction process, the propargyl group was transformed to an allene intermediate **218** that underwent 5-*exo*-*trig* ring closure followed by aromatization to form the furan ring (Scheme 28).



Scheme 27. Addition of propargyl magnesium bromide **215** to the lactone **210**.



Scheme 28. Proposed reaction mechanism for the formation of furan derivative **217**.

As the essential Grignard addition step in this synthetic route provided an unexpected product **216**, the route was abandoned, and attention was turned to a different route.

2.2.2 Retrosynthetic analysis of Pse donor from D-glucose

The next synthetic plan was established based on the strategic disconnections made after rotation of the Pse Fischer projection by 180° (Figure 7), leading to the chiral pool material, mono acetone D-glucose **230**. Thus, it was considered that the target donor **172** could be accessed from the intermediate **204**, which could be obtained from the corresponding open-chain olefin **223** by ozonolysis. Chain elongation would be accomplished by In-mediated Barbier reaction with methyl 2-(bromomethyl)acrylate from the corresponding aldehyde **221**. The hexose aldehyde **221** could obtained by selective oxidation of a primary alcohol using TEMPO after cleavage of TBS from intermediate **225**. Deoxygenation of the anomeric carbon of glucose was thought to be possible by the reduction of cyclic sulfate **226,** which might be easily obtained from the intermediate **227**, which is the alditol from reduction of the furanose sugar moiety **228**. Introduction of two azides at C3 and C4 with inversion of configuration would be accomplished by S_N2 displacement of triflates. This planned synthetic pathway would deliver the target Pse donor **172** in 13 steps starting from commercial monoacetone D-glucose **230** (Scheme 29).

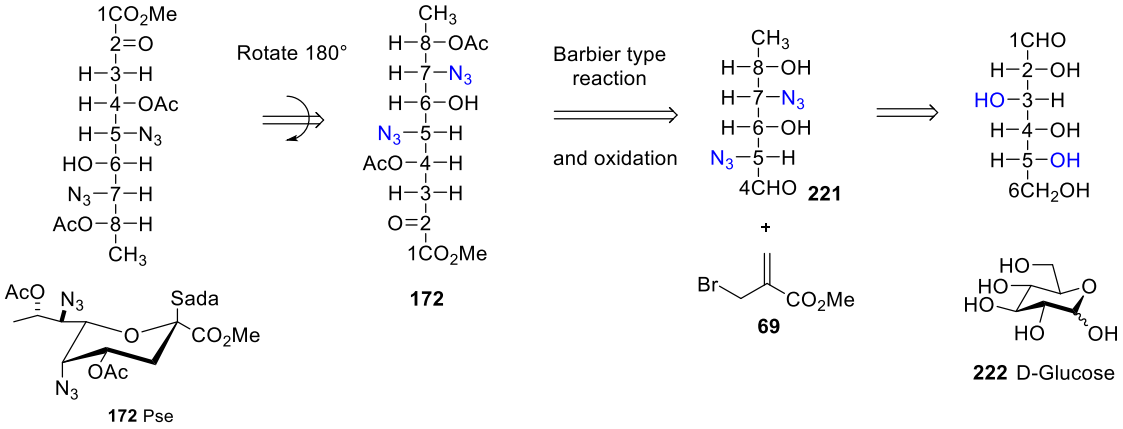
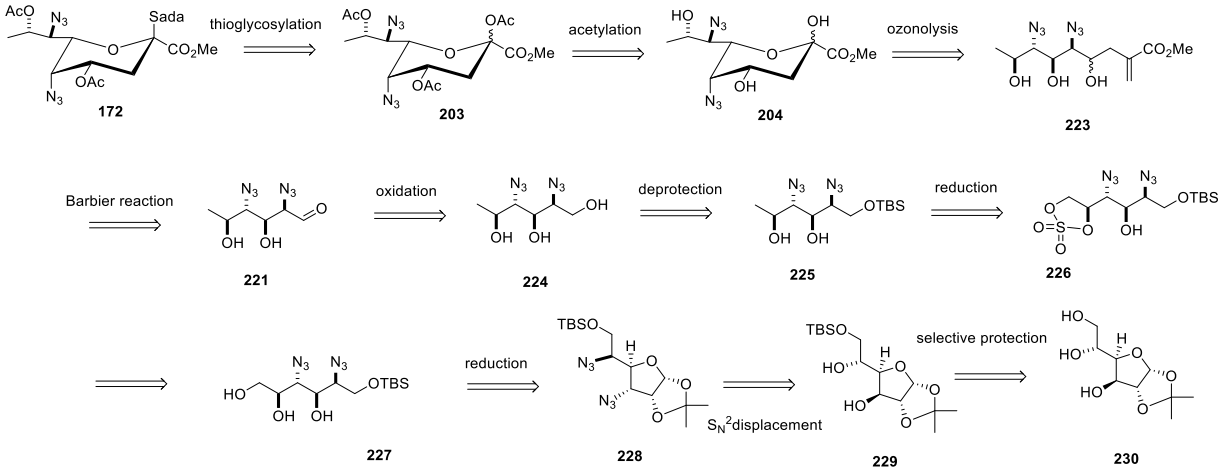


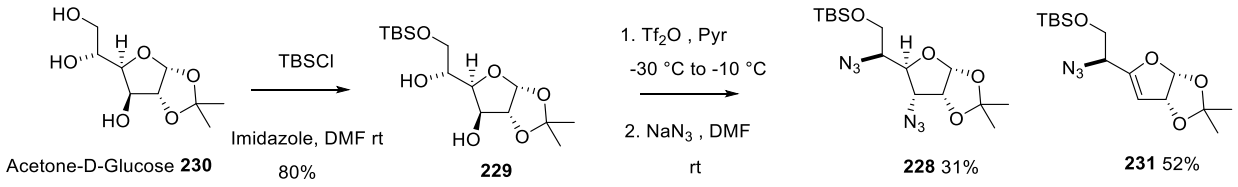
Figure 7. Strategic Disconnections.



Scheme 29. Retrosynthetic plan for Pse donor **172** from monoacetone D-glucose **230**.

2.2.2.1 Synthesis of a 3,5-diazido talofuranoside 228

The primary alcohol of monoacetone D-glucose **230** was protected selectively with a TBS group giving **229** in 80% yield. Next, the remaining two secondary alcohols at C3 and C5 were converted to the ditriflate derivative, which was then treated with sodium azide in DMF. This displacement reaction afforded the diazido sugar **228** in 31% yield with inversion of configuration at C3 and C5, along with the elimination product **231** in 52% yield (Scheme 30). Several reaction conditions were attempted using different azide salts in an attempt to favor the formation **228** over the elimination, as described in Table 4. Unfortunately, no conditions were found to afford substituted product **228** as major product, although tetrabutylammonium azide minimized the elimination product compared to other reagents.

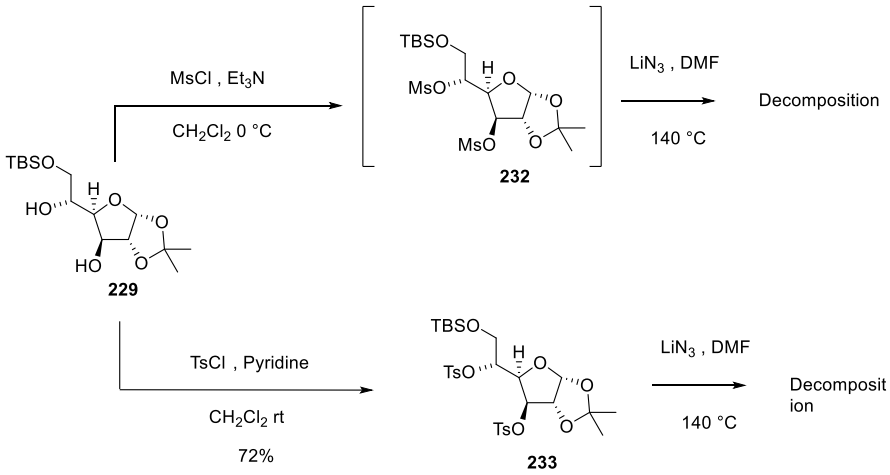


Scheme 30. Synthesis of 3,5-diazido talofuranoside **228**.

Table 4. Conditions attempted for diazide formation from diol **229**.

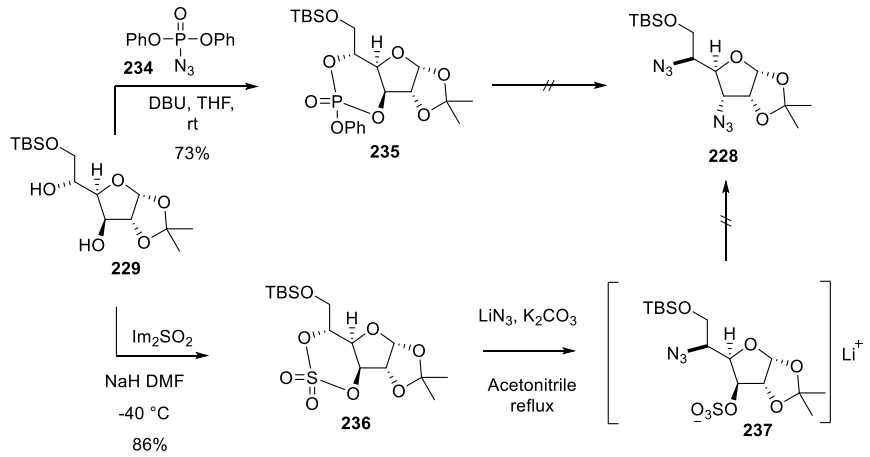
Azide reagent	Solvent	Condition	228: 231
NaN_3	DMF	0 °C to RT	1: 1.5
NaN_3	Acetone: Water (3:1)	RT	1: 2.3
NaN_3 with nBu_4NHSO_4	THF	RT	1: 2.5
LiN_3	DMF	0 °C to RT	1: 1.7
LiN_3	DMSO	RT	1: 1.5
$TBAN_3$	Toluene	RT	1: 1.5
$TBAN_3$	Acetonitrile	-30 °C to RT	1: 1.7
$TBAN_3$	CH_2Cl_2	0 °C to RT	1: 1.3
$TBAN_3$	Acetonitrile	10 °C	1: 1.3
$TBAN_3$	CH_2Cl_2	10 °C	1: 1.3
$TBAN_3$	1,2-Dichloroethane	20 °C	1: 1.3
$TBAN_3$	Hexafluoroisopropanol	RT	No Rn
nBu_3SnN_3		60 °C	No Rn

In further attempts to minimize the elimination during formation of 3,5-diazido talofuranoside **228**, the mesylate **232** and tosylate **233** derivatives of the diol **229** were examined (Scheme 31). The crude mesylate **232** was treated with lithium azide, but no reaction was observed below 140 °C. After reaching that temperature, the mesylate decomposed. The tosylate **233** was isolated in 72% yield but behaved similarly to the mesylate and decomposed around at 140 °C.



Scheme 31. Attempted reactions of mesylate and tosylate derivatives of diol **229**.

Reaction of diol **229** with diphenylphosphoryl azide **234** in the presence of DBU as a base,[116] gave cyclic phosphate derivative **235** in 73% yield, proving that diphenyl phosphate was not an adequate leaving group on this substrate. In yet a further variation the diol was reached with sulfonylimidazole to give the cyclic sulfate intermediate **236** in 86% yield.[117, 118] Attempted conversion of the cyclic sulfate to the target 3,5-diazido talofuranoside **228** with lithium azide at reflux in acetonitrile did not lead to the desired **228** but stopped after a single displacement at the level of **237** (Scheme 32) as deduced by mass spectrometry and NMR spectrometry.

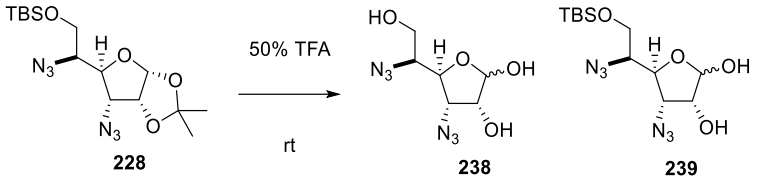


Scheme 32. Attempts were made to synthesis 3,5-diazido talofuranoside **228**.

2.2.2.2 Selective cleavage of the acetonide

The removal of the acetonide in **228** using harsh acidic conditions resulted in cleavage of both the acetonide and the silyl ether. Unfortunately, milder conditions (Table 5) were also unbale to bring above the selective deprotection.

Table 5. Attempted conditions for selective cleavage of an acetonide.

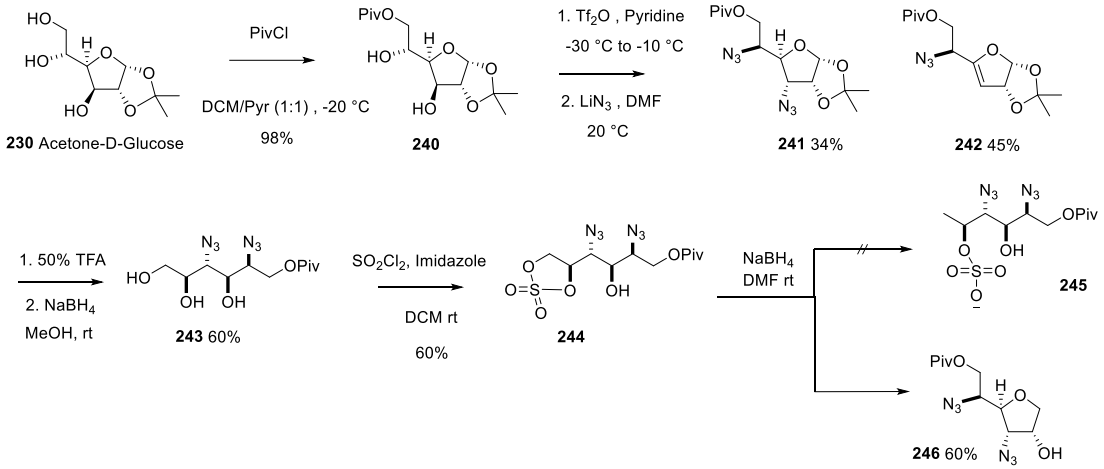


Compound	Condition	Product
228	50% TFA, rt	**238**
	60% AcOH, 110 °C	**238**
	I_2 MeOH, RT	**238**

2.2.2.3 Synthesis and reduction of an open chain cyclic sulfate

To circumvent the selective deprotection issue the primary hydroxy group in monoacetone D-glucose was protected as the pivaloyl derivative **240** in 98% yield, which was then subjected to the displacement of its ditriflate by sodium azide in DMF at 20 °C leading to the 3,5-diazido talofuranoside **241** in 34% yield along with the eliminated product **242** in 45% yield. After selective cleavage of the acetonide with 50% trifluoroacetic acid the resulting furanose was reduced with sodium borohydride to afford the alditol **243** in 60% yield. In order to deoxygenate C6, **243** was converted to cyclic sulfate **244** in 60% yield using sulfuryl chloride in the presence

of imidazole. However, sodium borohydride mediated reduction of this cyclic sulfate **244**,[119] resulted in formation of the 1,4-anhydro-D-altritol derivative **246** after elimination of the bisulfite group, instead of providing the desired C6-deoxy product **245** (Scheme 33).



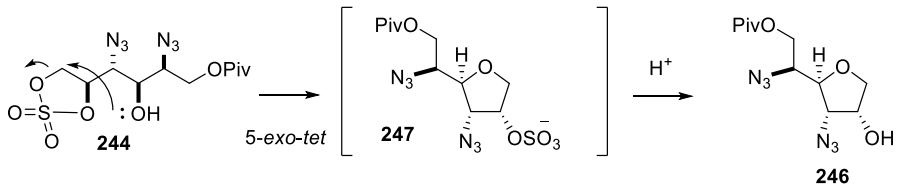
Scheme 33. Synthesis and reduction of an open chain cyclic sulfate **244**.

Various reducing reagents were investigated to reach the desired **245,** but surprisingly, all gave the 1,4-anhydro-D-altritol derivative **246** (Table 6).

Table 6. Conditions attempted to reduce cyclic sulfate **244**.

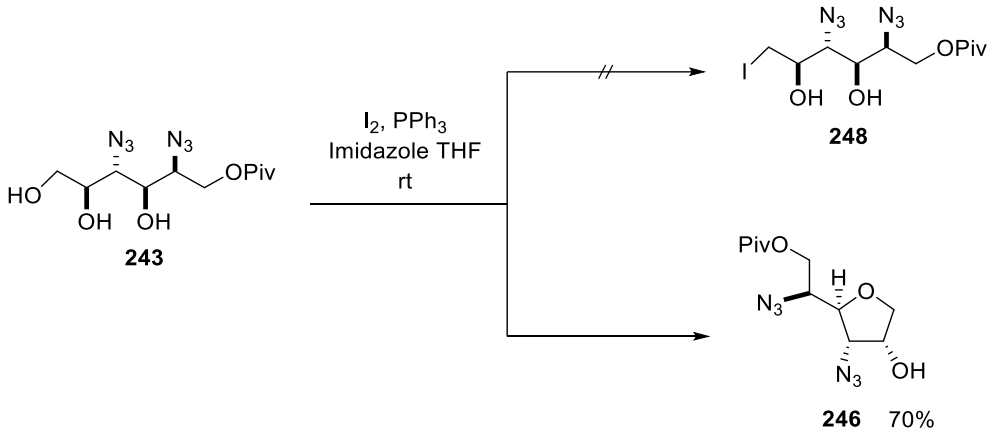
Conditions	Product
$NaBH_4$, DMAC, 4 Å MS	**246**
$NaBH_4$, DMF	**246**
$NaBH_3CN$, THF	**246**
$LiEt_3BH$	**246**

Under the basic condition alcohol **244** undergoes intramolecular cyclization by attack of O5 on C1 with the formation of the intermediate **247** (Scheme 34). On workup acidic hydrolysis of the sulfate group in **247** affords the 1,4-anhydro-D-altritol derivative **246**.



Scheme 34. Proposed mechanism for formation of 1,4-anhydro-D-altritol derivative **246**.

In yet a further attempt to remove the hydroxy group at C1, triol **243** was treated with iodine and triphenylphosphine in the presence of imidazole. Resulting in the formation of 1,4-anhydro-D-altritol derivative **246** in 70% yield rather than the desired iodide **248** (Scheme 35).



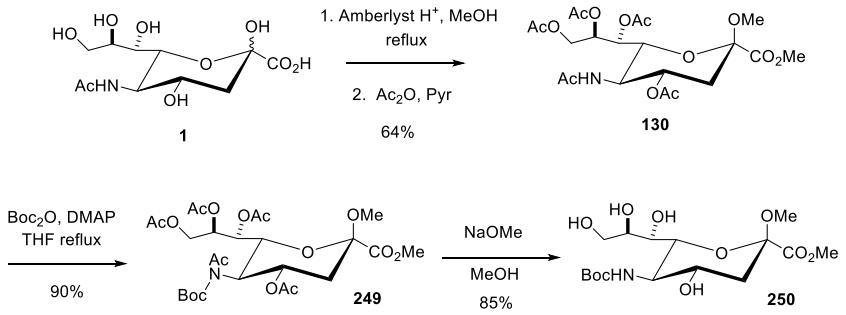
Scheme 35. Attempted synthesis of iodide derivative **248**.

All these results suggested the necessity of protection of the C4 hydroxy group in order to achieve deoxygenation at C1. As the addition of extra protection/deprotection stop would result in an overly long synthesis of the target Pse donor **172**, this approach was abandoned.

2.2.3 Attempted side chain modifications of *N*-acetylneuraminic acid

Inspired by Crich and Dhakal's earlier syntheses of Pse and Leg donors (Scheme 7 and 16) starting from cheap readily available *N*-acetylneuraminic acid **1**, attention was refocused on development of a more convenient second generation of synthesis from the same starting material. Clearly this new approach would have to make less use of protecting groups than the earlier one to be more efficient.

For the exploratory work the methyl glycoside of *N*-acetylneuraminic acid was used to develop reaction conditions because of its relative ease of access. Therefore, the 5-*N*-Boc protected methyl sialoside **250** was synthesized from the commercial *N*-acetylneuraminic acid **1** by a known literature protocol (Scheme 36).[99, 120]

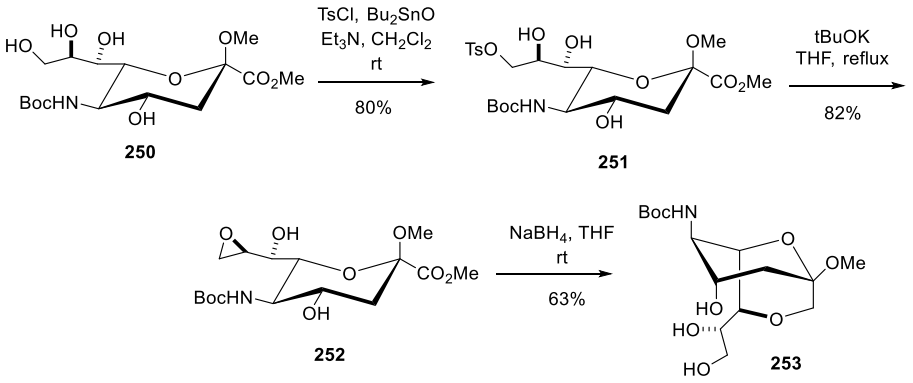


Scheme 36. Synthesis of 5-*N*-Boc protected methyl sialoside **250**.

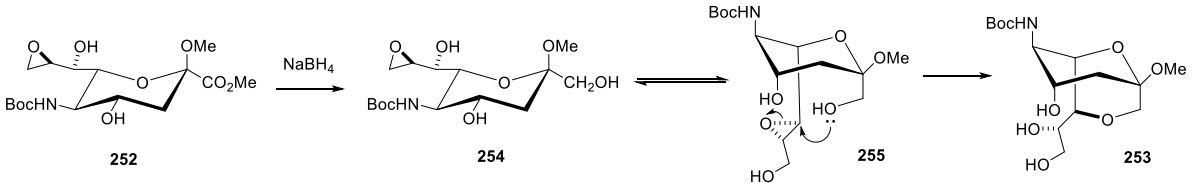
2.2.3.1 Attempted synthesis of a 9-deoxy sialoside via reduction of an 8,9-epoxide

Kiefel and coworkers were unable to tosylate the C9 hydroxy group in sialoside derivatives with tosyl chloride and pyridine,[23] however, dibutyltin catalyzed selective tosylation of tetraol **250** provided the mono tosyl derivative **251** in 80% yield in the presence of triethylamine as a base.[121] Heating the tosylate in the presence of tertiary butoxide transformed it to terminal epoxide **252** in 82% yield. Unfortunately, sodium borohydride reduction of **252**, afforded the undesired bicyclic

derivative **253** in 63% yield. This product arises by reduction of the anomeric methyl ester followed by base-catalyzed Payne rearrangement (Scheme 37). The rearranged epoxide **255** is then attacked by the C1 hydroxyl group on to C7, which opens the epoxide ring via 6-*exo*-*tet* to form the bicyclic sugar **253** (Scheme 38).



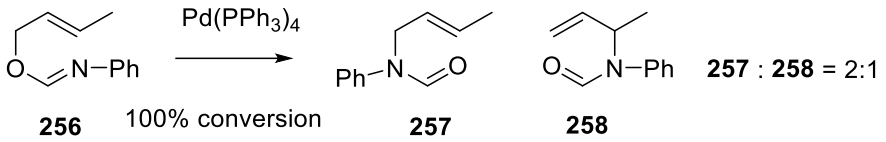
Scheme 37. Attempted synthesis of a 9-deoxy sialoside via reduction of an 8,9-epoxide.



Scheme 38. Mechanism of formation of bicyclic sugar **253**.

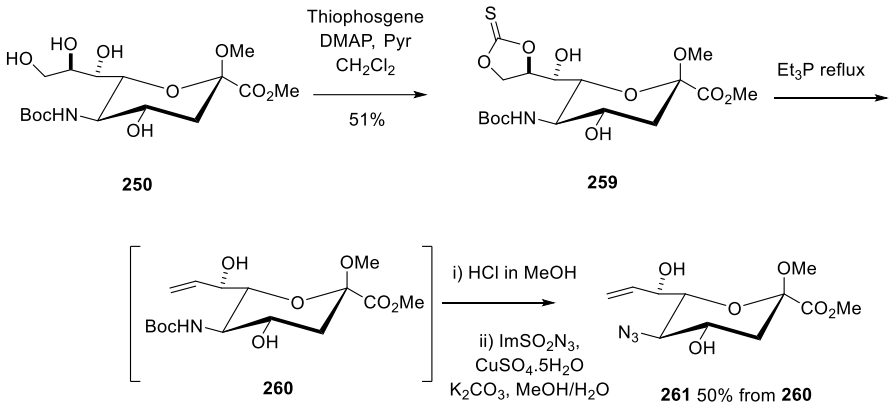
2.2.3.2 Attempt of introducing amino functionality via 1,3-Overmann rearrangement

Ikariya and coworkers reported the 1,3-Overmann rearrangement of allylic *N*-phenylformimidates with palladium (0) complexes (Scheme 39).[122] It was considered that a similar reaction might be used to install the needed amino-functionality at C7 in a derivative of sialic acid. To achieve this, the 8,9-diol would need to be converted to an olefin.



Scheme 39. 1,3-Overmann rearrangement of allylic *N*-phenylformimidates.

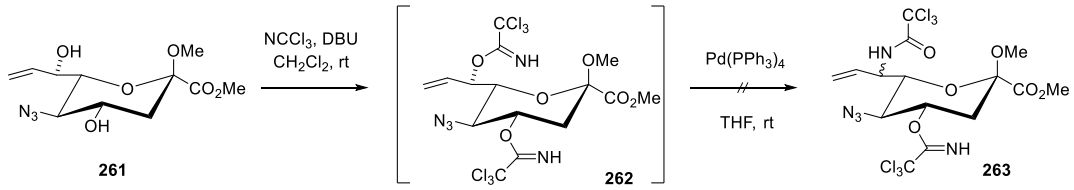
The elimination of two hydroxyl groups at C9 and C8 in sialoside **250** to provide 8,9-olefin is feasible via the Corey-Winter olefin synthesis.[123] Therefore, tetraol **250** was converted to corresponding 8,9-thiocarbonyl derivative **259** in 51% yield by treatment with thiophosgene. Upon heating to 140 °C in triethyl phosphite, **259** furnished the desired 8,9-alkene **260**. Purification of **260** was difficult, therefore, the crude product was used for the conversion to the corresponding 5-azide. For this, acid-mediated deprotection of the Boc group was followed by reaction with Stick's reagent in the presence of catalytic copper sulfate and potassium carbonate in aqueous methanol affording the 5-azido-alkene **261** in 50% yield after three steps (Scheme 40).



Scheme 40. Synthesis of unsaturated sialoside **261**.

The unsaturated sialoside **261** was treated with trichloroacetonitrile in the presence of DBU to obtain the trichloroacetimidate **262**, which was then treated with the

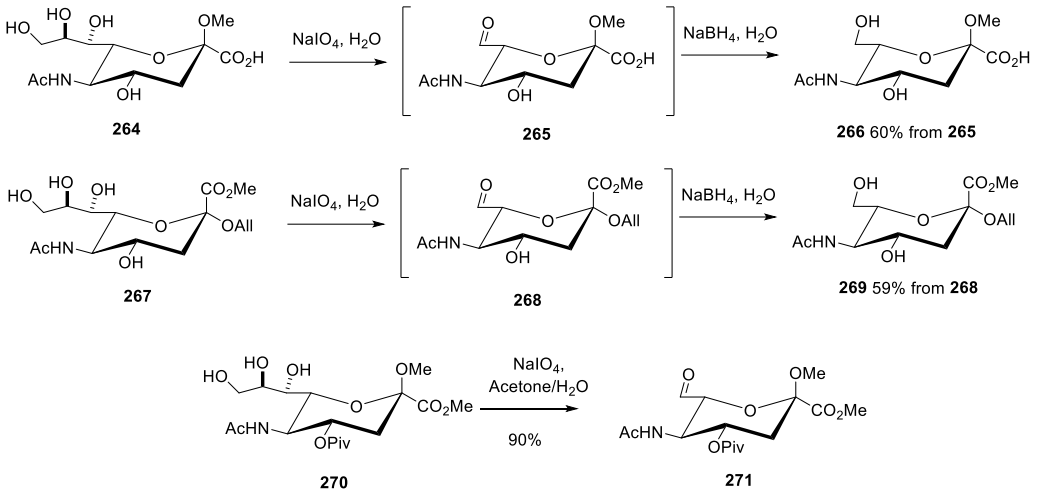
tetrakis(triphenylphosphine)palladium (0) complex in tetrahydrofuran. Unfortunately, no reaction was observed, and this substrate was recovered unchanged (Scheme 41).



Scheme 41. Attempted 1,3-Overmann rearrangement.

2.2.4 Literature precedent of oxidative cleavage of side chain

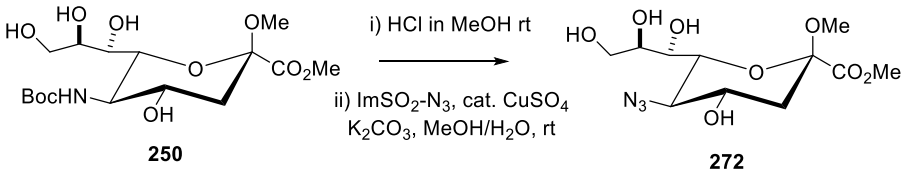
Attention was next toward to the possibility of oxidative cleavage of the side chain, followed by reinstallation of the desired one. The possibility of sodium periodate mediated oxidative cleavage of the side chain was first reported for the methyl glycoside of the *N*-acetylneuraminic acid **265** by Robert and Ledeen in 1969 (Scheme 42).[124] They obtained the corresponding aldehyde after oxidation and reduced it with sodium borohydride to give the isolated 7-carbon ulosonic acid **266**. In addition, Roy and Laferriere also obtained allyl heptulopyranoside methyl ester **269** after periodate mediated oxidation followed by reduction of *N*-acetylneuraminic methyl ester **267**.[125] In 2000, Honda and coworkers also applied the same strategy to synthesize the 4-pivaloyl aldehyde derivative **271**.[126] More recently, Fessner and coworkers have used this oxidation to obtain aldehyde **265**, which was used to synthesized terminally modified sialic acid analogs.[127]



Scheme 42. Literature precedent for oxidative cleavage of the side chain.

2.2.5 Oxidative cleavage of the side chain and synthesis of an aldehyde

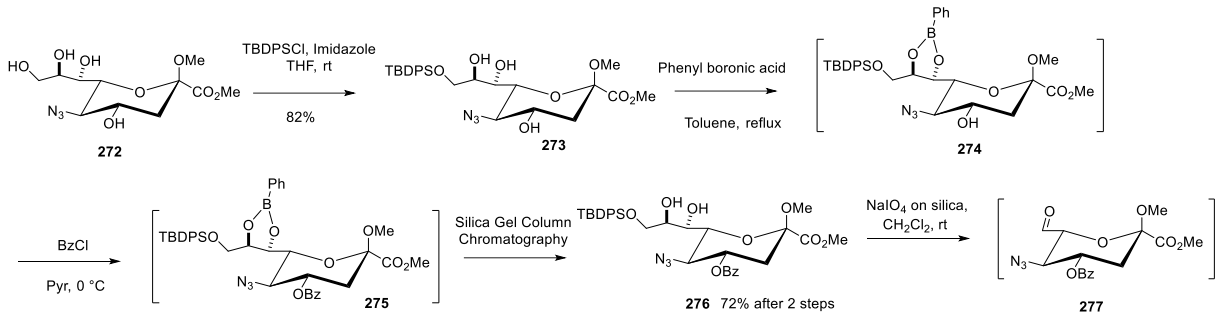
Two different aldehydes were synthesized differing in protection of the C4 hydroxy group as it proved difficult to isolate the corresponding aldehyde lacking protection at O4. The 5-*N*-Boc group in precursor **250** is problematic for acid-sensitive reactions, therefore, tetraol **250** was transformed into the 5-azido derivative **272** according to a known literature procedure (Scheme 43).[99, 120]



Scheme 43. Conversion of a 5-*N*-Boc derivative to the corresponding 5-azide.

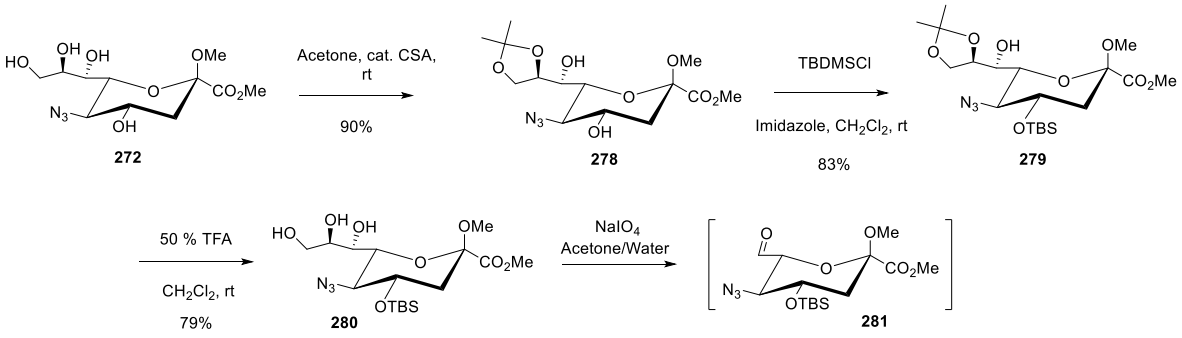
Selective protection of C9 hydroxy group with a TBDPS ether gave **273** in 82% yield, whose two adjacent secondary hydroxyl groups at C8 and C7 were temporarily protected as a boronate ester using phenylboronic acid in toluene.[128] The remaining C4 hydroxyl group was then benzoylated to give **275** from which the boronate was cleaved during column purification over

silica gel to give diol **276** in 72% yield after three steps. Sodium periodate on silica[129] mediated oxidation of the **276** afforded the corresponding aldehyde **277**, which was further used without purification (Scheme 44).



Scheme 44. Synthesis of 4-benzoyl aldehyde **277**.

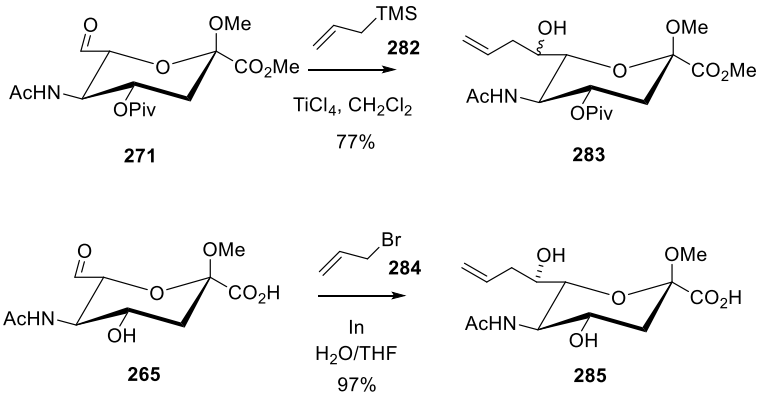
The acetonide-protected sialoside **278** was obtained from precursor 5-azido **272** according to literature protocol. The selective installation of a TBS ether on the C4 hydroxy group was accomplished in the presence of imidazole in dichloromethane and provided **279** in 83% yield. After selective cleavage of the acetonide without affecting the TBS ether with 50% trifluoroacetic acid, the resulting tetraol **280** was treated with sodium periodate to afford the aldehyde **281** (Scheme 45).



Scheme 45. Synthesis of 4-*O*-TBS aldehyde **281**.

2.2.5.1 Attempted reactions of the aldehydes

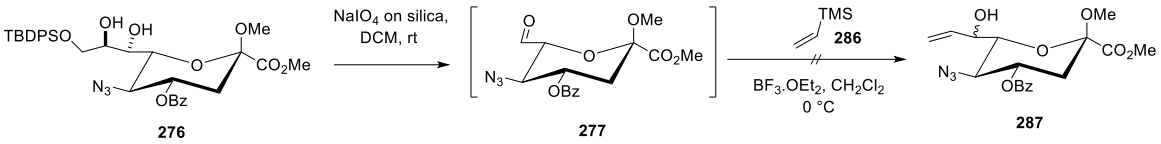
In addition to the reduction of sialoside aldehydes, there are a few other reactions reported in the literature (Scheme 46). Thus, Honda and coworkers successfully obtained sialoside **283** in good yield from sialoside aldehyde **271** by Sakurai reaction.[126] Fessner and coworkers on the other hand have synthesized sialic acid analogs based on indium-mediated Barbier type chain extension of sialoside aldehyde **265** in good to moderate yields (Scheme 46).[127]



Scheme 46. Reactions of side chain aldehydes reported in the literature.

2.2.5.2 Reactions with vinyl nucleophiles

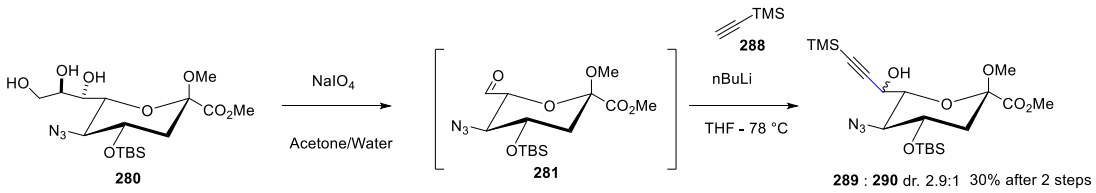
Reconstruction of the side chain of Pse or Leg from any C7 aldehyde sialoside requirs the addition of two carbons. Therefore, the 4-*O*-benzoyl aldehyde **277** was treated with vinyltrimethylsilane in the presence of $BF_3.OEt_2$ in order to obtain the corresponding sialoside **287**. Unfortunately, due to the less reactive nature of vinyltrimethylsilane compared to allyltrimethylsilane, this transformation did not proceed (Scheme 47). Complex mixtures were obtained with vinyl magnesium bromide.



Scheme 47. Attempted reaction of aldehyde **277** with vinyltrimethylsilane.

2.2.5.3 Reactions with alkynyl nucleophiles

Attention was next turned to installation of the required carbons in the form of an alkyne. Aldehyde **281** was treated with lithium trimethylsilylacetylide at -78 °C in THF and afforded the alcohol as a 2.9:1 mixture of diastereomers in 30% yield (Scheme 48).



Scheme 48. Synthesis of sialosides **289** and **290**.

After separating the so-formed diastereomers, the configuration at C7 of the two isomers was established by converting to the corresponding (*R*)-Mosher esters. In a Mosher ester the methoxy and trifluoromethyl groups tend to orient the phenyl group in such a manner as to shield one of the two substituents on the (secondary) alcohol (Figure 8).[130] Therefore, the Mosher ester shifts the back group (blue) upfield in the ^{1}H NMR spectrum while the front group (red) is shielded compared to the present alcohol.[130]

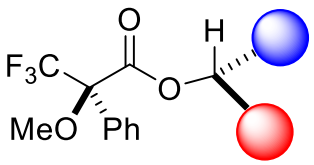
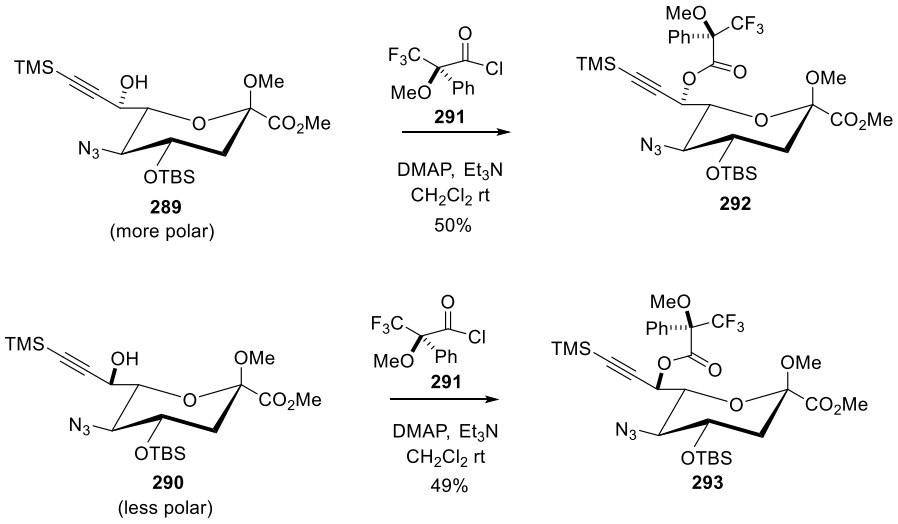


Figure 8. The conformation of (*R*)-Mosher ester leading to selective shielding of the blue group.

The more polar derivative **289** was transformed to the (*R*)-Mosher ester **292** in 50% yield by treatment with (*S*)-Mosher acid chloride **291** in the presence of DMAP and triethylamine (Scheme 49). On the other hand, the less polar derivative **290** provided corresponding (*R*)-Mosher ester **293** in 49% yield under the same conditions. On analysis of the chemical shifts in less polar derivative **290** and desired ester **293**, H6 in Mosher ester **293** showed a downfield shift of δ 0.16 compared its alcohol, that implies the sugar ring is not shielded by phenyl group and is in front side (Figure 9). In the more polar isomer Mosher ester, H6 showed a smaller downfield shift leading to the conclusion that its sugar ring is in the shielding zone on the back side (Figure 9, Table 7). Hence, compound **289** was recognized as the D-galacto derivative, while compound **290** was the L-altro-isomer.



Scheme 49. Synthesis of Mosher esters.

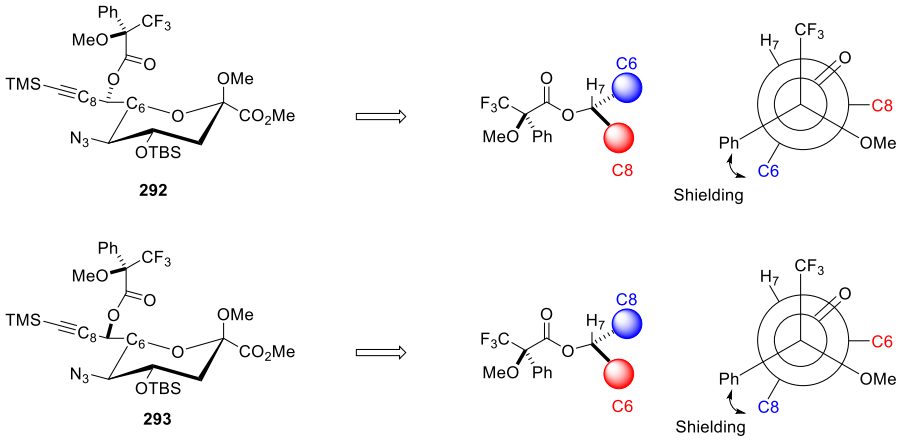


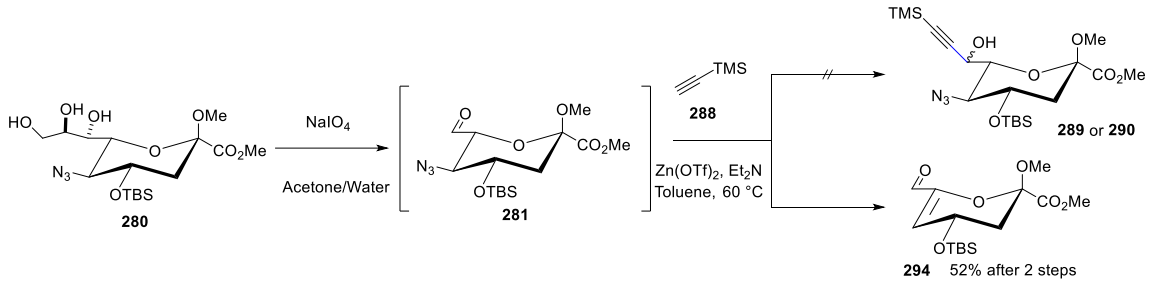
Figure 9. Shielding in the Mosher ester **292** and **293**.

Table 7. Chemical shifts of alcohols and their Mosher esters.

Proton	Alcohol	ME	Δ(ME-Alcohol)
	290	**293**	
H6	δ 3.42	δ 3.58	δ 0.16
TMS	δ 0.14	δ 0.15	δ -0.01
	289	**292**	
H6	δ 3.49	δ 3.54	δ 0.05
TMS	δ 0.21	δ 0.21	δ 0

The low yield of adduct formation with lithium trimethylsilylacetylide lead to the consideration of milder conditions and the in situ generation of zinc acetylides as first reported by Carreira and coworkers for the synthesis of propargyl alcohols.[131] Accordingly, the aldehyde sialoside **281** was treated with of zinc acetylides generated in situ from trimethylsilyl acetylene in the presence of $Zn(OTf)_2$ and triethylamine. Although all previously reported reactions were

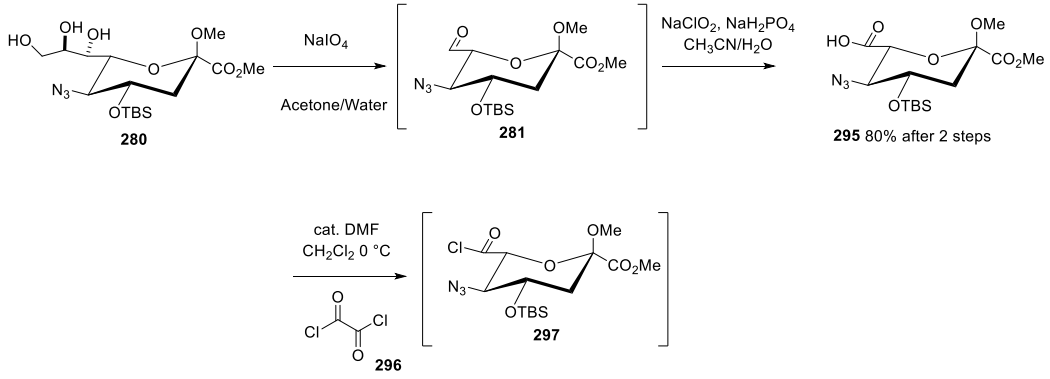
conducted at room temperature, aldehyde **281** was unreactive under those conditions. Upon heating the reaction mixture to 60 °C, consumption of the starting aldehyde was observed and the α,β-unsaturated sialoside **294** isolated in 52% yield (Scheme 50). A similar outcome was obtained when the starting aldehyde was heated to 60 °C with triethylamine in toluene, demonstrating the acidic nature of the H6 proton.



Scheme 50. Attempted propargylation with a zinc acetylide.

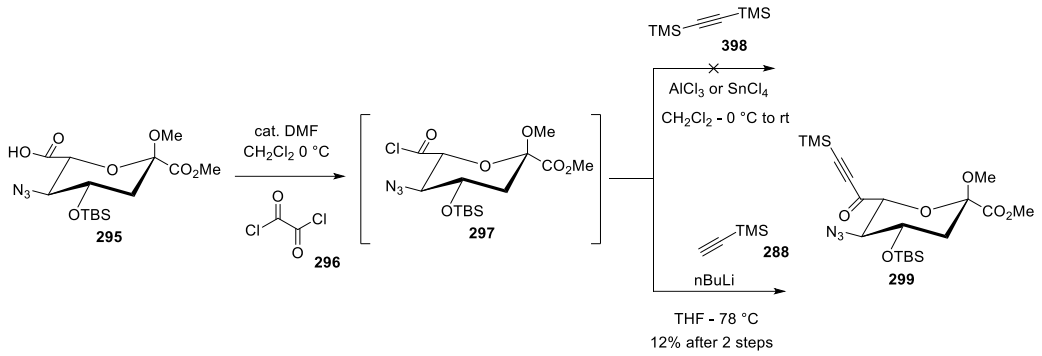
2.2.5.4 Reaction of a C7 acyl chloride with bistrimethylacetylene

To increase the reactivity of the C7 electrophile the sialyl acid **295** was prepared in 80% yield from the aldehyde **281** via Pinnick oxidation.[132] The acid **295** was then converted to the acyl chloride **297** using oxalyl chloride (Scheme 51). The acid chloride **297** was used as a crude preparation for further nucleophilic addition reactions without isolation.



Scheme 51. Synthesis of acyl chloride **297**.

Acyl chlorides can couple with bistrimethylacetylene via a Friedel craft acylation type in the presence of a Lewis acid.[133, 134] However, acyl chloride **297** failed to lead under typical conditions. The addition of lithium trimethylsilylacetylide to **297** on the other hand gave the desired alkynyl ketone **299** but only in 12% yield (Scheme 52).



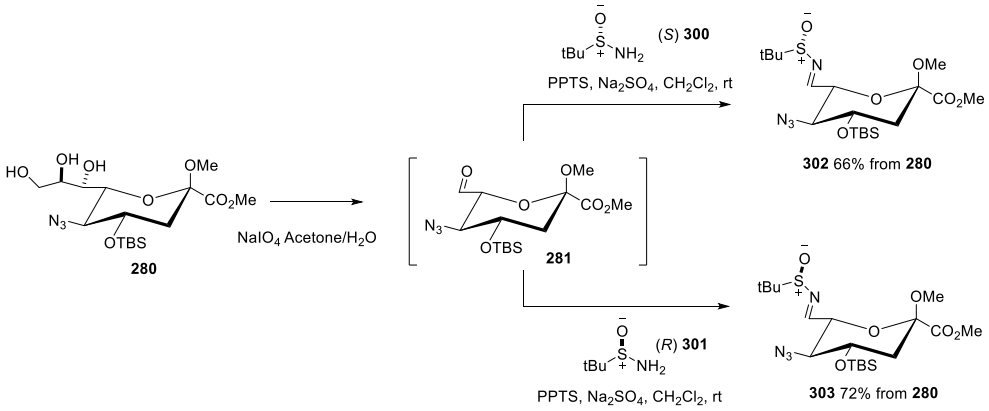
Scheme 52. Formation of alkynyl ketone **299**.

2.2.6 Synthesis of chiral *N*-sulfinyl imines

In view of the complications and/or lack of reactivity with C7 aldehydes and acid derivatives attention was redirected to *N*-sulfinyl imines as introduced by Ellman and coworkers.[135, 136] Such sulfinimines have played an important role in asymmetric synthesis by facilitating the production of structurally diverse nitrogen-containing molecules and are a general solution to the problem of addition of organometallic reagents to chiral imines.[135, 136] The presence of the electron-withdrawing sulfinyl group activates the CN bond for nucleophilic addition, which allow reactions to proceed at lower temperatures.[136] The *N*-sulfinyl auxiliary also exerts powerful stereo-directing effects and provides excellent stereoselectivity in many cases.

The use of chiral *N*-sulfinyl imines derived from the sialic acid C7 aldehyde potentially allows direct introducing of an amine at C7 after the addition of carbon nucleophiles with control of configuration. To examine the selectivity of chiral sialic acid-derived *N*-sulfinyl imines towards

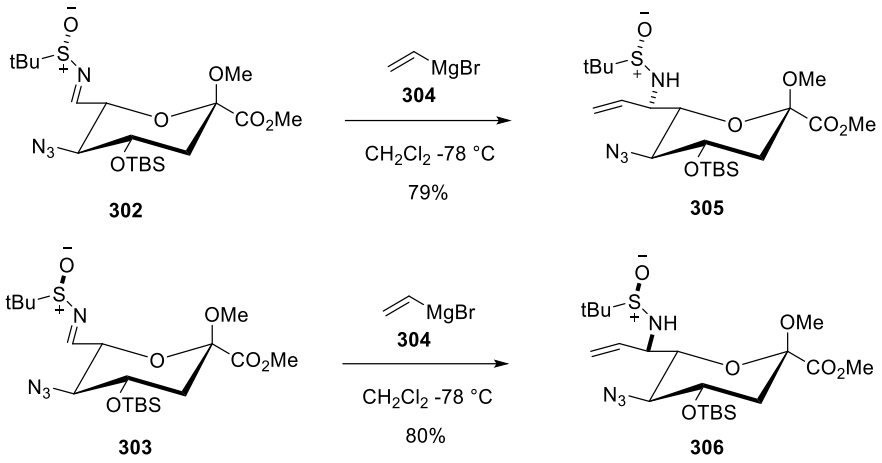
carbon nucleophiles, both (*S)* and (*R) N*-sulfinyl imines were synthesized (Scheme 53). The (*S)*-*N*-sulfinyl imine sialoside **302** was obtained in 66% yield by treating the crude aldehyde **281** with (*S)*-butanesulfinamide **300** in the presence of a catalytic amount of PPTS and dehydrating agent Na_2SO_4 in dichloromethane. The (*R)*-*N*-sulfinyl imine sialoside **303** was also obtained in 72% yield under the same conditions with (*R)*-butanesulfinamide **301**.



Scheme 53. Synthesis of (*S*)- and (*R*)-*N*-sulfinyl imines.

2.2.6.1 Reaction of chiral *N*-sulfinyl imines with vinyl magnesium bromide

Previous reports of Grignard additions to chiral *N*-sulfinyl imines showed improved diastereoselectivities when the non-coordinating solvent dichloromethane was used.[137] The addition of vinylmagnesium bromide to (*S)*-*N*-sulfinyl imine sialoside **302** in dichloromethane at -78 °C provided the 7-(*S*)-allylic amine derivative **305** in 79% yield while the (*R*)-*N*-sulfinyl imine **303** gave the corresponding 7-(*R*)-allylic amine derivative **306** in 80% yield as single diastereomer demonstrating the excellent stereocontrol possible with these derivatives (Scheme 54).



Scheme 54. Synthesis of allylic amine sialosides.

The configuration at C7 in these allylic amines was identified from the corresponding (*R*)-Mosher amides using the established model (Figure 10) which parallels that discussed earlier for esters.[130, 138]

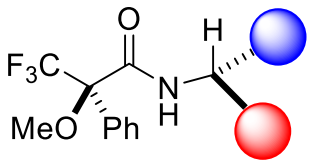
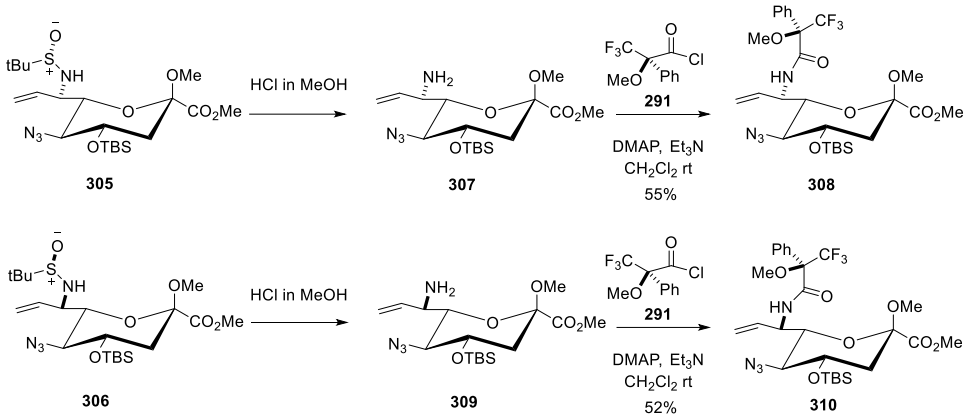


Figure 10. Stable Z-conformer of (*R*)-Mosher amide.

Methanolysis of the sulfinamide group in both 7-allylamino sialosides **305** and **306** with methanolic hydrogen chloride provided the naked amines, which were coupled with the (*S*)-Mosher acid in the presence of DMAP and triethylamine in dichloromethane to give the corresponding (*R*)-Mosher amides. The amine obtained from **305** gave the Mosher amide sialoside **308** in 55% yield, and amine obtained from **306** afforded its Mosher amide sialoside **310** in 52% yield under the same conditions (Scheme 55).



Scheme 55. Synthesis of (*R*)-Mosher amide sialosides.

Analysis of the chemical shifts in Mosher amide **308** revealed that its H6 proton is shifted upfield by δ 0.19 compared to 7-(*S*)-amino silaloside **307** H6 proton. This implies the sugar ring is shielded by the phenyl group and positioned in the backside of the model. The H8 proton did not show a significant change in chemical shift indicating C8 is sitting on the front side, which confirms C7 has the (*S)* configuration (Figure 11). In contrast Mosher amide **310** showed an upfield shift of H8 by δ 0.13 as well as a downfield shift of H6 by δ 0.09 (Table 8); therefore, the phenyl group sits above C8 and shields it while the sugar ring is in front side confirming C7 has the (*R)*-configuration (Figure 11).

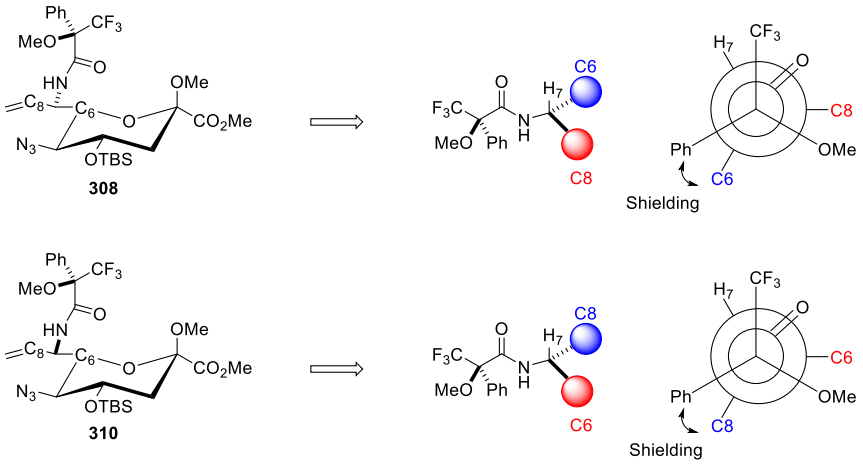
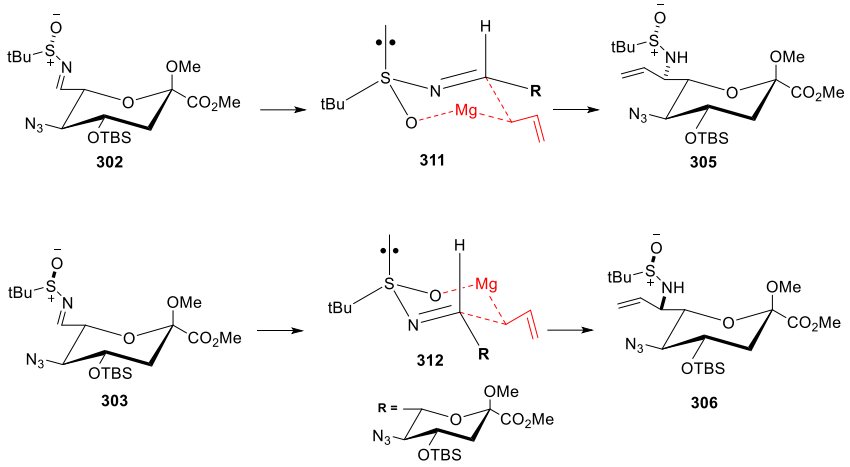


Figure 11. Mosher analysis of amides **308** and **310**.

Table 8. Mosher analysis of amides **308** and **310**.

Proton	Amine	MT-Amide	Δ(MT-Amine)
	307	**308**	
H6	δ 3.48	δ 3.29	δ -0.19
H8	δ 5.99	δ 5.91	δ -0.08
	309	**310**	
H6	δ 3.31	δ 3.40	δ 0.09
H8	δ 6.0	δ 5.87	δ -0.13

These addition reactions indicated that the *N*-sulfinyl group serves as a powerful chiral directing group and likely directs the stereoselectivity via a six-membered cyclic transition state (Scheme 56).[139] Hence, the (*S*)-*N*-sulfinyl imine reaction proceeds through transition state **311** and afforded the Leg-like configuration at C7, while the Pse-like configuration is provided by the (*R*)-*N*-sulfinyl imine via an analogues transition state **312**.



Scheme 56. Six membered cyclic transition states for vinylmagnesium bromide addition to sulfinyl imines.

With the success of these vinylmagnesium bromide additions to *N*-sulfinyl imines, it remained to introduce the 8-hydroxy group ideally by simple cyclization of the sulfoxide oxygen onto the alkene (Figure 12).

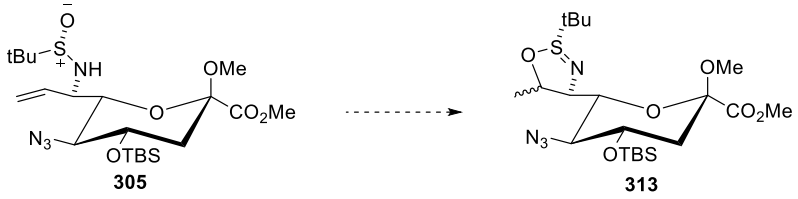
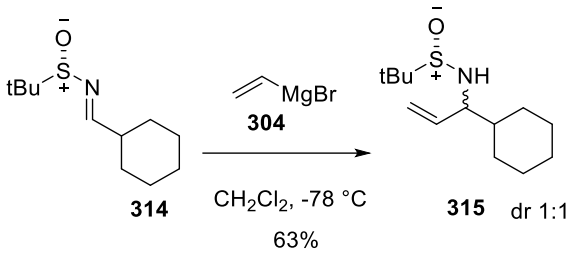


Figure 12. Hypothetical cyclization of an allylic sulfinamide.

2.2.6.2 Attempted cyclization of allylic sulfinamides

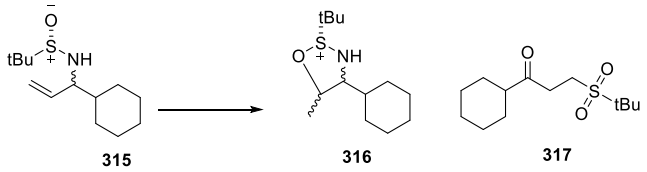
The cyclization of sulfinamide oxygen to an olefin carbon has not been reported yet in the literature, necessitating a search for suitable reaction conditions. Hence, the sulfinamide **315**, which has a cyclohexyl group that resembles ring segment in sulfinamide sialosides, was prepared for the use as a model. The cyclohexyl sulfinamide **315** was synthesized from (*S*)-*N*-sulfinyl imine **314** according to the known literature procedure (Scheme 57).[140]



Scheme 57. Synthesis of cyclohexyl sulfinamide **315**.

Turning to the cyclization, Pd complexes are known for activation of olefins,[141] therefore, $Pd(OAc)_2$ was studied under different conditions, but starting sulfinamide **315** was always recovered unchanged. The use of various Ru, Rh, Cu, and Sc complexes also failed to catalyze the desired cyclization (Table 9). The used the Bronsted acids, triflic acid, and trifluoro acid provided a keto sulfone **317** instead of the cyclized product **316** upon heating to 100 °C in toluene.

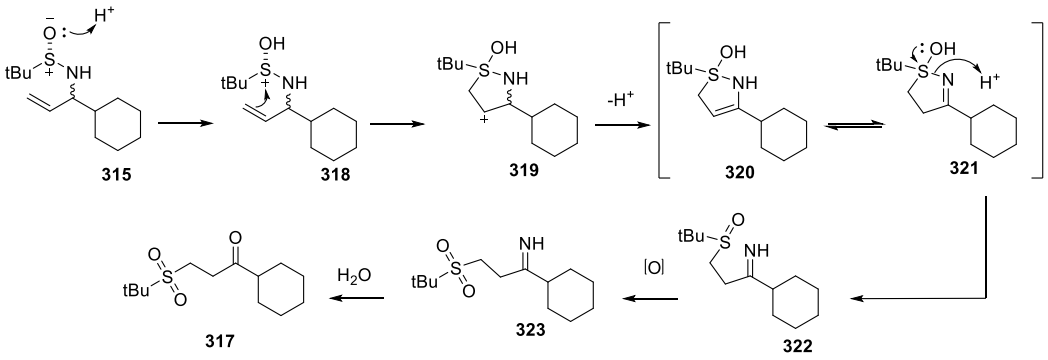
Table 9. Attempted conditions for cyclization of *N*-vinyl sulfinamide **315**.



Reagent	Solvent	Temperature	Product
$Pd(OAc)_2$	DMSO	rt	No reaction
	CH_3CN	rt to 50 °C	No reaction
$RuCl_2(PPh_3)_3$	EtOH	rt to reflux	No reaction
Rh_2Ac_2	CH_2Cl_2	rt	No reaction
$Sc(OTf)_2$	CH_2Cl_2	rt	No reaction
$Cu(OTf)_2$	CH_2Cl_2	rt	No reaction
TFA	CH_2Cl_2	rt	No reaction

TFA	Toluene	100 °C	**317**, 37%
Triflic acid	CH_2Cl_2	rt	No reaction
Triflic acid	Toluene	100 °C	**317**, 10%

The formation of keto sulfone **317** can be rationalized by the following mechanism (Scheme 58). In the presence of Bronsted acid, the sulfinamide **315** oxygen is protonated to form the intermediate **318** that gives cyclic carbocation **319** via cyclization of the olefin to the positively charged sulfur. Removal of a proton from this carbocation provides a dihydroisothiazole **320** whose tautomer **321** gives the sulfinyl imine **322** after opening the dihydroisothiazole ring. The oxidation of sulfur converts imine **322** to sulfonyl imine **323,** which was hydrolyzed to give keto sulfonyl compound **317** during the workup.

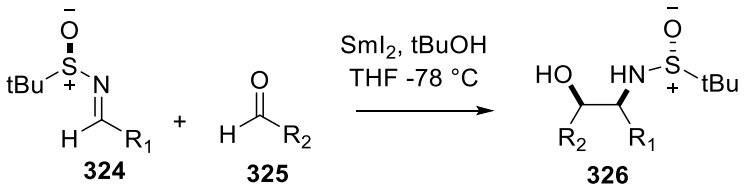


Scheme 58. Proposed mechanism for formation of keto sulfone compound **317**.

2.2.6.3 Samarium iodide-mediated aza pinacol reaction

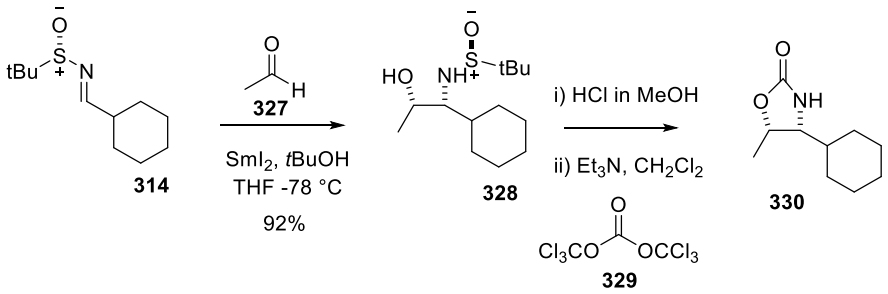
The reductive cross-coupling of (*R*)-*N*-*tert*-butylsulfinyl imines with aldehydes was reported by both Lin *et al*. and Bentley *et al*. in 2005 to give enantiopure β-amino alcohols in high yields and with high diastereomeric ratios (Scheme 59).[142, 143] This pinacol-type reductive coupling

is induced by SmI_2 at -78 °C in the presence of *t*BuOH, and is reported to selectively give *syn* β-amino alcohols.[142, 143]



Scheme 59. Samarium iodide-mediated aza pinacol reaction.

Application of this reaction to C7 sialic and derived chiral *N*-sulfinimides provides a potentially very direct entry into the Leg and Pse side chains. To examine the coupling of acetaldehyde with a chiral *N*-sulfinyl imine, the imine **314** was subjected to samarium iodide-mediated cross-coupling with acetaldehyde in the presence of *t*BuOH at -78 °C. After several attempts, the use of five equivalents of samarium iodide and six equivalents of acetaldehyde freshly distilled over a drop of conc. H_2SO_4 gave the corresponding β-amino alcohol **328** in 92% yield as a single diastereomer. In order to establish the relative configurations, β-amino alcohol **328** was transformed to the corresponding oxazolidinone derivative **330** (Scheme 60).



Scheme 60. Synthesis of cross-coupled amino alcohol **328** and oxazolidinone **330**.

The configuration at C3 in **330** is identified as (*S*) become it is derived from (*S*)-*N*-sulfinyl imine as described in the work of Lin and Bentley.[142, 143] The relative configuration of C2 and C3

was established by the analysis of NOE interactions in **330**. Two key interactions, were observed between H2 and H3, and between the methyl group and H4. Together with the 2,3-coupling constant of 7.7 Hz these measurements established the oxazolidinone to be *cis*-disubstituted and so the configuration at C2 was established as (*S*) (Figure 13).

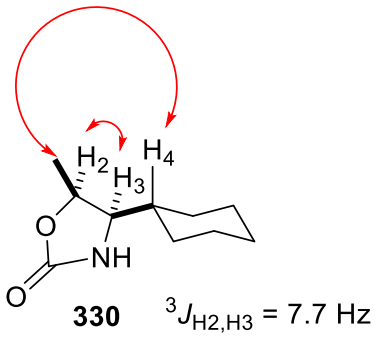
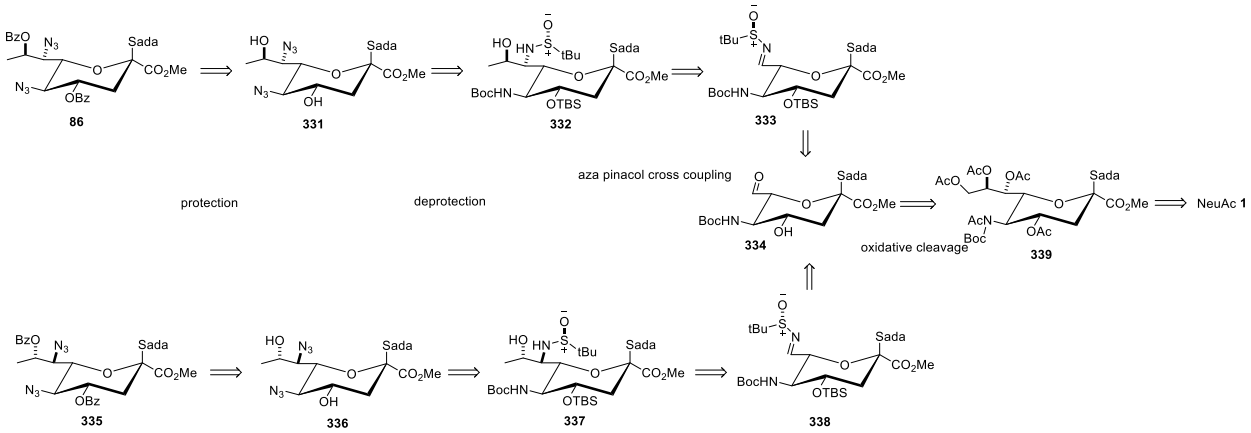


Figure 13. NOE interaction in oxazolidinone **330**.

2.2.7 Syntheses of legionaminic acid and acetaminic acid donors

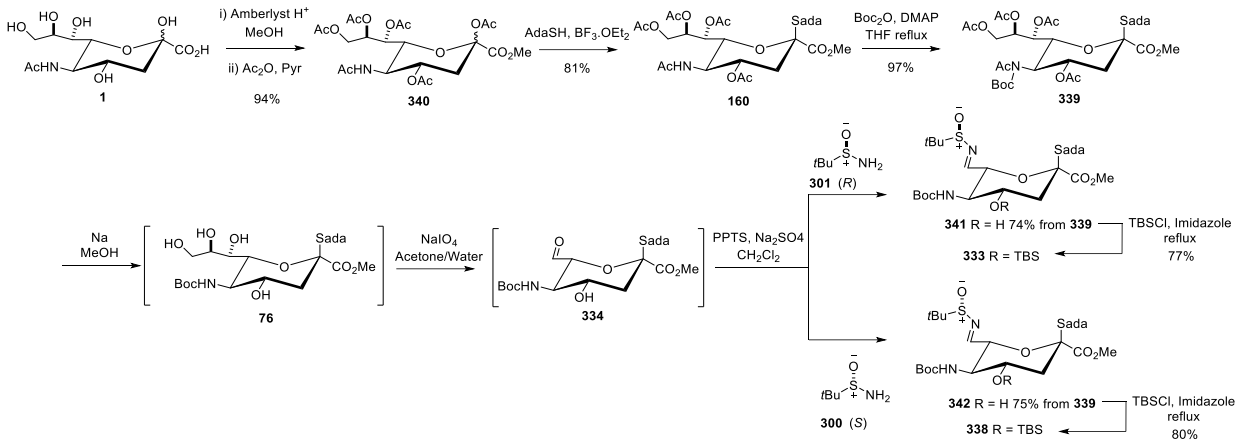
Syntheses of legionaminic acid and acetaminic acid glycosyl donors from *N*-acetylneuraminic acid were designed based on the chiral *N*-sulfinyl imines by developed samarium iodide-mediated aza-pinacol reaction with acetaldehyde (Scheme 61). According to this scheme, legionaminic acid and acetaminic acid donors could be obtained from the aza-pinacol adduct by straightforward one pot deprotection of the Boc, sulfinamide and TBS groups followed by benzoyl protection of the diol. Following on from the model study it was apparent that the (*R*)-*N*-sulfinyl imine **333** would give the legionaminic acid configuration of the side chain, while the (*S*)-*N*-sulfinyl imine **338** would give the acetaminic acid configuration. The common aldehyde intermediate **334** was considered accessible from the 5-*N*-Boc tetraacetyl glycoside **339**, which was reported in Crich's previous Leg synthesis form *N*-acetylneuraminic acid **1**.



Scheme 61. Strategic disconnections for legionaminic acid, and acetaminic acid glycosyl donors.

2.2.7.1 Synthesis of chiral *N*-sulfinyl imines

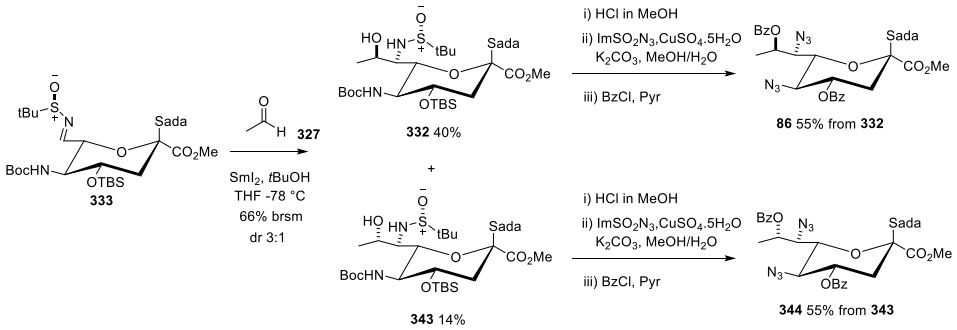
The 5-*N*-Boc tetraacetyl glycoside **339** was synthesized from NeuAc **1** by a three-step literature protocol in 74% overall yield.[120, 144] In order to cleave the side chain, this fully protected glycoside was deacetylated by treatment with sodium in methanol to give tetraol **76**. The immediate oxidative cleavage of **76** with sodium metaperiodate in aqueous acetone afforded the common precursor aldehyde **334**, which was immediately condensed with the two enantiomers of the Ellman sulfinamide in the presence of PPTS and Na_2SO_4 in dichloromethane (Scheme 62). The (*R*)-enantiomer **301** of the auxiliary gave (*R*)-*N*-sulfinyl imine **341** in 74% yield after three steps, whose remaining secondary alcohol was silylated with TBSCl and imidazole in hot THF to obtain protected imine **333** in 77% yield. The other enantiomer of the auxiliary gave (*S*)-*N*-sulfinyl imine **342** in 75% yield after three steps, and silylation of its 4-hydroxy groups provided protected imine **338** in 80% yield.



Scheme 62. Synthesis of (*R*)- and (*S*)-*N*-sulfinyl imines.

2.2.7.2 Synthesis of a legionaminic acid donor and an 8-*epi*-legionaminic acid donor

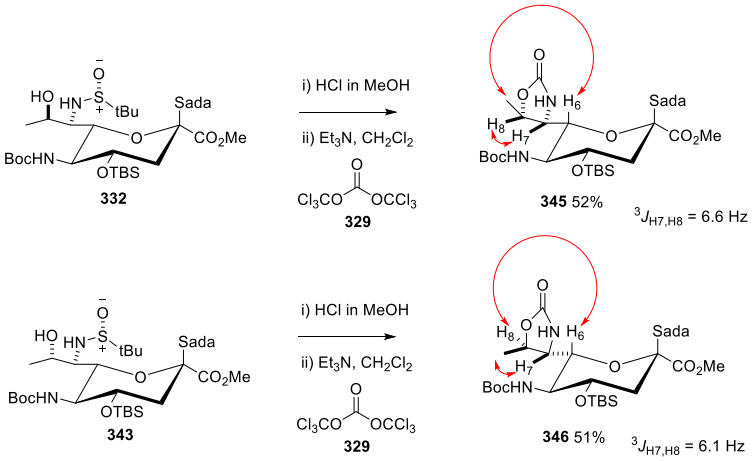
The samarium iodide-mediated aza-pinacol cross coupling reaction of imine **333** with acetaldehyde generated the diastereomeric α-hydroxy sulfinamides **332** and **343** in 54% overall yield, and 3:1 selectivity. After separation of the diastereomers, treatment of the less polar D-glycero-D-galacto **332** isomer with methanolic HCl followed by exposure to Stick's reagent and then standard benzoylation conditions afforded the target Leg donor **86** in 55% yield for the three steps, with spectral data identical to that from the previous Crich group synthesis (Scheme 63). Analogous treatment of the more polar L-glycero-D-galacto **343** isomer gave 8-*epi*-legionaminic acid donor **344** in 55% yield for the three steps (Scheme 63).



Scheme 63. Synthesis of legionaminic acid donor **86** and 8-*epi*-legionaminic acid donor **344**.

2.2.7.3 Assignment of relative configuration in aza-pinacol adducts

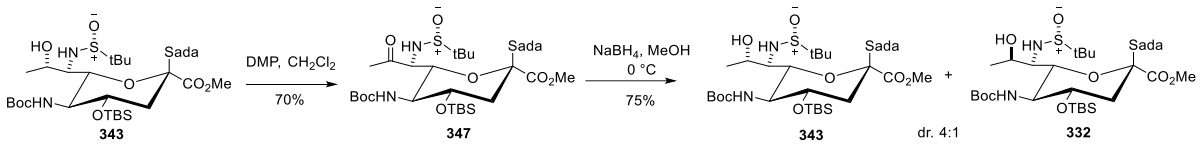
The relative configuration of both adducts **332** and **343** was determined by conversion to the corresponding 8-*O*-7-*N*-oxazolidinones. Selective cleavage of the TBS and sulfinamide groups in the less polar isomer **332** gave the 7-amino glycoside, which was treated with triphosgene in the presence of triethylamine in dichloromethane to afford oxazolidinone **345** in 52% yield. This compound showed NOE interactions between the terminal methyl group and H6, and between H7 and H8, and had a 6.6 Hz $^{3}J_{H7,H8}$ coupling constant, proving the *anti*-configuration at C7-C8 (Scheme 64). The polar isomer **343** provided the oxazolidinone **346** in 51% yield under the same conditions: it was displayed NOE interactions between the terminal methyl group and H7, and between H6 and H8 and had a 6.1 Hz $^{3}J_{H7,H8}$ coupling constant, showing the C7-C8 configuration to be *syn* (Scheme 64).



Scheme 64. Assignment of relative configuration in aza-pinacol adducts **332** and **343**.

2.2.7.4 Attempted conversion of the L-glycero-D-galacto adduct to its D-glycero-D-galacto counterpart

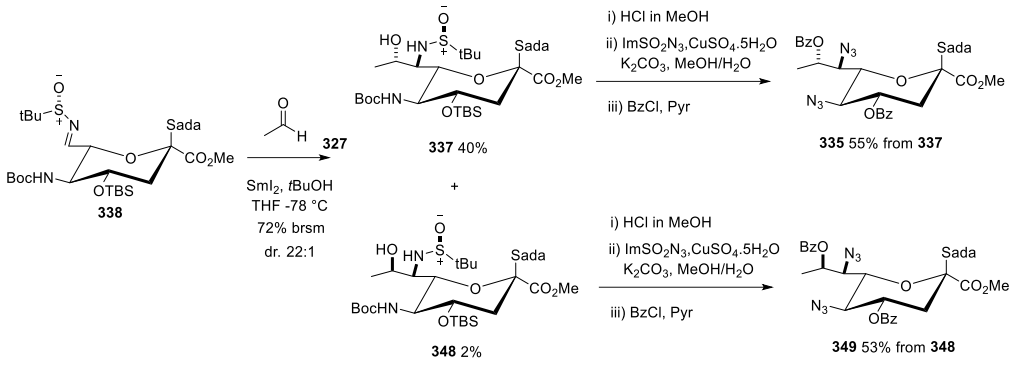
In an attempt to transform the minor adduct **343** to the D-glycero-D-galacto isomer **332**, Dess-Martin oxidation of **343** was conducted and gave ketone glycoside **347** in 70% yield. Subsequent reduction with sodium borohydride at 0 °C afforded L-glycero-D-galacto **332** and D-glycero-D-galacto **343** in 75% yield as a 1:4 mixture (Scheme 65).



Scheme 65. Attempted conversion of minor isomer **343** to major isomer **332**.

2.2.7.5 Synthesis of an acetaminic acid donor and an 8-*epi*-acetaminic acid donor

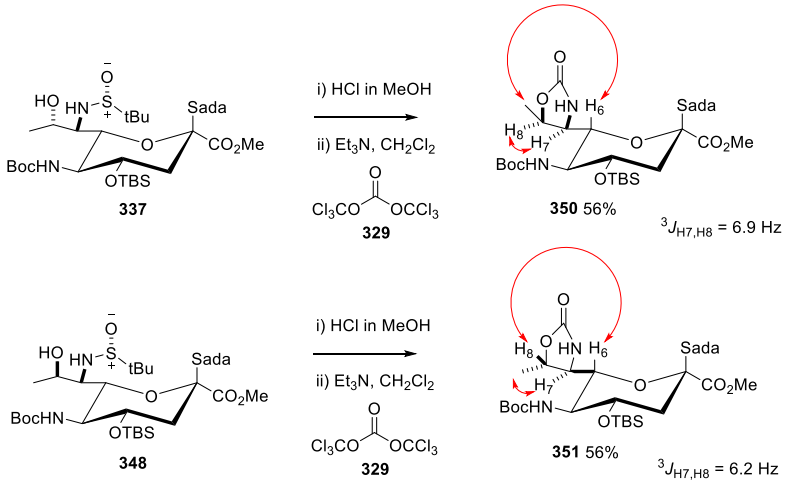
Samarium iodide-mediated cross coupling of imine **338** with acetaldehyde afforded the hydroxy sulfinamides **337** and **348** in 58% combined yield and 22:1 selectivity. Processing the of polar isomer **337** by exposure to methanolic HCl, followed by treatment with Stick's reagent and finally benzoylation gave the acetaminic acid donor **335** with the L-glycero-L-altro configuration in 55% yield (Scheme 66). An analogous sequence of reactions was applied to the less polar isomer **348** and gave the D-glycero-L-altro-configured 8-*epi*-acetaminic acid donor **349** in 53% yield (Scheme 66).



Scheme 66. Synthesis of acetaminic acid donor **335** and 8-*epi*-acetaminic acid donor **349**.

2.2.7.6 Assignment of relative configuration in coupled adducts 337 and 348

Similarly to the Leg synthesis, after selective cleavages of the TBS and Boc groups from isomer **337**, treatment with triphosgene afforded oxazolidinone **350** in 56% yield. This displayed a 6.9 Hz $^{3}J_{H7,H8}$ coupling constant and NOE interactions between the terminal methyl group and H6 and, and between H7 and H8, which proves *anti*-configuration in the side chain (Scheme 67). The oxazolidinone **351** was afforded in 56% from the less polar isomer **348**. It had showed NOE interactions between the terminal methyl group and H7 and, and between H6 and H8, and a 6.2 Hz $^{3}J_{H7,H8}$ coupling constant, establishing the *syn*-configured side chain (Scheme 67).

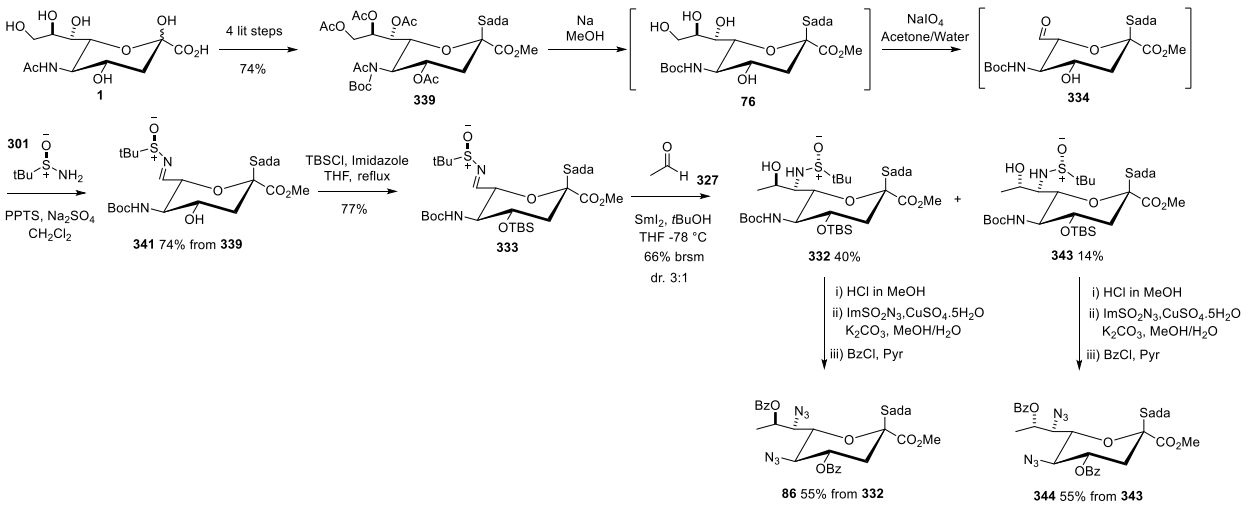


Scheme 67. Assignment of relative configuration in coupled adducts **337** and **348**.

2.2.8 Selectivities in the samarium iodide-mediated aza-pinacol coupling

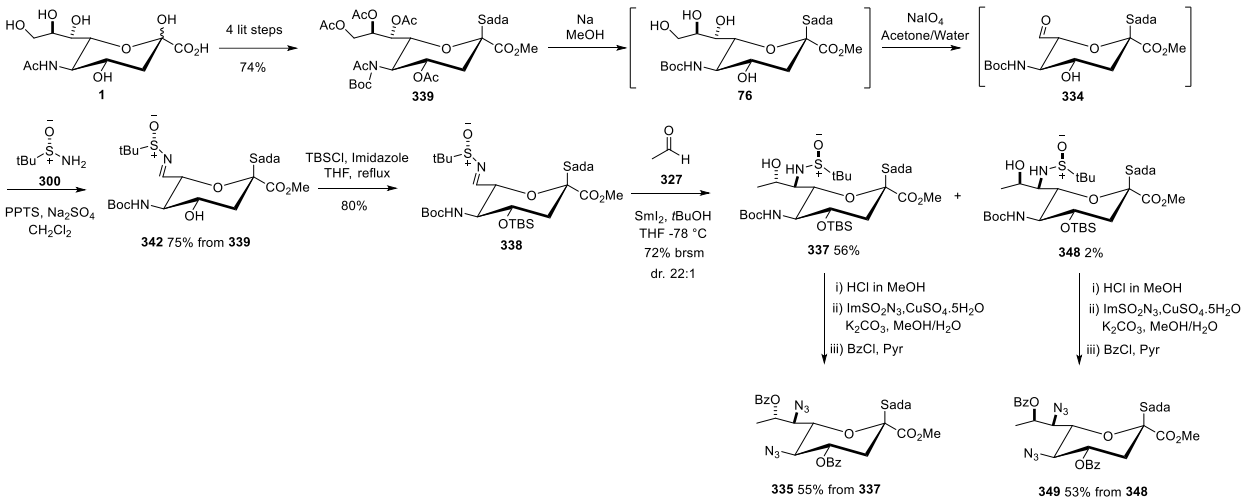
The isomeric sulfinamides derived from the (*R*)- and (*S*)- isomers of the Ellman auxiliary exhibited very different selectivities in the samarium iodide-mediated coupling: imine **333** with the (*R*)-configuration at sulfur provided a 3:1 mixture (Scheme 63) while (*S*)-configured **338** gave a 22:1 ratio (Scheme 66). In both cases the imines exhibited complete stereocontrol at C7 due to the high degree of facial discrimination by the adjacent chiral auxiliary. Less control was observed at the aldehyde-derived C8 for the (*R*)-configured auxiliary. The lower degree of asymmetric induction at the 8-position in the preference of the (*R*)-auxiliary probably arises from a mismatch between the (*R*)-auxiliary and the chirality of the pyranoside ring at C6.

Overall, a practical synthesis of the Leg donor **86** was achieved in 12 steps and 18% overall yield starting from *N*-acetylneuraminic acid **1**, which is shorter than Crich's previous synthesis. This synthetic pathway also provided the novel 8-*epi*-Leg donor **344** in 4% yield overall. The complete synthesis of Leg and 8-*epi*-Leg donors from NeuAc is summarized in Scheme 68.



Scheme 68. Total syntheses of Leg donor **86** and 8-*epi*-Leg donor **344**.

In addition to the target Leg synthesis, a total synthesis of the novel acetaminic acid donor **335** was developed in 17% overall yield, and one of the 8-*epi*-acetaminic acid donor **349** in 1% overall yield from NeuAc in 12 steps. The total syntheses of the acetaminic acid donor and the 8-*epi*-acetaminic acid donor from NeuAc are summarized in Scheme 69.

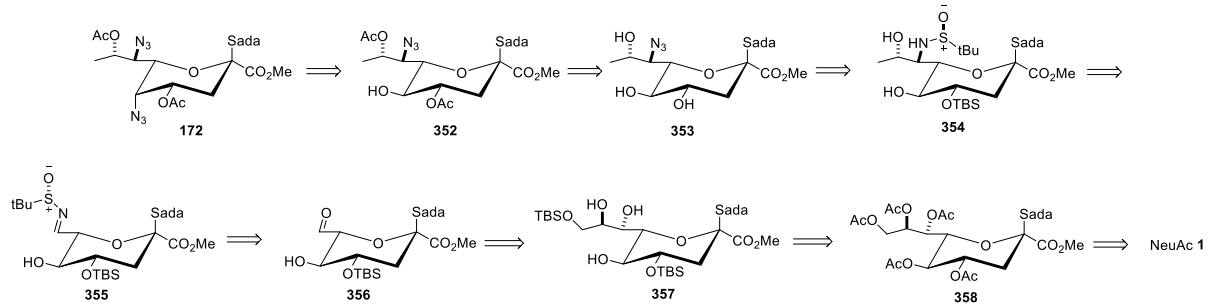


Scheme 69. Total syntheses of acetaminic acid donor **335** and 8-*epi*-acetaminic acid donor **349**.

2.2.9 Synthesis of a pseudaminic acid donor

Based on the selectivities observed in Leg and acetaminic acid donor syntheses employing the samarium iodide-mediated aza-pinacol coupling reaction, the synthesis of Pse donor **172** was designed via an (*S*)-*N*-sulfinyl imine intermediate. It was envisaged that late-stage inversion of C5 would be afforded by triflate displacement after regioselective acetylation of the 4- and 8-hydroxy groups. Cross-coupling of the (*S*)-*N*-sulfinyl imine with acetaldehyde was expected to install the side chain, and the conversion of a 7-amino group to the corresponding azide is possible by treatment with Stick's reagent. The (*S*)-configured imine **355** could be obtained from di-silylated derivative **357**, which should be available by regioselective silylation of deprotected deaminated intermediate **358**. The synthesis of the deaminated pentaacetate **358** is straightforward

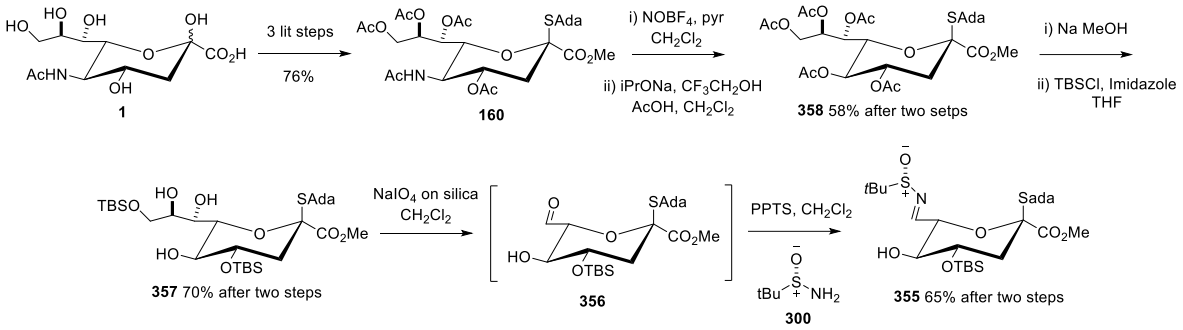
and requires 5 steps from NeuAc **1** following a protocol developed in Crich lab. The outlined strategic disconnections for Pse donor **172** are summarized in Scheme 70.



Scheme 70. Strategic disconnections for Pse donor **172**.

2.2.9.1 Synthesis of (*S*)-*N*-sulfinyl imine 355

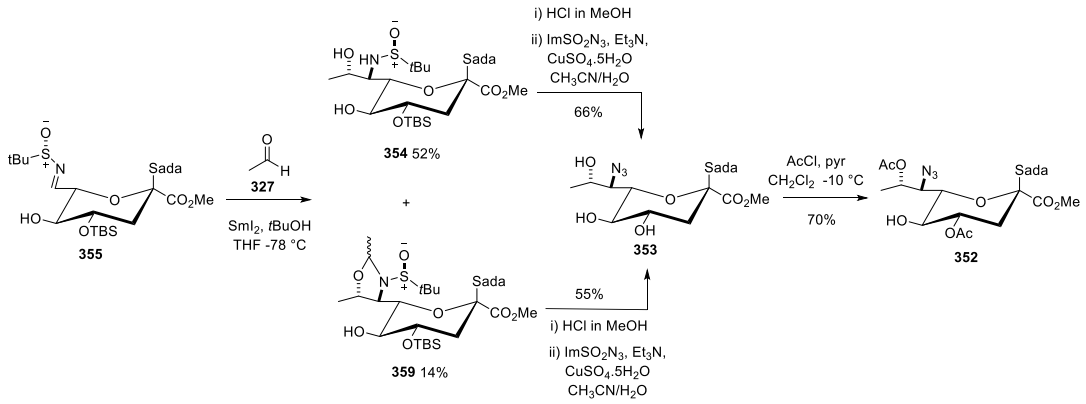
The acetamido derivative **160** was obtained from the NeuAc **1** according to the literature protocol in 76% overall yield.[144] The conversion of the C-N to a C-O bond at C5 was achieved by a well-developed deamination protocol in the Crich lab giving the pentaacetate **358** in 58% yield.[145] This fully protected glycoside was then deacetylated with sodium methoxide to afford a pentaol, which was immediately subjected to controlled regioselective silylation[146, 147] with TBSCl in the presence of imidazole in THF to provide **357** in 70% yield. The oxidative cleavage of the side chain with sodium periodate on silica furnished the aldehyde **356** that was immediately condensed with the (*S*)-enantiomer **300** of the Ellman sulfinamide to give imine **355** in 65% yield (Scheme 71).



Scheme 71. Synthesis of (*S*)-*N*-sulfinyl imine **355**.

2.2.9.2 Synthesis of 4,8-*O*-di-acetyl glycoside 352

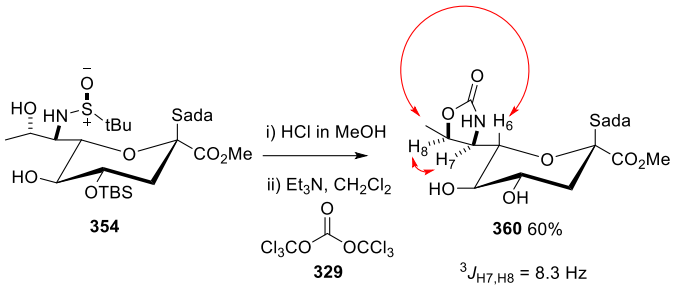
Treatment of imine **355** with acetaldehyde under the samarium iodide-mediated coupling conditions in the presence of *t*-butanol at -78 °C afforded the adduct **354** as a single diastereomer in 52% yield along with aminal **359** in 14% yield. This extreme selectivity is consistent with the formation **337** of from **338**, in which the influence of the (*S*)-auxiliary and the pyranoside side are matched. The adduct **354** was then treated with methanolic HCl followed by Stick's reagent to give the azide **353** in 66% yield. The aminal **359** was also converted into azide **353** in 55% yield, which confirmed the configuration of **359**. Regioselective acetylation of **353** with acetyl chloride and pyridine in cold dichloromethane gave **352** in 70% yield (Scheme 72).



Scheme 72. Synthesis of 4,8-*O*-di-acetyl glycoside **352**.

2.2.9.3 Assignment of the relative configuration of adduct 354

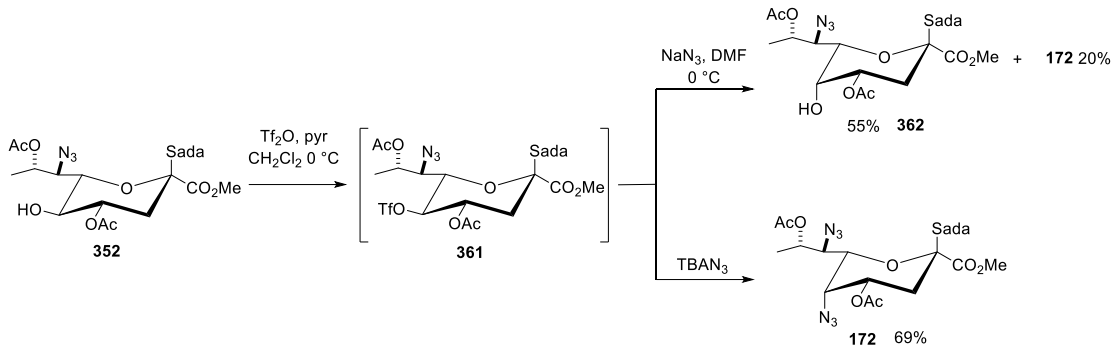
The relative configuration of the side chain in aza-pinacol adduct **354** was determined by transformation to the oxazolidinone derivative **360** in 60% yield, which displayed a 8.3 Hz $^{3}J_{H7,H8}$ coupling constant, and NOE interactions between the terminal methyl group and H6 and, between H7 and H8, proving the *anti*-configuration (Scheme 73).



Scheme 73. Assignment of relative configuration in adduct **360**.

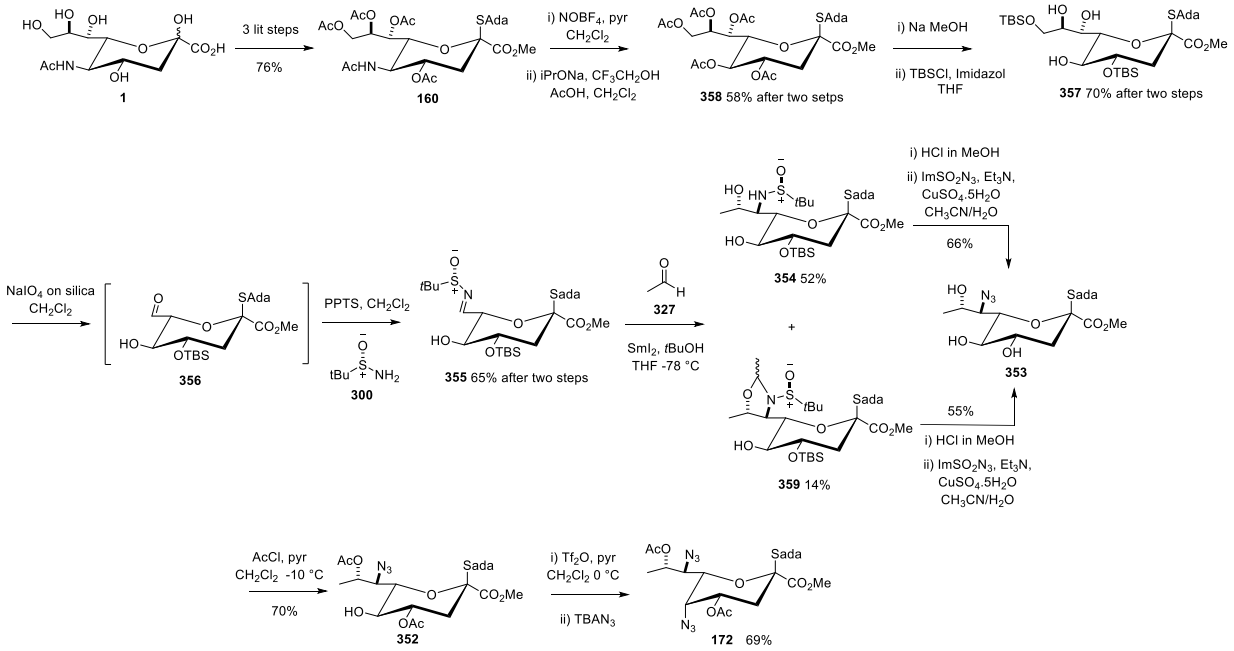
2.2.9.4 Synthesis of the 5,7-diazido Pse donor 172

The conversion of the free alcohol in **352** to the azide with inversion of configuration was attempted via displacement of the derived triflate with sodium azide in DMF. A similar S_N2 displacement at C5 was reported in Crich's previous Pse synthesis[109] and in Kiefel's synthesis[105]. However, employing the previous reported conditions resulted in formation of the inverted alcohol **362** in 55% yield along with the target Pse donor **172** in only 20% yield. Conversion of the triflate **361** to alcohol **362** was observed by TLC on simple heating. Therefore, a cold solution of tetrabutylammonium azide was added to the crude triflate finally affording Pse donor **172** in 69% yield (Scheme 74).



Scheme 74. Synthesis of the 5,7-diazido Pse donor **172**.

Overall, a practical synthesis of the Pse donor **172** was developed in 15 steps from NeuAc **1** in 4% overall yield, which is shorter than the previous synthesis. This new total synthesis of the Pse donor from *N*-acetylneuraminic acid is summarized in Scheme 75.



Scheme 75. Total synthesis of the Pse donor **172**.

2.2.10 Side chain conformation of the synthesized donors

The previously synthesized Leg **86** and Pse **172** donors have predominant *gauche,gauche* (*gg*) and *trans,gauche* (*tg*) conformations respectively of the C6-C7 bond as apparent from their $^{3}J_{H6,H7}$ coupling constants of 1.8 and 9.8 Hz (Figure 14) according to previous analyses. Small $^{3}J_{H6,H7}$ coupling constants (1.5-2.1 Hz) were observed for 8-*epi*-Leg donor **344**, acetaminic acid donor **335** and 8-*epi*-acetaminic acid donor **349**, indicating the *gauche* orientation of H-6 and H-7 (Figure 14). Therefore, the L-glycero-D-galacto donor **344** has the *gg* conformation of its side chain, while the D-glycero-L-altro **335** and L-glycero-L-altro **349** donors have the predominant *gt* conformation. These conformations are consistent with Tsvetko's analysis[104] of side chain conformation in *O*-acetylated derivatives of Leg, 8-*epi*-Leg, acetaminic and 8-*epi*- acetaminic acid derivatives.

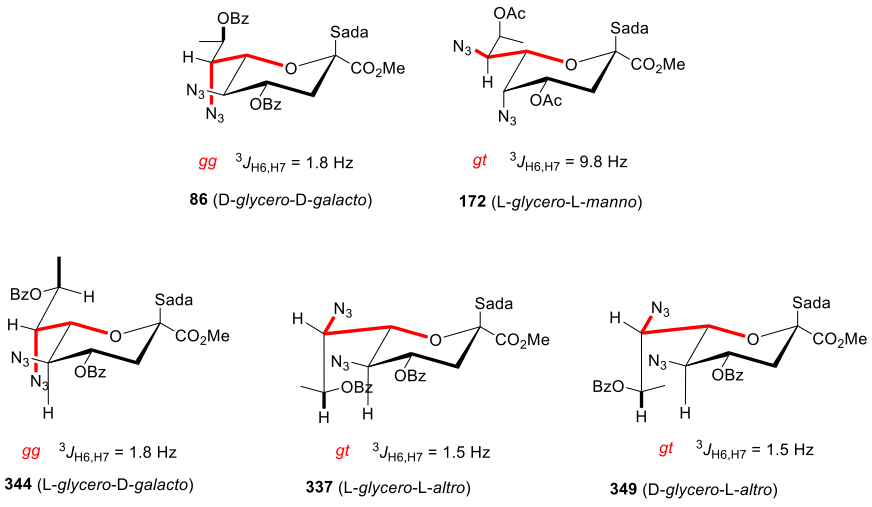


Figure 14. Side chain in the synthesized donors.

2.3 Conclusion

In conclusion, effective syntheses of Leg, 8-*epi*-Leg, acetaminic and 8-*epi*-acetaminic thioglycoside donors were developed from NeuAc in 12 steps, and as well as one of a Pse thioglycoside donor in 15 steps. This approach to bacterial sialoside donors trims multiple steps from Crich's previous syntheses of both Leg and Pse donors.

CHAPTER THREE

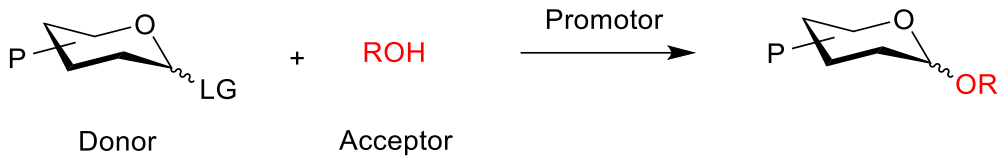
INFLUENCE OF SIDE CHAIN CONFORMATION IN GLYCOSYLATION

3.1 Importance of oligosaccharide synthesis

Oligosaccharides are recognized as an important class of biomolecules due to their essential biological roles. However, oligosaccharides occur in nature heterogeneous mixtures from which it is hard to purify sufficient quantities for biological research. The chemical synthesis of oligosaccharides is one way to overcome this problem and obtain enough homogeneous material to support biological research. In addition, the chemical synthesis of oligosaccharides allows to produce both natural and unnatural oligosaccharides and is not limited by the availability of specific enzymes. The chemical method of forming a glycosidic bond is termed chemical glycosylation.

3.2 Chemical glycosylation

A chemical glycosylation reaction involves two reactants, named the glycosyl donor and acceptor, which are coupled to form a glycosidic bond (Scheme 76). The coupling process involves displacement of a leaving group from the anomeric sp^3 carbon of the glycosyl donor by an incoming acceptor nucleophile with the formation of a new carbon-heteroatom bond.[148]



Scheme 76. General glycosylation reaction.

3.2.1 Mechanism of glycosylation

Glycosylation reactions can be considered as a subset of nucleophilic displacement at sp^3 carbon atom. The glycosyl donor, which can exist either in one or both of two possible anomeric configurations, is activated by a promotor to the form either an axial or equatorial activated intermediate, which then equilibrates with its tightly associated ion pairs (contact ion pair - CIP), and then with more loosely associated ion pairs (solvent separated ion pair - SSIP) (Figure 15).[149, 150] The axial intermediate and its CIP favor the formation of the equatorial glycoside via an S_N2-like pathway, while the corresponding equatorial intermediates favor the formation of the axial glycoside (Figure 15), and the loosely associated ion pair (SSIP) provides both glycosides via S_N1-like pathway.[150] The location of a particular reaction on the spectrum of covalent intermediates and ion pairs is influenced by factors such as substituent effects, leaving group, temperature, activator, and solvent.[151-153] The ion pair concept was first introduced for the chemical glycosylation mechanism by Rhind-Tutt[149] and Vernon, with subsequent contributions from Lemieux and coworkers who modified it to a more graphical form[154-156].

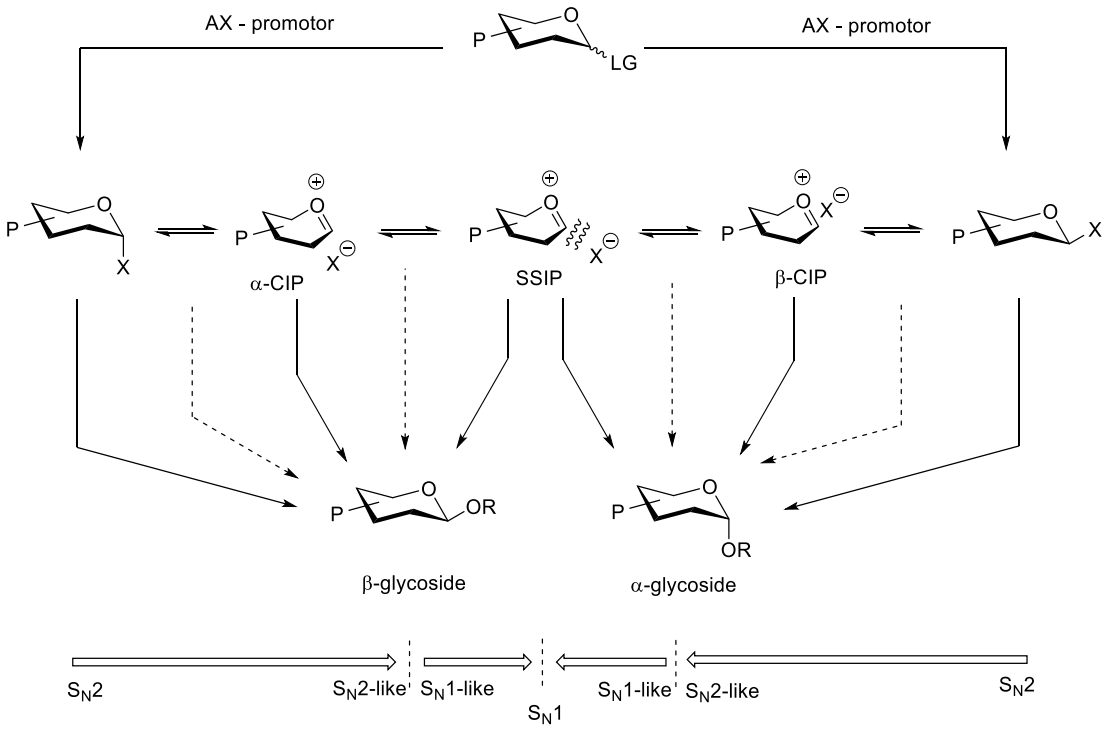


Figure 15. S_N1-S_N2 Continuum for the ion pair mechanism of glycosylation reactions.

3.3 Role of side chain conformation in stereo-controlled glycosylation

The side chain of the hexopyranoses can be described as an equilibrium mixture of three staggered conformations: *gauche*,*gauche* (*gg*), *gauche*,*trans* (*gt*), and *trans*,*gauche* (*tg*) conformers (Figure 16) according to the relationship of the C6-O6 bond to the C5-C4 and C5-O5 bonds.[157-159] Experimentally it is found that the three staggered conformations for the glucose series are populated in an approximate ratio of 6:4:0, *gg*:*gt*:*tg*, whereas the galactose series has an approximate population ratio of 2:6:2, *gg*:*gt*:*tg*, with only slight variations in different solvent systems (Figure 16).

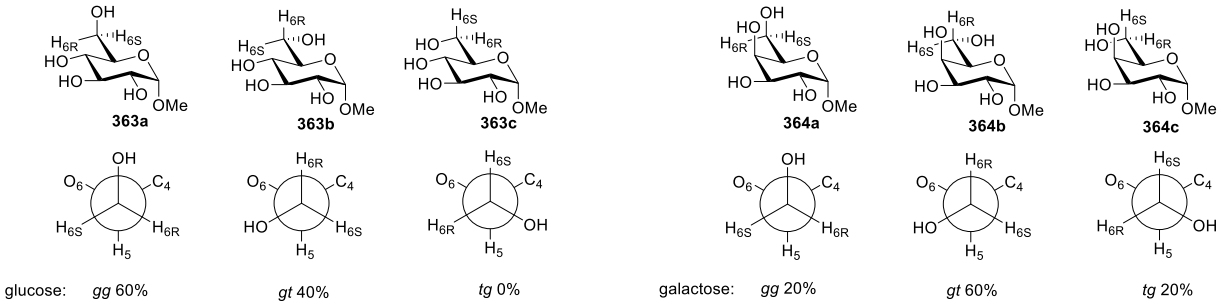


Figure 16. The staggered conformations of the side chains of gluco and galactopyranose.

3.3.1 4,6-*O*-Benzyledine-protected mannosyl donors

Crich and coworkers reported that 4,6-*O*-benzylidene-protected mannosyl sulfoxide donor **365** in dichloromethane at −78 °C, with pre-activation with triflic anhydride prior to addition of an acceptor, displayed excellent equatorial selectivities compared to 4,6-di-*O*-benzyl mannosyl sulfoxide donor **366** (Figure 17).[160, 161] This is consistent with the disarming effect of a 4,6-*O*-benzylidene acetal noted by Fraser-Reid,[162] leading the Crich group to reason that the presence of the disarming 4,6-*O*-benzylidene group, favors formation of a covalently bonded axial triflate intermediate, which is displaced by an acceptor from the equatorial face leading to the formation of equatorial glycosides.[163]

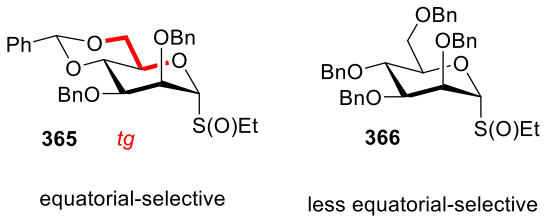
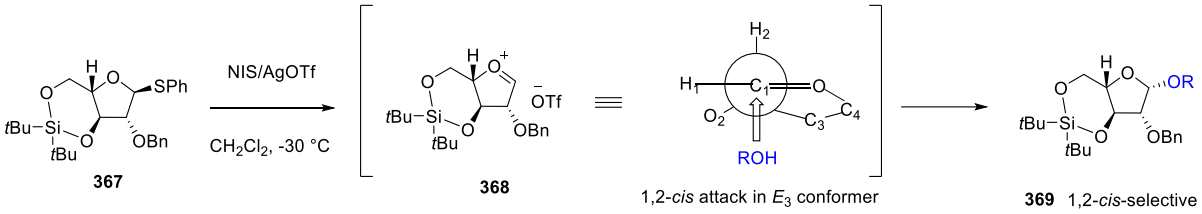


Figure 17. 4,6-*O*-Benzyledine-protected mannosyl sulfoxide donor **365** and 4,6-di-*O*-benzyl mannosyl sulfoxide donor **366**.

3.3.2 3,5-*O*-Di-*tert*-butylsilylene-protected arabino furanosyl donors

The coupling reactions of 3,5-*O*-di-*tert*-butylsilylene-protected arabinofuranosyl thioglycoside donor **367** showed 1,2-*cis* selectivity. Boons and coworkers explained this by invoking 1,2-*cis*-face attack on an arabinofuranosyl oxacarbenium ion intermediate favoring the E_3 conformer to minimize interaction with the incoming acceptor (Scheme 77).[164] However, in an investigation of intermediates by variable-temperature NMR spectroscopy, Crich and coworkers observed formation of the stable arabinofuranosyl 1,2-*trans* triflate at low temperature, leading them suggest that the displacement of triflate by an acceptor from the 1,2-*cis* face favored the formation of 1,2-*cis*-glycosides in donors **370** and **371**.[165] The cyclic silylene acetal adpots the ideal chair conformation, and the five-membered takes up a ^3E envelop conformation. Thus, the C5-O5 bond is oriented antiperiplanar to the C4-O4, bond, which is similar to benzylidene-protected mannosyl sulfoxides.



Scheme 77. Boons's explanation of 1,2-*cis* selectivity in donor **367**.

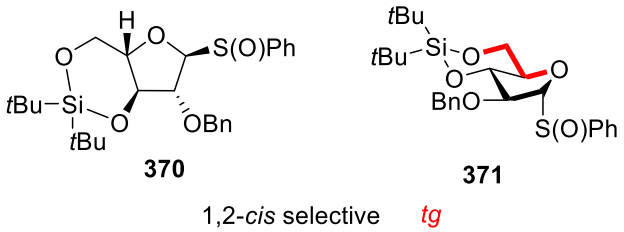
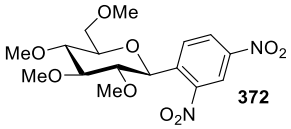
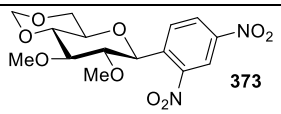
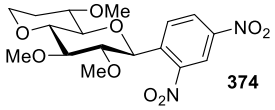
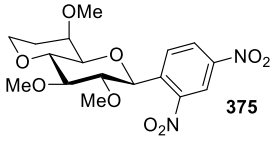


Figure 18. 3,5-*O*-Di-*tert*-butylsilylene-protected arabino furanosyl donors **370** and **371**.

3.3.3 Probing the influence of the side chain conformation

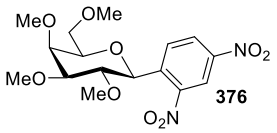
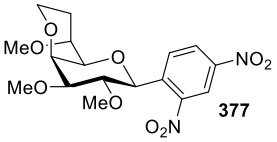
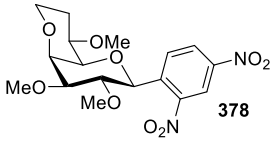
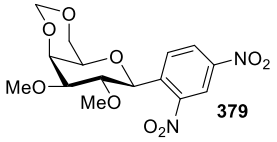
The influence of C-O bonds on the anomeric reactivity of glycosyl donors was highlighted in the work of Bols and coworkers.[166] This study demonstrated that the restriction free monocyclic derivative **372** was hydrolyzed faster than conformationally restricted analogues locked in the *gg* and *gt* conformations, which nevertheless showed 0.3 and 0.4 times more reactivity than the *tg* conformer, respectively (Table 10).[166] According to Bols, the torsional disarming effect, as well as the imposition of the *tg* conformation on the glucopyranosyl side chain by 4,6-*O*-acetal, results in the less reactive nature of **373**. Due to the imposition of the *tg* conformation in **373**, the electron-withdrawing effect of the C6−O6 bond is maximized and destabilizes the formation of the CIP and SSIP.[166]

Table 10. Relative hydrolysis rates of glucopyranosides as examined by Bols and co-workers.

Compound	Relative hydrolysis rate	O5-C5-C6-O6 Conformation
 **372**	1	-
 **373**	0.07	*tg*
 **374**	0.16	*gt*
 **375**	0.24	*gg*

Another study on the influence of C−O bonds on the anomeric reactivity of glycosyl donors was carried out by Crich group who conducted experiments to determine the relative rates of hydrolysis of methyl or dinitrophenyl galactopyranosides under acidic conditions (Table 11).[167] This study revealed that the bicyclic dinitrophenyl galactopyranosides were less reactive in comparison to the monocyclic derivative **376**. The compound **377** with the enforced *tg* conformation was the least reactive consistent with Bols observations in the glucose series.

Table 11. Relative hydrolysis rates of galactopyranosides as examined by Crich and coworkers.

Compound	Relative hydrolysis rate	O5-C5-C6-O6 Conformation
 **376**	1	-
 **377**	0.17	*tg*
 **378**	0.23	*gt*
 **379**	0.43	*gg*

The above observations from the Bols and Crich groups were rationalized based on the interaction of O6 electron density and the π* orbital of the oxocarbenium ion.[168] Hence, the *gg* conformation can stabilize the oxocarbenium ion by through-space donation of O6 electron density

into the π* orbital of the C1-O5. The *gt*-conformation can only stabilize oxocarbenium ion through electrostatic interaction to the π-system of any anomeric oxocarbenium ion due to the inappropriate location of the C6−O bond for interaction with the π* orbital (Figure 19), and so is less reactive than the *gg* conformation.[168] The most electron-withdrawing *tg* conformation destabilizes the formation of the oxocarbenium ion and was the least reactive of the model compounds.

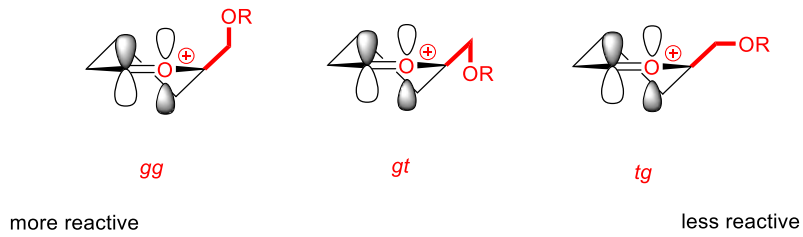


Figure 19. Orientations of the C6-O6 bond in the hexosyl-oxocarbenium ions and their relative reactivity.

3.4 Influence of side chain conformation in sialosides

To further understand the relationship of the side chain configuration and conformation to the reactivity and selectivity in glycosylation, various modified sialic acid donors were synthesized and studied by the Crich group.

The Crich group demonstrated that a change in the configuration at C7 in the O4,N5-oxazolidinone thioglycoside donor **380** to the 7-*epi*-isomer **381** resulted in a change in the conformation of the side chain from *gg* to *gt* (Figure 20).[169] The donor **381** was less reactive than **380** such that higher temperatures had to be used to activate **381** and led to lower selectivities.[169] That is, the isomer with gt conformation of the side chain was less reactive.

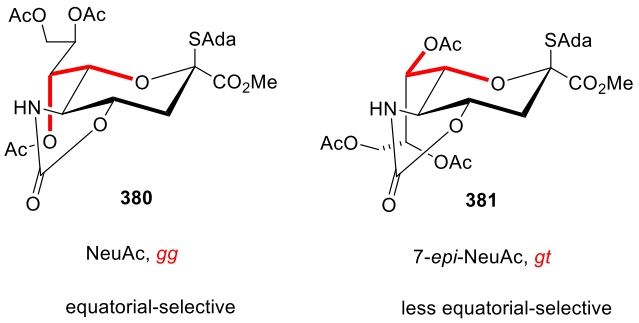


Figure 20. NeuAc and 7-*epi*-NeuAc donors.

Subsequently it was demonstrated that the 5-*epi*-NeuAc donor **383**, with the predominant *gt* conformation of the side chain displayed increased equatorial selectivity than NeuAc donor **382** with *gg* conformation of the side chain in coupling reactions (Figure 21).[170]

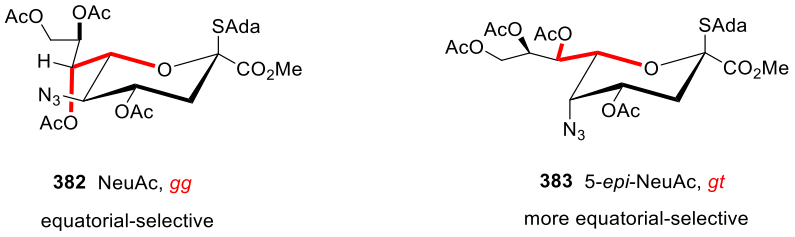


Figure 21. NeuAc donor **382** and 5-*epi*-NeuAc donor **383**.

This lead to the development of the Pse donor **172** (5,7,8-tri-*epi* NeuAc config), with the predominant *tg* conformation (Figure 22) of its side chain and excellent equatorial-selectivity.[109]

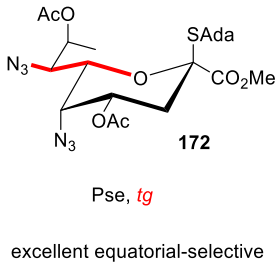
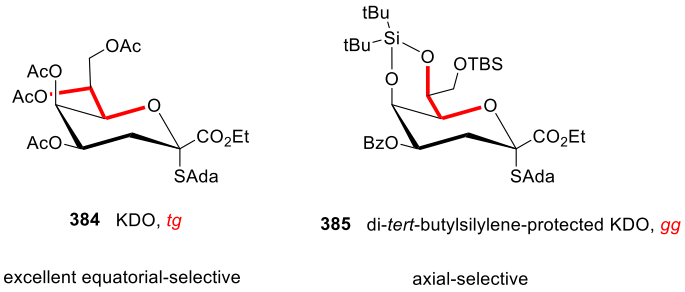


Figure 22. Pse donor **172**.

The 3-deoxy-D-manno-oct-2-ulosonic acid (KDO) **383** (Figure 23), which is pseudoenantiomeric to Pse **172**, also had the *tg* conformation of its side chain and displayed excellent equatorial-selectivity in the coupling reactions.[171] However, the di-*tert*-butylsilylene-protected KDO donor **385** (Figure 23) locked in the *gg* conformation, showed opposite selectivity and provided predominantly the axial glycosides.



384 KDO, *tg*

excellent equatorial-selective

385 di-*tert*-butylsilylene-protected KDO, *gg*

axial-selective

Figure 23. KDO donors.

3.5 Influence of the side chain conformation in 7-Deoxyheptopyranosyl donors

To further understand the role of side chain conformation in simple monocyclic pyranose systems the Crich group turned to a series of simple 6-methyl hexopyranosyl donors.

The D-glycero-D-galacto configured donor **386** with the predominant *tg* conformation (Figure 24) showed excellent selectivity for the formation of the equatorial glycoside in the glycosylation reactions.[172] The epimeric L-glycero-D-galacto donor **387** with the *gt* conformation, was less equatorially selective.[172]

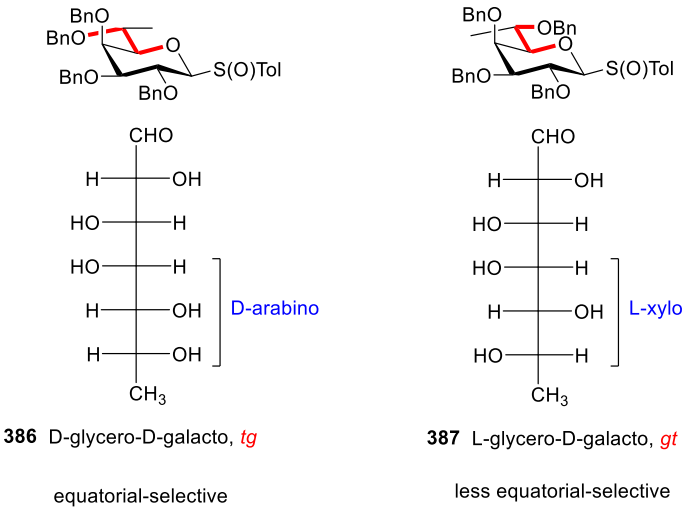


Figure 24. D-glycero-D-galacto donor **386** and L-glycero-D-galacto donor **387**.

Low-temperature NMR studies of these two donors revealed that the D-glycero-D-galacto donor **386** favored the formation an axial-triflate intermediate **388** upon activation at -80 °C that was stable up to -20 °C, while the epimeric L-glycero-D-galacto axial-triflate **389** decomposed by -70 °C (Figure 25).[172] Therefore, the disarming *tg* side-chain conformation promoted a more S_N2-like displacement of the triflate leading greater equatorial selectivity.

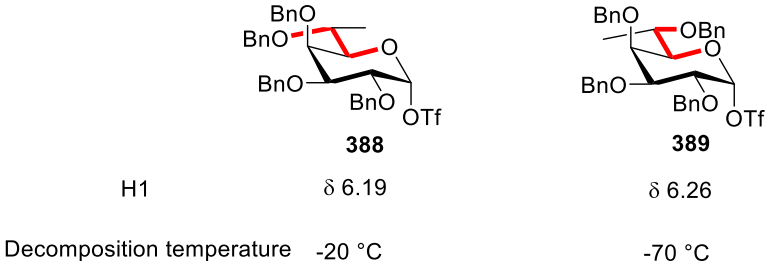


Figure 25. Triflate intermediates from D-glycero-D-galacto **386** and L-glycero-D-galacto **387** donors.

The coupling reactions of L-glycero-D-gluco donor **390** with the predominant *gg* conformation of its side chain (Figure 26) surprisingly displayed high selectivity for the formation

of equatorial glycosides.[172] The epimeric D-glycero-D-gluco donor **391**, with the *gt* conformation of its side chain, had little to no selectivity in its coupling reaction under the same conditions.

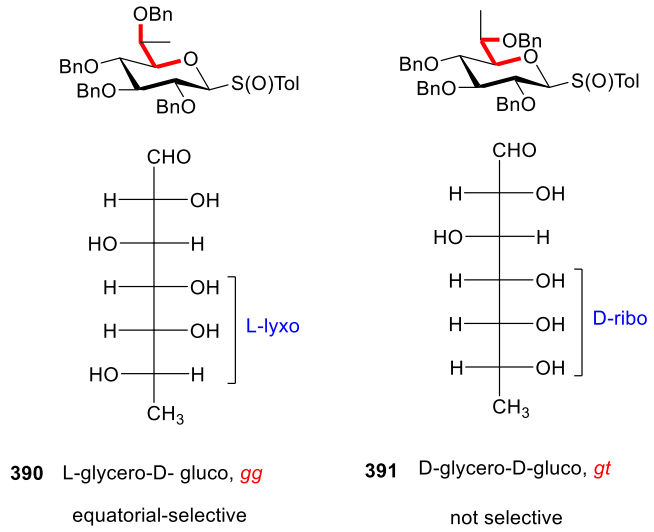


Figure 26. D-glycero-D-gluco donor **391** and L-glycero-D- gluco donor **390**.

The unexpected equatorial selectivity of **390** was reasoned in terms of stereodirecting donor−acceptor hydrogen bonding in the L-glycero-D-gluco isomer **390** with O6 of the donor serving as a H-bond acceptor.[172] VT-NMR analysis of the triflate intermediates from these two donors showed little difference in stability (Figure 27).

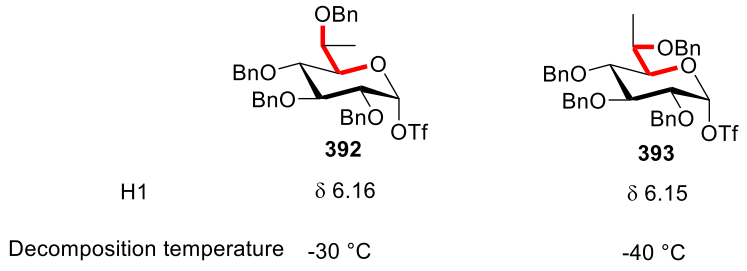


Figure 27. Triflate intermediates from D-glycero-D-gluco **391** and L-glycero-D-gluco **390** donors.

3.6 Goal

As discussed above, side chain configuration and conformation have significant influence on the rate and selectivity of glycosylation reactions, and the Crich group demonstrated that this influence was not limited to constrained bicyclic donors by studying isomers in the sialic acid series and simple 6-methyl pyranosyl donors. The goal of this project was to extend these studies to furanosyl donors and to determine if the conformations of hexofuranosyl side chains could be analogously predicted and their reactivity influenced by side chain conformation. A series of four 6-deoxy hexofuranosyl donors **394-397** were designed and their side chain conformations predicted by extension of the rules developed in the heptopyranose series (Figure 28).[173] The subsequent chapter describes the synthesis, conformational analysis, VT-NMR, and selectivities of these donors.

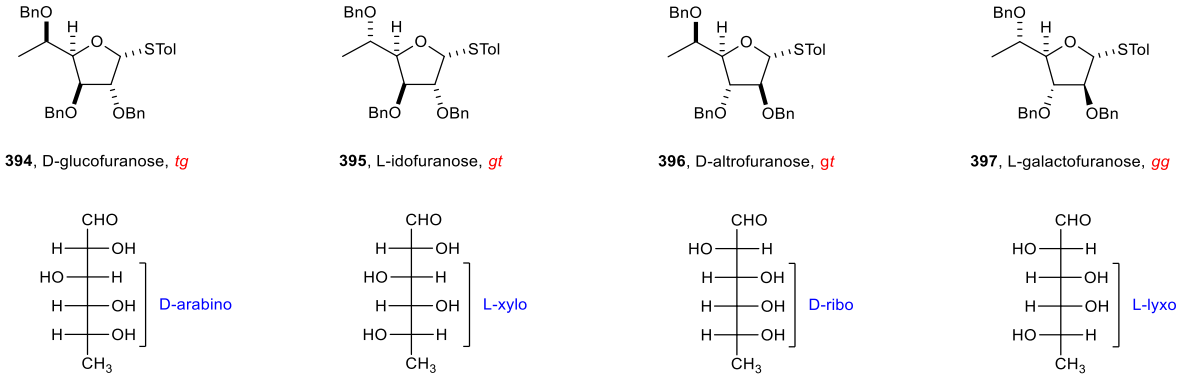


Figure 28. Thiofuranosides targeted for synthesis and their predicted side chain conformations.

CHAPTER FOUR

SIDE CHAIN CONFORMATION AND ITS INFLUENCE ON GLYCOSYLATION SELECTIVITY IN HEXOFURANOSIDES

4.1 Existing literature on side chain conformations in furanoses

The population distribution of side chain conformations in the pentofuranosides was assigned by Serianni and coworkers in the 1980's based on NMR population analysis (Figure 29).[174] Lowry and coworkers subsequently reported that the relative stability of 1,2-anhydro-5-*O*-benzoyl-α- and β-D-lyxofuranosyl triflates varied according to side chain *tg* > *gt* > *gg* order conformation, with based on DFT calculation methods.[175] Recently, a molecular dynamic study by Wang and Woods found that the side chain conformation is influenced by the ring conformation in simple pentofuranosides.[176] However, Nester and Plazinski reported that correlation between ring and side chain conformation in pentofuranosides is minimal with differences <0.7 kcalmol^{-1}.[177]

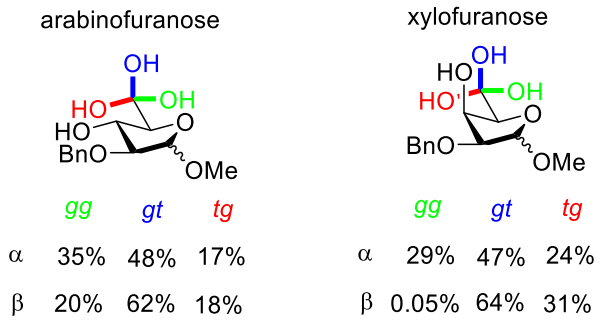
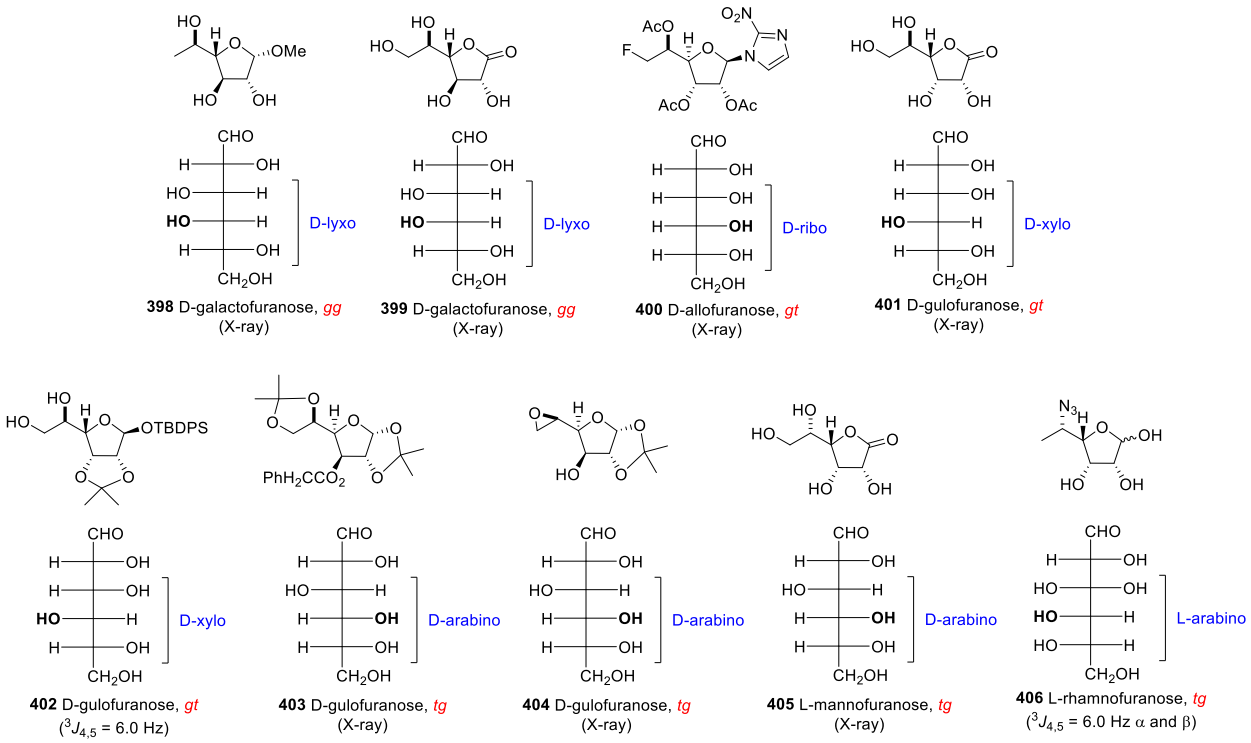


Figure 29. The staggered conformations of the side chains of methyl arabino and xylofuranosides and their approximate populations in the free solution.[174]

Regarding the side chain conformation of the hexofuranosides a literature survey revealed the nine compounds in Figure 30,[178-183] where conformations were established by eighter x-ray crystallography or NMR spectroscopy. All fit the model established for the higher carbon pyranosides[173], giving rise to the possibility that relative configuration and consequently side chain conformation may influence the reactivity and selectivity of hexo- and higher carbon furanosides.



398 D-galactofuranose, *gg* (X-ray)
399 D-galactofuranose, *gg* (X-ray)
400 D-allofuranose, *gt* (X-ray)
401 D-gulofuranose, *gt* (X-ray)
402 D-gulofuranose, *gt* ($^3J_{4,5}$ = 6.0 Hz)
403 D-gulofuranose, *tg* (X-ray)
404 D-gulofuranose, *tg* (X-ray)
405 L-mannofuranose, *tg* (X-ray)
406 L-rhamnofuranose, *tg* ($^3J_{4,5}$ = 6.0 Hz α and β)

Figure 30. Literature hexofuranose derivatives and their approximate side chain conformations.

On this basis, the 6-deoxy-D-gluco, L-ido, D-altro, and L-galactothio- furanosides **394-397** (Figure 31) were targeted in order to analysis their side chain conformation and its influence on glycosylation reactivity and selectivity.

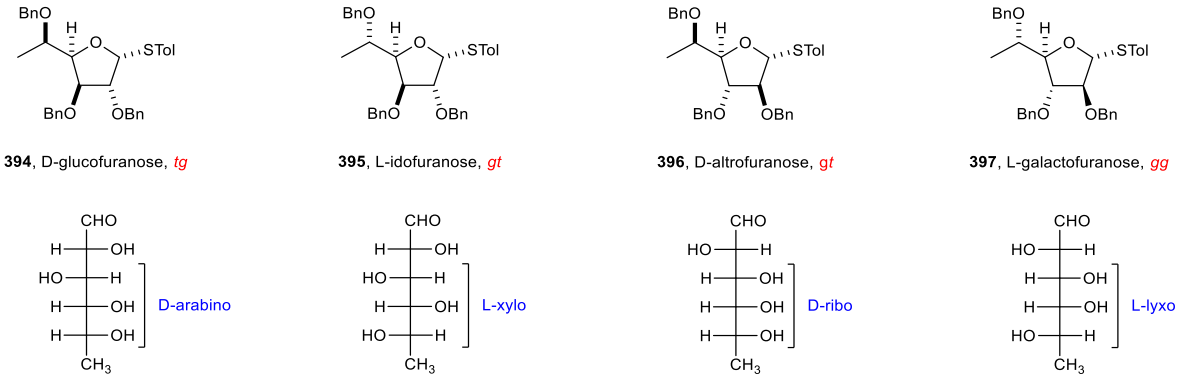


Figure 31. Hexofuranosyl donors targeted for synthesis and investigation.

4.2 Results and Discussion

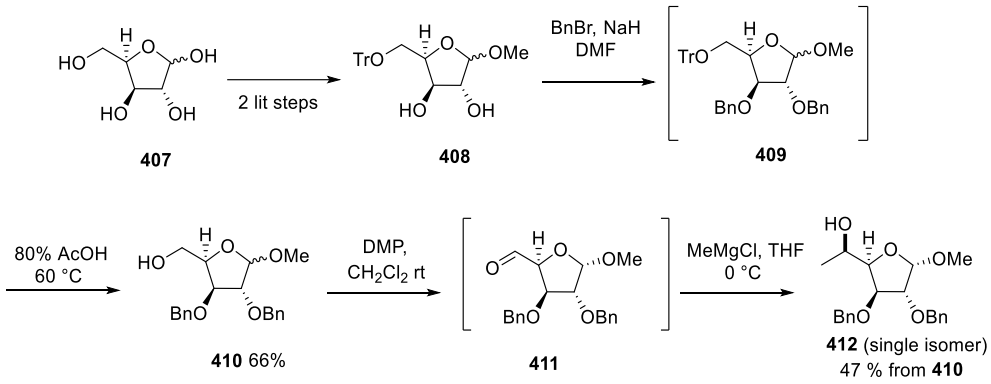
To avoid potential confusion arising from the comparison of selectivities between donors in the D- and L-series the anomeric configuration of all higher carbon furanosyl glycosides are described as 1,2-*cis*-, or 1,2-*trans* in this chapter abbreviated to *cis*- or *trans*- in the compound numbers. However, in the experimental section compounds are named formally according to the Rosanoff convention.

4.2.1 Synthesis of 6-Deoxy-D-glucofuranose and 6-deoxy-L-idofuranose donors

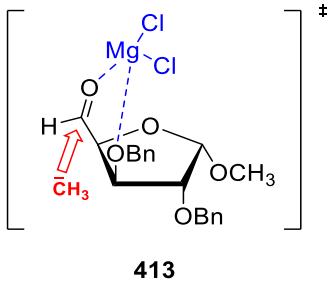
4.2.1.1 Synthesis of 6-Deoxy-D-glucofuranose derivative

Commercial D-xylose **407** was converted to tritylated methyl glycoside **408** according to the known literature protocol.[184, 185] In the anomeric mixture **408**, these two secondary alcohols were protected as benzyl ethers to give **409** by a standard benzylation protocol, and subsequent cleavage of the trityl group in **409** afforded the anomeric methyl furanosides **410-(1,2-*cis*)** and **410-(1,2-*trans*)** in 32% and 34% yield, respectively. Dess-Martin oxidation of the primary alcohol in **410-(1,2-*cis*)** delivered the corresponding aldehyde **411**, which was treated with MeMgCl at 0 °C in THF to give **412** as a single isomer in 47% yield after two steps (Scheme 78). The chelation

of magnesium between the more basic O3 and O5 (Figure 32) is probably the reason for the excellent stereoselectivity observed in this Grignard reaction.



Scheme 78. Synthesis of 6-Deoxy-D-glucofuranose derivative **412**.

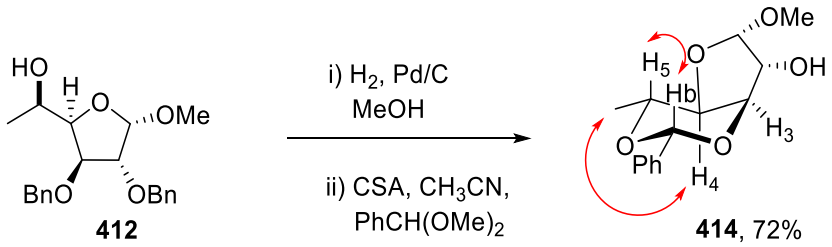


413

Figure 32. Chelation control in the Grignard reaction of **411**.

4.2.1.2 Assignment of configuration at C5 in 6-Deoxy-D-glucofuranose derivative

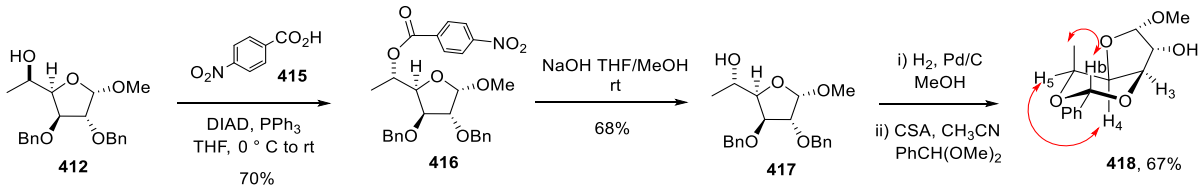
In order to establish the configuration at C5, a cyclic protecting group spanning O5 and O6 was introduced. Cleavage of the benzyl ethers in **412** by hydrogenolysis afforded the corresponding tetraol, which was subsequently treated with benzaldehyde dimethyl acetal in the presence of a catalytic amount of camphor sulfonic acid to give benzylidene acetal **414** in 72% yield after two steps (Scheme 79). Compound **414** had strong NOE interactions between the benzylidene proton and H5, and between the methyl group and H4. Therefore, the configuration was established as gluco for **412**, **414**, and other members of the same series.



Scheme 79. Assignment of configuration at C5 in 6-deoxy-D-glucofuranose derivative **412**.

4.2.1.3 Inversion of the 6-deoxy-D-glucofuranose derivative to a 6-deoxy-L-idofuranose derivative

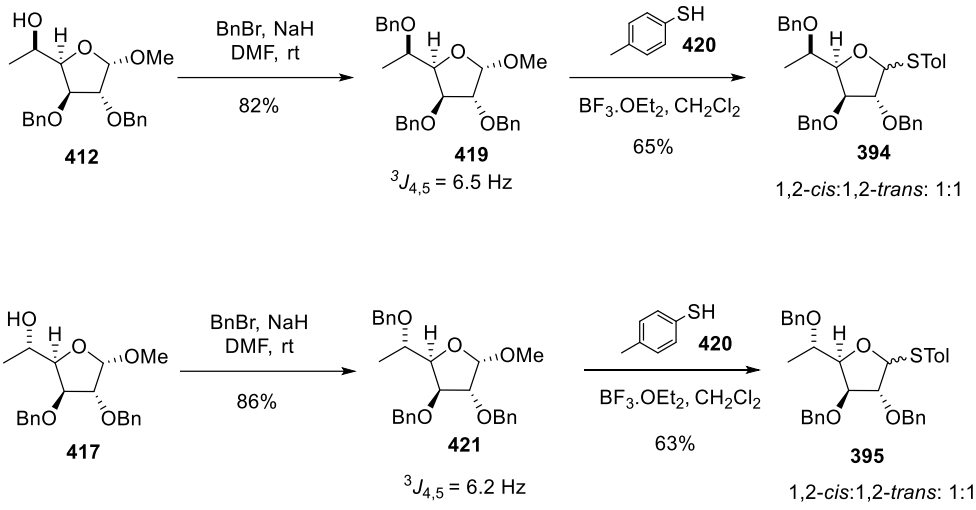
To obtain the other epimer at the 5-position, the D-gluco-derivative **412** was subjected to Mitsunobu inversion with *p*-nitrobenzoic acid giving the corresponding ester **416** in 70% yield, which was hydrolyzed with sodium hydroxide to afford inverted alcohol **417** in 68% yield (Scheme 80). The inverted configuration at C5 in **417** was proved by synthesizing benzylidene acetal **418** in 67% yield under the same conditions employed for the D-gluco-derivative. The benzylidene acetal **418** displayed NOE interactions between H's 4 and 5, and the benzylidene proton and the methyl group, confirming the overall L-ido configuration for **418** and **417**.



Scheme 80. Synthesis of 6-deoxy-L-idofuranose derivative **417**, and assignment of configuration at C5 in **417**.

4.2.1.4 Synthesis of 6-deoxy-D-glucofuranose and 6-deoxy-L-idofuranose donors

Benzylation of the remaining secondary alcohol in the D-gluco-derivative **412** gave the fully protected methyl glycoside **419** in 82% yield, which was then subjected to transglycosylation with *p*-thiocresol to give thioglycoside **394** in 65% yield as 1:1 1,2-*cis*:1,2-*trans* mixture. On the other hand, the remaining hydroxyl group in the L-ido-derivative **417** was also benzylated to give the fully protected methyl glycoside **421** in 68% yield. Transglycosylation of **421** with *p*-thiocresol afforded thioglycoside **395** in 63% yield as 1:1 1,2-*cis*:1,2-*trans* mixture.



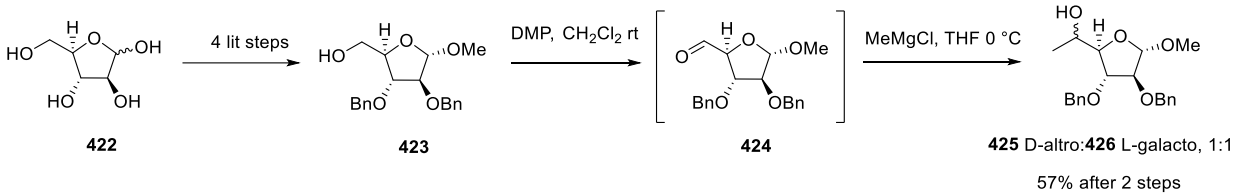
Scheme 81. Synthesis of 6-deoxy-D-glucofuranose thioglycoside **394** and 6-deoxy-L-idofuranose thioglycoside **395**.

4.2.2 Synthesis of 6-deoxy-D-altrofuranose and 6-deoxy-L-galactofuranose donors

4.2.2.1 Synthesis of 6-deoxy-D-altro- and L-galacto- derivatives

Commercial D-arabinose **422** was converted to the 1,2-*cis*-methyl arabinofuranoside intermediate **423** by a known literature protocol.[186, 187] Dess-Martin periodinane oxidation of **424** afforded corresponding aldehyde **423** which was then treated with MeMgCl at 0 °C to give the

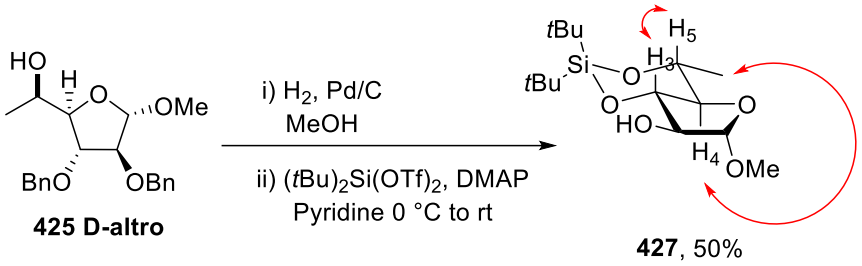
homologs **425** and **426** in 57% yield as 1:1 mixture of diastereomers (Scheme 82). In the arabino aldehyde **424** no selectivity was seen in the Grignard addition, with chelation to O3 on the opposite side of the ring being less favorable.



Scheme 82. Synthesis of 6-deoxy-D-altro- and L-galacto- derivatives.

4.2.2.2 Assignment of configuration at C5 in the D-altro and L-galacto series

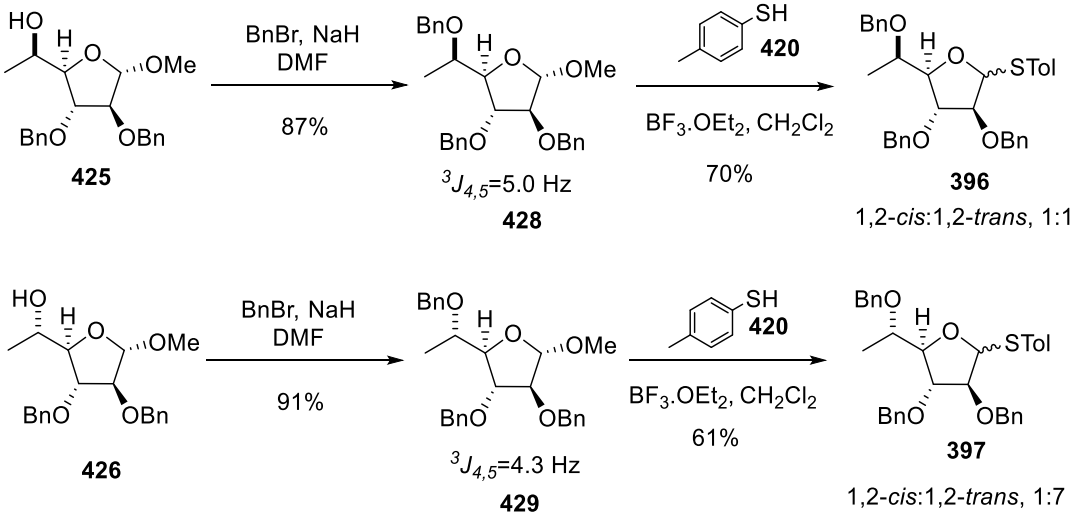
The installation of 3,5-*O*-benzylidene acetals in the arabinofuranosides is difficult and reports in the literature are rare.[188] Therefore, the use of the 3,5-*O*-di-*tert*-butylsilylene group was selected to establish the configuration at C5. Hydrogenolysis of the less polar isomer **425** gave a tetrol intermediate, which was converted to 3,5-*O*-di-*tert*-butylsilylene protected methyl furanoside **427** in 50% yield (Scheme 83). The so-formed silylene acetal **427** had NOE interactions between H's 3 and 5, as well as between H4 and the methyl group that identify the overall configuration as D-altro for **425** and **427**. Installation of 3,5-*O*-di-*tert*-butylsilylene group in the polar isomer **426** was unsuccessful, and the configuration therefore assigned as L-galacto by default.



Scheme 83. Assignment of configuration at C5 in **425**.

4.2.2.3 Synthesis of 6-deoxy-D-altrofuranose and 6-deoxy-L-galactofuranose donors

Benzylation of the D-altro-derivative **425** afforded the benzyl ether **428** in 87% yield, which was then subjected to transglycosylation with *p*-thiocresol to give D-altrofuranosyl thioglycoside **396** in 70% yield as 1:1 1,2-*cis*:1,2-*trans*-anomeric mixture. The conversion of epimer **426** to its benzyl ether gave fully protected methyl glycoside **429** in 91% yield that was transformed to thioglycoside **397** in 61% yield as 1:7 1,2-*cis*:1,2-*trans* mixture by transglycosylation.



Scheme 84. Synthesis of 6-deoxy-D-altrofuranose thioglycoside **396** and 6-deoxy-L-galactofuranose thioglycoside **397**.

4.2.3 Side chain conformation

Analysis of the ^{1}H NMR spectrum of the D-glucofuranosyl donor **394-(1,2-*cis*)**, revealed it to have a $^{3}J_{4,5}$ = 7.5 Hz coupling constant, and an NOE interaction between H1 and the terminal methyl group, leading to the assignment of a predominant *tg* conformation for the 6-deoxy-D-glucofuranose series. On the other hand, the L-idofuranosyl derivative **395-(1,2-*cis*)** displayed a $^{3}J_{4,5}$ = 8.7 Hz coupling constant in its ^{1}H NMR spectrum and an NOE interaction between H3 and the terminal methyl group indicative of a predominant *gt* conformation. The D-altrofuranose derivative **396-(1,2-*trans*)** had a $^{3}J_{4,5}$ = 5.1 Hz and showed a NOE between H5 and H4, but H1 did not show a NOE with the terminal methyl group, establishing predominance of the *gt* conformer. Finally, an NOE interaction was observed between H1 and terminal methyl group for L-galactofuranosyl derivative **397-(1,2-*trans*)**, which together with the $^{3}J_{4,5}$ = 4.2 Hz, points to its predominant side chain conformation being *gg*. Overall, the relationships observed in the pyranose series between relative configuration of higher carbon sugars and the conformation of their side chains, as also seen in the literature hexofuranosides (Figure 30) carries over to the hexo- donors **394-397** as in the higher pyranosides the side chain conformation of hexo- and higher-carbon furanosides can be predicted by simple inspection of their Fischer projection (Figure 34).

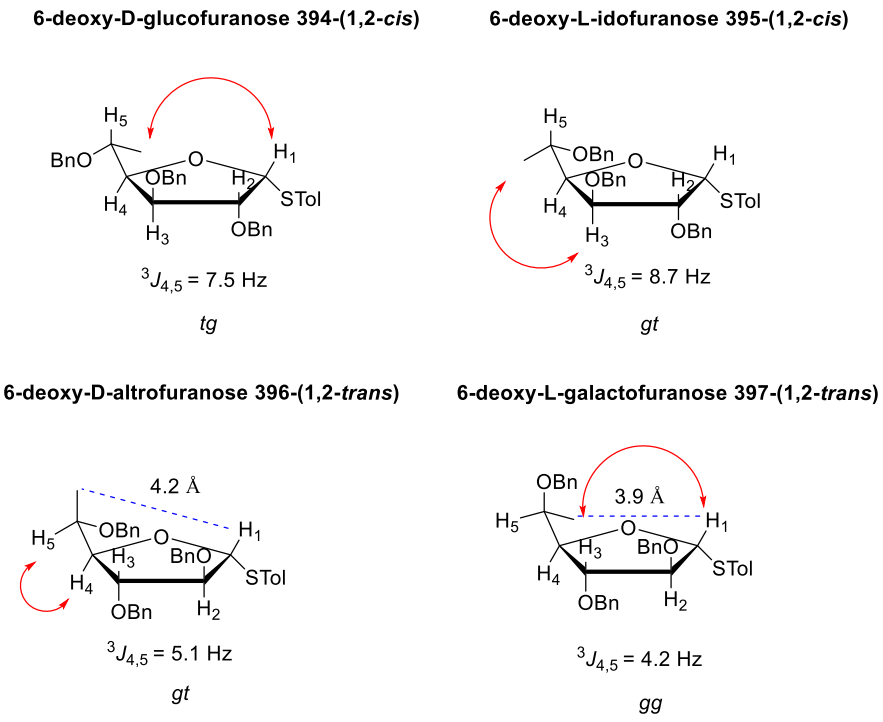


Figure 33. Diagnostic NOE and coupling constants for side chain conformation assignment.

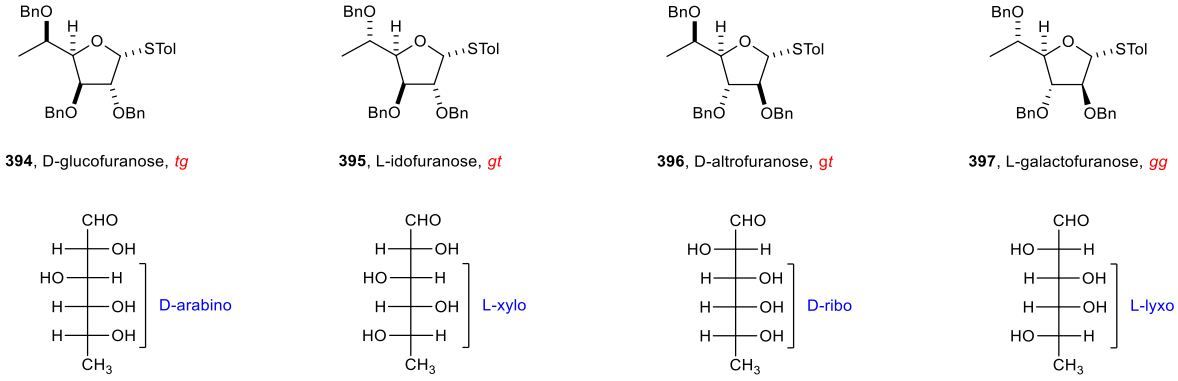


Figure 34. Fischer projections of the four hexofuranosyl donors **394-397** and their side chain conformations.

4.2.4 Glycosylation

Glycosylation reactions were carried out for the four donors by activating 0.2 M dichloromethane solutions of the thioglycosides in the presence of 1.1 equivalents of acceptor

alcohol with 1.4 equivalents of NIS and 0.2 equivalents of AgOTf at -30 °C.[189, 190] The configuration at anomeric center in the various glycosides formed was assigned based on the $^{3}J_{1,2}$ coupling constants. Typically, in the furanosides, 1,2-*cis*-glycosides have larger $^{3}J_{1,2}$ coupling constants than the corresponding 1,2-*trans*-glycosides (Figure 35).[190, 191] Therefore, the 1,2-*trans* glycosides in all four series were assigned on the basis of $^{3}J_{1,2}$ coupling constants of 0-2 Hz, while the 1,2-*cis* isomers had $^{3}J_{1,2}$ coupling constants of 4-5 Hz.

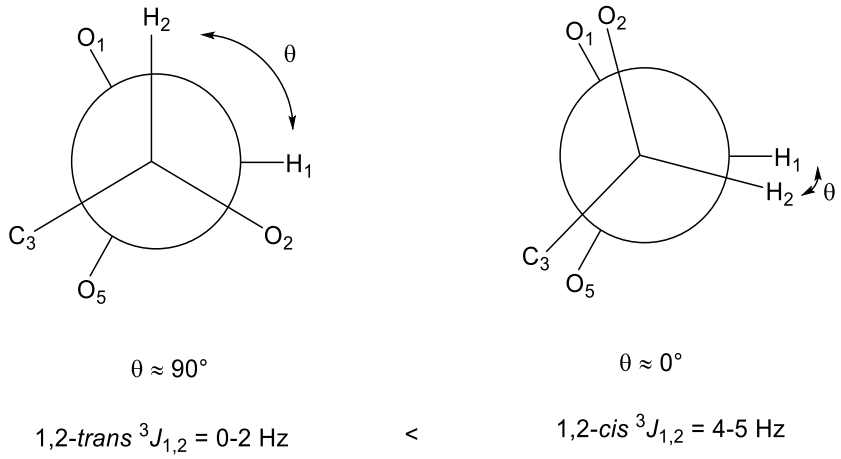
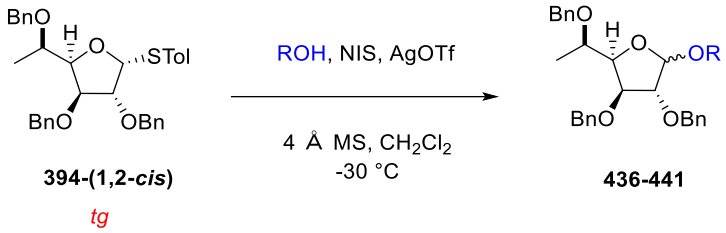


Figure 35. Comparison of $^{3}J_{1,2}$ coupling constants in 1,2-*cis* and 1,2-*trans* furanosides.

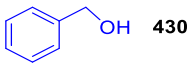
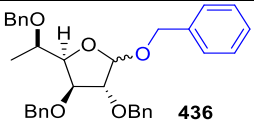
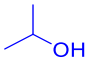
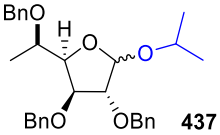
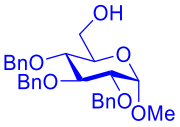
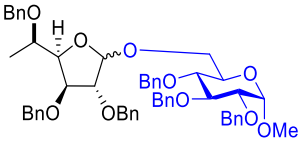
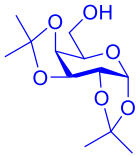
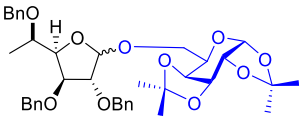
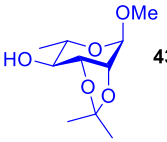
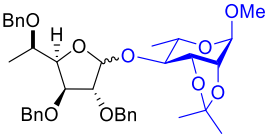
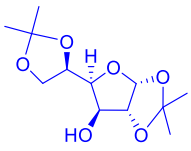
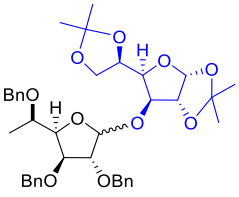
4.2.4.1 Glycosylation of donor 394-(1,2-*cis*)

The D-glucofuranose donor **394-(1,2-*cis*)** with the predominant *tg* side chain conformation displayed modest selectivity for the formation of 1,2-*trans*-glycosides in good yields with simple primary and secondary alcohols (Table 12, entries 1-2). With the primary carbohydrate acceptors, it showed excellent 1,2-*trans*-selectivity along with modest yields (Table 12, entries 3-4), while exclusive formation of 1,2-*trans*-glycosides was seen with secondary carbohydrate acceptors (Table 12, entries 5-6).

Table 12. Glycosylation of donor **394-(1,2-*cis*)**.



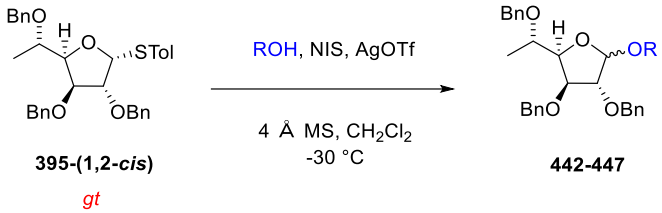
394-(1,2-*cis*) *tg* | **436-441**

Entry	Acceptor	Product	Yield (%)	1,2-*cis*:1,2-*trans*	1,2-*trans* $^3J_{1,2}$ (Hz)	1,2-*cis* $^3J_{1,2}$ (Hz)
1	 **430**	 **436**	75	1:3.2	1.2	4.5
2	 **431**	 **437**	69	1:5.7	1.9	4.6
3	 **432**	 **438**	89	1:10	1.6	4.0
4	 **433**	 **439**	58	1:11	1.4	4.3
5	 **434**	 **440**	59	*trans* only	1	
6	 **435**	 **441**	40	*trans* only	0	

4.2.4.2 Glycosylation of donor 395-(1,2-*cis*)

The L-idofuranose donor **395-(1,2-*cis*)** with the predominant *gt* side chain conformation showed nearly 2:1 1,2-*cis*:1,2-*trans* selectivity with simple primary and secondary alcohols in good yields. Continuing the trend, **395-(1,2-*cis*)** also displayed similar selectivity with the primary and secondary carbohydrate acceptors with moderate yields. However, greater selectivity for the formation of the 1,2-*cis*-glycoside was seen with diacetoneglucose as acceptor (Table 13, entry 6) compared to other secondary carbohydrate acceptors.

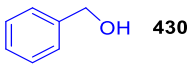
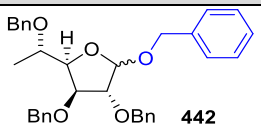
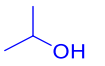
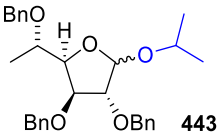
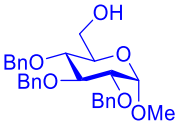
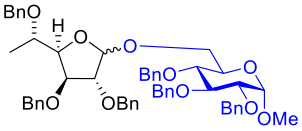
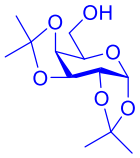
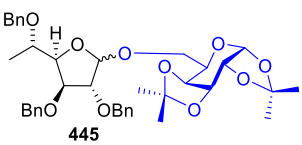
Table 13. Glycosylation of donor **395-(1,2-*cis*)**.

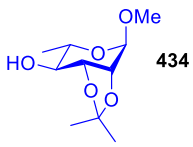
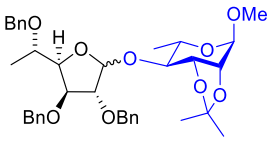
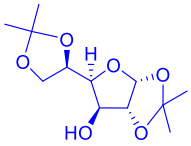
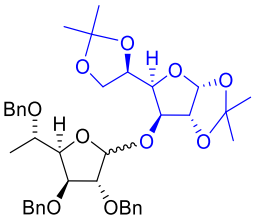


395-(1,2-*cis*)

gt

442-447

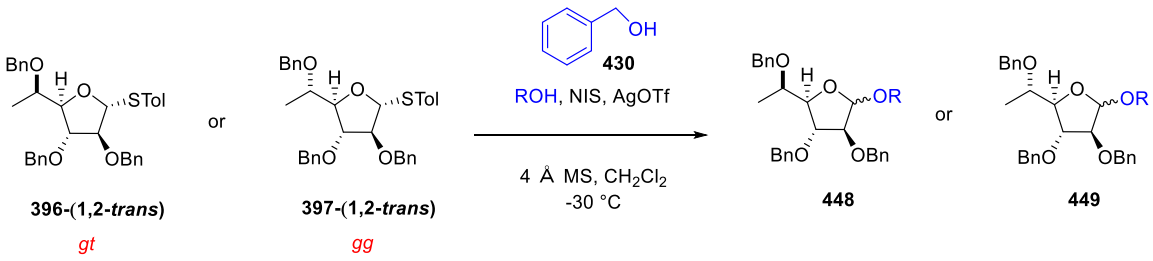
Entry	Acceptor	Product	Yield (%) [b]	1,2-*cis*:1,2-*trans*	1,2-*trans* $^3J_{1,2}$ (Hz)	1,2-*cis* $^3J_{1,2}$ (Hz)
1	 **430**	 **442**	73	2:1	1.2	4.3
2	 **431**	 **443**	80	2.5:1	1.8	4.3
3	 **432**	 **444**	82	2.3:1	1.3	4.1
4	 **433**	 **445**	77	2:1	1.2	4.3

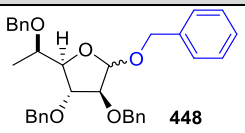
5	 **434**	 **446**	60	2.2:1	0	4.1
6	 **435**	 **447**	73	3.7:1	0	4.3

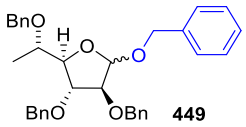
4.2.4.3 Glycosylation of D-altro 396-(1,2-*trans*) donor and L-galacto 397-(1,2-*trans*) donor

The coupling reactions of the D-altro **396-(1,2-*trans*)** donor and L-galacto **397-(1,2-*trans*)** donor displayed comparable modest 1,2-*cis*-selectivity even with a primary alcohol acceptor (Table 14). As these donors differ only in configuration at the 5-position and in their predominant side chain conformations (*gt* in **396-(1,2-*trans*)** and *gg* in **397-(1,2-*trans*)**), this suggested these donors are minimally influenced by the side chain and further examples were not pursued.

Table 14. Glycosylation of D-altro **396-(1,2-*trans*)** donor and L-galacto **397-(1,2-*trans*)** donor.



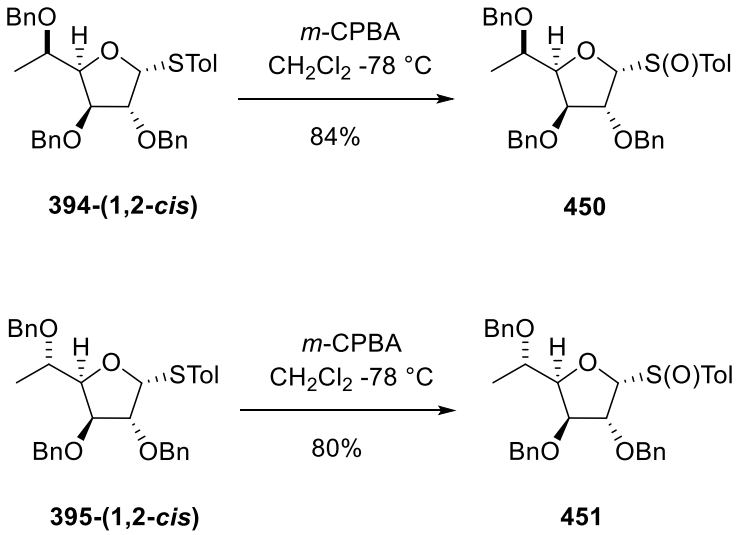
Entry	Donor	Product	Yield (%) [b]	1,2-*cis*:1,2-*trans*	1,2-*trans* $^3J_{1,2}$ (Hz)	1,2-*cis* $^3J_{1,2}$ (Hz)
1	**396-(1,2-*trans*)**	 **448**	82	2.4:1	0	4.4

2	**397-(1,2-*trans*)**	 **449**	81	2.9:1	0	4.3

Overall, 1,2-*cis* selectivity was seen for the three donors with the L-idofuranose (**395-(1,2-*cis*)**), D-altrofuranose (**396-(1,2-*trans*)**), and L-galactofuranose (**397-(1,2-*trans*)**) configurations, while the D-glucofuranose donor (**394-(1,2-*cis*)**) configuration was 1,2-*trans* selective.

4.2.5 Low temperature NMR studies

In view of the change in selectivity seen from 1,2-*trans* selective D-glucofuranose donor **394-(1,2-*cis*)** and the 1,2-*cis* selective L-idofuranose donor **395-(1,2-*cis*)**, low temperature NMR spectroscopy was employed to investigate the intermediates formed during their activation. In order to obtain clear NMR spectra without complicating issues, glycosyl sulfoxides **450** and **451** were prepared as unassigned mixtures of diastereomers in 84% and 80% yield, respectively, from the thioglycosides **394-(1,2-*cis*)** and **395-(1,2-*cis*)** by controlled reaction with *m*-chloroperoxybenzoic acid (Scheme 85).



Scheme 85. Synthesis of sulfoxide donors **450** and **451**.

The NMR spectra of the two sulfoxides were recorded in deuteriodichloromethane at -80 °C in the presence of the hindered base 1,3,5-tri-*tert*-butylpyrimidine (TTBP). After ejection of the NMR tube from the probe, cold Tf_2O was added, and the tube returned to the cold probe. Immediately ^{1}H and ^{13}C NMR spectra of reaction mixture were recorded and then the NMR probe temperature was raised in 10 °C increments with ^{1}H NMR spectra obtained at each step until decomposition of the intermediates was seen. The formation of multiple species was observed in both cases at -80 °C with complex ^{1}H NMR spectra. These species evolved gradually with increased temperature until a more abrupt change between -20 °C and -10 °C indicated decomposition of the various activated intermediates. Purification of crude reaction mixture from sulfoxide donor **450** gave decomposition product **452** in 13% yield, while sulfoxide donor **451** afforded the L-ido analog **453** in 6% yield (Figure 38). These intramolecular Freidel-Crafts products are consistent with decomposition products seen previously for the 3,5-*O*-(di-*tert*-butylsilylene)-2-*O*-benzyl arabinothiofuranosyl donor **454**, which gave **455**.[188]

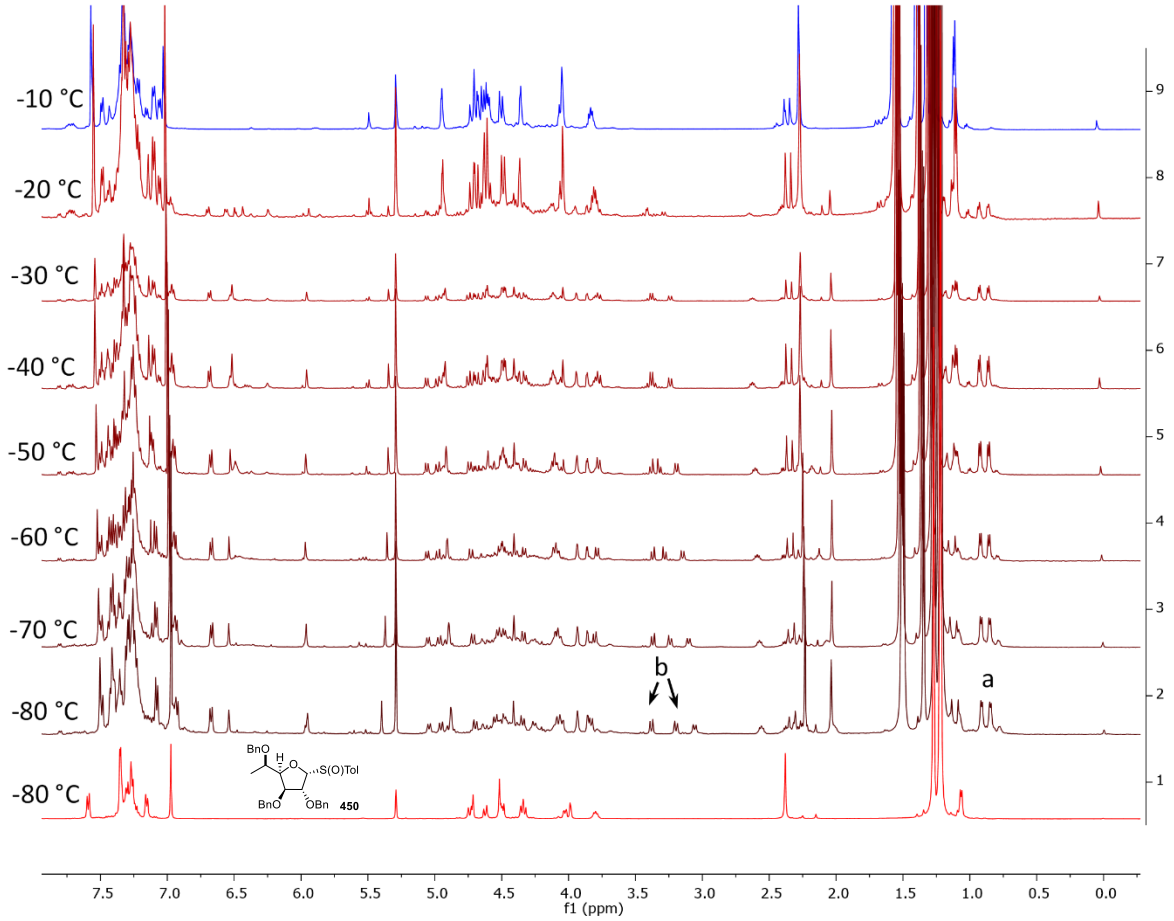


Figure 36. Variable temperature ^{1}H NMR spectra for activated sulfoxide donor **450** with characteristic signals a) = δ 0.87 and 0.94 (J = 6.1 Hz), and b) = δ 3.00-3.50 (J = 10.6 Hz).

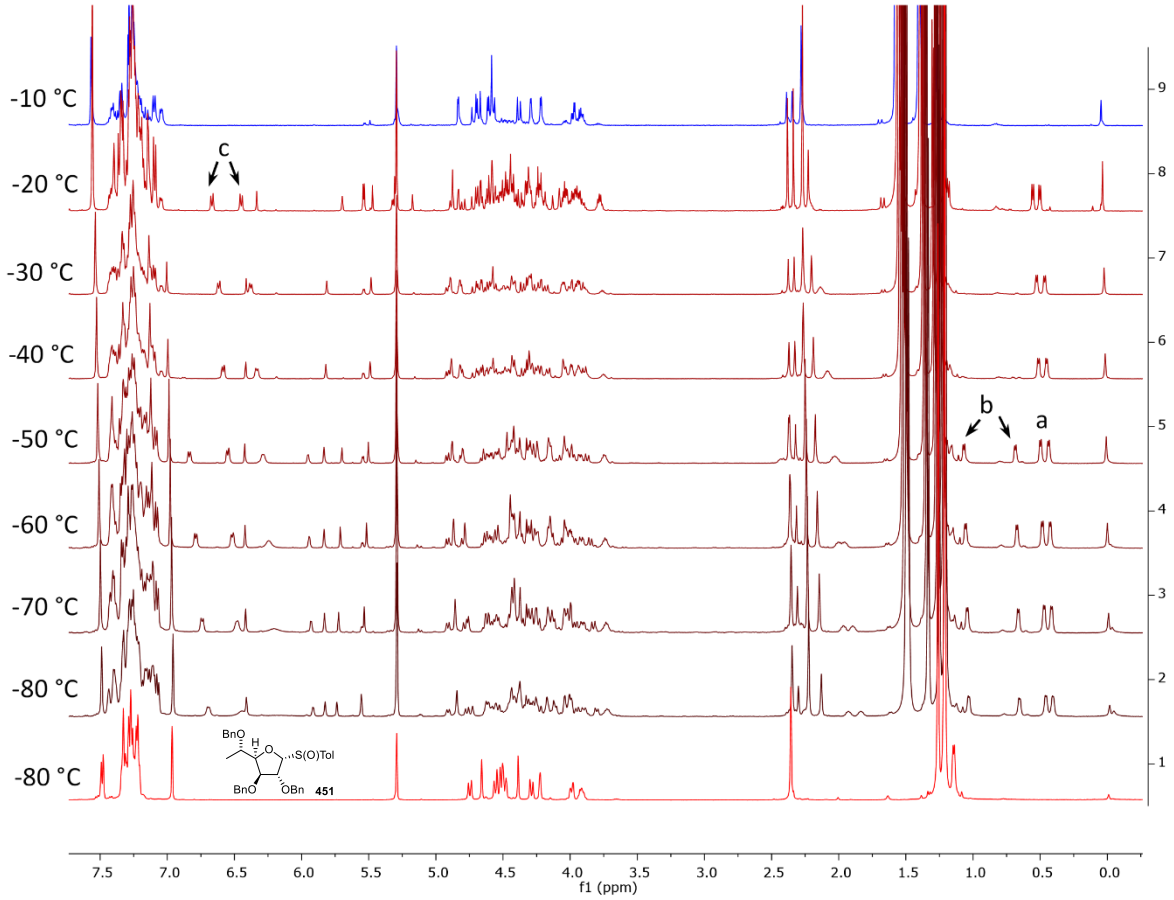


Figure 37. Variable temperature ^{1}H NMR spectra for activated sulfoxide donor **451** with characteristic signals a) δ 0.44 and 0.49 (J = 5.9 Hz), b) δ 0.68 and 1.06 (J = 6.1 Hz), and c) δ 6.45 and 6.67 (J = 8.0 Hz).

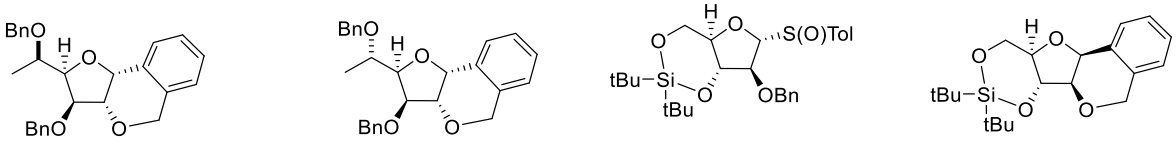


Figure 38. Decomposition products **452** and **453** from VT-NMR studies of donors **450** and **451**, and the literature product **455** seen on decomposition of activated **454**.

In the VT NMR spectra of both activated thioglycosides a series of characteristic singlets and doublets were observed in the downfield window (δ 5.25−7.00), while the upfield region (δ 1.25−0.4) had multiple deshielded methyl doublets. Additionally, on activation **450** showed upfield-shifted signals in the δ3.00−3.50 region. These characteristic signals varied in line shape and chemical shifts with the change of temperature. Unfortunately, obtaining quality 2D spectra for further characterization of the various intermediates formed was not possible due to complexity of the spectra in Figure 33 and Figure 34. In the, ^{13}C NMR spectra recorded at 60 °C no resonances were observed in the δ 200−250 window of the ^{13}C NMR spectra of the activated forms of **450** and **451** (Figure 39) indicating that none of the features observed in the ^{1}H NMR spectra are due to long-lived oxocarbenium ions.

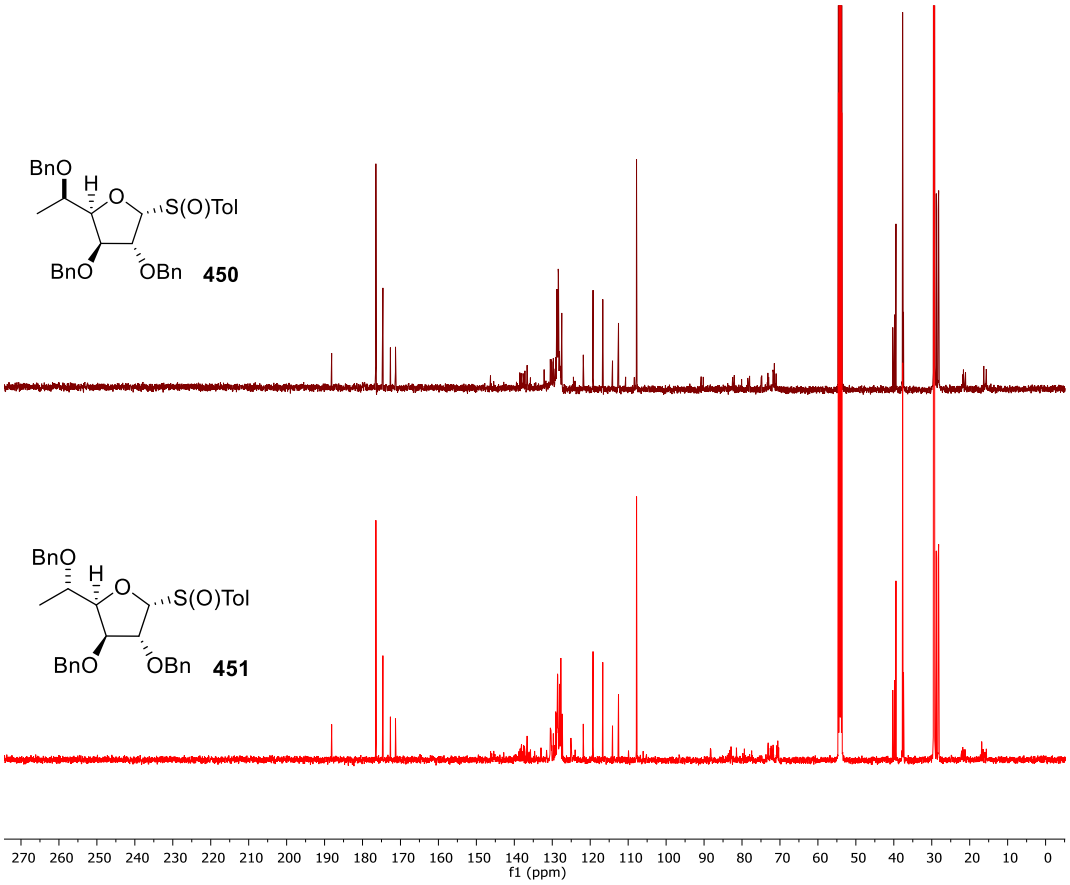
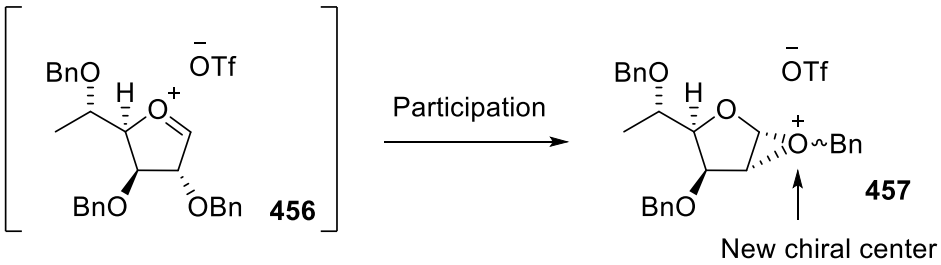


Figure 39. ^{13}C spectra for donors **450** and **451** at -60 °C after activation.

On activation of sulfoxide donor **451** at -80 °C, four apparent methyl doublets were observed at δ 0.44, 0.49, 0.68, and 1.06 in the upfield region of the spectrum, indicative of at least four substances. An approximate 1:1 pair of the signals at δ 0.68 and 1.06 (labeled b in Figure 37) were lost between -50 °C and -40 °C, while a second approximate 1:1 pair persisted until -20 °C. This implies that two sets of two intermediates were formed on the activation of **451** at -80 °C, with one pair being considerably less stable than the other. The mutually coupled doublets (δ6.45 and 6.67) with a coupling constant of 8.0 Hz at -20 °C (labeled c in Figure 37) at the low field end of the spectrum must represent the diastereotopic protons of a strongly deshielded benzyl ether. These spectral features and temperature-dependent changes are hypothesized to arise from the formation of a transient oxocarbenium ion, which was trapped by cyclization on to one or more of the benzyl ethers, giving a series of cyclic oxonium ions of differing ring sizes. The strong deshielded signals are thus assigned to benzyl groups that are involved in oxonium ion formation. Participation in this way creates a new chiral center giving rise to two diastereomers and consequently the downfield AB quartets (Scheme 86). These signals are strongly suggestive of participation by benzyl ethers.



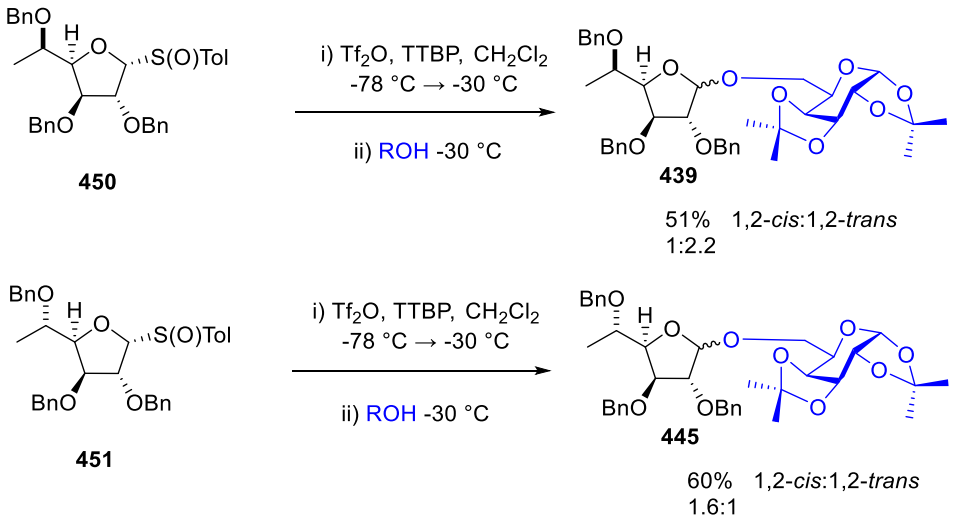
Scheme 86. Formation of new chiral center by benzyl ether participation.

Two clearly resolved upfield doublets at δ 0.88 and 0.94 (labeled a in Figure 36) and other unresolved ones in the adjacent broad signal in isomer **450** were observed along with the down

field signals arising from strongly deshielded benzylic methylene groups. Noticeably, in addition the spectra of activated **450** had signals in the δ 3.00−3.50 region that was not present in **451**. These signals took the form an apparent AB quartet with a coupling constant of 10.6 Hz (labeled b in Figure 36) suggesting a benzylic ether methylene group that is present in the shielding zone of a benzyl group pendant to a bridging oxonium ion.

4.2.6 Glycosylation by the sulfoxide method

To verify that the sulfoxide method[192] used in the VT-NMR studies gives analogues results to the thioglycoside method used in the preparative work (Tables 12 and 13), the glycosylation reactions of sulfoxide donors with 1,2:3,4-diacetone-α-D-galactopyranose by the sulfoxide method[192] was investigated. To this end, 0.2 M solutions of **450** and **451** in dichloromethane with 2 equiv of TTBP were cooled to -78 °C and treated with 1.5 equiv of triflic anhydride. After the reaction mixtures were warmed to -30 °C, and 0.4 M solution of acceptor (1.1 equiv) was added before triethylamine was added. The donor **450** showed 1:2.2 1,2-*cis*:1,2-*trans* selectivity in the formation of saccharide for **439**, while epimeric donor **451** displayed 1.6:1 1,2-*cis*:1,2-*trans* selectivity in **445** that of (Scheme 87). Not surprisingly, the observed product ratios differ with those reported under the preparative conditions (Tables 12 and 13, entry 4) due to the different glycosylation conditions.[193] However, the overall pattern observed from sulfoxide method is similar to that observed with the NIS/AgOTf method.

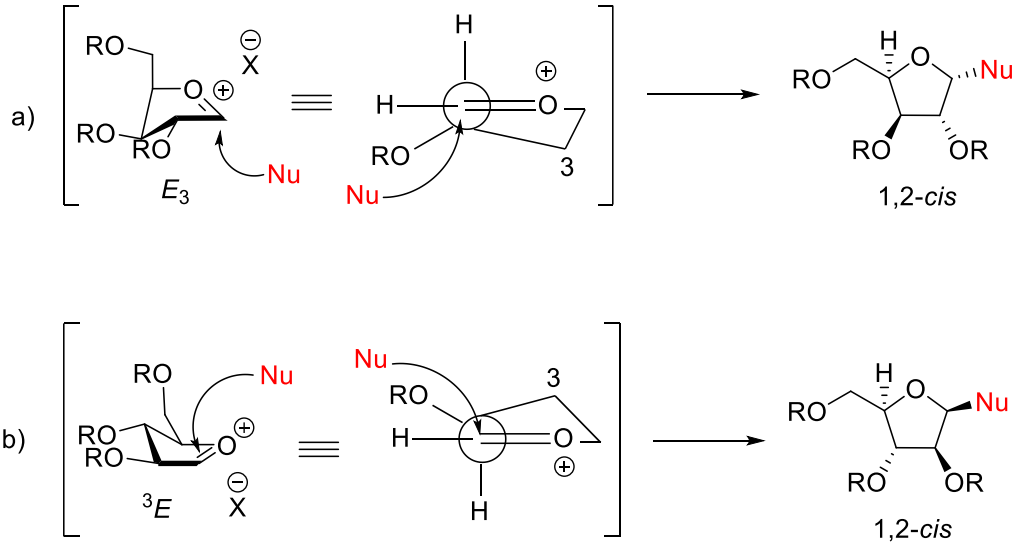


Scheme 87. Glycosylation of acceptor with D-gluco sulfoxide **450** and the L-ido sulfoxide **451**.

The difference in the magnitudes of the selectivities between the above sulfoxide and thioglycoside methods is due to the type of equivalence of the counterions and the concentration of the activated donors, as all reactions were conducted at the same temperature and concentration. In the preparative experiments, a combination of 1.4 equiv of NIS and 0.2 equiv of AgOTf was employed for activation, while the sulfoxide donors were preactivated by a molar equivalent of triflic anhydride. Thus, glycosylation the reaction mixtures employing sulfoxide donors contained a higher concentration of activated donors and triflate anion than those employing **394-(1,2-*cis*)** and **395-(1,2-*cis*)**, which only had a catalytic amount of AgOTf for the activation. Additionally, the reaction mixtures for couplings with donors **394-(1,2-*cis*)** and **395-(1,2-*cis*)** also contained iodide and succinimide as alternate counterions.[194] These changes influence the outcome of reactions taking place at the S_N1/S_N2 mechanistic border, even if the overall trends observed in both methods were same.

4.3 Discussion

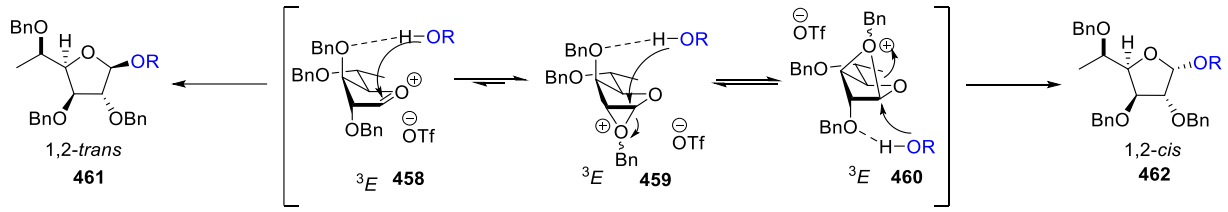
Woerpel and coworkers, and subsequently Codée and workers showed that furanosyl oxocarbenium ions undergo nucleophilic attack by carbon nucleophiles and hydride donors on the inside face of envelope conformations in order to minimize the torsional interactions, result in the formation of 1,2-*cis* isomers (Scheme 88).[195-202]



Scheme 88. Inside attack model for furanosyl oxocarbenium ions, a) E_3 conformer b) ^3E conformer.

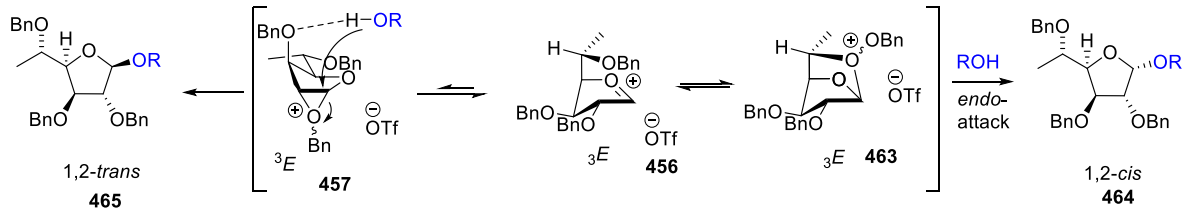
This inside attack model can be adopted to explain the observed selectivities for the four donors. The 1,2-*trans*-selective D-gluco donor **394-(1,2-*cis*)** with the *tg* conformation displayed higher levels of *trans*-selectivity with the less reactive acceptors via an S_N1-like mechanism. Thus, incoming acceptor attacks from the *endo* side on the highly reactive oxocarbenium ion **458** in an approximate ^3E conformation possibly with H-bonding assistance from the pseudoaxial O3. On the other hand, the moderate selectivity was observed with the more reactive acceptors suggests a move to the S_N2-like end of the mechanistic spectrum. In this hypothesis, the oxocarbenium ion

458 formed upon activation of donor **394-(1,2-*cis*)** is in equilibrium with the two bridged oxonium ions **459** and **460** as a result of participation by the C2 and C3 benzyl ethers. The formation of third bridged ion by participation of the C5 benzyl ether is not possible due to an inevitable steric clash between the terminal methyl group and the C3 benzyl ether. The two bridged ions, **459** and **460**, both with two possible epimers at oxygen, are consistent with the experimental observation of four upfield methyl doublets in the VT-NMR studies and favor the formation of both anomers via S_N2-like attack. The highly electron withdrawing *tg* conformation of donor **394-(1,2-*cis*)** destabilizes the oxocarbenium ion formation and favors the bridged ions (Scheme 89).



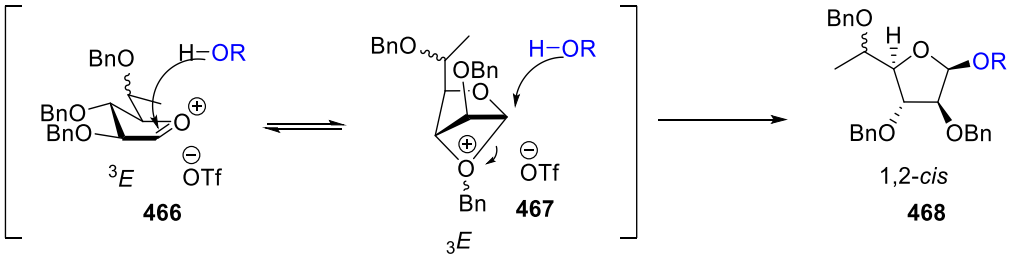
Scheme 89. Model for the explanation of selectivities observed with donor **394-(1,2-*cis*)**.

The donor **395-(1,2-*cis*)** with the lower energy *gt* side chain conformation can access bridged oxonium ion **463** in a $_3E$ conformer with participation by the C5 benzyloxy group (Scheme 90). In this ion, the C3−C6 carbon backbone is in a low energy approximate zigzag conformation with no unfavorable steric or dipolar repulsions. Therefore, the 1,2-*cis*-selectivity in the donor **395-(1,2-*cis*)** likely arises from *endo*-attack on bridged oxonium ion **463**.



Scheme 90. Model for the explanation of selectivities observed with donor **395-(1,2-*cis*)**.

The D-altro and L-galacto configured pair of donors **396-(1,2-*cis*)** and **397-(1,2-*cis*)** had comparable 1,2-*cis*-selectivity, which presumably arises from *endo* attack on the oxocarbenium ion **466** in a ^{3}E conformer and/or via bridged oxonium ion **467** in a $_{3}E$ conformer (Scheme 91).



Scheme 91. Model for the explanation of selectivities observed with donor **396-(1,2-*cis*)** and **397-(1,2-*cis*)**.

Furanosyl oxocarbenium ions contains fewer electron withdrawing C-O bonds than their pyranosyl counterparts and so are less inductively destabilized. Additionally, sp^2 hybridized atoms are well accommodated in five-membered due to the reduction in torsional strain. Therefore, the formation of covalent furanosyl triflates is less favorable than that of pyranosyl triflates.[203] The low temperature NMR studies of donors **450** and **451** revealed that formation of furanosyl covalent triflates is not the dominant mode of reaction upon activation unlike typical pyranosyl donors. However, it is apparent that furanosyl oxocarbenium ions are also not dominant, rather they are stabilized by the formation of bridged bicyclic oxonium ions via participation of various benzyl ethers. Overall, different picture emerges for furanosyl donors than for pyranosyl donors, with the preferential intervention of participation by benzyl ethers (Figure 40).

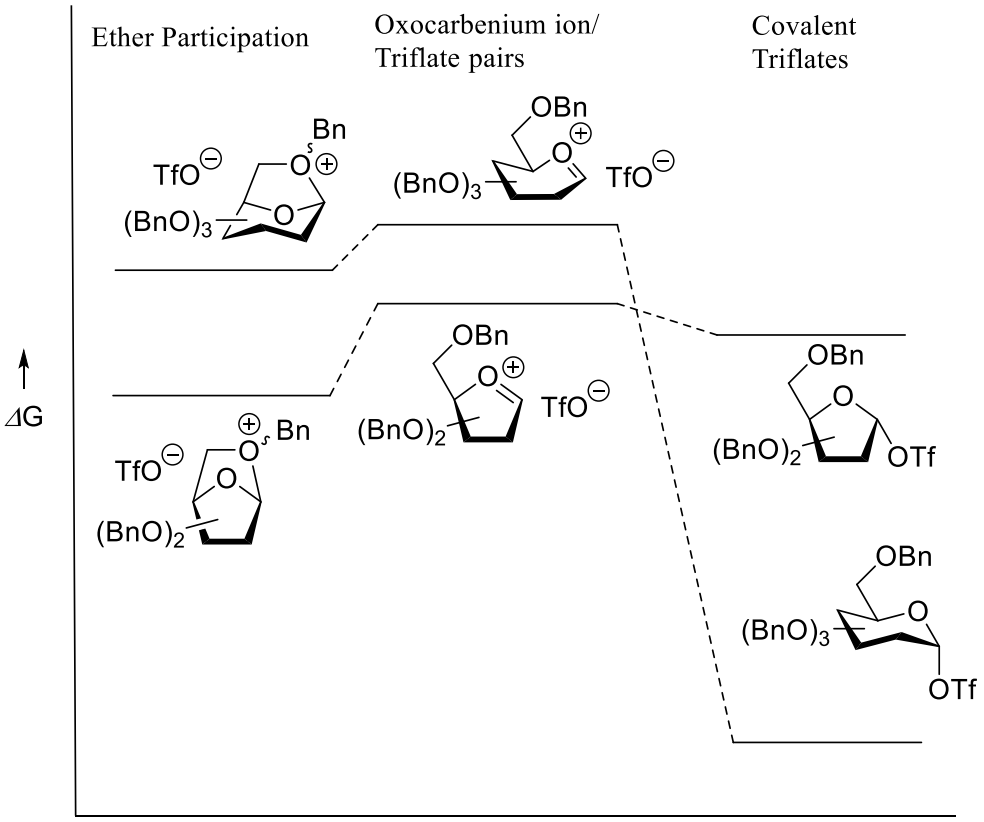


Figure 40. Relative stabilities of intermediates on the activation of glycosyl donors in the furanosyl and pyranosyl series in the presence of the triflate ion.

4.4 Conclusion

Studies of the side chain conformation in four diastereomeric furanosyl donors revealed that the relative configuration of C3, C4, and C5 in hexofuranosides dictates their side chain conformation. Further, the side chain conformation in D-gluco and L-ido furanosyl donors influenced both reactivity and selectivity in their glycosylation reactions. On the other hand, the D- altro and L-galacto donors displayed little or no influence of the side chain on selectivity. Low temperature NMR experiments with activated sulfoxide donors gave configuration dependent mixtures, which were explained by the formation of multiple equilibrating bridged oxonium ions due to the participation by various benzyl ethers. The observed diastereoselectivities were

rationalized on the basis of these observations. Finally, benzyl ether participation is a more important factor in furanosyl donors than the formation of covalent glycosyl triflates.

CHAPTER FIVE

OVERALL CONCLUSION

The cleavage of the side chain in *N*-acetyl neuraminic acid by sodium periodate oxidation resulted in an aldehyde, which gave diastereomeric imines after condensation with chiral sulfinimides. In aza pinacol coupling reactions of these imines with acetaldehyde, the (*R*)-configured sufinyl imine showed 4:1 selectivity affording the legionaminic acid and 8-*epi*-legionaminic acid configuration in the side chain. The (*S*)-configured sulfinyl imine displayed 22:1 selectivity for the acetaminic acid over the 8-*epi*-acetaminic acid configuration, while a KDO-derived (*S*)-configured sulfinyl imine was highly selective and led to a single isomer with the pseudaminic acid configuration in the side chain. These reactions enabled the development of syntheses of various 9-deoxy sialic acid donors from *N*-acetyl neuraminic acid with significant improvements over the literature syntheses most notably reduced step counts.

Analysis of side chain conformation in the hexofuranosides revealed it to depend on the relative configuration of C3, C4, and C5, which parallels observations in the higher carbon pyranosides. A D-gluco-configured furanosyl donor with the *tg* conformation of the side chain showed 1,2-*trans*-selectivity in glycosylation reactions. Inversion of the configuration at C5 in this donor resulted in a L-ido-configured furanosyl donor, which adopted to *gt* conformation of the side chain and showed 1,2-*cis*-selectivity. A D-altro-configured furanosyl donor with the *gt* of the side chain conformation and a L-galacto-configured furanosyl donor with the *gg* conformation displayed 1,2-*cis*-selective in their glycosylation reactions. These observations show that the

stereoselectivity in glycosylation reactions of furanosyl donors with the gluco- and ido- relative configurations are influenced by the side chain conformation. On the other hand, altro- and galacto-configured donors were little influenced by side chain conformation. Low-temperature NMR studies of activated donors revealed with the gluco- and ido- configurations complex mixtures of intermediates, which were interpreted as involving multiple bicyclic bridged oxonium ions due to participation by various benzyl ethers. The observed patterns of diastereoselectivity in the glycosylation reactions are rationalized according to this participation. This study concludes that benzyl ether participation is a more important factor in furanosyl donors compared to the pyranosyl donors.

CHAPTER SIX

EXPERIMENTAL SECTION

General Experimental. Commercially available starting materials were used without further purification. All solvents were dried according to standard methods. All reactions were carried out under argon using oven dried glassware. Heating of reaction mixtures was carried out on a thermostatically-controlled aluminum heating block of appropriate size. TLC was performed on pre-coated glass plates employing UV absorption and charring with 10% sulfuric acid, or ceric ammonium molybdate (CAM) for visualization. Silica gel 60, 230−400 mesh, 40−63 μM was used for column chromatography. ^{1}H and ^{13}C NMR spectra were recorded on 400, 600 and 900 MHz instruments at 300 K. Chemical shifts were calibrated from residual solvent peaks. Specific rotations were measured using a digital polarimeter and are given with units of $10^{-1}deg \cdot cm^{2} \cdot g^{-1}$. High-resolution mass spectra were recorded with an electrospray source coupled to an Orbitrap Mass analyzer.

3,5-*O*-Benzylidene-6-deoxy-2-*O*-(trimethylsilyl)-L-gulono-1,4-lactone (210).

To a stirred solution of compound **212**[114] (1.3 g, 6.2 mmol) in benzaldehyde (10 mL, 25 mmol), concentrated HCl (0.50 mL, 6.2 mmol) was added and stirred at room temperature overnight. After completion, the reaction mixture was diluted with diethyl ether (30 mL) and the resulting precipitate was filtered before it was washed with diethyl ether. After drying under vacuum, the white precipitate (1.4 g) was dissolved in anhydrous acetonitrile (10 mL), and the resulting solution was treated with bis(trimethylsilyl)amine (1.5 mL, 7.1 mmol) and stirred at room temperature for

5 h. Removal of the solvents gave compound **210** (1.8 g, 92% after two steps) as a white powder; R_f = 0.48 (7:13 ethyl acetate/hexane); $[\alpha]^{25}_D$ = +78 (*c* = 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.45 (m, 2H, ArH), 7.38 – 7.33 (m, 3H, ArH), 5.56 (s, 1H, PhCH), 4.61 – 4.55 (m, 2H, H-3, H-2), 4.16 (qd, *J* = 6.6, 1.8 Hz, 1H, H-5), 4.04 (t, *J* = 1.9 Hz, 1H, H-4), 1.46 (d, *J* = 6.6 Hz, 3H, CH_3), 0.20 (s, 9H, $Si(CH_3)_3$) ; ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.2 (CO_2C), 137.2 (Ar), 129.3 (Ar), 128.3 (Ar), 126.5 (Ar), 99.6 (PhCH), 75.0 (C-2), 72.6 (C-3), 72.3 (C-4), 71.9 (C-5), 16.7 (CH_3), 0.4 ($Si(CH_3)_3$); HRMS (ESI) m/z calcd for $C_{16}H_{22}O_5SiNa$ $[M + Na]^+$ 345.1134, found 345.1128.

(2*S*,4*S*,5*R*,6*S*)-4-(3-acetoxy-5-methylfuran-2-yl)-6-methyl-2-phenyl-1,3-dioxan-5-yl acetate (217).

Preparation of propagyl magnesium bromide solution; To a stirred suspension of magnesium turnings (12 mg, 0.48 mmol) and mercuric chloride (1.0 mg) in diethyl ether (2.0 mL), the propagyl bromide (1.0 µL) was added. The reflux of the solution was induced by heat gun before the mixture was cooled in an iced bath. To this cold mixture, the propagyl bromide (10 µL) in diethyl ether (0.50 mL) was added slowly and the resulting mixture was stirred at 0 °C for 1 h.

To a stirred solution of compound **210** (20 mg, 60 µmol) in anhydrous THF (0.30 mL) at -40 °C, a freshly prepared propagyl magnesium bromide solution was added dropwise, and the mixture was stirred at -40 °C for 2 h before it was allowed to warm to 0 °C. The resulting reaction mixture was quenched by addition of saturated aqueous NH_4Cl and extracted with ethyl acetate. The extracts were washed with brine and dried over Na_2SO_4. Removal of the solvent gave an orange color oil (30 mg) that was dissolved in anhydrous CH_2Cl_2 (0.60 mL) and cooled to 0 °C. To this cold reaction mixture, triethyl amine (17 µL, 0.12 mmol) and acetic anhydride (12 µL, 0.12 mmol) were added and stirred at room temperature overnight. After dilution of the reaction mixture by

addition of CH_2Cl_2, the organic layer was washed with saturated aqueous $NaHCO_3$, 1 M HCl, brine and dried over Na_2SO_4. Removal of the solvent gave compound **217** as a colorless oil (3.0 mg, 13% yield after two steps); R_f = 0.41 (3:7 ethyl acetate/hexane); $[\alpha]^{25}_D$ = +4 (*c* = 0.15, $CHCl_3$) ; ^{1}H NMR (600 MHz, C_6D_6) δ 7.67 (d, *J* = 7.0 Hz, 2H, ArH), 7.11 (dd, *J* = 23.3, 7.4 Hz, 3H, ArH), 6.04 (s, 1H, H-2), 5.47 (s, 1H, PhCH), 5.07 (s, 1H, H-6), 4.92 (s, 1H, H-5), 3.53 (qd, *J* = 6.5, 1.6 Hz, 1H, H-7), 1.84 (s, 6H, Ac, CH_3), 1.74 (s, 3H, Ac), 1.17 (d, *J* = 6.5 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, C_6D_6) δ 170.2 (Ac), 167.7 (Ac), 150.6 (Ar), 138.8 (Ar), 137.2 (Ar), 136.5 (Ar), 129.0 (Ar), 126.9 (Ar), 103.9 (C-2), 101.6 (PhCH), 74.4 (C-7), 74.1 (C-5), 68.0 (C-6), 20.5 (Ac), 20.3 (Ac), 17.1 (CH_3), 13.6 (CH_3); HRMS (ESI) m/z calcd for $C_{20}H_{22}O_7Na$ $[M + Na]^+$ 397.1263, found 397.1260.

1,2-*O*-isopropylidene-6-*O*-(*tert*-butyldimethylsilyl)-α-D-glucofuranose (229).

A stirred solution of compound **230** (2.3 g, 10 mmol) in anhydrous DMF (50 mL) was cooled to 0 °C, and to this reaction mixture imidazole (1.1 g, 16 mmol) and TBSCl (2.0 g, 12 mmol) were added. The resulting reaction mixture was allowed to warm to room temperature for 1 h before it was poured in to iced cold water. The resulting aqueous suspension was extracted with ethyl acetate and extract was washed with cold water followed by brine and dried over Na_2SO_4. After removal of the solvent, the crude product was purified by column chromatography (1:4 ethyl acetate/hexane) to give **229** (3.3 g, 94%) as a white solid with spectral data consistent with those reported in the literature[204]; R_f = 0.26 (1:4 ethyl acetate/hexane); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.95 (d, *J* = 3.6 Hz, 1H, H-1), 4.53 (d, *J* = 3.7 Hz, 1H, H-2), 4.35 (d, *J* = 2.7 Hz, 1H, H-3), 4.08 (dd, *J* = 6.4, 2.7 Hz, 1H, H-4), 4.01 (ddd, *J* = 6.4, 5.2, 3.8 Hz, 1H, H-5), 3.88 (dd, *J* = 10.4, 3.8 Hz, 1H, H-6), 3.72 (dd, *J* = 10.4, 5.2 Hz, 1H, H-6), 1.47 (s, 3H, $C(CH_3)$), 1.31 (s, 3H, $C(CH_3)$), 0.90 (s, 9H $C(CH_3)_3$), 0.09 (s, 6H, $Si(CH_3)_2$); ^{13}C NMR (151 MHz, $CDCl_3$) δ 111.6 ($C(CH_3)_2$), 104.9

(C-1), 85.0 (C-2), 79.7 (C-4), 75.9 (C-3), 70.5 (C-5), 64.0 (C-6), 26.8 (C(CH$_3$)$_2$), 25.8 (C(CH$_3$)$_3$), 18.3 (C(CH$_3$)$_3$), -5.5 (Si(CH$_3$)$_2$).

3,5-Diazido-3,5-dideoxy-1,2-*O*-isopropylidene-6-*O*-*tert*-butyldimethylsilyl)-β-L-tallofuranose (228) and 5-azido-3,5-dideoxy-3-en-1,2-*O*-isopropylidene-6-*O*-(*tert*-butyldimethylsilyl)-L-glycero-β-D- glycerofuranose (231).

To stirred solution of compound **229** (0.54 g, 1.2 mmol) in anhydrous CH_2Cl_2 (6.0 mL) and pyridine (0.30 mL, 3.5 mmol) at -30 °C, Tf_2O (1.1 mL, 5.0 mmol) was added dropwise. The resulting reaction mixture was allowed to warm to 0 °C with stirring for 2 h. After completion, the reaction mixture was diluted with CH_2Cl_2 and the resulting solution was washed with 1 M HCl, saturated aqueous $NaHCO_3$ and brine. The extract was dried over Na_2SO_4, and the solvent was removed under reduced pressure at room temperature to give the crude triflate, which was dissolved in DMF (2.5 mL). To the resulting reaction mixture, lithium azide (0.28 g, 5.8 mmol) was added and stirred for 20 h at 20 °C before it was poured in to iced water. The resulting aqueous solution was extracted with ethyl acetate, and the extract was washed with brine and dried over Na_2SO_4. After removal the solvent under reduced pressure, a mixture of **228** and **231** that was separated by flash column chromatography (hexane/ethyl acetate 97:3) to give compound **228**, and compound **231**.

228 (0.14 g, 31%) colorless oil; R_f = 0.16 (1:19 ethyl acetate/hexane); $[\alpha]^{25}_D$ = +10.61 (*c* = 1.3, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.81 (d, *J* = 3.6 Hz, 1H, H-1), 4.74 (dd, *J* = 4.7, 3.6 Hz, 1H, H-2), 4.14 (dd, *J* = 9.5, 2.3 Hz, 1H, H-4), 3.96 (dd, *J* = 10.3, 7.9 Hz, 1H, H-6), 3.90 (dd, *J* = 10.3, 5.2 Hz, 1H, H-6), 3.63 – 3.57 (m, 2H, H-3, H-5), 1.56 (s, 3H, C(CH$_3$)), 1.36 (s, 3H, C(CH$_3$)), 0.92 (s, 9H, C(CH$_3$)$_3$), 0.11 (d, *J* = 2.5 Hz, 6H, Si(CH$_3$)$_2$); ^{13}C NMR (151 MHz, $CDCl_3$) δ 113.5 (C(CH$_3$)$_2$), 104.4 (C-1), 79.9 (C-2), 76.4 (C-4), 63.8 (C-6), 61.7 (C-5), 61.1 (C-3), 26.6 (C(CH$_3$)$_2$),

26.5 (C(CH_3)$_2$), 25.9 (C(CH_3)$_3$), 18.3 (C(CH_3)$_3$), -5.4 (Si(CH_3)$_2$); HRMS (ESI) m/z calcd for $C_{15}H_{28}N_6O_4SiNa$ [M + Na] $^+$ 407.1839, found 407.1839.

231 (0.20 g, 52%) colorless oil; R_f = 0.29 (1:19 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -1.76 (*c* = 2.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.05 (d, *J* = 5.3 Hz, 1H, H-1), 5.30 – 5.27 (m, 1H, H-2), 5.26 – 5.25 (m, 1H, H-3), 4.00 (dd, *J* = 7.3, 4.1 Hz, 1H, H-5), 3.93 (ddd, *J* = 10.4, 4.1, 0.6 Hz, 1H, H-6), 3.76 (ddd, *J* = 10.5, 7.3, 0.6 Hz, 1H, H-6), 1.46 (s, 3H, C(CH_3)), 1.44 (s, 3H, C(CH_3)), 0.89 (s, 9H, C(CH_3)$_3$), 0.08 (d, *J* = 2.3 Hz, 6H, Si(CH_3)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.1 (C-4), 112.7 (C(CH_3)$_2$, 106.5 (C-1), 100.8 (C-3), 83.4 (C-2), 64.2 (C-6), 60.6 (C5), 28.3 (C(CH$_3$)$_2$), 28.0 (C(CH$_3$)$_2$), 25.9 (C(CH$_3$)$_3$), 18.4 (C(CH_3)$_3$), -5.4 (Si(CH_3)$_2$); HRMS (ESI) m/z calcd for $C_{15}H_{27}N_3O_4SiNa$ [M + Na]$^+$ 364.1669, found 364.1668.

1,2-*O*-Isopropylidene-6-*O*-(*tert*-butyldimethylsilyl)-3,5-*O*-di((methylphenyl)sulfonyl)-α-D-glucofuranose (233).

To a stirred solution of compound **229** (0.18 g, 5.3 mmol) in pyridine (2.6 mL) at 0 °C, TsCl (1.0 g, 10 mmol) was added and stirred for 132 h at room temperature. After completion, the reaction mixture was diluted with ethyl acetate and the resulting organic layer was washed with 1 M HCl followed by saturated aqueous $NaHCO_3$, brine and dried over Na_2SO_4. After removal of the solvent under reduced pressure, the crude product was purified by flash column chromatography (hexane/ethyl acetate 13:1) to give compound **233** (0.25 g, 72%) as a white solid; R_f = 0.15 (1:9 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -2.28 (*c* = 2.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 – 7.89 (m, 2H, Ar), 7.77 – 7.71 (m, 2H, ArH), 7.39 (d, *J* = 8.0 Hz, 2H, ArH), 7.28 (d, *J* = 7.9 Hz, 2H, ArH), 5.78 (d, *J* = 3.7 Hz, 1H, H-1), 4.94 (d, *J* = 2.7 Hz, 1H, H-3), 4.85 (d, *J* = 3.7 Hz, 1H, H-2), 4.71 (dt, *J* = 6.8, 3.5 Hz, 1H, H-5), 4.46 (dd, *J* = 6.7, 2.7 Hz, 1H, H-4), 3.67 (d, *J* = 3.5 Hz, 2H, H-6), 2.46 (s, 3H, ArCH_3), 2.42 (s, 3H, ArCH_3), 1.41 (s, 3H, C(CH_3)), 1.27 (s, 3H, C(CH_3)), 0.78 (s,

9H, C(CH_3)$_3$), -0.07 (s, 3H, SiCH_3), -0.12 (s, 3H, SiCH_3); $_{13}$C NMR (101 MHz, $CDCl_3$) δ 145.6 (Ar), 144.6 (Ar), 134.9 (Ar), 132.8 (Ar), 130.2 (Ar), 129.7 (Ar), 128.6 (Ar), 128.0 (Ar), 112.7 (*C*(CH_3)$_2$), 104.5 (C-1), 82.6 (C-3), 81.1 (C-2), 78.3 (C-5), 76.6 (C-4), 60.9 (C-6), 26.6 (C(*C*H_3)$_2$), 26.4 (C(*C*H_3)$_2$), 25.8 (C(*C*H_3)$_3$), 21.9 (ArCH_3), 21.7 (ArCH_3), 18.3 (*C*(CH_3)$_3$), -5.6 (SiCH_3), -5.7 (SiCH_3); HRMS (ESI) m/z calcd for $C_{29}H_{42}O_{10}SiS_2Na$ $[M + Na]^+$ 665.1886 found 665.1888.

1,2-*O*-Isopropylidene-6-*O*-(*tert*-butyldimethylsilyl)-3,5-*O*-(phenoxyphosphoryl)-α-D-glucofuranose (235).

A stirred solution of compound **229** (0.15 g, 0.44 mmol) in anhydrous THF (2.2 mL) at 0 °C, was treated with DBU (0.33 mL, 2.2 mmol) and dphenylphosphoryl azide (0.50 mL, 2.2 mmol). The resulting reaction mixture was allowed to warm to 0 ℃ to room temperature with stirring for 12 h before the mixture was diluted with ethyl acetate. The resulting solution was washed with 1M HCl followed by saturated aqueous $NaHCO_3$, brine and dried over Na_2SO_4. Removal of the solvent under reduced pressure gave a crude product that was purified by flash column chromatography (hexane/ethyl acetate 5:1) to give compound **235** (0.15 g, 73%) as a colorless oil; R_f = 0.27 (1:5 ethyl acetate/hexane); $[\alpha]^{25}_D$ = +2.87 (*c* = 1.7, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35 – 7.30 (m, 2H, ArH), 7.23 – 7.16 (m, 3H, ArH), 5.80 (d, *J* = 3.7 Hz, 1H, H-1), 5.00 (dd, *J* = 5.8, 2.9 Hz, 1H, H-3), 4.70 – 4.66 (m, 2H, H-5, H-2), 4.47 (q, *J* = 2.5 Hz, 1H, H-4), 3.98 (dd, *J* = 11.2, 5.0 Hz, 1H, H-6), 3.93 (ddd, *J* = 11.3, 3.9, 2.2 Hz, 1H, H-6), 1.49 (s, 3H, C(CH_3)), 1.32 (s, 3H, C(CH_3)), 0.91 (s, 9H, C(CH_3)$_3$), 0.11 (d, *J* = 8.9 Hz, 6H, Si(CH_3)$_2$); ^{13}C NMR (151 MHz, $CDCl_3$) δ 150.7 (Ar), 129.8 (Ar), 125.4 (Ar), 120.3 (Ar), 112.8 (*C*(CH_3)$_2$), 104.6 (C-1), 84.3 (C-5), 82.8 (C-3), 81.0 (C-2), 74.7 (C-4), 63.7 (C-6), 26.8 (C(*C*H_3)$_2$), 26.4 (C(*C*H_3)$_2$), 25.9 (C(*C*H_3)$_3$), 18.4 (*C*(CH_3)$_3$), -5.4 (Si(CH_3)$_2$); HRMS (ESI) m/z calcd for $C_{21}H_{33}O_8SiPNa$ $[M + Na]^+$ 495.1580 found 4951581.

1,2-*O*-Isopropylidene-6-*O*-(*tert*-butyldimethylsilyl)-3,5-*O*-sulfuryl-α-D-glucofuranose (236).

To a stirred solution of compound **229** (0.12 g, 0.35 mmol) in anhydrous dimethylformamide at 0 °C, sodium hydride (26 mg, 24 mmol) was added, and the stirring was continued for 0.5 h at 0 °C. The resulting reaction mixture was cooled to -40 °C and Im_2SO_2 (0.21 g, 1.0 mmol) in anhydrous dimethylformamide (2.0 mL) was added dropwise and stirred for 0.5 h min at -40 °C before the mixture was poured in to iced-cold water. The resulting residual aqueous was extracted with ethyl acetate and extract was washed with brine and dried over Na_2SO_4. Removal of the solvent gave a crude product that was purified by using flash column chromatography (hexane/ethyl acetate 9:1) to give compound **236** (0.12 g, 86%) as a colorless oil; R_f = 0.24 (1:9 ethyl acetate/hexane); $[\alpha]^{25}_D$ = +1.73 (*c* = 1.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.05 (d, *J* = 3.7 Hz, 1H, H-1), 5.13 (d, *J* = 2.3 Hz, 1H, H-3), 4.82 (ddd, *J* = 7.2, 5.1, 2.5 Hz, 1H, H-5), 4.76 (d, *J* = 3.7 Hz, 1H, H-2), 4.51 (t, *J* = 2.5 Hz, 1H, H-4), 4.07 (qd, *J* = 11.3, 6.1 Hz, 2H, H-6), 1.50 (s, 3H, $C(CH_3)$), 1.36 (s, 3H, $C(CH_3)$), 0.90 (s, 9H, $C(CH_3)_3$), 0.10 (s, 6H, $Si(CH_3)_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 113.4 ($C(CH_3)_2$), 105.0 (C-1), 86.0 (C-5), 85.4 (C-3), 82.8 (C-2), 71.7 (C-4), 61.5 (C-6), 26.7 ($C(CH_3)_2$), 26.5 ($C(CH_3)_2$), 25.8 ($C(CH_3)_3$), 18.3 ($C(CH_3)_3$), -5.3 ($Si(CH_3)_2$); HRMS (ESI) m/z calcd for $C_{15}H_{28}O_8SiSNa$ $[M + Na]^+$ 419.1172 found 419.1169.

Lithium (5-azido-1,2-*O*-Isopropylidene-6-*O*-(*tert*-butyldimethylsilyl)-β-L-3-mannofuranosid)sulfate (237).

A stirred solution of compound **236** (20 mg, 0.50 mmol), lithium azide (12 mg, 0.25 mmol) and potassium carbonate (35 mg, 0.25 mmol) in CH_3CN (2.5 mL) was heated to reflux for overnight. After completion, the reaction mixture was evaporated to dryness to give a residue that was dissolved in chloroform. The resulting mixture was filtered through Celite, and removal of the solvent afforded the crude **237** (33 mg).

Data for **237**; ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.00 (d, *J* = 3.8 Hz, 1H, H-1), 5.01 (d, *J* = 3.8 Hz, 1H, H-2), 4.74 (d, *J* = 2.9 Hz, 1H, H-3), 4.45 (s, 1H, H-4), 3.87 (ddd, *J* = 28.0, 10.9, 4.8 Hz, 2H, H-6), 3.70 – 3.63 (m, 1H, H-5), 1.47 (s, 3H, $C(CH_3)$), 1.33 (s, 3H, $C(CH_3)$), 0.90 (s, 9H, $C(CH_3)_3$), 0.10 – 0.09 (m, 6H, $Si(CH_3)_2$); ^{13}C NMR (151 MHz, $CDCl_3$) δ 112.5 ($C(CH_3)_2$), 104.7 (C-1), 83.6 (C-2), 81.0 (C-3), 77.3 (C-4), 63.3 (C-6), 60.6 (C-5), 26.8 ($C(CH_3)_2$), 26.6 ($C(CH_3)_2$), 25.9 ($C(CH_3)_3$), 18.3 ($C(CH_3)_3$), -5.4 ($Si(CH_3)_2$); HRMS (ESI) m/z calcd for $C_{15}H_{28}O_8N_3SiS$ $[M]^-$ 438.1366 found 438.1360.

1,2-*O*-Isopropylidene-6-*O*-(pivaloyl)-α-D-glucofuranose (240).

To a solution of commercial 1,2-*O*-isopropylidene-α-D-glucofuranose **230** (0.50 g, 2.3 mmol) in anhydrous CH_2Cl_2 / pyridine (1:1) (22 mL) at -20 °C, pivaloyl chloride (0.31 mL, 2.5 mmol) was added dropwise and stirred for 12 h at -20 °C. After completion, the reaction mixture was diluted with CH_2Cl_2, and the resulting solution was washed with 1 M HCl followed by saturated aqueous $NaHCO_3$, brine and dried over Na_2SO_4. Removal of the solvent under reduced pressure afforded a crude product that was purified by flash column chromatography (1:9 ethyl acetate/hexane) to give **240** (0.68 g, 98%) as a white solid; R_f = 0.25 (2:3 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -0.44 (*c* = 1.9, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.96 (d, *J* = 3.5 Hz, 1H, H-1), 4.53 (d, *J* = 3.5 Hz, 1H, H-2), 4.45 – 4.39 (m, 1H, H-6), 4.36 (s, 1H, H-3), 4.25 (d, *J* = 5.6 Hz, 1H, H-6), 4.23 (d, J = 3.8 Hz, 1H, H-5), 4.08 (dd, *J* = 6.0, 2.6 Hz, 1H, H-4), 3.26 (d, *J* = 3.4 Hz, 1H, OH), 3.16 (d, *J* = 3.8 Hz, 1H, OH), 1.48 (s, 3H, $C(CH_3)$), 1.32 (s, 3H, $C(CH_3)$), 1.23 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (151 MHz, $CDCl_3$) 179.6 (*t*Bu*C*O_2C), 112.0 ($C(CH_3)_2$), 105.1 (C-1), 85.3 (C-2), 79.4 (C-4), 75.7 (C-3), 69.6 (C-5), 66.2 (C-6), 39.1 ($C(CH_3)_3$), 27.2 ($C(CH_3)_3$), 27.4 ($C(CH_3)_3$), 26.4 ($C(CH_3)_2$), 26.3 ($C(CH_3)_2$); HRMS (ESI) m/z calcd for $C_{14}H_{24}O_7Na$ $[M + Na]^+$ 327.1420, found 327.1427.

3,5-Diazido-3,5-dideoxy-1,2-*O*-isopropylidene-6-*O*-(pivaloyl)-β-L-tallofuranose (241) and 5-azido-3,5-dideoxy-3-en-1,2-*O*-isopropylidene-6-*O*-(pivaloyl)-L-glycero-β-D-glycerofuranose (242).

To a stirred solution of compound **240** (0.63 g, 2.1 mmol) and pyridine (2.0 mL, 25 mmol) in anhydrous CH_2Cl_2 (10 mL) at -30 °C, Tf_2O (2.0 mL, 12 mmol) was added dropwise. The resulting reaction mixture was allowed to warm to 0 °C with stirring for 2 h before the mixture was poured in to iced cold water. The resulting aqueous solution was extracted with CH_2Cl_2, and the extract was washed with 1 M HCl followed by saturated aqueous $NaHCO_3$, brine and dried over Na_2SO_4. Removal of the solvent under reduced pressure at room temperature gave the crude triflate that was dissolved in dimethylformamide (10 mL). The resulting reaction mixture was treated with lithium azide (0.50 g, 10.4 mmol) and stirred for 20 h at 20 °C before the reaction mixture was poured in to iced water. The resulting aqueous solution was extracted with ethyl acetate, and the extract was washed with brine and dried over Na_2SO_4. After removal of the solvent under reduced pressure, a mixture of **241** and **242** was separated by flash column chromatography (hexane/ethyl acetate 1:9) to give compound **241**, and compound **242**.

241 (0.25 g, 34%) colorless oil; R_f = 0.20 (1:19 ethyl acetate/hexane); $[\alpha]^{25}_D$ = +8.53 (*c* = 1.3, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.82 (d, *J* = 3.5 Hz, 1H, H-1), 4.76 (t, *J* = 4.0 Hz, 1H, H-3), 4.39 (qd, *J* = 11.7, 6.8 Hz, 2H, H-6), 4.12 (dd, *J* = 9.4, 2.3 Hz, 1H, H-4), 3.73 (td, *J* = 5.1, 2.4 Hz, 1H, H-5), 3.61 (dd, *J* = 9.4, 4.5 Hz, 1H, H-3), 1.55 (s, 3H, C(CH_3)), 1.37 (s, 3H, C(CH_3)), 1.24 (s, 9H, C(CH_3)$_3$) ; ^{13}C NMR (151 MHz, $CDCl_3$) δ 178.1 (*t*Bu*C*O_2C), 113.7 (*C*(CH_3)$_2$), 104.5 (C-1), 79.9 (C-2), 77.0 (C-4), 64.2 (C-6), 61.1 (C-3), 59.0 (C-5), 39.0 (*C*(CH_3)$_3$), 27.2 (C(*C*H_3)$_3$), 26.6 (C(*C*H_3)$_2$, 2C); HRMS (ESI) m/z calcd for $C_{14}H_{22}N_6O_5Na$ $[M + Na]^+$ 377.1549, found 377.1548.

242 (0.25 g, 45%) colorless oil; R_f = 0.30 (1:19 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -3.01 (*c* = 2.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) 6.08 (d, *J* = 4.9 Hz, 1H, H-1), 5.31 – 5.26 (m, 2H, H-2, H-3), 4.35 – 4.30 (m, 1H, H-5), 4.24 – 4.20 (m, 2H, H-6), 1.46 (s, 3H, C(CH_3)), 1.44 (s, 3H, C(CH_3)), 1.21 (s, 9H, C(CH_3)$_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ 178.0 (*t*Bu*C*O_2C), 156.2 (C-4), 112.9 (*C*(CH_3)$_2$), 106.6 (C-1), 101.3 (C-3), 83.3 (C-2), 63.7 (C-6), 57.6 (C-5), 39.0 (*C*(CH_3)$_3$), 28.3 (C(*C*H_3)$_3$), 27.9 (C(*C*H_3)$_2$), 27.2 (C(*C*H_3)$_2$); HRMS (ESI) m/z calcd for $C_{14}H_{21}N_3O_5Na$ [M + Na]$^+$ 334.1379, found 334.1377.

3,5-Diazido-3,5-dideoxy-6-*O*-(pivaloyl)-L-talitol (243).

Compound **241** (0.23 g, 0.64 mmol) was dissolved in 50% trifluoroacetic acid (3.0 mL), and the resulting reaction mixture was stirred at room temperature for 6 h. After completion, solution was cooled in an ice bath before the reaction was quenched by addition of saturated aqueous $NaHCO_3$. The resulting aqueous solution was extracted with ethyl acetate and the extract was washed with brine and dried over Na_2SO_4. After removal of the solvent under reduced pressure, the crude product was dissolved in anhydrous MeOH (6.4 mL) and cooled to 0 °C. To the resulting solution was treated with sodium borohydride (73 mg, 1.9 mmol) and stirred at 0 °C for 1 h before it was diluted with methanol and neutralized by addition of Amberlyst H^+. The resulting mixture was filtered, and the solvent of the filtrate was evaporated to give a crude product that was purified by flash column chromatography ($CHCl_3$/ethyl acetate 3:7) to give compound **243** (0.12 g, 60% after 2 steps) as a colorless oil; R_f = 0.33 (4:1 ethyl acetate/$CHCl_3$); $[\alpha]^{25}_D$ = -1.73 (*c* = 0.8, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.41 (dd, *J* = 11.6, 4.8 Hz, 1H, H-1), 4.36 (dd, *J* = 11.6, 8.4 Hz, 1H, H-1), 4.00 (s, 1H, H-5), 3.93 (d, *J* = 5.0 Hz, 1H, OH), 3.92 (d, *J* = 5.0 Hz, 1H, H-2), 3.87 (dd, *J* = 11.4, 3.2 Hz, 1H, H-6), 3.80 (dd, *J* = 11.4, 5.1 Hz, 1H, H-6), 3.71 (d, *J* = 2.9 Hz, 2H, H-4, H-3), 2.89 (br s, 1H, OH), 1.96 (br s, 1H, OH), 1.24 (s, 9H, C(CH_3)$_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ

178.9 (*t*Bu*C*O$_2$C), 73.5 (C-5), 71.4 (C-3), 64.7 (C-1), 63.7 (C-6), 63.3 (C-4), 61.5 (C-2), 39.1 (*C*(CH$_3$)$_3$), 27.2 (C(*C*H$_3$)$_3$); HRMS (ESI) m/z calcd for $C_{11}H_{20}N_6O_5Na$ $[M + Na]^+$ 339.1393, found 339.1398.

3,5-Diazido-3,5-dideoxy-1,2-*O*-(sulfuryl)-6-*O*-(pivaloyl)-L-talitol (244).

To a stirred solution of compound **243** (0.10 g, 0.34 mmol) in anhydrous CH_2Cl_2 (1.1 mL) at -20 °C, imidazole (81 mg, 1.2 mmol) was added followed by dropwise addition of sulfuryl chloride (45 µL, 0.54 mmol). The resulting reaction mixture was stirred at -20 °C for 1 h and allowed to warm to 20°C before it was stirred at 20°C for overnight. Then the reaction mixture was diluted with CH_2Cl_2, and the resulting organic solution was washed with water and brine. After drying over Na_2SO_4, the solvent was removed under reduced pressure to give a crude product that was purified by flash column chromatography (hexane/ethyl acetate 5:1) to give **244** (0.18 mg, 60%) as an orange oil; R_f = 0.56 (1:5 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -5.98 (*c* = 3.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.49 – 5.44 (m, 1H, H-5), 4.41 – 4.37 (m, 2H, H-1, OH), 4.32 – 4.26 (m, 2H, H-4, H-6), 4.22 (dd, *J* = 11.7, 2.1 Hz, 1H, H-6), 3.93 (dd, *J* = 8.4, 2.1 Hz, 1H, H-3), 3.77 – 3.71 (m, 1H, H-2), 1.24 (s, 9H, C(CH$_3$)$_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ 178.1 (*t*Bu*C*O$_2$C), 85.2 (C-5), 79.4 (C-3), 71.0 (C-6), 64.2 (C-1), 61.9 (C-4), 59.6 (C-2), 39.0 (*C*(CH$_3$)$_3$), 27.2 (C(*C*H$_3$)$_3$); HRMS (ESI) m/z calcd for $C_{11}H_{18}N_6O_7SNa$ $[M-H]^-$ 377.0879, found 377.0886.

3,5-Diazido-3,5-dideoxy-6-*O*-(pivaloyl)-1,4-anhydro-L-altritol (246).

A stirred solution of **244** (62 mg, 0.16 mmol) in anhydrous DMF (1.0 mL) was cooled to 0 °C and treated with sodium boron hydride (8.0 mg, 0.12 mmol). The stirring was continued for 0.5 h at room temperature before the reaction mixture was evaporated to dryness. The resulting crude product was purified by column chromatography (3:7 ethyl acetate/hexane) to give **246** (34 mg,

70%) as a colorless oil; R_f = 0.18 (1:5 ethyl acetate/hexane); $[\alpha]^{25}_D$ = +6.10 (*c* = 1.7, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.46 (td, *J* = 4.2, 2.3 Hz, 1H, H-4), 4.41 – 4.33 (m, 2H, H-6), 4.08 (dd, *J* = 10.1, 4.3 Hz, 1H, H-1), 3.97 – 3.96 (m, 2H, H-5, H-2), 3.83 (dd, *J* = 10.1, 2.5 Hz, 1H, H-1), 3.69 – 3.61 (m, 1H, H-5), 1.23 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ 178.3 (*t*Bu*C*O_2C), 79.3 (C-2), 73.9 (C-1), 72.0 (C-4), 64.5 (C-6), 64.3 (C-3), 60.4 (C-5), 39.0 (*C*$(CH_3)_3$), 27.2 (C(*C*$H_3)_3$); HRMS (ESI) m/z calcd for $C_{11}H_{18}N_6O_4Na$ $[M + Na]^+$ 321.11297, found 321.1290.

Preparation from **243**; To a stirred solution of compound **243** (30 mg, 95 µmol) in anhydrous CH_2Cl_2 (0.20 mL), PPh_3 (27 mg, 0.10 mmol) was added followed by imidazole (7.0 mg, 0.10 mmol) and iodine (27 mg, 0.10 mmol). The resulting reaction mixture was stirred at room temperature for 12 h before it was diluted with CH_2Cl_2. The resulting organic solution was washed with saturated aqueous $Na_2S_2O_3$, brine and dried over Na_2SO_4. After removal of the solvent, the crude product was purified by column chromatography (3:7 ethyl acetate/hexane) to give **246** (20 mg, 70%) with spectra identical to the above-described sample.

Methyl (Methyl 3,5-dideoxy-5-*N*-(*tert*-butoloxycarbonyl)-9-*O*-((4-methylphenyl)sulfonyl)-D-glycero-β-D-galacto-non-2-ulopyranosid)onate (251).

To a stirred solution of compound **250**[99, 120] (0.10 g, 0.25 mmol) in anhydrous CH_2Cl_2 (0.50 mL), dibutyltin oxide (1.5 mg, 20 µmol) and *p*-toluenesulfonyl chloride (54 mg, 0.28 mmol) were added followed by triethyl amine (39 µL, 0.28 mmol). The resulting mixture was stirred at room temperature for 1.5 h before it was filtered through Celite, and after removal of the solvent under reduced pressure, the crude product was purified by flash column chromatography (hexane/ethyl acetate 3:7) to give compound **251** (0.11 g, 79%) as a white foam; R_f = 0.75 (1:8 methanol/ ethyl acetate); $[\alpha]^{25}_D$ = -2.8 (*c* = 0.50, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.75 (m, 3H, Ar), 7.34 (d, *J* = 8.1 Hz, 3H, Ar), 5.07 (d, *J* = 8.4 Hz, 1H, NH), 4.37 (dd, *J* = 10.2, 2.3 Hz, 1H, H-9),

4.20 (dd, *J* = 10.2, 5.8 Hz, 1H, H-9), 4.11 (dd, *J* = 8.5, 5.9 Hz, 1H, H-8), 3.96 (td, *J* = 10.3, 4.7 Hz, 1H, H-4), 3.76 (s, 3H, CO_2CH_3), 3.74 – 3.65 (m, 1H, H-6), 3.63 – 3.51 (m, 2H, H-7, H-5), 3.21 (s, 3H, OCH_3), 2.44 – 2.39 (m, 4H, H-3_{eq}, $ArCH_3$), 1.70 (t, *J* = 12.0 Hz, 1H, H-3_{ax}), 1.42 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.9 (CO_2Me), 157.9 ($HNCO_2$*t*Bu), 145.2 (Ar), 132.5 (Ar), 130.1 (Ar), 128. (Ar)1, 99.1 (C-2), 81.1 (*C*$(CH_3)_3$), 73.0 (C-9), 71.4 (C-6), 68.6 (C-7), 68.4 (C-8), 67.1 (C-4), 53.7 (C-5), 52.9 (CO_2*C*H_3), 51.2 (OCH_3), 40.3 (C-3), 28.4 (C(*C*$H_3)_3$), 21.8 ($ArCH_3$); HRMS (ESI) m/z calcd for $C_{23}H_{35}NO_{12}SNa$ $[M+Na]^+$ 572.1778, found 572.1778.

Methyl (Methyl 8,9-anhydro-3,5-dideoxy-5-*N*-(*tert*-butoloxycarbonyl)-D-glycero-β-D-galacto-non-2-ulopyranosid)onate (252).

A stirred solution of compound **251** (50 mg, 90 μmol) in anhydrous THF (0.50 mL) was treated with potassium tertiary butoxide (16 mg, 0.14 mmol) and resulting solution was heated to reflux for 1.5 h. After completion, the reaction mixture was diluted with CH_2Cl_2 and neutralized by addition of Amberlyst H^+ followed by filtered through Celite. Removal of the solvent under reduce pressure gave compound **252** (28 mg, 82%) as a white solid; R_f = 0.17 (7:3 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -4.8 (*c* = 0.50, $CHCl_3$) ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.83 (d, *J* = 7.8 Hz, 1H, NH), 4.44 (br s, 1H, OH), 4.10 – 3.91 (m, 1H, H-4), 3.80 (s, 3H, CO_2CH_3), 3.65 (q, *J* = 9.2, 8.5 Hz, 1H, H-5), 3.54 (d, *J* = 10.2 Hz, 1H, H-6), 3.38 – 3.26 (m, 2H, H-7, H-8), 3.26 (s, 3H, OCH_3), 2.90 (t, *J* = 4.3 Hz, 1H, H-9), 2.75 (dd, *J* = 5.1, 2.2 Hz, 1H, H-9), 2.47 (dd, *J* = 12.9, 5.1 Hz, 1H, H-3_{eq}), 1.86 – 1.75 (m, 1H, H-3_{ax}), 1.42 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.8 (CO_2Me), 157.6 ($HNCO_2$*t*Bu), 99.3 (C-2), 81.2 (*C*$(CH_3)_3$), 73.4 (C-6), 70.5 (C-7), 67.4 (C-4), 53.8 (C-5), 52.9 (CO_2*C*H_3), 51.4 (C-8), 51.1 (OCH_3), 47.7 (C-9), 40.5 (C-3), 28.4 ($C(CH_3)_3$); HRMS (ESI) m/z calcd for $C_{16}H_{27}NO_9Na$ $[M+Na]^+$ 400.1580, found 400.1584.

***tert*-Butyl ((1*S*,4*S*,5*R*,6*R*,7*R*)-4-((*S*)-1,2-dihydroxyethyl)-7-hydroxy-1-methoxy-3,9-dioxabicyclo[3.3.1]nonan-6-yl)carbamate (253).**

The compound **252** (19 mg, 50 µmol) was dissolved in anhydrous methanol (0.26 mL) and cooled to 0 °C followed by addition of sodium borohydride (4.0 mg, 1.0 mmol). After stirring at 0 °C for 1 h, the reaction mixture was quenched by addition of saturated aqueous NH_4Cl and evaporated to dryness. The resulting crude product was purified by flash column chromatography (ethyl acetate/methanol 20:1) to give compound **253** (11 mg, 63%) as a colorless oil; R_f = 0.45 (1:19 methanol/ethyl acetate); $[\alpha]^{25}_D$ = -3.3 (*c* = 0.60, MeOH); ^{1}H NMR (600 MHz, CD_3OD) δ 4.34 (t, *J* = 9.8 Hz, 1H, H-4`), 4.03 (ddd, *J* = 10.4, 9.1, 5.2 Hz, 1H, H-2), 3.97 (t, *J* = 9.9 Hz, 1H, H-5), 3.88 – 3.83 (m, 2H, H-5`, H-6`), 3.81 – 3.76 (m, 1H, H-6`), 3.70 (d, *J* = 11.9 Hz, 1H, H-2`), 3.45 (d, *J* = 11.9 Hz, 1H, H-2`), 3.29 – 3.25 (m, 3H, OCH_3), 2.99 (t, *J* = 9.5 Hz, 1H, H-4), 2.29 (dd, *J* = 13.8, 5.1 Hz, 1H, H-2_{eq}), 1.52 (s, 9H, $C(CH_3)_3$), 1.48 (d, *J* = 4.8 Hz, 1H, H-2_{ax}); ^{13}C NMR (151 MHz, CD_3OD) δ 159.6 ($HNCO_2$*t*Bu), 103.3 (C-1), 83.1 (*C*$(CH_3)_3$), 75.0 (C-5), 71.8 (C-5`), 70.3 (C-2`), 64.2 (C-3), 63.7 (C-4), 62.5 (C-6`), 60.4 (C-4), 48.3 (OCH_3), 40.3 (C-2), 28.5 (C(*C*$H_3)_3$); HRMS (ESI) m/z calcd for $C_{15}H_{27}NO_8Na$ $[M + Na]^+$ 372.1634, found 372.1627.

Methyl (1-Methyl 3,5-dideoxy-8,9-*O*-thiocarbonyl-5-*N*-(*tert*-butoloxycarbonyl)-D-glycero-*β*-D-galacto-non-2-ulopyranosid)onate (259).

To a stirred mixture of compound **250**[99, 120] (2.3 g, 5.8 mmol) in anhydrous CH_2Cl_2 (25 mL) at 0°C, pyridine (1.0 g, 13 mmol) was added followed by DMAP (71 mg, 0.58 mmol). The resulting reaction mixture was treated with thiophosgene (1.0 g, 8.8 mmol) and stirred for 3 h at room temperature. After completion, the mixture was directly adsorbed on silica gel and purified by flash column chromatography (toluene/acetone 4:1) to give compound **259** (1.3 g, 51%) as a white solid; R_f = 0.57 (4:1 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -7.0 (*c* = 1.6, MeOH); ^{1}H NMR (400 MHz,

CD_3OD) δ 5.15 (td, *J* = 8.2, 3.3 Hz, 1H, H-8), 4.94 (dd, *J* = 9.2, 7.5 Hz, 1H, H-9), 4.75 (t, *J* = 8.9 Hz, 1H, H-9), 4.09 (dd, *J* = 3.4, 1.7 Hz, 1H, H-7), 3.92 (ddd, *J* = 11.2, 9.4, 4.9 Hz, 1H, H-4), 3.79 (s, 3H, CO_2CH_3), 3.59 – 3.48 (m, 2H, H-6, H-5), 3.16 (s, 3H, OCH_3), 2.33 (dd, *J* = 13.0, 4.9 Hz, 1H, H-3_{eq}), 1.60 (dd, *J* = 13.0, 11.3 Hz, 1H, H-3_{ax}), 1.46 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (101 MHz, CD_3OD) δ 192.6 (CS), 168.3 (CO_2Me), 158.0 ($HNCO_2$*t*Bu), 99.0 (C-2), 83.1 (C-8), 79.6 (*C*$(CH_3)_3$), 72.8 (C-6), 70.5 (C-9), 67.7 (C-7), 65.6 (C-4), 53.0 (C-5), 51.7 (CO_2*C*H_3), 50.1 (OCH_3), 40.0 (C-3), 27.3 ($C(CH_3)_3$); HRMS (ESI) m/z calcd for $C_{17}H_{27}NO_{10}SNa$ $[M + Na]^+$ 460.1253, found 460.1263.

Methyl (Methyl 5-azido-3,5,8,9-tetradeoxy-8-en-*β*-D-galacto-non-2-ulopyranosid)onate (261).

The compound **259** (1.3 g, 3.0 mmol) was treated with triethylphosphite (10 mL) and heated to reflux for 12 h. After completion, triethylphosphite was evaporated to dryness under high vacuum before the resulting residue was dissolved in 2 M HCl in methanol and was stirred at room temperature for 1 h, after removal of solvent gave a crude amine that was dissolved in a mixture of methanol and water (1:1, 20 mL) and treated with potassium carbonate (2.0 g, 15.0 mmol), copper(II) sulfate pentahydrate (0.30 g, 1.2 mmol), and imidazole-1-sulfonyl azide hydrochloride (0.78 g, 4.5 mmol). The resulting solution was stirred at room temperature for 1 h and after completion, the reaction mixture was evaporated to dryness to give a residue that was dissolved in acetone and filtered. The filtrate was adsorbed on silica gel and purified by flash column chromatography (dichloromethane/methanol 19:1) to give compound **261** (0.43 g, 50% after 3 steps) as a brown oil ; R_f = 0.30 (1:19 methanol/DCM); $[\alpha]^{25}_D$ = -5.16 (*c* = 0.57, MeOH); ^{1}H NMR (400 MHz, CD_3OD) δ 6.05 (ddd, *J* = 17.0, 10.5, 6.3 Hz, 1H, H-8), 5.33 (dt, *J* = 17.3, 1.5 Hz, 1H, H-9), 5.18 (dt, *J* = 10.5, 1.5 Hz, 1H, H-9), 4.37 – 4.25 (m, 1H, H-7), 4.00 – 3.84 (m, 1H, H-4),

3.80 (s, 3H, CO_2CH_3), 3.46 (t, *J* = 9.9 Hz, 1H, H-5), 3.34 – 3.24 (m, 2H, H-6, OH), 3.13 (s, 3H, OCH_3), 2.28 (dd, *J* = 13.0, 5.1 Hz, 1H, H-3_{eq}), 1.64 (dd, *J* = 13.0, 11.3 Hz, 1H, H-3_{ax}); ^{13}C NMR (101 MHz, CD_3OD) δ 169.4 (CO_2Me), 137.8 (C-8), 114.9 (C-9), 99.0 (C-2), 74.9 (C-6), 70.8 (C-7), 67.9 (C-8), 63.5 (C-5), 52.0 (CO_2CH_3), 50.0 (OCH_3), 39.9 (C-3); HRMS (ESI) m/z calcd for $C_{11}H_{17}N_3O_6Na$ $[M+Na]^+$ 310.1022, found 310.1015.

Methyl (Methyl 5-azido-4,7-*O*-di(trichloroacetamido)-8-en-3,5,8,9-tetradeoxy-*β*-D-galacto-non-2-ulopyranosid)onate (262).

To a stirred solution of compound **261** (34 mg, 0.12 mmol) in anhydrous CH_2Cl_2 (0.50 mL) at 0 °C, DBU (11 mg, 71 µmmol) was added followed by trichloro acetonitrile (25 µL). The resulting solution was stirred at 0 °C for 0.5 h before it was evaporated to dryness to give a crude product that was filtered through pad of basified silica gel (40% ethyl acetate in hexane) to give crude **262**.

Data for **262**; R_f = 0.23 (1:9 ethyl acetate/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, *J* = 8.4 Hz, 2H, NH), 6.12 – 6.02 (m, 1H, H-8), 5.82 – 5.78 (m, 1H, H-7), 5.56 (dt, *J* = 17.4, 1.3 Hz, 1H, H-9), 5.42 (dd, *J* = 10.6, 1.2 Hz, 1H, H-9), 5.33 (dd, *J* = 5.1, 1.6 Hz, 1H, H-4), 3.85 – 3.74 (m, 4H, H-5, CO_2CH_3), 3.70 (dd, *J* = 10.2, 2.6 Hz, 1H, H-6), 3.25 (s, 3H), 2.79 (dd, *J* = 12.8, 5.2 Hz, 1H, H-3_{eq}), 1.84 (dd, *J* = 12.9, 11.2 Hz, 1H, H-3_{ax}).

Methyl (Methyl 5-azido-9-*O*-(*tert*-butyldiphenylsilyl)-3,5-dideoxy-D-glycero-β-D-galacto-non-2-ulopyranosid)onate (273).

A stirred solution of compound **272**[99, 120] (90 mg, 0.28 mmol) in anhydrous THF (6.0 mL) was treated with imidazole (19 mg, 0.28 mmol), DMAP (17 mg, 0.14 mmol) and *tert*-butyldiphenylsilane chloride (80 µL, 0.80 mmol). The resulting reaction mixture was stirred at room temperature for 28 h, and after completion the reaction mixture was diluted with ethyl

acetate. The resulting organic solution was washed with 1 M HCl followed by saturated aqueous $NaHCO_3$ and brine. After drying over Na_2SO_4, removal of the solvent gave a crude product that was purified by flash column chromatography (3:2 hexane/ethyl acetate) to give compound **273** (0.13 mg, 81%) as a white powder; R_f = 0.34 (2:23 methanol/ $CHCl_3$); $[\alpha]^{25}_D$ = -44.5 (*c* = 1.2, $CHCl_3$) ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (ddt, *J* = 7.9, 6.6, 1.6 Hz, 4H, Ar), 7.48 – 7.36 (m, 6H, Ar), 4.09 (ddd, *J* = 11.3, 9.5, 5.0 Hz, 1H, H-4), 3.92 (dd, *J* = 4.1, 2.5 Hz, 2H, H-9), 3.88 – 3.81 (m, 2H, H-7, H-6), 3.80 (d, *J* = 4.7 Hz, 1H, H-8), 3.77 (s, 3H, CO_2CH_3), 3.54 (t, *J* = 9.9 Hz, 1H, H-5), 3.21 (s, 3H, OCH_3), 2.73 (s, 1H, OH), 2.64 (d, *J* = 6.7 Hz, 1H, OH), 2.44 (s, 1H), 2.38 (dd, *J* = 13.1, 5.0 Hz, 1H, H-3_{eq}), 1.67 (dd, *J* = 13.1, 11.3 Hz, 1H, H-3_{ax}), 1.08 (s, 9H, $C(CH_3)_3$) ; ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.6 (CO_2CH_3), 135.6 (Ar), 135.5 (Ar), 133.0 (Ar), 132.7 (Ar), 129.9 (Ar, 2C), 127.8 (Ar, 2C), 99.0 (C-2), 70.7 (C-8), 70.5 (C-6), 69.2 (C-7), 68.3 (C-4), 64.8 (C-9), 63.3 (C-5), 52.8 (CO_2CH_3), 51.3 (OCH_3), 39.7 (C-3), 26.9 ($C(CH_3)_3$), 19.3 ($C(CH_3)_3$); HRMS (ESI) m/z calcd for $C_{27}H_{37}N_3O_8SiNa$ $[M+Na]^+$ 582.2248, found 582.2239.

Methyl (Methyl 5-azido-9-*O*-(*tert*-butyldiphenylsilyl)-4-*O*-benzoyl-3,5-dideoxy-D-glycero-β-D-galacto-non-2-ulopyranosid)onate (276).

A stirred solution of **273** (0.11 g 0.20 mmol) in anhydrous toluene (1.0 mL) was treated with phenyl boric acid (32 mg, 0.26 mmol). The resulting reaction mixture was heated to reflux for overnight before it was evaporated to dryness. The resulting crude product was dissolved in pyridine (2.0 mL) and cooled to 0 °C. Benzyl chloride (35 µL, 0.30 mmol) was added to the reaction mixture at 0 °C and stirred for 1 h at room temperature. After completion, the reaction mixture was diluted with ethyl acetate and washed with 1M HCl followed by saturated aqueous Na_2CO_3, saturated aqueous NaCl and dried over Na_2SO_4. After removal of the solvent, the crude product was dissolved in 1 M arabitol solution and stirred at room temperature for overnight before

the solution was extracted with ethyl acetate. Removal of the solvent gave a crude product that was purified by flash column chromatography (toluene/acetone 4:1) to give compound **276** (95 mg, 72% after 3 steps) as a colorless oil; R_f = 0.17 (3:7 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -60 (*c* = 1.0, $CHCl_3$) ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 – 8.03 (m, 2H, Ar), 7.69 (td, *J* = 7.9, 1.6 Hz, 4H, Ar), 7.61 – 7.55 (m, 1H), 7.48 – 7.39 (m, 8H, Ar), 5.52 (dddd, *J* = 9.7, 6.8, 5.0, 1.5 Hz, 1H, H-4), 4.01 – 3.89 (m, 5H, H-9, H-7, H-6, H-5), 3.83 (q, *J* = 4.1 Hz, 1H, H-8), 3.75 (s, 3H, CO_2CH_3), 3.26 (s, 3H, OCH_3), 2.73 (dd, *J* = 12.8, 5.1 Hz, 1H, H-3_{eq}), 2.68 (br s, 1H, OH), 2.20 (br s, 1H, OH), 1.80 (dd, *J* = 12.8, 11.3 Hz, 1H, H-3_{ax}), 1.09 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.8 (CO_2CH_3) 165.3 (CO_2Bz), 135.6 (Ar), 135.5 (Ar), 133.3 (Ar), 133.0 (Ar), 132.8 (Ar), 130.0 (Ar), 129.7 (Ar), 129.5 (Ar), 128.5 (Ar), 127.8 (Ar), 98.8 (C-2), 71.3 (C-4), 70.8 (C-8), 70.4 (C-6), 69.2 (C-7), 64.9 (C-9), 60.05 (C-5), 52.6 (CO_2CH_3), 51.4 (OCH_3), 37.1 (C-3), 26.9 ($C(CH_3)_3$), 19.3 ($C(CH_3)_3$); HRMS (ESI) m/z calcd for $C_{34}H_{41}N_3O_9SiNa$ $[M + Na]^+$ 686.2510, found 686.2504.

Methyl (Methyl 5-azido-4-*O*-(*tert*-butyldimethylsilyl)-3-deoxy-8,9-*O*-isopropylidene-D-glycero-β-D-galacto-non-2-ulopyranosid)onate (279).

To a stirred solution of compound **278**[99] (0.83 g, 2.3 mmol) in CH_2Cl_2 (20 mL), Imidazole (0.31 g, 4.6 mmol) was added followed by TBSCl (0.42 g, 2.8 mmol). The resulting reaction mixture was stirred at room temperature for 12 h before it was filtered through Celite. After evaporation of the reaction mixture to dryness, the crude product was purified by flash column chromatography (1:2 ethyl acetate/hexane) to give **279** (0.86 g, 79%) as a white solid; R_f = 0.33 (3:7 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -61.4 (*c* = 0.70, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.18 – 4.12 (m, 2H, H-9, H-7), 4.11 – 4.05 (m, 2H, H-9, H-4), 3.82 (s, 3H, CO_2CH_3), 3.81 (t, *J* = 9.3 Hz, 1H, H-8), 3.64 (dd, *J* = 10.6, 1.2 Hz, 1H, H-6), 3.51 (dd, *J* = 10.6, 9.1 Hz, 1H, H-5), 3.24 (s, 3H, OCH_3), 2.39 (d, *J* = 11.7 Hz, 1H, OH), 2.27 (dd, *J* = 13.2, 5.1 Hz, 1H, H-3_{eq}), 1.69 (dd, *J* = 13.2, 11.0 Hz,

1H, H-3_{ax}), 1.43 (s, 3H, $C(CH_3)_2$), 1.32 (s, 3H, $C(CH_3)_2$), 0.92 (s, 9H, $C(CH_3)_3$), 0.19 (s, 3H, $SiCH_3$), 0.13 (s, 3H, $SiCH_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.5 (CO_2Me), 109.3 ($C(CH_3)_2$), 99.2 (C-2), 75.0 (C-7), 70.8 (C-6), 70.5 (C-8), 69.3 (C-4), 67.5 (C-9), 63.6 (C-5), 52.8 (CO_2CH_3), 51.1 (OCH_3), 40.8 (C-3), 27.0 ($C(CH_3)_2$), 25.7 ($C(CH_3)_2$), 25.4 ($C(CH_3)_3$), 17.8 ($C(CH_3)_3$), -4.6 ($SiCH_3$), -5.0 ($SiCH_3$); HRMS (ESI) m/z calcd for $C_{20}H_{37}O_8N_3SiNa$ $[M+Na]^+$ 498.2242, found 498.2227.

Methyl (Methyl 5-azido-4-*O*-(*tert*-butyldimethylsilyl)-3-deoxy-D-glycero-β-D-galacto-non-2-ulopyranosid)onate (280).

A stirred solution of compound **279** (0.86 g, 1.8 mmol) in CH_2Cl_2 (30 mL) was cooled to 0 °C before 50% TFA (2.3 mL) was added. The reaction mixture was warmed to room temperature and stirred at the same temperature for 2 h. After completion, solid Na_2CO_3 was added to the mixture and filtered through Celite. After removal of the solvent, the crude product was purified using flash column chromatography (1:19 MeOH/CH_2Cl_2) to give **280** (0.66 g, 83%) as a white foam; R_f = 0.13 (1:19 methanol/CH_2Cl_2); $[\alpha]^{25}_D$ = -29.3 (*c* = 0.15, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.06 (ddd, *J* = 10.9, 9.1, 4.9 Hz, 1H, H-4), 3.92 (d, *J* = 9.8 Hz, 1H, H-9), 3.89 – 3.78 (m, 2H, H-9, H-7), 3.82 – 3.80 (m, 4H, H-8, CO_2CH_3), 3.74 (d, *J* = 10.5 Hz, 1H, H-6), 3.52 (dd, *J* = 10.5, 9.2 Hz, 1H, H-5), 3.28 (d, *J* = 10.0 Hz, 1H, OH), 3.23 (s, 3H, OCH_3), 2.87 (br s, 1H, OH), 2.77 (d, *J* = 5.9 Hz, 1H, OH), 2.26 (dd, *J* = 13.1, 5.0 Hz, 1H, H-3_{eq}), 1.66 (dd, *J* = 13.1, 10.9 Hz, 1H, H-3_{ax}), 0.90 (s, 9H, $C(CH_3)_3$), 0.17 (s, 3H, $SiCH_3$), 0.11 (s, 3H, $SiCH_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ 169.3 (CO_2Me), 99.4 (C-2), 71.2 (C-8), 70.7 (C-6), 70.0 (C-7), 69.5 (C-4), 64.4 (C-9), 63.9 (C-5), 53.1 (CO_2CH_3), 51.4 (OCH_3), 40.9 (C-3), 25.8 ($C(CH_3)_3$), 18.0 ($C(CH_3)_3$), -4.4 ($SiCH_3$), -4.9 ($SiCH_3$); HRMS (ESI) m/z calcd for $C_{17}H_{33}O_8N_3SiNa$ $[M+Na]^+$ 458.1929, found 458.1908.

General procedure for cleavage of the side chain and synthesis of aldehyde GP1.

A stirred 0.05 M solution of compound **280** in acetone/water (1:1) was treated with $NaIO_4$ (4 equiv) and the resulting solution was stirred at room temperature for 5 h before the acetone was evaporated. The resulting aqueous residual was extracted with ethyl acetate and the extracts were washed with brine and dried over Na_2SO_4. After removal of the solvent, the crude aldehyde was used directly for the next step.

Methyl (Methyl 5-azido-4-*O*-(*tert*-butyldimethylsilyl)-3,8,9-trideoxy-9-*C*-trimethylsilyl-8-yn-D-galacto-β-non-2-ulopyranosid)onate (289) Methyl (Methyl 5-azido-4-*O*-(*tert*-butyldimethylsilyl)-3,8,9-trideoxy-9-*C*-trimethylsilyl-8-yn-L-α-altro-non-2-ulopyranosid)onate (290).

The aldehyde was prepared from **280** (35 mg, 80 µmol), acetone/water (1.6 mL) and $NaIO_4$ (52 mg, 0.24 mmol) according to GP1. A stirred solution of the crude aldehyde in anhydrous THF (0.60 mL) at 0 °C was treated with 0.18 M solution of lithium TMS-acetylide (0.45 mL). The resulting reaction mixture was stirred at the same temperature for 15 min before it was quenched by addition of aqueous NH_4Cl. The resulting aqueous solution was extracted with ether and the extract was washed with brine and dried over Na_2SO_4. After removal of solvent, a mixture of diastereomers (**289:290** 2.9:1) was separated by column chromatography (1:9 ethyl acetate/hexane).

289; (8.0 mg, 23%) colorless oil; R_f = 0.22 (1:4 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -30 (*c* = 0.10, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.71 (d, *J* = 3.3 Hz, 1H, H-7), 4.02 (ddd, *J* = 10.9, 9.1, 5.1 Hz, 1H, H-4), 3.81 (s, 3H, CO_2CH_3), 3.49 (dd, *J* = 10.4, 3.3 Hz, 1H, H-6), 3.41 – 3.30 (m, 1H, H-5), 3.22 (s, 3H, OCH_3), 2.27 (dd, *J* = 13.2, 5.1 Hz, 1H, H-3$_{eq}$), 1.72 (dd, *J* = 13.2, 10.9 Hz, 1H, H-

3_{ax}), 0.91 (s, 9H, $C(CH_3)_3$), 0.21 (d, *J* = 0.8 Hz, 9H, TMS), 0.17 (s, 3H, $SiCH_3$), 0.12 (s, 3H, $SiCH_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.3 (CO_2Me), 101.6 (C-8), 99.2 (C-2), 92.6 (C-9), 73.5 (C-6), 69.2 (C-4), 65.6 (C-5), 63.3 (C-7), 52.9 (CO_2CH_3), 51.2 (OCH_3), 40.9 (C-3), 25.8 ($C(CH_3)_3$), 18.0 ($C(CH_3)_3$), -0.1 (TMS), -4.5 ($SiCH_3$), -4.9 ($SiCH_3$); HRMS (ESI) m/z calcd for $C_{20}H_{37}O_6N_3Si_2Na$ $[M+Na]^+$ 494.2113, found 494.2091.

290; (6.0 mg, 17%) colorless oil; R_f = 0.38 (1:4 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -80 (*c* = 0.10, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 4.65 (d, *J* = 1.5 Hz, 1H, H-7), 4.02 (ddd, *J* = 10.8, 9.0, 5.0 Hz, 1H, H-4), 3.82 (s, 3H, CO_2CH_3), 3.49 – 3.42 (m, 1H, H-5), 3.39 (dd, *J* = 10.4, 1.5 Hz, 1H, H-6), 3.27 (s, 3H, OCH_3), 2.24 (dd, *J* = 13.2, 5.1 Hz, 1H, H-3_{eq}), 1.72 (dd, *J* = 13.2, 10.8 Hz, 1H, H-3_{ax}), 0.90 (s, 9H, $C(CH_3)_3$), 0.16 (s, 3H, $SiCH_3$), 0.14 (s, 9H, TMS), 0.11 (s, 3H, $SiCH_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.4 (CO_2Me), 104.0 (C-8), 99.4 (C-2), 90.0 (C-9), 74.4 (C-6), 69.6 (C-4), 63.8 (C-5), 61.8 (C-7), 52.9 (CO_2CH_3), 51.0 (OCH_3), 40.9 (C-3), 25.8 ($C(CH_3)_3$), 18.0 ($C(CH_3)_3$), -0.1 (TMS), -4.4 ($SiCH_3$), -4.9 ($SiCH_3$); HRMS (ESI) m/z calcd for $C_{20}H_{37}O_6N_3Si_2Na$ $[M+Na]^+$ 494.2113, found 494.2091.

General procedure for synthesis of Mosher esters GP2.

A stirred solution of alcohol (5.0 mg, 11 µmol) in anhydrous CH_2Cl_2 (0.10 mL) at 0 °C was treated with Et_3N (50 µL, 12 µmol), DMAP (1.3 mg, 11 µmol) and (*S*)-Mosher acid (2.5 mg, 11 µmol). The stirring was continued at room temperature for overnight before the reaction mixture was evaporated to dryness to give a crude ester that was purified by column chromatography (1:19 ethyl acetate/hexane) to give pure Mosher ester.

Methyl (Methyl 5-azido-4-*O*-(*tert*-butyldimethylsilyl)-3,8,9-trideoxy-7-*O*-(3,3,3-trifluoro-2-methoxy-2-phenylpropanoyl)-9-*C*-trimethylsilyl-8-yn-D-galacto-β-non-2-ulopyranosid)onate (292).

Prepared from **289** according to GP2 and obtained **292** (1.0 mg, 15%) as a colorless oil; R_f = 0.63 (1:4 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -8.0 (*c* = 0.10, $CHCl_3$); ^{1}H NMR (900 MHz, $CDCl_3$) δ 7.60 (dt, *J* = 6.7, 1.5 Hz, 2H, Ar), 7.41 – 7.35 (m, 3H, Ar), 5.95 (d, *J* = 2.0 Hz, 1H, H-7), 3.92 (ddd, *J* = 10.9, 9.1, 5.1 Hz, 1H, H-4), 3.78 (s, 3H, CO_2CH_3), 3.64 (s, 3H, OCH_3), 3.52 (dd, *J* = 10.4, 2.1 Hz, 1H, H-6), 3.18 (dd, *J* = 10.3, 9.1 Hz, 1H, H-5), 3.05 (s, 3H, OCH_3), 2.16 (dd, *J* = 13.1, 5.1 Hz, 1H, H-3_{eq}), 1.58 (dd, *J* = 13.2, 11.0 Hz, 1H, H-3_{ax}), 0.89 (s, 9H, $C(CH_3)_3$), 0.21 (s, 9H, TMS), 0.14 (s, 3H, $SiCH_3$), 0.08 (s, 3H, $SiCH_3$); ^{13}C NMR (226 MHz, $CDCl_3$) δ 168.0 (CO_2Me), 165.1 ($CO2C_q$), 132.6 (Ar), 129.7 (Ar), 128.5 (Ar), 127.5 (Ar), 99.3 (C-2), 96.5 (C-8), 95.2 (C-9), 72.9 (C-6), 68.9 (C-4), 65.9 (C-7), 64.4 (C-5), 55.7 (OCH_3), 52.7 (CO_2CH_3), 51.0 (OCH_3), 40.7 (C-3), 25.8 ($C(CH_3)_3$), 18.0 ($C(CH_3)_3$), 1.2 (TMS), -4.5 ($SiCH_3$), -4.9 ($SiCH_3$); HRMS (ESI) m/z calcd for $C_{30}H_{44}O_8N_3F_3Si_2Na$ $[M+Na]^+$ 710.2511, found 710.2477.

Methyl (Methyl 5-azido-4-*O*-(*tert*-butyldimethylsilyl)-3,8,9-trideoxy-7-*O*-(3,3,3-trifluoro-2-methoxy-2-phenylpropanoyl)-9-*C*-trimethylsilyl-8-yn-L-altro-α-non-2-ulopyranosid)onate (293).

Prepared from **290** according to GP2 and obtained **293** (1.5 mg, 20%) as a colorless oil; R_f = 0.63 (1:4 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -40 (*c* = 0.10, $CHCl_3$); ^{1}H NMR (900 MHz, $CDCl_3$) δ 7.59 (d, J = 8.0 Hz, 2H, Ar), 7.42 – 7.41 (m, 3H, Ar), 5.85 (d, J = 3.3 Hz, 1H, H-7), 3.98 (ddd, J = 11.0, 9.0, 5.1 Hz, 1H, H-4), 3.77 (s, 3H, CO_2CH_3), 3.57 (s, 3H, OCH_3), 3.56 – 3.55 (m, 1H, H-6), 3.24 (s, 3H, OCH_3), 3.16 (dd, J = 10.4, 9.0 Hz, 1H, H-5), 2.22 (dd, J = 13.1, 5.1 Hz, 1H, H-3_{eq}), 1.69 (dd, J = 13.2, 11.0 Hz, 1H, H-3_{ax}), 0.90 (s, 9H, $C(CH_3)_3$), 0.16 (s, 3H, $SiCH_3$), 0.15 (s, 9H, TMS),

0.10 (s, 3H, $SiCH_3$); ^{13}C NMR (226 MHz, $CDCl_3$) δ 168.0 (CO_2Me), 165.7 (CO_2C_q), 131.7 (Ar), 129.9 (Ar), 128.6 (Ar), 128.0 (Ar), 99.2 (C-2), 97.6 (C-8), 93.9 (C-7), 72.7 (C-6), 69.6 (C-4), 65.8 (C-7), 64.6 (C-5), 55.6 (OCH_3), 52.8 (CO_2CH_3), 51.1 (OCH_3), 40.8 (C-3), 25.8 ($C(CH_3)_3$), 18.0 ($C(CH_3)_3$), -0.4 (TMS), -4.5 ($SiCH_3$), -4.9 ($SiCH_3$); HRMS (ESI) m/z calcd for $C_{30}H_{44}O_8N_3F_3Si_2Na$ $[M+Na]^+$ 710.2511, found 710.2477.

Methyl (Methyl 4-*O*-(*tert*-butyldimethylsilyl)-5-en-5,3-dideoxy-D-glycero-β-hept-6-ulo-2,6-pyranosid)uronate aldose (294).

The aldehyde was prepared from **280** (0.10 g, 0.27 mmol), acetone/water (2.0 mL) and $NaIO_4$ (0.20 g, 1.3 mmol) according to GP1. Pre-dried $Zn(OTf)_2$ (0.11 g, 0.30 mmol) was dissolved in anhydrous toluene (0.50 mL) and Et_3N (51 µL, 0.37 mmol), TMS-acetylene (51 µL, 0.37 mmol) were added and stirred at room temperature for 0.5 h before the solution of the crude aldehyde in toluene (0.40 mL) was added. The stirring was continued at 60 °C for 7 h and the reaction mixture was evaporated to dryness. The crude product that was purified using column chromatography (2:3 ethyl acetate/hexane) to give **294** (46 mg, 52% after 2 steps) as a white solid; R_f = 0.35 (3:17 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -86.7 (*c* = 0.60, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 9.24 (s, 1H, H-1), 5.88 (dd, *J* = 2.7, 1.4 Hz, 1H, H-3), 4.72 (ddd, *J* = 9.2, 6.6, 2.6 Hz, 1H, H-4), 3.83 (s, 3H, CO_2CH_3), 3.35 (s, 3H, OCH_3), 2.35 (dd, *J* = 13.2, 6.5, 1H, H-3_{eq}), 2.03 (dd, *J* = 13.3, 9.2 Hz, 1H, H-3_{ax}), 0.90 (s, 9H, $C(CH_3)_3$), 0.13 (s, 3H, $SiCH_3$), 0.11 (s, 3H, $SiCH_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ 186.6 (C-1), 168.3 (CO_2Me), 145.7 (C-2), 119.5 (C-3), 95.7 (C-6), 64.5 (C-4), 53.1 (CO_2CH_3), 51.3 (OCH_3), 38.0 (C-5), 25.6 ($C(CH_3)_3$), 18.0 ($C(CH_3)_3$), -4.5 ($Si(CH_3)_2$); HRMS (ESI) m/z calcd for $C_{15}H_{26}O_6SiNa$ $[M+Na]^+$ 353.1390, found 353.1375.

Methyl (Methyl 5-azido-4-*O*-(*tert*-butyldimethylsilyl)-3-deoxy-L-arabino-α-hept-2-diulopyranosid)onate (295).

The aldehyde was prepared from **280** (0.10 g, 0.27 mmol), acetone/water (2.0 mL) and $NaIO_4$ (0.20 g, 1.3 mmol) according to GP1. The crude aldehyde was dissolved in THF/*t*BuOH (1:1 2.0 mL) and cooled to 0 °C. The resulting reaction mixture was treated with water (1.0 mL), 2-butyl-2-butene (0.50 mL), NaH_2PO_4 (0.19 g, 1.6 mmol), $NaClO_2$ (0.20 g, 2.3 mmol) and stirred at 0 °C for 1 h. After completion, the reaction mixture was diluted with ethyl acetate and the organic layer was decanted before it was washed with brine. The organic layer was dried over Na_2SO_4 and after removal of solvent, the crude acid was purified by flash column chromatography (3:17 MeOH/$CHCl_3$) to give **295** (81 mg, 88%) as a colorless oil; R_f = 0.47 (3:17 methanol/ $CHCl_3$); $[\alpha]^{25}_D$ = -18.6 (*c* = 0.22, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.03 – 3.95 (m, 1H, H-4), 3.88 (d, *J* = 10.4 Hz, 1H, H-6), 3.84 (s, 3H, CO_2CH_3), 3.54 (dd, *J* = 10.4, 9.1 Hz, 1H, H-5), 3.28 (s, 3H, OCH_3), 2.28 (dd, *J* = 13.3, 5.1 Hz, 1H, H-3_{eq}), 1.78 (dd, *J* = 13.3, 11.0 Hz, 1H, H-3_{ax}), 0.90 (s, 9H, $C(CH_3)_3$), 0.17 (s, 3H, $SiCH_3$), 0.11 (s, 3H, $SiCH_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.8 (CO_2H), 168.2 (CO_2Me), 99.8 (C-2), 71.5 (C-6), 68.7 (C-4), 64.8 (C-5), 53.3 (CO_2CH_3), 51.5 (OCH_3), 40.5 (C-3), 25.8 ($C(CH_3)_3$), 18.0 ($C(CH_3)_3$), -4.5 ($SiCH_3$), -4.9 ($SiCH_3$); HRMS (ESI) m/z calcd for $C_{15}H_{27}O_7N_3SiNa$ $[M+Na]^+$ 412.1511, found 412.1492.

Methyl (Methyl 5-azido-4-*O*-(*tert*-butyldimethylsilyl)-3,7,8,9-tetradeoxy-9-*C*-trimethylsilyl-8-yn-L-arabino-α-non-2-diulopyranosid)onate (299).

To a stirred solution of **295** (50 mg, 0.12 mmol) in anhydrous CH_2Cl_2 (1.4 mL) at 0 °C, oxalyl chloride (19 mg, 0.14 mmol) was added followed by drop of anhydrous DMF. The stirring was continued at same temperature for 1 h before it was evaporated to dryness. After drying, the resulting crude acid chloride was dissolved in anhydrous THF (1.4 mL) and cooled to 0 °C before

it was treated with 0.1 M lithium TMS-acetylide (0.85 equiv). After completion, the reaction mixture was quenched by adding saturated aqueous NH_4Cl and extracted with ether. The extract was washed with brine and dried over Na_2SO_4. After removal of the solvent, the crude ketone was purified using column chromatography (1:19 ethyl acetate/hexane) to give **299** (7.0 mg, 12%) as a colorless oil; R_f = 0.36 (1:9 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -174 (*c* = 0.30, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.98 (ddd, *J* = 11.0, 9.1, 5.2 Hz, 1H, H-4), 3.82 (s, 3H, CO_2CH_3), 3.80 (d, *J* = 10.4 Hz, 1H, H-6), 3.51 (dd, *J* = 10.4, 9.0 Hz, 1H, H-5), 3.30 (s, 3H, OCH_3), 2.26 (dd, *J* = 13.3, 5.2 Hz, 1H, H-3_{eq}), 1.76 (dd, *J* = 13.3, 11.0 Hz, 1H, H-3_{ax}), 0.90 (s, 9H, $C(CH_3)_3$), 0.27 (s, 9H, TMS), 0.16 (s, 3H, $SiCH_3$), 0.11 (s, 3H, $SiCH_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ 180.9 (C_7OC_8), 167.8 (CO_2Me), 103.2 (C-8), 100.5 (C-9), 99.9 (C-2), 76.2 (C-6), 68.9 (C-4), 64.4 (C-5), 53.0 (CO_2CH_3), 51.3 (OCH_3), 40.6 (C-3), 25.8 ($C(CH_3)_3$), 18.0 ($C(CH_3)_3$), -0.7 (TMS), -4.5 ($SiCH_3$), -4.9 ($SiCH_3$); HRMS (ESI) m/z calcd for $C_{20}H_{35}O_6N_3Si_2Na$ $[M+Na]^+$ 492.1962, found 492.1968.

General procedure for synthesis of sulfinylimine GP3.

The aldehyde was prepared from **280** (90 mg, 0.21 mmol) according to GP1, and the resulting aldehyde in anhydrous CH_2Cl_2 (1.0 mL) was treated with PPTS (3.0 mg, 10 µL), Na_2SO_4 (0.15 g, 1.0 mmol) and (*S*) or (*R*) *tert*-butanesulfinamide (51 mg, 0.42 mmol), and stirred at room temperature for 36 h. After completion, the reaction mixture was filtered through Celite, and removal of the solvent afforded a crude sulfinyl imine that was purified by flash column chromatography (1:5 ethyl acetate/hexane).

Methyl (Methyl 5-azido-4-*O*-(*tert*-butyldimethylsilyl)-3,5-dideoxy-L-lyxo-α-hept-6-ulo-2,6-pyranosid)uronate 7-(*S*S)-*N*-(*tert*-butylsulfinyl)imine (302).

Prepared from **280** by using (*S*)-*tert*-butanesulfinamide according to GP3 and obtained **302** (68 mg, 70% after 2 steps) as a colorless oil; R_f = 0.58 (3:7 ethyl acetate/hexane); $[\alpha]^{25}_D$ = +30 (*c* = 0.10, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.08 (d, *J* = 5.2 Hz, 1H, H-1), 4.13 – 4.05 (m, 2H, H-4, H-2), 3.81 (s, 3H, CO_2CH_3), 3.38 (dd, *J* = 10.4, 9.0 Hz, 1H, H-3), 3.26 (s, 3H, OCH_3), 2.31 (dd, *J* = 13.2, 5.1 Hz, 1H, H-3_{eq}), 1.79 (dd, *J* = 13.3, 11.0 Hz, 1H, H-3_{ax}), 1.26 (s, 9H, $C(CH_3)_3$), 0.91 (s, 9H, $C(CH_3)_3$), 0.17 (s, 3H, $SiCH_3$), 0.13 (s, 3H, $SiCH_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.9 (CO2Me), 164.0 (C-1), 99.5 (C-6), 73.0 (C-2), 69.3 (C-4), 65.3 (C-5), 57.6 ($C(CH_3)_3$), 53.0 (CO_2CH_3), 51.4 (OCH_3), 40.7 (C-3), 25.8 ($C(CH_3)_3$), 22.6 ($C(CH_3)_3$), 18.0 ($C(CH_3)_3$), -4.4 ($SiCH_3$), -4.9 ($SiCH_3$); HRMS (ESI) m/z calcd for $C_{19}H_{36}O_6N_4SSiNa$ $[M+Na]^+$ 499.2017, found 499.2000.

Methyl (Methyl 5-azido-4-*O*-(*tert*-butyldimethylsilyl)-3,5-dideoxy-L-lyxo-α-hept-6-ulo-2,6-pyranosid)uronate 7-(*R*S)-*N*-(*tert*-butylsulfinyl)imine (303).

Prepared from **280** by using (*R*)-*tert*-butanesulfinamide according to GP3 and obtained **303** (69 mg, 72% after 2 steps) as a colorless oil; R_f = 0.58(3:7 ethyl acetate/hexane); $[\alpha]^{25}_D$ = +30 (*c* = 0.10, $CHCl_3$); ^{1}H NMR (900 MHz, $CDCl_3$) δ 8.12 (d, *J* = 3.6 Hz, 1H, H-1), 4.10 – 4.06 (m, 1H, H-2), 4.08 – 4.03 (m, 1H, H-4), 3.81 (s, 3H, CO_2CH_3), 3.52 (dd, *J* = 10.3, 9.0 Hz, 1H, C-5), 3.27 (s, 3H, OCH_3), 2.28 (dd, *J* = 13.3, 5.1 Hz, 1H, H-3_{eq}), 1.78 (dd, *J* = 13.3, 11.1 Hz, 1H, H-3_{ax}), 1.25 (s, 9H, $C(CH_3)_3$), 0.91 (s, 9H, $C(CH_3)_3$), 0.17 (s, 3H, $SiCH_3$), 0.12 (s, 3H, $SiCH_3$); ^{13}C NMR (226 MHz, $CDCl_3$) δ 167.9 (CO2Me), 163.9 (C-1), 99.6 (C-6), 72.2 (C-2), 69.3 (C-4), 65.3 (C-5), 57.4 ($C(CH_3)_3$), 53.0 (CO_2CH_3), 51.4 (OCH_3), 40.6 (C-5), 25.8 ($C(CH_3)_3$), 22.6 ($C(CH_3)_3$),

18.0(*C*(CH_3)$_3$), -4.5 ($SiCH_3$), -4.9 ($SiCH_3$); HRMS (ESI) m/z calcd for a $C_{19}H_{36}O_6N_4SSiNa$ $[M+Na]^+$ 499.2017, found 499.2000.

General procedure for vinyl Grignard addition to sulfinyl imine GP4.

A stirred 0.2 M solution of sulfinyl imine in anhydrous CH_2Cl_2 at -78 °C was treated with 1 M vinyl magnesium bromide (1.5 equiv). The resulting mixture was stirred at -78 °C for 5 h before it was quenched by addition of saturated aqueous NH_4Cl. The resulting aqueous solution was extracted with ether and the extract was washed with brine and dried over Na_2SO_4. The removal of solvent gave the pure addition product.

Methyl (Methyl 5-azido-4-*O*-(*tert*-butyldimethylsilyl)-7-(*S*s)-*N*-(*tert*-butylsulfinyl)amino-8-en-3,8,9-trideoxy-β-D-galacto-non-2-ulopyranosid)onate (305).

Prepared from **302** (54 mg, 0.11 mmol) with vinyl magnesium bromide (0.17 mL, 0.17 mmol) according to GP4 and gave **305** (49 mg, 97%) as a colorless oil; R_f = 0.19 (3:7 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -14 (*c* = 1.5, $CHCl_3$); ^{1}H NMR (900 MHz, $CDCl_3$) δ 5.91 (ddd, *J* = 17.2, 10.2, 8.6 Hz, 1H, H-8), 5.36 – 5.31 (m, 2H, H-9), 4.15 (td, *J* = 8.9, 2.8 Hz, 1H, H-7), 4.02 (ddd, *J* = 11.0, 9.1, 5.0 Hz, 1H, H-4), 3.94 (d, *J* = 9.4 Hz, 1H, NH), 3.80 (s, 3H, CO_2CH_3), 3.71 (dd, *J* = 10.6, 2.8 Hz, 1H, H-6), 3.28 (s, 3H, OCH_3), 3.14 (dd, *J* = 10.6, 9.1 Hz, 1H, H-5), 2.24 (dd, *J* = 13.2, 5.0 Hz, 1H, H-3$_{eq}$), 1.64 (dd, *J* = 13.2, 11.0 Hz, 1H, H-3$_{eq}$), 1.20 (s, 9H, C(CH_3)$_3$), 0.89 (s, 9H, C(CH_3)$_3$), 0.16 (s, 3H, $SiCH_3$), 0.11 (s, 3H, $SiCH_3$); ^{13}C NMR (226 MHz, $CDCl_3$) δ 168.4 (CO_2Me), 133.9 (C-8), 119.3 (C-9), 99.2 (C-2), 74.6 (C-6), 69.3 (C-4), 65.6 (C-5), 60.8 (C-7), 56.2 (*C*(CH_3)$_3$), 52.8 (CO_2CH_3), 51.8 (OCH_3), 41.1 (C-3), 25.8 (C(*C*H_3)$_3$), 22.7 (C(*C*H_3)$_3$), 18.0 (*C*(CH_3)$_3$), -4.5 ($SiCH_3$), -4.9 ($SiCH_3$); HRMS (ESI) m/z calcd for $C_{21}H_{40}O_6N_4SSiNa$ $[M+Na]^+$ 527.2330, found 527.2317.

Methyl (Methyl 5-azido-4-*O*-(*tert*-butyldimethylsilyl)-7-(*R*S)-*N*-(*tert*-butylsulfinyl)amino-8-en-3,8,9-trideoxy-α-L-altro-non-2-ulopyranosid)onate (306).

Prepared from **303** (34 mg, 71 µmol) with vinyl magnesium bromide (0.10 mL, 0.10 mmol) according to GP4 and gave **306** (31 mg, 87%) as a colorless oil; R_f = 0.37 (7:13 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -57 (*c* = 0.28, $CHCl_3$); ^{1}H NMR (900 MHz, $CDCl_3$) δ 5.92 – 5.86 (m, 1H, H-8), 5.32 (dt, *J* = 17.1, 1.5 Hz, 1H, H-9), 5.19 (dt, *J* = 10.3, 1.4 Hz, 1H, H-9), 4.24 (ddd, *J* = 8.9, 5.8, 1.7 Hz, 1H, H-7), 4.21 (d, *J* = 8.7 Hz, 1H, NH), 4.01 (ddd, *J* = 11.0, 9.2, 4.9 Hz, 1H, H-4), 3.78 (s, 3H, CO_2CH_3), 3.70 (dd, *J* = 10.4, 9.2 Hz, 1H, H-5), 3.37 (dd, *J* = 10.4, 1.8 Hz, 1H, H-6), 3.15 (s, 3H, OCH_3), 2.20 (dd, *J* = 13.2, 4.9 Hz, 1H, H-3_{eq}), 1.74 (dd, *J* = 13.2, 11.0 Hz, 1H, H-3_{ax}), 1.27 (s, 9H, $C(CH_3)_3$), 0.89 (s, 9H, $C(CH_3)_3$), 0.16 (s, 3H, $SiCH_3$), 0.09 (s, 3H, $SiCH_3$); ^{13}C NMR (226 MHz, $CDCl_3$) δ 168.3 (CO_2Me), 137.3 (C-8), 116.5 (C-9), 99.3 (C-2), 74.6 (C-6), 69.7 (C-4), 64.1 (C-5), 59.3 (C-7), 56.3 ($C(CH_3)_3$), 52.8 (CO_2CH_3), 51.1 (OCH_3), 40.9 (C-3), 25.8 ($C(CH_3)_3$), 22.9 ($C(CH_3)_3$), 18.0 ($C(CH_3)_3$), -4.5 ($SiCH_3$), -5.0 ($SiCH_3$); HRMS (ESI) m/z calcd for $C_{21}H_{40}O_6N_4SSiNa$ $[M+Na]^+$ 527.2330, found 527.2317.

General procedure for synthesis of Mosher amides GP5.

A stirred solution of Grignard addition product **305** or **306** (13 mg, 26 µmol) in MeOH (0.90 mL) at 0 °C was treated with 2 M HCl in MeOH and stirred at the 0 °C for 1 h before saturated aqueous $NaHCO_3$ was added. The resulting aqueous solution was extracted with ethyl acetate and the extract was washed with brine and dried over Na_2SO_4. After removal of the solvent, the crude amine **307** or **309** was dissolved in pyridine (0.30 mL) and cooled to 0 °C. The resulting solution was treated with DMAP (1.0 mg) and (*S*)-Mosher acid (10 mg, 39 µmol) at 0 °C, and was allowed to warm to room temperature with stirring for overnight before it was evaporated to dryness. The

crude amide was purified by column chromatography (1:17 ethyl acetate/hexane) to give pure Mosher amide.

Data for **307**; ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.99 (ddd, J = 17.2, 10.2, 8.6 Hz, 1H, H-8), 5.27 – 5.19 (m, 2H, H-9), 3.99 (ddd, J = 10.9, 9.1, 5.1 Hz, 1H, H-4), 3.80 (s, 3H, CO_2CH_3), 3.63 (dd, J = 8.7, 2.6 Hz, 1H, H-7), 3.48 (dd, J = 10.6, 2.6 Hz, 1H, H-6), 3.24 (s, 3H, OCH_3), 3.16 – 3.11 (m, 1H, H-5), 2.23 (dd, J = 13.1, 5.1 Hz, 1H, H-3_{eq}), 1.65 (dd, J = 13.2, 10.9 Hz, 1H, H-3_{ax}), 0.89 (s, 9H, $C(CH_3)_3$), 0.15 (s, 3H, $SiCH_3$), 0.10 (s, 3H, $SiCH_3$).

Data for **309**; ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.01 (ddd, *J* = 17.3, 10.3, 7.1 Hz, 1H, H-8), 5.21 (dt, *J* = 17.2, 1.3 Hz, 1H, H-9), 5.10 (dt, *J* = 10.2, 1.2 Hz, 1H, H-9), 3.99 (ddd, *J* = 11.0, 9.2, 5.1 Hz, 1H, H-4), 3.79 (s, 3H, CO_2CH_3), 3.61 – 3.55 (m, 2H, H-7, H-6), 3.29 (dd, *J* = 10.2, 2.4 Hz, 1H, H-5), 3.15 (s, 3H, OCH_3), 2.22 (dd, *J* = 13.1, 5.1 Hz, 1H, H-3_{eq}), 1.70 (dd, *J* = 13.1, 11.0 Hz, 1H, H-3ax), 0.90 (s, 9H, $C(CH_3)_3$), 0.16 (s, 3H, $SiCH_3$), 0.10 (s, 3H, $SiCH_3$).

Methyl (Methyl 5-azido-4-*O*-(*tert*-butyldimethylsilyl)-3,8,9-trideoxy8-en-7-*N*-(3,3,3-trifluoro-2-methoxy-2-phenylpropanoyl)-D-galacto-β-non-2-ulopyranosid)onate (308).

Obtained **308** (2.0 mg, 12%) as a colorless oil; R_f = 0.53 (3:7 ethyl acetate/hexane); $[\alpha]^{25}_{D}$ = -20 (*c* = 0.10, $CHCl_3$); ^{1}H NMR (900 MHz, $CDCl_3$) δ 7.57 – 7.52 (m, 2H, Ar), 7.37 – 7.33 (m, 2H, Ar), 7.03 (d, *J* = 9.3 Hz, 1H, Ar), 5.91 (ddd, *J* = 17.2, 10.2, 9.0 Hz, 1H, H-8), 5.51 (dt, *J* = 17.2, 1.1 Hz, 1H, H-9), 5.42 (dd, *J* = 10.1, 1.2 Hz, 1H, H-9), 4.96 (td, *J* = 9.1, 2.7 Hz, 1H, H-7), 3.93 (ddd, *J* = 10.9, 9.0, 5.0 Hz, 1H, H-4), 3.78 (s, 3H, CO_2CH_3), 3.50 (s, 3H, OCH_3), 3.29 (dd, *J* = 10.6, 2.7 Hz, 1H, H-6), 3.13 (dd, *J* = 10.6, 9.1 Hz, 1H, H-5), 2.65 (s, 3H, OCH_3), 2.17 (dd, *J* = 13.3, 5.1 Hz, 1H, H-3_{eq}), 1.62 (dd, *J* = 13.4, 11.0 Hz, 1H, H-3_{ax}), 0.88 (s, 9H, $C(CH_3)_3$), 0.14 (s, 3H, $SiCH_3$), 0.08 (s, 3H, $SiCH_3$); ^{13}C NMR (226 MHz, $CDCl_3$) δ 167.9 (CO_2Me), 165.2

($HNCOC_q$), 134.2 (C-8), 133.1 (Ar), 131.4 (Ar), 129.5 (Ar), 129.4 (Ar), 128.4 (Ar), 127.1 (Ar), 121.4 (C-9), 98.9 (C-2), 73.3 (C-6), 69.0 (C-4), 64.9 (C-5), 55.2 (OCH_3), 52.7 (CO_2CH_3), 52.4 (OCH_3), 50.2 (C-7), 40.7 (C-3), 25.7 ($C(CH_3)_3$), 17.8 ($C(CH_3)_3$), -4.7 ($SiCH_3$), -5.1 ($SiCH_3$); HRMS (ESI) m/z calcd for $C_{27}H_{39}O_7N_4F_3SiNa$ $[M+Na]^+$ 639.2432, found 639.2404.

Methyl (Methyl 5-azido-4-*O*-(*tert*-butyldimethylsilyl)-3,8,9-trideoxy-8-en-7-*N*-(3,3,3-trifluoro-2-methoxy-2-phenylpropanoyl)-L-altro-α-non-2-ulopyranosid)onate (310).

Obtained **310** (3.0 mg, 19%) as a colorless oil; R_f = 0.28 (1:4 ethyl acetate/hexane); $[\alpha]^{25}_D$ = +24 (*c* = 0.10, $CHCl_3$); ^{1}H NMR (900 MHz, $CDCl_3$) δ 7.58 – 7.55 (m, 1H, Ar), 7.50 (dd, *J* = 6.8, 2.9 Hz, 1H, Ar), 7.43 – 7.37 (m, 2H, Ar), 7.34 (d, *J* = 9.8 Hz, 1H, Ar), 5.92 – 5.83 (m, 1H, H-8), 5.25 – 5.16 (m, 2H), 5.08 – 5.06 (m, 1H, H-7), 4.04 – 3.98 (m, 1H, H-4), 3.81 (s, 3H, CO_2CH_3), 3.47 (s, 3H, OCH_3), 3.40 (d, *J* = 10.4 Hz, 1H, H-5), 3.17 (s, 3H, OCH_3), 3.12 – 3.03 (m, 1H, H-5), 2.23 (dd, *J* = 13.2, 5.0 Hz, 1H, H-3_{eq}), 1.71 – 1.62 (m, 1H, H-3_{ax}), 0.91 (s, 9H, $C(CH_3)_3$), 0.17 (s, 3H, $SiCH_3$), 0.11 (s, 3H, $SiCH_3$); ^{13}C NMR (226 MHz, $CDCl_3$) δ 168.1 (CO_2Me), 165.8 ($HNCOC_q$), 134.8 (C-8), 129.5 (Ar), 129.2 (Ar), 128.6 (Ar), 128.3 (Ar), 127.9 (Ar), 126.6 (Ar), 117.4 (C-9), 99.1 (C-2), 74.0 (C-6), 69.2 (C-4), 65.1 (C-5), 55.1 (OCH_3), 52.7 (CO_2CH_3), 51.0 (OCH_3), 50.9 (C-7), 40.8 (C-3), 25.7 ($C(CH_3)_3$), 17.8 ($C(CH_3)_3$), -4.6 ($SiCH_3$), -5.1; HRMS (ESI) m/z calcd for $C_{27}H_{39}O_7N_4F_3SiNa$ $[M+Na]^+$ 639.2432, found 639.2404.

3-(*tert*-butylsulfonyl)-1-cyclohexylpropan-1-one (317).

A stirred solution of **315**[140] (20 mg, 93 μmol) and TFA (10 mg, 93 μL) in toluene (0.50 mL) was heated to 100 °C for 16 h. After completion, solid Na_2CO_3 was added to the reaction mixture and filtered through Celite before the solvent was removed under reduced pressure. The crude product was purified by column chromatography (2:3 ethyl acetate/hexane) to give **317** (9.0 mg, 37%) as

a white solid; R_f = 0.25 (1:1 ethyl acetate/hexane); ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.20 (dd, *J* = 8.2, 6.8 Hz, 2H, H-2), 3.04 (dd, *J* = 8.3, 6.7 Hz, 2H, H-1), 2.43 (tt, *J* = 11.4, 3.5 Hz, 1H, H-$4_{cyclohex}$), 1.92 – 1.86 (m, 2H, cyclohex), 1.81 – 1.77 (m, 2H, cyclohex), 1.70 – 1.66 (m, 1H, cyclohex), 1.43 (s, 9H, $C(CH_3)_3$), 1.41 – 1.18 (m, 5H, cyclohex); ^{13}C NMR (151 MHz, $CDCl_3$) δ 210.4 (C-3), 59.2 ($C(CH_3)_3$), 51.1 (C-$4_{cyclohex}$), 40.2 (C-2), 31.2 (C-1), 28.6 (cyclohex), 25.9 (cyclohex), 25.7 (cyclohex), 23.5 ($C(CH_3)_3$); HRMS (ESI) m/z calcd for $C_{13}H_{24}O_3SNa$ $[M+Na]^+$ 283.1338, found 283.1333.

Procedure for purifying commercial 1,2-diiodoethane (GP6).

Commercial 1,2-diiodoethane (10 g) was dissolved in diethyl ether (200 mL) and washed with saturated aqueous $Na_2S_2O_3$ solution (4 × 50 mL) followed by water (50 mL).[205] The organic layer was dried over Na_2SO_4 and evaporated to dryness under reduced pressure at 0 °C to give a white solid, which was dried under vacuum for 1 h in a flask shielded from the light by aluminum foil.

Preparation of 0.1 M samarium iodide solution (GP7).

An oven-dried round bottom flask equipped with a Teflon-coated magnetic stir was purged with argon, charged with samarium metal (2 equiv), capped with a septum, and maintained under argon with the aid of a balloon. Sufficient anhydrous THF (Sigma-Aldrich, anhydrous, used as received) was added to give an eventual 0.1 M solution.[205] After which, freshly washed 1,2-diiodoethane (GP6, 1 equiv) was added and the mixture was stirred for 24 h under argon.

Procedure for purifying commercial acetaldehyde (GP8).

Commercial acetaldehyde was treated with a drop of concentrated sulfuric acid and distilled into a receiver cooled in an acetone dry ice bath.

General procedure for samarium iodide-mediated aza-pinacol reaction (GP9).

The sulfinyl imine was placed in an oven-dried round bottom flask under argon and dissolved in anhydrous THF to give a 0.2 M solution, before anhydrous *t*BuOH (3 equiv) was added. The resulting solution was cooled to -78 °C and freshly purified acetaldehyde (GP8, 5 equiv) was added under stirring. Freshly prepared 0.1 M samarium iodide solution in THF (GP7, 4-5 equiv) was then added, and stirring was continued for 20 h at -78 °C, before the reaction mixture was quenched with saturated aqueous $Na_2S_2O_3$. The resulting mixture was warmed to the room temperature, the aqueous phase was extracted with ethyl acetate, and the extracts were washed with brine. After drying over Na_2SO_4, the solvent was removed under reduced pressure to give a mixture of diastereomers that was separated by flash column chromatography.

***N*-((1R,2S)-1-cyclohexyl-2-hydroxypropyl)-2-methylpropane-2-sulfinamide (*S*s) (328).**

The sulfinyl imine **314**[140] (55 mg, 0.26 mmol) was treated with *t*BuOH (73 µL, 0.77 mmol), acetaldehyde (85 µL, 1.5 mmol) and 0.1 M SmI_2 (13 mL, 5 equiv) according to GP9 to give a crude product that was purified by flash chromatography (7:3 ethyl acetate/hexane) to give **330** as a white solid; R_f = 0.42 (4:1 ethyl acetate/hexane); $[\alpha]^{25}_D$ = +27 (*c* = 1.7, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.95 – 3.85 (m, 1H, H-1), 3.19 – 3.03 (m, 2H, H-2), 2.05 (d, *J* = 7.5 Hz, 1H, OH), 1.99 (d, *J* = 13.2 Hz, 1H, cyclohex), 1.81 – 1.73 (m, 2H, cyclohex), 1.64 (d, *J* = 11.2 Hz, 2H, cyclohex), 1.49 – 1.32 (m, 1H, cyclohex), 1.26 (s, 9H, $C(CH_3)_3$), 1.23 – 1.19 (m, *J* = 10.7 Hz, 4H, cyclohex), 1.05 – 0.99 (m, 3H, CH_3), 1.02 (q, *J* = 12.0 Hz, 1H, cyclohex); ^{13}C NMR (151 MHz, $CDCl_3$) δ 68.1 (C-1), 66.9 (C-2), 56.7 ($C(CH_3)_3$), 39.7 (cyclohex), 30.6 (cyclohex), 29.7 (cyclohex), 26.4 (cyclohex), 26.3 (cyclohex), 26.2 (cyclohex), 23.2 ($C(CH_3)_3$), 18.1 (CH_3); HRMS (ESI) m/z calcd for $C_{13}H_{27}O_2NSNa$ $[M+Na]^+$ 284.1654, found 284.1641.

(4R,5S)-4-cyclohexyl-5-methyloxazolidin-2-one (330).

To a stirred solution of compound **328** (35 mg, 0.13 mmol) in MeOH (3.0 mL), HCl in MeOH (0.30 mL, 0.65 mmol) was added. The stirring was continued for 5 h at room temperature before the reaction mixture was evaporated to dryness. The crude amine was dissolved in anhydrous dichloromethane (2.0 mL) and cooled to 0 °C. To the cold reaction mixture triethylamine (56 µL, 0.40 mmol) was added followed by triphosgene (39 mg, 0.13 mmol) and stirred at room temperature for 7 h. After completion, diluted with dichloromethane and the extract was washed with water followed by brine. After drying over Na_2SO_4, removal of the solvent afforded **330** (17 mg, 71%) as a colorless oil; $[\alpha]^{25}_D$ = -16 (*c* = 0.85, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.38 (s, 1H, NH), 4.72 (p, *J* = 6.7 Hz, 1H, H-1), 3.54 (t, *J* = 7.7 Hz, 1H, H-2), 1.78 – 1.66 (m, 4H, cyclohex), 1.56 – 1.48 (m, 2H, cyclohex), 1.35 (d, *J* = 6.6, 3H, CH_3), 1.28 – 1.21 (m, 2H, cyclohex), 1.19 – 1.13 (m, 1H, cyclohex), 1.09 – 0.84 (m, 2H, cyclohex); ^{13}C NMR (151 MHz, $CDCl_3$) δ 160.4 (HN*C*OC), 76.5 (C-1), 61.3 (C-2), 37.4 (cyclohex), 30.2 (cyclohex), 29.5 (cyclohex), 26.1 (cyclohex), 25.7 (cyclohex), 25.6 (cyclohex), 14.7 (CH_3); HRMS (ESI) m/z calcd for $C_{10}H_{17}O_2NNa$ $[M+Na]^+$ 206.1151, found 206.1147.

General procedure for side chain cleavage and synthesis of sulfinyl imines (GP10).

To a stirred 0.1 M solution of compound **339**[144] in anhydrous methanol at 0 °C, sodium metal (0.1 equiv) was added. After complete dissolution of the sodium, the solution was warmed to room temperature and stirred for 5 h or until completion before it was evaporated to dryness to give the crude product, which was dissolved in acetone/water 1:1 to give a 0.05 M solution. To this solution, sodium periodate (2.5 equiv) was added and stirring continued at room temperature for 2 h before the acetone was evaporated. The residual aqueous phase was extracted with ethyl acetate and the extracts were washed with brine, dried over Na_2SO_4, and evaporated to dryness under reduced

pressure. After drying under vacuum, the crude aldehyde was dissolved in anhydrous CH_2Cl_2 to give a 0.2 M solution and treated with Na_2SO_4 (5 equiv), PPTS (0.05 equiv), (*R*)- or (*S*)-*tert*-butylsulfinamide (2 equiv), and stirred at room temperature for 36 h. Subsequently, the crude reaction mixture was filtered through Celite, concentrated under vacuum, and purified by flash column chromatography (2:1 ethyl acetate/hexane) to give the corresponding sulfinyl imine.

General procedure for TBS protection of sulfinyl imines (GP11).

A stirred 0.1 M solution of sulfinyl imine in anhydrous THF, was treated with imidazole (3 equiv) and TBSCl (2.5 equiv) followed by heating to reflux overnight. After completion, the mixture was filtered through Celite, and the solvent was removed under vacuum to give the crude product that was purified by flash column chromatography (1:5 ethyl acetate/hexane).

General procedure for converting sulfylamines to azides followed by protection of alcohols with benzoyl group (GP12).

A stirred 0.1 M solution of aza-pinacol product in MeOH was treated with 2 M HCl in MeOH (18 equiv), and the reaction progress monitored by mass spectrometry. After cleavage of the sulfinamide, Boc, and TBS groups was observed, the reaction mixture was evaporated to dryness to give a crude amine, that was dissolved in MeOH/H_2O (1:1) to give a 0.05 M solution. The resulting solution was cooled to 0 °C and K_2CO_3 (3 equiv) was added followed by $CuSO_4.5H_2O$ (0.1 equiv) and $ImSO_2N_3$ (3 equiv). Stirring was continued at room temperature for 20 h before the reaction mixture was evaporated to dryness to give a crude product, that was redissolved in ethyl acetate and filtered through Celite. After removal of the solvent under reduced pressure, the crude diazido product was dissolved in pyridine to give a 0.2 M solution that was cooled to 0 °C. Benzoyl chloride (2.5 equiv) was added to the cold reaction mixture which was allowed to warm

to room temperature overnight before evaporation to dryness. The crude product was dissolved in ethyl acetate and the resulting organic solution was washed with saturated aqueous Na_2CO_3, brine and dried over Na_2SO_4. Removal of solvent gave a crude product that was purified by flash column chromatography.

General procedure for synthesis of 8-*O*-7-*N*-oxazolidinone derivative for the configuration assignment (GP13).

A stirred 0.1 M solution of aza-pinacol product in MeOH was treated with 2 M HCl in MeOH (10 equiv), and the reaction progress monitored by mass spectrometry. After cleavage of the sulfinamide and TBS groups was observed, the reaction mixture was quenched by addition of solid Na_2CO_3. The resulting mixture was filtered through Celite before the filtrate was evaporated to dryness. The residue was redissolved in ethyl acetate and filtered through Celite again after which concentration gave the crude amine which was dissolved in anhydrous CH_2Cl_2 to give a 0.2 M solution that was cooled 0 °C. After addition of Et_3N (3 equiv) to this solution, a 0.2 M solution of triphosgene (1 equiv) in CH_2Cl_2 was added dropwise. The resulting solution was stirred at room temperature for 3 h before the reaction mixture was evaporated to dryness to give a crude oxazolidinone product that was purified using flash column chromatography (7:3 ethyl acetate/hexane).

Methyl (1-Adamantanyl 3-*N*-(*tert*-butyloxycarbonyl)-3,5-dideoxy-6-thio-α-L-lyxo-hept-6-ulo-2,6-pyranosid)uronate (R_s)-*N*-(*tert*-butylsulfinyl)imine (341).

Prepared from compound **339** (4.2 g, 6.9 mmol) with following quantities of reagents according to general procedure GP10: -

i) Na (16 mg, 0.69 mmol), MeOH (70 mL)

ii) $NaIO_4$ (3.7 g, 17 mmol), acetone/H_2O (140 mL)

iii) PPTS (8.5 mg, 34 µmol), Na_2SO_4 (5.0 g, 35 mmol) and (*R*)- *tert*-butylsulfinamide (1.7 g, 14 mmol), CH_2Cl_2 (35 mL)

Obtained **341** (3.0 g, 74% after 3 steps) as a white foam; R_f = 0.42 (3:2 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -174 (*c* = 0.30, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$, T = 313 K) δ 8.11 (d, *J* = 5.6 Hz, 1H, H-7), 4.90 (d, *J* = 5.6 Hz, 1H, H-6), 4.88 (d, *J* = 6.1 Hz, 1H, NH), 4.11 (ddd, *J* = 11.4, 9.6, 4.9 Hz, 1H, H-4), 3.81 (s, 3H, OCH_3), 3.55 (q, *J* = 9.2 Hz, 1H, H-5), 2.54 (dd, *J* = 14.0, 5.0 Hz, 1H, H-3_{eq}), 2.00 – 1.92 (m, 6H, Ada), 1.91 – 1.82 (m, 4H, Ada, H-3_{ax}), 1.63 (s, 6H, Ada), 1.42 (s, 9H, ($C(CH_3)_3$), 1.21 (s, 9H, ($C(CH_3)_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.9 (CO_2Me), 165.4 (C-7), 156.8 ($NHCO_2$*t*Bu), 86.6 (C-2), 81.4 (*C*(CH_3)$_3$), 73.9 (C-6), 68.4 (C-4), 57.4 (C-5), 56.5 (*C*(CH_3)$_3$), 52.9 (OCH_3), 50.6 (Ada), 43.6 (Ada), 43.5 (Ada), 42.4 (C-3), 36.2 (Ada), 30.0 (Ada), 28.5 (C(*C*H_3)$_3$), 22.6 (C(*C*H_3)$_3$); HRMS (ESI) m/z calcd for $C_{27}H_{44}O_7N_2S_2Na$ $[M+Na]^+$ 595.2488, found 595.2479.

Methyl (1-Adamantanyl 5-*N*-(*tert*-butyloxycarbonyl)-3,5-dideoxy-6-thio-α-L-lyxo-hept-6-ulo-2,6-pyranosid)uronate 7-(S_s)-*N*-(*tert*-butylsulfinyl)imine (342).

Prepared from compound **339** (3.3 g, 4.4 mmol) with following quantities of reagents according to general procedure GP10: -

Na (20 mg, 0.88 mmol), MeOH (44 mL)

i) $NaIO_4$ (2.3 g, 11 mmol), acetone/H_2O (90 mL)

ii) PPTS (57 mg, 0.23 mmol), Na_2SO_4 (3.2 g, 23 mmol) and (*S*)- *tert*-butylsulfinamide (1.1 g, 9.1 mmol), CH_2Cl_2 (22 mL)

Obtained **342** (1.89g, 75% after 3 steps) as a white form; R_f = 0.35 (3:2 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -47.9 (*c* = 0.30, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$, T = 313 K) δ 8.17 (d, *J* = 4.1 Hz, 1H, H-7), 5.22 (s, 1H, NH), 4.98 (dd, *J* = 10.6, 4.1 Hz, 1H, H-6), 4.45 (d, *J* = 15.9 Hz, 1H, OH), 4.16 (td, *J* = 10.4, 9.8, 4.8 Hz, 1H, H-4), 3.83 (s, 3H, OCH_3), 3.40 (ddd, *J* = 10.6, 9.2, 6.0 Hz, 1H, H-5), 2.55 (dd, *J* = 14.1, 4.9 Hz, 1H, H-3_{eq}), 1.98 (d, *J* = 11.1 Hz, 6H, Ada), 1.87 (dd, *J* = 18.4, 7.8 Hz, 1H, H-3_{ax}), 1.83 – 1.81 (m, 3H, Ada), 1.64 (s, 6H, Ada), 1.43 (s, 9H, $C(CH_3)_3$), 1.23 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (226 MHz, $CDCl_3$) δ 170.8 (CO_2Me), 166.5 (C-7), 157.5 (NHCO_2*t*Bu), 86.3 (C-2), 81.4 (*C*$(CH_3)_3$), 72.9 (C-6), 70.1 (C-4), 57.3 (C-5), 56.3(*C*$(CH_3)_3$), 53.0 (OCH_3), 50.7 (Ada), 43.4 (Ada), 42.1 (C-3), 36.1 (Ada), 29.9 (Ada), 28.4 (C(*C*$H_3)_3$), 22.6 (C(*C*$H_3)_3$); HRMS (ESI) m/z calcd for $C_{27}H_{44}O_7N_2S_2Na$ $[M+Na]^+$ 595.2488, found 595.2479.

Methyl (1-Adamantanyl 4-*O*-(*tert*-butyldimethylsilyl)-3,5-dideoxy-5-*N*-(*tert*-butyloxycarbonyl)-6-thio-α-L-lyxo-hept-6-ulo-2,6-pyranosid)uronate 7-(R_s)-*N*-(*tert*-butylsulfinyl)imine (333).

Compound **341** (2.7 g, 4.7 mmol) was treated with imidazole (0.96 g, 14 mmol) and TBSCl (1.8 g, 12 mmol) according to the general procedure GP11 to give compound **333** (2.5 g, 77%) as a white foam; R_f = 0.84 (3:2 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -123 (*c* = 0.25, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.09 (d, *J* = 5.8 Hz, 1H, H-7), 4.93 (dd, *J* = 10.6, 5.8 Hz, 1H, H-6), 4.42 (d, *J* = 9.0 Hz, 1H, NH), 4.10 (td, *J* = 10.6, 4.9 Hz, 1H, H-4), 3.81 (s, 3H, OCH_3), 3.53 (q, *J* = 9.7 Hz, 1H, H-5), 2.37 (dd, *J* = 14.1, 5.0 Hz, 1H, H-3_{eq}), 1.99 – 1.92 (m, 6H, Ada), 1.89 (dd, *J* = 14.1, 11.0 Hz, 1H, H-3_{ax}), 1.84 (d, *J* = 12.0 Hz, 3H, Ada), 1.65 – 1.58 (m, 6H, Ada), 1.37 (s, 9H, $C(CH_3)_3$), 1.19 (s, 9H, $C(CH_3)_3$), 0.84 (s, 9H, $C(CH_3)_3$), 0.06 (d, *J* = 7.4 Hz, 6H, $Si(CH_3)_2$); ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.1 (CO_2Me), 165.4 (C-7), 155.0 (NHCO_2*t*Bu), 86.7 (C-2), 79.6 (*C*$(CH_3)_3$), 74.8 (C-6), 68.0 (C-4), 57.0 (*C*$(CH_3)_3$), 55.8 (C-5), 53.0 (OCH_3), 50.6 (Ada), 43.8 (C-3), 43.5 (Ada), 36.1

(Ada), 30.2 (Ada), 29.9 (C(CH_3)$_3$), 28.5 (C(CH_3)$_3$), 28.4 ((C(CH_3)$_3$), 2C), 25.8 (C(CH_3)$_3$), 25.7 (C(CH_3)$_3$, 2C), 22.5 (C(CH_3)$_3$), 18.0 (C(CH_3)$_3$), -4.3 ($SiCH_3$), -4.7 ($SiCH_3$); HRMS (ESI) m/z calcd for $C_{33}H_{58}O_7N_2S_2SiNa$ $[M+Na]^+$ 709.3346, found 709.3326.

Methyl (1-Adamantanyl 4-*O*-(*tert*-butyldimethylsilyl)-3,5-dideoxy-5-*N*-(*tert*-butyloxycarbonyl)-6-thio-α-L-lyxo-hept-6-ulo-2,6-pyranosid)uronate 7-(S_s)-*N*-(*tert*-butylsulfinyl)imine (338).

Compound **342** (0.93 g, 1.6 mmol) was treated with imidazole (0.33 g, 4.9 mmol) and TBSCl (1 g, 4.1 mmol) according to the general procedure GP11 to give compound **338** (0.9 g, 80%) as a white foam; R_f = 0.72 (1:1 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -32 (*c* = 0.25, $CHCl_3$); ^{1}H NMR (900 MHz, $CDCl_3$) δ 8.10 (d, *J* = 4.1 Hz, 1H, H-7), 5.09 (dd, *J* = 11.0, 4.1 Hz, 1H, H-6), 4.45 (d, *J* = 8.9 Hz, 1H, NH), 4.18 (br s, 1H, H-4), 3.83 (s, 3H, OCH_3), 3.47 (q, *J* = 9.9 Hz, 1H, H-5), 2.40 (dd, *J* = 14.2, 5.0 Hz, 1H, H-3$_{eq}$), 2.02 – 1.94 (m, 6H, Ada), 1.93 – 1.88 (m, 1H, H-3$_{ax}$), 1.85 (d, *J* = 11.8 Hz, 3H, Ada), 1.64 (s, 6H, Ada), 1.40 (s, 9H, C(CH_3)$_3$), 1.22 (s, 9H, C(CH_3)$_3$), 0.86 (s, 9H, C(CH_3)$_3$), 0.10 (s, 3H, $SiCH_3$), 0.08 (s, 3H, $SiCH_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.0 (CO_2Me), 165.0 (C-7), 154.8 ($NHCO_2tBu$), 86.7 (C-2), 79.9 (C(CH_3)$_3$), 73.7 (C-6), 68.5 (C-4), 57.0 (C(CH_3)$_3$), 56.4 (C-5), 53.0 (OCH_3), 50.7 (Ada), 43.7 (C-3), 43.5 (Ada), 36.2 (Ada), 30.0 (Ada), 28.6 (C(CH_3)$_3$), 25.8 (C(CH_3)$_3$), 22.6 ((C(CH_3)$_3$), 2C), 18.0 (C(CH_3)$_3$), -4.3 ($SiCH_3$), -4.6 ($SiCH_3$); HRMS (ESI) m/z calcd for $C_{33}H_{58}O_7N_2S_2SiNa$ $[M+Na]^+$ 709.3346, found 709.3326.

Methyl (1-Adamantanyl 4-*O*-(*tert*-butyldimethylsilyl)-7-(R_S)-*N*-(*tert*-butylsulfinyl)amino-3,5,7,9-tetradeoxy-5-*N*-(*tert*-butyloxycarbonyl)-2-thio-D-glycero-β-D-galacto-non-2-ulopyranosid)onate (332) and Methyl (1-Adamantanyl 4-*O*-(*tert*-butyldimethylsilyl)-7-(R_S)-*N*-(*tert*-butylsulfinyl)amino-3,5,7,9-tetradeoxy-5-*N*-(*tert*-butyloxycarbonyl)-2-thio-L-glycero-α-D-galacto-non-2-ulopyranosid)onate (343).

The sulfinyl imine **333** (1.5 g, 2.2 mmol) was treated with *t*BuOH (0.62 mL, 6.5 mmol), acetaldehyde (0.61 mL, 11 mmol) and 0.1 M SmI_2 (110 mL, 5 equiv) according to GP9 to give mixture of **332**, **343** and unreacted **333**, which were separated using flash chromatography (1:5 acetone/toluene). The sulfinylimine **333** (0.28 g, 19%) also was recovered after column chromatography.

332; white foam (0.64 g, 40%); R_f = 0.15 (1:9 acetone/toluene); $[\alpha]^{25}_D$ = -67 (*c* = 0.50, $CHCl_3$); ^{1}H NMR (600 MHz, C_6D_6, T = 333 K) δ 5.57 (br s, 1H, NH), 4.82 (br s, 1H, H-6), 4.53 (d, *J* = 9.1 Hz, 1H, NH), 4.16 (br s, 1H, H-8), 3.81 (d, *J* = 9.8 Hz, 1H, H-4), 3.58 (d, *J* = 9.3 Hz, 1H, H-7), 3.42 (s, 3H, OCH_3), 2.76 (dd, *J* = 14.2, 4.5 Hz, 1H, H-3_{eq}), 2.18 – 2.14 (m, 3H, Ada), 2.10 – 2.05 (m, 4H, H-3_{ax}, Ada), 1.89 – 1.81 (m, 3H, Ada), 1.58 (d, *J* = 12.1 Hz, 3H, Ada), 1.50 – 1.43 (m, 12H, Ada, $C(CH_3)_3$), 1.39 – 1.35 (m, 3H, CH_3), 1.07 (s, 9H, $C(CH_3)_3$), 0.95 (s, 9H, $C(CH_3)_3$), 0.18 (s, 3H, $SiCH_3$), 0.12 (s, 3H, $SiCH_3$); ^{13}C NMR (151 MHz, C_6D_6, T=333 K) δ 171.5 (CO_2Me), 155.6 ($NHCO_2tBu$), 86.8 (C-2), 79.3 ($C(CH_3)_3$), 69.0 (C-6), 67.7 (C-5), 63.5 (C-7), 57.0 (C-4), 56.0 ($C(CH_3)_3$), 52.0 (OCH_3), 50.2 (Ada), 45.0 (C-3), 44.1 (Ada), 36.5 (Ada), 30.5 (Ada), 28.7 ($C(CH_3)_3$), 26.1 ($C(CH_3)_3$), 22.9 ($C(CH_3)_3$), 21.8 (CH_3), 18.2 ($C(CH_3)_3$), -4.4 ($Si(CH_3)_2$); HRMS (ESI) m/z calcd for $C_{35}H_{64}O_8N_2S_2SiNa$ $[M+Na]^+$ 755.3765, found 755.3752.

343; white foam (0.22 g, 14%); R_f = 0.19 (1:9 acetone/toluene); $[\alpha]^{25}_D$ = -78 (*c* = 0.75, $CHCl_3$); ^{1}H NMR (600 MHz, C_6D_6, T = 333 K) δ 5.89 (br s, 1H, NH), 5.43 (br s, 1H, H-6), 4.90 (br s, 1H, H-

5), 4.60 (d, *J* = 9.6 Hz, 1H, NH), 4.36 (p, *J* = 5.9 Hz, 1H, H-8), 3.70 – 3.65 (m, 1H, H-4), 3.62 (ddd, *J* = 9.6, 4.3, 2.0 Hz, 1H, H-7), 3.41 (s, 3H, OCH_3), 2.79 (dd, *J* = 13.7, 4.7 Hz, 1H, H-3_{eq}), 2.15 – 2.11 (m, 3H, Ada), 2.05 – 1.98 (m, 4H, H-3_{ax}, Ada), 1.83 (s, 3H, Ada), 1.57 – 1.51 (m, 3H, Ada), 1.48 – 1.43 (m, 12H, Ada, $C(CH_3)_3$), 1.42 (d, *J* = 6.2 Hz, 3H, CH_3), 1.06 (s, 9H, $C(CH_3)_3$), 0.95 (s, 9H, $C(CH_3)_3$), 0.18 (s, 3H, $SiCH_3$), 0.12 (s, 3H, $SiCH_3$); ^{13}C NMR (151 MHz, C_6D_6, T=333 K) δ 171.2 (CO_2Me), 155.8 ($NHCO_2tBu$), 87.0 (C-2), 79.3 ($C(CH_3)_3$), 72.8 (C-6), 67.9 (C-8), 66.9 (C-5), 63.3 (C-7), 57.3 (C-4), 56.5 ($C(CH_3)_3$), 52.0 (OCH_3), 50.3 (Ada), 45.4 (C-3), 44.1 (Ada), 36.4 (Ada), 30.4 (Ada), 28.7 ($C(CH_3)_3$), 26.1 ($C(CH_3)_3$), 22.9 ($C(CH_3)_3$), 21.0 (CH_3), 18.2 ($C(CH_3)_3$), -4.4 $Si(CH_3)_2$; HRMS (ESI) m/z calcd for $C_{35}H_{64}O_8N_2S_2SiNa$ $[M+Na]^+$ 755.3765, found 755.3752.

Methyl (1-Adamantanyl 3,5,7,9-tetradeoxy-5-*N*-(*tert*-butyloxycarbonyl)-8-*O*-7-*N*-oxazolidinone-2-thio-D-glycero-β-D-galacto-non-2-ulopyranosid)onate (345).

Prepared from **332** (21 mg, 29 µmol) with the following quantities of reagents according to GP13 : -

i) HCl in MeOH (0.15 mL, 0.29 mmol), MeOH (0.30 mL)

ii) $CO(OCCl_3)_2$ (9.0 mg, 29 µmol), Et_3N (12 µL, 87 µmol), CH_2Cl_2 (0.30 mL)

Obtained **345** (8.0 mg, 52%) white solid; R_f = 0.29 (4:1 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -107 (*c* = 0.15, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 5.61 (s, 1H, NH), 4.73 (p, *J* = 6.6 Hz, 1H, H-8), 4.60 (s, 1H, NH), 4.23 (t, *J* = 8.8 Hz, 1H, H-6), 4.17 (t, *J* = 7.5 Hz, 1H, H-7), 4.05 – 3.99 (m, 1H, H-4), 3.82 (s, 3H, OCH_3), 3.36 (d, *J* = 10.2 Hz, 1H, H-5), 2.61 (dd, *J* = 14.1, 4.6 Hz, 1H, H-3_{eq}), 2.03 – 1.95 (m, 6H, Ada), 1.92 – 1.83 (m, 4H, Ada, H-3_{ax}), 1.66 (s, 6H, Ada), 1.49 – 1.44 (m, 12H, $C(CH_3)_3$, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.8 (CO_2Me), 158.3 (OCONH), 156.2

(NHCO$_2$*t*Bu), 86.0 (C-2), 81.1 (*C*(CH$_3$)$_3$), 75.3 (C-8), 71.0 (C-6), 67.4 (C-4), 58.6 (C-7), 57.7 (C-5), 53.1 (OCH$_3$), 50.8 (Ada), 43.9 (Ada), 43.0 (C-3), 36.1 (Ada), 30.0 (Ada), 28.4 (C(*C*H$_3$)$_3$), 16.8 (CH$_3$); HRMS (ESI) m/z calcd for $C_{26}H_{40}O_8N_2NaS$ $[M+Na]^+$ 563.2397, found 563.2406.

Methyl (1-Adamantanyl 3,5,7,9-tetradeoxy-5-*N*-(*tert*-butyloxycarbonyl)-8-*O*-7-*N*-oxazolidinone-2-thio-L-glycero-α-D-galacto-non-2-ulopyranosid)onate (346).

Prepared from **343** (21 mg, 29 µmol) with the following quantities of reagents according to GP13 : -

i) HCl in MeOH (0.15 mL, 0.29 mmol), MeOH (0.30 mL)

ii) CO(OCCl$_3$)$_2$ (9.0 mg, 29 µmol), Et$_3$N (12 µL, 87 µmol), CH$_2$Cl$_2$ (0.30 mL)

Obtained **346** (7.0 mg, 51%) white solid; R_f = 0.46 (4:1 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -102 (*c* = 0.35, CHCl$_3$); ^{1}H NMR (600 MHz, CDCl$_3$) δ 6.10 (s, 1H, NH), 4.83 (p, *J* = 6.1 Hz, 1H, H-8), 4.70 (d, *J* = 9.2 Hz, 1H, NH), 4.02 – 3.97 (m, 2H, H-4, H-6), 3.82 (s, 3H, OCH$_3$), 3.61 (t, *J* = 4.9 Hz, 1H, H-7), 3.40 – 3.32 (m, 1H, H-5), 2.62 (dd, *J* = 13.7, 4.6 Hz, 1H, H-3$_{eq}$), 2.01 – 2.00 (m, 3H, Ada), 1.99 – 1.95 (m, 3H, Ada), 1.85 (dd, *J* = 13.7, 11.5 Hz, 1H, H-3$_{ax}$), 1.80 (d, *J* = 11.8 Hz, 3H, Ada), 1.66 (s, 6H, Ada), 1.45 (s, 9H, C(CH$_3$)$_3$), 1.42 (d, *J* = 6.4 Hz, 3H, CH$_3$); ^{13}C NMR (151 MHz, CDCl$_3$) δ 170.5 (CO$_2$Me), 158.7 (OCONH), 156.8 (NHCO$_2$*t*Bu), 86.4 (C-2), 81.2 (*C*(CH$_3$)$_3$), 74.2 (C-8), 71.5 (C-6), 67.5 (C-4), 60.8 (C-7), 56.4 (C-5), 53.0 (OCH$_3$), 50.6 (Ada), 43.8 (Ada), 43.2 (C-3), 36.1 (Ada), 30.0 (Ada), 28.4 (C(*C*H$_3$)$_3$), 20.7 (CH$_3$); HRMS (ESI) m/z calcd for $C_{26}H_{40}O_8N_2NaS$ $[M+Na]^+$ 563.2397, found 563.2388.

Methyl (1-Adamantanyl 4-*O*-(*tert*-butyldimethylsilyl)-7-(R_S)-*N*-(*tert*-butylsulfinyl)amino-3,5,7,9-tetradeoxy-5-*N*-(*tert*-butyloxycarbonyl)-2-thio-D-β-galacto-non-2,7-diulopyranosid)onate (347).

A solution of **343** (0.10 g, 0.14 mmol) in anhydrous CH_2Cl_2 (0.70 mL), was treated with DMP (89 mg, 0.21 mmol) and stirred for 1 h at room temperature before it was diluted with ether and saturated aqueous $Na_2S_2O_3$ was added followed by saturated aqueous $NaHCO_3$. The resulting mixture was stirred until two separate layers were formed, after which the ether layer was decanted off and washed with brine, dried over Na_2SO_4, and evaporated to dryness. The crude product was purified by flash column chromatography (3:7 ethyl acetate/hexane) to give **347** as a white foam (71 mg, 70%); R_f = 0.48 (2:3 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -52 (*c* = 0.20, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.15 – 5.12 (m, 2H, H-6, NH), 4.68 – 4.63 (m, 1H, NH), 4.45 – 4.39 (m, 1H, H-4), 4.18 (d, *J* = 9.2 Hz, 1H, H-7), 3.78 (s, 3H, OCH_3), 3.17 (q, *J* = 9.4 Hz, 1H, H-5), 2.36 (dd, *J* = 13.9, 4.6 Hz, 1H, H-3_{eq}), 2.30 (s, 3H, CH_3), 1.98 – 1.93 (m, 3H, Ada), 1.92 – 1.86 (m, 3H, Ada), 1.81 – 1.70 (m, 4H, H-3_{ax}, Ada), 1.63 (s, 6H, Ada), 1.44 (s, 9H, $C(CH_3)_3$), 1.29 (s, 9H, $C(CH_3)_3$), 0.84 (s, 9H, $C(CH_3)_3$), 0.06 (d, *J* = 7.2 Hz, 6H, $Si(CH_3)_2$); ^{13}C NMR (151 MHz, $CDCl_3$) δ 206.7 (C-8), 171.3 (CO_2Me), 154.9 ($NHCO_2$*t*Bu), 86.3 (C-2), 79.6 (*C*$(CH_3)_3$), 71.6 (C-6), 66.4 (C-4), 65.5 (C-7), 56.8 (C-5), 56.5 (*C*$(CH_3)_3$), 52.8 (OCH_3), 50.2 (Ada), 44.6 (C-3), 43.6 (Ada), 36.2 (Ada), 30.0 (Ada), 28.9 (C-8), 28.6 (C(*C*$H_3)_3$), 25.9 (C(*C*$H_3)_3$), 22.9 C(*C*$H_3)_3$), 18.0 *C*$(CH_3)_3$), -4.5 ($SiCH_3$), -4.7 ($SiCH_3$); HRMS (ESI) m/z calcd for $C_{35}H_{62}O_8N_2S_2SiNa$ $[M+Na]^+$ 753.3609, found 753.3609.

Reduction of ketone (347).

The ketone **347** (0.10 g, 0.14 mmol) was dissolved in MeOH (1.4 mL) and was cooled to 0 °C followed by addition of sodium boro hydride (8.0 mg, 0.21 mmol). The reaction mixture was

stirred at the same temperature for 2 h before it was quenched by addition of saturated aqueous NH_4Cl. The aqueous phase was extracted with the ethyl acetate and the organic layer was washed with brine. After drying over Na_2SO_4, the solvent was evaporated and the resulting mixture of diastereomers (**343**:**332** 4:1) was separated by flash chromatography (1:5 acetone/toluene) to give **343** (61 mg, 60%) and **332** (19 mg, 19%) with spectra identical to the above-described samples.

Methyl (1-Adamantanyl 5,7-diazido-4,8-di-*O*-benzoyl-3,5,7,9-tetradeoxy-2-thio-D-glycero-β-D-galacto-non-2-ulopyranosid)onate (86).

Prepared from **332** (0.89 g, 1.2 mmol) with the following quantities of reagents according GP12: -

i) HCl in MeOH (11 mL, 22 mmol), MeOH (20 mL)

ii) K_2CO_3 (0.50 g, 3.6 mmol), $CuSO_4.5H_2O$ (30 mg, 0.12 mmol), $ImSO_2N_3$ (0.76 g, 3.6 mmol) and $MeOH/H_2O$ (20 mL)

iii) BzCl (0.24 mL, 2.1 mmol), Pyridine (4.0 mL)

The crude product was purified by flash column chromatography (1:19 ethyl acetate/hexane) to give **86** (0.45 g, 55% after 3 steps) as a white foam with spectral data consistent with those reported in the literature[99]; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.06 (ddd, *J* = 11.6, 8.3, 1.4 Hz, 4H, ArH), 7.60 (td, *J* = 7.3, 1.8 Hz, 2H, ArH), 7.47 (dt, *J* = 9.7, 7.6 Hz, 4H, ArH), 5.66 (ddd, *J* = 11.7, 9.7, 4.7 Hz, 1H, H-4), 5.39 (t, *J* = 6.3 Hz, 1H, H-8), 4.48 (dd, *J* = 10.1, 1.8 Hz, 1H, H-6), 3.91 – 3.84 (m, 2H, H-7, H-5), 3.79 (s, 3H, OCH_3), 2.89 (dd, *J* = 13.5, 4.7 Hz, 1H, H-3_{eq}), 1.99 (dd, *J* = 13.5, 11.7 Hz, 1H, H-3_{ax}), 1.92 – 1.86 (m, 6H, Ada), 1.73 (d, *J* = 12.0, 3H, Ada), 1.69 (d, *J* = 6.1 Hz, 3H, CH_3), 1.57 (d, *J* = 12.5 Hz, 3H, Ada), 1.46 (d, *J* = 12.3 Hz, 3H, Ada); ^{13}C NMR (151 MHz, $CDCl_3$) δ 169.8 (CO_2Me), 165.5 (CO_2Ar), 165.4 (CO_2Ar), 133.7 (Ar), 133.5 (Ar), 130.0 (Ar), 129.9 ((Ar),

2C), 129.4 (Ar), 128.7 ((Ar), 2C), 86.0 (C-2), 71.4 (C-6), 71.2 ((C-8, C-4), 2C), 64.2 (C-7), 61.7 (C-5), 52.9 (OCH_3), 50.6 (Ada), 43.4 (Ada), 40.0 (C-3), 35.9 (Ada), 29.8 (Ada), 17.4 (CH_3); HRMS (ESI) m/z calcd for $C_{34}H_{38}O_7N_6SNa$ $[M+Na]^+$ 697.2414, found 697.2408.

Methyl (1-Adamantanyl 5,7-diazido-4,8-di-*O*-benzoyl-3,5,7,9-tetradeoxy-2-thio-L-glycero-α-D-galacto-non-2-ulopyranosid)onate (344).

Prepared from **343** (0.22 g, 0.30 mmol) with the following quantities of reagents according GP12 : -

i) HCl in MeOH (2.7 mL, 5.4 mmol), MeOH (5.0 mL)

ii) K_2CO_3 (0.12 g, 0.90 mmol), $CuSO_4.5H_2O$ (8.0 mg, 30 µmol), $ImSO_2N_3$ (0.19 g, 0.90 mmol) and $MeOH/H_2O$ (4.3 mL)

iii) BzCl (87 µL, 0.75 mmol), Pyridine (1.5 mL)

The crude product was purified by flash column chromatography (1:19 ethyl acetate/hexane) to give **344** (0.10 g, 55% after 3 steps) as a white foam; R_f = 0.22 (1:4 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -19 (*c* = 0.40, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.14 (dd, *J* = 8.2, 1.4 Hz, 2H, ArH), 8.06 – 8.02 (m, 2H, ArH), 7.62 – 7.56 (m, 2H, ArH), 7.47 (td, *J* = 7.6, 5.1 Hz, 4H, ArH), 5.61 (ddd, *J* = 11.3, 9.4, 4.7 Hz, 1H, H-4), 5.55 – 5.48 (m, 1H, H-8), 4.31 (dd, *J* = 10.0, 1.8 Hz, 1H, H-6), 3.91 (t, *J* = 9.7 Hz, 1H, H-5), 3.73 (s, 3H, OCH_3), 3.70 (dd, *J* = 7.4, 1.8 Hz, 1H, H-7), 2.89 (dd, *J* = 13.7, 4.7 Hz, 1H, H-3_{eq}), 2.09 (dd, *J* = 13.7, 11.3 Hz, 1H, H-3_{ax}), 2.03 – 1.98 (m, 6H, Ada), 1.88 – 1.83 (m, 3H, Ada), 1.64 (d, *J* = 12.7 Hz, 3H, Ada), 1.61 – 1.55 (m, 3H, Ada), 1.56 (d, *J* = 6.3, 6H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 169.8 (CO_2Me), 165.8 (CO_2Ar), 165.3 (CO_2Ar), 133.9 (Ar), 133.7 (Ar), 133.4 (Ar), 133.3 (Ar), 130.1 (Ar, 2C), 130.0 (Ar), 129.9 (Ar), 129.3 (Ar), 128.8 (Ar), 128.7 (Ar), 128.6 (Ar), 128.5 (Ar), 86.0 (C-2), 72.3 (C-6), 71.4 (C-4), 71.2 (C-8), 64.2 (C-7), 61.9

(C-5), 52.8 (OCH_3), 50.9 (Ada), 43.7 (Ada), 39.8 (C-3), 36.1 (Ada), 29.9 (Ada), 18.3 (CH_3); HRMS (ESI) m/z calcd for $C_{34}H_{38}O_7N_6SNa$ $[M+Na]^+$ 697.2414, found 697.2408.

Methyl (1-Adamantanyl 4-*O*-(*tert*-butyldimethylsilyl)-7-(*S*$_S$)-*N*-(*tert*-butylsulfinyl)amino-3,5,7,8-tetradeoxy-5-*N*-(*tert*-butyloxycarbonyl)-2-thio-L-glycero-α-L-altro-non-2-ulopyranosid)onate (337) and Methyl (1-Adamantanyl 4-*O*-(*tert*-butyldimethylsilyl)-7-(*S*$_S$)-*N*-(*tert*-butylsulfinyl)amino-3,5,7,8-tetradeoxy-5-*N*-(*tert*-butyloxycarbonyl)-2-thio-D-glycero-β-L-altro-non-2-ulopyranosid)onate (348).

The sulfinyl imine **338** (0.4 g, 0.56 mmol) was treated with *t*BuOH (0.16 mL, 1.7 mmol), acetaldehyde (0.16 mL, 2.8 mmol) and 0.1 M SmI_2 (28 mL, 5 equiv) according to GP9 to give a mixture of **337**, **348** and unreacted **338**, which were separated using flash chromatography (1:5 ethyl acetate/hexane). The sulfinylimine **338** (80 mg, 20%) was recovered.

337; white foam (0.22 g, 54%); R_f = 0.28 (3:7 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -57 (*c* = 0.25, $CHCl_3$); ^{1}H NMR (900 MHz, $CDCl_3$) δ 4.66 (d, *J* = 9.7 Hz, 1H, NH), 4.52 (d, *J* = 11.2 Hz, 1H, H-6), 4.19 – 4.12 (m, 1H, NH), 3.98 (p, *J* = 6.2 Hz, 1H, H-8), 3.87 (ddd, *J* = 11.4, 9.4, 4.5 Hz, 1H, H-4), 3.83 (s, 3H, OCH_3), 3.70 (dt, *J* = 11.2, 9.6 Hz, 1H, H-5), 3.46 (dd, *J* = 11.0, 4.7 Hz, 1H, H-7), 2.36 (dd, *J* = 13.8, 4.6 Hz, 1H, H-3$_{eq}$), 1.99 – 1.98 (m, 6H, Ada), 1.96 – 1.92 (m, 3H, Ada), 1.82 (dd, *J* = 13.8, 11.2 Hz, 1H, H-3$_{ax}$), 1.69 – 1.64 (m, 6H, Ada), 1.43 (s, 9H, $C(CH_3)_3$), 1.42 (d, *J* = 6.7 Hz, 3H, CH_3), 1.21 (s, 9H, $C(CH_3)_3$), 0.85 (s, 9H, $C(CH_3)_3$), 0.09 (s, 3H, $SiCH_3$), 0.06 (s, 3H, $SiCH_3$); ^{13}C NMR (226 MHz, $CDCl_3$) δ 171.2 (CO_2Me), 156.5 ($NHCO_2tBu$), 86.0 (C-2), 79.9 ($C(CH_3)_3$), 79.0 (C-6), 70.6 (C-8), 68.5 (C-4), 62.2 (C-7), 56.3 ($C(CH_3)_3$), 56.0 (C-5), 53.0 (OCH_3), 50.4 (Ada), 43.7 (C-3), 43.6 (Ada), 36.1 (Ada), 30.0 (Ada), 28.5 ($C(CH_3)_3$), 25.8 ($C(CH_3)_3$), 22.8 ($C(CH_3)_3$), 21.7 (CH_3), 18.0 ($C(CH_3)_3$), -4.2 ($SiCH_3$), -4.7 ($SiCH_3$); HRMS (ESI) m/z calcd for $C_{35}H_{64}O_8N_2S_2SiNa$ $[M+Na]^+$ 755.3765, found 755.3740.

348; white foam (10 mg, 2%); R_f = 0.52 (3:7 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -32 (*c* = 0.10, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.67 – 4.63 (m, 1H, NH), 4.50 (d, *J* = 11.0 Hz, 1H, H-6), 4.41 (q, *J* = 6.3 Hz, 1H, H-8), 4.16 (d, *J* = 11.3 Hz, 1H, NH), 3.91 – 3.87 (m, 1H, H-4), 3.84 (s, 3H, OCH_3), 3.41 (q, *J* = 10.1 Hz, 1H, H-5), 3.30 (d, *J* = 11.1 Hz, 1H, H-7), 2.38 (dd, *J* = 13.8, 4.6 Hz, 1H, H-3_{eq}), 1.97 – 1.95 (m, 8H, Ada), 1.80 – 1.71 (m, 1H, H-3_{ax}), 1.66 – 1.63 (m, 6H, Ada), 1.48 – 1.47 (m, 1H, Ada), 1.43 (s, 9H, $C(CH_3)_3$), 1.25 (s, 9H, $C(CH_3)_3$), 0.85 (s, 9H, $C(CH_3)_3$), 0.09 (s, 3H, $SiCH_3$), 0.07 (s, 3H, $SiCH_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.5 (CO_2Me), 156.1 ($NHCO_2tBu$), 85.8 (C-2), 79.9 ($C(CH_3)_3$), 79.8 (C-6), 68.0 (C-4), 66.0 (C-8), 60.8 (C-7), 56.8 ($C(CH_3)_3$), 55.2 (C-5), 53.2 (OCH_3), 50.6 (Ada), 44.1 (C-3), 43.6 (Ada), 36.1 (Ada), 30.0 (Ada), 28.4 ($C(CH_3)_3$), 25.8 ($C(CH_3)_3$), 23.0 ($C(CH_3)_3$), 20.2 (CH_3), 18.0 ($C(CH_3)_3$), -4.3 ($SiCH_3$), -4.7 ($SiCH_3$); HRMS (ESI) m/z calcd for $C_{35}H_{64}O_8N_2S_2SiNa$ $[M+Na]^+$ 755.3765, found 755.3740.

Methyl (1-Adamantanyl 5,7-diazido-4,8-di-*O*-benzoyl-3,5,7,9-tetradeoxy-2-thio-L-glycero-*α*-L-altro-non-2-ulopyranosid)onate (335).

Prepared from **337** (0.20 g, 0.27 mmol) with the following quantities of reagents according GP12 : -

i) HCl in MeOH (2.0 mL, 4.3 mmol), MeOH (3.0 mL)

ii) K_2CO_3 (0.11 g, 0.81 mmol), $CuSO_4.5H_2O$ (8.0 mg, 30 µmol), $ImSO_2N_3$ (0.17 g, 0.81 mmol) and $MeOH/H_2O$ (5.0 mL)

iii) BzCl (78 µL, 0.67 mmol), Pyridine (1.4 mL)

The crude product was purified by flash column chromatography (1:19 ethyl acetate/hexane) to give **335** (99 mg, 55%) as a white foam; R_f = 0.23 (1:9 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -31 (*c* = 0.30, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.07 (dd, *J* = 7.9, 1.5 Hz, 2H, ArH), 8.01 (dd, *J* = 8.0, 1.6 Hz, 2H, ArH), 7.62 – 7.55 (m, 2H, ArH), 7.45 (q, *J* = 8.1 Hz, 4H, ArH), 5.51 (ddd, *J* = 11.2,

9.4, 4.7 Hz, 1H, H-4), 5.41 (p, *J* = 6.4 Hz, 1H, H-8), 4.52 (dd, *J* = 10.2, 1.5 Hz, 1H, H-6), 4.12 (dd, *J* = 7.2, 1.5 Hz, 1H, H-7), 3.93 (t, *J* = 9.7 Hz, 1H, H-5), 3.80 (s, 3H, OCH_3), 2.77 (dd, *J* = 13.7, 4.9 Hz, 1H, H-3_{eq}), 2.06 (d, *J* = 11.7 Hz, 6H, Ada), 1.97 – 1.90 (m, Ada, H-3_{ax}), 1.70 (s, 6H, Ada), 1.59 (d, *J* = 6.2 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.4 (CO_2Me), 165.4 (CO_2Ar), 165.3 (CO_2Ar), 133.6 (Ar), 133.4 (Ar), 130.1 (Ar), 129.9 (Ar), 129.8 (Ar), 129.4 (Ar), 128.6 (Ar, 2C), 85.7, 71.9 (C-6, C-4, 2C), 70.4 (C-8), 67.6 (C-7), 60.8 (C-5), 52.9 (OCH_3), 50.6 (Ada), 43.5 (Ada), 39.3 (C-3), 36.2 (Ada), 30.0 (Ada), 18.0 (CH_3); HRMS (ESI) m/z calcd for $C_{34}H_{38}O_7N_6SNa$ $[M+Na]^+$ 697.2414, found 697.2408.

Methyl (1-Adamantanyl 5,7-diazido-4,8-di-*O*-benzoyl-3,5,7,9-tetradeoxy-2-thio-D-glycero-β-L-altro-non-2-ulopyranosid)onate (349).

Prepared from **348** (10 mg, 14 μmol) with the following quantities of reagents according GP12: -

i) HCl in MeOH (0.11 mL, 0.22 mmol), MeOH (0.14 mL)

ii) K_2CO_3 (30 mg, 0.22 mmol), $CuSO_4.5H_2O$ (1.0 mg, 1.4 μmol), $ImSO_2N_3$ (46 mg, 0.22 mmol) and MeOH/H_2O (0.30 mL)

iii) BzCl (4.0 μL, 0.55 mmol), Pyridine (0.10 mL)

The crude product was purified by flash column chromatography (5:95 ethyl acetate/hexane) to give **349** (5.0 mg, 53%) as a white foam; R_f = 0.40 (1:4 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -31 (*c* = 0.30, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.11 – 8.08 (m, 2H, ArH), 8.05 – 8.01 (m, 2H, ArH), 7.59 (ddd, *J* = 8.5, 7.0, 1.2 Hz, 2H, ArH), 7.50 – 7.44 (m, 4H, ArH), 5.62 – 5.57 (m, 2H, H-8, H-4), 4.47 (dd, *J* = 10.1, 2.1 Hz, 1H, H-6), 4.04 (t, *J* = 9.8 Hz, 1H, H-5), 3.85 (dd, *J* = 7.9, 2.1 Hz, 1H, H-7), 3.66 (s, 3H, OCH_3), 2.77 (dd, *J* = 13.6, 4.8 Hz, 1H, H-3_{eq}), 2.05 (d, *J* = 10.2 Hz, 6H, Ada), 1.98 (dd, *J* = 13.6, 11.3 Hz, 1H, H-3_{ax}), 1.89 (d, *J* = 11.6 Hz, 3H, Ada), 1.69 (d, *J* = 3.0 Hz,

6H, Ada), 1.53 (d, J = 6.3 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.2 (CO_2Me), 165.7 (CO_2Ar), 165.4 (CO_2Ar), 133.7 (Ar), 133.3 (Ar), 130.1 (Ar), 130.0 (Ar), 129.9 (Ar), 129.4 (Ar), 128.7 (Ar), 128.6 (Ar), 86.1 (C-2), 71.9 (C-8), 71.4 (C-6), 71.0 (C-4), 68.2 (C-7), 60.7 (C-5), 52.8 (OCH_3), 50.6 (Ada), 43.5 (Ada), 39.3 (C-3), 36.2 (Ada), 30.0 (Ada), 18.5 (CH_3); HRMS (ESI) m/z calcd for $C_{34}H_{38}O_7N_6SNa$ $[M+Na]^+$ 697.2414, found 697.2408.

Methyl (1-Adamantanyl 3,5,7,8-tetradeoxy-5-*N*-(*tert*-butyloxycarbonyl)-8-*O*-7-*N*-oxazolidinone-2-thio-L-glycero-α-L-altro-non-2-ulopyranosid)onate (350).

Prepared from **337** (24 mg, 33 µmol) with the following quantities of reagents according to GP13:-

i) HCl in MeOH (0.16 mL, 0.33 mmol), MeOH (0.33 mL)

ii) $CO(OCCl_3)_2$ (10 mg, 33 µmol), Et_3N (14 µL, 99 µmol), CH_2Cl_2 (0.16 mL)

Obtained **350** (10 mg, 56%) white solid; R_f = 0.29 (7:3 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -63 (c = 0.40, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 5.26 (s, 1H, NH), 4.91 (p, J = 6.9 Hz, 1H, H-8), 4.67 (br s, 1H, NH), 4.11 (dd, J = 10.6, 2.8 Hz, 1H, H-6), 4.02 (dd, J = 7.8, 2.8 Hz, 1H), 3.96 (ddd, J = 11.2, 9.4, 4.6 Hz, 1H, H-4), 3.82 (s, 3H, OCH_3), 3.56 – 3.50 (m, 1H, H-5), 2.57 (dd, J = 13.9, 4.6 Hz, 1H, H-3_{eq}), 2.02 – 1.96 (m, 6H, Ada), 1.88 (dd, J = 13.9, 11.3 Hz, 1H, H-3_{ax}), 1.83 (d, J = 11.8 Hz, 3H, Ada), 1.68 (d, J = 6.7 Hz, 3H, CH_3), 1.66 (d, J = 3.1 Hz, 6H, Ada), 1.46 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.8 (CO_2Me), 159.2 (OCONH), 156.6 ($NHCO_2tBu$), 86.1 (C-2), 81.1 ($C(CH_3)_3$), 76.6 (C-8), 73.7 (C-6), 68.3 (C-4), 56.0 (C-7), 55.3 (C-5), 53.0 (OCH_3), 50.7 (Ada), 43.9 (Ada), 42.8 (C-3), 36.1 (Ada), 30.0 (Ada), 28.5 ($C(CH_3)_3$), 16.0 (CH_3); HRMS (ESI) m/z calcd for $C_{26}H_{40}O_8N_2NaS$ $[M+Na]^+$ 563.2397, found 563.2406.

Methyl (1-Adamantanyl 3,5,7,8-tetradeoxy-5-*N*-(*tert*-butyloxycarbonyl)-8-*O*-7-*N*-oxazolidinone-2-thio-D-glycero-β-L-altro-non-2-ulopyranosid)onate (351).

Prepared from **348** (10 mg, 14 µmol) with the following quantities of reagents according to GP13 : -

i) HCl in MeOH (68 µL, 0.14 mmol), MeOH (0.14 mL)

ii) $CO(OCCl_3)_2$ (4.0 mg, 14 µmol), Et_3N (7 µL, 33 µmol), CH_2Cl_2 (0.10 mL)

Obtained **351** (4.0 mg, 56%) white solid; R_f = 0.37 (4:1 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -72 (*c* = 0.15, $CHCl_3$); ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.46 (s, 1H, NH), 4.78 (p, *J* = 6.2 Hz, 1H, H-8), 4.74 – 4.59 (m, 1H, NH), 4.09 – 4.03 (m, 1H, H-6), , 4.01 – 3.94 (m, 1H, H-4), 3.81 (s, 3H, OCH_3), 3.66 (td, *J* = 5.3, 1.3 Hz, 1H, H-7), 3.35 (s, 1H, H-5), 2.57 (dd, *J* = 13.7, 4.7 Hz, 1H, H-3_{eq}), 2.02 – 1.95 (m, 6H, Ada), 1.85 – 1.78 (m, 4H, Ada, H-3_{ax}), 1.71 – 1.62 (m, 6H, Ada), 1.52 (d, *J* = 6.3 Hz, 3H, CH_3), 1.46 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.6 (CO_2Me), 158.9 (OCONH), 156.8 ($NHCO_2tBu$), 86.0 (C-2), 81.4 ($C(CH_3)_3$), 76.1 (C-8), 73.7 (C-6), 68.2 (C-4), 61.7 (C-7), 56.8 (C-5), 52.9 (OCH_3), 50.6 (Ada), 43.7 (Ada), 43.0 (C-3), 36.1 (Ada), 30.0 (Ada), 28.5 ($C(CH_3)_3$), 21.1 (CH_3); HRMS (ESI) m/z calcd for $C_{26}H_{40}O_8N_2NaS$ $[M+Na]^+$ 563.2397, found 563.2401.

Methyl (1-Adamantanyl 4,9-di-*O*-(*tert*-butyldimethylsilyl)-3-deoxy-2-thio-D-glycero-β-D-galacto-non-2-ulopyranosid)onate (357).

A stirred solution of **160**[145] (5.0 g, 7.8 mmol) in anhydrous MeOH was treated with Na (18 mg, 0.78 mmol, 0.1 equiv) at 0 °C and stirred for 5 h before it was evaporated to dryness. The residual was dissolved in anhydrous THF (80 mL), cooled to 0 °C and imidazole (2.6 g, 39 mmol, 5 equiv), TBSCl (2.3 g, 16 mmol, 2 equiv), DMAP (95 mg, 0.78 mmol, 0.1 equiv) were added, and the

reaction mixture was allowed to warm with stirring to room temperature overnight. The reaction mixture was filtered through Celite, and after removal of solvent gave a crude product that was purified by flash column chromatography (3:7 ethyl acetate/hexane) to give **357** as a white solid (3.4 g, 66%); R_f = 0.64 (3:2 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -64 (*c* = 1.2, $CHCl_3$); ^{1}H NMR (900 MHz, $CDCl_3$) δ 4.37 (dd, *J* = 9.8, 2.4 Hz, 1H, H-6), 4.09 (ddd, *J* = 11.4, 8.5, 4.7 Hz, 1H, H-4), 3.89 (dd, *J* = 10.0, 4.3 Hz, 1H, H-9), 3.87 – 3.84 (m, 2H, H-7, H-9), 3.81 (s, 3H, OCH_3), 3.77 – 3.72 (m, 1H, H-8), 3.54 (dd, *J* = 9.8, 8.5 Hz, 1H, H-5), 2.32 (dd, *J* = 13.8, 4.7 Hz, 1H, H-3_{eq}), 2.00 – 1.98 (m, 6H, Ada), 1.93 – 1.90 (m, 3H, Ada), 1.77 (dd, *J* = 13.9, 11.4 Hz, 1H, H-3_{ax}), 1.65 (s, 6H, Ada), 0.90 (s, 9H, $C(CH_3)_3$), 0.88 (s, 9H, $C(CH_3)_3$), 0.12 (s, 3H, $SiCH_3$), 0.10 (d, *J* = 1.2 Hz, 6H, $Si(CH_3)_2$), 0.10 (s, 3H, $SiCH_3$); ^{13}C NMR (226 MHz, $CDCl_3$) δ 171.4 (CO_2Me), 86.3 (C-2), 72.4 (C-6), 72.2 (C-5), 71.4 (C-7), 70.6 (C-4), 70.3 (C-8), 64.9 (C-9), 52.9 (OCH_3), 50.2 (Ada), 43.5 (Ada), 42.9 (C-3), 36.2 (Ada), 30.0 (Ada), 26.0 $Si(C(CH_3)_3)$, 25.9 $Si(C(CH_3)_3)$, 18.4 $Si(C(CH_3)_3)$, 18.1 $Si(C(CH_3)_3)$, -4.4 ($SiCH_3$), -5.2 ($SiCH_3$), -5.3 ($SiCH_3$); HRMS (ESI) m/z calcd for $C_{32}H_{60}O_8SSi_2Na$ $[M+Na]^+$ 683.3439, found 683.3412.

Methyl (1-Adamantanyl 4-*O*-(*tert*-butyldimethylsilyl)-3-deoxy-6-thio-α-L-lyxo-hept-6-ulo-2,6-pyranosid)uronate 7-(S_s)-*N*-(*tert*-butylsulfinyl)imine (355).

A stirred solution of **357** (3.5 g, 5.3 mmol) in CH_2Cl_2 (50 mL) was treated with $NaIO_4$ on silica gel[129] (10 g) and stirred for overnight. After completion, the reaction mixture was filtered through Celite and evaporated to dryness to give the corresponding aldehyde. The crude aldehyde was dissolved in anhydrous CH_2Cl_2 (27 mL) and Na_2SO_4 (3.7 g, 26 mmol, 5 equiv) was added followed by PPTS 67 mg, 0.26 mmol, 0.05 equiv) and (*S*)-*tert*-butylsulfinamide (1.3 g, 11 mmol, 2 equiv). The resulting mixture was stirred at room temperature for 36 h before it was filtered through Celite concentrated under the reduced pressure to afford a crude product that was purified by flash

column chromatography (3:7 ethyl acetate/hexane) to give **355** as a white foam (2.0 g, 64%); R_f = 0.42 (1:2 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -13 (*c* = 1.5, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.24 (d, *J* = 2.8 Hz, 1H, H-7), 4.97 (dd, *J* = 9.7, 2.8 Hz, 1H, H-6), 4.15 (ddd, *J* = 11.4, 8.5, 5.0 Hz, 1H, H-4), 3.82 (d, *J* = 1.4 Hz, 3H, OCH_3), 3.48 (t, *J* = 9.1 Hz, 1H, H-5), 2.96 (d, *J* = 8.4 Hz, 1H, OH), 2.33 (dd, *J* = 14.0, 5.0 Hz, 1H, H-3_{eq}), 2.04 – 1.95 (m, 6H, Ada), 1.88 – 1.81 (m, 4H, H-3_{ax}, Ada), 1.65 (s, 6H, Ada), 1.23 (s, 9H, $C(CH_3)_3$), 0.88 (s, 9H, $C(CH_3)_3$), 0.12 (s, 3H, $SiCH_3$), 0.11 (s, 3H, $SiCH_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.0 (CO_2Me), 167.3 (C-7), 86.8 (C-2), 74.4 (C-5), 74.3 (C-6), 70.3 (C-4), 57.4 ($C(CH_3)_3$), 53.0 (OCH_3), 50.7 (Ada), 43.4 (Ada), 42.7 (C-3), 36.2 (Ada), 30.0 (Ada), 25.9 ($Si(C(CH_3)_3$, 2C), 22.6 ($Si(C(CH_3)_3$, 2C), 18.2 ($Si(C(CH_3)_3$), -4.4 ($SiCH_3$), -4.5 ($SiCH_3$); HRMS (ESI) m/z calcd for $C_{28}H_{49}O_6NS_2SiNa$ $[M+Na]^+$ 610.2662, found 610.2653.

Methyl (1-Adamantanyl 4-*O*-(*tert*-butyldimethylsilyl)-7-(S_S)-*N*-(*tert*-butylsulfinyl)amino-3,7,9-trideoxy-2-thio-L-glycero-α-L-altro-non-2-ulopyranosid)onate (354) and Methyl (1-Adamantanyl 4-*O*-(*tert*-butyldimethylsilyl)-7-(S_S)-*N*-(*tert*-butylsulfinyl)amino-3,7,9-trideoxy-8-*N*-7-*O*-ethylidine-2-thio-L-glycero-α-L-altro-non-2-ulopyranosid)onate (359).

The sulfinyl imine **355** (2.0 g, 3.4 mmol) was treated with *t*BuOH (1.0 mL, 10 mmol), acetaldehyde (1.7 mL, 20 mmol) and 0.1 M SmI_2 (136 mL, 4 equiv) according to GP9 to give a mixture of **354** and **359** which was separated by flash chromatography (1:5 ethyl acetate/hexane).

354; white foam (1.1 g,52%); R_f = 0.20 (2:3 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -73 (*c* = 0.25, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.26 (dd, *J* = 9.4, 5.3 Hz, 1H, H-6), 4.09 – 3.98 (m, 3H, NH, H-8, H-4), 3.81 (s, 3H, OCH_3), 3.57 – 3.52 (m, 2H, H-7, H-5), 2.32 (dd, *J* = 13.8, 4.7 Hz, 1H, H-3_{eq}), 2.01 – 1.99 (m, 6H, Ada), 1.90 – 1.83 (m, 4H, H-3_{ax}, Ada), 1.66 (s, 6H, Ada), 1.29 (d, *J* = 6.4 Hz, 3H, CH_3), 1.26 (s, 9H, $C(CH_3)_3$), 0.87 (s, 9H, $C(CH_3)_3$), 0.11 (s, 3H, $SiCH_3$), 0.09 (s, 3H, $SiCH_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.0 (CO_2Me), 86.2 (C-2), 75.6 (C-6), 74.3 (C-7), 70.2 (C-4),

69.7 (C-8), 64.5 (C-5), 56.7 (*C*(CH_3)$_3$), 53.0 (OCH_3), 50.2 (Ada), 43.6 (Ada), 42.7 (C-3), 36.2 (Ada), 30.0 (Ada), 26.0 (C(*C*H_3)$_3$), 23.0 (*C*(CH_3)$_3$), 20.5 (CH_3), 18.2 (*C*(CH_3)$_3$), -4.3 ($SiCH_3$), -4.5 ($SiCH_3$); HRMS (ESI) m/z calcd for $C_{30}H_{55}O_7NS_2SiNa$ $[M+Na]^+$ 656.3081, found 656.3080.

359; white foam (0.30 g,14%); R_f = 0.36 (2:3 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -97 (*c* = 0.10, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.36 (q, *J* = 5.9 Hz, 1H, CHMe), 4.59 – 4.52 (m, 1H, H-7), 4.49 (dd, *J* = 10.3, 1.2 Hz, 1H, H-6), 4.15 (t, *J* = 6.7 Hz, 1H, H-8), 3.99 (ddd, *J* = 11.6, 8.2, 4.7 Hz, 1H, H-4), 3.80 (s, 3H, OCH_3), 3.44 (ddd, *J* = 10.2, 8.1, 1.8 Hz, 1H, H-5), 2.33 (dd, *J* = 13.7, 4.7 Hz, 1H, H-3$_{eq}$), 2.00 – 1.95 (m, 6H, Ada), 1.88 (d, *J* = 11.5, 3H, Ada), 1.75 (dd, *J* = 13.8, 11.6 Hz, 1H, H-3$_{ax}$), 1.69 – 1.58 (m, 6H, Ada), 1.55 (d, *J* = 6.0 Hz, 3H, C*H*$_3$CH), 1.50 (d, *J* = 6.7 Hz, 3H, CH_3), 1.28 (s, 9H, C(CH_3)$_3$), 0.88 (s, 9H, C(CH_3)$_3$), 0.12 (s, 3H, $SiCH_3$), 0.10 (s, 3H, $SiCH_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.9 (CO_2Me), 90.8 (CHMe), 86.7 (C-2), 76.3 (C-8, C-6), 73.1 (C-5), 71.0 (C-4), 57.5 (*C*(CH_3)$_3$), 55.8 (C-7), 52.8 (OCH_3), 50.0 (Ada), 43.7 (Ada), 43.0 (C-3), 36.2 (Ada), 30.0 (Ada), 25.9 (C(*C*H_3)$_3$), 23.6 (C(*C*H_3)$_3$), 18.2 (CH*C*H_3), 18.1 (*C*(CH_3)$_3$), 16.7 (CH_3), -4.3 ($SiCH_3$), -4.4 ($SiCH_3$); HRMS (ESI) m/z calcd for $C_{32}H_{57}O_7NS_2SiNa$ $[M+Na]^+$ 682.3237, found 682.3236.

Methyl (1-Adamantanyl 7-azido-3,7,9-trideoxy-2-thio-L-glycero-α-L-altro-non-2-ulopyranosid)onate (353).

A stirred solution of aza-pinacol product **354** (1.3 g, 2.1 mmol) in MeOH (21 mL) was treated with 2 M HCl in MeOH (5.0 mL, 10 mmol, 5 equiv) and the reaction progress was monitored by mass spectrometry. After cleavage of the sulfinamide and TBS groups was observed by mass spectrometry, the reaction mixture was evaporated to dryness to give the amine which was dissolved in CH_3CN/H_2O (4:1) (34 mL) and cooled to 0 °C. To this cold solution Et_3N (0.85 mL, 6.1 mmol, 3 equiv) was added followed by $CuSO_4.5H_2O$ (53 mg, 0.21 mmol, 0.1 equiv) and

$ImSO_2N_3$ (0.63 g, 3.0 mmol, 1.5 equiv). The reaction mixture was warmed to room temperature and the stirring was continued for 12 h before the reaction mixture was evaporated to dryness to give a crude product that was purified by column chromatography (1:19 MeOH/CH_2Cl_2) to give **353** (0.80 g, 66%) as a white foam; R_f = 0.30 (1:2 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -96 (*c* = 0.50, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.48 (dd, *J* = 9.4, 2.5 Hz, 1H, H-6), 4.13 (ddd, *J* = 11.9, 8.7, 4.9 Hz, 1H, H-4), 4.05 (p, *J* = 6.4 Hz, 1H, H-8), 3.81 (s, 3H, OCH_3), 3.74 (dd, *J* = 5.9, 2.5 Hz, 1H, H-7), 3.58 (t, *J* = 9.0 Hz, 1H, H-5), 3.36 (s, 1H, OH), 2.77 (s, 1H, OH), 2.46 (dd, *J* = 13.7, 4.9 Hz, 1H, H-3_{eq}), 2.02 – 1.99 (m, 6H, Ada), 1.88 – 1.85 (m, 3H, Ada), 1.83 (dd, *J* = 13.8, 11.9 Hz, 1H, H-3_{ax}), 1.67 – 1.66 (m, 6H, Ada), 1.34 (d, *J* = 6.5 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.2 (CO_2Me), 86.2 (C-2), 73.0 (C-6), 71.3 (C-5), 69.6 (C-4), 69.5 (C-7), 68.0 (C-8), 52.9 (OCH_3), 50.1 (Ada), 43.5 (Ada), 41.4 (C-3), 36.2 (Ada), 30.0 (Ada), 19.5 (CH_3); HRMS (ESI) m/z calcd for $C_{20}H_{31}O_6N_3SNa$ $[M+Na]^+$ 464.1825, found 464.1823.

Preparation from **359**; A stirred solution of compound **359** (0.50 g, 0.76 mmol) in MeOH (7.5 mL) was treated with 2 M HCl in MeOH (6.0 mL, 12 mmol, 16 equiv), and the reaction mixture was stirred at room temperature until cleavage of the TBS, sulfinamide and acetal groups was observed by mass spectrometry. After completion, the reaction mixture was evaporated to dryness to give a crude amine that was dissolved in CH_3CN/H_2O (4:1) (13 mL) and cooled to 0 °C. To this reaction mixture Et_3N (0.30 mL, 2.3 mmol, 3 equiv) was added followed by $CuSO_4.5H_2O$ (19 mg, 76 µmol, 0.1 equiv) and $ImSO_2N_3$ (0.23 g, 1.1 mmol, 1.5 equiv). The resulting mixture was warmed to room temperature and the stirring was continued for 12 h before the reaction mixture was evaporated to dryness to give a crude product that was purified by column chromatography (1:19 MeOH/CH_2Cl_2) to give **353** (0.18 g, 55%) with spectra identical to the above-described sample.

Methyl (1-Adamantanyl 4,8-di-*O*-acetyl-7-azido-3,7,9-trideoxy-2-thio-L-glycero-α-L-altro-non-2-ulopyranosid)onate (352).

A stirred solution of **353** (0.67 g, 1.5 mmol) in anhydrous CH_2Cl_2 (22 mL) and pyridine (0.31 mL, 3.8 mmol, 2.5 equiv) at -20 °C was treated dropwise with AcCl (0.27 mL, 3.8 mmol, 2.5 equiv) in anhydrous CH_2Cl_2 (8.5 mL) and stirred at -20 °C for 5 h before it was quenched by addition of saturated aqueous NH_4Cl. The resulting mixture was extracted with CH_2Cl_2, the extracts were washed with brine, dried over Na_2SO_4, and the solvent removed to afford a crude product that was purified by flash column chromatography (1:5 ethyl acetate/hexane) to give **353** (0.55 g, 69%) as a white foam; R_f = 0.42 (2:3 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -143 (*c* = 0.35, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.23 – 5.17 (m, 2H, H-8, H-4), 4.40 (dd, *J* = 9.7, 2.2 Hz, 1H, H-6), 3.96 (dd, *J* = 6.3, 2.2 Hz, 1H, H-7), 3.80 (s, 3H, OCH_3), 3.75 (t, *J* = 9.2 Hz, 1H, H-5), 2.83 (s, 1H, OH), 2.51 (dd, *J* = 13.7, 4.9 Hz, 1H, H-3_{eq}), 2.09 (s, 3H, Ac), 2.07 (s, 3H, Ac), 2.04 – 1.99 (m, 6H, Ada), 1.92 – 1.84 (m, 4H, Ada, H-3_{ax}), 1.68 – 1.67 (m, 6H, Ada), 1.41 (d, *J* = 6.3 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.3 (Ac), 170.7 (CO_2Me), 170.3 (Ac), 85.8 (C-2), 73.2 (C-6), 72.4 (C-8), 70.4 (C-5, C-4, 2C), 67.0 (C-7), 52.9 (OCH_3), 50.4 (Ada), 43.6 (Ada), 39.2 (C-3), 36.2 (Ada), 30.0 (Ada), 21.5 (Ac), 21.2 (Ac), 17.2 (CH_3); HRMS (ESI) m/z calcd for $C_{24}H_{35}O_8N_3SNa$ $[M+Na]^+$ 548.2037, found 548.2028.

Methyl (1-Adamantanyl 3,7,9-trideoxy-8-*O*-7-*N*-oxazolidinone-2-thio-L-glycero-α-L-altro-non-2-ulopyranosid)onate (360).

Prepared from **354** (24 mg, 38 µmol) with the following quantities of reagents according to GP13:-

i) 2 M HCl (0.10 mL, 0.20 mmol), MeOH (0.40 mL)

ii) Et_3N (16µL, 0.11 mmol), (11 mg, 38 µmol), CH_2Cl_2 (0.20 mL)

The crude product was purified by flash column chromatography (1:9 methanol/DCM) and to give **360** (10 mg, 60%) as a white solid; R_f = 0.27 (1:9 methanol/DCM); $[\alpha]^{25}_D$ = -90 (*c* = 0.50, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.76 (s, 1H, NH), 4.93 – 4.87 (m, 1H, H-8), 4.35 (dd, *J* = 9.6, 2.6 Hz, 1H, H-6), 4.08 (ddd, *J* = 11.6, 8.8, 4.9 Hz, 1H, H-4), 4.03 (dd, *J* = 8.3, 2.6 Hz, 1H, H-7), 3.81 (s, 3H, OCH_3), 3.41 (t, *J* = 9.2 Hz, 1H, H-5), 2.47 (dd, *J* = 13.9, 4.8 Hz, 1H, H-3_{eq}), 2.00 – 1.94 (m, 6H, Ada), 1.86 – 1.79 (m, 4H, Ada, H-3_{ax}), 1.66 – 1.66 (m, 6H, Ada), 1.60 (d, *J* = 6.7 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.6 (CO_2Me), 160.7 (OCONH), 86.4 (C-2), 76.5 (C-8), 72.8 (C-5), 72.0 (C-6), 69.9 (C-4), 59.3 (C-7), 53.0 (OCH_3), 50.2 (Ada), 43.7 (Ada), 41.8 (C-3), 36.2 (Ada), 30.0 (Ada), 15.7 (CH_3); HRMS (ESI) m/z calcd for $C_{21}H_{31}O_7NNaS$ $[M+Na]^+$ 464.1713, found 464.1713.

Methyl (1-Adamantanyl 4,8-di-*O*-acetyl-5,7-di-azido-3,5,7,9-tetra-deoxy-2-thio-L-glycero-α-L-manno-non-2-ulopyranosid)onate (172).

To a stirred solution of **352** (0.50 g, 0.95 mmol) in anhydrous CH_2Cl_2 (20 mL) at 0 °C, pyridine (0.15 mL, 1.9 mmol, 2 equiv) was added. To this cold reaction mixture, Tf_2O (0.19 mL, 1.1 mmol, 1.2 equiv) was added dropwise and the resulting solution stirred at the same temperature for 1 h. After complete conversion, a cold solution of nBu_4NN_3 (1.2 g, 4.7 mmol, 5 equiv) in anhydrous CH_2Cl_2 (10 mL) was added and the reaction mixture was stirred for 0.5 h before it was evaporated to dryness. The crude product was purified by flash column chromatography (1:5 ethyl acetate/hexane) to give **172** (0.36 g, 68%) as a white foam with spectral data consistent with those reported in the literature;[109] ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.36 – 5.30 (m, 2H, H-8, H-4), 4.13 – 4.07 (m, 2H, H-6, H-5), 4.02 (dd, *J* = 9.8, 2.3 Hz, 1H, H-7), 3.81 (s, 3H, OCH_3), 2.33 (dd, *J* = 13.5, 4.9 Hz, 1H, H-3_{eq}), 2.27 (dd, *J* = 13.5, 12.2 Hz, 1H, H-3_{ax}), 2.11 (s, 3H, Ac), 2.09 (s, 3H, Ac), 2.02 – 2.01 (m, 3H, Ada), 1.98 – 1.94 (m, 3H, Ada), 1.81 (d, *J* = 12.4, 3H, Ada), 1.67 – 1.62 (m, 6H,

Ada), 1.32 (d, *J* = 6.3 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 169.9 (CO_2Me, Ac, 2C), 86.3 (C-2), 70.6 (C-8), 69.3 (C-4), 69.2 (C-6), 65.2 (C-7), 59.2 (C-5), 52.9 (OCH_3), 50.7 (Ada), 43.8 (Ada), 36.1 (Ada), 34.9 (C-3), 30.0 (Ada), 21.3 (Ac), 20.8 (Ac), 14.3 (CH_3); HRMS (ESI) m/z calcd for $C_{24}H_{34}N_6O_7NaS$ $[M+Na]^+$ 573.2107, found 573.2110.

Methyl (1-Adamantanyl 4,8-di-*O*-acetyl-7-azido-3,7,9-tri-deoxy-2-thio-L-glycero-α-L-manno-non-2-ulopyranosid)onate (364) and Methyl (1-Adamantanyl 4,8-di-*O*-acetyl-5,7-di-azido-3,5,7,9-tetra-deoxy-2-thio-L-glycero-α-L-manno-non-2-ulopyranosid)onate (172).

A stirred solution of compound **352** (49 mg, 93 µmol) in anhydrous CH_2Cl_2 (1.0 mL) and pyridine (22 µL, 0.28 mmol, 3 equiv) at 0 °C was treated with Tf_2O (0.19 mL, 1.1 mmol, 1.2 equiv) and was stirred at 0 °C for 1.5 h. After complete conversion, the reaction mixture was diluted with CH_2Cl_2 and washed with cold 1 M HCl, saturated aqueous $NaHCO_3$, brine and dried over Na_2SO_4. Removal of the solvent under reduced pressure at 0 °C gave the crude triflate that was dissolved in anhydrous DMF (0.50 mL) and cooled to 0 °C. To the resulting reaction mixture NaN_3 (30 mg, 0.64 mmol, 5 eq) was added and was stirred at 0 °C for overnight. After completion, the mixture was diluted with ether and washed with water, brine and dried over Na_2SO_4. Removal of the solvent gave a mixture of **362** and **172** that was separated by column chromatography (1:9 ethyl acetate/hexane) to give **362** and **172**.

172 (14 mg, 23%) had spectral data identical to the above-described sample.

362 (27 mg, 55%) as a colorless oil; R_f = 0.18 (3:7 ethyl acetate/hexane); $[\alpha]^{25}_D$ = -90 (*c* = 0.50, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 5.31 – 5.25 (m, 1H, H-8), 5.22 (ddd, *J* = 10.1, 6.9, 2.8 Hz, 1H, H-4), 4.18 (dd, *J* = 7.7, 1.4 Hz, 1H, H-6), 4.11 (dd, *J* = 2.9, 1.3 Hz, 1H, H-7), 4.07 (dd, *J* = 7.7, 3.2 Hz, 1H, H-5), 3.81 (s, 3H, OCH_3), 2.29 – 2.24 (m, 2H, H-3_{ax}, H-3_{eq}), 2.09 (s, 3H, Ac),

2.09 (s, 3H, Ac), 2.03 – 1.97 (m, 6H, Ada), 1.88 – 1.82 (m, 3H, Ada), 1.66 (s, 6H, Ada), 1.35 (d, *J* = 6.3 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.5 (Ac), 170.2 (Ac), 169.9 (CO_2Me), 86.4 (C-2), 70.9 (C-6), 70.5 (C-8), 69.4 (C-4), 65.6 (C-7), 65.5 (C-5), 52.9 (OCH_3), 50.4 (Ada), 43.7 (Ada), 36.2 (Ada), 33.8 (C-3), 30.0 (Ada), 21.3 (Ac), 21.2 (Ac), 15.1 (CH_3); HRMS (ESI) m/z calcd for $C_{24}H_{35}O_8N_3SNa$ $[M+Na]^+$ 548.2037, found 548.2028.

Methyl 2,3-di-*O*-benzyl-α-D-xylofuranoside (410α) and Methyl 2,3-di-*O*-benzyl-β-D-xylofuranoside (410β).

A stirred solution of compound **408**[184, 185] (11.5 g, 28.2 mmol) in anhydrous DMF (130 mL) at 0 °C was treated with NaH (8.0 g, 76.2 mmol) and stirring was continued for 10 min at 0 °C before BnBr (26 mL, 76.2 mmol) was added, and the reaction mixture was stirred at 30 °C overnight. Then water was added slowly to the reaction mixture and the aqueous phase was extracted with ether. The organic layer was washed with brine, dried over Na_2SO_4 and the solvent was evaporated under reduced pressure to give a crude product which was dissolved in 80% acetic acid (100 mL) and stirred at 75 °C for 4 h. The solvent was evaporated under reduced pressure and the anomers were separated using flash column chromatography (1:5 ethyl acetate/hexane).

410α. 3.1 g (32 %) colorless oil ; Rf = 0.22 (7:3 hexane-ethyl acetate); $[\alpha]^{25}_D$ = +69 (*c* = 0.70, $CHCl_3$); 1H NMR (600 MHz, $CDCl_3$) δ 7.39 – 7.27 (m, 10H, ArH), 4.81 (d, *J* = 4.2 Hz, 1H, H-1), 4.74 (d, *J* = 11.8 Hz, 1H, OCH_2Ph), 4.66 (d, J = 11.9 Hz, 1H, OCH_2Ph), 4.59 (d, *J* = 11.7 Hz, 2H, OCH_2Ph), 4.44 (dd, *J* = 7.8, 6.4 Hz, 1H, H-3), 4.22 (dt, *J* = 7.8, 3.9 Hz, 1H, H-4), 4.06 (dd, *J* = 6.5, 4.2 Hz, 1H, H-2), 3.80 (dt, *J* = 12.4, 4.1 Hz, 1H, H-5), 3.74 (ddd, *J* = 12.5, 8.6, 4.1 Hz, 1H, H-5'), 3.38 (s, 3H, OCH_3), 2.37 (dd, *J* = 8.9, 4.9 Hz, 1H, OH); ^{13}C NMR (151 MHz, $CDCl_3$) δ 137.7 (Ar), 137.6 (Ar), 128.7 (Ar), 128.6 (Ar), 128.4 (Ar), 128.2 (Ar), 128.1 (Ar), 127.9 (Ar),

100.3 (C-1), 84.7 (C-2), 82.4 (C-3), 76.3 (C-4), 72.9 (OCH_2Ph), 72.8 (OCH_2Ph), 62.4 (C-5), 55.2 (OCH_3); HRMS (ESI) m/z calcd for $C_{20}H_{24}O_5Na$ $[M+Na]^+$ 367.1516, found 367.1513.

410β. 3.3 g (34%) colorless oil; R_f = 0.27 (7:3 hexane-ethyl acetate); $[\alpha]^{25}_D$ = -30 (*c* = 1.6, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 7.39 – 7.29 (m, 10H, ArH), 4.91 (d, *J* = 1.9 Hz, 1H, H-1), 4.64 (d, *J* = 12.0 Hz, 1H, OCH_2Ph), 4.59 (d, *J* = 11.8 Hz, 1H, OCH_2Ph), 4.52 (dd, *J* = 22.7, 11.9 Hz, 2H, OCH_2Ph), 4.33 (dt, *J* = 6.9, 4.8 Hz, 1H, H-4), 4.20 (dd, *J* = 6.9, 3.9 Hz, 1H, H-3), 4.11 (dd, *J* = 3.9, 1.9 Hz, 1H, H-2), 3.80 (qd, *J* = 12.1, 4.8 Hz, 2H, H-5), 3.42 (s, 3H, OCH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 137.6 (Ar), 128.7 (Ar), 128.6 (Ar), 128.1 (2C, Ar), 128.0 (Ar), 127.9 (Ar), 108.1 (C-1), 87.3 (C-2), 83.0 (C-3), 80.7 (C-4), 72.6 (OCH_2Ph), 72.3 (OCH_2Ph), 62.4 (C-5), 55.8 (OCH_3); HRMS (ESI) m/z calcd for $C_{20}H_{24}O_5Na$ $[M+Na]^+$ 367.1516, found 367.1513.

Methyl 2,3-di-*O*-benzyl-6-deoxy-α-D-glucofuranoside (412).

To a stirred solution of compound **410α** (2.5 g, 7.4 mmol) in anhydrous CH_2Cl_2 (25 mL), Dess-Martin periodinane (4.8 g, 11 mmol) was added and then stirring was continued at room temperature for 3 h. After completion, the reaction mixture was diluted with ether and saturated $NaHCO_3$, saturated NaS_2O_3, were added and stirring was continued until two layers were formed, and the aqueous phase was extracted with ether. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to give a crude aldehyde which was dried and used for the next step. To a stirred solution of the crude aldehyde in anhydrous THF (20 mL) at 0 °C, methylmagnesium chloride (3.5 mL, 10 mmol) was added dropwise and stirring was continued for 1 h. After completion, saturated NH_4Cl was added, and the aqueous phase was extracted with ether. The organic layer was washed with brine, dried over Na_2SO_4 and the solvent was evaporated under reduced pressure to give a crude product which was purified using flash column chromatography (9:1 hexane/ethyl acetate) to give compound **412** (1.3 g, 47% after 2

steps) as a colorless oil; R_f = 0.26 (7:3 hexane-ethyl acetate); $[\alpha]^{25}_D$ = +67 (*c* = 0.80, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 7.39 – 7.27 (m, 10H, ArH), 4.86 (d, *J* = 4.2 Hz, 1H, H-1), 4.72 (d, *J* = 11.7 Hz, 1H, OCH_2Ph), 4.66 (d, *J* = 11.9 Hz, 1H, OCH_2Ph), 4.58 (d, *J* = 3.7 Hz, 1H, OCH_2Ph), 4.56 (d, *J* = 3.6 Hz, 1H, OCH_2Ph), 4.35 (dd, *J* = 7.5, 5.9 Hz, 1H, H-4), 4.06 (ddd, *J* = 8.8, 6.2, 4.0 Hz, 2H, H-2, H-5), 4.00 (dd, *J* = 7.5, 2.8 Hz, 1H, H-3), 3.39 (s, 3H, OCH_3), 1.23 (d, *J* = 6.6 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 137.6 (2C, Ar), 128.6 (2C, Ar), 128.4 (Ar), 128.2 (Ar), 128.1 (Ar), 127.9 (Ar), 100.2 (C-1), 84.8 (C-2), 82.6 (C-4), 79.4 (C-3), 72.8 (2C, OCH_2Ph), 66.3 (C-5), 55.3 (OCH_3), 18.5 (CH_3); HRMS (ESI) m/z calcd for $C_{21}H_{26}O_5Na$ $[M+Na]^+$ 381.1672, found 381.1675.

Methyl 3,5-*O*-benzylidene-6-deoxy-α-D-glucofuranoside (414).

Compound **412** (40 mg, 0.11 mmol) was dissolved in MeOH (1.0 mL) and Pd/C (10 mg) was added, then the reaction mixture was stirred at room temperature overnight. After completion, the reaction mixture was filtered through Celite and evaporated to dryness under reduced pressure to give a crude product which was dissolved in anhydrous CH_3CN (1.1 mL), and treated with benzaldehyde dimethyl acetal (34 µL, 0.22 mL) and camphorsulfonic acid (14 mg, 60 µmol). Then the reaction mixture was stirred at room temperature for 4 h before it was quenched with Et_3N. The reaction mixture was evaporated to dryness to give a crude product which was purified using column chromatography (9:1 toluene/acetone) to give compound **414** (21 mg, 72% after 2 steps) as a white solid; R_f = 0.31 (9:1 toluene-acetone); $[\alpha]^{25}_D$ = +52 (*c* = 0.60, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 7.51 – 7.48 (m, 2H, ArH), 7.38 – 7.33 (m, 3H, ArH), 5.50 (s, 1H, ArCH), 5.30 (d, *J* = 4.1 Hz, 1H, H-1), 4.36 – 4.33 (m, 1H, H-3), 4.26 (dd, *J* = 4.0, 0.9 Hz, 1H, H-2), 4.12 (qd, *J* = 6.6, 1.8 Hz, 1H, H-5), 4.02 (t, *J* = 2.0 Hz, 1H, H-4), 3.58 (s, 3H, OCH_3), 1.46 (d, *J* = 6.6 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.0 (Ar), 129.1 (Ar), 128.4 (Ar), 126.3 (Ar), 103.8 (C-1),

99.6 (ArCH), 81.6 (C-3), 75.5 (C-2), 74.3 (C-5), 73.0 (C-4), 56.8 (OCH_3), 17.6 (CH_3); HRMS (ESI) m/z calcd for $C_{14}H_{18}O_5Na$ $[M+Na]^+$ 289.1046, found 289.1048.

Methyl 2,3-di-*O*-benzyl-6-deoxy-5-*O*-(*p*-nitrocarbonyl)-β-L-idofuranoside (416).

To a stirred solution of compound **412** (0.89 g, 2.5 mmol) in anhydrous THF (6.2 mL) at -20 °C, PPh_3 (0.78 g, 3.0 mmol) and *p*-nitrobenzoic acid (0.51 g, 3.0 mmol) were added. After that, DIAD (0.6 mL, 3.0 mmol) was added and then the resulting solution was stirred at -20 °C to room temperature for 12 h. After completion, saturated $NaHCO_3$ was added, and the aqueous phase was extracted with ether. The organic layer was washed with brine, dried over Na_2SO_4 and the solvent was evaporated under reduced pressure to give a crude product which was purified using flash column chromatography (9:1 – 5:1 hexane/ethyl acetate) to give compound **416** as a colorless oil (0.88 g, 70%); R_f = 0.63 (7:3 hexane-ethyl acetate); $[\alpha]^{25}_D$ = +17 (*c* = 0.80, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.24 – 8.20 (m, 2H, ArH), 8.09 (dd, *J* = 8.8, 1.8 Hz, 2H, ArH), 7.40 – 7.30 (m, 5H, ArH), 7.21 – 7.12 (m, 5H, ArH), 5.48 – 5.42 (m, 1H, H-5), 4.89 (dd, *J* = 4.3, 1.6 Hz, 1H, H-1), 4.68 (dd, *J* = 11.9, 1.6 Hz, 1H, OCH_2Ph), 4.59 (ddd, *J* = 21.8, 11.9, 1.6 Hz, 2H, OCH_2Ph), 4.44 (dd, *J* = 11.8, 1.6 Hz, 1H, OCH_2Ph), 4.40 – 4.36 (m, 1H, H-4), 4.30 (ddd, *J* = 6.8, 4.9, 1.6 Hz, 1H, H-3), 4.03 – 3.98 (m, 1H, H-2), 3.44 (d, *J* = 1.6 Hz, 3H, OCH_3), 1.44 (dd, *J* = 6.5, 1.6 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.8 (Ar-CO_2), 150.5 (Ar), 137.6 (Ar), 136.1 (Ar), 130.8 (2C, Ar), 128.6 (Ar), 128.4 (Ar), 128.3 (Ar), 128.2 (Ar), 127.8 (Ar), 123.5 (2C, Ar), 101.1 (C-1), 83.9 (C-2), 81.3 (C-3), 78.1 (C-4), 72.9 (OCH_2Ph), 72.5 (OCH_2Ph), 71.1 (C-5), 55.6 (OCH_3), 16.4(CH_3); HRMS (ESI) m/z calcd for $C_{28}H_{29}NO_8Na$ $[M+Na]^+$ 530.1785, found 530.1790.

Methyl 2,3-di-*O*-benzyl-6-deoxy-β-L-idofuranoside (417).

To a stirred solution of compound **416** (0.88 g, 1.3 mmol) in THF (1.3 mL)/MeOH (1.0 mL), NaOH (99 mg, 0.54 mmol) in water (0.80 mL) was added at 0 °C. The resulting solution was stirred at room temperature for 1 h before the reaction mixture was diluted with water and extracted with ether. The organic layer was washed with brine, dried over Na_2SO_4 and the solvent was evaporated under reduced pressure to a crude product which was subjected to flash column chromatography (7:3 hexane/ethyl acetate) to give compound **417** (0.32 g, 68%) as a colorless oil; R_f = 0.32 (7:3 hexane-ethyl acetate); $[\alpha]^{25}_D$ = +40 (*c* = 0.80, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 – 7.27 (m, 10H, ArH), 4.79 (d, *J* = 4.2 Hz, 1H, H-1), 4.75 (d, *J* = 11.6 Hz, 1H, OCH_2Ph), 4.66 (d, *J* = 11.8 Hz, 1H, OCH_2Ph), 4.55 (dd, *J* = 11.7, 5.0 Hz, 2H, OCH_2Ph), 4.44 (dd, *J* = 7.2, 5.8 Hz, 1H, H-4), 4.03 (dd, *J* = 5.8, 4.2 Hz, 1H, H-2), 3.96 – 3.90 (m, 1H, H-5), 3.88 (t, *J* = 7.4 Hz, 1H, H-3), 3.38 (s, 3H, OCH_3), 1.23 (d, *J* = 6.2 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 137.5 (Ar), 137.4 (Ar), 128.8 (Ar), 128.7 (Ar), 128.5 (Ar), 128.3 (Ar), 128.2 (Ar), 128.0 (Ar), 100.3 (C-1), 84.7 (C-2), 82.5 (C-4), 79.2 (C-3), 72.7 (OCH_2Ph), 72.4 (OCH_2Ph), 67.5 (C-5), 55.2 (OCH_3), 19.6 (CH_3); HRMS (ESI) m/z calcd for $C_{21}H_{26}O_5Na$ $[M+Na]^+$ 381.1672, found 381.1675.

Methyl 3,5-*O*-benzylidene-6-deoxy-β-L-idofuranoside (418).

Compound **417** (32 mg, 90 μmol) was dissolved in MeOH (1.0 mL), and Pd/C (10 mg) was added, then the reaction mixture was stirred at room temperature overnight. After completion, the reaction mixture was filtered through Celite and evaporated to dryness to give a crude product which was dissolved in anhydrous CH_3CN (1.1 mL), and treated with benzaldehyde dimethyl acetal (28 μL, 0.18 mmol) and camphorsulfonic acid (12 mg, 50 μmol). Then the reaction mixture was stirred at room temperature for 4 h before it was quenched with Et_3N. The reaction mixture was evaporated to dryness to give crude a product which was purified using column chromatography (9:1

toluene/acetone) to give compound **418** (16 mg, 67% after 2 steps) as a white solid; R_f = 0.36 (7:3 toluene-acetone); $[\alpha]^{25}_D$ = +108 (*c* = 0.40, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.53 – 7.43 (m, 2H, ArH), 7.41 – 7.31 (m, 3H, ArH), 5.73 (s, 1H, ArCH), 5.25 (dd, *J* = 4.2, 0.5 Hz, 1H, H-1), 4.44 – 4.38 (m, 2H, H-3, H-5), 4.27 (d, *J* = 4.2 Hz, 1H, H-2), 3.97 (t, *J* = 2.4 Hz, 1H, H-4), 3.57 (s, 3H, OCH_3), 2.97 (s, 1H, OH), 1.47 (d, *J* = 7.1 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.3 (Ar), 129.1 (Ar), 128.4 (Ar), 126.3 (Ar), 103.3 (C-1), 93.0 (ArCH), 79.0 (C-3), 76.1 (C-2), 75.9 (C-4), 69.7 (C-5), 56.6 (OCH_3), 16.5 CH_3); HRMS (ESI) m/z calcd for $C_{14}H_{18}O_5Na$ $[M+Na]^+$ 289.1046, found 289.1048.

Methyl 2,3,5-tri-*O*-benzyl-6-deoxy-α-D-glucofuranoside (419).

A stirred solution of compound **412** (0.56 g, 1.6 mmol) in anhydrous DMF (8.0 mL) at 0 °C was treated with NaH (83 mg, 2.0 mmol) and stirring was continued for 10 min at 0 °C before BnBr (0.25 mL, 2.0 mmol) was added, and then the reaction mixture was stirred at room temperature for 5 h. After completion, water was added slowly to the reaction mixture and the aqueous phase was extracted with ether. The organic layer was washed with brine, dried over Na_2SO_4 and the solvent was evaporated under reduced pressure to give a crude product which was purified using flash column chromatography (9:1-5:1 hexane/ethyl acetate) to give compound **419** (0.58 g, 82%) as a colorless oil; R_f = 0.65 (7:3 hexane-ethyl acetate); $[\alpha]^{25}_D$ = +70 (*c* = 0.80, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 – 7.25 (m, 15H, Ar), 4.86 (d, *J* = 4.4 Hz, 1H, H-1), 4.66 (dd, *J* = 11.9, 9.9 Hz, 2H, OCH_2Ph), 4.60 – 4.54 (m, 3H, OCH_2Ph), 4.53 – 4.49 (m, 1H, OCH_2Ph), 4.21 (dd, *J* = 6.6, 5.6 Hz, 1H, H-3), 4.18 (dd, *J* = 5.6, 4.4 Hz, 1H, H-2), 4.06 (dd, *J* = 6.6, 4.6 Hz, 1H, H-4), 3.77 (qd, *J* = 6.4, 4.6 Hz, 1H, H-5), 3.41 (s, 3H, OCH_3), 1.17 (d, *J* = 6.4 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.2 (Ar), 138.2 (Ar), 138.0 (Ar), 128.5 (2C, Ar), 128.3 (2C, Ar), 128.1 (Ar), 128.0 (Ar), 127.9 (Ar), 127.8 (Ar), 127.4 (Ar), 101.0 (C-1), 83.2 (C-2), 82.1 (C-3), 80.6 (C-4), 73.5 (C-

5), 72.8 (OCH_2Ph), 72.5 (OCH_2Ph), 71.9 (OCH_2Ph), 55.5 (OCH_3), 16.9 (CH_3); HRMS (ESI) m/z calcd for $C_{28}H_{32}O_5Na$ $[M+Na]^+$ 471.2124, found 471.2142.

Methyl 2,3,5-tri-*O*-benzyl-6-deoxy-β-L-idofuranoside (421).

A stirred solution of compound **417** (0.52 g, 1.3 mmol) in anhydrous DMF (6.5 mL) at 0 °C was treated with NaH (68 mg, 1.7 mmol) and then stirring was continued for 10 min at 0 °C before BnBr (0.21 mL, 1.7 mmol) was added, and the reaction mixture was stirred at room temperature for 5 h. After completion, water was added slowly to the reaction mixture and aqueous phase was extracted with ether. The organic layer was washed with brine, dried over Na_2SO_4, and the solvent was evaporated under reduced pressure to give a crude product which was purified using flash column chromatography (9:1-17:3 hexane/ethyl acetate) to give compound **421** (0.50 g, 86%) as a colorless oil; R_f = 0.56 (4:1 hexane-ethyl acetate); $[\alpha]^{25}_D$ = +30 (*c* = 0.30, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36 – 7.25 (m, 13H, ArH), 7.22 – 7.20 (m, 2H, ArH), 4.88 (d, *J* = 4.2 Hz, 1H, H-1), 4.65 (d, *J* = 12.0 Hz, 1H, OCH_2Ph), 4.60 – 4.54 (m, 3H, OCH_2Ph), 4.50 (d, *J* = 11.9 Hz, 1H, OCH_2Ph), 4.42 (d, *J* = 11.7 Hz, 1H, OCH_2Ph), 4.26 (dd, *J* = 6.4, 4.6 Hz, 1H, H-3), 4.22 (t, *J* = 6.2 Hz, 1H, H-4), 3.97 (t, *J* = 4.4 Hz, 1H, H-2), 3.85 (t, *J* = 6.1 Hz, 1H, H-5), 3.42 (s, 3H, OCH_3), 1.28 (d, *J* = 6.2 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.0 (Ar), 138.4 (Ar), 137.9 (Ar), 128.5 (2C, Ar), 128.4 (Ar), 128.2 (Ar), 128.0 (Ar), 127.7 (2C, Ar), 127.5 (Ar), 101.2 (C-1), 84.0 (C-2), 82.0 (C-3), 79.6 (C-4), 73.3 (C-5), 72.8 (OCH_2Ph), 72.6(OCH_2Ph), 70.7(OCH_2Ph), 55.6 (OCH_3), 16.1 (CH_3); HRMS (ESI) m/z calcd for $C_{28}H_{32}O_5Na$ $[M+Na]^+$ 471.2124, found 471.2142.

General Procedure for transglycosylation of methyl furanosides with *p*-thiocresol (GP14).

To a stirred solution of methyl furanoside (1.0 equiv.) in anhydrous CH_2Cl_2 (0.06 M in the substrate) at 0 °C, *p*-thiocresol (1.1 equiv.) was added and stirring continued for 10 min at 0 °C.

Then $BF_3.OEt_2$ (2.0 equiv.) was added, and the reaction mixture stirred at 0 °C for 2 h before it was quenched with Et_3N. Then the reaction mixture was evaporated to dryness under reduced pressure and the anomers were separated using column chromatography to give the α- and β-anomers.

_p_-Cresyl 2,3,5-tri-*O*-benzyl-6-deoxy-1-thio-α-D-glucofuranoside (394α) and _p_-Cresyl 2,3,5-tri-*O*-benzyl-6-deoxy-1-thio-β-D-glucofuranoside (394β).

According to the general transglycosylation procedure (GP14), compound **419** (0.58 g, 1.3 mmol) was treated with *p*-thiocresol (0.18 g, 1.4 mmol) and $BF_3.OEt_2$ (0.26 mL, 2.6 mmol) in anhydrous CH_2Cl_2 (20 mL). The anomers were separated using column chromatography (0.3:99.7 acetone/toluene) to give the α- and β-anomers (α/β = 1:1).

394α: (0.23 g, 33%) colorless oil; R_f = 0.78 (49:1 toluene-acetone); $[\alpha]^{25}_D$ = +103 (*c* = 0.60, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.52 – 7.27 (m, 16H, ArH), 7.24 – 7.20 (m, 2H, ArH), 7.09 – 7.06 (m, 2H, ArH), 5.84 (d, *J* = 5.3 Hz, 1H, H-1), 4.80 (d, *J* = 11.9 Hz, 1H, OCH_2Ph), 4.72 (d, *J* = 11.6 Hz, 1H, OCH_2Ph), 4.59 (d, *J* = 5.3 Hz, 1H, OCH_2Ph), 4.57 (d, *J* = 5.5 Hz, 1H, OCH_2Ph), 4.47 (d, *J* = 11.7 Hz, 1H, OCH_2Ph), 4.36 (dd, *J* = 7.5, 4.3 Hz, 1H, H-4), 4.35 (d, *J* = 11.9 Hz, 1H, OCH_2Ph) 4.29 (dd, *J* = 5.3, 2.0 Hz, 1H, H-2), 3.96 (dd, *J* = 4.3, 1.9 Hz, 1H, H-3), 3.90 – 3.85 (m, 1H, H-5), 2.32 (s, 3H, $ArCH_3$), 1.16 (d, *J* = 6.3 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.5 (Ar), 137.6 (Ar), 137.5 (Ar), 137.0 (Ar), 132.3 (Ar), 131.9 (Ar), 129.6 (Ar), 128.7 (Ar), 128.6 (Ar), 128.3 (Ar), 128.2 (2C, Ar), 128.1 (Ar), 128.0 (Ar), 127.8 (Ar), 127.3 (Ar), 91.0 (C-1), 83.5 (C-4), 83.2 (C-2), 83.1 (C-3) 74.1 (C-5), 73.4 (OCH_2Ph), 72.2 (OCH_2Ph), 71.9 (OCH_2Ph), 21.2 (Ar-CH_3), 17.1 (CH_3); HRMS (ESI) m/z calcd for $C_{34}H_{36}O_4SNa$ $[M+Na]^+$ 563.2226, found 563.2238.

394β: (0.22 g, 32%) colorless oil R_f = 0.77 (49:1 toluene-acetone); $[\alpha]^{25}_D$ = -45 (*c* = 0.30, $CHCl_3$) ^1H NMR (600 MHz, $CDCl_3$) δ 7.44 (d, *J* = 7.9 Hz, 2H, ArH), 7.39 – 7.26 (m, 16H, ArH), 7.08 (d, *J* = 7.9 Hz, 2H, ArH), 5.36 (d, *J* = 2.5 Hz, 1H, H-1), 4.78 (d, *J* = 11.8 Hz, 1H, OCH_2Ph), 4.65 (dd, *J* = 19.5, 11.8 Hz, 2H, OCH_2Ph), 4.51 (dd, *J* = 11.8, 3.3 Hz, 2H, OCH_2Ph), 4.31 (d, *J* = 11.7 Hz, 1H, OCH_2Ph), 4.15 (dd, *J* = 2.7, 1.2 Hz, 1H, H-2), 4.07 (dd, *J* = 8.2, 4.0 Hz, 1H, H-4), 4.00 (dq, *J* = 8.0, 6.2 Hz, 1H, H-5), 3.87 (dd, *J* = 4.0, 1.1 Hz, 1H, H-3), 2.31 (s, 3H, Ar-CH_3), 1.12 (d, *J* = 6.2 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.4 (Ar), 137.5 (Ar), 137.4 (Ar), 137.2 (Ar), 131.9 (Ar), 131.8 (Ar), 129.7 (Ar), 128.7 (Ar), 128.5 (Ar), 128.3 (Ar), 128.2 (Ar), 128.1 (Ar), 128.0 (2C, Ar), 127.9 (Ar), 127.4 (Ar), 90.7 (C-1), 87.2 (C-4), 85.8 (C-2), 82.3 (C-3), 74.8 (C-5), 72.4 (OCH_2Ph), 72.0 (OCH_2Ph), 71.6 (OCH_2Ph), 21.2 (Ar-CH_3), 16.9 (CH_3); HRMS (ESI) m/z calcd for $C_{34}H_{36}O_4SNa$ $[M+Na]^+$ 563.2226, found 563.2238.

***p*-Cresyl 2,3,5-tri-*O*-benzyl-6-deoxy-1-thio-β-L-idofuranoside (395β) and *p*-Cresyl 2,3,5-tri-*O*-benzyl-6-deoxy-1-thio-α-L-idofuranoside (395α).**

According to general transglycosylation procedure (GP14), compound **421** (0.59 g, 1.3 mmol) was treated with *p*-thiocresol (0.18 g, 1.4 mmol) and $BF_3.OEt_2$ (0.26 mL, 2.6 mmol) in anhydrous CH_2Cl_2 (20 mL). The anomers were separated using column chromatography (0.3: 99.7 acetone/toluene) to give the α- and β-anomers (α/β = 1:1).

395β. (0.23 g, 33%) colorless oil; R_f = 0.78 (9:0.5:0.5 DCM-iPrOH-acetone); $[\alpha]^{25}_D$ = +50 (*c* = 0.60, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 7.45 – 7.42 (m, 2H, ArH), 7.41 – 7.35 (m, 4H, ArH), 7.33 – 7.30 (m, 3H, ArH), 7.29 – 7.26 (m, 6H, ArH), 7.22 – 7.19 (m, 2H, ArH), 7.11 – 7.08 (m, 2H, ArH), 5.69 (d, *J* = 4.7 Hz, 1H, H-1), 4.63 (dd, *J* = 14.0, 11.7 Hz, 2H, OCH_2Ph), 4.56 (d, *J* = 11.9 Hz, 1H, OCH_2Ph), 4.44 (d, *J* = 4.8 Hz, 2H, OCH_2Ph), 4.40 (d, *J* = 11.4 Hz, 1H, OCH_2Ph), 4.25 (dd, *J* = 8.7, 3.6 Hz, 1H, H-4), 4.16 (dd, *J* = 4.7, 1.4 Hz, 1H, H-2), 4.12 (dd, *J* = 3.7, 1.4 Hz,

1H, H-3), 3.94 (dq, *J* = 8.7, 6.1 Hz, 1H, H-5), 2.32 (s, 3H, Ar-CH_3), 1.37 (d, *J* = 6.2 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.9 (Ar), 138.0 (Ar), 137.6 (Ar), 136.9 (Ar), 132.3 (Ar), 131.7 (Ar), 129.7 (Ar), 128.6 (Ar), 128.5 (Ar), 128.4 (Ar), 128.1 (Ar), 128.0 (Ar), 127.9 (Ar), 127.8 (Ar), 127.7 (Ar), 127.6 (Ar), 90.9 (C-1), 83.7 (C-2), 82.6 (C-4), 81.6 (C-3), 73.1 (OCH_2Ph), 72.4 (C-5), 72.3 (OCH_2Ph), 70.7 (OCH_2Ph), 21.2 (Ar-CH_3), 17.3 (CH_3); HRMS (ESI) m/z calcd for $C_{34}H_{36}O_4SNa$ $[M+Na]^+$ 563.2228, found 563.2238.

395α. (0.20 g, 30%) colorless oil; R_f = 0.77 (9:0.5:0.5 DCM-iPrOH-acetone); $[\alpha]^{25}_D$ = -97 (*c* = 0.10, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43 – 7.39 (m, 2H, ArH), 7.35 – 7.26 (m, 15H, ArH), 7.13 – 7.10 (m, 2H, ArH), 5.33 (d, *J* = 2.1 Hz, 1H, H-1), 4.63 (d, *J* = 11.3 Hz, 1H, OCH_2Ph), 4.55 (dd, *J* = 11.8, 2.5 Hz, 2H, OCH_2Ph), 4.49 (dd, *J* = 11.7, 1.4 Hz, 2H, OCH_2Ph), 4.42 (d, *J* = 11.3 Hz, 1H, OCH_2Ph), 4.13 (dd, *J* = 2.3, 0.9 Hz, 1H, H-2), 4.12 (dd, *J* = 3.8, 1.0 Hz, 1H, H-3), 4.11 – 4.08 (m, 1H, H-5), 4.04 (dd, *J* = 8.8, 3.9 Hz, 1H, H-4), 2.34 (s, 3H, Ar-CH_3), 1.39 (d, *J* = 6.0 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.0 (Ar), 138.0 (Ar), 137.5 (Ar), 137.2 (Ar), 132.0 (Ar), 131.6 (Ar), 129.8 (Ar), 128.6 (Ar), 128.5 (Ar), 128.4 (Ar), 128.0 (Ar), 127.9 (Ar), 127.8 (2C, Ar), 127.7 (Ar), 127.5 (Ar), 91.0 (C-1), 86.8 (C-4), 85.6 (C-2), 81.3 (C-3), 72.8 (OCH_2Ph), 72.1 (C-5), 71.9 (OCH_2Ph), 70.9 (OCH_2Ph), 21.2 (Ar-CH_3), 17.5 (CH_3); HRMS (ESI) m/z calcd for $C_{34}H_{36}O_4SNa$ $[M+Na]^+$ 563.2228, found 563.2238.

Methyl 2,3-di-*O*-benzyl-6-deoxy-α-D-altrofuranoside (425) and Methyl 2,3-di-*O*-benzyl-6-deoxy-β-L-galactofuranoside (426).

To a stirred solution of compound **423**[186, 187] (0.75 g, 2.2 mmol) in anhydrous CH_2Cl_2 (7.3 mL), Dess-Martin periodinane (1.4 g, 3.3 mmol) was added and the resulting suspension was stirred at room temperature for 3 h. After completion, the reaction mixture was diluted with ether and saturated $NaHCO_3$, and saturated NaS_2O_3, were added. Then stirring was continued until two

layers were formed after which the aqueous phase was extracted with ether. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to give a crude aldehyde which was dried and used for the next step. To a stirred solution of the crude aldehyde in anhydrous THF (6.0 mL) at 0 °C, methylmagnesium chloride (1.5 mL, 4.4 mmol) was added dropwise and stirring continued for 1 h. After completion, saturated NH_4Cl was added, and the aqueous phase was extracted with ether. The organic layer was washed with brine, dried over Na_2SO_4 and the solvent was evaporated under reduced pressure, and two isomers were separated using flash column chromatography (9:1 hexane/ethyl acetate) to give the **D-altro-425** (0.41 g, 56%) as a colorless oil and then the **L-galacto-426** (0.36 g, 46%) as a colorless oil.

D-altro-425: R_f = 0.63 (3:2 hexane-ethyl acetate); $[\alpha]^{25}_D$ = +44 (*c* = 0.80, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 – 7.27 (m, 10H, ArH), 4.94 (s, 1H, H-1), 4.57 (d, *J* = 11.9 Hz, 1H, OCH_2Ph), 4.50 (d, *J* = 11.3 Hz, 3H, OCH_2Ph), 4.06 – 4.02 (m, 2H, H-4, H-5), 3.98 (dd, *J* = 7.9, 2.4 Hz, 2H, H-2, H-3), 3.38 (s, 3H, OCH_3), 1.15 (d, *J* = 6.6 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 137.7 (Ar), 137.4 (Ar), 128.7 (Ar), 128.6 (Ar), 128.2 (Ar), 128.1 (2C, Ar), 107.3 (C-1), 87.0 (C-2), 86.3 (C-3), 81.6 (C-4), 72.3 (OCH_2Ph), 71.8 (OCH_2Ph), 66.9 (C-5), 54.9 (OCH_3), 18.2 (CH_3); HRMS (ESI) m/z calcd for $C_{21}H_{26}O_5Na$ $[M+Na]^+$ 381.1672, found 381.1661.

L-galacto-426: R_f = 0.60 (3:2 hexane-ethyl acetate); $[\alpha]^{25}_D$ = +15 (c=0.20, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 – 7.29 (m, 10H, ArH), 4.95 (s, 1H, H-1), 4.58 (dd, *J* = 16.8, 11.8 Hz, 2H, OCH_2Ph), 4.53 – 4.48 (m, 2H, OCH_2Ph), 4.00 (dd, *J* = 2.1, 0.9 Hz, 1H, H-2), 3.92 – 3.86 (m, 2H, H-3, H-4), 3.85 – 3.79 (m, 1H, H-5), 3.40 (s, 3H, OCH_3), 1.22 (d, *J* = 6.4 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 137.9 (Ar), 137.7 (Ar), 128.9 (Ar), 128.8 (Ar), 128.3 (4C, Ar), 107.4 (C-1), 87.9 (C-2), 86.0 (C-4), 84.1 (C-3), 72.6 (OCH_2Ph), 72.3(OCH_2Ph), 68.4 (C-5), 55.2 (OCH_3), 19.8 (CH_3); HRMS (ESI) m/z calcd for $C_{21}H_{26}O_5Na$ $[M+Na]^+$ 381.1672, found 381.1661.

Methyl 3,5-*O*-(Di-*tert*-butylsilylene)-6-deoxy-α-D-altrofuranoside (427).

D-altro-425 (50 mg, 0.14 mmol) was dissolved in MeOH (1.0 mL), and Pd/C (15 mg) was added, and the reaction mixture was stirred at room temperature overnight. After completion, the reaction mixture was filtered through Celite and evaporated to dryness to give a crude product which was dissolved in pyridine (0.55 mL) at 0 °C, and treated with DMAP (9.0 mg, 70 µmol) and di-*tert*-butylsilyl bis(trifluoromethanesulfonate) (50 µL, 0.15 mmol). Then the reaction mixture was allowed to reach room temperature and then stirred for 12 h before it was quenched with MeOH (0.2 mL). The crude reaction mixture was concentrated under reduced pressure to give a crude product which was purified by flash chromatography on silica gel (hexane/ethyl acetate 9:1) to give **427** (22 mg, 50% after 2 steps) as a colorless oil; R_f = 0.35 (4:1 hexane-ethyl acetate); $[\alpha]^{25}_D$ = +20 (*c* = 0.20, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.77 (d, *J* = 3.4 Hz, 1H, H-1), 4.10 – 4.04 (m, 2H, H-2, H-5), 3.95 (dd, *J* = 9.6, 7.7 Hz, 1H, H-3), 3.44 (t, *J* = 9.4 Hz, 1H, H-4), 3.41 (s, 3H, OCH_3), 1.30 (d, *J* = 6.0 Hz, 3H, CH_3), 1.05 (s, 9H, $3CH_3$), 0.98 (s, 9H, $3CH_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ 108.7 (C-1), 82.1 (C-2), 81.3 (C-3), 79.8 (C-4), 74.2 (C-5), 56.1 (OCH_3), 27.7 ($3CH_3$), 27.3 ($3CH_3$), 22.8 ((CH_3)$_3$C), 21.5 (CH_3), 19.9 ((CH_3)$_3$C); HRMS (ESI) m/z calcd for $C_{15}H_{30}O_5SiNa$ $[M+Na]^+$ 341.1754, found 341.1754.

Methyl 2,3,5-tri-*O*-benzyl-6-deoxy-α-D-altrofuranoside (428).

A stirred solution of compound **425** (0.12 g, 0.35 mmol) in anhydrous DMF (2.0 mL) at 0 °C was treated with NaH (21 mg, 0.53 mmol) and stirring was continued for 10 min at 0 °C before BnBr (71 µL, 0.53 mmol) was added, and the reaction mixture was stirred at room temperature for 5 h. After completion, water was added slowly to the reaction mixture and the aqueous phase was extracted with ether. The organic layer was washed with brine, dried over Na_2SO_4 and the solvent was evaporated under reduced pressure to give a crude product which was purified using flash

column chromatography (9:1-17:3 hexane/ethyl acetate) to give compound **428** (0.14 g, 87%) as a colorless oil; R_f = 0.65 (7:3 hexane-ethyl acetate); $[\alpha]^{25}_D$ = +78 (*c* = 0.5, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 – 7.25 (m, 15H, ArH), 4.98 (s, 1H, H-1), 4.64 – 4.57 (m, 2H, OCH_2Ph), 4.56 (s, 2H, OCH_2Ph), 4.51 – 4.43 (m, 2H, OCH_2Ph), 4.09 (t, *J* = 5.0 Hz, 1H, H-4), 4.03 (dd, *J* = 5.2, 1.7 Hz, 1H, H-3), 3.99 (dd, *J* = 1.7, 0.9 Hz, 1H, H-2), 3.69 (dd, *J* = 6.4, 4.9 Hz, 1H, H-5), 3.41 (s, 3H, OCH_3), 1.27 (d, *J* = 6.4 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.9 (Ar), 138.1 (Ar), 137.7 (Ar), 128.5 (Ar), 128.4 (2C, Ar), 128.0 (Ar), 127.9 (3C, Ar), 127.8 (Ar), 127.5 (Ar), 107.4 (C-1), 87.8 (C-2), 85.9 (C-4), 83.4 (C-3), 74.6 (C-5), 72.0 (OCH_2Ph), 71.7 (OCH_2Ph), 71.3 (OCH_2Ph), 54.9 (OCH_3), 16.4 (CH_3); HRMS (ESI) m/z calcd for $C_{28}H_{32}O_5Na$ $[M+Na]^+$ 471.2142, found 471.2137.

Methyl 2,3,5-tri-*O*-benzyl-6-deoxy-β-L-galactofuranoside (429).

To a stirred solution of **426** (0.11 g, 0.30 mmol) in anhydrous DMF (1.5 mL) at 0 °C, NaH (18 mg, 0.45 mmol) was added and stirring was continued for 10 min at 0 °C. Then BnBr (60 µL, 0.45 mmol) was added and the reaction mixture was stirred at room temperature for 5 h. After completion, water was added slowly to the reaction mixture and the aqueous phase was extracted with ether. The organic layer was washed with brine, dried over Na_2SO_4 and the solvent was evaporated under reduced pressure to give a crude product which was purified using flash column chromatography (9:1-17:3 hexane/ethyl acetate) to give compound **429** (0.13 g, 91%) as a colorless oil; R_f = 0.68 (7:3 hexane-ethyl acetate); $[\alpha]^{25}_D$ = +10 (*c* = 0.2, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36 – 7.22 (m, 15H, ArH), 4.96 (s, 1H, H-1), 4.63 (d, *J* = 12.0 Hz, 1H, OCH_2Ph), 4.57 – 4.52 (m, 2H, OCH_2Ph), 4.51 – 4.45 (m, 2H, OCH_2Ph), 4.40 (d, *J* = 11.8 Hz, 1H, OCH_2Ph), 4.02 (d, *J* = 6.6, 4.3 Hz, 1H, H-4), 3.98 (dd, *J* = 2.8, 1.1 Hz, 1H, H-2), 3.95 (ddd, *J* = 6.7, 2.8, 0.7 Hz, 1H, H-3), 3.70 (dd, *J* = 6.4, 4.3 Hz, 1H, H-5), 3.38 (s, 3H, OCH_3), 1.23 (d, *J* = 6.5 Hz, 3H, CH_3);

^{13}C NMR (151 MHz, $CDCl_3$) δ 138.8 (Ar), 138.0 (Ar), 137.8 (Ar), 128.6 (Ar), 128.5 (Ar), 128.4 (Ar), 128.2 (Ar), 128.1 (Ar), 128.0 (2C, Ar), 127.9 (Ar), 127.6 (Ar), 107.0 (C-1), 88.4 (C-2), 84.3 (C-4), 83.3 (C-3), 73.6 (C-5), 72.3 (OCH_2Ph), 71.9 (OCH_2Ph), 71.4 (OCH_2Ph), 54.9 (OCH_3), 16.0 (CH_3); HRMS (ESI) m/z calcd for $C_{28}H_{32}O_5Na$ $[M+Na]^+$ 471.2142, found 471.2137.

***p*-Cresyl 2,3,5-tri-*O*-benzyl-6-deoxy-1-thio-α-D-altrofuranoside (396α) and *p*-Cresyl 2,3,5-tri-*O*-benzyl-6-deoxy-1-thio-β-D-altrofuranoside (396β).**

According to general transglycosylation procedure (GP14), compound **428** (0.11 g, 0.24 mmol) was treated with *p*-thiocresol (33 mg, 0.26 mmol) and $BF_3.OEt_2$ (0.13 mL, 0.48 mmol) in anhydrous CH_2Cl_2 (4.0 mL). The anomers were separated using column chromatography (1: 19 Ethyl acetate/Hexane) to give the α- and β-anomers (α/β = 1:1).

396α. (50 mg, 39%) colorless oil; R_f = 0.27 (19:1 hexane-ethyl acetate); $[\alpha]^{25}_D$ = +110 (*c* = 0.20, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43 – 7.41 (m, 2H, ArH), 7.38 – 7.23 (m, 15H, ArH), 7.14 – 7.11 (m, 2H, ArH), 5.55 (d, *J* = 2.4 Hz, 1H, H-1), 4.62 (d, *J* = 11.9 Hz, 1H, OCH_2Ph), 4.60 (d, *J* = 4.0 Hz, 1H, OCH_2Ph), 4.59 – 4.57 (m, 2H, OCH_2Ph), 4.55 (d, *J* = 12.2 Hz, 1H, OCH_2Ph), 4.47 (d, *J* = 11.7 Hz, 1H, OCH_2Ph), 4.27 (t, *J* = 5.1 Hz, 1H, H-4), 4.16 (ddd, *J* = 5.5, 2.4, 0.7 Hz, 1H, H-3), 4.13 (t, *J* = 2.4 Hz, 1H, H-2), 3.77 (qd, *J* = 6.4, 4.7 Hz, 1H, H-5), 2.35 (s, 3H, Ar-CH_3), 1.27 (d, *J* = 6.4 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.9 (Ar), 138.0 (Ar), 137.6 (Ar), 137.4 (Ar), 132.1 (Ar), 131.3 (Ar), 129.8 (Ar), 128.6 (Ar), 128.5 (Ar), 128.4 (Ar), 128.0 (2C, Ar), 127.9 (Ar), 127.8 (Ar), 127.5 (Ar), 90.9 (C-1), 88.5 (C-2), 85.3 (C-4), 83.8 (C-3), 74.3 (C-5), 72.1 (OCH_2Ph), 72.0 (OCH_2Ph), 71.5 (OCH_2Ph), 21.2 (Ar-CH_3), 16.7 (CH_3); HRMS (ESI) m/z calcd for $C_{34}H_{36}O_4SNa$ $[M+Na]^+$ 563.2228, found 563.2238.

396β. (39 mg, 30%) colorless oil; R_f = 0.25 (19:1 hexane-EtOAc); $[\alpha]^{25}_D$ = -56 (*c* = 0.20, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.44 (dd, *J* = 8.3, 2.4 Hz, 2H, ArH), 7.38 – 7.36 (m, 4H, ArH), 7.34 – 7.24 (m, 11H, ArH), 7.14 – 7.11 (m, 2H, ArH), 5.62 (d, *J* = 4.6 Hz, 1H, H-1), 4.66 (d, *J* = 11.7 Hz, 1H, OCH_2Ph), 4.56 (dd, *J* = 12.0, 3.7 Hz, 2H, OCH_2Ph), 4.50 (dd, *J* = 12.0, 3.4 Hz, 2H, OCH_2Ph), 4.45 (d, *J* = 11.7 Hz, 1H, OCH_2Ph), 4.21 (dd, *J* = 4.7, 2.6 Hz, 1H, H-2), 4.19 (t, *J* = 2.6 Hz, 1H, H-3), 3.90 – 3.82 (m, 2H, H-4, H-5), 2.34 (s, 3H, Ar-CH_3), 1.33 (d, *J* = 5.6 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.4 (Ar), 137.5 (Ar), 137.4 (Ar), 137.2 (Ar), 131.9 (Ar), 131.8 (Ar), 129.7 (Ar), 128.5 (Ar), 128.3 (Ar), 128.2 (Ar), 128.1 (Ar), 128.0 (2C, Ar), 127.9 (Ar), 127.4 (Ar), 90.7 (C-1), 87.2 (C-4), 84.5 (C-2), 83.2 (C-3), 75.0 (C-5), 72.3 (OCH_2Ph), 71.6 (OCH_2Ph), 71.0 (OCH_2Ph), 21.2 (Ar-CH_3), 17.0 (CH_3); HRMS (ESI) m/z calcd for $C_{34}H_{36}O_4SNa$ $[M+Na]^+$ 563.2228, found 563.2238.

***p*-Cresyl 2,3,5-tri-*O*-benzyl-6-deoxy-1-thio-β-L-galactofuranoside (397β) and *p*-Cresyl 2,3,5-tri-*O*-benzyl-6-deoxy-1-thio-α-L-galactofuranoside (397*α*).**

According to general transglycosylation procedure (GP14), compound **429** (0.12 g, 0.25 mmol) was treated with *p*-thiocresol (53 mg, 0.41 mmol) and $BF_3.OEt_2$ (0.14 mL, 0.54 mmol) in anhydrous CH_2Cl_2 (4.5 mL). The anomers were separated using column chromatography (19: 1 hexane/ethyl acetate) to give the α- and β-anomers (α/β = 1:6).

397β. (70 mg, 52%) colorless oil; R_f = 0.31 (19:1 hexane-ethyl acetate); $[\alpha]^{25}_D$ = +85 (c = 0.30, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.44 – 7.41 (m, 2H, ArH), 7.39 – 7.25 (m, 15H, ArH), 7.12 – 7.09 (m, 2H, ArH), 5.57 (d, *J* = 2.6 Hz, 1H, H-1), 4.66 (d, *J* = 11.8 Hz, 1H, OCH_2Ph), 4.62 (d, *J* = 11.9 Hz, 1H, OCH_2Ph), 4.58 (s, 1H, OCH_2Ph), 4.52 – 4.50 (m, 1H, OCH_2Ph), 4.49 (d, *J* = 5.2 Hz, 1H, OCH_2Ph), 4.42 (d, *J* = 11.6 Hz, 1H, OCH_2Ph), 4.23 (dd, *J* = 7.1, 4.2 Hz, 1H, H-4), 4.10 (t, *J* = 3.0 Hz, 1H, H-2), 4.05 (dd, *J* = 7.2, 3.2 Hz, 1H, H-3), 3.74 (dd, *J* = 6.5, 4.2 Hz, 1H, H-

5), 2.34 (s, 3H, Ar-CH_3), 1.26 (d, *J* = 6.5 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.7 (Ar), 138.4 (Ar), 137.9 (Ar), 137.6 (Ar), 137.5 (Ar), 132.3 (Ar), 131.1 (Ar), 129.7 (Ar), 128.6 (Ar), 128.5 (2C, Ar), 128.4 (Ar), 128.2 (Ar), 128.1 (Ar), 128.0 (Ar), 127.9 (2C, Ar), 127.8 (Ar), 127.6 (Ar), 90.4 (C-1), 88.7 (C-2), 83.6 (C-4), 83.5 (C-3), 73.3 (C-5), 72.4 (OCH_2Ph), 72.2 (OCH_2Ph), 72.1 (OCH_2Ph), 71.4 (OCH_2Ph), 21.2 (Ar-CH3), 16.2 (CH_3); HRMS (ESI) m/z calcd for $C_{34}H_{36}O_4SNa$ $[M+Na]^+$ 563.2228, found 563.2238.

397α. (12 mg, 9%) colorless oil; R_f = 0.22 (7:3 Hexane-EtOAc); $[\alpha]^{25}_D$ = -100 (*c* = 0.30, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.45 (d, *J* = 7.8 Hz, 2H, ArH), 7.42 (d, *J* = 8.3 Hz, 2H, ArH), 7.37 (t, *J* = 7.5 Hz, 2H, ArH), 7.33 – 7.24 (m, 11H, ArH), 7.09 (d, *J* = 7.9 Hz, 2H, ArH), 5.68 (d, *J* = 5.0 Hz, 1H, H-1), 4.74 (d, *J* = 11.6 Hz, 1H, OCH_2Ph), 4.61 (d, *J* = 8.1 Hz, 3H, OCH_2Ph), 4.57 (d, *J* = 11.6 Hz, 1H, OCH_2Ph), 4.52 (d, *J* = 11.6 Hz, 1H, OCH_2Ph), 4.31 (t, *J* = 4.7 Hz, 1H, H-2), 4.08 (t, *J* = 4.7 Hz, 1H, H-3), 3.97 (dd, *J* = 7.3, 5.3 Hz, 1H, H-4), 3.89 (p, *J* = 6.5 Hz, 1H, H-5), 2.32 (s, 4H, Ar-CH_3), 1.17 (d, *J* = 6.3 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.1 (Ar), 137.8 (Ar), 137.5 (Ar), 136.9 (Ar), 131.9 (Ar), 131.2 (Ar), 129.8 (Ar), 128.6 (Ar), 128.5 (Ar), 128.3 (Ar), 128.2 (Ar), 128.1 (Ar), 128.0 (Ar), 127.9 (Ar), 127.8 (Ar), 127.4 (Ar), 89.8 (C-1), 86.3 (C-4), 84.6 (C-2), 82.9 (C-3), 76.2 (C-5), 72.6 (OCH_2Ph), 72.1 (OCH_2Ph), 71.9 (OCH_2Ph), 21.2 (Ar-CH_3), 16.3 (CH_3); HRMS (ESI) m/z calcd for $C_{34}H_{36}O_4SNa$ $[M+Na]^+$ 563.2228, found 563.2238.

Acid-Washed Molecular Sieves.

Molecular sieves (4 Å, 30.0 g) were soaked in 2 N HCl (80.0 mL) for 12 h before the mixture was concentrated under reduced pressure. Water (100 mL) was added and the resulting suspension was filtered. The filter cake was washed with water (200 mL) and dried at 254 °C for 24 h to give acid-washed molecular sieves (28.0 g), which were used directly in the glycosylation reactions.

General glycosylation Protocol with Donor (GP15).

A mixture of donor **(394α, 395β, 396α, 397β)**, acceptor (1.1 equiv.), and activated 4 Å acid washed powdered molecular sieves (2 g/mmol of donor) in CH_2Cl_2 (0.2 M in the substrate) was stirred for 1 h at room temperature under argon and cooled to -30 °C. Then it was treated with *N*-iodosuccinimide (1.2 equiv.) and AgOTf (0.2 equiv.) and the reaction mixture was stirred at -30 °C for 30 min before it was quenched with Et_3N. The reaction mixture was diluted with CH_2Cl_2, filtered through Celite, washed with 20% aqueous $Na_2S_2O_3$, dried over Na_2SO_4, and concentrated under reduced pressure. Purification by flash column chromatography on silica gel afforded the corresponding α/β-glycofuranosides. The anomeric ratio of the products was determined by the integration of the ^{1}H NMR spectrum of the crude product mixture.

Benzyl 2,3,5-tri-*O*-benzyl-6-deoxy-α-D-glucofuranoside (436α) and Benzyl 2,3,5-tri-*O*-benzyl-6-deoxy-β-D-glucofuranoside (436β).

According to the general glycosylation procedure (GP15), the reaction mixture of donor **394α** (47 mg; 87 µmol) and benzyl alcohol (0.11 mL, 10 µmol) in anhydrous CH_2Cl_2 (0.44 mL) at -30 °C was treated with *N*-iodosuccinimide (26 mg, 11 µmol) and AgOTf (5.0 mg, 20 µmol). After chromatographic purification over silica gel eluting with 0.2% acetone in toluene, inseparable two anomers were obtained as a colorless oil. (34 mg, 75%); α/β: 1:3.2; R_f = 0.35 (49:1 toluene-acetone); HRMS (ESI) m/z calcd for $C_{34}H_{36}O_5Na$ $[M+Na]^+$ 547.2455, found 547.2453.

436α: ^{1}H NMR (900 MHz, $CDCl_3$) δ 7.40 – 7.21 (m, 20H, ArH), 5.10 (d, *J* = 4.5 Hz, 1H, H-1), 4.82 (d, *J* = 12.2 Hz, 1H, OCH_2Ph), 4.70 (d, *J* = 11.7 Hz, 1H, OCH_2Ph), 4.63 (d, *J* = 11.7 Hz, 1H, OCH_2Ph), 4.60 – 4.58 (m, 2H, OCH_2Ph), 4.55 (d, *J* = 11.3 Hz, 1H, OCH_2Ph), 4.51 (d, *J* = 11.7 Hz, 1H, OCH_2Ph), 4.47 (d, *J* = 11.7 Hz, 1H, OCH_2Ph), 4.28 (t, *J* = 6.2 Hz, 1H, H-3), 4.18 (t, *J* = 5.0

Hz, 1H, H-2), 4.13 (dd, *J* = 6.7, 4.8 Hz, 1H, H-4), 3.81 – 3.77 (m, 1H, H-5), 1.19 (d, *J* = 6.5 Hz, 3H, CH_3); ^{13}C NMR (226 MHz, $CDCl_3$) δ 139.3 (Ar), 138.3 (Ar), 138.0 (2C, Ar), 128.5 (Ar), 128.4 (Ar), 128.3 (Ar), 128.2 (Ar), 128.1 (Ar), 128.0 (Ar), 127.9 (2C, Ar), 127.8 (2C, Ar), 127.4 (Ar), 98.6 (C-1), 83.3 (C-2), 82.3 (C-3), 80.9 (C-4), 73.6 (C-5), 72.6 (2C, OCH_2Ph), 72.5 (OCH_2Ph), 69.3 (OCH_2Ph), 16.9 (CH_3).

436β: ^1H NMR (900 MHz, $CDCl_3$) δ 7.40 – 7.21 (m, 20H, ArH), 5.22 (d, *J* = 1.2 Hz, 1H, H-1), 4.88 (d, *J* = 12.0 Hz, 1H, OCH_2Ph), 4.72 (d, *J* = 11.9 Hz, 1H, OCH_2Ph), 4.62 (d, *J* = 11.9 Hz, 1H, OCH_2Ph), 4.58 – 4.56 (m, 3H, OCH_2Ph), 4.50 (d, *J* = 11.8 Hz, 1H, OCH_2Ph) 4.37 (d, *J* = 11.7 Hz, 1H, OCH_2Ph), 4.15 (dd, *J* = 8.2, 4.6 Hz, 1H, H-4), 4.12 (s, 1H, H-2), 3.94 (dq, *J* = 8.2, 6.2 Hz, 1H, H-5), 3.89 (dd, *J* = 4.6, 1.4 Hz, 1H, H-3), 1.14 (d, *J* = 6.2 Hz, 3H, CH_3); ^{13}C NMR (226 MHz, $CDCl_3$) δ 139.5 (Ar), 138.3 (Ar), 137.7 (2C, Ar), 128.6 (Ar), 128.5 (2C, Ar), 128.4 (Ar), 128.3 (Ar), 128.1 (Ar), 127.9 (2C, Ar), 127.8 (Ar), 127.6 (Ar), 127.4 (Ar), 106.4 (C-1), 86.1 (C-4), 85.0 (C-2), 81.5 (C-3), 75.1 (C-5), 72.1 (2C, OCH_2Ph), 72.0 (OCH_2Ph), 69.8 (OCH_2Ph), 16.8 (CH_3);

Isopropyl 2,3,5-tri-*O*-benzyl-6-deoxy-α-D-glucofuranoside (437α) and Isopropyl 2,3,5-tri-*O*-benzyl-6-deoxy-β-D-glucofuranoside (437β).

According to the general glycosylation procedure (GP15), the reaction mixture of donor **394α** (36 mg, 67 μmol) and isopropyl alcohol (6.1 μL, 80 μmol) in anhydrous CH_2Cl_2 (0.34 mL) at -30 °C was treated with *N*-iodosuccinimide (20 mg, 83 μmol) and AgOTf (3.5 mg, 13 μmol). After chromatographic purification over silica gel eluting with 0.2% acetone in toluene, two anomers were obtained (22 mg, 69%); α/β: 1:5.7.

437α. colorless oil : R_f = 0.28 (66:1 toluene-acetone); $[\alpha]^{25}_D$ = +20 (*c* = 0.10, $CHCl_3$); ^1H NMR (900 MHz, $CDCl_3$) δ 7.37 – 7.27 (m, 15H, ArH), 5.16 (d, *J* = 4.6 Hz, 1H, C-1), 4.67 (dd, *J* = 20.1,

11.8 Hz, 2H, OCH_2Ph), 4.61 (d, *J* = 11.3 Hz, 1H, OCH_2Ph), 4.54 (d, *J* = 11.4 Hz, 1H, OCH_2Ph), 4.50 (dd, *J* = 14.6, 11.7 Hz, 2H, OCH_2Ph), 4.21 (dd, *J* = 6.6, 5.2 Hz, 1H, H-3), 4.13 (t, *J* = 4.9 Hz, 1H, H-2), 4.11 (dd, *J* = 6.6, 5.0 Hz, 1H, H-4), 3.94 (p, *J* = 6.2 Hz, 1H, $(CH_3)_2CH$), 3.78 (dd, *J* = 6.5, 5.1 Hz, 1H, H-5), 1.27 (d, *J* = 6.2 Hz, 3H, CH_3), 1.19 (d, *J* = 6.1 Hz, 3H, CH_3), 1.17 (d, *J* = 6.4 Hz, 3H, CH_3); ^{13}C NMR (226 MHz, $CDCl_3$) δ 139.4 (Ar), 138.3 (Ar), 138.1 (Ar), 128.5 (Ar), 128.5 (Ar), 128.4 (Ar), 128.3 (Ar), 128.0 (2C, Ar), 127.9 (Ar), 127.8 (Ar), 127.3 (Ar), 98.7 (C-1), 83.4 (C-2), 82.5 (C-3), 80.7 (C-4), 73.7 (C-5), 72.5 (OCH_2Ph), 72.4 (OCH_2Ph), 72.0 (OCH_2Ph), 70.5 ($(CH_3)_2CH$), 23.8 (CH_3), 22.2 (CH_3), 17.0 (CH_3); HRMS (ESI) m/z calcd for $C_{30}H_{36}O_5Na$ $[M+Na]^+$ 499.2455, found 499.2453.

437β. colorless oil: R_f = 0.31 (66:1 toluene-acetone); $[\alpha]^{25}_D$ = -27 (*c* = 0.40, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 7.41 – 7.23 (m, 15H, ArH), 5.17 (d, *J* = 1.9 Hz, 1H, H-1), 4.76 (d, *J* = 11.9 Hz, 1H, OCH_2Ph), 4.65 (d, *J* = 4.4 Hz, 1H, OCH_2Ph), 4.63 (d, *J* = 4.3 Hz, 1H, OCH_2Ph), 4.57 (dd, *J* = 11.8, 8.7 Hz, 2H, OCH_2Ph), 4.35 (d, *J* = 11.8 Hz, 1H, OCH_2Ph), 4.04 (dd, *J* = 8.1, 4.5 Hz, 1H, H-4), 4.02 – 3.98 (m, 2H, H-2, $(CH_3)_2CH$), 3.94 (dq, *J* = 8.1, 6.2 Hz, 1H, H-5), 3.84 (dd, *J* = 4.5, 1.4 Hz, 1H, H-3), 1.27 (d, *J* = 6.2 Hz, 3H, CH_3), 1.22 (d, *J* = 6.1 Hz, 3H, CH_3), 1.13 (d, *J* = 6.2 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.6 (Ar), 137.9 (Ar), 137.8 (Ar), 128.6 (Ar), 128.4 (Ar), 128.3 (Ar), 128.0 (Ar), 127.9 (Ar), 127.8 (2C, Ar), 127.3 (Ar), 106.1 (C-1), 85.9 (C-2), 85.1 (C-4), 81.6 (C-3), 74.9 (C-5), 72.1 (OCH_2Ph), 71.9 (OCH_2Ph), 71.2 (OCH_2Ph), 70.6 ($(CH_3)_2CH$), 23.7 (CH_3), 22.0 (CH_3), 16.8 (CH_3); HRMS (ESI) m/z calcd for $C_{30}H_{36}O_5Na$ $[M+Na]^+$ 499.2455, found 499.2453.

Methyl 2,3,4-tribenzyl-6-*O*-(2,3,5-tri-*O*-benzyl-6-deoxy-β-D-glucofuranosyl)-α-D-glucopyranoside (438β).

According to the general glycosylation procedure (GP15), the reaction mixture of donor **394α** (29 mg; 54 µmol) and methyl 2,3,4-*O*-tribenzyl-α-D-glucopyranoside (30 mg, 65 µmol) in anhydrous CH_2Cl_2 (0.27 mL) at -30 °C was treated with *N*-iodosuccinimide (18 mg, 76 µmol) and AgOTf (2.7 mg, 11 µmol). After chromatographic purification over silica gel eluting with 0.5% acetone in toluene, **438β** was obtained as a colorless oil (43 mg, 89%). α/β: 1:10; R_f = 0.17 (66:1 toluene-acetone); $[\alpha]^{25}_D$ = -2.9 (*c* = 0.4, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35 – 7.22 (m, 30H, ArH), 5.15 (d, *J* = 1.6 Hz, 1H, H-1′), 4.97 (d, *J* = 10.9 Hz, 1H, OCH_2Ph), 4.86 – 4.76 (m, 3H), 4.72 (d, *J* = 11.8 Hz, 1H, OCH_2Ph), 4.65 (d, *J* = 12.2 Hz, 1H, OCH_2Ph), 4.60 (d, *J* = 2.5 Hz, 1H, OCH_2Ph), 4.58 (dd, *J* = 4.3, 2.9 Hz, 3H, OCH_2Ph), 4.55 (d, *J* = 10.9 Hz, 1H), 4.53 – 4.49 (m, 2H, H-1, OCH_2Ph), 4.34 (d, *J* = 11.7 Hz, 1H, OCH_2Ph), 4.11 – 4.05 (m, 3H, H-6, H-2′, H-4′), 4.00 (t, *J* = 9.3 Hz, 1H, H-3), 3.92 (dq, *J* = 8.2, 6.2 Hz, 1H, H-5′), 3.85 (dd, *J* = 4.6, 1.4 Hz, 1H, H-3′), 3.84 – 3.81 (m, 1H, H-4), 3.69 (dd, *J* = 11.0, 5.8 Hz, 1H, H-6), 3.53 – 3.46 (m, 2H, H-2, H-5), 3.28 (s, 3H, OCH_3), 1.12 (d, *J* = 6.2 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.5 (Ar), 138.9 (Ar), 138.3 (Ar), 137.7 (Ar), 137.6 (Ar), 128.6 (2C, Ar), 128.5 (3C, Ar), 128.3 (Ar), 128.2 (Ar), 128.1 (Ar), 128.0 (2C, Ar), 127.9 (2C, Ar), 127.8 (3C, Ar), 127.7 (Ar), 127.8 (Ar), 127.3 (Ar), 108.1 (C-1′), 98.0 (C-1), 85.7 (C-2′), 85.1 (C-4′), 82.3 (C-3), 81.5 (C-3′), 80.1 (C-2), 78.3 (C-5), 75.9 (OCH_2Ph), 75.1 (C-5′), 75.0, 73.5 (OCH_2Ph), 72.3 (OCH_2Ph), 72.0 (OCH_2Ph), 71.5 (OCH_2Ph), 70.2 (C-4), 67.7 (C-6), 55.1 (OCH_3), 16.9 (CH_3); HRMS (ESI) m/z calcd for $C_{55}H_{60}O_{10}Na$ $[M+Na]^+$ 903.4078, found 903.4089.

1,2:3,4-Di-*O*-isopropylidene-6-*O*-(2,3,5-tri-*O*-benzyl-6-deoxy-β-D-glucofuranosyl)-α-D-galactopyranose (439β).

According to the general glycosylation procedure (GP15), the reaction mixture of donor **394α** (30 mg; 56 µmol) and methyl 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside (17 mg, 67 µmol) in anhydrous CH_2Cl_2 (0.28 mL) at -30 °C was treated with *N*-iodosuccinimide (16 mg, 69 µmol) and AgOTf (3.0 mg, 11 µmol). After chromatographic purification over silica gel eluting with 5% ethyl acetate in hexane, **439β** was obtained as a colorless oil (22 mg, 58%). α/β: 1:11; R_f = 0.19 (17:3 hexane-ethyl acetate); $[\alpha]^{25}_D$ = -27 (*c* = 0.7, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 – 7.22 (m, 15H, ArH), 5.55 (d, *J* = 5.0 Hz, 1H, H-1), 5.21 (d, *J* = 1.4 Hz, 1H, H-1′), 4.78 (d, *J* = 11.8 Hz, 1H, OCH_2Ph), 4.70 (d, *J* = 11.9 Hz, 1H, OCH_2Ph), 4.63 (d, *J* = 11.8 Hz, 1H, OCH_2Ph), 4.54 (d, *J* = 11.8 Hz, 2H, OCH_2Ph), 4.52 (dd, *J* = 7.9, 2.3 Hz, 1H, H-3), 4.31 (d, *J* = 11.6 Hz, 1H, OCH_2Ph), 4.29 (dd, *J* = 5.0, 2.4 Hz, 1H, H-2), 4.17 (dd, *J* = 7.9, 1.8 Hz, 1H, H-4), 4.12 – 4.09 (m, 2H, H-2′, H-4′), 4.04 (dd, *J* = 10.5, 4.7 Hz, 1H, H-6), 4.00 (dd, *J* = 6.8, 1.9 Hz, 1H, H-5), 3.93 (dt, *J* = 8.3, 6.2 Hz, 1H, H-5′), 3.84 (dd, *J* = 4.5, 1.4 Hz, 1H, H-3′), 3.70 (dd, *J* = 10.5, 6.9 Hz, 1H, H-6), 1.50 (s, 3H, CH_3), 1.41 (s, 3H, CH_3), 1.33 (s, 3H, CH_3), 1.27 (s, 3H, CH_3), 1.12 (d, *J* = 6.2 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.6 (Ar), 137.9 (Ar), 137.7 (Ar), 128.6 (Ar), 128.5 (Ar), 128.3 (Ar), 128.2 (Ar), 128.1 (Ar), 128.0 (Ar), 127.9 (Ar), 127.8 (Ar), 127.3 (Ar), 109.3 ($(CH_3)_2C$), 108.6 ($(CH_3)_2C$), 107.8 (C-1′), 96.5 (C-1), 85.9 (C-2′), 84.6 (C-4′), 81.5 (C-3′), 75.2 (C-5′), 72.3 (OCH_2Ph), 71.8 (OCH_2Ph), 71.5 (OCH_2Ph), 71.3 (C-4), 70.8 (C-2), 70.8 (C-3), 67.9 (C-5), 67.6 (C-6), 26.3 (CH_3), 26.2 (CH_3), 25.2 (CH_3), 24.5 (CH_3), 16.9 (CH_3); HRMS (ESI) m/z calcd for $C_{39}H_{48}O_{10}Na$ $[M+Na]^+$ 699.3139, found 699.3136.

Methyl 2,3-*O*-isopropylidene-4-*O*-(2,3,5-tri-*O*-benzyl-6-deoxy-β-D-glucofuranosyl)-6-deoxy-α-L-mannopyranoside (440β).

According to the general glycosylation procedure (GP15), the reaction mixture of donor **394α** (38 mg, 70 µmol) and methyl 6-deoxy-L-mannopyranose (18 mg, 84 µmol) in anhydrous CH_2Cl_2 (0.35 mL) at -30 °C was treated with *N*-iodosuccinimide (24 mg, 87 µmol) and AgOTf (3.2 mg, 14 µmol). After chromatographic purification over silica gel eluting with 0.5% acetone in toluene, **440β** was obtained as a colorless oil (26 mg, 59%); R_f = 0.28 (66:1 toluene-acetone); $[\alpha]^{25}_D$ = -36.4 (*c* = 0.6, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 – 7.22 (m, 15H, ArH), 5.59 (d, *J* = 1.0 Hz, 1H, H-1′), 4.87 (s, 1H, H-1), 4.77 (d, *J* = 11.8 Hz, 1H, OCH_2Ph), 4.72 (d, *J* = 11.7 Hz, 1H, OCH_2Ph), 4.63 (d, *J* = 11.7 Hz, 1H, OCH_2Ph), 4.56 (dd, *J* = 11.6, 1.2 Hz, 2H, OCH_2Ph), 4.33 (d, *J* = 11.7 Hz, 1H, OCH_2Ph), 4.19 (dd, *J* = 6.9, 5.5 Hz, 1H, H-4), 4.16 (dd, *J* = 8.0, 4.4 Hz, 1H, H-4′), 4.11 (dd, *J* = 5.8, 0.9 Hz, 2H, H-2, H-2′), 3.90 (dq, *J* = 8.1, 6.3 Hz, 1H, H-5′), 3.85 (dd, *J* = 4.4, 1.3 Hz, 1H, H-3′), 3.63 – 3.57 (m, 2H, H-3, H-5), 3.37 (s, 3H, OCH_3), 1.56 (s, 3H, CH_3), 1.36 (s, 3H, CH_3), 1.30 – 1.27 (m, 3H, CH_3), 1.14 (d, *J* = 6.3 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.5 (Ar), 137.9 (Ar), 137.8 (Ar), 128.6 (Ar), 128.4 (2C, Ar), 128.0 (Ar), 127.9 (2C, Ar), 127.7 (Ar), 127.4 (Ar), 109.5 ($(CH_3)_2C$), 106.5 (C-1′), 98.1 (C-2), 86.7 (C-4′), 84.5 (C-2′), 81.4 (C-3′), 78.8 (C-3), 78.6 (C-4), 76.1 (C-2), 75.3 (C-5′), 72.3 (OCH_2Ph), 71.8 (OCH_2Ph), 71.4 (OCH_2Ph), 64.7 (C-5), 54.9 (OCH_3), 28.3 (CH_3), 26.6 (CH_3), 17.8 (CH_3), 16.9 (CH_3); HRMS (ESI) m/z calcd for $C_{37}H_{46}O_9Na$ $[M+Na]^+$ 657.3034, found 657.3013.

1,2:5,6-Di-*O*-isopropylidene-3-*O*-(2,3,5-tri-*O*-benzyl-6-deoxy-β-D-glucofuranosyl)-α-D-glucofuranose (441β).

According to the general glycosylation procedure (GP15), the reaction mixture of donor **394α** (34 mg, 63 µmol) and 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranoside (20 mg, 76 µmol) in

anhydrous CH_2Cl_2 (0.32 mL) at -30 °C was treated with *N*-iodosuccinimide (21 mg, 78 µmol) and AgOTf (3.0 mg, 13 µmol). After chromatographic purification over silica gel eluting with 0.5% acetone in toluene, **441β** was obtained as a colorless oil (13 mg, 30%); R_f = 0.24 (97:3 toluene-acetone); $[\alpha]^{25}_D$ = -25 (*c* = 0.2, $CHCl_3$); ^{1}H NMR (900 MHz, $CDCl_3$) δ 7.38 – 7.37 (m, 4H, ArH), 7.33 – 7.28 (m, 11H, ArH), 5.83 (d, *J* = 3.6 Hz, 1H, H-1), 5.23 (s, 1H, H-1′), 4.78 (d, *J* = 11.7 Hz, 1H, OCH_2Ph), 4.63 (d, *J* = 11.7 Hz, 1H, OCH_2Ph), 4.59 (d, *J* = 12.2 Hz, 3H, OCH_2Ph), 4.46 (d, *J* = 3.7 Hz, 1H, H-2), 4.41 (d, *J* = 3.1 Hz, 1H, H-3), 4.34 (d, *J* = 11.4 Hz, 1H, OCH_2Ph), 4.28 (q, *J* = 6.4 Hz, 1H, H-5), 4.16 (dd, *J* = 8.3, 4.5 Hz, 1H, H-4′), 4.12 (dd, *J* = 7.0, 3.0 Hz, 1H, H-4), 4.09 (s, 1H, H-2′), 4.03 – 3.99 (m, 1H, H-5′), 3.92 – 3.88 (m, 2H, H-6), 3.86 (dd, *J* = 4.5, 1.0 Hz, 1H, H-3′), 1.49 (s, 3H, CH_3), 1.30 (s, 3H, CH_3), 1.29 (s, 3H, CH_3), 1.17 (s, 3H, CH_3), 1.13 (d, *J* = 6.3 Hz, 3H, CH_3); ^{13}C NMR (226 MHz, $CDCl_3$) δ 139.5 (Ar), 137.6 (Ar), 137.3 (Ar), 128.7 (Ar), 128.6 (Ar), 128.4 (Ar), 128.2 (Ar), 128.1 (Ar), 127.9 (2C, Ar), 127.4 (Ar), 111.9 ($(CH_3)_2C$), 108.8 ($(CH_3)_2C$), 105.3 (C-1′), 105.2 (C-1), 87.0 (C-4′), 84.7 (C-2′), 82.9 (C-2), 81.3 (C-3′), 81.0 (C-4), 77.4 (C-3), 75.2 (C-5′), 72.5 (OCH_2Ph), 72.5 (OCH_2Ph), 72.4 (C-4), 71.8 (OCH_2Ph), 66.7 (OCH_2Ph), 27.0 (CH_3), 26.9 (CH_3), 26.4 (CH_3), 25.5 (CH_3), 16.8 (CH_3); HRMS (ESI) m/z calcd for $C_{39}H_{48}O_{10}Na$ $[M+Na]^+$ 699.3139, found 699.3142.

Benzyl 2,3,5-tri-*O*-benzyl-6-deoxy-β-L-idofuranoside (442β) and Benzyl 2,3,5-tri-*O*-benzyl-6-deoxy-α-L-idofuranoside (442α).

According to the general glycosylation procedure (GP15), the reaction mixture of donor **395β** (33 mg, 60 µmol) and benzyl alcohol (5.4 µL, 72 µmol) in anhydrous CH_2Cl_2 (0.30 mL) at -30 °C was treated with *N*-iodosuccinimide (18 mg, 73 µmol) and AgOTf (3.0 mg, 13 µmol). After chromatographic purification over silica gel eluting with 0.1% acetone in toluene, two anomers were obtained (23 mg, 81%); α/β: 1:2.

442β. colorless oil; R_f = 0.27 (66:1 toluene-acetone); $[\alpha]^{25}_D$ = +69 (*c* = 0.40, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 7.39 (d, *J* = 7.1 Hz, 2H, ArH), 7.36 – 7.25 (m, 16H, ArH), 7.23 – 7.20 (m, 2H, ArH), 5.10 (d, *J* = 4.3 Hz, 1H, H-1), 4.82 (d, *J* = 12.3 Hz, 1H, OCH_2Ph), 4.63 – 4.57 (m, 4H, OCH_2Ph), 4.50 (dd, *J* = 16.7, 11.8 Hz, 3H, OCH_2Ph), 4.43 (d, *J* = 11.7 Hz, 1H, OCH_2Ph), 4.33 (dd, *J* = 6.5, 4.6 Hz, 1H, H-3), 4.29 (t, *J* = 6.2 Hz, 1H, H-4), 3.98 (t, *J* = 4.4 Hz, 1H, H-2), 3.87 (p, *J* = 6.1 Hz, 1H, H-5), 1.28 (d, *J* = 6.2 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.0 (Ar), 138.4 (Ar), 138.0 (Ar), 137.9 (Ar), 128.5 (2C, Ar), 128.4 (2C, Ar), 128.3 (Ar), 128.1 (Ar), 127.9 (Ar), 127.8 (Ar), 127.7 (2C, Ar), 127.6 (Ar), 127.5 (Ar), 98.9 (C-1), 84.1 (C-2), 82.1 (C-3), 79.6 (C-4), 73.3 (C-5), 72.6 (OCH_2Ph), 72.5 (OCH_2Ph), 70.8 (OCH_2Ph), 69.4 (OCH_2Ph), 16.1 (CH_3); HRMS (ESI) m/z calcd for $C_{34}H_{36}O_5Na$ $[M+Na]^+$ 547.2455, found 547.2453.

442α. colorless oil; R_f = 0.32 (66:1 toluene-acetone); $[\alpha]^{25}_D$ = -67 (*c* = 0.2, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 7.37 – 7.23 (m, 20H, ArH), 5.12 (d, *J* = 1.2 Hz, 1H, H-1), 4.83 (d, *J* = 12.1 Hz, 1H, OCH_2Ph), 4.58 (dd, *J* = 17.3, 11.6 Hz, 3H, OCH_2Ph), 4.51 (dd, *J* = 12.0, 5.0 Hz, 2H, OCH_2Ph), 4.47 (s, 2H, OCH_2Ph), 4.42 (d, *J* = 11.3 Hz, 1H, OCH_2Ph), 4.13 (dd, *J* = 8.3, 4.7 Hz, 1H, H-4), 4.10 (dd, *J* = 4.8, 1.4 Hz, 1H, H-3), 4.05 (d, *J* = 1.2 Hz, 1H, H-2), 4.04 – 4.00 (m, 1H, H-5), 1.35 (d, *J* = 6.1 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.0 (Ar), 138.3 (Ar), 138.1 (Ar), 137.7 (Ar), 128.6 (Ar), 128.4 (2C, Ar), 128.0 (Ar), 127.9 (Ar), 127.8 (Ar), 127.8 (2C, Ar), 127.7 (2C, Ar), 127.5 (Ar), 106.3 (C-1), 85.9 (C-2), 84.5 (C-4), 80.9 (C-3), 73.3 (C-5), 72.1 (OCH_2Ph), 71.9 (OCH_2Ph), 70.9 (OCH_2Ph), 69.8 (OCH_2Ph), 17.4 (CH_3); HRMS (ESI) m/z calcd for $C_{34}H_{36}O_5Na$ $[M+Na]^+$ 547.2455, found 547.2453.

Isopropyl 2,3,5-tri-*O*-benzyl-6-deoxy-β-L-idofuranoside (443β) and Isopropyl 2,3,5-tri-*O*-benzyl-6-deoxy-α-L-idofuranoside (443*α*).

According to the general glycosylation procedure (GP15), the reaction mixture of donor **395β** (36 mg, 67 µmol) and isopropyl alcohol (6.1 µL, 80 µmol) in anhydrous CH_2Cl_2 (0.34 mL) at -30 °C was treated with *N*-iodosuccinimide (20 mg, 83 µmol) and AgOTf (3.5 mg, 13 µmol). After chromatographic purification over silica gel eluting with 0.2% acetone in toluene, two anomers were obtained (22 mg, 69%); α/β: 1:2.5.

443β. colorless oil; R_f = 0.20 (66:1 toluene-acetone); $[\alpha]^{25}_D$ = +35 (*c* = 0.40, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36 – 7.19 (m, 15H, ArH), 5.12 (d, *J* = 4.3 Hz, 1H, H-1), 4.63 (d, *J* = 11.8 Hz, 1H, OCH_2Ph), 4.61 – 4.55 (m, 2H, OCH_2Ph), 4.50 (dd, J = 11.9, 3.2 Hz, 2H, OCH_2Ph), 4.41 (d, *J* = 11.7 Hz, 1H, OCH_2Ph), 4.27 – 4.21 (m, 2H, H-3, H-4), 3.95 – 3.90 (m, 2H, H-2, H-4), 3.87 – 3.82 (m, 1H, $(CH_3)_2CH$), 1.26 (d, *J* = 6.3 Hz, 3H, CH_3), 1.25 (d, *J* = 6.2 Hz, 3H, CH_3), 1.18 (d, *J* = 6.2 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$ ^{13}C NMR (151 MHz, CDCl3) δ 139.0 (Ar), 138.5 (Ar), 138.1 (Ar), 128.5 (Ar), 128.4 (2C, Ar), 128.2 (Ar), 127.9 (Ar), 127.7 (Ar), 127.6 (2C, Ar), 127.5 (Ar), 98.9 (C-1), 84.2 (C-2), 82.3 (C-4), 79.3 (C-3), 73.3 ($(CH_3)_2CH$), 72.4 (2C, OCH_2Ph), 70.7 (OCH_2Ph), 70.6 (C-5), 23.7 (CH_3), 22.2 (CH_3), 16.3 (CH_3); HRMS (ESI) m/z calcd for $C_{30}H_{36}O_5Na$ $[M+Na]^+$ 499.2455, found 499.2445.

443α. colorless oil; R_f = 0.23 (66:1 toluene-acetone); $[\alpha]^{25}_D$ = -30 (*c* = 0.10, $CHCl_3$); ^{1}H NMR (900 MHz, $CDCl_3$) δ 7.35 – 7.23 (m, 15H, ArH), 5.09 (d, *J* = 1.9 Hz, 1H, H-1), 4.59 – 4.56 (m, 2H, OCH_2Ph), 4.55 – 4.52 (m, 2H, OCH_2Ph), 4.51 – 4.48 (m, 1H, OCH_2Ph), 4.40 (d, *J* = 11.3 Hz, 1H, OCH_2Ph), 4.06 (dd, *J* = 4.5, 1.8 Hz, 1H, H-3), 4.03 – 3.99 (m, 2H, H-4, H-5), 3.94 (t, *J* = 1.8 Hz, 1H, H-2), 3.92 (p, *J* = 6.2 Hz, 1H, $(CH_3)_2CH$), 1.33 (d, *J* = 5.7 Hz, 3H, CH_3), 1.23 (d, *J* = 6.2 Hz, 3H, CH_3), 1.18 (d, *J* = 6.2 Hz, 3H, CH_3); ^{13}C NMR (226 MHz, $CDCl_3$) δ 139.1 (Ar), 138.5 (Ar),

137.9 (Ar), 128.6 (Ar), 128.4 (2C, Ar), 127.9 (Ar), 127.8 (2C, Ar), 127.7 (Ar), 127.6 (Ar), 127.5 (Ar), 105.6 (C-1), 86.7 (C-2), 83.5 (C-4), 81.0 (C-3), 73.3 (C-5), 71.9 (OCH_2Ph), 71.8 (OCH_2Ph), 70.9 (OCH_2Ph), 70.3 ($(CH_3)_2CH$), 23.6 (CH_3), 21.9 (CH_3), 17.3 (CH_3); HRMS (ESI) m/z calcd for $C_{30}H_{36}O_5Na$ $[M+Na]^+$ 499.2455, found 499.2445.

Methyl 2,3,4-tribenzyl-6-*O*-(2,3,5-tri-*O*-benzyl-6-deoxy-β-L-idofuranosyl)-α-D-glucopyranoside (444β) and Methyl 2,3,4-tribenzyl-6-*O*-(2,3,5-tri-*O*-benzyl-6-deoxy-α-L-idofuranosyl)-α-D-glucopyranoside (444α).

According to the general glycosylation procedure (GP15), the reaction mixture of donor **395β** (30 mg; 56 µmol) and methyl 2,3,4-*O*-tribenzyl-α-D-glucopyranoside (31 mg, 67 µmol) in anhydrous CH_2Cl_2 (0.28 mL) at -30 °C was treated with *N*-iodosuccinimide (21 mg, 78 µmol) and AgOTf (2.5 mg, 11 µmol). After chromatographic purification over silica gel eluting with 0.5% acetone in toluene, two anomers were obtained (41 mg, 82%); α/β: 1:2.3.

444β. colorless oil; R_f = 0.13 (66:1 toluene-acetone); $[\alpha]^{25}_D$ = +2.8 (*c* = 0.40, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35 – 7.20 (m, 30H, ArH), 5.18 (d, *J* = 4.1 Hz, 1H, H-1′), 4.95 (d, *J* = 11.0 Hz, 1H, OCH_2Ph), 4.82 (dd, *J* = 10.8, 6.8 Hz, 2H, OCH_2Ph), 4.74 (d, *J* = 12.1 Hz, 1H, OCH_2Ph), 4.70 – 4.64 (m, 2H, OCH_2Ph), 4.61 (d, *J* = 11.9 Hz, 1H, OCH_2Ph), 4.58 – 4.56 (m, 2H, H-1, OCH_2Ph), 4.54 (d, *J* = 11.7 Hz, 1H, OCH_2Ph), 4.48 (dd, *J* = 13.8, 11.7 Hz, 2H, OCH_2Ph), 4.38 (d, *J* = 11.7 Hz, 1H, OCH_2Ph), 4.26 – 4.21 (m, 2H, H-3′, H-4′), 4.11 (dd, *J* = 11.4, 3.5 Hz, 1H, H-6), 3.99 – 3.94 (m, 2H, H-3, H-2′), 3.83 (p, *J* = 6.2 Hz, 1H, H-5′), 3.75 (ddd, *J* = 10.0, 3.6, 1.8 Hz, 1H, H-5), 3.71 – 3.65 (m, 2H, H-4, H-6), 3.42 (dd, *J* = 9.6, 3.5 Hz, 1H, H-2), 3.34 (s, 3H, OCH_3), 1.24 (d, *J* = 6.2 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.1 (Ar), 139.0 (Ar), 138.5 (Ar), 138.4 (2C, Ar), 138.3 (Ar), 128.6 (Ar), 128.5 (2C, Ar), 128.4 (2C, Ar), 128.2 (Ar), 128.0 (2C, Ar), 127.8 (2C, Ar), 127.7 (2C, Ar), 127.6 (2C, Ar), 127.5 (Ar), 101.4 (C-1′), 98.3 (C-1), 83.5 (C-2′), 82.1

(C-3), 82.1 (C-4′), 80.2 (C-2, C-3′), 77.9 (C-4), 75.7 (OCH_2Ph), 75.3 (OCH_2Ph), 73.6 (OCH_2Ph), 73.2 (C-5′), 72.5 (OCH_2Ph), 72.4 (OCH_2Ph), 70.7 (OCH_2Ph), 70.3 (C-5), 66.9 (C-6), 55.3 (OCH_3), 16.2 (CH_3); HRMS (ESI) m/z calcd for $C_{55}H_{60}O_{10}Na$ $[M+Na]^+$ 903.4078, found 903.4075.

444α. colorless oil; R_f = 0.16 (66:1 toluene-acetone); $[\alpha]^{25}_D$ = -12 (*c* = 0.30, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 7.37 – 7.26 (m, 20H, ArH), 7.24 (dd, *J* = 5.4, 3.4 Hz, 10H, ArH), 5.07 (d, *J* = 1.4 Hz, 1H, H-1`), 4.98 (d, *J* = 10.8 Hz, 1H, OCH_2Ph), 4.85 (d, *J* = 10.9 Hz, 1H, OCH_2Ph), 4.80 (dd, *J* = 17.1, 11.5 Hz, 2H, OCH_2Ph), 4.65 (d, *J* = 12.1 Hz, 1H, OCH_2Ph), 4.59 – 4.56 (m, 2H, H-1, OCH_2Ph), 4.53 (dd, *J* = 13.8, 11.5 Hz, 2H, OCH_2Ph), 4.48 – 4.45 (m, 3H, OCH_2Ph), 4.36 (d, *J* = 11.3 Hz, 1H, OCH_2Ph), 4.06 – 4.03 (m, 2H, H-4, H-5), 4.01 (d, *J* = 1.8 Hz, 1H, H-2`), 4.00 – 3.96 (m, 3H, H-3, H-6, H-5`), 3.79 (ddd, *J* = 10.2, 6.0, 1.8 Hz, 1H, H-3`), 3.61 (dd, *J* = 10.9, 6.0 Hz, 1H, H-6), 3.51 (dd, *J* = 9.6, 3.6 Hz, 1H, H-2), 3.44 (t, *J* = 9.5 Hz, 1H, H-4`), 3.29 (s, 3H, OCH_3), 1.28 (d, *J* = 6.0 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.0 (2C, Ar), 138.4 (Ar), 138.3 (2C, Ar), 137.7 (Ar), 128.6 (3C, Ar), 128.5 (Ar), 128.4, (2C, Ar), 128.2 (Ar), 128.1 (Ar), 128.0 (Ar), 127.9, (2C, Ar), 127.8 (Ar), 127.7 (4C, Ar), 127.5 (Ar), 107.7 (C-1`), 98.0 (C-1), 85.9 (C-2`), 84.2 (C-4), 82.3 (C-3),. 80.8 (C-5), 80.1 (C-2), 78.4 (C-4`), 75.9 ($OCH_2Ph$), 75.1 ($OCH_2Ph$), 73.5 ($OCH_2Ph$), 73.2 (C-5`), 72.0 (OCH_2Ph), 71.9 (OCH_2Ph), 70.9 (OCH_2Ph), 70.3 (C-3`), 67.2 (C-6), 55.1 (OCH_3), 17.3 (CH_3); HRMS (ESI) m/z calcd for $C_{55}H_{60}O_{10}Na$ $[M+Na]^+$ 903.4078 found 903.4075

1,2:3,4-Di-*O*-isopropylidene-6-*O*-(2,3,5-tri-*O*-benzyl-6-deoxy-β-L-idofuranosyl)-α-D-galactopyranoside (445β) and 1,2:3,4-di-*O*-isopropylidene-6-*O*-(2,3,5-tri-*O*-benzyl-6-deoxy-α-L-idofuranosyl)-α-D-galactopyranoside (445α).

According to the general glycosylation procedure (GP15), the reaction mixture of donor **395β** (30 mg; 56 μmol) and methyl 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside (17 mg, 67 μmol)

in anhydrous CH_2Cl_2 (0.28 mL) at -30 °C was treated with *N*-iodosuccinimide (16 mg, 69 µmol) and AgOTf (3.0 mg, 11 µmol). After chromatographic purification over silica gel eluting with 0.5% acetone in toluene, two anomers were obtained (29 mg, 77%); α/β: 1:2.

445β. colorless oil; R_f = 0.07 (66:1 toluene-acetone); $[\alpha]^{25}_D$ = +20 (*c* = 0.10, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 – 7.19 (m, 15H, ArH), 5.52 (d, *J* = 5.0 Hz, 1H, H-1), 5.13 (d, *J* = 4.2 Hz, 1H, H-1′), 4.71 (d, *J* = 11.8 Hz, 1H, OCH_2Ph), 4.62 – 4.56 (m, 3H, OCH_2Ph, H-3), 4.42 (d, *J* = 11.6 Hz, 1H, OCH_2Ph), 4.32 – 4.28 (m, 2H, H-2, H-4), 4.27 – 4.26 (m, 1H, H-3′), 4.23 *J* (t, = 6.4 Hz, 1H, H-4′), 4.07 (ddd, *J* = 8.2, 6.0, 2.2 Hz, 1H, H-5), 3.98 (t, *J* = 4.3 Hz, 1H, H-2′), 3.90 – 3.83 (m, 2H, H-6, H-5′), 3.72 (dd, *J* = 9.9, 8.4 Hz, 1H, H-6), 1.52 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.32 (s, 3H, CH_3), 1.31 (s, 3H, CH_3), 1.27 (d, *J* = 6.2 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.0 (Ar), 138.4 (Ar), 138.1 (Ar), 128.5 (Ar), 128.4 (2C, Ar), 128.0 (Ar), 127.9 (Ar), 127.7 (2C, Ar), 127.6 (Ar), 127.5 (Ar), 109.3 ($(CH_3)_2C$), 108.7 ($(CH_3)_2C$), 100.6 (C-1′), 96.5 (C-1), 84.0 (C-2′), 82.1 (C-3′), 79.8 (C-4′), 73.2 (C-5′), 72.4 (OCH_2Ph), 72.3 (OCH_2Ph), 70.9 (C-4), 70.9 (C-3), 70.8 (OCH_2Ph), 70.7 (C-3), 66.3 (C-6), 65.7 (C-5), 26.3 (CH_3), 26.2 (CH_3), 25.1 (CH_3), 24.7 (CH_3), 16.3 (CH_3); HRMS (ESI) m/z calcd for $C_{39}H_{48}O_{10}Na$ $[M+Na]^+$ 699.3139, found 699.3163.

445α. colorless oil; R_f = 0.13 (66:1 toluene-acetone); $[\alpha]^{25}_D$ = -13 (*c* = 0.20, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35 – 7.31 (m, 4H, ArH), 7.30 – 7.27 (m, 3H, ArH), 7.26 – 7.22 (m, 8H, ArH), 5.54 (d, *J* = 5.0 Hz, 1H, H-1), 5.11 (d, *J* = 1.2 Hz, 1H, H-1′), 4.62 – 4.57 (m, 2H, OCH_2Ph), 4.56 – 4.50 (m, 3H, H-3, OCH_2Ph), 4.45 (d, *J* = 11.7 Hz, 1H, OCH_2Ph), 4.39 (d, *J* = 11.3 Hz, 1H, OCH_2Ph), 4.30 (dd, *J* = 5.0, 2.4 Hz, 1H, H-2), 4.21 (dd, *J* = 7.9, 1.8 Hz, 1H, H-4), 4.10 – 4.05 (m, 3H, H-2′, H-3′, H-4′), 4.02 – 3.99 (m, 1H, H-5′), 3.97 (dd, *J* = 6.8, 1.8 Hz, 1H, H-5), 3.95 (dd, *J* = 10.2, 5.1 Hz, 1H, H-6), 3.62 (dd, *J* = 10.2, 6.7 Hz, 1H, H-6), 1.51 (s, 3H, CH_3), 1.44 (d, *J* = 0.6 Hz, 3H, CH_3), 1.34 – 1.32 (m, 6H, $2CH_3$), 1.28 (d, *J* = 0.7 Hz, 3H, CH_3); ^{13}C NMR (151 MHz,

$CDCl_3$) δ 139.1 (Ar), 138.3 (Ar), 137.9 (Ar), 128.5 (Ar), 128.4 (Ar), 127.9 (2C, Ar), 127.7 (2C, Ar), 127.5 (Ar), 109.3 ($(CH_3)_2C$), 108.7 ($(CH_3)_2C$), 107.4 (C-1′), 96.5 (C-1), 85.6 (C-2′), 84.3 (C-4′), 81.0 (C-3′), 73.3 (C-5′), 72.0 (OCH_2Ph), 71.8 (OCH_2Ph), 71.3 (C-4), 70.9 (OCH_2Ph), 70.8 (C-2, C-3), 67.7 (C-5), 67.2 (C-6), 26.3 (CH_3), 26.2 (CH_3), 25.2 (CH_3), 24.5 (CH_3), 17.4 (CH_3); HRMS (ESI) m/z calcd for $C_{39}H_{48}O_{10}Na$ $[M+Na]^+$ 699.3139, found 699.3163.

Methyl 2,3-*O*-isopropylidene-4-*O*-(2,3,5-tri-*O*-benzyl-6-deoxy-β-L-idofuranosyl)-6-deoxy-α-L-mannopyranoside (446β) and Methyl 2,3-*O*-isopropylidene-4-*O*-(2,3,5-tri-*O*-benzyl-6-deoxy-α-L-idofuranosyl)-6-deoxy-α-L-mannopyranoside (446α).

According to the general glycosylation procedure (GP15), the reaction mixture of donor **395β** (32 mg; 60 µmol) and methyl 6-deoxy-L-mannopyranose (16 mg, 72 µmol) in anhydrous CH_2Cl_2 (0.30 mL) at -30 °C was treated with *N*-iodosuccinimide (20 mg, 73 µmol) and AgOTf (2.7 mg, 12 µmol). After chromatographic purification over silica gel eluting with 0.5% acetone in toluene, two anomers were obtained (23 mg, 60%); α/β: 1:2.2.

446β. colorless oil; R_f = 0.12 (66:1 toluene-acetone); $[\alpha]^{25}_D$ = +39 (*c* = 0.20, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36 – 7.20 (m, 15H, ArH), 5.18 (d, *J* = 4.1 Hz, 1H, H-1′), 4.83 (s, 1H, H-1), 4.66 (d, *J* = 11.9 Hz, 1H, OCH_2Ph), 4.62 – 4.52 (m, 4H, OCH_2Ph), 4.45 (t, *J* = 6.6 Hz, 1H, H-4′), 4.42 (d, *J* = 11.6 Hz, 1H, OCH_2Ph), 4.34 (dd, *J* = 6.9, 5.3 Hz, 1H, H-3′), 4.20 (dd, *J* = 7.3, 5.6 Hz, 1H, H-3), 4.10 – 4.07 (m, 1H, H-2), 3.97 (dd, *J* = 5.3, 4.1 Hz, 1H, H-2′), 3.86 (p, *J* = 6.2 Hz, 1H, H-5′), 3.71 (dq, *J* = 9.9, 6.3 Hz, 1H, H-5), 3.50 (dd, *J* = 10.0, 7.3 Hz, 1H, H-4), 3.35 (s, 3H, OCH_3), 1.52 (s, 3H, CH_3), 1.31 (s, 3H, CH_3), 1.28 (dd, *J* = 6.3, 2.1 Hz, 6H, $2CH_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.1 (Ar), 138.6 (Ar), 137.9 (Ar), 128.6 (Ar), 128.4 (2C, Ar), 128.0 (Ar), 127.6 (3C, Ar), 127.4 (Ar), 109.3 ($(CH_3)_2C$), 99.4 (C-1′), 98.3 (C-1), 84.7 (C-2′), 82.0 (C-3′), 79.2 (C-4), 78.9 (C-4′), 77.1 (C-3), 76.1 (C-2), 73.6 (C-5′), 72.9 (OCH_2Ph), 72.8 (OCH_2Ph), 70.6

(OCH_2Ph), 64.9 (C-5), 54.9 (OCH_3), 28.1 (CH_3), 26.6 (CH_3), 18.0 (CH_3), 16.2 (CH_3); HRMS (ESI) m/z calcd for $C_{37}H_{46}O_9Na$ $[M+Na]^+$ 657.3034, found 657.3027.

446α. colorless oil; R_f = 0.24 (66:1 toluene-acetone); $[\alpha]^{25}_D$ = -52 (*c* = 0.20, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) 7.36 – 7.23 (m, 15H, ArH), 5.51 (s, 1H, H-1′), 4.86 (s, 1H, H-1), 4.59 (d, *J* = 11.3 Hz, 2H, OCH_2Ph), 4.55 – 4.51 (m, 2H, OCH_2Ph), 4.45 – 4.38 (m, 2H, OCH_2Ph), 4.17 (dd, *J* = 7.3, 5.6 Hz, 1H, H-3), 4.12 – 4.08 (m, 2H, H-2, H-4′), 4.06 (d, *J* = 4.5 Hz, 1H, H-3′), 4.04 (s, 1H, H-2′), 4.00 (dq, *J* = 8.9, 6.1 Hz, 1H, H-5′), 3.59 (dq, *J* = 9.7, 6.2 Hz, 1H, H-5), 3.52 (dd, *J* = 10.0, 7.4 Hz, 1H, H-4), 3.37 (s, 3H, OCH_3), 1.55 (s, 3H, CH_3), 1.35 (s, 3H CH_3), 1.34 (d, *J* = 6.1 Hz, 3H, CH_3), 1.25 (d, J = 6.2 Hz, 3H CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.1 (Ar), 138.3 (Ar), 137.9 (Ar), 128.6 (Ar), 128.4 (Ar), 128.3 (Ar), 127.9 (Ar), 127.8 (Ar), 127.8 (Ar), 127.7 (Ar), 127.6 (Ar), 127.5 (Ar), 109.5 ($(CH_3)_2C$), 106.0 (C-1′), 98.1 (C-1), 85.4 (C-2′), 85.1 (C-4′), 80.6 (C-3′), 78.7 (C-3), 77.9 (C-4), 76.1 (C-2), 73.0 (C-5′), 71.9 (OCH_2Ph), 71.8 (OCH_2Ph), 70.9 (OCH_2Ph), 64.7 (C-5), 54.9 (OCH_3), 28.2 (CH_3), 26.7 (CH_3), 17.7 (CH_3), 17.4 (CH_3); HRMS (ESI) m/z calcd for $C_{37}H_{46}O_9Na$ $[M+Na]^+$ 657.3034, found 657.3027.

1,2:5,6-Di-*O*-isopropylidene-3-*O*-(2,3,5-tri-*O*-benzyl-6-deoxy-β-L-idofuranosyl)-α-D-glucofuranoside (447β) and 1,2:5,6-di-*O*-isopropylidene-3-*O*-(2,3,5-tri-*O*-benzyl-6-deoxy-α-L-idofuranosyl)-α-D-glucofuranoside (447α).

According to the general glycosylation procedure (GP15), the reaction mixture of donor **395β** (29 mg; 53 µmol) and 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranoside (18 mg, 64 µmol) in anhydrous CH_2Cl_2 (0.27 mL) at -30 °C was treated with *N*-iodosuccinimide (17 mg, 64 µmol) and AgOTf (2.5 mg, 11 µmol). After chromatographic purification over silica gel eluting with 0.5% acetone in toluene, two anomers were obtained (26 mg, 73%); α/β: 1:3.7.

447β. colorless oil; R_f = 0.29 (97:3 toluene-acetone); $[\alpha]^{25}_D$ = +74 (*c* = 0.20, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 – 7.16 (m, 15H, ArH), 5.87 (d, *J* = 3.5 Hz, 1H, H-1), 5.30 (d, *J* = 4.3 Hz, 1H, H-1′), 4.73 (dd, *J* = 7.7, 4.2 Hz, 2H, H-2, OCH_2Ph), 4.58 (t, *J* = 11.8 Hz, 2H, OCH_2Ph), 4.50 (dd, *J* = 11.9, 4.1 Hz, 2H, OCH_2Ph), 4.41 (d, *J* = 11.5 Hz, 1H, OCH_2Ph), 4.31 (ddd, *J* = 8.7, 6.1, 4.8 Hz, 1H, H-5), 4.25 (dd, *J* = 6.2, 4.4 Hz, 1H, H-3′), 4.22 (d, *J* = 3.0 Hz, 1H, H-3), 4.19 (t, *J* = 6.5 Hz, 1H, H-4′), 4.10 (dd, *J* = 8.6, 3.0 Hz, 1H, H-4), 4.04 (dd, *J* = 8.8, 6.1 Hz, 1H, H-6), 4.01 (dd, *J* = 8.8, 4.8 Hz, 1H, H-6), 3.98 (t, *J* = 4.32 Hz, 1H, H-2′), 3.89 (p, *J* = 6.3 Hz, 1H, H-5′), 1.50 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 1.30 (d, *J* = 5.0 Hz, 3H, CH_3), 1.29 (s, 3H, CH_3), 1.23 (s, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.9 (Ar), 138.3 (Ar), 138.0 (Ar), 128.6 (Ar), 128.5 (2C, Ar), 128.0 (Ar), 127.8 (Ar), 127.7 (3C, Ar), 127.6 (Ar), 112.0 ($(CH_3)_2C$), 109.3 ($(CH_3)_2C$), 105.5 (C-1), 101.8 (C-1′), 84.0 (C-2′), 84.0 (C-2), 81.8 (C-3′), 81.8 (C-3), 81.4 (C-4), 80.1 (C-4′), 73.1 (C-5′), 72.6 (C-5), 72.4 (OCH_2Ph), 72.4 (OCH_2Ph), 70.9 (OCH_2Ph), 67.7 (C-6), 27.1 (CH_3), 27.1 (CH_3), 26.4 (CH_3), 25.5 (CH_3), 16.4 (CH_3); HRMS (ESI) m/z calcd for $C_{39}H_{48}O_{10}Na$ $[M+Na]^+$ 699.3139, found 699.3138.

447α. colorless oil; R_f = 0.32 (97:3 toluene-acetone); $[\alpha]^{25}_D$ = -36 (*c* = 0.20, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 – 7.24 (m, 15H, ArH), 5.83 (d, *J* = 3.7 Hz, 1H, H-1), 5.13 (s, 1H, H-1′), 4.60 – 4.55 (m, 3H, OCH_2Ph), 4.48 (dd, *J* = 16.6, 11.6 Hz, 2H, OCH_2Ph), 4.42 (d, *J* = 3.7 Hz, 1H, H-2), 4.39 (d, *J* = 11.2 Hz, 1H, OCH_2Ph), 4.32 – 4.30 (m, 2H, H-4, H-5), 4.13 – 4.10 (m, 3H, H-3, H-4′, H-5′), 4.08 (d, *J* = 4.0 Hz, 1H, H-3′), 4.02 (s, 1H, H-2′), 3.99 – 3.92 (m, 2H, H-6), 1.49 (s, 3H, CH_3), 1.37 (s, 3H, CH_3), 1.34 (d, *J* = 5.5 Hz, 3H, CH_3), 1.31 (s, 3H, CH_3), 1.22 (s, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.1 (Ar), 138.0 (Ar), 137.6 (Ar), 128.7 (Ar), 128.5 (Ar), 128.4 (Ar), 128.1 (Ar), 127.9 (Ar), 127.8 (2C, Ar), 127.6 (Ar), 127.5 (Ar), 111.9 ($(CH_3)_2C$), 108.8 ($(CH_3)_2C$), 105.3 (C-1), 105.0 (C-1′), 85.6 (C-2′), 85.4 (C-4′), 82.6 (C-2), 80.9 (C-3), 80.5 (C-3′),

77.21 (C-4), 72.9 (C-5′), 72.5 (C-5), 72.2 (OCH_2Ph), 70.8 (OCH_2Ph), 66.8 (C-6), 26.9 (CH_3), 26.4 (CH_3), 25.5 (CH_3), 17.4 (CH_3); HRMS (ESI) m/z calcd for $C_{39}H_{48}O_{10}Na$ $[M+Na]^+$ 699.3139, found 699.3138.

Benzyl 2,3,5-tri-*O*-benzyl-6-deoxy-α-D-altrofuranoside (448α) and Benzyl 2,3,5-tri-*O*-benzyl-6-deoxy-β-D-altrofuranoside (448β).

According to the general glycosylation procedure (GP15), the reaction mixture of donor **396α** (52 mg; 96 μmol) and benzyl alcohol (11 μL, 0.11 mmol) in anhydrous CH_2Cl_2 (0.48 mL) at -30 °C was treated with *N*-iodosuccinimide (27 mg, 0.12 mmol) and AgOTf (5.0 mg, 2.0 μmol). After chromatographic purification over silica gel eluting with 8% ethyl acetate in hexane, two anomers were obtained (41 mg, 82%); α/β: 1:2.4.

448α. colorless oil; R_f = 0.55 (17:3 hexane-ethyl acetate); $[\alpha]^{25}_D$ = +88 (*c* = 0.30, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 – 7.26 (m, 20H, ArH), 5.14 (s, 1H, H-1), 4.80 (d, *J* = 12.2 Hz, 1H, OCH_2Ph), 4.62 (d, *J* = 11.9 Hz, 1H, OCH_2Ph), 4.58 (d, *J* = 11.9 Hz, 1H, OCH_2Ph), 4.54 (d, *J* = 13.0 Hz, 3H, OCH_2Ph), 4.47 (d, *J* = 11.9 Hz, 1H, OCH_2Ph), 4.42 (d, *J* = 11.8 Hz, 1H, OCH_2Ph), 4.13 (dd, *J* = 5.5, 4.7 Hz, 1H, H-4), 4.07 (dd, *J* = 2.1, 0.9 Hz, 1H, H-2), 4.04 (dd, *J* = 5.5, 2.0 Hz, 1H, H-3), 3.70 (qd, *J* = 6.4, 4.7 Hz, 1H, H-5), 1.25 (d, *J* = 6.4 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.0 (Ar), 138.2 (Ar), 138.1 (Ar), 137.7 (Ar), 128.7 (Ar), 128.6 (Ar), 128.5 (Ar), 128.4 (2C, Ar), 128.0 (Ar), 128.0 (Ar), 127.9 (3C, Ar), 127.7 (Ar), 127.5 (Ar), 105.2 (C-1), 88.0 (C-2), 85.6 (C-4), 83.8 (C-3), 74.7 (C-5), 72.0 (OCH_2Ph), 71.8 (OCH_2Ph), 71.4 (OCH_2Ph), 68.8 (OCH_2Ph), 16.4 (CH_3); HRMS (ESI) m/z calcd for $C_{34}H_{36}O_5Na$ $[M+Na]^+$ 547.2455, found 547.2458.

448β. colorless oil; R_f = 0.34 (17:3 Hexane-EtOAc); $[\alpha]^{25}_D$ = -65 (*c* = 0.40, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 – 7.20 (m, 20H, ArH), 4.96 (d, *J* = 4.4 Hz, 1H, H-1), 4.76 (d, *J* = 12.3 Hz, 1H, OCH_2Ph), 4.66 – 4.61 (m, 3H, OCH_2Ph), 4.57 (d, *J* = 11.8 Hz, 1H, OCH_2Ph), 4.52 (d, *J* = 12.3 Hz, 1H, OCH_2Ph), 4.50 (d, *J* = 11.8 Hz, 1H, OCH_2Ph), 4.45 (d, *J* = 11.5 Hz, 1H, OCH_2Ph), 4.27 (dd, *J* = 6.7, 5.3 Hz, 1H, H-3), 4.06 (dd, *J* = 6.8, 4.5 Hz, 1H, H-2), 3.85 (dd, *J* = 7.6, 5.3 Hz, 1H, H-4), 3.64 (dq, *J* = 7.7, 6.1 Hz, 1H, H-5), 1.30 (d, *J* = 6.1 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.6 (2C, Ar), 137.8 (Ar), 137.5 (Ar), 128.6 (Ar), 128.5 (Ar), 128.4 (3C, Ar), 128.1 (Ar), 128.0 (2C, Ar), 127.8 (Ar), 127.7 (Ar), 127.5 (Ar), 99.2 (C-1), 84.7 (C-2), 84.4 (C-4), 84.1 (C-3), 76.8 (C-5), 72.5 (2C, OCH_2PH), 71.1 (OCH_2Ph), 69.3 (OCH_2Ph), 16.3 (CH_3); HRMS (ESI) m/z calcd for $C_{34}H_{36}O_5Na$ $[M+Na]^+$ 547.2455, found 547.2458.

Benzyl 2,3,5-tri-*O*-benzyl-6-deoxy-β-L-galactofuranoside (449β) and Benzyl 2,3,5-tri-*O*-benzyl-6-deoxy-α-L-galactofuranoside (449*α*).

According to the general glycosylation procedure (GP15), the reaction mixture of donor **397β** (60 mg; 0.11 mmol) and benzyl alcohol (13 μL, 0.12 mmol) in anhydrous CH_2Cl_2 (0.55 mL) at -30 °C was treated with *N*-iodosuccinimide (35 mg, 0.14 mmol) and AgOTf (6.0 mg, 2.5 μmol). After chromatographic purification over silica gel eluting 5% ethyl acetate in hexane, two anomers were obtained (41 mg, 82%); α/β: 2.9:1.

449β. colorless oil; R_f = 0.11 (17:3 hexane-ethyl acetate); $[\alpha]^{25}_D$ = +66 (*c* = 0.40, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 – 7.22 (m, 20H, ArH), 5.15 (s, 1H, H-1), 4.77 (d, *J* = 12.1 Hz, 1H, OCH_2Ph), 4.64 (d, *J* = 11.9 Hz, 1H, OCH_2Ph), 4.52 (ddd, *J* = 12.0, 6.4, 2.7 Hz, 4H, OCH_2Ph), 4.45 (d, *J* = 11.8 Hz, 1H, OCH_2Ph), 4.39 (d, *J* = 11.7 Hz, 1H, OCH_2Ph), 4.08 (dd, *J* = 3.1, 1.2 Hz, 1H, H-2), 4.06 (dd, *J* = 7.1, 4.2 Hz, 1H, H-4), 3.99 (dd, *J* = 7.1, 3.0 Hz, 1H, H-3), 3.70 (qd, *J* = 6.4, 4.2 Hz, 1H, H-5), 1.23 (d, *J* = 6.5 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.8 (Ar),

138.0 (Ar), 137.8 (Ar), 128.5 (2C, Ar), 128.4 (Ar), 128.4 (Ar), 128.1 (2C, Ar), 128.0 (Ar), 127.8 (2C, Ar), 127.6 (Ar), 105.0 (C-1), 88.6 (C-2), 84.2 (C-4), 83.5 (C-3), 73.5 (C-5), 72.2 (OCH_2Ph), 72.0 (OCH_2Ph), 71.4 (OCH_2Ph), 69.0 (OCH_2Ph), 16.1 (CH_3); HRMS (ESI) m/z calcd for $C_{34}H_{36}O_5Na$ $[M+Na]^+$ 547.2455, found 547.2456.

449α. colorless oil; R_f = 0.31 (17:3 hexane-ethyl acetate); $[\alpha]^{25}_D$ = -90 (*c* = 0.20, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 7.39 – 7.23 (m, 20H, ArH), 4.96 (d, *J* = 4.3 Hz, 1H, H-1), 4.80 (d, *J* = 11.6 Hz, 1H, OCH_2Ph), 4.70 (d, *J* = 12.3 Hz, 1H, OCH_2Ph), 4.65 (d, *J* = 11.9 Hz, 1H, OCH_2Ph), 4.59 (d, *J* = 3.1 Hz, 1H, OCH_2Ph), 4.58 – 4.55 (m, 2H, OCH_2Ph), 4.46 (dd, *J* = 11.9, 5.0 Hz, 2H, OCH_2Ph), 4.21 (t, *J* = 7.1 Hz, 1H, H-3), 4.08 (dd, *J* = 7.4, 4.3 Hz, 1H, H-2), 3.89 (t, *J* = 7.0 Hz, 1H, H-4), 3.68 – 3.62 (m, 1H, H-5), 1.19 (d, *J* = 6.3 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.0 (Ar), 138.3 (Ar), 137.7 (Ar), 137.6 (Ar), 128.6 (Ar), 128.5 (2C, Ar), 128.4 (Ar), 128.2 (Ar), 128.1 (Ar), 128.0 (2C, Ar), 127.9 (Ar), 127.8 (Ar), 127.6 (Ar), 98.5 (C-1), 84.5 (C-2), 83.9 (C-4), 82.1 (C-3), 77.1 (C-5), 72.4 (2C, OCH_2Ph), 71.2 (OCH_2Ph), 68.7 (OCH_2Ph), 15.7 (CH_3); HRMS (ESI) m/z calcd for $C_{34}H_{36}O_5Na$ $[M+Na]^+$ 547.2455, found 547.2456.

***p*-Cresyl 2,3,5-tri-*O*-benzyl-6-deoxy-1-thio-α-D-glucofuranoside *S*-Oxide (450).**

To a stirred solution of compound **394α** (65 mg, 0.12 mmol) in anhydrous CH_2Cl_2 (3.0 mL) at -78 °C, mCPBA (29 mg, 0.13 mmol) in anhydrous CH_2Cl_2 (1.0 mL) was added dropwise. Then the reaction mixture was stirred at -78 °C for 15 min before sat. $NaHCO_3$ was added. The aqueous phase was extracted with ether and the organic layer was washed with brine and dried over Na_2SO_4. The solvent was evaporated under reduced pressure to give a crude product, which was purified using flash column chromatography 20% ethyl acetate in hexane to give compound **450** as a colorless oil (64 mg, 84%); R_f = 0.20 (7:3 hexane-ethyl acetate); $[\alpha]^{25}_D$ = +42 (*c* = 0.30, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 7.67 – 7.64 (m, 2H, ArH), 7.53 – 7.49 (m, 2H, ArH), 7.44 – 7.40

(m, 2H, ArH), 7.38 – 7.34 (m, 1H, ArH), 7.33 – 7.25 (m, 6H, ArH), 7.24 – 7.19 (m, 4H, ArH), 7.16 – 7.11 (m, 2H, ArH), 4.98 (d, *J* = 11.7 Hz, 1H, OCH_2Ph), 4.78 (d, *J* = 4.4 Hz, 1H, H-1), 4.73 (d, *J* = 11.6 Hz, 1H OCH_2Ph), 4.53 (dd, *J* = 4.4, 1.1 Hz, 1H, H-2), 4.51 (d, *J* = 11.8 Hz, 1H, OCH_2Ph), 4.39 (dd, *J* = 24.9, 11.7 Hz, 2H, OCH_2Ph), 4.26 (dd, *J* = 8.3, 3.0 Hz, 1H, H-4), 4.18 (d, *J* = 11.6 Hz, 1H, OCH_2Ph), 3.84 (dd, *J* = 3.1, 1.1 Hz, 1H, H-3), 3.69 (dq, *J* = 8.3, 6.3 Hz, 1H, H-5), 2.38 (s, 3H, Ar-CH_3), 1.04 (d, *J* = 6.3 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 141.5 (Ar), 139.4 (2C, Ar), 137.5 (Ar), 136.9 (Ar), 129.5 (Ar), 128.8 (Ar), 128.7 (Ar), 128.6 (Ar), 128.4 (Ar), 128.3 (2C, Ar), 128.1 (Ar), 127.3 (Ar), 125.8 (Ar), 100.2 (C-1), 88.1 (C-4), 82.7 (C-3), 80.1 (C-2), 74.5 (OCH_2Ph), 74.2 (OCH_2Ph), 72.1 (C-5), 72.0 (OCH_2Ph), 21.6 (Ar-CH_3), 16.9 (CH_3); HRMS (ESI) m/z calcd for $C_{34}H_{36}O_5SNa$ $[M+Na]^+$ 579.2175, found 579.2187.

***p*-Cresyl 2,3,5-tri-*O*-benzyl-6-deoxy-1-thio-β-L-idoofuranoside *S*-Oxide (451)**

To a stirred solution of compound **395β** (60 mg, 0.11 mmol) in anhydrous CH_2Cl_2 (2.8 mL) at -78 °C, mCPBA (29 mg, 0.13 mmol) in anhydrous CH_2Cl_2 (1.0 mL) was added dropwise. Then the reaction mixture was stirred at -78 °C for 15 min before sat. $NaHCO_3$ was added. The aqueous phase was extracted with ether and the organic layer was washed with brine and dried over Na_2SO_4. The solvent was evaporated under reduced pressure to give a crude product, which was purified using flash column chromatography 20% ethyl acetate in hexane to give compound **451** as a colorless oil (49 mg, 80%); R_f = 0.27 (7:3 hexane-ethyl acetate); $[\alpha]^{25}_D$ = -58 (*c* =0.30, $CHCl_3$); ^1H (600 MHz, $CDCl_3$) δ 7.62 – 7.59 (m, 2H, ArH), 7.48 – 7.46 (m, 2H, ArH), 7.41 – 7.37 (m, 2H, ArH), 7.36 – 7.33 (m, 1H, ArH), 7.30 – 7.25 (m, 8H, ArH), 7.24 – 7.20 (m, 2H, ArH), 7.16 – 7.13 (m, 2H, ArH), 4.84 (d, *J* = 11.4 Hz, 1H, OCH_2Ph), 4.69 – 4.64 (m, 2H, H-1, OCH_2Ph), 4.55 (d, *J* = 11.4 Hz, 1H, OCH_2Ph), 4.48 (dd, *J* = 4.2, 0.9 Hz, 1H, H-2), 4.38 – 4.29 (m, 3H, OCH_2Ph), 4.12 (dd, *J* = 9.0, 2.8 Hz, 1H, H-4), 4.10 (dd, *J* = 2.8, 0.9 Hz, 1H, H-3), 3.76 (dq, *J* = 9.0, 6.1 Hz, 1H,

H-5), 2.40 (s, 3H, Ar-CH_3), 1.20 (d, *J* = 6.1 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 141.6 (Ar), 139.5 (Ar), 138.6 (Ar), 137.5 (Ar), 137.3 (Ar), 129.6 (Ar), 128.7 (Ar), 128.6 (2C, Ar), 128.5 (Ar), 128.3 (Ar), 128.1 (Ar), 127.9 (Ar), 127.7 (2C, Ar), 125.5 (Ar), 99.7 (C-1), 86.1 (C-4), 81.4 (C-3), 81.1 (C-2), 74.2 (OCH_2Ph), 72.3 (OCH_2Ph), 71.8 (C-5), 70.9 (OCH_2Ph), 21.6 (Ar-CH_3), 17.3 (CH_3); HRMS (ESI) m/z calcd for $C_{34}H_{36}O_5SNa$ $[M+Na]^+$ 579.2175, found 579.2187.

General Protocol for Glycosylation by the Sulfoxide Method (GP16).

A mixture of the donor (1.0 equiv), TTBP (2.0 equiv), and activated 4 Å powdered molecular sieves (2 g/mmol of the donor) in CH_2Cl_2 (0.2 M in the substrate) was stirred for 1 h at room temperature under argon and then cooled to -78 °C and treated with Tf_2O (1.1 equiv). After 15 min of stirring at -78 °C, the reaction mixture was warmed to -30 °C before a solution of the glycosyl acceptor (1.1 equiv) in CH_2Cl_2 (0.4 M in acceptor) was added slowly. The reaction mixture was stirred for further 4 h at -30 °C and then quenched with triethylamine. The reaction mixture was warmed to room temperature and diluted with dichloromethane, the molecular sieves were filtered off through a pad of Celite, and the filtrate was washed with saturated $NaHCO_3$. The organic layer was separated, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by flash column chromatography on silica gel afforded the corresponding α/β-glycofuranosides. The anomeric ratio of the products was determined by integration of the 1 H NMR spectrum of the crude product mixture.

6-*O*-(2,3,5-Tri-*O*-benzyl-6-deoxy-α-D-glucofuranosyl)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (439α) and 6-*O*-(2,3,5-Tri-*O*-benzyl-6-deoxy-β-D-glucofuranosyl)-1,2:3,4-di-*O*-isopropylidene-αD-galactopyranose (439β) by the Sulfoxide Method.

Coupling of donor **450** (29 mg, 52 μmol) and 1,2:3,4-di-*O*-isopropylidene-α-Dgalactopyranoside (15 mg, 57 μmol) following the general protocol for sulfoxide glycosylation (GP16) gave 46α and 46β (eluent: 0.5% acetone in toluene); combined yield (18 mg, 51%), α/β = 1: 2.2. Glycoside 46β had spectral data identical to the above-described sample.

439α. Colorless oil; R_f = 0.07 (66:1 toluene/acetone); $[\alpha]\ ^{25}_{D}$ = +25 (*c* = 0.10, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 (d, *J* = 7.3 Hz, 2H, ArH), 7.35−7.22 (m, 13H, ArH), 5.52 (d, *J* = 5.0 Hz, 1H, H-1′), 5.14 (d, *J* = 4.4 Hz, 1H, H-1), 4.71 (dd, *J* = 19.6, 11.8 Hz, 3H, OCH_2Ph), 4.59−4.56 (m, 2H, H-3′, OCH_2Ph), 4.51 (dd, *J* = 13.4, 11.7 Hz, 4H, OCH_2Ph), 4.31−4.28 (m, 2H, H-2′), 4.23 (t, *J* = 6.1 Hz, 1H, H-3), 4.19 (t, *J* = 5.0 Hz, 1H, H-2), 4.10 (dd, *J* = 6.6, 4.7 Hz, 1H, H-4), 4.07 (ddd, *J* = 8.1, 5.9, 1.8 Hz, 1H, H-5′), 3.89 (dd, J = 9.9, 6.0 Hz, 1H, H-6′), 3.79−3.74 (m, 1H, H-5), 3.71 (t, *J* = 9.2 Hz, 1H, H6′), 1.52 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.32 (s, 3H, CH_3), 1.31 (s, 3H, CH_3), 1.17 (d, *J* = 6.5 Hz, 3H, CH3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.3 (2C, Ar), 138.2 (Ar), 128.5 (2C, Ar), 128.3 (Ar), 128.1 (2C, Ar), 127.9 (Ar), 127.8 (Ar), 127.4 (Ar), 109.2 ($C(CH_3)_2$), 108.7 ($C(CH_3)_2$), 100.4 (C-1), 96.5 (C-1′), 83.1 (C-2), 82.2 (C-3), 81.0 (C-4), 73.5 (C-5), 72.4 (OCH_2Ph), 72.2 (OCH_2Ph), 71.9 (OCH_2Ph), 70.9 (C-2′), 70.8 (C-3′), 70.7 (C-6′), 66.3 (C-5′), 65.7 (CH_3), 26.3 (CH_3), 26.2 (CH_3), 25.1 (CH_3), 24.7 (CH_3), 16.9 (CH_3); HRMS (ESI) m/z calcd for C39H48O10Na $[M+Na]^+$ 699.3139, found 699.3136.

6-*O*-(2,3,5-Tri-*O*-benzyl-6-deoxy-β-L-idofuranosyl)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (445β) and 6-*O*-(2,3,5-Tri-*O*-benzyl-6-deoxy-α-L-idofuranosyl)-1,2:3,4-di-*O*-isopropylidene-α-Dgalactopyranose (445α) by the Sulfoxide Method.

Coupling of donor 58 (31 mg, 56 μmol) and 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside (16 mg, 61 μmol) following the general protocol for sulfoxide glycosylation (GP16) gave **445α** and **445β** (eluent: 0.5% acetone in toluene); combined yield (23 mg, 61%), α/β = 1: 1.6. Glycoside **445α** and **445β** had spectral data identical to the above-described sample.

VT-NMR studies of *p*-Cresyl 2,3,5-tri-*O*-benzyl-6-deoxy-1-thio-α-D-glucofuranoside *S*-Oxide (450).

A solution of the sulfoxide **450** (22 mg, 41 μmol) and TTBP (20 mg, 82 μmol) in CD_2Cl_2 (0.70 mL) were placed in a 5 mm NMR tube under argon and cooled to -80 °C in the NMR probe. The starting sulfoxide reaction mixture ^{1}H spectrum was obtained; then, the sample was quickly removed from the probe, and the precooled Tf_2O (13.0 μL, 82 μmol) at -78 °C was added quickly. The sample was returned to the NMR probe and the ^{1}H spectrum was recorded after 10 min. The temperature was increased by 10 °C /10 min increments until -10 °C and with ^{1}H NMR recorded at each temperature. The decomposition product **452** (2 mg, 13%) was isolated from the mixture by chromatography following warming to room temperature (eluent: 95:5 hexane/ethyl acetate).

1*R*-1,4-Anhydro-3,5-di-*O*-benzyl-6-deoxy-1-*C*-2-*O*-(*o*-phenylenemethylene)-D-glucitol (452).

Colorless oil; R_f = 0.67 (7:3 hexane-ethyl acetate); $[\alpha]^{25}_D$ = -46 (*c* = 0.05, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.5 Hz, 1H, ArH), 7.40 – 7.34 (m, 5H, ArH), 7.33 – 7.27 (m, 2H, ArH), 7.27 – 7.21 (m, 1H, ArH), 7.05 (d, *J* = 7.5 Hz, 1H, ArH), 5.02 (d, *J* = 3.7 Hz, 1H, H-1), 4.81 (d, *J* = 11.9 Hz, 1H, OCH_2Ph), 4.74 (dd, *J* = 13.1, 9.2 Hz, 2H, OCH_2Ph), 4.64 (dd, *J* = 21.6, 13.2

Hz, 2H, OCH_2Ph), 4.56 (d, *J* = 11.6 Hz, 1H, OCH_2Ph), 4.35 (d, *J* = 3.7 Hz, 1H, H-2), 4.17 (dd, *J* = 8.0, 3.7 Hz, 1H, H-4), 4.08 (d, *J* = 3.8 Hz, 1H, H-3), 3.95 (tt, *J* = 8.5, 6.2 Hz, 1H, H-5), 1.15 (d, *J* = 6.3 Hz, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.6 (Ar), 137.6 (Ar), 134.4 (Ar), 131.9 (Ar), 130.4 (Ar), 128.5 (Ar), 128.1 (Ar), 128.0 (Ar), 127.9 (Ar), 127.8 (Ar), 127.7 (Ar), 127.5 (Ar), 127.1 (Ar), 124.0 (Ar), 85.0 (C-4), 84.5 (C-3), 79.1 (C-2), 74.9 (C-5), 73.2 (C-1), 72.3 (OCH_2Ph), 72.0 (OCH_2Ph), 66.9 (OCH_2Ph), 17.0 (CH3); HRMS (ESI) m/z calcd for $C_{27}H_{28}O_4Na$ $[M+Na]^+$ 439.1872, found 439.1869.

VT-NMR studies of *p*-Cresyl 2,3,5-tri-*O*-benzyl-6-deoxy-1-thio-β-L-idofuranoside *S*-Oxide (451).

A solution of the sulfoxide **451** (23 mg, 42 μmol) and TTBP (21 mg, 84 μmol) in CD_2Cl_2 (0.70 mL) were placed in a 5 mm NMR tube under argon and cooled to -80 °C in the NMR probe. The starting ^1H spectrum was obtained and the sample was quickly removed from the probe. Precooled Tf_2O (14.0 μL, 84 μmol) at -78 °C was added quickly, the sample was returned to the NMR probe and the ^1H spectrum was recorded after 10 min. The temperature was increased by 10 °C /10 min increments until -10 °C and the ^1H NMR spectrum recorded at each temperature. The decomposition product **453** (1 mg, 6%) was isolated by chromatography following warming to room temperature (eluent: 95:5 hexane/ethyl acetate)

1*R*-1,4-Anhydro-3,5-di-*O*-benzyl-6-deoxy-1-*C*-2-*O*-(*o*-phenylenemethylene)-L-iditol (453).

Colorless oil; R_f = 0.40 (9:1 hexane-ethyl acetate); $[\alpha]^{25}_D$ = -63 (*c* = 0.08, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 7.50 – 7.47 (m, 1H, ArH), 7.34 – 7.25 (m, 12H, ArH), 7.06 (d, *J* = 7.3 Hz, 1H, ArH), 4.91 (d, *J* = 3.1 Hz, 1H, H-1), 4.77 (d, *J* = 14.6 Hz, 1H, OCH_2Ph), 4.71 (d, *J* = 11.6 Hz, 1H, OCH_2Ph), 4.66 – 4.60 (m, 3H, OCH_2Ph), 4.44 (d, *J* = 11.4 Hz, 1H, OCH_2Ph), 4.29 (dd, *J* = 11.3,

3.3 Hz, 2H, H-2,H-3), 4.12 (dd, *J* = 8.9, 3.4 Hz, 1H, H-4), 4.01 (dq, *J* = 9.3, 6.3 Hz, 1H, H-5), 1.35 (d, *J* = 6.2 Hz, 3H, CH_3), ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.1 (Ar), 138.3 (Ar), 134.7 (Ar), 131.6 (Ar), 130.6 (Ar), 128.5 (Ar), 128.4 (Ar), 128.2 (Ar), 127.8 (Ar), 127.7 (Ar), 127.6 (Ar), 127.5 (Ar), 124.3 (Ar), 83.7 (C-4), 83.6 (C-3), 79.7 (C-2), 73.3 (C-1), 72.9 (C-5), 72.7 (OCH_2Ph), 70.7 (OCH_2Ph), 67.0 (OCH_2Ph), 17.5 (CH_3); HRMS (ESI) m/z calcd for $C_{27}H_{28}O_4Na$ $[M+Na]^+$ 439.1872, found 439.1864.

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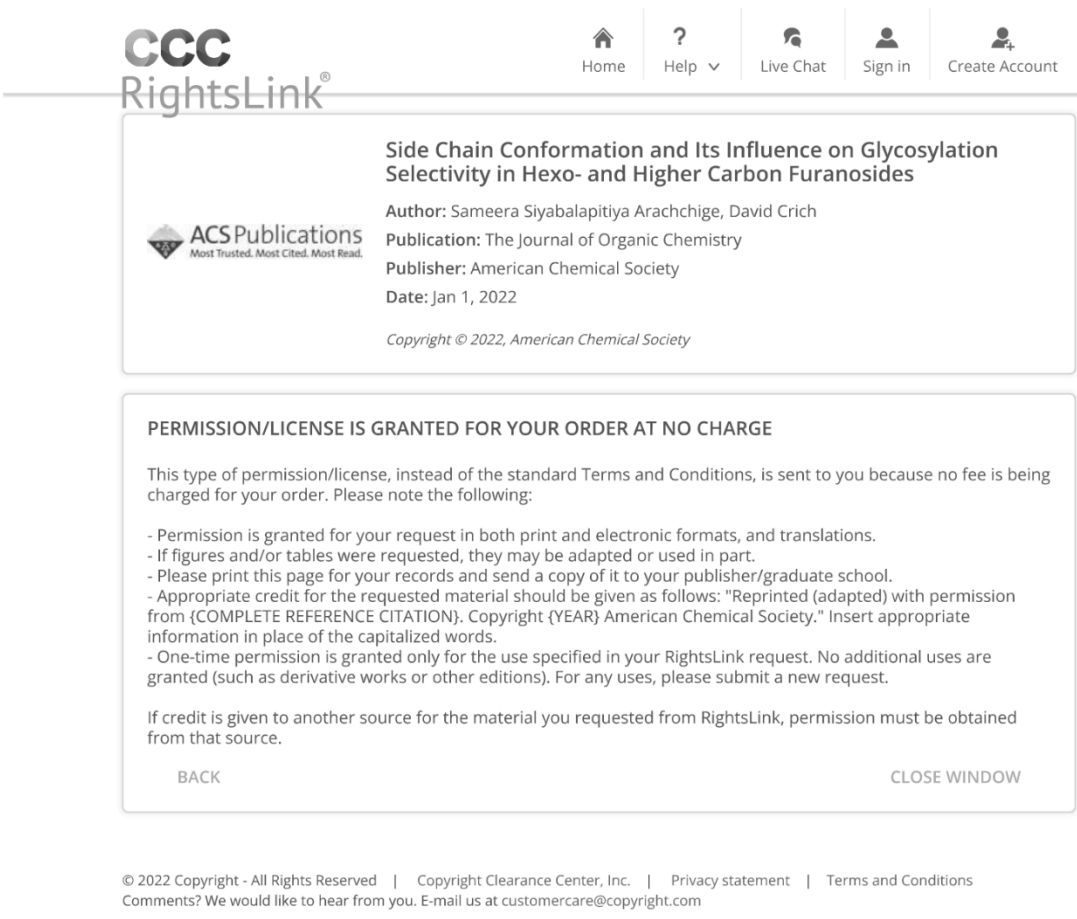
APPENDIX



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Side Chain Conformation and Its Influence on Glycosylation Selectivity in Hexo- and Higher Carbon Furanosides

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Publications

- **Siyabalapitiya Arachchige, S**.; Crich, D., Side Chain Conformation, and Its Influence on Glycosylation Selectivity in Hexo- and Higher Carbon Furanosides. *J. Org. Chem.* **2022**, 87, 316-339.
- **Siyabalapitiya Arachchige, S**.; Crich, D., Syntheses of Legionaminic Acid, Pseudoaminic Acid, Acetaminic Acid, 8-*epi*-Acetaminic Acid and 8-*epi*-Legionaminic Acid Glycosyl Donors from *N*-Acetylneuraminic Acid by Side Chain Exchange. (Organic Letters, Accepted)

Conferences

- Presented an oral talk at ACS Spring 2022 Meeting at San Diego, CA on March 22, 2022, Title: Concise Syntheses of Pseudaminic Acid and Legionaminic Acid Donors and their Analogues.