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Synthesis and NMR Characterization of the Six Regioisomeric Mono-*O*-Phosphates of Octyl 2-acetamido-2-deoxy-4-*O*-(β-*D*-galactopyranosyl)-β-*D*-glucopyranoside

By

David Rabuka

A thesis submitted to the Faculty of Graduate Studies and Research in partial fulfillment of the requirements for the degree of

Master of Science

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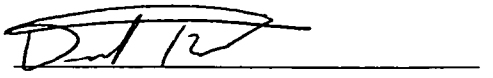

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Abstract

All six regioisomeric mono-*O*-phosphates of octyl 2-acetamido-2-deoxy-4-*O*-(β-*D*-galactopyranosyl)-β-*D*-glucopyranoside have been chemically synthesized and characterized by high resolution ^{1}H, ^{13}C and ^{31}P NMR spectroscopy. Phosphorylation causes characteristic downfield shifts of the substituted site in the ^{1}H and ^{13}C NMR signals and a unique ^{31}P signal. ^{31}P NMR was utilized to detect the phosphorylated products in mixture of disaccharides resulting from phosphorylation of octyl 2-acetamido-2-deoxy-4-*O*-(β-*D*-galactopyranosyl)-β-*D*-glucopyranoside.

UNIVERSITY OF ALBERTA

FACULTY OF GRADUATE STUDIES AND RESEARCH

The undersigned certify that they have read, and recommended to the Faculty of Graduate Studies and Research for acceptance, a thesis entitled **Synthesis and NMR Characterization of the Six Regioisomeric Mono-*O*-Phosphates of Octyl 2-acetamido-2-deoxy-4-*O*-(β-*D*-galactopyranosyl)-β-*D*-glucopyranoside** by **David Rabuka** in partial fulfillment of the requirements for the degree of **Master of Science.**

Dr. Ole Hindsgaul (Supervisor)

Dr. Derrick L.J. Clive

Dr. Edward E. Knaus

Dated: June 29th, 2000

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My deepest gratitude goes to my family who have always supported me and encouraged me during my entire time spent in university.

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List of Abbreviations

Ac	acetyl
All	allyl
anal.	analysis
Asn	asparagine
Bn	benzyl
b	broad
Bu	butyl
calcd	calculated
d	doublet
DBU	1,8-diazobicyclo[4.3.0]undec-5-ene
DCM	dichloromethane
DCP	dichlorophthaloyl
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DMAP	4-dimethylaminopyridine
DMF	N,N-dimethylformamide
DMSO	dimethylsulfoxide
eq.	equivalent
Et	ethyl
Fuc	*L*-fucopyranose
Gal	*D*-galactopyranose
GalNAc	*D*-2-acetamido-2-deoxy-glucopyranose

GC	gas chromatography
Glc	*D*-glucopyranose
GlcNAc	*D*-2-acetamido-2-deoxy-glucopyranose
GlcNPhth	*D*-2-deoxy-2-phthalimido-glucopyranose
GPI	glycosyl-phosphatidyl-inositol
GPL	glycopeptide
HMBC	heteronuclear multiple bond coherence
HMQC	heteronuclear multiple quantum coherence
HPLC	high performance liquid chromatography
HR-ESMS	high resolution electrospray mass spectrometry
IdA	iduronic acid
Hz	hertz
J	coupling constant
Kan-Nacyl	*N*-acylkanosamine
LacNAc	2-acetamido-2-deoxy-4-*O*-(β-*D*-galactopyranosyl)-β-*D*-glucopyranoside
LOS	lipo-oligosaccharide
m	multiplet
Man	*D*-mannopyranose
Me	methyl
mg	milligram
MHz	megahertz
min	minute(s)

mL	millileter(s)
mol	mole(s)
mmol	millimole(s)
MS	mass spectrometry or molecular sieves
NMR	nuclear magnetic resonance
NOE	Nuclear Overhauser Effect
Oct	octyl
PGL	phenolic glycolipid
Ph	phenyl
Phth	phthaloyl
PMB	*p*-methoxybenzyl
ppm	parts per million
Pr	propyl
quant	quantitative
s	singlet
Ser	*L*-serine
sm	starting material
Tf	trifluoromethanesulfonyl
TCP	tetrachlorophthaloyl
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TIS	triisopropylsilyl
Thr	*L*-threonine

TLC	thin layer chromatography
TMS	trimethylsilyl
TOCSY	total correlation spectroscopy
Tr	trityl
TROESY	transverse rotating frame Nuclear Overhauser Enhancement spectroscopy
Ts	*p*-toluensulfonyl

Chapter 1

Introduction

1.1 Introduction to Carbohydrates

Carbohydrates make up the most abundant and disparate class of biological molecules [1]. Essential to living organisms, sugars are present in all aspects of biological chemistry. Saccharides found in nature are derived from simple molecules through gluconeogenesis [2], or from carbon dioxide and water through photosynthesis in plants. They sustain living systems as an essential energy source via their metabolic breakdown and as essential structural components, such as cellulose in plants or as chitin in shellfish [3]. In the last fifty years the role of carbohydrates in other biological events has become increasingly apparent. A large number of other biological processes involving carbohydrates have been discovered and, as a result, the interest of the scientific community in sugars has subsequently grown.

1.1.1 The Structures of Naturally Occurring Carbohydrates

The diversity and complexity of oligosaccharide structure is a key difference between carbohydrates and other natural building blocks, such as amino acids and nucleotides. Carbohydrates found in living systems usually consist of several monosaccharides covalently linked together. The connectivity of these units is limited only by the number of available hydroxyl groups present on the molecules, leading to a

large variety of possible branching structures [4]. Glycosidic linkages constitute another element of structural diversity in oligosaccharides as connectivity at the C-1 position of monosaccharides can result in either α- or β-anomers.

Carbohydrates can be present in living systems as independent entities but most often they are attached to proteins or lipids forming glycoproteins or glycolipids, respectively. Glycoproteins, the most abundant conjugates of oligosaccharides found in nature, are classified as *N*-linked or *O*-linked, in accordance with the amino acid connecting the sugar moiety to the protein [5]. In *O*-linked glycoproteins the attachment site is at the hydroxyl group of serine (Ser) or threonine (Thr) (Fig 1-1). The *N*-linked glycoproteins have the sugars attached to the amide group of asparagine (Asn), which is part of a consensus sequence of Asn-X-Ser/Thr, where X can be any amino acid other then proline. *N*-linked glycans of glycoproteins can be placed in one of three categories:

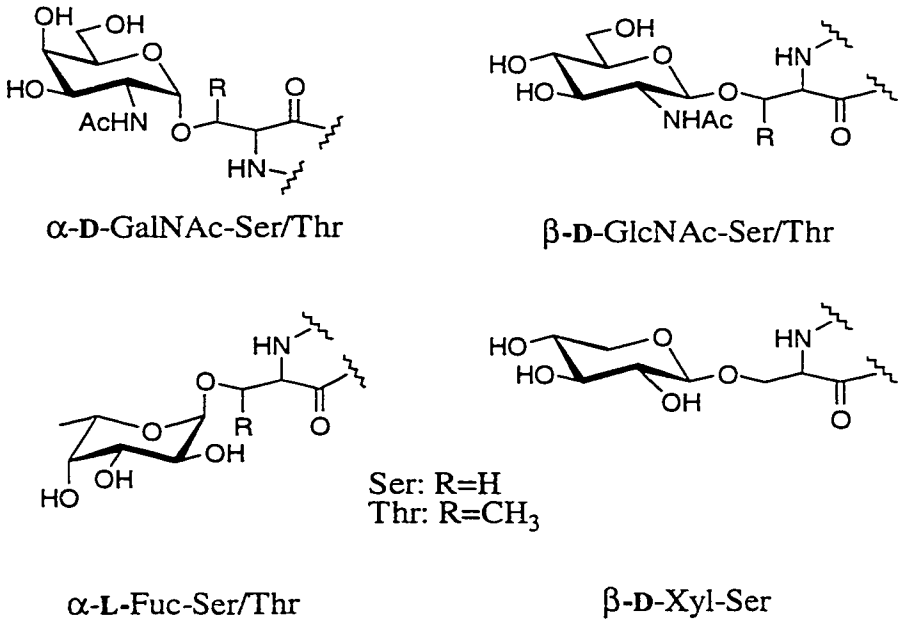


Fig 1-1 Examples of O-linked glycoproteins

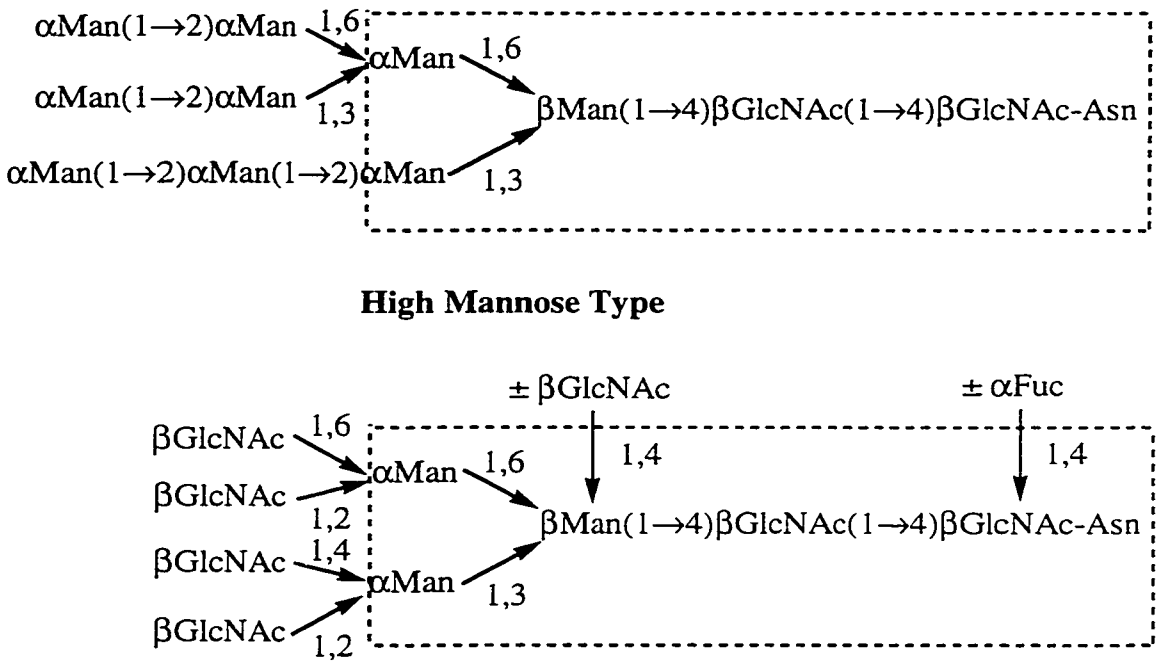


Fig 1-2 Three types of N-linked glycoproteins

the high mannose type, complex type and hybrid type. All have a common pentasaccharide core, Manα1→6[Manα1→3] Manβ1→4GlcNAc1→4GlcNAcβ (Fig 1-2).

There are a large possible number of branched structures attached to the pentasaccharide core. These various side chains provide tremendously diverse

asparagine-linked oligosaccharides. One of the commonly occurring side chains in complex *N*-glycans, the disaccharide unit Galβ1→4GlcNAc also known as LacNAc (*N*-acetyllactosamine), plays a role in a variety of biological processes. Examples of additional LacNAc units modifying *N*-glycans include blood type activity (Fig 1-3), fetal erythrocytes and a highly branched poly-*N*-acetyllacto-lactosamine glycan called embryoglycan, present in early mouse embryos [6]. In glycans of the complex type, up to five units of LacNAc can be β-linked to the pentasaccharide core [7].

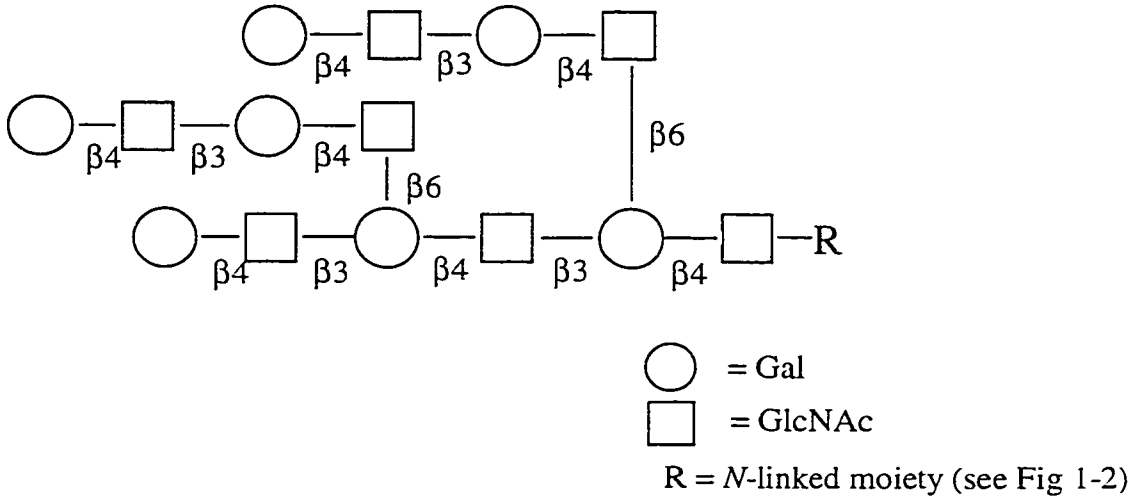


Fig 1-3 Blood group I antigen

Glycolipids contain oligosaccharides linked to the hydroxyl group of hydrophobic moieties such as ceramide. They are placed into three broad categories: glycosphingolipids (found predominantly on mammalian cells), glycoglycerolipids (found in bacteria and plants) and glycosyl-phosphatidyl-inositols (GPIs) [8].

1.1.2 Biological Roles of Carbohydrates

The roles the carbohydrates play in the biological realm are vast. The involvement of oligosaccharides in such diverse activities as intracellular trafficking and cell-cell recognition events is only now being recognized [9]. Carbohydrates have been found to be participants in oncogenesis [10], utilized in metastasis and have been implicated in the fertilization and early development of embryos [11]. They serve as receptors for cell-cell adhesion and cellular binding of bacteria, toxins, viruses, and hormones [12].

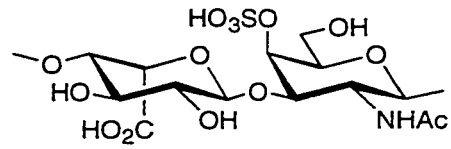
In order for biological events to transpire the carbohydrate must interact with other molecular species, such as proteins. Carbohydrate binding proteins are classified as lectins, immunoglobins and carbohydrate binding enzymes [13]. The nature of carbohydrate protein interactions is very site and structure specific.

1.2 Modified Sugars in Biological Systems

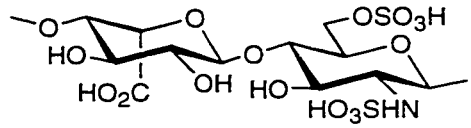
The biological interactions of carbohydrates are further increased by the presence of additional structural motifs. Modifications on oligosaccharides include the addition of phosphates, phosphonates, acyl groups, alkyl ether groups, sulfates, sulfonates, pyruvyl groups and carbamoylation [14]. In eukaryotic cells the modifications are generally limited to phosphorylation, sulfation and acetylation.

1.2.1 Eukaryotic Modifications

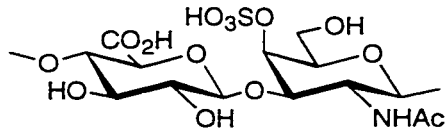
Sulfation can be found on Gal, GlcNAc, Glc, IdA and GalNAc moieties. In eukaryotes there are a number of examples of oligosaccharides modified with sulfates. Chondroiton-4-sulfate and chondroiton-6-sulfate are major components of cartilage and other connective tissue. Dermatan sulfate is found predominantly in the skin. Heparin inhibits the clotting of blood and heparan sulfate is found ubiquitously in cells (Fig 1-4) [15]. Another example of modification with sulfates is 4-*O*-sulfate GalNAc residues on glycoprotein hormones [16]. Sulfatides, galactocerebroside-3-sulfate account for 15% of the lipids of white matter in the brain [17].



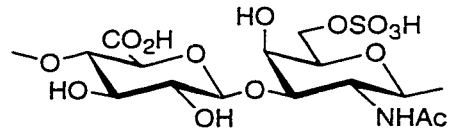
Dermatan 4-sulfate



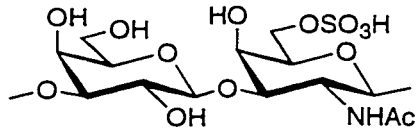
Heparin



Chondroitin 4-sulfate



Chondroitin 6-sulfate



Keratan Sulfate

Fig 1-4 Modification with sulfates in nature

Phosphorylation is a common modification on oligosaccharides in eukaryotic systems. Fructose-2,6-biphosphate activates glycolysis. Phosphorylated high mannose-type oligosaccharides on lysosomal enzymes are thought to play an important role in trafficking newly synthesized lysosomal enzymes [18]. Mannose 6-*O*-phosphate and glucose 6-*O*-phosphate are key intermediates in oligosaccharide synthesis. Additional ethanolamine phosphates are a unique feature of GPIs in higher eukaryotes [19].

1.2.2 Prokaryotic Modifications

The greatest number of interesting oligosaccharide modifications are found in prokaryotic cells. Bacteria produce a variety of glycoconjugates and polysaccharides consisting of unusual sugars not found in eukaryotes [20]. Modifications of sugar moieties are often species specific and provide markers for classification. The list of prokaryotic oligosaccharide modification is extensive.

One of the most thoroughly studied prokaryotes are members of the genus *Mycobacterium*, which have been implicated in a large number of diseases [21]. The modifications found in *Mycobacterium* provide an interesting example of the structural diversity found in prokaryotic systems.

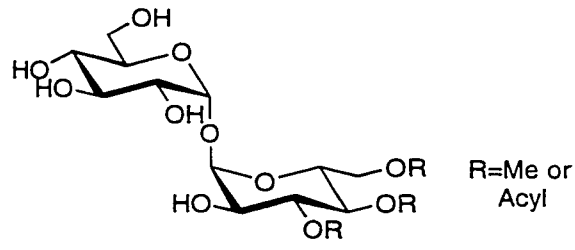


Fig 1-5 α,α-Trehalose

Glycopetidolipids (GPLs) are characteristically found in *M. avium* and associated complexes [22]. The core of the oligosaccharide consists of α-*L*-Rha-(1→2)-6-deoxy-*L*-Tal. Methyl ethers, especially of 6-deoxy hexoses, are constituents of all but one GPL and many are modified with uronic acids and acetal-linked pyruvic acid moieties [23]. Other members of the *M. avium* GPL complex exhibit extensive methylation, dideoxygenation, acetylation and chain branching [24].

The trelose-containing lipo-oligosaccharides (LOSs) from *Mycobacterium* species also contain many novel structural features. These glycolipids are based on α,α-trehalose units in which one α-*D*-glucopyranoside residue contains two or three fatty acyl substituents and occasionally an *O*-methyl group [25]. The other α-*D*-glucopyranose residue carries one of several oligoglycosyl groups consisting of a variety of sugar types and composition (Fig 1-5). The single most unique characteristic of the LOSs of *Mycobacterium* is the 4,6-dideoxy-(2-methoxypropanamido)-3-*C*-methyl-2-*O*-methyl-*L*-manno-hexapyranose unit. Its trivial name is *N*-acylkanosamine (Kan-NAcyl) (Fig 1-6) [26].

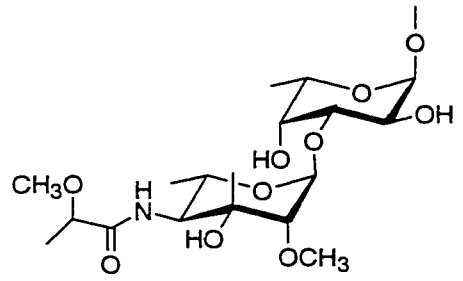


Fig 1-6 The structure of Kan-NAcyl

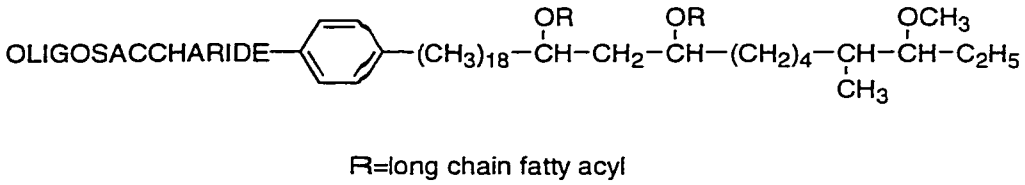


Fig 1-7 Phenolic glycolipid core

LOSs from *M. malmoense*, a group of typical *Mycobacteria* implicated in pulmonary infections, contains *O*-methylated 2-linked α-*L*-rhamnopyransyl residues [27]. Examples of acylation can be found in *M. tuberculosis* where saturated acyl groups are located at the 2-O and 3-O positions of the terminal Glc on the terminal trehalose. At least six molecular species differing only in fatty acid content have been discovered and comprise a family of di-*O*-acylated trehaloses [28].

Glycolipids that are devoid of amino acids and have the base core structure as shown in Fig 1-7 have been termed phenolic glycolipids (PGLs). The oligosaccharides demonstrate immense variation including *O*-methyl groups and dideoxy moieties. For example, the carbohydrate composition of PGL-I of *M. leprae* consists of 3,6-di-*O*-methyl-β-*D*-glucopyranose, 2,3,-di-*O*-methyl-α-*L*-rhamnopyranose and 3-*O*-methyl-α-*L*-rhamnopyranose (Fig 1-8) [29].

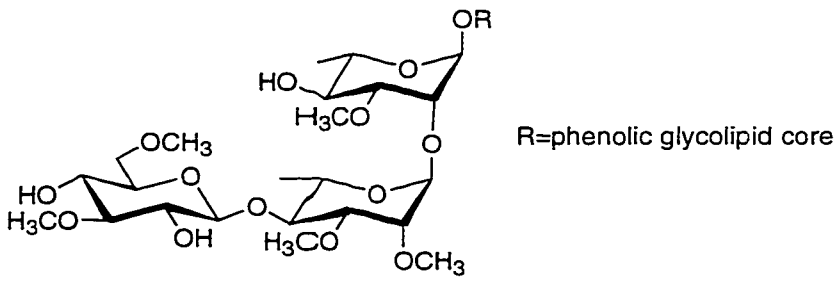


Fig 1-8 Structure of PGL-I

1.3 NMR Structural Analysis of Oligosaccharides

Up until the 1970's, the complexity of oligosaccharides severely hindered attempts to elucidate their structure. However, in the past thirty years a number of different techniques have become available to the researcher in analyzing conformations, connectivity and the makeup of complex sugars. Methods for identifying the presence of carbohydrates include the phenol-sulfuric acid assay, detecting the presence of hexose, and hydrazinolysis which releases *N*-linked chains. High performance liquid chromatography (HPLC), lectin affinity interactions, gas chromatography (GC) and mass spectrometry (MS) have all constituted vital roles and increasing usefulness in structural analysis [30]. However, no single technique has had more impact in the field of carbohydrate analysis than high field nuclear magnetic resonance spectroscopy [31].

Since the first investigation by Lemieux [32] of carbohydrate derivatives by ^{1}H NMR, this technique has become firmly established as a powerful tool in oligosaccharide structural analysis. Provided a sufficient amount of purified material is available, complete structural elucidation can be carried out, in solution, with ^{1}H NMR and ^{13}C NMR. Structural analysis is usually carried out using a combination of one-dimensional (1-D) and two-dimensional (2-D) experiments including correlation spectroscopy (COSY), total correlation spectroscopy (TOCSY), heteronuclear multiple quantum coherence (HMQC) and heteronuclear multiple bond coherence (HMBC) experiments [33].

The chemical shifts of protons are related primarily to the surroundings of individual protons and provide information about ring conformation. The chemical shifts

for the anomeric proton in a α anomer is usually greater than 4.75 ppm and less than 4.75 ppm in β anomers. Chemical shifts are indicative of axial versus equatorial protons. The chemical shift of H-4 on Gal generally is greater than 4 ppm. When a sugar is glycosylated, H-1 will shift approximately 0.5 ppm downfield. Regiochemistry of substitutions can be evaluated according to chemical shifts at specific positions. The ^{13}C shifts are also consistent for certain positions on various monosaccharide units. The C-1 shift can provide information on the type of anomers; α-C-1 generally resonates at less than 100 ppm and β-C-1 at greater than 100 ppm. A large database of chemical shifts and couplings has been compiled in the literature, providing an easily accessible source of comprehensive data [34].

The J splitting (scalar coupling constants) of protons can provide useful information about the ring conformations of monosaccharides. ^{1}H-^{1}H geminal coupling, found for H_{6a}/H_{6b}, is generally around 11-12 Hz, while the vicinal coupling is between 1-10 Hz and is strongly conformation dependent. From the proton-proton coupling it is possible to identify the stereochemistry of the sugar units, for example glucose vs galactose vs mannose. The coupling at the anomeric position of hexoses is indicative of α or β linkages; the α $J_{H1,H2}$ is 3-4 Hz, the β $J_{H1,H2}$ 7-8 Hz generally (although not for mannosides). The carbon-proton coupling at the anomeric position, obtained from coupled HMQC experiments, has a $J_{C1,H1}$ for α-anomers of 166-172 Hz and for β-anomers it is 158-164 Hz.

Through-space effects, or Nuclear Overhauser Effects (NOEs) can provide evidence for the linking position and sequence of oligosaccharides. NOEs along with J coupling can be used to determine the glycosidic angles (ϕ, ψ, ω) (Fig 1-9). Meaningful

structural data can also be obtained by incorporating NMR data and computer graphics simulation to provide further insight into oligosaccharide conformation and solution behavior [35].

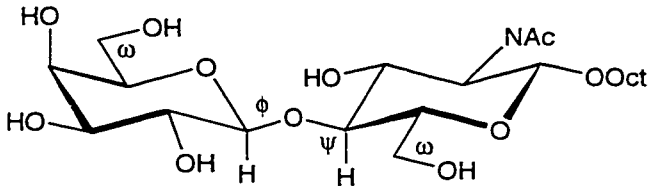


Fig 1-9 Glycosidic angles of octyl β-LacNAc

NMR data is now beginning to accumulate on intermolecular and intramolecular interactions of oligosaccharides and proteins with the transfer NOEs being an especially useful tool [36]. Effective protocols for the elucidation of the conformation of oligosaccharides bound to proteins are now available and should lead to a deeper understanding of the molecular events involved in oligosaccharide-acceptor binding.

1.4 Chemical Synthesis of Carbohydrates

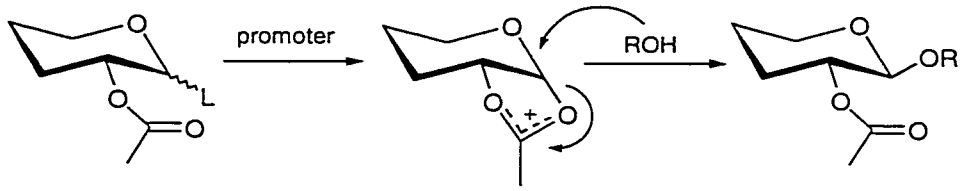
1.4.1 Introduction to Chemical Synthesis

The synthesis of oligosaccharides presents a number of unique challenges due to the complexity of the structures involved and the large number of linkages possible [37]. Complicated protecting strategies need to be invoked and suitable procedures for activation of the anomeric carbon atom are required. The coupling step must also be diastereoselective with respect to formation of α- or β-anomers. A number of donors

have been utilized in glycosidic bond formation including glycosyl halides, orthoesters, thioglycosides, sulfoxides, glycals, epoxides, glycosyl phosphites, glycosyl acetates, seleno glycosides, imidates and *n*-pentenyl glycosides. The methods utilized in the present work will discussed in further detail.

1.4.2 1,2-Trans-Glycosylation

1,2-Trans-glycosylation is generally less difficult then 1,2-cis-glycosylation and usually proceeds with neighboring group participation. The neighboring group at the C-2 position is generally an acyl group although other groups have been used. The ester in the presence of a promoter goes through the dioxolanium intermediate followed by attack of the glycosyl acceptor. The attack occurs trans to the neighboring group, giving β-glycosides in the gluco/galacto-series (Fig 1-10) and the α-glycosides in the manno-series [38].



L=Leaving group

Fig 1-10 Neighboring group participation

1.4.3 1,2-Cis-Glycosylation

In 1,2-cis-glycosylation a non-participating group must be present at C-2. 1,2-Cis-glycosylation is more difficult than 1,2-trans-glycosylation because of the lack of a neighboring group to direct glycosylation. The *in situ* anomerization of α-halides was the first reliable method to make 1,2-cis-glycosides (Fig 1-11) [39]. The preferred α-glycoside formation is rationalized on the basis of two factors. The less thermodynamically stable β-halide is closer to the transition state for glycosylation and reactions proceed more quickly from the α-face as a result of the anti-periplanar arrangement of the nucleophile oxygen with the ring oxygen lone pair.

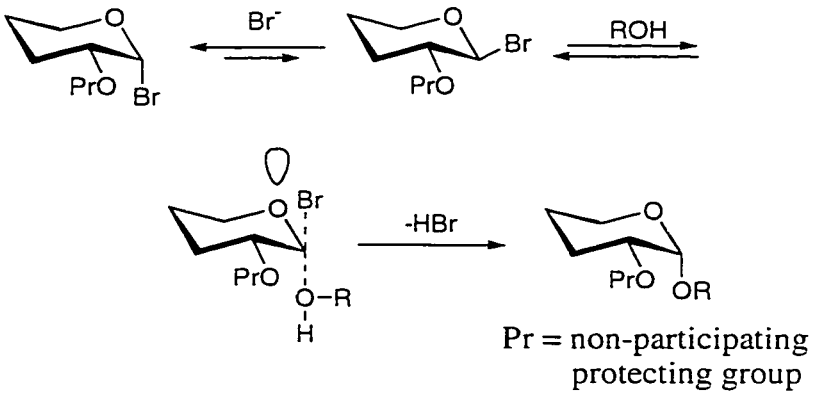


Fig 1-11 α Glycosylation

1.4.4 Synthesis of 2-Amino-2-deoxy-Glycosides

The synthesis of 2-amino-2-deoxy sugars has attracted much attention largely due to their ubiquitous presence in nature as N-acetylglucosamine (GlcNAc) and N-acetylgalactosamine (GalNAc) [40]. The amino group has to always be protected in

order to avoid N-glycosylation. Since the amino group is positioned at C-2, the choice of protecting group will also dictate the stereocontrol of the reaction. As with any protecting group, the ideal N-protecting group should be relatively easy to install and remove. It should also be stable to the conditions employed in the synthesis.

Glycosyl donors containing N-acetyl groups have not been widely used since they tend to from stable oxazoline intermediates which are unreactive with many acceptors [41]. Other protecting groups have become more favored and commonly employed. The most widely used protection for amino groups is the phthalimido group introduced by Lemiex in 1976 [42]. The phthalimido group behaves as a participating neighboring group giving rise to β-anomers (Fig 1-12).

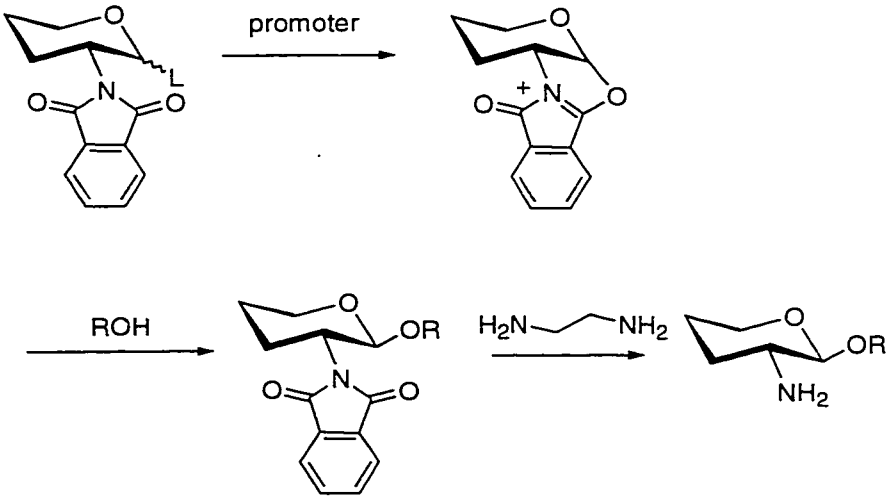


Fig 1-12 Glycosylation with the phthalimido group at C-2

The conditions required to remove the phthalimido group can be quite harsh, involving excess hydrazine, butylamine, hydoxylamine, ethylene diamine or sodium borohydride at temperatures of 80-100 °C [43]. The dichlorophthaloyl (DCP) and

tetrachlorophthaloyl (TCP) have been applied as protecting groups, both of which can be removed under milder conditions.

1.4.5 The Koenigs-Knorr Method of Glycosylation

The Koenigs-Knorr method of gycosylation dates back to 1901 [44]. The activation of the donor is achieved from glycosyl halides (bromine or chlorine) that react with an acceptor in the presence of a heavy metal salt (Fig 1-12). Diastereoselectivity is achieved by participation of neighboring groups to give β-glycosides of *D*-glucose, *D*-glucosamine, *D*-galactose and *D*-galactosamine and α-glycosides of *D*-mannose and *L*-rhamnose.

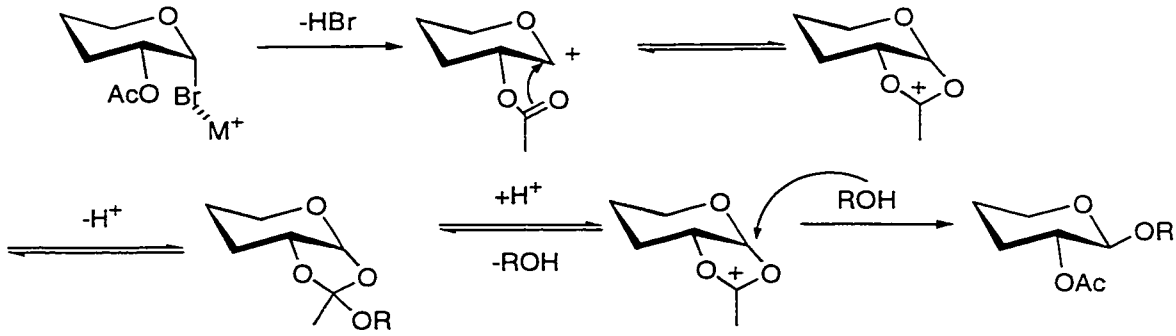


Fig 1-13 Koenigs-Knorr glycosylation

Disadvantages of the Koenigs-Knorr method in the synthesis of oligosaccharides include the harsh conditions needed to generate the glycosyl halide, and the relative instability of the glycosyl bromides or chlorides used. These drawbacks have prompted

researchers to investigate and use alternate glycosyl donors such as those mentioned previously.

1.4.6 Orthoesters in Glycoside Synthesis

In any displacement reaction at an anomeric center with neighboring group participation from an acyloxy group, the transient acyloxonium ion can be trapped by nucleophiles (Fig 1-13). In the presence of basic reagents high yields of orthoesters can be formed, particularly so with 1,2-trans-acylglycosyl halides. It is also possible to prepare 1,2-orthoesters from 1,2-cis-glycosyl halides using alcohols in the presence of tetraalklylammonium halides and sym-collidine or lead carbonate and ethyl acetate [45]. Many orthoesters are stable under basic conditions and can be further functionalized before being used in glycosylation.

Orthoesters can be used as glycosylating agents when activated by protic or Lewis acids followed by reaction with an alcohol or thiol [46]. Orthoesters are generally not used with unreactive acceptors because side products are generated from the alcohol.

1.4.7 Thioglycosides

The development of alternative donors for glycosylations yielded thioglycosides as donors [47]. Thioglycosides are easy to prepare and are relatively stable to many reaction conditions utilized in a synthetic scheme and can therefore be used as temporary

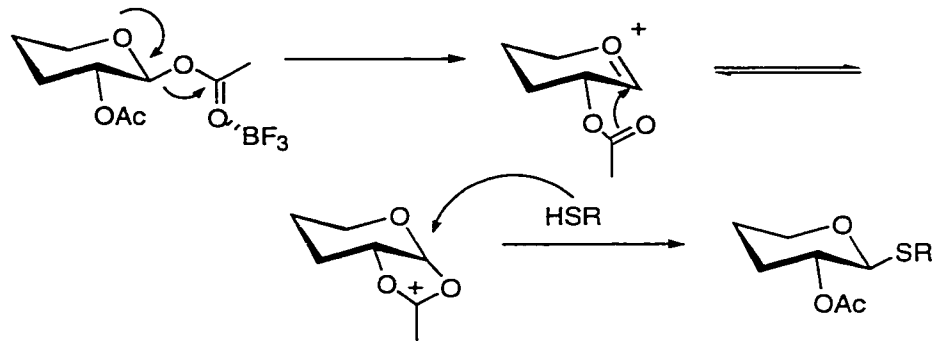


Fig 1-14 Generation of thioglycosides

protecting groups. Conversion of thioglycosides to other donors is feasible, making them particularly useful in oligosaccharide synthesis.

Thioglycosides can be prepared in a number of ways. Thiols react in the presence of Lewis acids, such as $BF_3 \bullet Et_2O$, to predominantly provide the 1,2-trans-product (Fig 1-14) [48]. Thiolate anions can react with a glycosyl halide to gain give the 1,2-trans thioglycoside.

Activation of thioglycosides can be carried out with a number of promoters. Common activators include *N*-iodosuccinimide with silver trifluoromethanesulfonate [49]

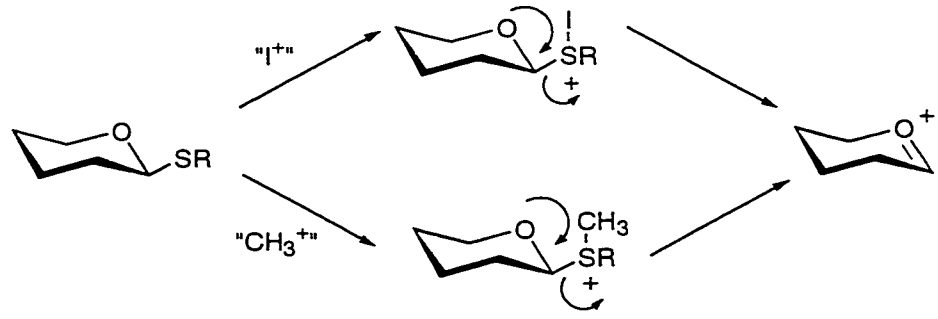


Fig 1-15 Activation of thioglycosides

or methylating agents such as methyl trifluoromethanesulfonate or dimethyl(methylthio)sulfonium trifluoromethane sulfonate (DMTST) (Fig 1-15) [50].

1.5 Scope of the Project

This work sets out to prepare a series of protected mono-*O*-hydroxyl octyl β-LacNAc compounds which would be useful intermediates for selective functionalization (Fig 1-15). These functionalized compounds can be utilized in protein binding studies [51], enzyme assays, as synthetic standards or in NMR studies. The present work focuses on the preparation of each of the six mono-*O*-phosphates of octyl β-LacNAc.

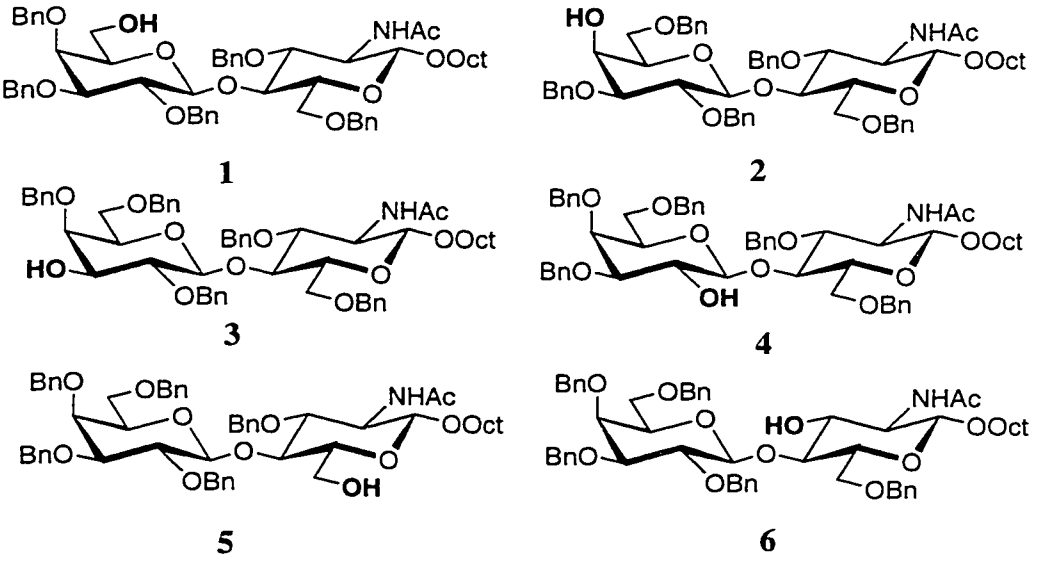


Fig 1-16 Mono-hydroxy synthetic targets

Phosphorylation of alcohols can be carried out in a variety of ways [52] and would be an ideal initial functionalization of the six mono-*O*-hydroxyl octyl β-LacNAc compounds at each of the six free OH groups (Fig 1-17). The presence of ^{31}P also provides a unique opportunity to use ^{31}P NMR techniques to examine how the chemical shifts of phosphates in different chemical environments vary and to look at how phosphates affect the chemical environments of the protons and carbon atoms present on the molecules of interest.

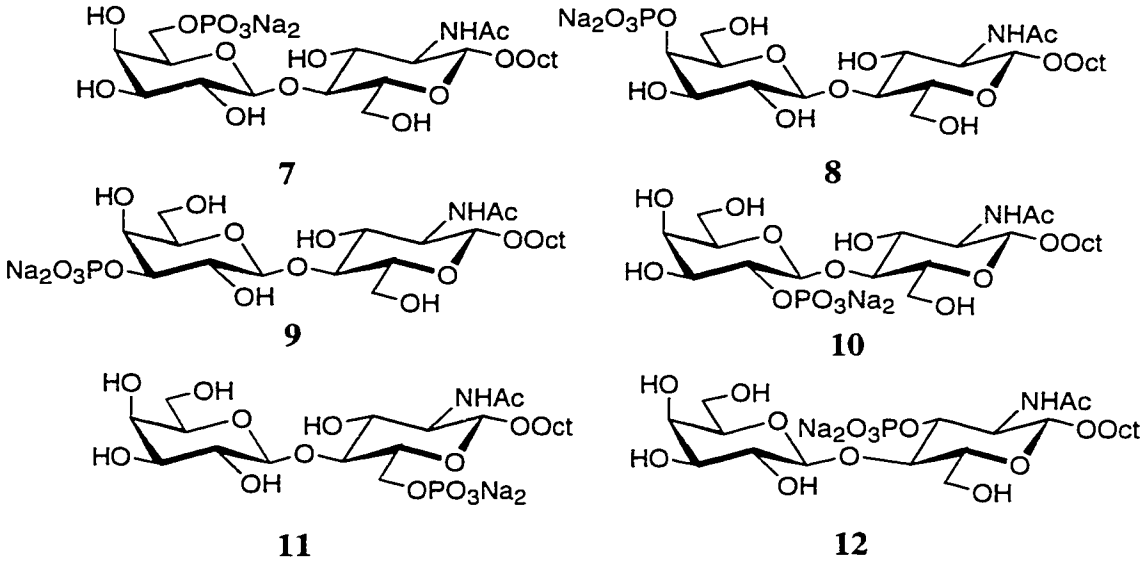


Fig 1-17 Mono-*O*-phosphate octyl β-LacNAc synthetic targets

Chapter 2

Chemical Synthesis and NMR Characterization of Mono-*O*-Phosphates of Octyl β-Glc and Octyl β-LacNAc

2.1 Introduction

The preparation and ^{1}H, ^{13}C and ^{31}P spectral analyses of the isomeric mono-*O*-phosphates of octyl β-*D*-glucopyranoside and octyl *O*-β-*D*-galactopyranosyl-(1→4)-2-acetamido-2-deoxy-β-*D*-glucopyranoside are presented in this chapter. The simpler monosaccharide phosphates were prepared first to establish the reaction conditions for selective protection, phosphorylation and deprotection that would later be applied to the more complex LacNAc targets.

2.2 Preparation of Mono-Hydroxy Monosaccharides

2.2.1 Retrosynthetic Analysis

The preparation of the desired target compounds required selectively protected glycosides for later functionalization to access the phosphates. The strategy for the chemical synthesis of monosaccharides **31**, **32**, **33** and **34** involved selective protection/deprotection steps, utilizing well-established procedures [53]. The general synthetic scheme involved four levels of manipulation as outlined in Fig 2-1. Readily available peracetylated glucose was used as the starting material. The formation of an octyl glycoside would allow easy purification of the deprotected final products using

reverse phase chromatography [54]. From the octyl glycoside, the key benzylidene protected glucoside **13** [55] could be prepared. All four of the desired final products could be derived from this benzylidene precursor.

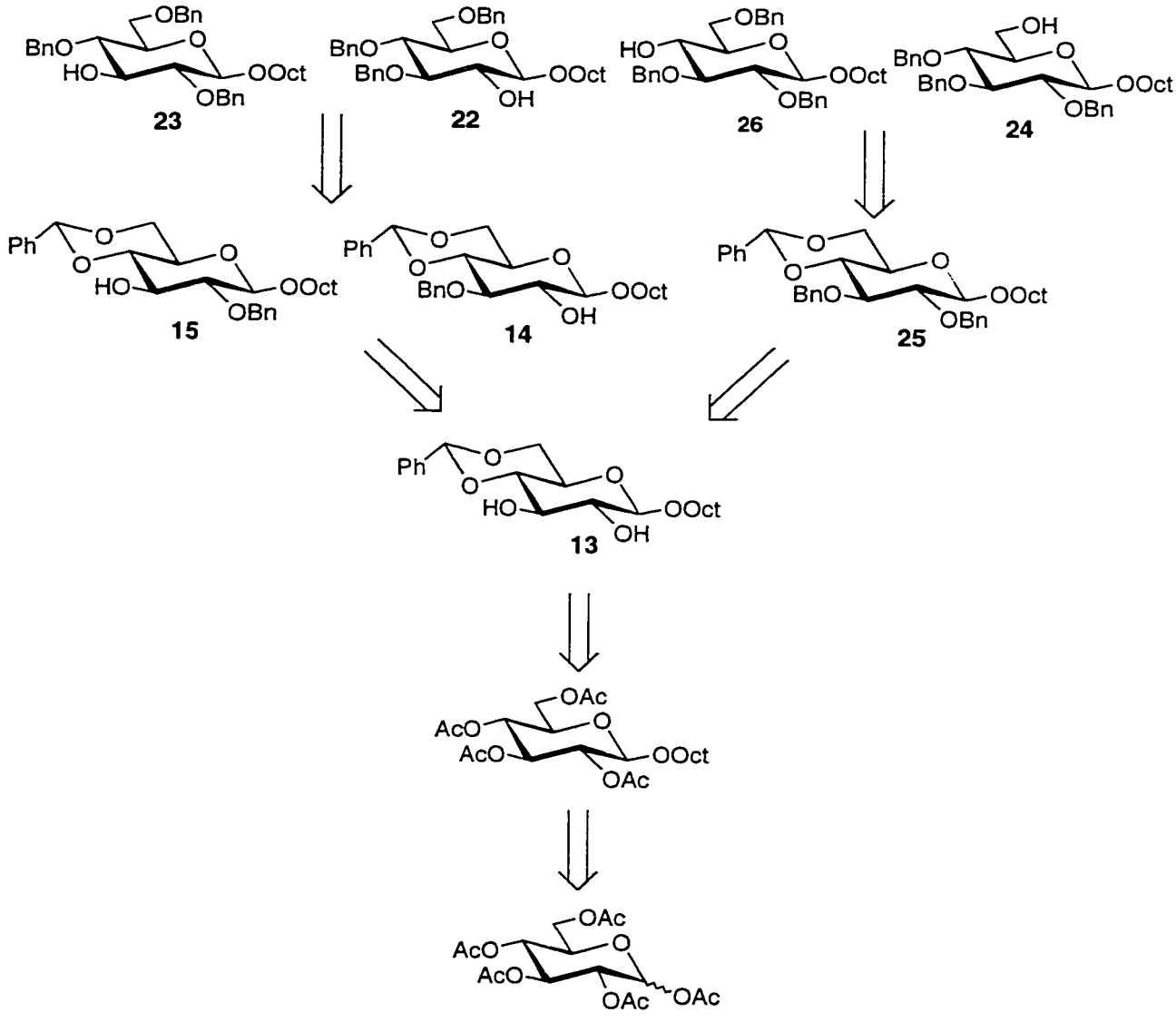


Fig 2-1 Retrosynthetic analysis for the synthesis of **22**, **23**, **24**, **26**

Selective protection of the two remaining hydroxyl groups using standard methods and regioselective acetal ring opening gave **22**, **23**, **24** and **26**. Benzyl ethers were chosen as persistent protecting groups to allow for a single deprotection step in the final stages of the synthesis.

2.2.2 Preparation of Mono-Hydroxy Monosaccharides

The synthesis of **13** from peracetylated glucose was carried out according to published procedures [55]. The glycosyl bromide was formed by reaction with 30% HBr/ HOAc and its glycosylation with octyl alcohol was carried out using Koenigs-Knorr type conditions. Zemplen deacetylation (NaOMe/MeOH) followed by formation of the benzylidene acetal afforded the diol **13** [55]. Subjecting diol **13** [55] to phase transfer conditions [56] for the selective benzylation reaction gave a mixture of the 3-*O*-benzyl **14** (13%) and 2-*O*-benzyl **15** (24%) ethers. The low isolated yields were due to the difficulty in separation of the two regioisomers. Further protection of **15** and **14** with *p*-methoxybenzyl chloride gave **16** (44%) and **17** (51%), respectively. The benzylidene acetal was regioselectively opened with lithium aluminum hydride and aluminum trichloride to give **18** (58%) and **19** (54%). This method proved useful since acidic conditions which often lead to *p*-methoxybenzyl ether cleavage could be avoided. Benzylation of **18** and **19** with benzyl bromide and sodium hydride afforded the fully protected compounds **20** (91%) and **21** (95%). Selective removal of the *p*-methoxybenzyl ether was accomplished using 2,3-dichloro-5,6-dicyano-1,4-

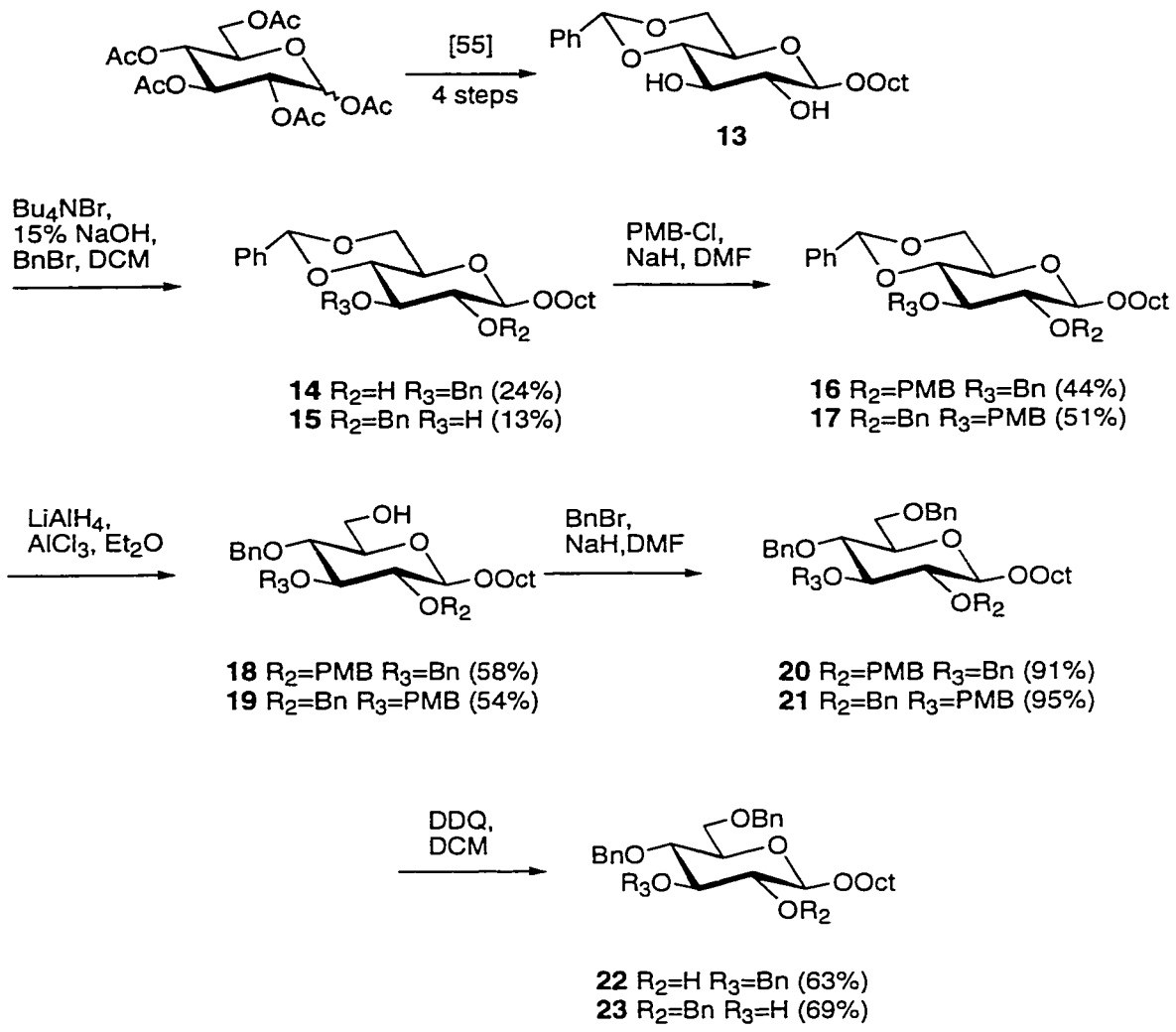


Fig 2-2 Preparation of the 2- and 3-OH octyl β-Glc, **22**, **23**

benzoquinone (DDQ) [57], providing the selectively protected octyl β-glycosides **22** (63%) and **23** (69%) (Fig 2-2).

Reaction of the diol **13** [55] with benzyl bromide and sodium hydride to provide **25**, followed by regioselective opening of the benzylidene acetal with sodium cyanoborohydride provided the 4-OH compound **26** as described by Lowary and Hindsgaul [58]. Opening of the acetal ring with lithium aluminum hydride and aluminum trichloride provided the desired 6-OH regioisomer **24** in modest yield of 55% (Fig 2-3).

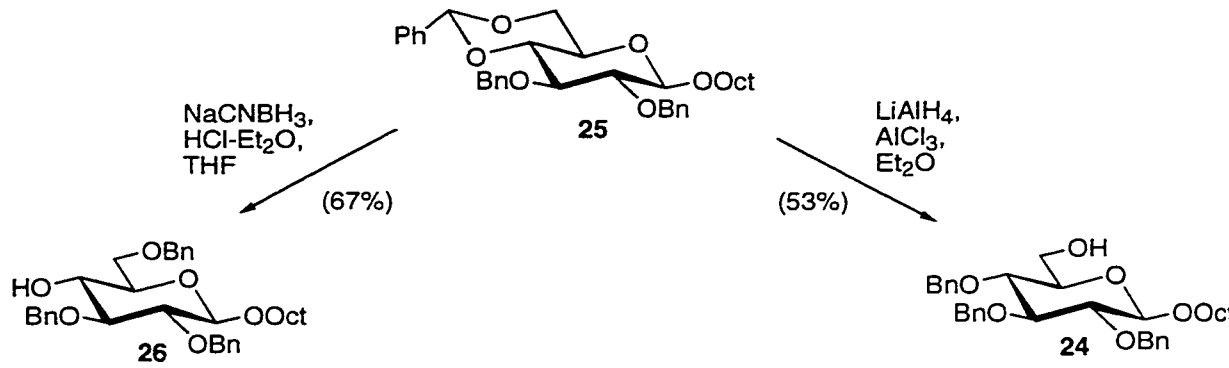


Fig 2-3 Preparation of the 4-, and 6-OH octyl β-Glc **24**, **25**

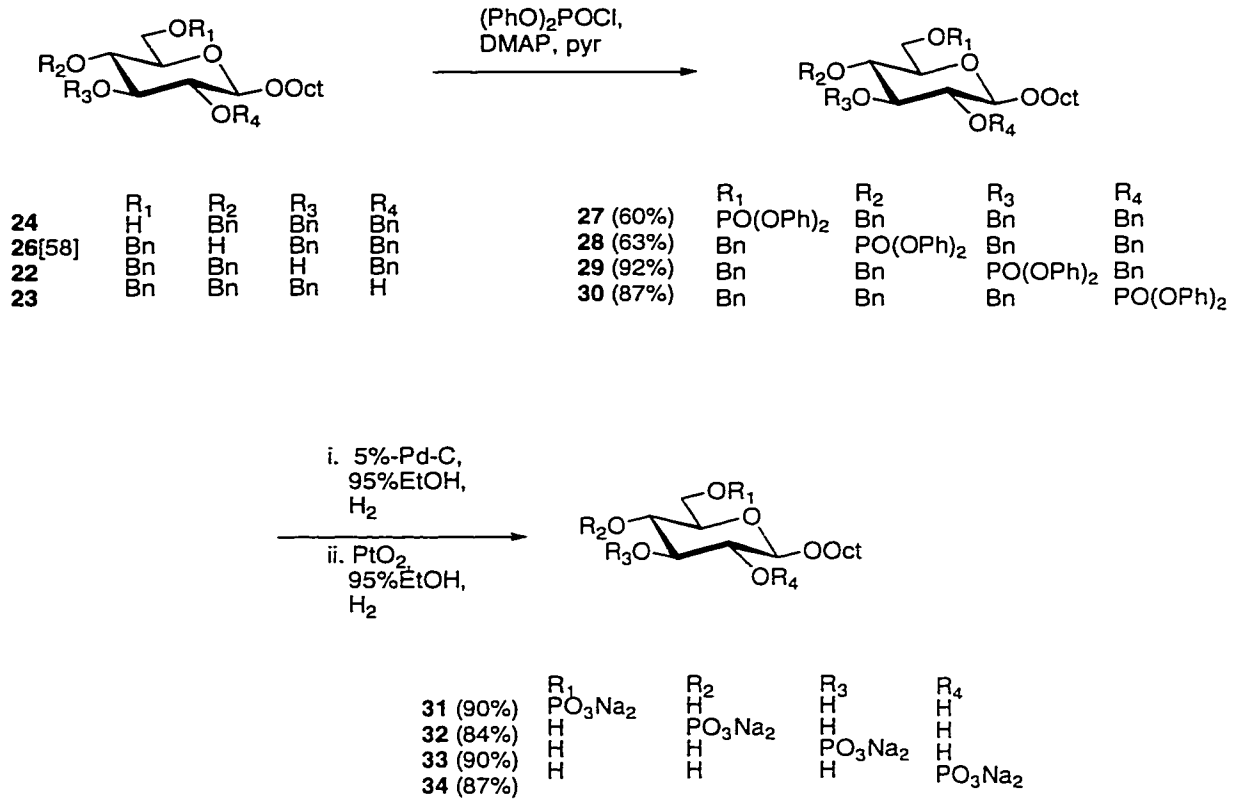
2.3 Preparation of Regioisomeric Octyl β-Glc Mono-*O*-Phosphates

Phosphorylation of the four alcohols **22**, **23**, **24** and **26** was carried out using diphenyl phosphorochloridate and 4-dimethylaminopyridine (DMAP) in pyridine, as described by Srivastava and Hindsgaul [59], to give the phosphoric triesters **27** (60%), **28** (63%), **29** (92%) and **30** (87%) (Fig 2-4). Hydrogenolysis of the benzyl ethers over palladium on carbon, followed removal of the phenyl phosphoesters over platinum dioxide (Adam's catalyst) provided the phosphates. These were treated with an anion exchange resin to yield the disodium salts **31** (90%), **32** (84%), **33** (90%) and **34** (78%).

2.4 Preparation of Mono-Hydroxy Disaccharides

2.4.1 Retrosynthetic Analysis

A retrosynthetic analysis of the six mono-hydroxy octyl β-LacNAc disaccharides suggested the use of temporary phthalimido protection during the glycosylation steps to



	R_1	R_2	R_3	R_4
24	H	Bn	Bn	Bn
26[58]	Bn	H	Bn	Bn
22	Bn	Bn	H	Bn
23	Bn	Bn	Bn	H

	R_1	R_2	R_3	R_4
27 (60%)	$PO(OPh)_2$	Bn	Bn	Bn
28 (63%)	Bn	$PO(OPh)_2$	Bn	Bn
29 (92%)	Bn	Bn	$PO(OPh)_2$	Bn
30 (87%)	Bn	Bn	Bn	$PO(OPh)_2$

	R_1	R_2	R_3	R_4
31 (90%)	PO_3Na_2	H	H	H
32 (84%)	H	PO_3Na_2	H	H
33 (90%)	H	H	PO_3Na_2	H
34 (87%)	H	H	H	PO_3Na_2

Fig 2-4 Preparation of the mono-*O*-phosphates of octyl β-Glc: **31**, **32**, **33** and **34**

be replaced with N-acetate protection at later stages in the synthesis. Selective deprotection would provide each mono-hydroxyl disaccharide protected with persistent *O*-benzyl ethers. The 6-OH (**5**), 3-OH (**6**) and 2'-OH (**4**) compounds could be derived by coupling of a common donor **45** with a series of selectively protected acceptors **41**, **44** and **38** (Fig 2-5).

The 6'-OH (**1**) and 4'-OH (**2**) compounds could be generated from a common benzylidene precursor **62**. The 3'-OH compound (**3**) could be generated from a selectively protected thioglycoside **51,** which is readily available via a stannylidene mediated regioselective alkylation (Fig 2-6).

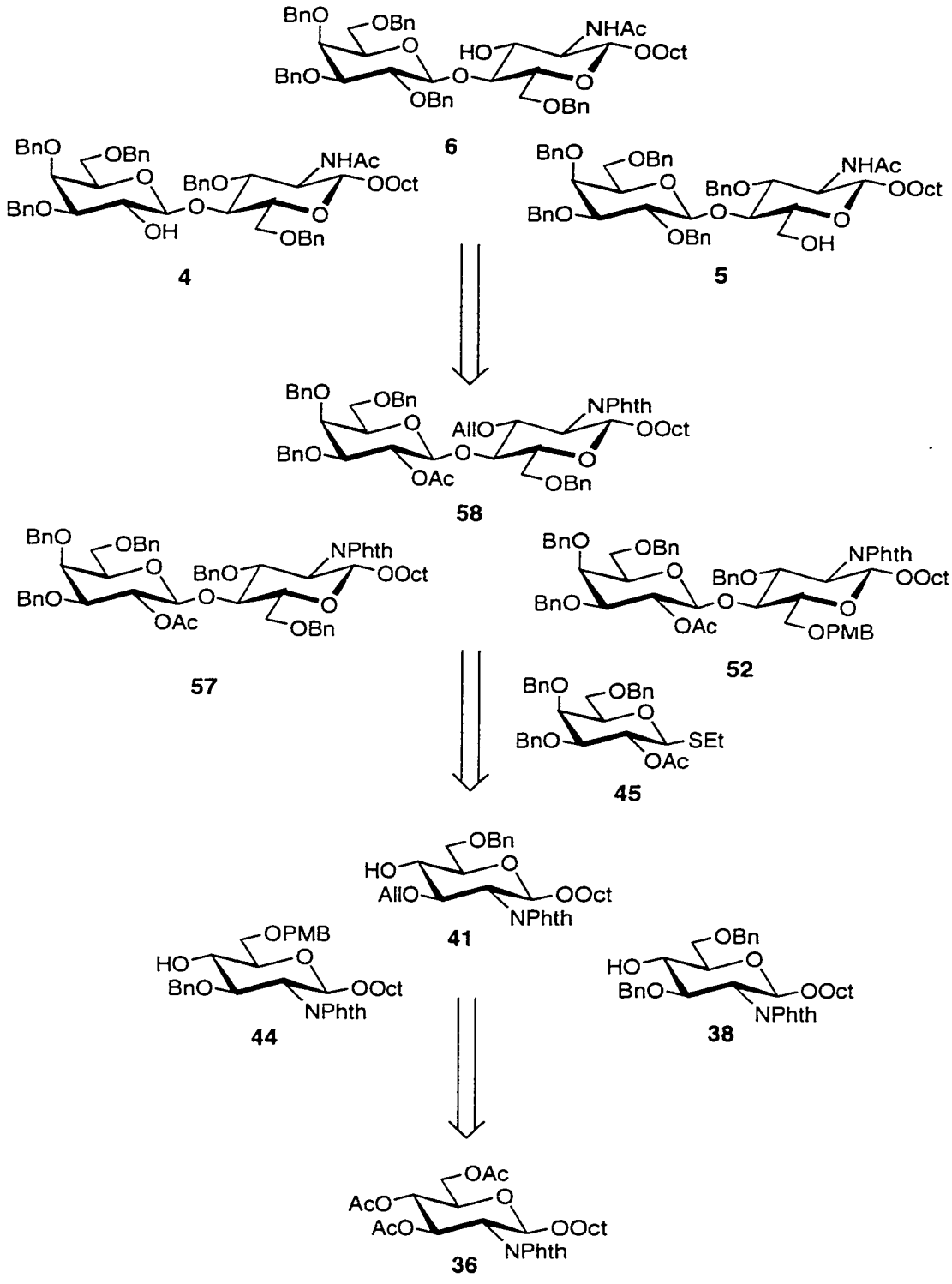


Fig 2-5 Retrosynthetic analysis for the synthesis of **4**, **5** and **6**

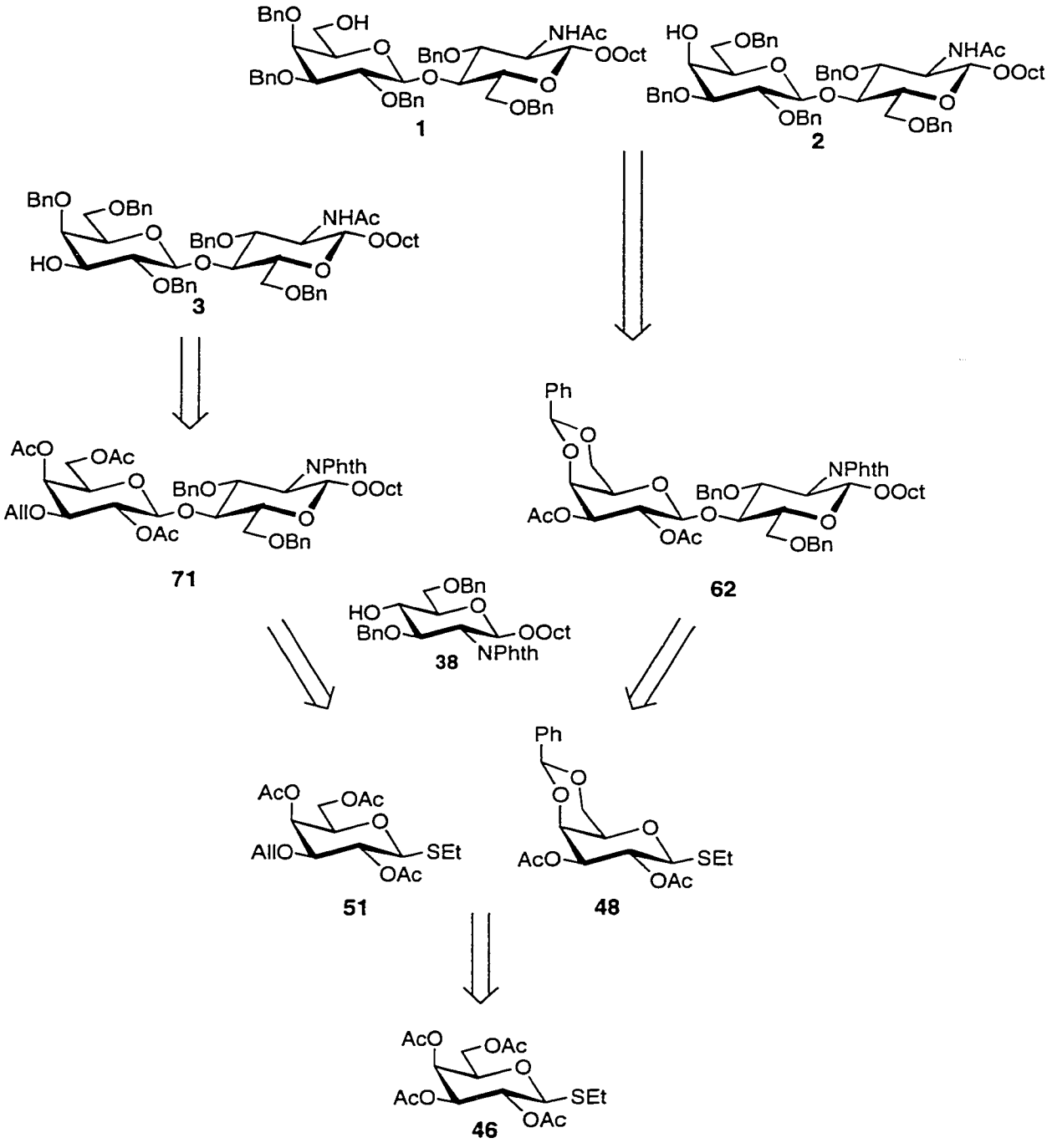


Fig 2-6 Retrosynthetic analysis for the synthesis of **1**, **2** and **3**

2.4.2 Preparation of GlcNPhth Acceptors

The synthesis of the required acceptors began by converting glucosamine hydrochloride to the phthalimido protected monosaccharide as previously described [60]. This involved stirring with phthalic anhydride in a sodium bicarbonate solution followed by acetylation with pyridine and acetic anhydride. The 1-*O*-acetate was then converted to the known bromide [61]. Glycosylation with octyl alcohol was carried out as reported [62]. An alternate method of glycosylation was established using silver zeolite, octyl alcohol, dichloromethane (DCM) and activated molecular sieves to provide **36** (88%, 2 steps). Silver zeolite as the activating species afforded a satisfactory yield and provided the advantage of an easier workup than previously reported methods as the removal of silver zeolite could be accomplished by a simple filtration step (Fig 2-8).

Octyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-*D*-glucopyranoside (**36**) was further manipulated to mask the 4- and 6-*O*-postitions with a benzylidene acetal. After the initial deacetylation the formation of the benzylidene derivative was effected, using dimethoxy toluene and *p*-toluene sulfonic acid monohydrate in acetonitrile, or formic acid and benzaldehyde in hexane to give the literature compound **37** [62]. Benzylation of OH-3 was followed by opening of the benzylidene ring to give the 4-OH compound **38** [62] using sodium cyanoborohydride as previously described [62].

The addition of *p*-methoxybenzyl chloride and sodium hydride to **37** [62] in dimethyl formamide (DMF) resulted in the protection of OH-3 as its *p*-methoxybenzyl ether **39**. The *p*-methoxybenzyl protecting group was intended to serve the dual purpose of a selectively removable group, to provide the free 3-OH group, as well as a persistent

protecting group that could be removed along with the remaining benzyl protecting groups in a global deprotection step. Upon reductive opening of the benzylidene acetal using sodium cyanoborohydride, however, the *p*-methoxybenzyl group was simultaneously removed, resulting in the undesired 3,4-diol (Fig 2-7). A synthetic scheme eliminating *p*-methoxybenzyl protection was therefore devised.

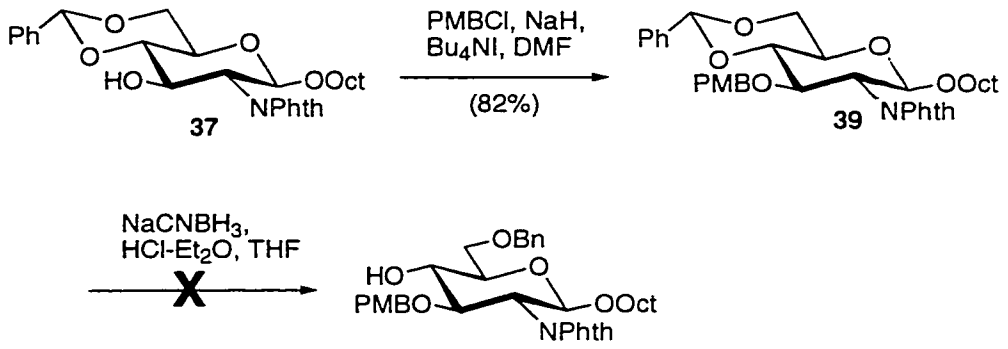


Fig 2-7 Unsuccessful attempt to prepare an acceptor

In order to introduce an alternate orthogonal protecting group for the 3-position, compound **37** [62] was reacted with allyl chloride and sodium hydride in DMF to give **40** (56%) along with 24% of unreacted starting material. The addition of excess reagents did not provide additional desired product and starting material was never entirely consumed. The benzylidene ring was then regioselectively opened with sodium cyanoborohydride to give the acceptor **41** in good yield (96%) (Fig 2-8).

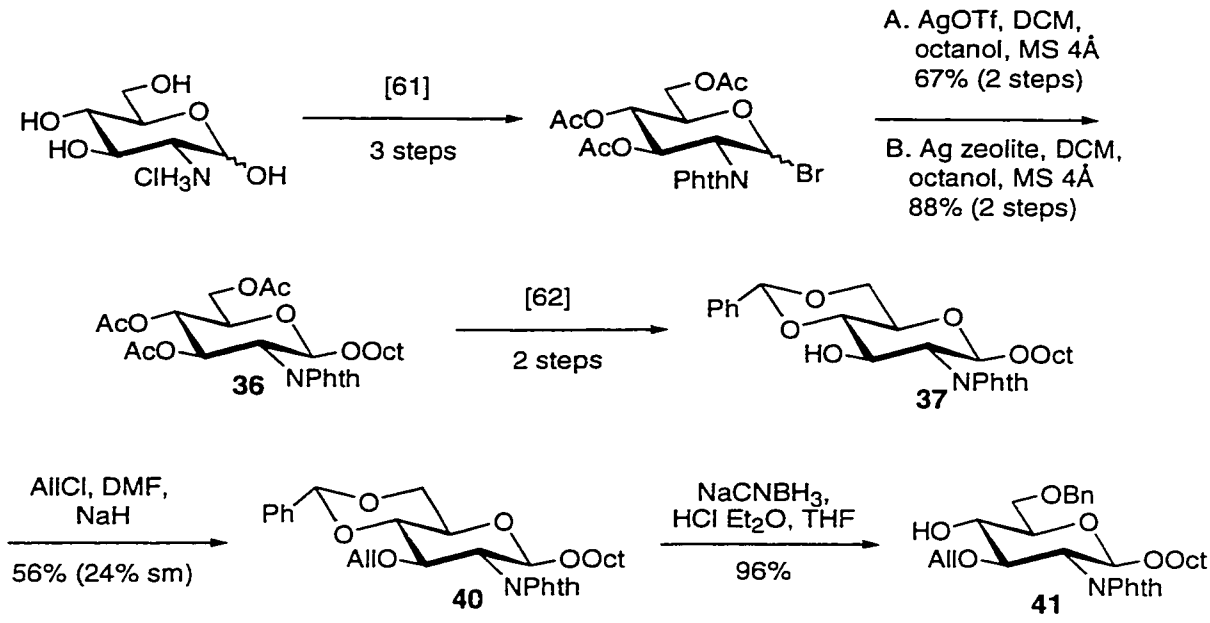


Fig 2-8 Preparation of acceptor **41**

Compound **36** was deacetylated and reacted with anisaldehyde dimethyl acetal and *p*-toluene sulfonic acid monohydrate in acetonitrile to afford **42** (83%). The free OH group was then converted to the benzyl ether to give the fully protected **43** (65%). The *p*-methoxybenzylidene acetal was regioselectively opened with sodium cyanoborohydride and ethereal hydrochloric acid to give **44** with OH-4 free (62%). Alternately, reaction with sodium cyanoborohydride and trifluroacetic acid provided the desired acceptor **44** (65%) (Fig 2-9).

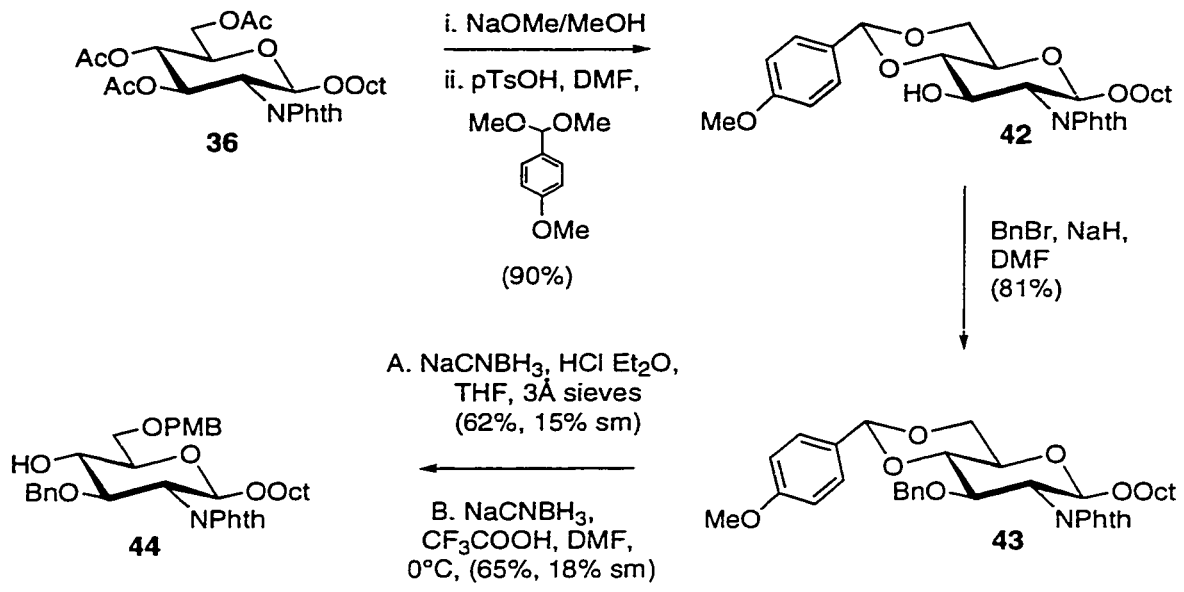


Fig 2-9 Preparation of compound **44**

2.4.3 Preparation of Thiogalactoside Donors

The syntheses of three different appropriately protected donors were required for the preparation of the desired mono-hydroxyl octyl β-LacNAc compounds. The ethyl thiogalactoside **45** was chosen as the donor, due to its versatility and relative stability [63]. Compound **45** was reported in the literature [64] and was synthesized accordingly from the galactose pentaacetate via the orthoester, followed by removal of the acetates and subsequent alkylation with benzyl bromide. The formation of the ethyl thiogalactoside was carried out from the orthoester with ethanethiol, trimethylsilyl triflate and activated molecular sieves in nitromethane to provide **45** (62%) (Fig 2-10).

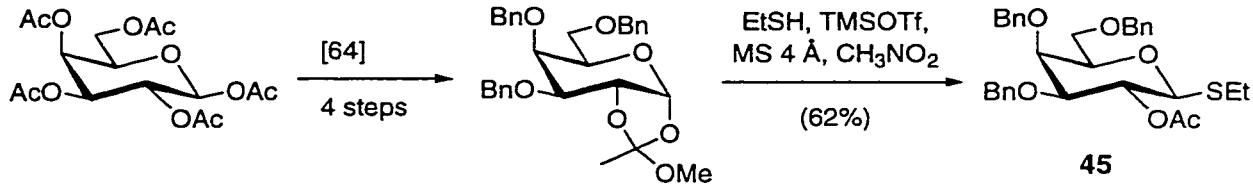


Fig 2-10 Preparation of thiogalactoside **45**

For the preparation of the required thiogalactoside donor **48**, compound **46** [65] was deacetylated and the product treated with benzaldehyde in formic acid to produce **47** (55%). Acetylation of **47** gave **48** (77%) (Fig 2-11).

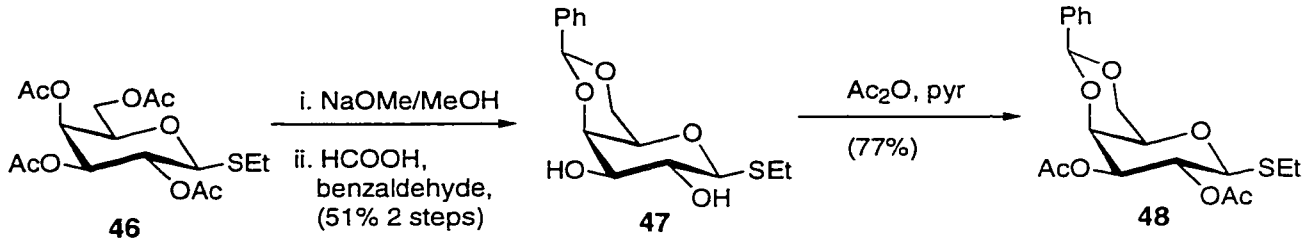


Fig 2-11 Preparation of thiogalactoside **48**

The third required donor, **51**, was derived from **49** [66], from which the 3,4-di-*O*-isopropylidene acetal was selectively removed with 70% acetic acid to provide **50** (95%) (Fig 2-12). Compound **50** and dibutyl tin oxide were mixed in refluxing toluene to produce the stannylidene intermediate which was regioselectively alkylated with allyl bromide. Three compounds were isolated from the reaction and ^{1}H NMR analysis revealed that although the regioselective alkylation was successful the acetate protecting groups had migrated during the course of the reaction. All three compounds were pooled

and collectively acetylated resulting in the formation of a single compound, **51** (77%) (Fig 2-12).

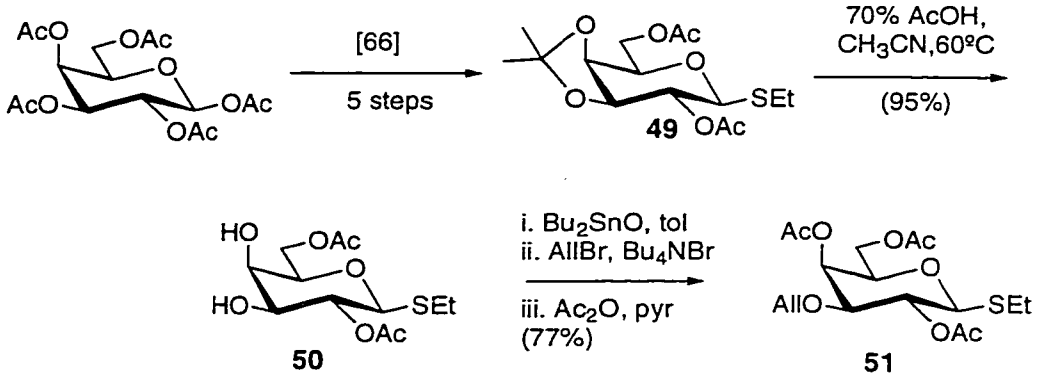


Fig 2-12 Preparation of thiogalactoside **51**

2.4.4 Preparation of Mono-Hydroxy Octyl β-LacNAc Disaccharides

Initial attempts at the synthesis of the desired octyl β-LacNAc compounds were carried out with donor **45** and the acceptor **44** with the intent of maintaining the 6-OH group functionalized as the *p*-methoxybenzyl ether. Glycosylation in dry DCM containing activated 4 Å sieves with dimethyl(methylthio)sulfonium triflate (DMTST) activation and the required donor and acceptor, was adapted from well-established procedures [67]. Upon workup, the major product recovered was a trisaccharide (**54**). The *p*-methoxybenzyl group was not stable under the glycosylation conditions and the free 6-OH group became available to react further with the donor. Therefore different glycosylation conditions were established. With *N*-iodosuccinimide and silver triflate as

the promoters, the desired disaccharide **52** was obtained in a yield of 88%. The disaccharide was deacetylated under standard conditions to give **53** (77%). The relatively lengthy time (24 hours) for the reaction to go to completion and the corresponding low yield was likely due to steric hinderance at the 2'-position. In all cases where

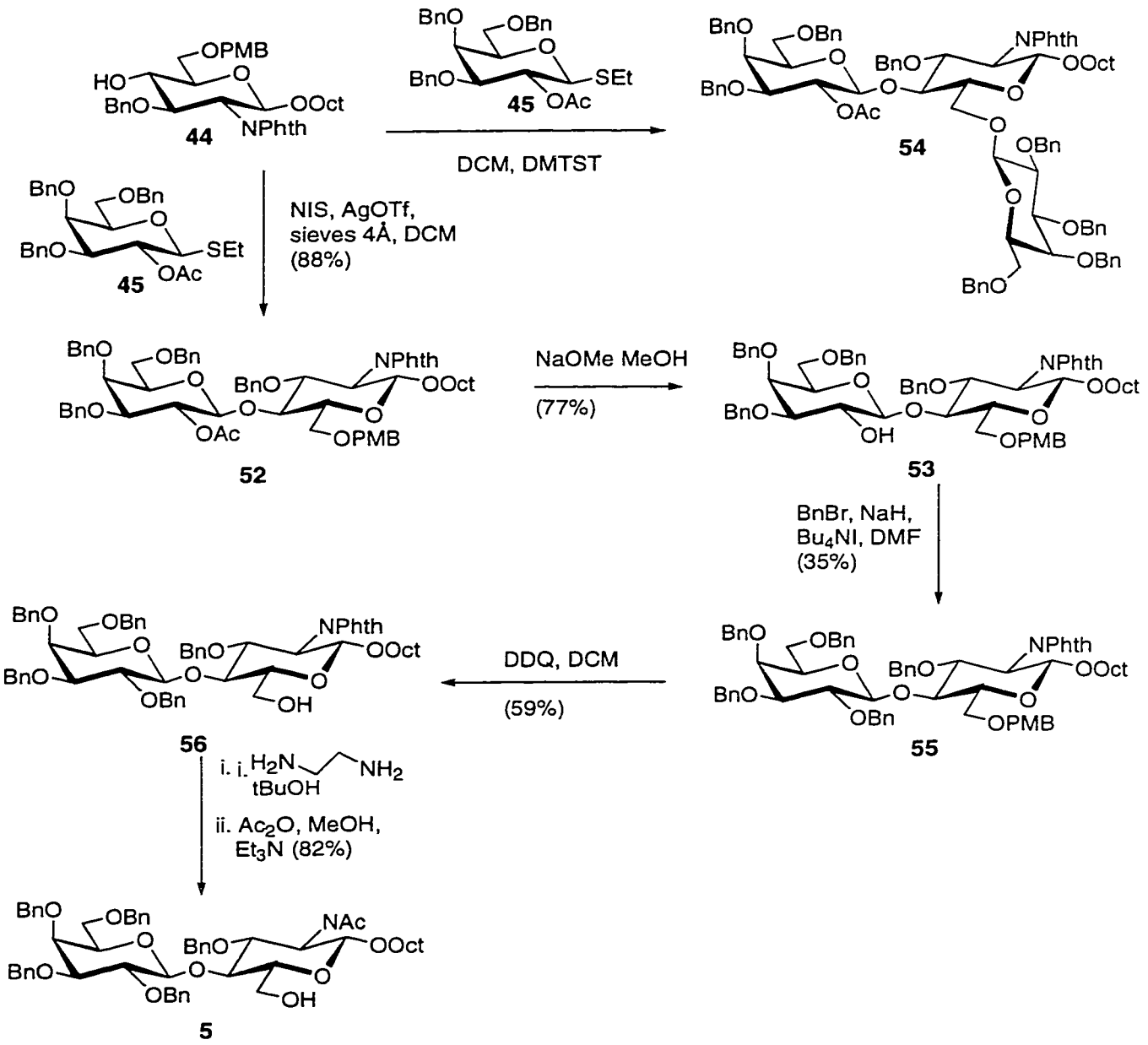


Fig 2-13 Preparation of 6-OH octyl β-LacNAc **5**

protection/deprotection steps were carried out at the 2'-position the reactions proceeded slowly, or in some cases, not at all, testifying to the hindered environment about OH-2'. The 2'-OH group was then benzylated using benzyl bromide, sodium hydride and tetrabutylammonium iodide in DMF to give **55** (33%). The reaction proceeded very slowly, consistent with previous observations of analogous reactions, and trace amounts of water present in the reaction resulted in the opening of the phthalimido ring affording the free acid or benzyl ester. In some cases, it was possible to reclose the phthalimido ring but the yields were always disappointing. Selective deprotection of the *p*-methoxybenzyl group was accomplished using DDQ in DCM [57], affording **56** in a moderate yield of 59%. Removal of the phthalimido group was carried out with ethylenediamine in tert-butanol, followed by *N*-acetylation with acetic anhydride in methanol in the presence of triethylamine to give **5** (82%) (Fig 2-13).

Octyl 3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-*D*-glucopyranoside (**38**) [62] was glycosylated with donor **45** using *N*-iodosuccinimide and silver triflate activation, as

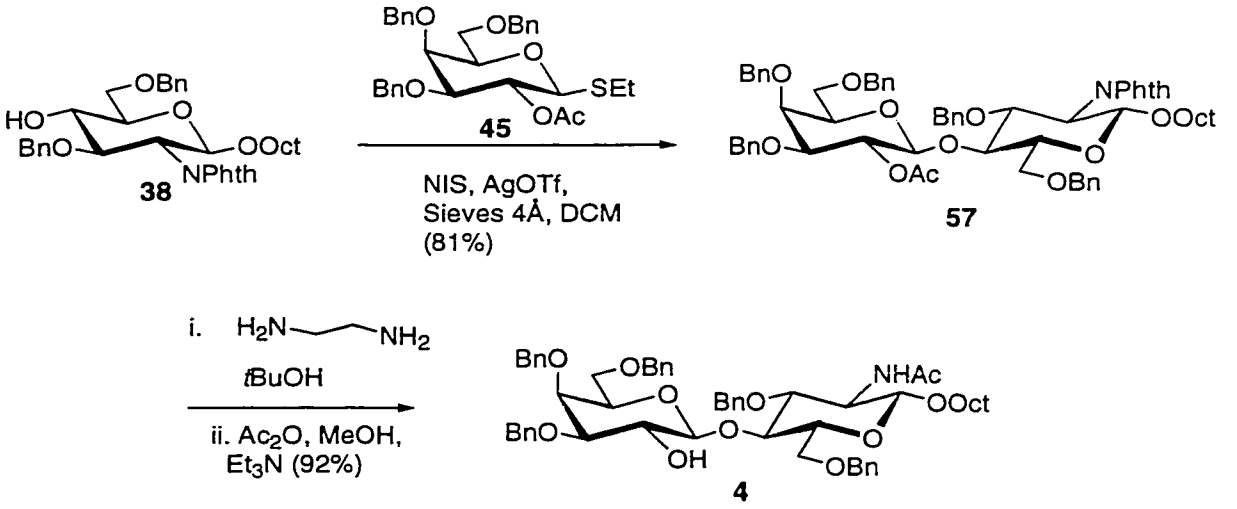


Fig 2-14 Preparation of 2'-OH octyl β-LacNAc **4**

described for the preparation of **52**, to give **57** in 81% yield based on the acceptor. The phthalimido and the acetate protecting groups were removed concurrently with ethylenediamine, and the *N*-acetylation was carried out as described for the preparation of **5** to give the desired 2'-OH compound **4** in a good yield of 92% (Fig 2-14).

In order to obtain the desired 3-OH octyl β-LacNAc, acceptor **41** was glycosylated with donor **45**, using the same conditions as described for compound **52**, to give **58** in 80% yield based on the acceptor. The removal of the acetate at the 2'-position gave **59** (78%) and subsequent alkylation with benzyl bromide provided **60** (45%). Slow degradation of the phthalimido group was observed so the benzylation reaction was

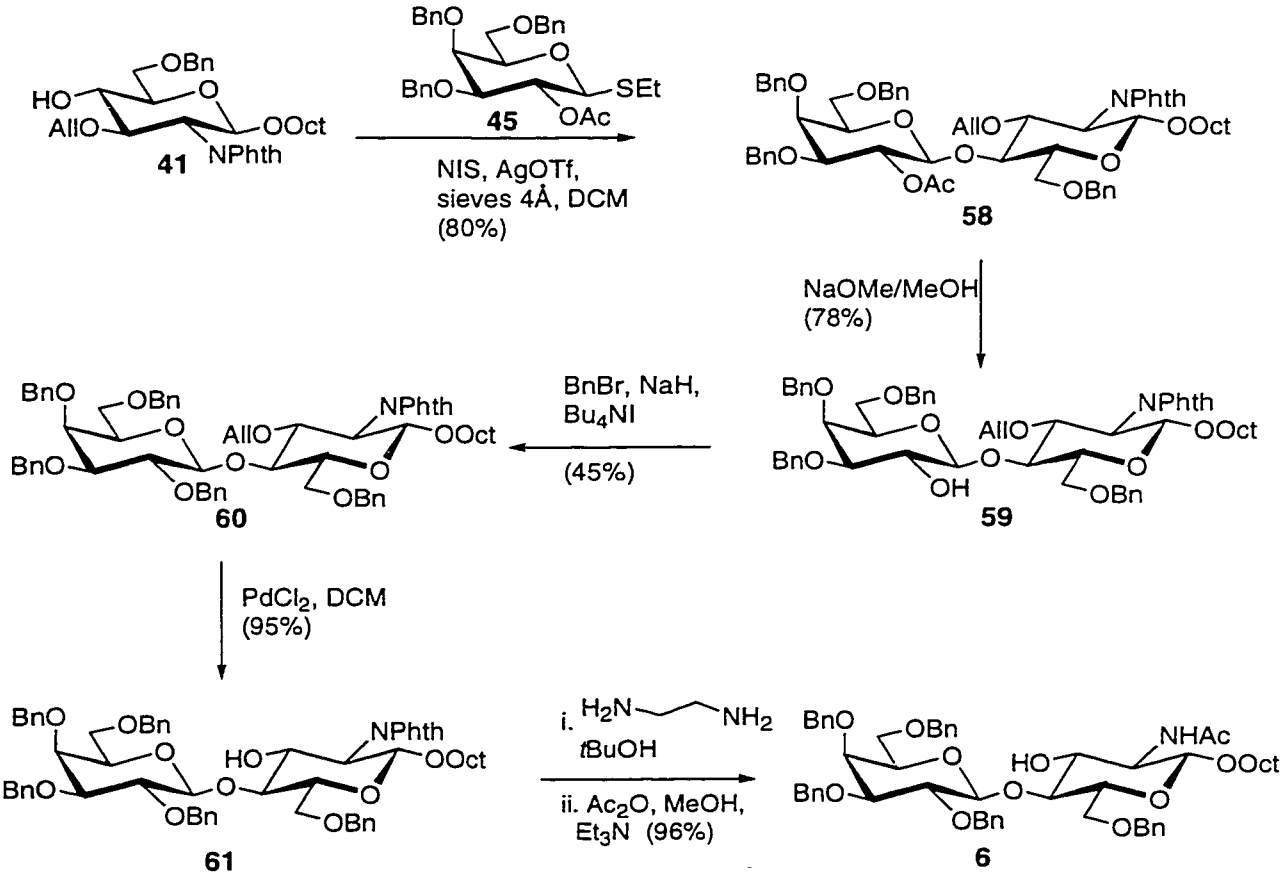


Fig 2-15 Preparation of 3-OH octyl β-LacNAc **6**

stopped prior to completion, resulting in isolation of product **60** (45%) and recovery of 30% of the starting material. The selective removal of the allyl protecting group was accomplished using palladium chloride in dry DCM [68], affording the desired 3-OH compound **61** in good yield (95%). The removal of the phthalimido group and subsequent installation of the N-acetamido was carried out as described for the preparation of **5** to give **6** (96%) (Fig.2-15).

The 4'- and 6'-OH octyl β-LacNAc compounds were prepared from a common disaccharide precursor containing a 4',6'-*O*-benzylidene group. Donor **48** was glycosylated with **38** [62] using N-iodosuccimide and silver triflate in DCM and 4 Å sieves to afford **62** as described for the preparation of **52** (Fig 2-16). Glycosylation was followed by removal of the acetates at the 2'- and 3'-positions to afford **63** (70%) followed by reprotection using benzyl bromide and sodium hydride providing **64** (66%). The benzylidene acetal was removed using 80% acetic acid providing **65** in 92% yield. The 6-OH group was selectively protected using trityl chloride and diisopropylethylamine giving **66** in quantitative yield. The 4-OH group was then benzylated under standard conditions to provide **67** (84%). The trityl group was removed using a solution of 5% trifluoroacetic acid and 5% triisopropylsilane in DCM [69] affording the 6-OH compound **68** in a very respectable 97% yield. Deprotection was carried out at room temperature, as opposed to the more standard method for removal of trityl groups where heating is required [70]. The phthalimido group was removed and the amine acetylated, as described for compound **5**, to provide **1** (86%) (Fig 2-16).

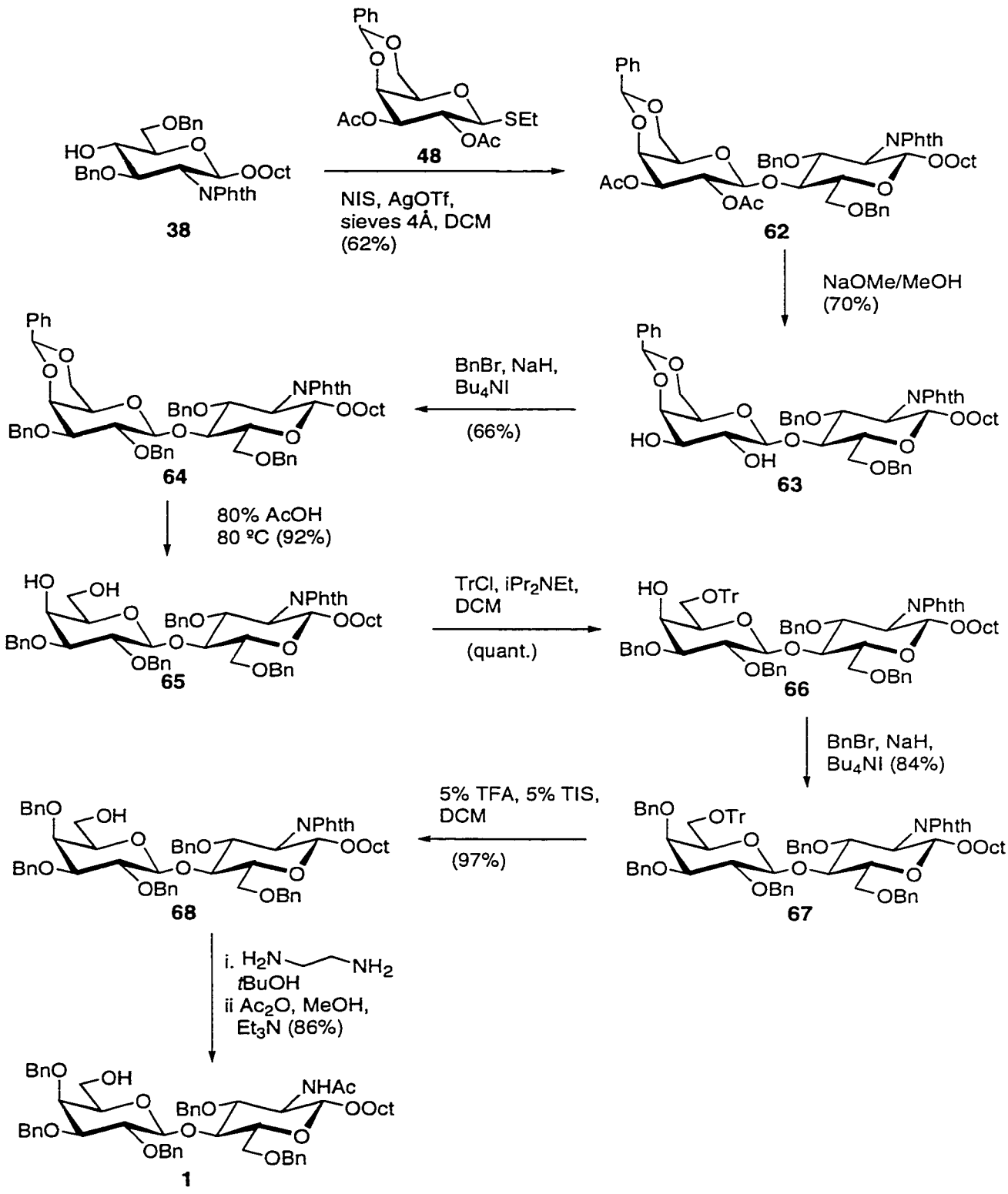


Fig 2-16 Preparation of 6'-OH octyl β-LacNAc **1**

The required free OH-4 was obtained through the regioselective opening of the acetal ring of **64**, using sodium cyanborohydride and ethereal hydrochloric acid to afford **69** (57%), followed by removal of the phthalimido group and subsequent acetylation, as described for compound **5**, to give **2** (90%) (Fig 2-17).

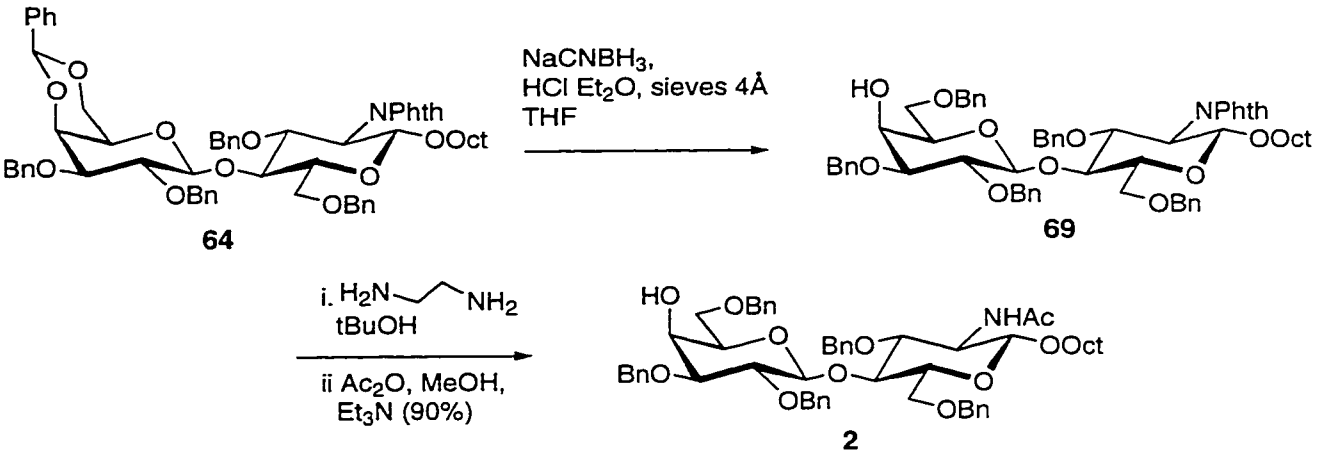


Fig 2-17 Preparation of 4'-OH octyl β-LacNAc **2**

The synthesis of the 3'-OH octyl β-LacNAc derivative was initially envisioned to involve a coupling of the donor **38** [62] with ethyl-2,6-*O*-acetyl-3,4-*O*-isopropylidene-thio-β-*D*-galactopyranoside [63] followed by the formation of a stannylidene derivative and allylation at the 3'-position. However, the glycosylation failed to provide the desired disaccharide using the conditions described for the preparation of **52** (Fig 2-18). The

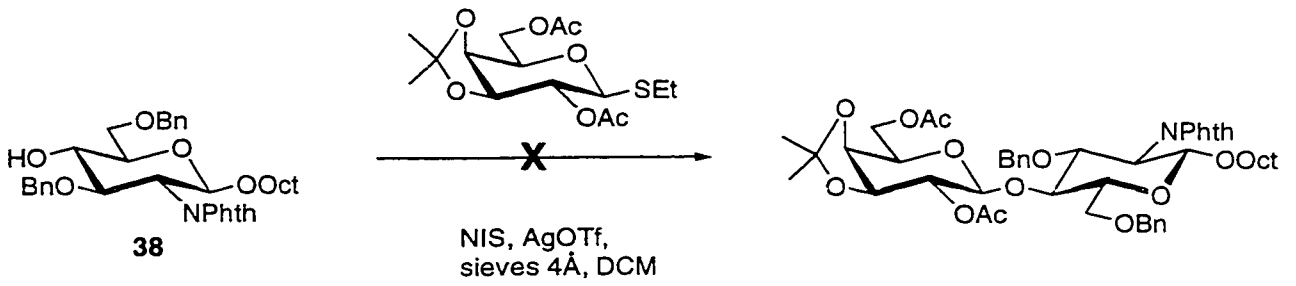


Fig 2-18. Unsuccessful glycosylation attempt

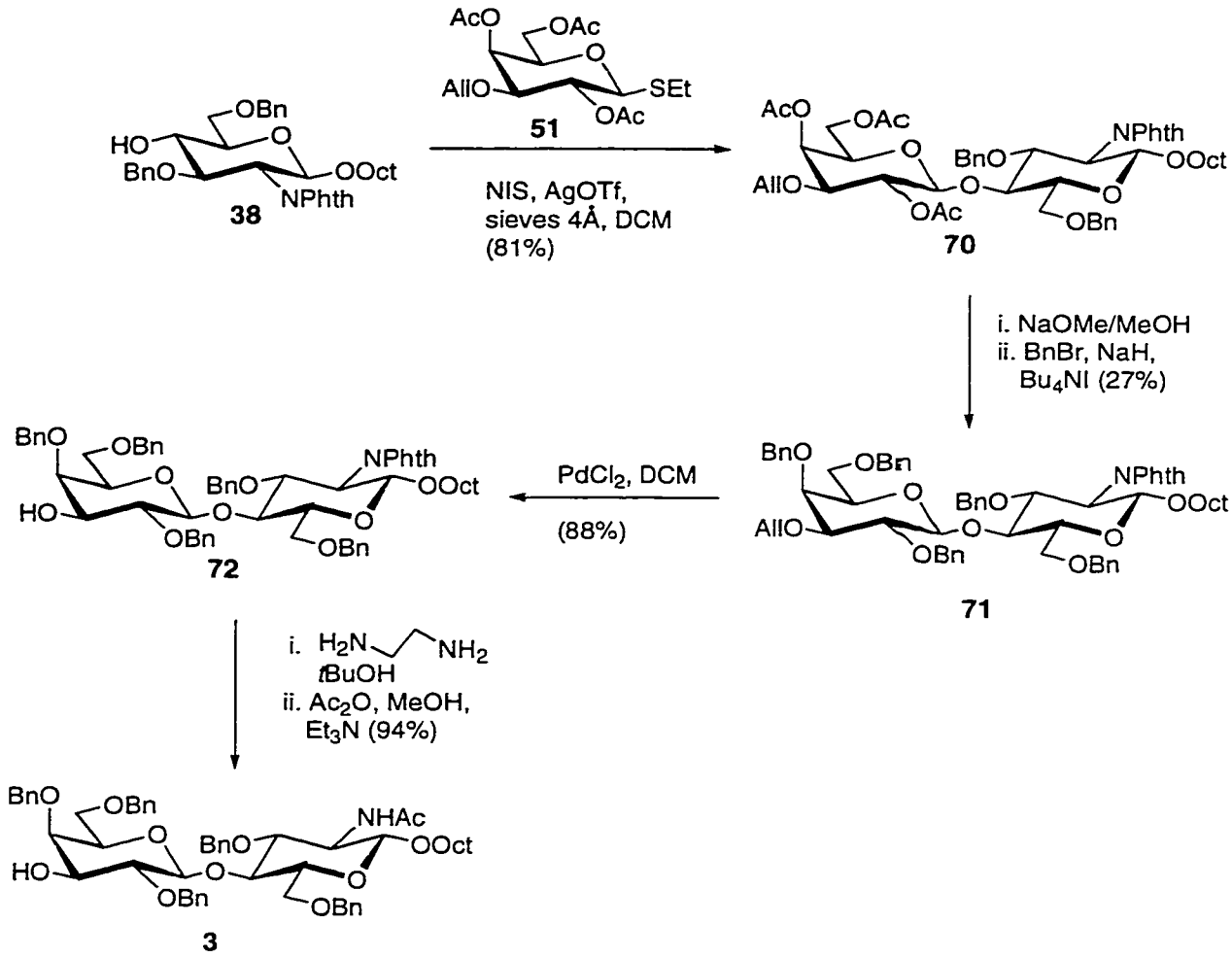


Fig 2-19 Preparation of 3'-OH octyl β-LacNAc **3**

donor was therefore converted to compound **51** and the reaction was attempted again. The glycosylation proceeded well, affording **70** in 81% yield, based on the acceptor. The disaccharide was deacetylated and benzylated to provide **71** (27%). The allyl protecting group was selectively removed using palladium chloride in DCM to provide **72** (88%). The phthalimido group was then removed and the resulting amine was converted to the N-acetamido group, as described for the preparation of **5**, yielding **3** (94%) (Fig 2-19).

2.5 Preparation of Regioisomeric Octyl β-LacNAc Mono-*O*-Phosphates

The six mono-hydroxy octyl β-LacNAc compounds **1-6** were functionalized and deprotected to give their respective phosphates. There are a number of established procedures for phosphorylating hydroxyl groups [71], and the initial phosphoryation conditions attempted were as described in section 2.3 for the octyl glucosides **27**, **28**, **29** and **30**. Compound **1** was reacted with diphenyl phosphorochloridate and 4-dimethylamino pyridine to provide the phosphorylated compound **73** (72%). Deprotection was carried out as described for the monsaccharide analogs **31**, **32**, **33** and **34** in section 2.3, using palladium on activated charcoal and platinum dioxide to provide the 6'-*O*-phosphate **7** (65%). Identical reaction conditions were used for phosphorylating **3** to give **74** (80%), and deprotection gave the 3'-*O*-phosphate **9** (56%) (Fig 2-20).

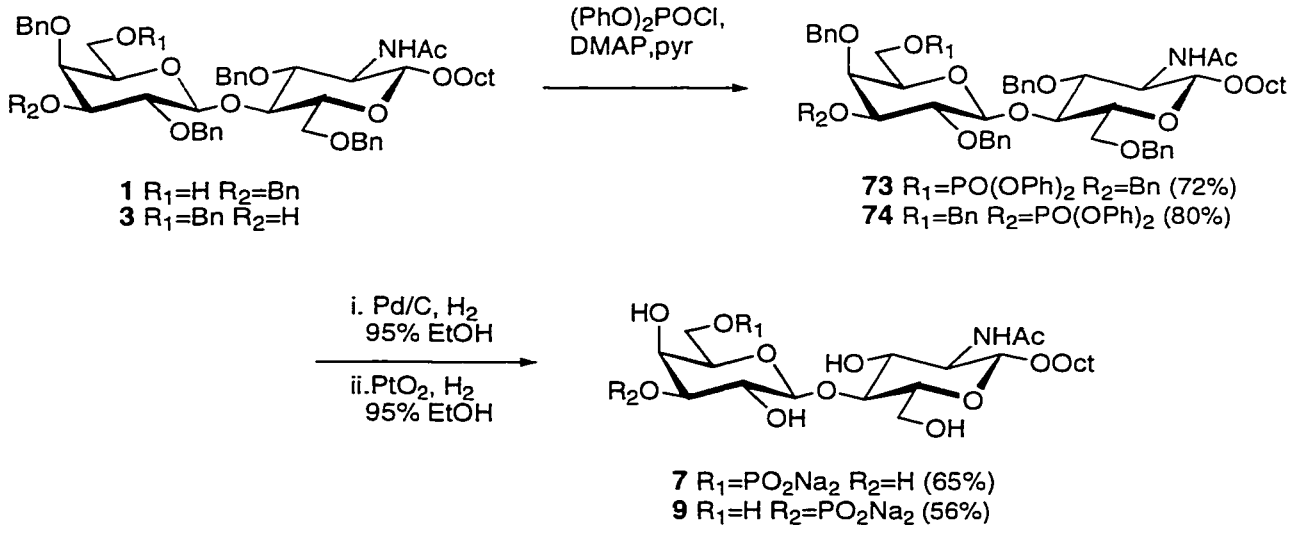
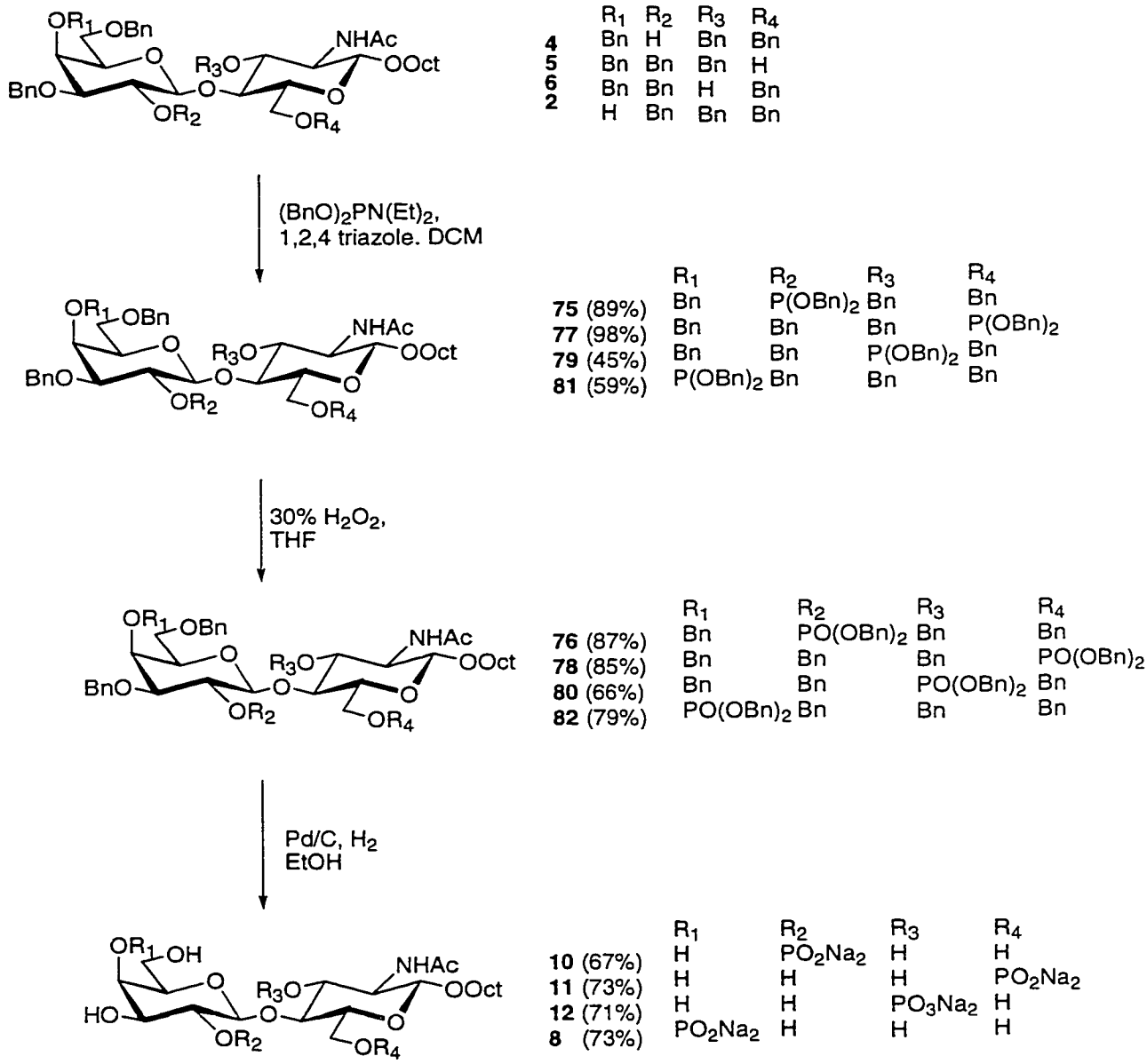


Fig 2-20 Preparation of 6'- and 3'-*O*-phosphate octyl β-LacNAc **7** and **9**

Initial attempts to synthesize the 3-*O*-phosphate in this manner were unsuccessful, with only starting material recovered. Therefore, a new approach was devised based on a procedure by Wong et al [72], involving an initial synthesis of the phosphite followed by oxidation to the phosphate and global deprotection (Fig 2-21). Compound **4** was reacted



	R_1	R_2	R_3	R_4
4	Bn	H	Bn	Bn
5	Bn	Bn	Bn	H
6	Bn	Bn	H	Bn
2	H	Bn	Bn	Bn

	R_1	R_2	R_3	R_4
75 (89%)	Bn	$P(OBn)_2$	Bn	Bn
77 (98%)	Bn	Bn	Bn	$P(OBn)_2$
79 (45%)	Bn	Bn	$P(OBn)_2$	Bn
81 (59%)	$P(OBn)_2$	Bn	Bn	Bn

	R_1	R_2	R_3	R_4
76 (87%)	Bn	$PO(OBn)_2$	Bn	Bn
78 (85%)	Bn	Bn	Bn	$PO(OBn)_2$
80 (66%)	Bn	Bn	$PO(OBn)_2$	Bn
82 (79%)	$PO(OBn)_2$	Bn	Bn	Bn

	R_1	R_2	R_3	R_4
10 (67%)	H	PO_2Na_2	H	H
11 (73%)	H	H	H	PO_2Na_2
12 (71%)	H	H	PO_3Na_2	H
8 (73%)	PO_2Na_2	H	H	H

Fig 2-21 Preparation of 4'-, 2'-, 6- and 3-*O*-phosphate octyl β-LacNAc **8**, **10**, **11** and **12**

with dibenzyl N,N-diethyl phosphoramidite and 1,2,4 triazole in DCM, which afforded the desired phosphite **75** in 89% yield. Oxidation to the phosphotriester was accomplished using 30% hydrogen peroxide producing **76** (78%). Hydrogenolysis over palladium on carbon, provided the target 2-*O*-phosphate **10** in 67% yield.

The 6-, 3-, and 4'-*O*-phosphates were synthesized in a similar fashion to **75** affording **77** (89%), **78** (45%) and **81** (59%), respectively. These compounds were then oxidized to phosphotriesters **78** (85%), **80** (66%) and **82** (79%), which were deprotected using standard hydrogenolysis conditions providing the 6-*O*-phosphate **11** (73%), the 3-*O*-phosphate **12** (71%) and the 4'-*O*-phosphate **8** (73%) (Fig 2-21).

2.6 NMR Spectral Analysis

2.6.1 NMR Spectral Analysis of the Octyl β-Glc Mono-*O*-Phosphate Regioisomers

The proton chemical shift and coupling constants of **31**, **32**, **33** and **34** are summarized in Tables 2-1 and 2-2 and the chemical shift changes induced by the substitution of a phosphate are presented in Fig 2-22. All samples were run in a buffer of sodium deuteroxide (0.045M) and sodium bicarbonate-d_1 (0.05M) in D_2O to ensure complete ionization of the phosphate. The pH of the solution was approximately 12.5.

The changes in chemical shift due to the substitution are 0.3-0.5 ppm downfield for the protons attached to the carbons bearing the phosphate group in the secondary alcohols and approximately 0.2 ppm downfield for the primary hydroxyl groups. The deshielding effects decrease with distance from the substitution with the exception of the 6-*O*-phosphate, where H-4 also showed a relatively large shift downfield possibly due to

deshielding resulting from spatial proximity of the anion on the freely rotating 6-*O*-phosphate and H-4. Analysis of the coupling constants suffers from spectral overlap and higher order effects such that no trends could be determined from the available data.

The ^{13}C chemical shifts are summarized in Table 2-3. The changes due to the substitution are approximately 3-4 ppm with the effects being very site specific. Very little change was observed in the ^{13}C chemical shifts for any of the unsubstituted positions.

The ^{31}P chemical shifts and coupling constants are shown in Table 2-4. The 6-*O*-phosphate had the expected "doublet of doublet" coupling pattern, while the other phosphates were doublets due to three bond coupling with vicinal protons.

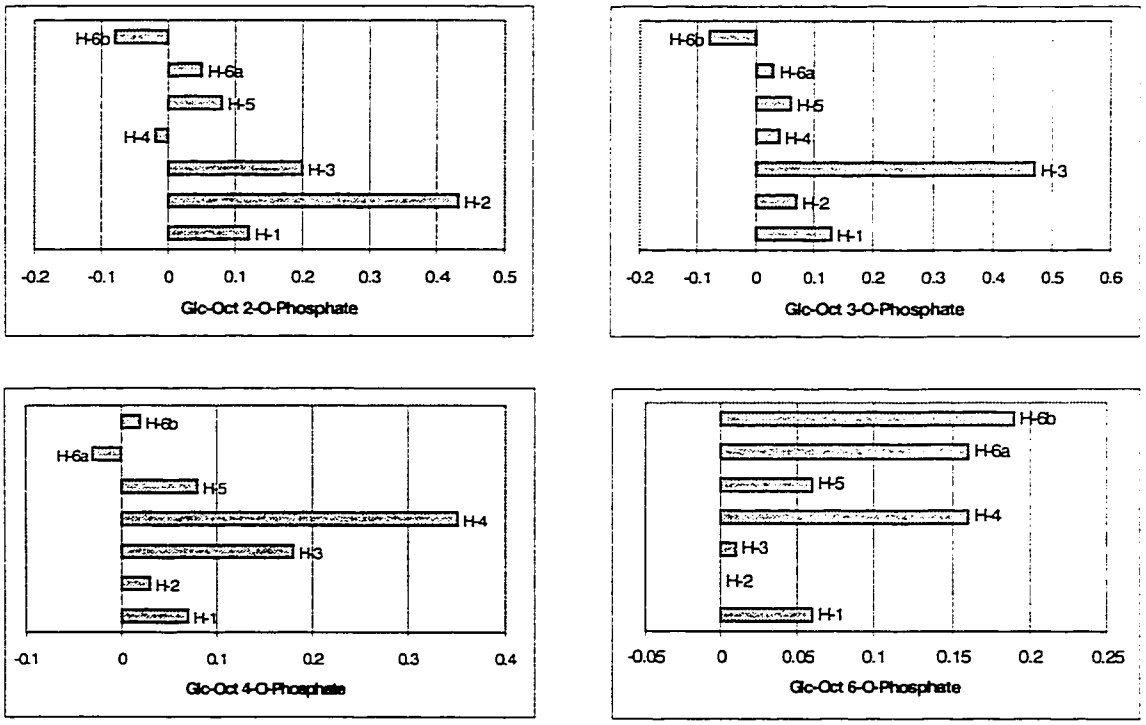


Fig.2-22 Proton chemical shift changes induced by phosphate substitution at different positions of octyl β-Glc. Chemical shift changes are quoted in ppm relative to the unsubstituted octyl β-Glc. Only changes larger than ±0.01 are shown.

Table 2-1

^{1}H Chemical shifts[a] of phosphorylated octyl β-Glc monosaccharides[b,c]

	H-1	H-2	H-3	H-4	H-5	H-6a	H-6b
Octyl β-Glc **35**	4.37	3.27	3.47	3.43	3.38	3.86	3.77
6-*O*-Phosphate **31**	4.43	3.27	3.48	3.59	4.02	3.96	3.44
4-*O*-Phosphate **32**	4.44	3.30	3.65	3.81	3.46	3.83	3.79
3-*O*-Phosphate **33**	4.50	3.34	3.94	3.47	3.47	3.89	3.69
2-*O*-Phosphate **34**	4.49	3.70	3.67	3.41	3.46	3.91	3.69

[a] Chemical shifts are referenced to external 0.1% acetone at 2.225 ppm.

[b] All data were recorded on a 600MHz Varian Inova spectrometer in D_2O buffered with 0.05M $NaDCO_3$ / 0.045M NaOD. The temperature was 30.0±0.1 °C.

[c] Geminal protons are not assigned stereospecifically. The higher chemical shift was arbitrarily assigned to H-6a and H-6a' respectively.

Table 2-2

^{1}H Coupling constants[a] of phosphorylated octyl β-Glc monosaccharides[b,c,d]

	J_{12}	J_{23}	J_{34}	J_{45}	J_{56a}	J_{56b}	J_{6a6b}
Octyl β-Glc **35**	8.0	8.4	8.8	8.9	2.4	4.8	12.2
6-*O*-Phosphate **31**	8.0	9.1	9.3	9.5	3.5	2.6	11.3
4-*O*-Phosphate **32**	8.1	9.3	9.0	9.7	2.4	4.9	12.8
3-*O*-Phosphate **33**	8.2	8.4	8.8	d	2.6	d	11.0
2-*O*-Phosphate **34**	7.5	d	9.8	9.8	2.2	6.1	12.3

[a,b,c] See footnotes a,b,c, Table 2-1

[d] Due to spectral overlap the coupling constants could not be accurately determined.

Table 2-3

^{13}C Chemical shifts[a] of phosphorylated octyl β-Glc monosaccharides[b]

	C-1	C-2	C-3	C-4	C-5	C-6
Octyl β-Glc **35**	102.8	73.8	76.9	70.1	76.5	61.7
6-*O*-Phosphate **31**	103.6	73.8	76.3	69.3	75.3	64.5
4-*O*-Phosphate **32**	103.0	74.2	76.9	73.4	75.9	61.4
3-*O*-Phosphate **33**	103.0	73.8	81.7	70.3	76.5	61.7
2-*O*-Phosphate **34**	102.1	76.9	77.7	70.3	76.4	61.6

[a] Chemical shifts are referenced to external 0.1% acetone at 2.225 ppm.
[b] All data were recorded on a 500MHz Varian Unity spectrometer in D_2O buffered with 0.05M $NaDCO_3$ / 0.045M NaOD. The temperature was 30.0±0.1 °C.

Table 2-4

^{31}P Chemical shifts[a] and coupling constants of octyl β-Glc monosaccharides[b]

Octyl β-Glc 6-*O*-Phosphate **31**	4.98	dd, 7.1 Hz
Octyl β-Glc 4-*O*-Phosphate **32**	4.63	d, 8.4 Hz
Octyl β-Glc 3-*O*-Phosphate **33**	4.58	d, 7.0 Hz
Octyl β-Glc 2-*O*-Phosphate **34**	3.92	d, 6.8 Hz

[a] Chemical shifts are referenced to external 5% phosphoric acid at 0.0 ppm.
[b] All data were recorded on a 500MHz Varian Unity spectrometer in D_2O buffered with 0.05M $NaDCO_3$ / 0.045M NaOD. The temperature was 30.0±0.1 °C.

2.6.2 NMR Spectral Analysis of the Octyl β-LacNAc Mono-*O*-Phosphate Regioisomers

The proton chemical shifts and coupling constants for the six mono-*O*-phosphate octyl β-LacNAc compounds **7**, **8**, **9**, **10**, **11** and **12** and the unsubstituted octyl β-LacNAc **83** are presented in Tables 2-5 and 2-6. The chemical shift changes due to phosphorylation are shown in Fig 2-23. The effects are strongest at the site of substitution with changes in chemical shift typically 0.4-0.6 ppm downfield for secondary alcohols and 0.2 ppm downfield for the primary alcohols. The deshielding effects dramatically drop off with distance from the site of substitution with immediate neighbouring sites exhibiting changes in the 0.1-0.2 ppm range or demonstrating no change at all. The one interesting exception is the 6-*O*-phosphate compound where H-1' exhibits a relatively large shift of 0.2 ppm downfield. The deshielding is possibly due to the orientation of H-1' and 6-*O*-phosphate and their potentially close spacial proximity. The negatively charged phosphate repels the electron density on the proton resulting in the observed deshielding. Phosphorylation at the 6'-position also lead to a distinct shift at the 4'-position, similar to what was observed with the octyl β-Glc 6-*O*-phosphate. Again, the spacial proximity of the negatively charged anion at the 6'-*O*-phosphate may be deshielding H-4'.

The analysis of the coupling constants for the phosphorylated octyl β-LacNAc compounds is severely hampered by spectral overlap and higher order effects. The chemical shifts of H-2, H-3, and H-4 are almost identical for many of the compounds, leading to higher order coupling and virtual coupling in the H-1 signal. Trends in coupling constants are difficult to discern with respect to the position of substitution.

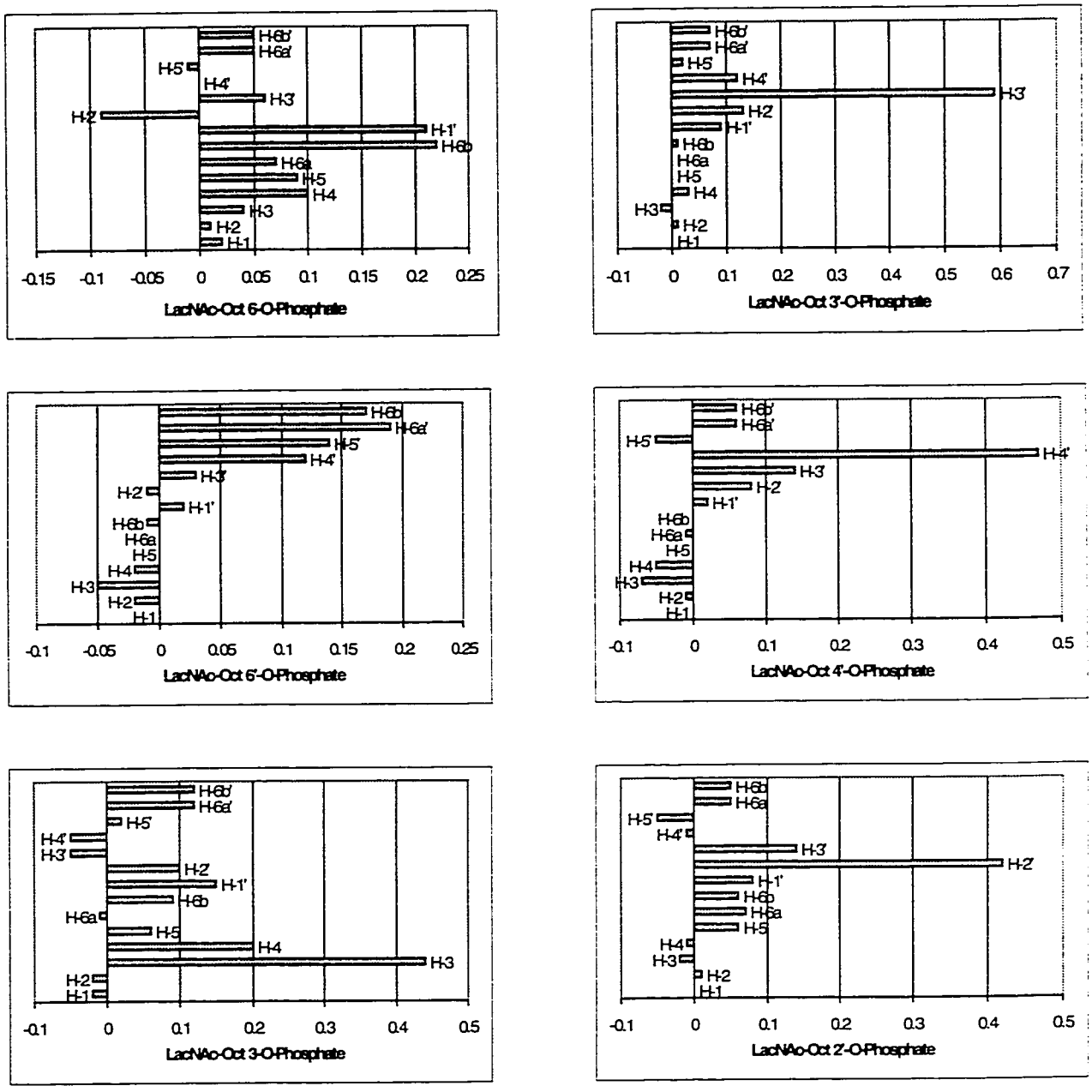


Fig 2-23 Proton chemical shift changes induced by phosphate substitution at different positions of octyl β-LacNAc. Chemical shift changes are quoted in ppm relative to the unsubstituted octyl β-LacNAc. Only changes larger then ±0.01 are shown

Table 2-5

^{1}H Chemical shifts[a] of phosphorylated octyl β-LacNAc disaccharides[b,c]

	H-1	H-2	H-3	H-4	H-5	H-6a	H-6b	H-1'	H-2'	H-3'	H-4'	H-5'	H-6a'	H-6b'
Octyl β-LacNAc **83**	4.64	3.91	3.75	3.71	3.56	3.97	3.82	4.45	3.53	3.64	3.91	3.67	3.69	3.69
6-*O*-Phosphate **11**	4.52	3.71	3.79	3.81	3.65	4.04	4.04	4.66	3.44	3.70	3.91	3.66	3.74	3.74
3-*O*-Phosphate **12**	4.48	3.68	4.19	3.91	3.62	3.98	3.81	4.47	3.52	3.67	4.03	3.81	3.88	3.86
6'-*O*-Phosphate **7**	4.50	3.68	3.70	3.69	3.56	3.97	3.81	4.47	3.52	3.67	4.03	3.81	3.88	3.86
4'-*O*-Phosphate **8**	4.50	3.69	3.68	3.66	3.56	3.96	3.82	4.47	3.61	3.78	4.38	3.61	3.75	3.75
3'-*O*-Phosphate **9**	4.50	3.71	3.73	3.74	3.56	3.97	3.83	4.54	3.66	4.23	4.03	3.69	3.76	3.76
2'-*O*-Phosphate **10**	4.50	3.71	3.73	3.70	3.62	4.05	3.88	4.53	3.95	3.78	3.90	3.61	3.74	3.74

[a,b,c] See footnotes a,b,c, Table 2-1

Table 2-6

^{1}H Coupling constants[a] of phosphorylated octyl β-LacNAc disaccharides[b,c]

	J_{12}	J_{23}	J_{34}	J_{45}	J_{56a}	J_{56b}	J_{6a6b}	$J_{1'2'}$	$J_{2'3'}$	$J_{3'4'}$	$J_{4'5'}$	$J_{5'6a'}$	$J_{5'6b'}$	$J_{6a'6b'}$
Octyl β-LacNAc **83**	7.9	d	d	d	2.4	5.1	12.5	7.8	10.0	3.3	d	d	d	d
6-*O*-Phosphate **11**	8.4	8.8	9.2	9.2	d	d	d	8.0	10.2	3.5	d	d	d	d
3-*O*-Phosphate **12**	8.3	9.4	9.4	9.2	2.6	d	12.3	7.5	9.9	3.5	d	d	d	d
6'-*O*-Phosphate **7**	7.7	d	d	9.2	2.3	6.5	12.2	7.9	10.0	3.6	d	d	d	d
4'-*O*-Phosphate **8**	7.1	d	d	d	2.2	5.1	12.2	7.7	d	1.1	d	d	d	d
3'-*O*-Phosphate **9**	8.1	d	d	d	2.0	d	12.1	7.9	8.4	3.3	d	d	d	d
2'-*O*-Phosphate **10**	8.0	d	d	d	1.5	d	12.7	7.7	9.2	3.5	d	d	d	d

[a,b,c] See footnotes a,b,c, Table 2-1

[d] Due to spectral overlap the coupling constants could not be determined with accuracy.

Table 2-7

^{13}C Chemical shifts[a] of phosphorylated octyl β-LacNAc disaccharides[b]

	C-1	C-2	C-3	C-4	C-5	C-6	C-1'	C-2'	C-3'	C-4'	C-5'	C-6'
Octyl β-LacNAc **83**	103.5	57.6	75.0	81.9	77.3	62.8	105.9	73.4	75.6	71.0	77.9	62.8
6-*O*-Phosphate **11**	102.0	55.9	76.2	79.0	75.3	62.9	103.5	71.8	74.4	69.5	74.3	61.9
3-*O*-Phosphate **12**	102.7	56.3	73.5	74.7	76.6	61.7	102.0	71.7	73.6	69.7	76.0	61.7
6'-*O*-Phosphate **7**	101.9	55.8	73.2	73.2	75.7	61.1	104.1	72.8	80.0	68.0	74.9	65.7
4'-*O*-Phosphate **8**	101.6	56.2	73.1	79.7	75.5	61.1	104.0	72.4	75.6	71.7	73.8	61.4
3'-*O*-Phosphate **9**	102.1	56.5	73.2	78.2	75.7	60.8	103.8	71.8	77.6	69.1	79.3	62.9
2'-*O*-Phosphate **10**	102.1	55.6	73.3	75.3	75.7	60.6	103.5	74.5	74.4	68.8	80.6	61.7

[a,b] See footnotes for Table 2-3

Table 2-8

^{31}P Chemical shifts[a] and coupling constants of octyl β-LacNAc disaccharides[b]

Octyl β-LacNAc 6-*O*-Phosphate **11**	4.10	s
Octyl β-LacNAc 3-*O*-Phosphate **12**	4.18	d, 9.4
Octyl β-LacNAc 6'-*O*-Phosphate **7**	4.64	dd, 6.5
Octyl β-LacNAc 4'-*O*-Phosphate **8**	5.43	d, 9.7
Octyl β-LacNAc 3'-*O*-Phosphate **9**	4.44	d, 8.4
Octyl β-LacNAc 2'-*O*-Phosphate **10**	4.13	d, 7.9

[a,b] See footnotes a,b Table 2-4

The ^{13}C chemical shifts of the phosphorylated octyl β-LacNAc compounds and the unsubstituted octyl β-LacNAc are presented in Table 2-7. Substitution on GlcNAc residue resulted in an upfield shift of approximately 1 ppm of the carbon signal at the position of substitution, while substitution on Gal gave downfield shifts of 3-4 ppm at the position of substitution, as was observed with octyl β-Glc (Section 2.5.1). The shifts of the carbon positions adjacent to substitutions do not change noticeably. There is less constistancy in the carbon shifts from one compound to the next, as was observed in octyl β-Glc, possibly due to conformational changes as a result of the introduction of the negative charge and the bulk of the phosphate.

The ^{31}P chemical shifts and coupling constants of the phosphorylated octyl β-LacNAc are presented in Table 2-8. The proton-phosphorous coupling of the 6-*O*-phosphate was too small to be observed resulting in a broad singlet. All the other coupling patterns were as expected, with all signals being doublets with the exception of the 6'-*O*-phosphate as a doublet of doublets. The chemical shifts for the phosphorous on the GlcNac moiety were all upfield from those on the Gal. The 4'-*O*-phosphate showed the most dramatic downfield shift.

2.6.3 Preparation of Mono-*O*-Phosphate Octyl β-LacNAc Mixture

The unique ^{31}P chemical shifts of the compounds **7**, **8**, **9**, **10**, **11** and **12** provided an opportunity to analyze the phosphorylation of unprotected octyl β-LacNAc. Hydrogenolysis of the benzyl ethers of compound **4** afforded literature compound **83** [73] in 73% yield. Phosphorylation of **83** was carried out with 0.5 eq. diphenyl

phosphorochloridate and DMAP in pyridine. Removal of the phenyl phospho-esters over Adam's catalyst was followed by purification using reverse phase chromatography and treatment with an anion exchange resin to provide the crude mixture ***A***.

Phosphorylation of **83** was also attempted using 0.5 eq. dibenzyl N,N-diethyl phosphoramidite and 1,2,4 triazole in acetonitrile followed by hydrogenolysis over palladium on carbon to afford the crude mixture ***B*** (Fig 2-24).

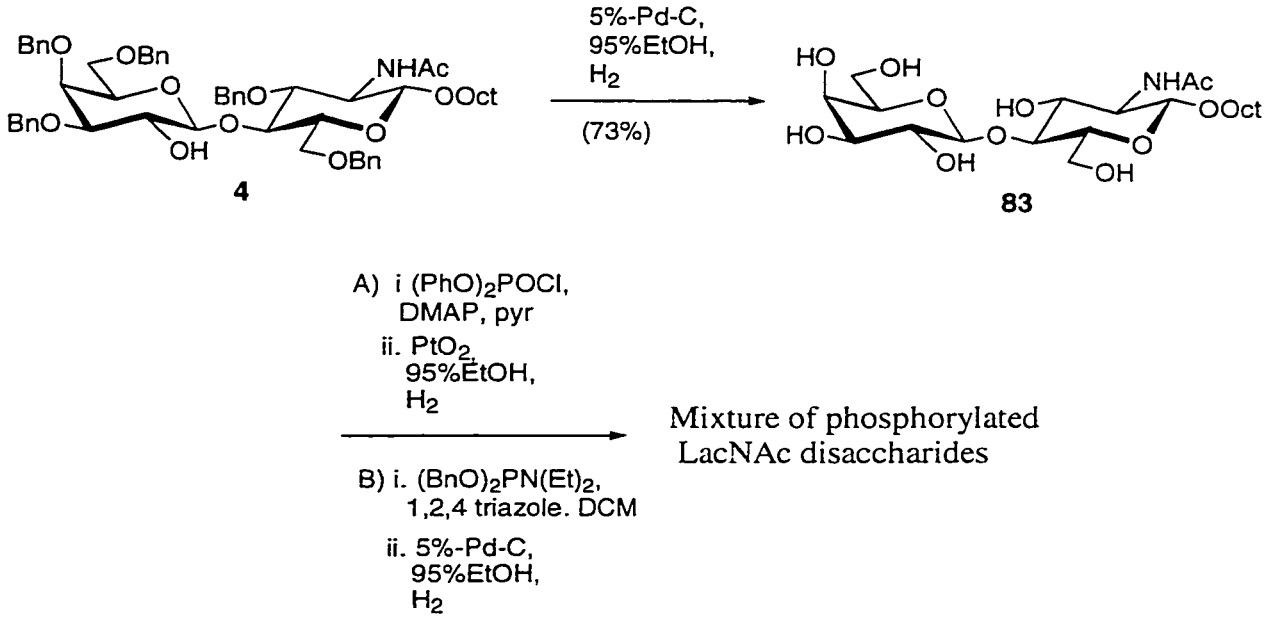


Fig 2-24 Phosphorylation of **83**

The unreacted octyl β-LacNAc was recovered by passing the crude mixture through a Bio-Rad AG 1-X8 ion exchange (Cl^-) column and purified using reverse phase chromatography. The phosphorylated compounds were eluted from the ion exchange column with 0.5 M NaCl.

2.6.4 NMR Spectral Analysis of Mono-*O*-Phosphate Octyl β-LacNAc Mixtures

The ^{31}P chemical shifts of a mixture of approximately 0.5 mg of each compound **7**, **8**, **9**, **10**, **11** and **12** are presented in table 2-9. The analysis was performed as described in section 2.5. There are no discernable differences between the chemical shifts of the mixture and those of the individual compounds.

Table 2-9
^{31}P Chemical shifts[a] of mixture of octyl β-LacNAc disaccharides[b]

	pure	mixture
Octyl β-LacNAc 6-*O*-Phosphate **11**	4.10	4.09
Octyl β-LacNAc 3-*O*-Phosphate **12**	4.18	4.18
Octyl β-LacNAc 6'-*O*-Phosphate **7**	4.64	4.66
Octyl β-LacNAc 4'-*O*-Phosphate **8**	5.43	5.43
Octyl β-LacNAc 3'-*O*-Phosphate **9**	4.44	4.45
Octyl β-LacNAc 2'-*O*-Phosphate **10**	4.13	4.13

[a,b] See footnotes a,b Table 2-4

The spectral analysis of mixtures ***A*** and ***B*** is presented in table 2-10. In both cases there is a signal at 4.66 ppm, corresponding with the 6'-*O*-phosphate, and signals at 4.45 ppm for ***A*** and 4.44 ppm for ***B***, corresponding with the 3'-*O*-phosphate. In both mixtures, small signals were observed in the ^{31}P NMR spectra that have a similar chemical shift as the 4'-*O*-phosphate. The signals that appear at 4.12 ppm are similar to the chemical shifts of 2- and 6-*O*-phosphates. Determining between the two possible compounds could not be accomplished with the available spectral data. No signal with a

chemical shift similar to the 3-*O*-phosphate was observed in either of the mixtures. The signals at 4.71 ppm in mixture ***A*** and 4.24 ppm in mixture ***B*** are from unknown impurities or possibly from di-phosphorylated dissaccharides. The poor signal to noise is possibly due to the poor solubility of octyl β-LacNAc in the solvents required for the phosphorylation procedure resulting in very little phosphorylated product.

While anomeric signals in the ^{1}H NMR spectral analysis of the mixtures were observed, the molecular ion of the expected mono-*O*-phosphates or di-*O*-phosphates could not be detected by electrospray MS for mixture ***A***. For mixture ***B*** the molecular ions of octyl β-LacNAc along with the mono-phosphorylated product was observed, however, no di-*O*-phosphate octyl β-LacNAc was detected.

Table 2-10
^{31}P Signals[a] and chemical shifts[b] from mixture ***A*** and ***B***

Mixture ***A***	Mixture ***B***
5.44 Octyl β-LacNAc 4'-O-phosphate	4.66 Octyl β-LacNAc 6'-*O*-phosphate
4.71 unknown	4.44 3'-*O*-phosphate
4.66 6'-*O*-phosphate	4.24 unknown
4.45 3'-*O*-phosphate	4.12 2'- or 6-*O*-phosphate
4.12 2'- or 6-*O*-phosphate	

[a,b] See footnotes a,b Table 2-4

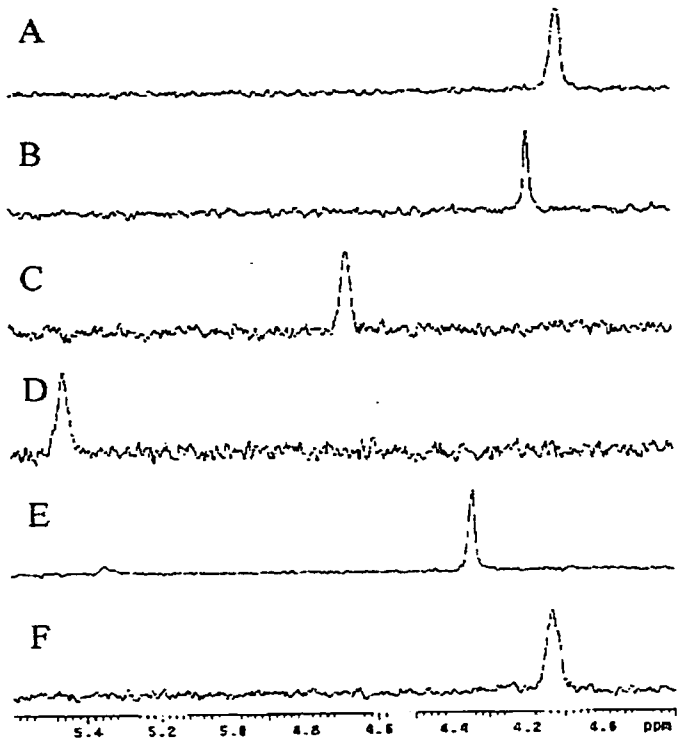


Fig 2-25 ^{31}P spectra of
A) Octyl β-LacNAc 6-*O*-phosphate **11**
B) 3-*O*-phosphate **12**
C) 6'-*O*-phosphate **7**
D) 4'-*O*-phosphate **8**
E) 3'-*O*-phosphate **9**
F) 2'-*O*-phosphate **10**

The ^{31}P NMR spectra of mixtures ***A*** and ***B*** are presented in Fig 2-25 along with the spectrum of the individual compounds and the mixture of the six mono-*O*-phosphates of octyl β-LacNAc.

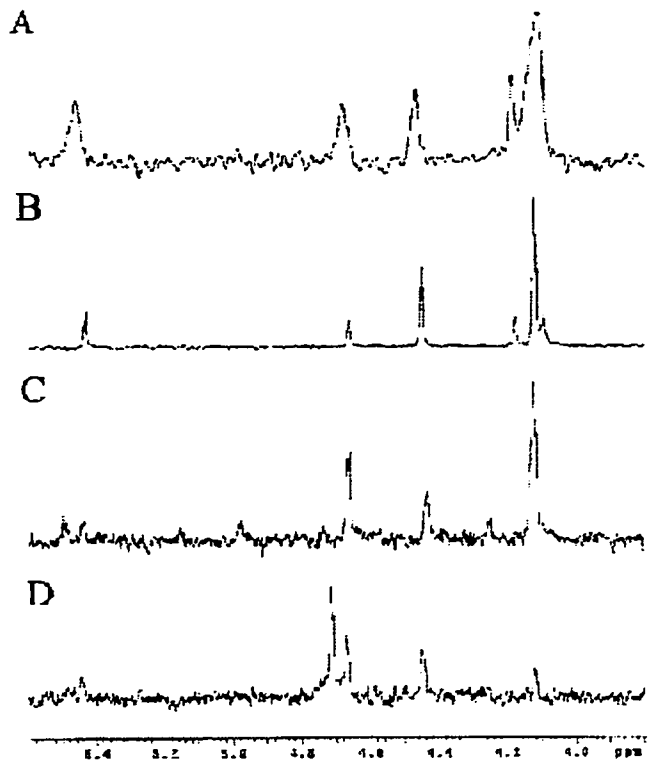


Fig 2-26 ^{31}P spectral analysis
A) combined FID of individual spectra of compounds **7**, **8**, **9**, **10**, **11** and **12**
B) mixture of compounds **7**, **8**, **9**, **10**, **11** and **12**
C) mixture ***B***
D) mixture ***A***

2.7 Conclusions and Future Perspectives

The six mono-hydroxy octyl β-LacNAc compounds have been prepared in sufficient quantity, over 100 mg of each, to provide advanced intermediates for the synthesis of functionalized dissacharides. Future derivatives of octyl β-LacNAc might include methyl ethers or sulfonates for use in probing protein-carbohydrate interactions.

The six mono-*O*-phosphates of octyl β-LacNAc were prepared and characterized by ^{1}H, ^{13}C and ^{31}P NMR spectroscopy. ^{31}P NMR spectroscopy was utilized to detect the products of a random mixture of phosphorylated compounds in solution. The low signal to noise ratios of the two prepared mixtures was problematic. The separation of the mono-*O*-phosphorylated compounds and di-*O*-phosphorylated compounds should also be addressed. Separation might be accomplished using DEAD-Sephadex A25 (Cl^- form) [74]. Molecular ions of the separated compounds should be obtained to verify the structures.

K. Parang, E. Fournier and O. Hindsgaul [75] have described the synthesis of mono-phosphorylated sugars using an immobolized phosphorylating agent. A 1% crosslinked divinylbenzenepolystyrene copolymer containing cyanoethoxy N,N-diisopropylamine phosphine was used as the phosphite donor. Loading the resin with an unprotected sugar was followed by oxidation to the phosphate. Cleavage and deprotection gave the mono-*O*-phosphorylated compounds (Fig 2.26).

A random phosphorylation of octyl β-LacNAc might be performed on the solid phase. Phosphorylating octyl β-LacNAc on the solid phase should afford mostly mono-*O*-phosphates and no starting material should be present after the loading step. In order to determine what compounds are present, the resulting mixture can be analyzed via ^{31}P NMR spectroscopy and the resulting signals compared to the spectra of the phosphorylated standards which have been prepared in solution and fully characterized.

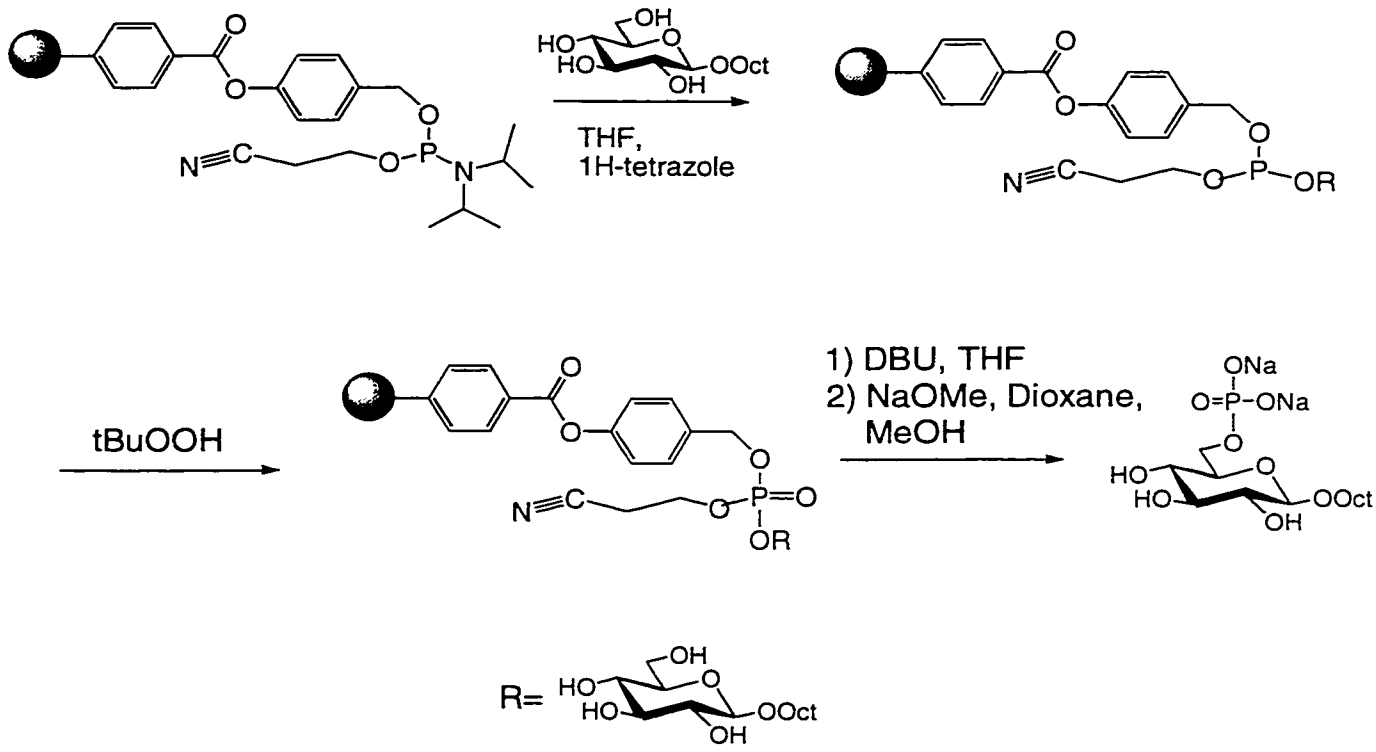


Fig 2.27 Solid phase phosphorylation strategy

Glycosyltransferases are a class of enzymes which assemble growing chains of oligosaccharides by catalyzing the transfer of a glycosyl residue from a donor to an acceptor [76]. A number of enzymes that use LacNAc-R as an acceptor have been cloned, including α1,3-galactosyltransferase, α2,3- and α2,6-sialyltransferases and α1,4- and α1,2-fucosyltransferase [77]. Each of the mono-*O*-phosphate octyl β-LacNAc compounds that have been prepared as described in section 2.4 can be tested against these enzymes to determine if: 1) the compounds of interest act as inhibitors of the enzymes or 2) the compounds of interest act as acceptors and result in the formation of a phosphorylated oligosaccharide. If the enzymatic synthesis is successful, the functionalized oligosaccharides can be utilized in further biological studies.

Chapter 3

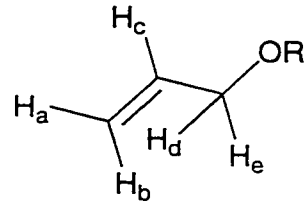
Experimental

3.1 Chemical Synthesis

3.1.1 General Methods

Analytical TLC was performed on Silica Gel 60-F254 (E. Merck, Darmstadt) with detection by charring with 5% sulfuric acid in EtOH, ninhydrin or permanganate. All commercial reagents were used as supplied, unless otherwise stated. Column chromatography was performed on Silica Gel 60 (E. Merck, 40-63 μm, Darmstadt). Millex-GV (0.22 μm) filter units were from Millipore (Missisauga, ON). C18 Sep-Pak sample preparation cartridges were from Waters Associates (Missisauga, ON). ^{1}H NMR spectra were recorded at 300 MHz (Varian Inova 300), 500 MHz (Varian Unity 500) or 600 MHz (Varian Inova 600). ^{13}C NMR spectra were recorded either at 75 MHz (Bruker AM-300) or 125 MHz (Varian Unity 500). ^{31}P NMR spectra were recorded at 202 MHz (Varian Unity 500). The proton chemical shifts were referenced to solvent residual peaks for solutions in $CDCl_3$ ($CHCl_3$, δ 7.26), CD_3OD (CHD_2OD δ 5.32) or external 1% acetone (δ 2.225). The carbon chemical shifts were referenced to solvent signals for solutions in $CDCl_3$ (δ 77.06), CD_3OD (δ 53.80) or external 1% acetone (δ 31.07). The phosphorous chemical shifts were referenced to external 5% phosphoric acid (δ 0.00). High resolution electrospray mass spectra were recorded on a Micro-mass ZabSpec Hydroid Sector-TOF. Microanalyses were carried out by the analytical services at the department of Chemistry at the University of Alberta. Melting points are uncorrected.

Protons of the allyl group present in compounds described in the thesis were designated H_a, H_b, H_c, H_d, H_e as shown below. These protons showed the same coupling constants and multiplicity patterns in all the compounds examined. Only the chemical shifts varied. The couplings observed are as follows: Ha, (dddd, $J_{a,c}$=10.5 Hz, $J_{a,b}=J_{a,d}=J_{a,e}$=1.5±0.5 Hz). Hb, (dddd, $J_{b,c}$=17.0 Hz, $J_{b,a}=J_{b,d}=J_{b,e}$=1.5±0.5 Hz). Hc, (dddd,

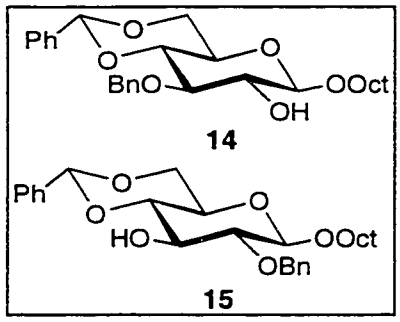


$J_{c,b}$=17.0 Hz, $J_{c,a}$=10.5 Hz, $J_{c,d}=J_{c,e}$=5.5 Hz). Hd, (dddd, $J_{d,e}$=13.5 Hz, $J_{d,c}$=5.5 Hz, $J_{d,a}=J_{d,b}$=1.5±0.5 Hz). He, (dddd, $J_{e,d}$=13.5 Hz , $J_{e,c}$=5.5 Hz, $J_{e,a}=J_{e,b}$=1.5±0.5 Hz).

3.1.2 Synthesis of Octyl β-Glc Mono-O-Phosphates

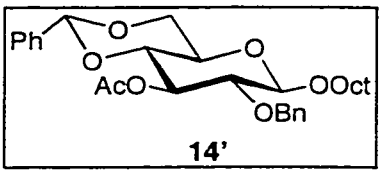
Octyl 4,6-O-benzylidene-3-O-benzyl-β-D-glucopyranoside (**14**) and

Octyl 4,6-O-benzylidene-2-O-benzyl-β-D-glucopyranoside (**15**)



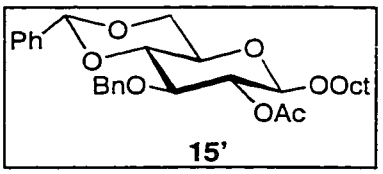
Octyl 4,6-O-benzylidene-β-D-glucopyranoside [55] (4.71 g, 12.4 mmol) was dissolved in DCM (200 mL) and tetrabutylammonium bromide (2.00 g, 6.2 mmol) was added followed by 15% sodium hydroxide (15 mL) and benzyl bromide (2.2 mL, 18 mmol). The solution was stirred at room temperature for 48 hours, washed successively with water and brine, dried over sodium sulfate and concentrated under reduced pressure. Column chromatography of the resulting clear oil (25:1 toluene/ethyl acetate) gave compound **14** (730 mg, 12.5%),

compound **15** (1.42 g, 24.0%) and a mixture of **14** and **15** (500 mg, 8.5%) as white solids. Compounds **14** and **15** (10 mg) were dissolved in pyridine (1 mL) and acetic anhydride (0.5 mL) and stirred at room temperature for 1 hour. Water (1 mL) was added to the mixture, followed by extraction with DCM. The solution was dried over sodium sulfate and concentrated under reduced pressure to afford a white solid. Column chromatography (10:1 hexane/ethyl acetate) resulted in the separation of the acetylated products, **14'** and **15'**:



14'

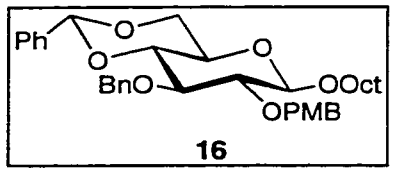
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43-7.25 (10H, Ph), 5.44 (s, 1H, PhC<u>H</u>O_2), 5.28 (dd, 1H, $J_{2,3}$=$J_{3,4}$=9.3 Hz, H-3), 4.86, 4.63 (d, 1H, J=11.9 Hz, PhC<u>H</u>$_2$), 4.57 (d, 1H, $J_{1,2}$=7.7 Hz, H-1), 4.33 (dd, 1H, $J_{5,6b}$=4.8, $J_{5,6a}$=10.5 Hz, H-5), 3.93 (dt, 1H, J=6.4, 9.4 Hz, OC<u>H</u>$_2$CH$_2$), 3.77 (dd, 1H, $J_{5,6a}$=$J_{6a,6b}$=10.0 Hz, H-6a), 3.62-3.38 (4H, H-2, H-4, H-6b, OC<u>H</u>$_2$CH$_2$), 1.95 (s, 3H, CH_3, acetyl), 1.72 (2H, OCH$_2$C<u>H</u>$_2$), 1.34-1.20 (10H, CH_2, octyl), 0.85 (t, 3H, J=7.0 Hz, CH_3, octyl).



15'

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43-7.21 (10H, Ph), 5.58 (s, 1H, PhC<u>H</u>O_2), 4.99 (dd, 1H, $J_{1,2}$=8.1, $J_{2,3}$=8.7 Hz, H-2) 4.96, 4.65 (d, 1H, J=11.7 Hz, PhC<u>H</u>$_2$), 4.43 (d, 1H, $J_{1,2}$=8.1 Hz, H-1), 4.34 (dd, 1H, J=5.0, 10.4 Hz, H-5), 3.87-3.67 (4H, H-3, H-6a, H-6b, OC<u>H</u>$_2$CH$_2$), 3.58-3.51 (2H, H-4, OC<u>H</u>$_2$CH$_2$), 1.95 (s, 3H, CH_3, acetyl), 1.55 (2H, OCH$_2$C<u>H</u>$_2$), 1.35-1.18 (10H, CH_2, octyl), 0.88 (t, 3H, J=7.0 Hz, CH_3, octyl).

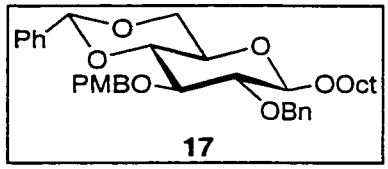
Octyl 3-O-benzyl-4,6-O-benzylidene-2-O-p-methoxybenzyl-β-D-glucopyranoside (**16**)



16

Compound **14** (720 mg 1.5 mmol) was dissolved in DMF (5 mL) and sodium hydride (118 mg, 60% dispersion in oil, 3.0 mmol) was added. The suspension was stirred at room temperature for 30 minutes followed by addition of *p*-methoxybenzyl chloride (450μL, 3.0mmol). The solution was stirred for an additional 2 hours and ice water added to decompose the excess sodium hydride. The reaction mixture was diluted with DCM, washed with water, dried over sodium sulfate and concentrated under reduced pressure. The resulting solid was recrystallized in isopropyl alcohol to give **16** (390mg, 44%) as a white solid: $[\alpha]_D$ +29.5° (c 1.2, $CHCl_3$); mp 83.3-83.5 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47 (2H, Ph), 7.40-7.22 (10H, Ph), 6.85 (d, 2H, J=7.5 Hz, Ph), 5.55 (s, 1H, PhC$\underline{H}O_2$), 4.93, 4,82, 4.78, 4.69 (d, 1H, J=11.5 Hz, PhC$\underline{H}_2$), 4.48 (d, 1H, $J_{1,2}$=7.7 Hz, H-1), 4.35 (dd, 1H, $J_{5,6b}$=4.9, $J_{5,6a}$=10.5 Hz, H-5), 3.91 (dt, 1H, J=6.4, 9.4 Hz, OC$\underline{H}_2CH_2$), 3.79 (5H, H-3, H-4, OCH_3), 3.68 (dd, 1H, $J_{5,6a}$=$J_{6a,6b}$=8.1 Hz, H-6a), 3.55 (dt, 1H J=9.4, 6.4 Hz, OC$\underline{H}_2CH_2$), 3.46-3.33 (2H, H-2, H-6b), 1.72 (2H, $OCH_2C\underline{H}_2$), 1.34-1.20 (10H, CH_2, octyl), 0.85 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.3, 138.7, 137.4, 130.6 (aromatic quat.), 129.8, 128.9, 128.3, 128.0, 127.6, 126.1, 113.8 (aromatic CH), 104.3 (C-1), 101.2 (Ph$\underline{C}HO_2$), 81.7, 81.6, 81.0, 75.1, 75.0, 70.7, 68.9, 66.1 (C-2, C-3, C-4, C-5, C-6, O$\underline{C}H_2CH_2$, Ph$\underline{C}H_2$x2), 55.3 (OCH_3), 31.9, 29.9, 29.5, 29.3, 26.2, 22.7 (CH_2 octyl), 14.1 (CH_3 octyl). *Anal.* Calcd for $C_{38}H_{52}O_6$ (604.90): C, 72.44; H, 8.16. Found: C, 72.68; H, 7.91.

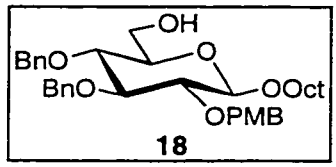
Octyl 2-O-benzyl-4,6-O-benzylidene-3-O-p-methoxybenzyl-β-D-glucopyranoside (**17**)



17

Compound **15** (1.42g, 3.0 mmol) was dissolved in DMF (10 mL) and sodium hydride (240 mg, 60% dispersion in oil, 6.0 mmol) was added. The solution was stirred at room temperature for 30 minutes followed by the addition of *p*-methoxybenzyl chloride (850 μL, 6.0 mmol). The reaction mixture was stirred for 1 hour and ice water was added to decompose the excess sodium hydride. The solution was diluted with DCM, washed with water, dried over sodium sulfate, and concentrated under reduced pressure. The resulting solid was recrystallized from isopropyl alcohol to give **17** (900 mg, 51%) as a white solid: $[\alpha]_D$ +30.2° (c 1.2, $CHCl_3$); mp 69.5-70.5 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54 (2H, Ph), 7.40-7.22 (10H, Ph), 6.80 (d, 2H, J=7.5 Hz, Ph), 5.55 (s, 1H, PhC$\underline{H}O_2$), 4.89, 4.83, 4.75, 4.71 (d, 1H, J=11.0 Hz, PhC$\underline{H}_2$), 4.47 (d, 1H, $J_{1,2}$=7.7 Hz, H-1), 4.35 (dd, 1H, J=5.0, 10.4 Hz, H-5), 3.90 (dt, 1H, J=6.4, 9.4 Hz, OC$\underline{H}_2CH_2$), 3.81-3.62 (6H, H-3, H-4, H-6a, OCH_3), 3.54 (dt, 1H J=9.4, 6.4 Hz, OC$\underline{H}_2CH_2$), 3.45-3.34 (2H, H-2, H-6b), 1.63 (2H, $OCH_2C\underline{H}_2$), 1.36 (10H, CH_2, octyl), 0.87 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.3, 138.5, 137.4, 130.7 (aromatic quat.), 129.7, 128.9, 128.3, 128.2, 127.7, 126.1, 113.7 (aromatic CH), 104.2 (C-1), 101.1 (Ph$\underline{C}HO_2$), 82.2, 81.5, 75.3, 74.8, 70.7, 68.9, 66.1 (C-2, C-3, C-4, C-5, C-6, O$\underline{C}H_2CH_2$, Ph$\underline{C}H_2$x2), 55.3 (OCH_3), 31.9, 29.9, 29.5, 29.3, 26.2, 22.7 (CH_2, octyl), 14.1 (CH_3, octyl).

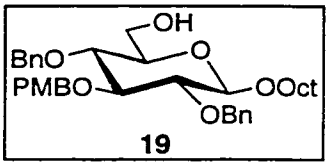
Octyl 3,4-di-O-benzyl-2-O-p-methoxybenzyl-β-D-glucopyranoside (**18**)



18

Compound **16** (290 mg, 0.52 mmol) was dissolved in diethyl ether and lithium aluminum hydride (200 mg, 5.2 mmol) was added. The solution was cooled to 0°C and aluminum trichloride (611 mg, 5.3 mmol) in diethyl ether (5 mL) was added dropwise over 30 minutes. The solution was warmed to room temp and stirring continued for 1 hour. The reaction was quenched with water (1 mL), filtered through celite, diluted with diethyl ether and washed successively with water and brine. Column chromatography (10:1 toluene/ethyl acetate) gave **18** (170 mg 58%) as a white solid: $[\alpha]_D$ +8.6° (c 0.7, $CHCl_3$); mp 59.0-60.5 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38-7.21 (12H, Ph), 6.82 (d, 2H, J=7.4 Hz, Ph), 4.92, 4.85, 4.83, 4.77, 4.64, 4.61 (d, 1H, J=11.1 Hz, PhC$\underline{H}_2$), 4.40 (d, 1H, $J_{1,2}$=7.9 Hz, H-1), 3.90 (dt, 1H, J=6.3, 9.5 Hz, OC$\underline{H}_2CH_2$), 3.84-3.68 (5H, H-4, H-5, OCH_3), 3.63 (dd, 1H $J_{2,3}$=$J_{3,4}$=9.0 Hz, H-3), 3.58-3.49 (2H, H-6a, OC$\underline{H}_2CH_2$), 3.41-3.30 (2H, H-2, H-6b), 1.87 (bs, 1H, OH), 1.64 (2H, $OCH_2C\underline{H}_2$), 1.50-1.22 (10H, CH_2, octyl), 0.94 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.1, 130.6, 129.8 (aromatic quat.), 128.5, 128.4, 128.1, 127.9, 127.6, 113.8 (aromatic CH), 103.8 (C-1), 84.6, 82.0, 77.7, 75.6, 75.1, 75.0, 74.6, 70.0, 62.2 (C-2, C-3, C-4, C-5, C-6, O$\underline{C}H_2CH_2$, Ph$\underline{C}H_2$x3), 55.3 (OCH_3), 31.9, 29.9, 29.5, 29.3, 26.2, 22.7 (CH_2, octyl), 14.1 (CH_3, octyl). *Anal.* Calcd for $C_{38}H_{54}O_6$ (606.83): C, 72.94; H, 8.16. Found: C, 72.43; H, 8.47.

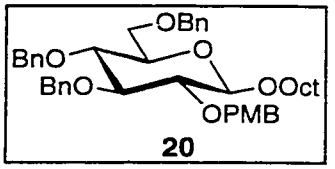
Octyl 2,4-di-O-benzyl-3-O-p-methoxybenzyl-β-D-glucopyranoside (**19**)



19

Compound **19** (430 mg, 54%) was synthesized from **17** (800 mg, 14.0 mmol), lithium aluminum hydride (532 mg, 140 mmol), and aluminum trichloride (1.82 g, 140 mmol) as described for **18**: $[\alpha]_D$ +2.9° (c 1.0, $CHCl_3$); mp 70.5-71.2 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38-7.19 (12H, Ph), 6.81 (d, 2H, J=7.6 Hz, Ph), 4.93, 4.85, 4.83, 4.72, 4.71, 4.61 (d, 1H, J=11.0 Hz, PhC$\underline{H}_2$), 4.41 (d, 1H, $J_{1,2}$=7.8 Hz, H-1), 3.90 (dt, 1H, J=6.4, 9.4 Hz, OC$\underline{H}_2CH_2$), 3.86-3.68 (5H, H-4, H-5, OCH_3), 3.64 (dd, 1H $J_{2,3}=J_{3,4}$=9.0 Hz, H-3), 3.57-3.48 (2H, H-6a, OC$\underline{H}_2CH_2$), 3.40-3.31 (2H, H-2, H-6b), 1.86 (bs, 1H, OH), 1.63 (2H, $OCH_2C\underline{H}_2$), 1.41-1.22 (10H, CH_2, octyl), 0.88 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.3, 138.5, 138.1, 130.8 (aromatic quat.), 129.6, 128.5, 128.4, 128.0, 127.9, 127.7, 113.8 (aromatic CH), 103.8 (C-1), 84.2, 82.5, 77.6, 75.0 (C-2, C-3, C-4, C-5), 75.4, 75.1, 74.9, 70.5, 62.2 (C-6, O$\underline{C}H_2CH_2$, Ph$\underline{C}H_2$x3), 55.3 (OCH_3), 31.8, 29.8, 29.5, 29.3, 26.2, 22.7 (CH_2, octyl), 14.1 (CH_3, octyl).

Octyl 3,4,6-tri-O-benzyl-2-O-p-methoxybenzyl-β-D-glucopyranoside (**20**)

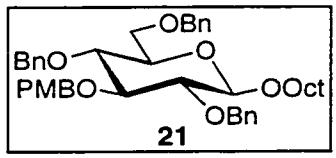


20

Compound **18** (130 mg, 0.20 mmol) was dissolved in dry DMF (1 mL) and sodium hydride (11 mg, 60% dispersion in oil, 0.28 mmol) was added and the solution was stirred at room temperature for 20 minutes. Benzyl Bromide (30 μL, 0.28 mmol) was added and the

reaction was stirred for three hours. Ice water was added to decompose the excess sodium hydride and the reaction was diluted with DCM and washed with water. The organic layer was dried with sodium sulfate and concentrated. Column chromatography (4:1 hexane/ethyl acetate) gave **20** (315 mg, 91%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.21 (15H, Ph), 7.17-7.12 (2H, Ph), 6.91 (d, 2H, J=7.0 Hz, Ph), 4.91, 4.86, 4.82, 4.75, 4.64, 4.59, 4,54, 4.50 (d, 1H, J=11.0 Hz, PhC$\underline{H}_2$), 4.36 (d, 1H, $J_{1,2}$=7.8 Hz, H-1), 3.94 (dt, 1H, J=6.2, 9.5 Hz, OC$\underline{H}_2CH_2$), 3.77 (s, 3H, OCH_3), 3.73 (dd, 1H $J_{3,4}$= 2.0, $J_{2,3}$=9.0 Hz, H-3), 3.65 (dd, 1H, $J_{3,4}$=4.8, $J_{4,5}$=10.8 Hz, H-4), 3.60 (dd, 1H, $J_{5,6a}$=$J_{6a,6b}$=8.4 Hz, H-6a), 3.46-3.38 (2H, H-5, OC$\underline{H}_2CH_2$), 3.46-3.38 (2H, H-2, H-6b), 1.67 (2H, $OCH_2C\underline{H}_2$), 1.50-1.22 (10H, CH_2, octyl), 0.86 (t, 3H, J=7.0 Hz, CH_3, octyl). *Anal.* Calcd for $C_{45}H_{60}O_6$ (682.88): C, 75.63; H, 7.97. Found: C, 75.44; H, 8.16.

Octyl 2,4,6-tri-O-*benzyl-3*-O-p-*methoxybenzyl-β*-D-*glucopyranoside* (**21**)

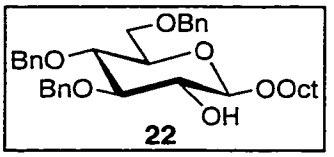


21

Compound **21** (430 mg, 95%) was synthesized from **19** (400 mg, 0.60 mmol) in dry DMF (4mL) containing sodium hydride (50 mg, 60% dispersion in oil, 1.3 mmol) and benzyl bromide (120 μL, 1.1 mmol) as described for **20**: $[\alpha]_D$ +3.8° (c 1.0, $CHCl_3$); mp 62.5-63.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37-7.23 (17H, Ph), 6.80 (d, 2H, J=8.7 Hz, Ph), 4.95, 4.83, 4.81, 4.71, 4.69, 4.59, 4,53, 4.51 (d, 1H, J=11.0 Hz, PhC$\underline{H}_2$), 4.36 (d, 1H, $J_{1,2}$=7.8 Hz, H-1), 3.92 (dt, 1H, J=6.4, 9.5 Hz, OC$\underline{H}_2CH_2$), 3.77 (s, 3H, OCH_3), 3.73 (dd, 1H $J_{3,4}$=1.9, $J_{2,3}$=10.8 Hz, H-3), 3.64 (dd, 1H, $J_{3,4}$=4.8, $J_{4,5}$=10.7 Hz, H-4), 3.61 (dd, 1H, $J_{5,6a}$=$J_{6a,6b}$=8.9 Hz, H-6a), 3.56-3.49 (2H, H-5, OC$\underline{H}_2CH_2$), 3.47-3.41 (2H, H-2, H-6b), 1.64 (2H, $OCH_2C\underline{H}_2$), 1.42-1.20

(10H, CH_2, octyl), 0.86 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.2, 138.6, 138.4, 138.3, 130.9 (aromatic quat.), 129.6, 128.4, 128.3, 128.2, 128.0, 127.8, 127.7, 113.8 (aromatic CH), 103.7 (C-1), 84.5, 82.4, 78.1, 74.9 (C-2, C-3, C-4, C-5), 75.4, 75.0, 74.8, 73.5, 70.2, 69.1 (C-6, O<u>C</u>H_2CH_2, Ph<u>C</u>H_2x4), 55.3 (OCH_3), 31.9, 29.9, 29.5, 29.3, 26.3, 22.7 (CH_2, octyl), 14.1 (CH_3, octyl). *Anal.* Calcd for $C_{43}H_{54}O_7$ (682.88): C, 75.63; H, 7.97. Found: C, 75.75; H, 8.27.

*Octyl 3,4,6-tri-*O*-benzyl-β-*D*-glucopyranoside* (**22**)

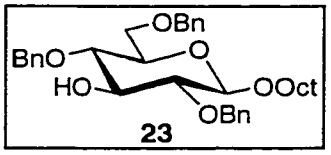


22

Compound **20** (135 mg, 0.18 mmol) was dissolved in DCM (2 mL) and DDQ (60 mg, 0.27 mmol) was added. The solution was stirred for two hours at room temperature and additional DDQ (28 mg, 0.13 mmol) was added before stirring for an additional 2 hours. The solution was diluted with DCM and washed with water. The organic layer was dried over sodium sulfate and concentrated under reduced pressure. Column chromatography (4:1 hexane/ethyl acetate) gave **22** (75 mg, 63%) as a white solid: $[\alpha]_D$ -5.6° (c 0.6, $CHCl_3$); mp 34.0-37.0 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.45-7.18 (15H, Ph), 4.95, 4.84, 4.62, 4.58, 4,55, 4.51 (d, 6H, J=11.0 Hz, PhC<u>H</u>$_2$), 4.24 (d, 1H, $J_{1,2}$=7.1 Hz, H-1), 3.91 (dt, 1H, J=6.4, 9.5 Hz, OC<u>H</u>$_2CH_2$), 3.75 (dd, 1H, $J_{3,4}$= 2.1, $J_{2,3}$=10.8 Hz, H-3), 3.62-3.44 (5H, H-2, H-5, H-6a , H-6b, OC<u>H</u>$_2CH_2$), 2.17 (bs, 1H, OH), 1.84 (2H, OCH_2C<u>H</u>$_2$), 1.42-1.22 (10H, CH_2, octyl), 0.86 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.4, 138.9, 138.8 (aromatic quat.), 129.2, 129.1, 129.0, 128.7, 128.6, 128.5, 128.4, 128.3 (aromatic CH), 103.4 (C-1), 85.2, 78.3, 75.4, 74.2 (C-2, C-3, C-4, C-5), 75.9, 75.3, 73.7, 70.8, 69.6

(C-6, O<u>C</u>H$_2$CH$_2$, Ph<u>C</u>H$_2$x3), 32.5, 30.3, 30.1, 29.9, 26.7, 23.4 (CH$_2$, octyl), 14.8 (CH$_3$, octyl).

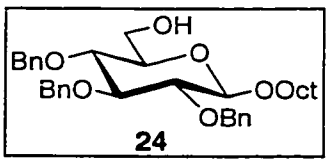
*Octyl 2,4,6-tri-*O*-benzyl-β-*D*-glucopyranoside* (**23**)



23

Compound **23** (225 mg, 69%) was prepared, as a white solid, from **21** (380 mg, 0.50 mmol) by reaction in DCM (5 mL) with DDQ (171 mg, 0.75 mmol) as described for the preparation of **22**: $[\alpha]_D$ +14.0° (c 1.2, $CHCl_3$); mp 47.0-49.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41-7.22 (15H, Ph), 4.88, 4.82, 4.65, 4.60, 4,58, 4.53 (d, 6H, J=11.3 Hz, PhC<u>H</u>$_2$), 4.36 (d, 1H, $J_{1,2}$=7.8 Hz, H-1), 3.92 (dt, 1H, J=6.4, 9.5 Hz, OC<u>H</u>$_2$CH$_2$), 3.78-3.63 (3H, H-3, H-4, H-6a), 3.55-3.40 (3H, H-2, H-5, OC<u>H</u>$_2$CH$_2$), 3.25 d, 1H, J=7.8, 9.2 Hz, H-6b), 2.40 (bs, 1H, OH), 1.65 (2H, OCH$_2$C<u>H</u>$_2$), 1.42-1.20 (10H, CH$_2$, octyl), 0.86 (t, 3H, J=7.0 Hz, CH$_3$, octyl); ^{13}C NMR (75 MHz,$CDCl_3$) δ 138.4, 138.2, 138.1 (aromatic quat.), 129.2, 129.1, 129.0, 128.7, 128.6, 128.5, 128.4, 128.3 (aromatic CH), 103.3 (C-1), 81.3, 77.4, 76.6, 74.3 (C-2, C-3, C-4, C-5), 74.6, 74.4, 73.5, 70.1, 69.2 (C-6, O<u>C</u>H$_2$CH$_2$, Ph<u>C</u>H$_2$x3), 31.9, 30.0, 29.8, 29.5, 26.2, 22.7 (CH$_2$, octyl), 14.1 (CH$_3$, octyl).

*Octyl 2,3,4-tri-*O*-benzyl-β-*D*-glucopyranoside* (**24**)

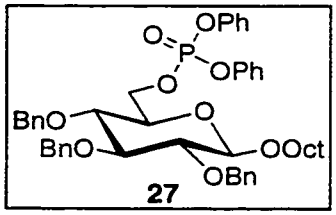


24

*Octyl 2,3-di-*O*-benzyl-4,6-di-*O*-benzylidene-β-*D*-glucopyranoside* [58] (757 mg, 1.12 mmol) was dissolved in diethyl ether (10 mL) and lithium aluminum hydride (80 mg, 2.1 mmol) was added.

The solution was heated to 40°C and aluminum trichloride (284 mg, 2.2 mmol) in diethyl ether (5 mL) was added dropwise. The solution was stirred for 3 hours at 40°C, diluted in ethyl acetate, washed with water, and concentrated under reduced pressure. Column chromatography (5:1 hexane/ethyl acetate) gave **24** (400 mg, 53%) as a white solid: $[\alpha]_D$ +2.4° (c 0.9, $CHCl_3$); mp 64.0-65.0 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.38-7.22 (15H, Ph), 4.94, 4.93, 4.85, 4.79, 4,71, 4.63 (d, 6H, J=11.3 Hz, $PhC\underline{H}_2$), 4.43 (d, 1H, $J_{1,2}$=7.8 Hz, H-1), 3.91 (dt, 1H, J=6.4, 9.5 Hz, $OC\underline{H}_2CH_2$), 3.84 (1H, H-6a), 3.71 (1H, H-6b), 3.64 (dd, 1H, $J_{2,3}=J_{3,4}$=8.9 Hz, H-3), 3.58-3.49 (2H, H-4, $OC\underline{H}_2CH_2$), 3.41 (dd, 1H, $J_{1,2}$=7.8, $J_{2,3}$=9.2 Hz, H-2), 3.34 (1H- H-5), 1.89(dd, 1H, J=7.9, 6.1 Hz, OH), 1.64 (2H, $OCH_2C\underline{H}_2$), 1.42-1.22 (10H, CH_2, octyl), 0.87 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.2, 139.1, 138.6 (aromatic quat.), 129.2, 129.1, 128.8, 128.7, 128.6, 128.4, 128.3 (aromatic CH), 104.4 (C-1), 85.2, 83.0, 78.3, 75.7 (C-2, C-3, C-4, C-5), 76.4, 75.8, 75.6, 71.2, 62.8 (C-6, $O\underline{C}H_2CH_2$, $Ph\underline{C}H_2$x3), 32.5, 30.5, 30.1, 30.0, 26.9, 23.4 (CH_2, octyl), 14.8 (CH_3, octyl). *Anal.* Calcd for $C_{35}H_{46}O_6$ (562.74): C, 74.73; H, 8.24. Found: C, 74.54; H, 8.23.

Octyl 2,3,4-tri-O-benzyl-6-O-diphenoxyphosphoryl-β-D-glucopyranoside (**27**)

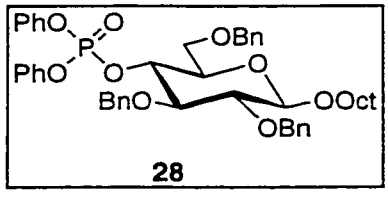


27

Compound **24** (50 mg, 0.09 mmol) was dissolved in pyridine (1 mL) and the solution was cooled to 0°C. To the cooled solution, DMAP (27 mg, 0.22 mmol) and diphenylphosphorochloridate (30 μL, 0.14 mmol) was added, and the solution was allowed to warm to room temperature. After 15 hours the solution was diluted with DCM, and washed sequentially

with water, sodium bicarbonate and water followed by concentration under reduced pressure. Column chromatography (3:1 hexane/ethyl acetate) resulted in **27** (43 mg, 60%) as an oil: $[\alpha]_D$ -3.6° (c 0.8, $CHCl_3$); mp 64.0-65.0 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.34-7.12 (25H, Ph), 4.93, 4.91, 4.77, 4.76, 4,69 (d, 6H, J=11.3 Hz, PhC$\underline{H}_2$), 4.51 (ddd, 1H, J= 1.7, 6.4, 11.0 Hz, H-6a), 4.45 (d, 6H, J=10.8 Hz, PhC$\underline{H}_2$), 4.38 (d, 1H, $J_{1,2}$=7.8 Hz, H-1), 4.32 (ddd, 1H, J=3.6, 7.2, 12.6 Hz, H-6b), 3.87 (dt, 1H, J=6.4, 9.5 Hz, OC$\underline{H}_2CH_2$), 3.63 (dd, 1H, $J_{2,3}$=$J_{3,4}$=8.9 Hz, H-3), 3.52-3.43 (3H, H-4, H-5, OC$\underline{H}_2CH_2$), 3.39 (dd, 1H, $J_{1,2}$=7.8, $J_{2,3}$=9.1 Hz, H-2), 1.60 (2H, $OCH_2C\underline{H}_2$), 1.39-1.20 (10H CH_2, octyl), 0.86 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.6, 150.5 (d, J=5.5 Hz, aromatic quat.), 138.5, 138.4, 137.8 (aromatic quat.), 129.8, 129.7, 128.5, 128.4, 128.2, 128.1, 128.0, 127.7 (aromatic CH), 125.4, 125.3 (d, $J_{C,P}$=1.5 Hz, aromatic CH), 120.3, 120.1 (d, $J_{C,P}$=4.5 Hz, aromatic CH), 103.5 (C-1), 85.5 (C-3), 82.2 (C-2), 77.1 (C-4), 76.5, 75.9, 71.5 (Ph$\underline{C}H_2$x3), 73.5 (d, $J_{5,P}$=7.6 Hz, C-5), 71.4 (O$\underline{C}H_2CH_2$), 67.7 (d, $J_{6,P}$=5.9 Hz, C-6), 31.9, 29.8, 29.4, 29.3, 26.2, 22.7 (CH_2, octyl), 14.1 (CH_3, octyl). HR-ESMS calcd for $C_{47}H_{55}NO_9Na$ 817.3481, found 817.3482. *Anal.* Calcd for $C_{47}H_{55}O_9$ (794.91): C, 71.01; H, 6.97. Found: C, 71.04; H, 6.96.

Octyl 2,3,6-tri-O-*benzyl-4*-O-*diphenoxyphosphoryl-β*-D-*glucopyranoside* (**28**)

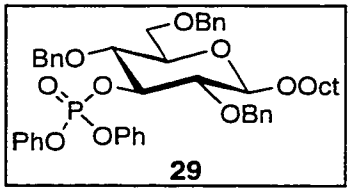


28

Compound **28** (83 mg, 63%) was synthesized from *Octyl 2,3,6-tri*-O-*benzyl-β*-D-*glucopyranoside* [62] (90 mg, 0.16 mmol), diphenylphosphorochloridate (80 μL, 0.35 mmol), DMAP (32 mg 0.26 mmol), and pyridine (2 mL) as described for the preparation of **27**:

$[\alpha]_D$ +3.6° (c 1.3, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.30-7.02 (25H, Ph), 4.92, 4.86, 4.72, 4.64, (d, 4H, J=10.8 Hz, PhC$\underline{H}_2$), 4.62 (ddd, 1H, $J_{3,4}$=$J_{4,5}$=9.3, $J_{4,P}$=9.5 Hz), 4.57 (d, 1H, J=12.0 Hz, PhC$\underline{H}_2$), 4.43 (d, 1H, $J_{1,2}$=7.5 Hz, H-1), 4.41 (d, 1H, J=11.8 Hz, PhC$\underline{H}_2$, H-2), 3.93 (dt, 1H, J=6.4, 9.5 Hz, OC$\underline{H}_2CH_2$), 3.75-3.71 (2H, H-3, H-6a), 3.66-3.60 (2H, H-5, H-6b), 3.52 (dt, 1H, J=6.7, 9.5 Hz, OC$\underline{H}_2CH_2$), 3.50 (dd, 1H, $J_{1,2}$=7.9, $J_{2,3}$=9.1 Hz), 1.63 (2H, $OCH_2C\underline{H}_2$), 1.41-1.22 (10H, CH_2, octyl), 0.88 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.6, 150.5 (d, $J_{C,P}$=5.5 Hz, aromatic quat.), 138.3, 138.2 (aromatic quat.), 129.7, 129.6, 128.3, 128.2, 128.1, 127.7, 127.6, 127.5, 127.3 (aromatic CH), 125.4, 125.3 (d, $J_{C,P}$=1.2 Hz, aromatic CH), 120.3, 120.1 (d, $J_{C,P}$=4.8 Hz, aromatic CH), 103.5 (C-1), 82.2 (d, $J_{3,P}$=2.8 Hz, C-3), 82.0 (C-2), 77.2 (C-4), 75.0, 74.8, 73.4 (Ph$\underline{C}H_2$x3), 74.2 (d, $J_{5,P}$=5.6 Hz, C-5), 70.3 (O$\underline{C}H_2CH_2$), 69.1 (C-6), 31.9, 29.8, 29.5, 29.3, 26.2, 22.7 (CH_2, octyl), 14.1 (CH_3, octyl). HR-ESMS calcd for $C_{47}H_{55}NO_9Na$ 817.3481, found 817.3488. *Anal.* Calcd for $C_{47}H_{55}O_9$ (794.91): C, 71.01; H, 6.97. Found: C, 70.84; H, 7.06.

*Octyl 2,4,6-tri-*O*-benzyl-3-*O*-diphenoxyphosphoryl-β-*D*-glucopyranoside* (**29**)

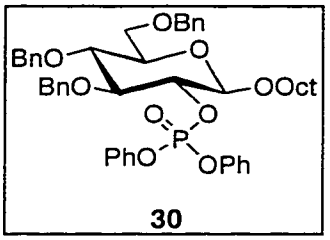


29

Compound **29** (57 mg, 92%) was synthesized from compound **22** (44 mg, 0.051 mmol), diphenylphosphorochloridate (40 μL, 0.17 mmol), DMAP (32 mg, 0.26 mmol) and pyridine (2 mL) as described for **27**: $[\alpha]_D$ +3.2° (c 0.3, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.18-7.00 (25H, Ph), 4.89 (d, 1H, J=10.8 Hz, PhC$\underline{H}_2$), 4.81 (ddd, 1H, $J_{2,3}$=$J_{3,4}$=8.9, $J_{3,P}$=17.8 Hz, H-3), 4.77, 4.65, 4.59, 4.53, 4.45 (d, 1H, J=10.8 Hz, PhC$\underline{H}_2$), 4.20 (d, 1H, $J_{1,2}$=7.6 Hz, H-

1), 3.92 (dt, 1H, J=6.6, 9.5 Hz, OC$\underline{H}_2CH_2$), 3.77 (dd, 1H, $J_{3,4}=J_{4,5}=9.5$ Hz, H-4), 3.72-3.67 (2H, H-6a, H-6b), 3.53 (dd, 1H, $J_{1,2}=7.8$, $J_{2,3}=9.2$ Hz, H-2), 3.51-3.44 (2H, H-5, OC$\underline{H}_2CH_2$), 1.50-1.42 (2H, $OCH_2C\underline{H}_2$), 1.30-1.14 (10H, CH_2, octyl), 0.88 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (75 MHz,$CDCl_3$) δ 150.6, 150.5 (d, $J_{C,P}=3.2$ Hz, aromatic quat.), 138.2, 138.0, 137.8 (aromatic quat.), 129.5, 128.4, 128.2, 128.1, 128.0, 127.9, 127.8, 127.6, 127.3 (aromatic CH), 125.0 (d, $J_{C,P}=1.2$ Hz, aromatic CH), 120.1 (d, $J_{C,P}=5.0$ Hz, aromatic CH), 103.4 (C-1), 83.9 (d, $J_{3,P}=8.0$ Hz, C-3), 82.0 (d, $J_{2,P}=2.4$ Hz, C-2), 76.8 (d, $J_{4,P}=4.2$ Hz, C-4), 74.5, 74.1, 73.6 (Ph$\underline{C}H_2$x3), 74.3 (C-5), 70.3 (O$\underline{C}H_2CH_2$), 68.6 (C-6), 31.8, 29.8, 29.3, 29.2, 26.1, 22.7 (CH_2, octyl), 14.1 (CH_3, octyl). *Anal.* Calcd for $C_{47}H_{55}O_9$ (794.91): C, 71.01; H, 6.97. Found: C, 71.08; H, 6.97.

*Octyl 3,4,6-tri-*O*-benzyl-2-*O*-diphenoxyphosphoryl-β-*D*-glucopyranoside* (**30**)

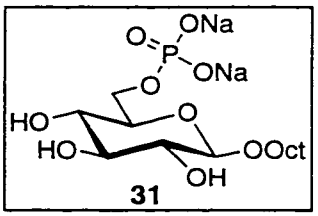


30

Compound **30** (42 mg, 87%) was synthesized from compound **23** (34 mg, 0.060 mmol), diphenylphosphorochloridate (30 μL, 0.13 mmol), DMAP (22 mg, 0.18 mmol) and pyridine (2 mL) as described for **24**: $[\alpha]_D$ –7.0° (c 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35-7.10 (25H, Ph), 4.84 (d, 1H, J=10.8 Hz, PhC$\underline{H}_2$), 4.75 (d, 2H, J=10.8 Hz, PhC$\underline{H}_2$), 4.61 (d, 1H, J=10.8 Hz, PhC$\underline{H}_2$), 4.58-4.49 (4H, H-1, H-2, PhC$\underline{H}_2$), 3.82-3.61 (5H, H-3, H-4, H-6a, H-6b, OC$\underline{H}_2CH_2$), 3.51 (ddd, 1H, J=2.0, 4.6, 9.8 Hz, H-5), 3.44 (dt, 1H, J=7.3, 9.2 Hz, OC$\underline{H}_2CH_2$), 1.48 (2H, $OCH_2C\underline{H}_2$), 1.30-1.14 (10H, CH_2, octyl), 0.88 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (75 MHz,$CDCl_3$) δ 150.9, 150.8 (d, $J_{C,P}=6.8$ Hz, aromatic quat.), 138.2, 138.1, 137.9 (aromatic quat.), 129.5, 128.4, 128.2,

128.1, 128.0, 127.8, 127.6, 127.5, 125.0 (aromatic CH), 120.2 (d, $J_{C,P}$=5.7 Hz, aromatic CH), 101.1 (d, $J_{1,P}$=3.2 Hz, C-1), 83.5 (d, $J_{3,P}$=4.1 Hz, C-3), 82.0 (d, $J_{2,P}$=7.1 Hz, C-2), 78.0 (C-4), 75.2, 75.0, 73.5 (Ph$\underline{C}H_2$x3), 75.1 (C-5), 70.2 (O$\underline{C}H_2CH_2$), 68.7 (C-6), 31.9, 29.5, 29.4, 29.2, 25.9, 22.7 (CH_2 octyl), 14.1 (CH_3 octyl). *Anal.* Calcd for $C_{47}H_{55}O_9$ (794.91): C, 71.01; H, 6.97. Found: C, 70.83; H, 6.96.

Octyl 6-O-disodiumphosphate-β-D-glucopyranoside (**31**)

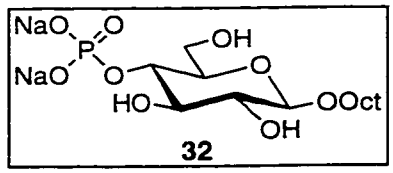


31

Compound **27** (43 mg, 0.05 mmol) was dissolved in 95% ethanol (2 mL) containing 5% palladium on charcoal (8 mg) and the mixture was stirred under hydrogen gas at ambient pressure for 15 hours. The catalyst was removed by filtration, the solvent concentrated and the residue was redisolved in 95% ethanol (4 mL). Adams' catalyst (PtO_2, 7 mg) was added and the mixture was stirred under hydrogen gas for 3 hours. The solution was filtered and concentrated. The resulting residue was dissolved in water and purified on a C-18 Sep-Pak cartridge using water and methanol. The carbohydrate containing fractions were pooled, concentrated and converted to the sodium salt by passage through Dowex 50-X8 (Na+) cation exchange resin. Lyophilization of the eluent provided **31** (19 mg, 90%): ^{1}H NMR (600 MHz, D_2O (0.05M $NaDCO_3$ 0.045M NaOD)) δ 4.43 (d, 1H, $J_{1,2}$=8.0 Hz, H-1), (4.02 (ddd, 1H, $J_{5,6a}$=4.0, $J_{6a,P}$=7.5, $J_{6a,6b}$=12.2 Hz), 3.89 (dt. 1H. J=7.0, 9.9 Hz, O$\underline{H}_2CH_2$), 3.64 (dt, 1H, J=7.0, 9.9 Hz, O$\underline{H}_2CH_2$), 3.59 (dd, 1H, $J_{3,4}$=$J_{4,5}$=9.5 Hz, H-4), 3.48 (dd, 1H, $J_{2,3}$=$J_{3,4}$=9.3 Hz, H-3), 3.44 (ddd, 1H, $J_{5,6b}$=2.6, $J_{5,6a}$= 3.5, $J_{4,5}$=9.7 Hz, H-5), 3.27 (dd, 1H, $J_{1,2}$=8.1, $J_{2,3}$=9.1 Hz, H-2), 1.61 (2H, $OCH_2C\underline{H}_2$), 1.56-1.22 (10H, CH_2,

octyl), 0.88 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (125 MHz, D_2O) δ 103.5 (C-1), 76.3 (C-3), 75.3 (d, J=10.2 Hz, C-5), 73.8 (C-2), 71.4 ($O\underline{C}H_2CH_2$), 69.7 (C-4), 64.5 (d, J=5.9 Hz, C-6), 31.8, 29.4, 29.2, 29.1, 25.7, 22.6 (CH_2, octyl), 14.1 (CH_3, octyl); HR-ESMS calcd for $C_{14}H_{28}O_9Na_2P$ 417.1266, found 417.1262.

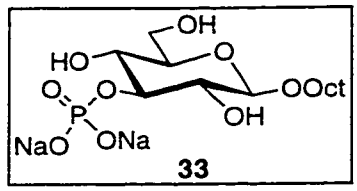
Octyl 4-O-disodiumphosphate-β-D-glucopyranoside (**32**)



32

Compound **32** (14 mg, 84%) was deprotected in the same fashion as **31** from compound **28** (31 mg, 0.039 mmol): ^1H NMR (600 MHz, D_2O(0.05M $NaDCO_3$ 0.045M NaOD)) δ 4.44 (d, 1H, $J_{1,2}$=8.1 Hz, H-1), 3.89 (dt, 1H, J=6.4, 9.5 Hz, $OC\underline{H}_2CH_2$), 3.85-3.78 (3H, H-4, H-6a, H-6b), 3.68-3.64 (2H, H-3, $OC\underline{H}_2CH_2$), 3.46 (dddd, 1H, J=2.4, 4.8, 7.1, 9.7 Hz, H-5), 3.30 (dd, 1H, $J_{1,2}$=8.2, $J_{2,3}$=9.3 Hz, H-2), 1.64-1.58 (2H, $OCH_2C\underline{H}_2$), 1.38-1.24 (10H, CH_2, octyl), 0.85 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (75 MHz, D_2O) δ 103.1 (C-1), 75.9 (d, $J_{3,P}$=2.0 Hz, C-3), 75.9 (d, $J_{5,P}$=6.0 Hz, C-5), 74.7 (d, J=6.0 Hz, C-2), 73.8 (C-4), 71.6 ($O\underline{C}H_2CH_2$), 61.4 (C-6), 31.9, 29.6, 29.3, 29.2, 25.9, 22.9 (CH_2 octyl), 14.3 (CH_3 octyl); HR-ESMS calcd for $C_{14}H_{28}O_9Na_2P$ 417.1266, found 417.1267.

Octyl 3-O-disodiumphosphate-β-D-glucopyranoside (**33**)

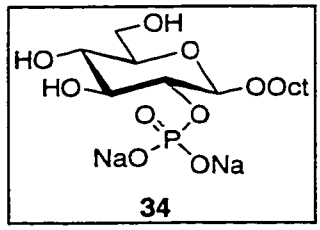


33

Compound **33** (7 mg, 90%) was deprotected in the same fashion as **31** from compound **29** (15 mg, 0.020 mmol): ^1H NMR (600 MHz, D_2O (0.05M $NaDCO_3$ 0.045M NaOD)) δ

4.50 (d, 1H, $J_{1,2}$=8.2 Hz, H-1), 3.97-3.88 (3H, H-3, H-6a, OC<u>H</u>$_2$CH$_2$), 3.73-3.63 (2H, H-5, OC<u>H</u>$_2$CH$_2$), 3.58-3.47 (2H, H-4, H-6b), 3.34 (dd, 1H, $J_{1,2}$=$J_{2,3}$=8.4 Hz, H-2), 1.64-1.60 (2H, OCH$_2$C<u>H</u>$_2$), 1.37-1.22 (10H, CH$_2$, octyl), 0.85 (t, 3H, J=7.0 Hz, CH$_3$, octyl); ^{13}C NMR (125 MHz, D_2O) δ 103.0 (C-1), 81.7 (d, $J_{3,P}$=6.1 Hz, C-3), 76.5 (C-5), 73.8 (d, $J_{2,P}$=3.7 Hz, C-2), 71.9 (O<u>C</u>H$_2$CH$_2$), 70.3 (d, $J_{4,P}$=3.7 Hz, C-4), 61.7 (C-6), 31.9, 29.6, 29.3, 29.2, 25.9, 22.8 (CH$_2$, octyl), 14.3 (CH$_3$, octyl); HR-ESMS calcd for $C_{14}H_{27}O_9Na_3P$ 439.1086, found 439.1082.

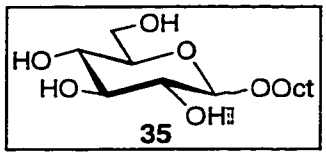
Octyl 2-O-disodiumphosphate-β-D-glucopyranoside (**34**)



34

Compound **34** (4 mg, 78%) was deprotected in the same fashion as **31** from compound **30** (10 mg, 0.012 mmol): ^{1}H NMR (600 MHz, D_2O (0.05M $NaDCO_3$ 0.045M NaOD)) δ 4.49 (d, 1H, $J_{1,2}$=7.5 Hz, H-1), 3.92-3.86 (2H, H-6a, OC<u>H</u>$_2$CH$_2$), 3.73-3.66 (4H, H-2, H-3, H-6b, OC<u>H</u>$_2$CH$_2$), 3.49-3.41 (2H, H-4, H-5), 1.65-1.60 (2H, OCH$_2$C<u>H</u>$_2$), 1.36-1.24 (10H CH$_2$ octyl), 0.86 (t, 3H, J=7.0 Hz, CH$_3$ octyl); ^{13}C NMR (75 MHz, D_2O) δ 103.0 (d, $J_{1,P}$=7.3 Hz, C-1), 81.7 (d, J=6.1 Hz, C-3), 76.5 (C-5), 73.8 (d, $J_{2,P}$=3.7 Hz, C-2), 71.9 (O<u>C</u>H$_2$CH$_2$), 70.3 (d, $J_{4,P}$=3.7 Hz, C-4), 61.7 (C-6), 31.9, 29.6, 29.3, 29.2, 25.9, 22.8 (CH$_2$ octyl), 14.3 (CH$_3$ octyl); HR-ESMS calcd for $C_{14}H_{27}O_9Na_3P$ 439.1086, found 439.1089.

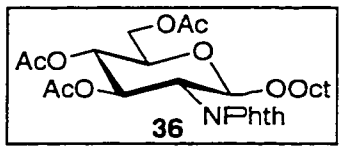
Octyl β-D-glucopyranoside (**35**)



Octyl 4,6-O-benzylidene-β-D-glucopyranoside [55] (50 mg, 0.13 mmol) was dissolved in 70% acetic acid and heated to 70°C for 2 hours. The solution was cooled to room temperature, diluted with toluene, and concentrated to provide a white solid. The resulting material was dissolved in water and purified on a C-18 Sep-Pak cartridge using water and methanol. The carbohydrate containing fractions were pooled, concentrated and lyophilized to afford **35** (36 mg, quant.): ^{1}H NMR (600 MHz, D_2O (0.05M $NaDCO_3$ 0.045M NaOD)) δ 4.37 (d, 1H, $J_{1,2}$=8.0 Hz, H–1), 3.88 (dt, 1H, J=7.0, 9.2 Hz, $OC\underline{H}_2CH_2$), 3.86 (dd 1H, $J_{5,6a}$=2.4, $J_{6a,6b}$=12.2 Hz, H-6a), 3.77 (dd 1H, $J_{5,6b}$=4.8, $J_{6a,6b}$=12.2 Hz, H-6a), 3.47 (1H, H-3), 3.43 (dd, 1H, $J_{3,4}$=$J_{4,5}$=8.8 Hz, H-4), 3.38 (1H, H-5), 3.27 (2H, H-2, $OC\underline{H}_2CH_2$), 1.65-1.60 (2H, $OCH_2C\underline{H}_2$), 1.36-1.24 (10H CH_2 octyl), 0.86 (t, 3H, J=7.0 Hz, CH_3 octyl); ^{13}C NMR (75 MHz, D_2O) δ 102.8 (C-1), 76.9 (C-3), 76.5 (C-5), 73.8 (C-2), 71.9 ($O\underline{C}H_2CH_2$), 70.1 (C-4), 61.7 (C-6), 31.9, 29.6, 29.3, 29.2, 25.9, 22.8 (CH_2, octyl), 14.3 (CH_3, octyl).

3.1.2 Synthesis of Octyl β-GlcNPhth Acceptors and ThioGal Donors

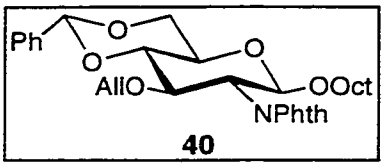
Octyl 3,4,6-tri-O-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (**36**)



1,3,4,6-tetra-O-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranoside [62] (6.79 g, 14.2 mmol) was dissolved in 30

mL 30% hydrobromic acid/acetic acid and stirred at room temperature for 3 hours. The solution was diluted with DCM (200 mL), washed twice with water (100 mL) and once with sodium bicarbonate (150 mL). The organic fraction was dried over magnesium sulfate and concentrated. Co-evaporation with toluene (2x60 mL) resulted in a white solid, which was carried directly on to the next step without further purification. The solid was dissolved in dry DCM (100 mL) containing activated 4 Å molecular sieves. 1-Octanol (10.0 mL, 63 mmol) was syringed into the mixture followed by the addition of crushed silver zeolite (823 mg 1.070 Ag mol/g). The solution was heated to 40°C, stirred for 48 hours, filtered through celite and concentrated under reduced pressure affording a colorless oil. Column chromatography (5:1 pentane/ethyl acetate) yielded **36** (6.81 g, 88%): $[\alpha]_D$ +21.1° (c 1.4, $CHCl_3$); mp 24.0-25.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84 (2H, Phth), 7.73 (2H, Phth), 5.77 (dd, 1H, $J_{2,3}$=9.1, $J_{3,4}$=10.8 Hz, H-3), 5.33 (d, 1H, $J_{1,2}$=8.5 Hz, H-1), 5.15 (dd, 1H, $J_{3,4}$=$J_{4,5}$=10.0 Hz, H-4), 4.35-4.26 (2H, H-2, H-6a), 4.15 (dd, 1H, $J_{5,6b}$=2.4, $J_{6a,6b}$=12.3 Hz, H-6b), 3.88-3.77 (2H, H-5, $OC\underline{H}_2CH_2$), 3.41 (dt, 1H, J=6.5, 9.7 Hz, $OC\underline{H}_2CH_2$), 2.09, 2.01, 1.84 (s, 3H, $COC\underline{H}_3$), 1.44-1.32 (2H, $OCH_2C\underline{H}_2$), 1.22-0.88 (10H, CH_2, octyl), 0.79 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (75 MHz $CDCl_3$) δ 170.8,170.2, 169.5 (CO, acetate), 134.3, 131.5, 123.6 (aromatic CH), 98.3 (C-1), 71.9, 70.9, 69.2 (C-3, C-4, C-5), 70.3 ($O\underline{C}H_2CH_2$), 62.2 (C-6), 54.8 (C-2), 31.7,.29.3, 29.1, 25.8, 22.6 (CH_2, octyl), 14.1 (CH_3, octyl). *Anal.* Calcd for $C_{28}H_{36}O_{10}$ (547.60): C, 71.01; H, 6.97. Found: C, 71.04; H, 6.96.

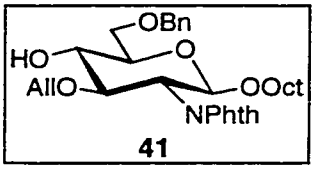
Octyl 3-O-allyl-4,6-O-benzylidene-2-deoxy-2-phthalimido-β-D-glucopyranoside (**40**)



40

Octyl 4,6-O-benzylidene-2-deoxy-2-phthalimido-β-D-glucopyranoside [62] (2.11 g, 4.17 mmol) was dissolved in DMF (20 mL) and cooled to 0°. Sodium hydride (180 mg, 60% dispersion in oil, 4.59 mmol) was added to the solution and allowed to stir for 30 minutes. Allyl bromide (550 μL, 6.23 mmol) was added and the solution was warmed to room temperature and stirred for an additional 3 hours. Methanol was added to decompose the excess sodium hydride and the solution was diluted with toluene, extracted with water and concentrated under reduced pressure. Column chromatography (10:1 hexane/ethyl acetate) gave unreacted starting material (520 mg 24%) and **40** (1.28 g 56%): $[\alpha]_D$ +21.3° (c 0.9, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.92-7.72 (4H, Phth), 7.28-7.15 (5H, Ph), 5.58 (s, 1H, $PhC\underline{H}O_2$), 5.56 (1H, H_c allyl), 5.23 (d, 1H, $J_{1,2}$=8.4 Hz, H-1), 5.02 (1H, H_a allyl), 4.85 (1H, H_b allyl), 4.44-4.35 (2H, H-3, H-6a), 4.30-4.19 (2H, H-2, H_d allyl), 3.96 (1H, H_e allyl), 3.88-3.70 (3H, H-4, H-6b, $OC\underline{H}_2CH_2$), 3.61 (ddd, 1H, J=4.8, 9.7, 9.7 Hz, H-5), 3.40 (dt, 1H, J=6.6, 9.8 Hz, $OC\underline{H}_2CH_2$), 1.52-1.30 (2H, $OCH_2C\underline{H}_2$), 1.20-0.92 (10H, CH_2, octyl), 0.80 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.1 (CO, Phth), 137.3, 131.7 (aromatic quat.), 134.5 ($CH_2=\underline{C}HCH_2O$), 134.1, 129.0, 128.2, 126.0 (aromatic CH), 116.8 ($\underline{C}H_2=CHCH_2O$), 101.3, 99.1, 82.8, 75.2, 66.2 (C-1, C-3, C-4, C-5, $Ph\underline{C}HO_2$), 73.1, 70.1, 68.8 (C-6, $O\underline{C}H_2CH_2$, $CH_2=CH\underline{C}H_2O$), 55.0 (C-2), 31.6, 29.3, 29.1, 29.0, 25.7, 22.6 (CH_2 octyl), 14.0 (CH_3 octyl). *Anal.* Calcd for $C_{32}H_{39}NO_7$ (553.29): C, 69.51; H, 6.96. Found: C, 69.71; H, 7.26.

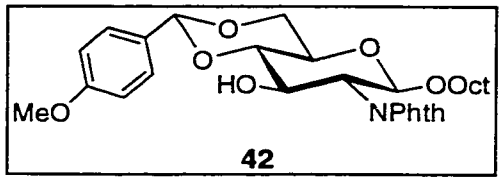
Octyl 6-O-benzyl-3-O-allyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (**41**)



41

Compound **40** (1.28 g, 2.39 mmol), sodium cyanoborohydride (753 mg, 11.95 mmol) and methyl orange indicator were dissolved in dry tetrahydrofuran (THF) containing crushed 4 Å molecular sieves. The solution was cooled to 0°C and ethereal hydrogen chloride was added dropwise until the red color of the solution persisted. The mixture was warmed to room temperature and stirred for an additional hour, filtered through celite, washed with water and brine and concentrated under reduced pressure. Column chromatography of the resulting pink oil (5:1 hexane/ethyl acetate) afforded **41** (1.24 g 96%) as a colorless oil: $[\alpha]_D$ +23.2° (c 0.4, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.91-7.68 (4H, Phth), 7.38-7.22 (5H, Ph), 5.60 (1H, H_c allyl), 5.14 (d, 1H, $J_{1,2}$=8.4 Hz, H-1), 5.05 (1H, H_a allyl), 4.87 (1H, H_b allyl), 4.63, 4.57 (d, 1H, J=12.0 Hz, $PhCH_2$), 4.22-4.13 (3H, H-2, H-3, H_d allyl), 3.97 (1H, H_e allyl), 3.84-3.71 (4H, H-4, H-6a, H-6b, OCH_2CH_2), 3.63 (ddd, 1H, H-5), 3.38 (dt, 1H, J=6.4, 9.2 Hz, OCH_2CH_2), 2.92 (bs, 1H, OH), 1.45-1.35 (2H, OCH_2CH_2), 1.20-0.90 (10H, CH_2, octyl), 0.89 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (75 MHz $CDCl_3$) δ 137.8, 131.8 (aromatic quat.), 134.7 (CH_2=$CHCH_2O$), 134.1, 128.6, 127. (aromatic CH), 117.1 (CH_2=$CHCH_2O$), 98.5 (C-1), 79.0, 74.0, 73.7 (C-3, C-4, C-5), 73.9, 73.1 ($PhCH_2$, CH_2=$CHCH_2O$), 70.8 (OCH_2CH_2,), 60.8 (C-6), 55.6 (C-2), 31.7, 29.4, 29.2, 25.9, 22.6 (CH_2, octyl), 14.1 (CH_3, octyl). *Anal.* Calcd for $C_{32}H_{41}NO_7$ (553.29): C, 69.67; H, 7.49. Found: C, 69.37; H, 7.19.

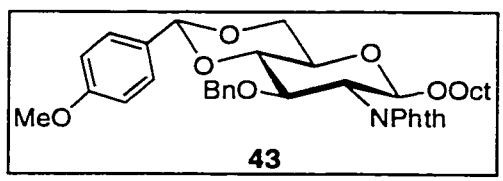
*Octyl 4,6-*p*-methoxybenzylidene-2-deoxy-2-phthalimido-β-*D*-glucopyranoside* (**42**)



42

Compound **36** (1.25 g, 2.3 mmol) was dissolved in dry methanol (40 mL) and sodium (8 mg) added. The reaction was stirred at room temperature for two hours, neutralized by adding amberlite IR-120(H^+) resin, filtered and concentrated. The resulting yellow syrup was dissolved in acetonitrile and *p*-toluene sulfonic acid monohydrate (30 mg, 17.0 mmol) and anisaldehyde dimethyl acetal (800 μL, 4.6 mmol) were added. The solution was heated to 60°C and stirred for 15 hours. The mixture was cooled to room temperature, neutralized with triethylamine and concentrated. Column chromatography (4:1 hexane/ethyl acetate) afforded **42** (1.03 g, 83%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92-7.70 (4H, Phth), 7.43 (d, 2H, J=8.2 Hz, Ph), 6.92 (d, 2H, J=8.2 Hz, Ph), 5.51 (s, 1H, PhC$\underline{H}O_2$), 5.25 (d, 1H, $J_{1,2}$=8.5 Hz, H-1), 4.61 (dd, 1H, $J_{3,4}$=8.4, $J_{2,3}$=10.4 Hz, H-3), 4.37 (dd, 1H, $J_{5,6a}$=4.2, $J_{6a,6b}$=10.4 Hz, H-6a), 4.23 (dd, 1H, $J_{1,2}$=8.4, $J_{2,3}$=10.4 Hz, H-2), 3.86-3.77 (5H, H-4, OC$\underline{H}_2$CH$_2$, OCH$_3$), 3.66-3.54 (2H, H-5, H-6b), 3.41 (dt, 1H, J=6.5, 9.7 Hz, OC$\underline{H}_2$CH$_2$), 1.48-1.30 (2H, OCH$_2$C$\underline{H}_2$), 1.23-0.92 (10H, CH$_2$, octyl), 0.82 (t, 3H, J=7.0 Hz, CH$_3$, octyl).

*Octyl 3-*O*-benzyl-4,6-*p*-methoxybenzylidene-2-deoxy-2-phthalimido-β-*D*-glucopyranoside* (**43**)

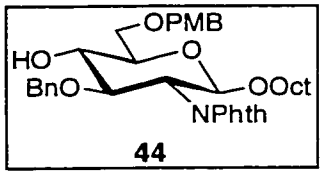


43

Compound **43** (778 mg, 65%) was synthesized from **42** (1.03 g, 1.91 mmol) as described for compound

20: $[\alpha]_D$ +34.4° (c 0.7, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.90-7.60 (4H, Phth), 7.43-6.85 (9H, Ph), 5.57 (s, 1H, PhC<u>H</u>O_2), 5.18 (d, 1H, $J_{1,2}$=8.5 Hz, H-1), 4.78, 4.48 (d, 1H, J=12.4 Hz. PhC<u>H</u>$_2$), 4.43-4.33 (2H, H-3, H-6a), 4.19 (dd, 1H, $J_{1,2}$=8.5, $J_{2,3}$=10.4 Hz, H-2), 3.88-3.72 (6H, H-4, H-6b, OC<u>H</u>$_2$CH_2, OCH_3), 3.61 (ddd, 1H, J=2.3, 4.9, 9.8 Hz, H-5), 3.36 (dt, 1H, J=6.5, 9.8 Hz, OC<u>H</u>$_2$CH_2), 1.22-1.12 (2H, OCH_2C<u>H</u>$_2$), 1.18-0.85 (10H, CH_2, octyl), 0.80 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.1 (CO, Phth), 138.0, 131.7, 130.0 (aromatic quat.), 133.8, 128.0, 127.4, 123.3 (aromatic CH), 113.6 (PhC<u>H</u>O_2), 101.3, 98.0, 83.1, 74.4 (C-1, C-3, C-4, C-5), 74.0 (PhC<u>H</u>$_2$), 70.0 (OC<u>H</u>$_2$CH_2), 68.8 (C-6), 66.1 (OCH_3), 55.9 (C-2), 31.6, 29.3, 29.1, 29.0, 25.7, 22.6 (CH_2, octyl), 14.0 (CH_3, octyl). *Anal.* Calcd for $C_{37}H_{43}NO_8$ (629.74): C, 70.57; H, 6.88. Found: C, 70.48; H, 6.83.

Octyl 3-O-benzyl-2-deoxy-6-O-p-methoxybenzyl-2-phthalimido-β-D-glucopyranoside (**44**)

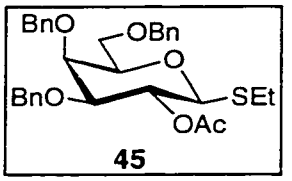


44

Compound **43** (778 mg, 1.24 mmol) and sodium cyanoborohydride (603 mg, 9.92 mmol) were dissolved in 5 mL DMF containing crushed molecular 4 Å sieves. The solution was cooled to 0°C and trifluoracetic acid (1 mL) in 4 mL DMF was added dropwise. The solution was allowed to warm to room temperature and stirred for 12 hours. The reaction was quenched by the addition of triethylamine, filtered through celite, diluted with DCM, washed with water and brine and concentrated under reduced pressure. Column chromatography (5:1 hexane/ethyl acetate) gave **44** (636 mg, 82%): ^1H NMR (300 MHz,

$CDCl_3$) δ 7.82-7.61 (4H, Phth), 7.24-6.82 (9H, Ph), 5.11 (d, 1H, $J_{1,2}$=8.0 Hz, H-1), 4.74 (d, 1H, J=12.2 Hz. $PhC\underline{H}_2$), 4.60-4.48 (3H, H-2, $PhC\underline{H}_2$), 4.25-4.08 (3H, H-3, H-4, $PhC\underline{H}_2$), 3.90-3.70 (6H, H-5, H-6a, H-6b, OCH_3), 3.63 (dt, 1H, J=4.8, 9.4 Hz, $OC\underline{H}_2CH_2$), 3.34 (dt, 1H, J=4.8, 9.7 Hz, $OC\underline{H}_2CH_2$), 2.96 (bs, 1H, OH), 1.40-1.25 (2H, $OCH_2C\underline{H}_2$), 1.20-0.85 (10H, CH_2, octyl), 0.80 (t, 3H, J=7.0 Hz, CH_3, octyl).

*Ethyl 3,4,6-tri-*O*-benzyl-2-*O*-acetyl-thio-β-*D*-galactopyranoside* (**45**)

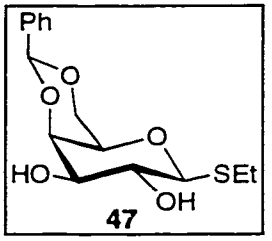


45

*3,4,6-tri-*O*-benzyl-1,2-*O*-methoxyethylidene-galactopyranose* [64] (2.29 g, 4.5 mmol) was dissolved in nitromethane (30 mL) containing crushed 4 Å molecular sieves. Ethanethiol (3 mL, 38 mmol) was added and the solution was cooled to 0°C followed by stirring for one hour. Trimethylsilyl-triflate (200 μL 1 mmol) was added to the cooled solution and allowed to stir for an additional three hours. The mixture was concentrated, diluted with diethyl ether, filtered through celite, washed with sodium bicarbonate and water, dried over magnesium sulfate and concentrated. Column chromatography (6:1 hexane/ethyl acetate) resulted in the corresponding α compound (476 mg, 19%) as a white solid and **45** (1.53 g, 62%) as a white solid: $[\alpha]_D$ -1.6° (c 1.2, $CHCl_3$); mp 61.5-63.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38-7.22 (15H, Ph), 5.40, (dd, 1H, $J_{1,2}$=$J_{2,3}$=9.7 Hz, H-2), 4.93, 4.66, 4.57, 4.52, 4.44, 4.40 (d, 1H, J=11.6 Hz, $PhC\underline{H}_2$), 4.32 (d, 1H, $J_{1,2}$=9.9 Hz, H-1), 3.98 (d, 1H, $J_{3,4}$=2.6 Hz, H-4), 3.63-3.58 (3H, H-5, H-6a, H-6b), 3.54 (dd, 1H, $J_{3,4}$=2.9, $J_{2,3}$=9.6 Hz, H-3), 2.68 (m, 2H, $SC\underline{H}_2CH_3$), 1.21 (t, 3H, J=8.5 Hz, $SCH_2C\underline{H}_3$); ^{13}C NMR (75 MHz, CD_3OD) δ 155.4 (CO, acetate), 139.8, 139.7, 139.5 (aromatic quat.), 129.4, 129.3, 128.9,

128.8, 128.7 (aromatic CH), 83.1, 78.5, 76.1, 72.2, 71.0 (C-1, C-2, C-3, C-4, C-5), 76.0, 74.3, 73.0 (Ph$\underline{C}H_2$), 70.1 (C-6), 24.6 (S$\underline{C}H_2CH_3$), 20.9 (CH_3, acetate), 15.1 ($SCH_2\underline{C}H_3$). *Anal.* Calcd for $C_{31}H_{36}O_6S$ (536.22): C, 69.38; H, 6.76. Found: C, 69.15; H, 6.95.

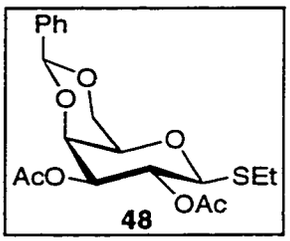
Ethyl 4,6-O-benzylidene-thio-β-D-galactopyranoside (**47**)



47

Ethyl 2,3,4,6-tetra-O-acetyl-thio-β-D-galactopyranoside [66] (2.00 g, 5.3 mmol) was deacetylated as described for the preparation of compound **42**. The crude material was dissolved in 5 mL formic acid and benzaldehyde (5 mL) added. The solution was stirred at room temperature for 5 minutes and added to potassium carbonate (14.0 g in 10 mL water) and 40 mL hexane. The solution was extracted twice with ethyl acetate, the organic fractions pooled, dried over sodium sulfate and concentrated under reduced pressure. Column chromatography 3:1 ethyl acetate/toluene) resulted in **47** (873 mg, 55%) as a white solid: $[\alpha]_D$ +26.3° (c 0.7, $CHCl_3$); mp 152.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32-7.15 (5H, Ph), 5.53 (s, 1H, PhC$\underline{H}O_2$), 4.33 (2H, H-1, H-6a), 4.24 (dd, 1H, $J_{4,5}$=1.2, $J_{3,4}$=3.7 Hz, H-4), 4.13 (dd, 1H, $J_{5,6b}$=1.3, $J_{6a,6b}$=12.1 Hz, H-6b), 3.80 (dd, 1H, $J_{1,2}$=$J_{2,3}$=9.3 Hz, H-2), 3.69 (1H, H-3), 3.51 (1H, H-5), 2.79 (m, 2H, S$\underline{C}H_2CH_3$), 2.56 (bs, 1H, OH), 1.34 (t, 3H, J=7.5 Hz, $SCH_2C\underline{H}_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 129.3, 128.3, 126.4 (aromatic CH), 101.5 (Ph$\underline{C}HO_2$), 85.3 (C-1), 75.6, 73.9, 70.1, 69.7 (C-2, C-3, C-4, C-5), 69.3 (C-6), 23.4 (S$\underline{C}H_2CH_3$), 15.1 ($SCH_2\underline{C}H_3$).

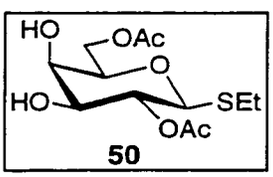
*Ethyl 2,3-di-*O*-acetyl-4,6-*O*-benzylidene-thio-β-*D*-galactopyranoside* (**48**)



48

Compound **47** (6.7 g, 20.4 mmol) was dissolved in acetic anhydride (5 mL) and pyridine (10 mL) and stirred for 15 hours. Water was added to quench the reaction and the solution was diluted with DCM, washed with 5% hydrochloric acid and sodium bicarbonate and concentrated under reduced pressure to give a red oil. Column chromatography (10:1 toluene/ethyl acetate), followed by recrystallization in diethyl ether resulted in **48** (6.5 g, 77%) as yellow crystals: $[\alpha]_D$ +34.4° (c 0.9, $CHCl_3$); mp 103.0-105.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37-7.18 (5H, Ph), 5.47 (s, 1H, PhC<u>H</u>O_2), 5.45 (dd, 1H, $J_{1,2}$=$J_{2,3}$=9.9 Hz, H-2), 4.97 (dd, 1H, $J_{3,4}$=3.5, $J_{2,3}$=9.0 Hz, H-3), 4.45 (d, 1H, $J_{1,2}$=10.0 Hz, H-1), 4.39 (dd, 1H, $J_{4,5}$=0.8, $J_{3,4}$=3.5 Hz, H-4), 4.32 (dd, 1H, $J_{5,6a}$=1.7, $J_{6a,6b}$=12.4 Hz, H-6a), 4.00 (dd, 1H, $J_{5,6b}$=1.7, $J_{6a,6b}$=12.4 Hz, H-6b), 3.57 (1H, H-5), 2.78 (m, 2H, SC<u>H</u>$_2$$CH_3$), 2.08 (s, 6H, CH_3 acetate), 1.04 (t, 3H, J=7.5 Hz, SCH_2C<u>H</u>$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 169.4 (CO, acetate), 137.6 (aromatic quat.), 129.1, 128.2, 126.4 (aromatic CH), 101.2 (PhC<u>H</u>O_2), 82.8 (C-1), 73.6, 73.0, 69.8, 66.6 (C-2, C-3, C-4, C-5), 69.1 (C-6), 22.8 (SC<u>H</u>$_2$$CH_3$), 20.9, 20.8 ($CH_3$, acetate), 14.8 ($SCH_2$C<u>H</u>$_3$). *Anal.* Calcd for $C_{19}H_{24}O_5S$ (396.45): C, 57.56; H, 6.10. Found: C, 57.34; H, 6.15.

*Ethyl 2,6-di-*O*-acetyl-thio-β-*D*-galactopyranoside* (**50**)

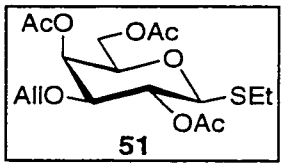


50

*Ethyl 2,6-di-*O*-acetyl-3,4-*O*-isopropylidene-thio-β-*D*-galactopyranoside* ([66] 790 mg, 1.7 mmol) was dissolved in

acetonitrile (2 mL) and as added to 70% acetic acid (20 mL). The solution was heated to 60°C and stirred for 13 hours. The mixture was cooled to room temperature and co-concentrated with toluene. Column chromatography (5:1 toluene/ethyl acetate) yielded **50** (624 mg, 95%): $[\alpha]_D$ +15.4° (c 0.5, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 4.99 (dd, 1H, $J_{1,2}=J_{2,3}=9.7$ Hz, H-2), 4.35 (d, 1H, $J_{1,2}=10.1$ Hz, H-1), 4.32 (dd, 1H, $J_{5,6a}=5.9$, $J_{6a,6b}=11.4$ Hz, H-6a), 4.23 (dd, 1H, $J_{5,6b}=6.7$, $J_{6a,6b}=11.5$ Hz, H-6b), 3.94 (bs, 1H, OH), 3.70-3.62 (2H, H-3, H-5), 3.70 (2H, H-4, OH), 2.65 (m, 2H, $SC\underline{H}_2CH_3$), 2.10, 2.07 (s, 3H, CH_3, acetate), 1.22 (t, 3H, J=7.5 Hz, $SCH_2C\underline{H}_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 169.5 (CO, acetate), 137.6 (aromatic quat.), 129.1, 128.2, 126.4 (aromatic CH), 101.2 ($Ph\underline{C}HO_2$), 82.8 (C-1), 73.6, 73.0, 69.8, 66.1 (C-2, C-3, C-4, C-5), 66.6 (C-6), 21.0 ($S\underline{C}H_2CH_3$), 14.8 ($SCH_2\underline{C}H_3$). *Anal.* Calcd for $C_{12}H_{20}O_7S$ (308.09): C, 46.74; H, 6.54. Found: C, 46.85; H, 6.46.

*Ethyl 2,4,6-tri-*O*-acetyl-3-*O*-allyl-thio-β-*D*-galactopyranoside* (**51**)



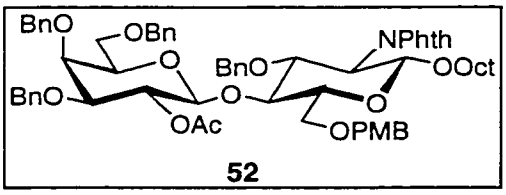
51

Compound **50** (589 mg, 1.5 mmol) was dissolved in toluene (50 mL) and was added to a flask equipped with a Dean-Stark separator containing dibutyl tin oxide (470 mg, 1.90 mmol). The solution was refluxed for 20 hours and cooled to room temperature. Allyl-bromide (2 mL, 23.0 mmol) and tetrabutylammonium bromide (214 mg, 0.66 mmol) were added and the solution was heated to 60°C. After stirring for 2 hours, the mixture was cooled to room temperature and concentrated. Column chromatography resulted in the recovery of three compounds, which were pooled and acetylated as described for the preparation of **48**,

affording **51** (447 mg 77%): $[\alpha]_D$ +18.1° (c 0.9, $CHCl_3$); mp 31.5-33.0 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 5.74 (1H, H_c allyl), 5.42 (d, 1H, $J_{3,4}$=3.3 Hz, H-4), 5.20 (1H, H_a allyl), 5.12 (1H, H_b allyl), 5.08 (dd, 1H, $J_{1,2}$=$J_{2,3}$=9.8 Hz, H-2), 4.39 (d, 1H, $J_{1,2}$=10.1 Hz, H-1), 4.12-4.04 (3H, H-6a, H-6b, H_d allyl), 3.89 (1H, H_e allyl), 3.79 (dd, 1H, $J_{5,6a}$=$J_{5,6b}$=6.5 Hz, H-5), 3.49 (dd, 1H, $J_{3,4}$=3.4, $J_{2,3}$= 9.6 Hz, H-3), 2.67 (m, 2H, $SC\underline{H}_2CH_3$), 2.10, 2.07, 2.03 (s, 3H, CH_3 acetate), 1.24 (t, 3H, J=7.5 Hz, $SCH_2C\underline{H}_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.5, 170.3, 169.5 (CO, acetate), 134.1 (CH_2=$\underline{C}HCH_2O$), 117.3 ($\underline{C}H_2$=$CHCH_2O$), 84.0 (C-1), 77.7, 74.7, 68.9, 66.4 (C-2, C-3, C-4, C-5), 70.3 (CH_2=$CH\underline{C}H_2O$), 62.2 (C-6), 24.1 ($S\underline{C}H_2CH_3$), 20.9, 20.8, 20.7 (CH_3, acetate), 14.9 ($SCH_2\underline{C}H_3$). *Anal.* Calcd for $C_{17}H_{26}O_8S$ (390.45): C, 52.29; H, 6.71. Found: C, 52.25; H, 6.78.

3.1.3 Synthesis of Octyl β-LacNAc Mono-O-Phosphates

Octyl 4-O-(2-O-acetyl-3,4,6-tri-O-benzyl-β-D-galactopyranosyl)-3-O-benzyl-2-deoxy-6-O-p-methoxybenzyl-2-phthalimido-β-D-glucopyranoside (**52**)

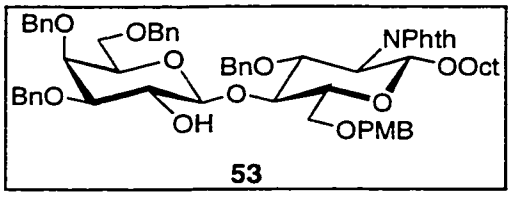


52

The acceptor compound **44** (636 mg, 1.0 mmol) and the donor compound **45** (1.00 g, 2.0 mmol) were dissolved in dry DCM (20 mL) containing crushed 4 Å molecular sieves. The solution was cooled to 0°C, followed by the addition of N-iodosuccinimide (450 mg 2.0 mmol) and stirred for 45 minutes. A catalytic amount of silver triflate was added, the solution stirred for an additional 2 hours, filtered through celite, washed successively with sodium bicarbonate, sodium thiosulfate, and water, dried

over magnesium sulfate and concentrated under reduced pressure. Column chromatography (10:1 toluene/ethyl aceate) resulted in **52** (977 mg, 88% based on the acceptor) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80-7.60 (4H, Phth), 7.38-6.78 (24H, Ph), 5.35 (dd, 1H, $J_{1',2'}$=7.9, $J_{2',3'}$=10.0 Hz, H-2'), 5.07 (d, 1H, $J_{1,2}$=8.5 Hz, H-1), 4.91, 4.84, 4.68, 4.67, 4.49, 4.47, 4.46, 4.43, 4.40, 4.25 (d, 1H, J=11.6 Hz, PhC$\underline{H}_2$), 4.42 (d, 1H, $J_{1',2'}$=8.1 Hz, H-1'), 4.23 (dd, 1H, $J_{3,4}$=8.4, $J_{2,3}$=10.8 Hz, H-3), 4.14 (dd, 1H, $J_{1,2}$=8.5, $J_{2,3}$=10.8 Hz, H-2), 3.97 (dd, 1H, $J_{3,4}$=8.5, $J_{4,5}$=9.9 Hz, H-4), 3.91 (d, 1H, $J_{3',4'}$=2.9 Hz, H-4'), 3.79-3.73 (6H, H-6a, H-6b, OC$\underline{H}_2$CH$_2$, CH_3), 3.52 (ddd, 1H, $J_{5,6a}$=$J_{5,6b}$=2.3, $J_{4,5}$=10.0 Hz, H-5), 3.46 (dd, 1H, $J_{6a',5'}$=$J_{6a',6b'}$=10.1 Hz, H-6a'), 3.42-3.32 (4H, H-3', H-5', H-6b', OC$\underline{H}_2$CH$_2$), 2.00 (s, 3H, CH_3, acetate), 1.42-1.30 (2H, OCH$_2$C$\underline{H}_2$), 1.20-0.85 (10H, CH_2, octyl), 0.80 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.3 (CO, acetate), 159.2 (CO, Phth), 139.0, 138.8, 138.2, 138.0, 130.4 (aromatic quat.), 133.7, 129.5, 128.4, 128.1, 127.8, 127.7, 127.6, 127.3, 127.2, 126.7, 123.2, 113.8 (aromatic CH), 100.9 (C-1'), 98.4 (C-1), 80.6 (C-3'), 78.0 (C-4), 77.1 (C-3), 75.2 (C-5), 74.5, 74.4, 73.4, 73.3, 71.8 (Ph$\underline{C}$H$_2$), 73.3 (C-5'), 72.8 (C-4'), 72.0 (C-2'), 69.6 (O$\underline{C}$H$_2$CH$_2$), 68.1 (C-6'), 67.6 (C-6'), 55.9 (C-2), 55.3 (OCH_3), 31.7, 29.3, 29.2, 29.1, 25.9, 22.6 (CH_2, octyl), 21.1 (CH_3, acetate), 14.1 (CH_3, octyl). *Anal.* Calcd for $C_{66}H_{75}NO_{14}$ (1106.30): C, 71.65; H, 6.83. Found: C, 71.42; H, 6.84.

Octyl 3-O-benzyl-4-O-(3,4,6-tri-O-benzyl-β-D-galactopyranosyl)-2-deoxy-6-O-p-methoxybenzyl-2-phthalimido-β-D-glucopyranoside (**53**)

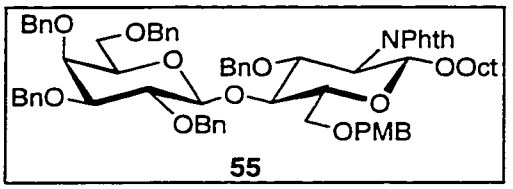


53

Compound **52** (30 mg, 0.026 mmol) was dissolved in dry methanol (1 mL) and sodium (0.5 mg) added. The solution was stirred at room temperature for 48 hours, neutralized with Amberlite IR-120(H^+) resin, filtered and concentrated. Column chromatography (5:1 hexane/ethyl acetate) resulted in **53** (22 mg, 77%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80-7.60 (4H, Phth), 7.38-6.80 (24H, Ph), 5.04 (d, 1H, $J_{1,2}$=8.6 Hz, H-1), 4.86, 4.84, 4.69, 4.66, 4.52, 4.51, 4.42, 4.31, 4.24 (d, 1H, J=11.6 Hz, PhC$\underline{H}_2$), 4.54 (d, 1H, $J_{1',2'}$=7.7 Hz, H-1'), 4.36 (dd, 1H, $J_{3,4}$=7.5, $J_{2,3}$=10.7 Hz, H-3), 4.14 (dd, 1H, $J_{1,2}$=8.6, $J_{2,3}$=10.9 Hz, H-2), 4.07 (dd, 1H, $J_{3,4}$=$J_{4,5}$=9.6 Hz, H-4) 3.99 (dd, 1H, $J_{5,6a}$=3.5, $J_{6a,6b}$=11.4 Hz, H-6a), 3.90 (dd, 1H, $J_{1',2'}$=7.5, $J_{2',3'}$=9.8 Hz, H-2'), 3.85 (d, 1H, $J_{3',4'}$=2.9 Hz, H-4'), 3.78-3.72 (5H, H-6a', H-6b, OCH_3), 3.61 (ddd, 1H, $J_{5,6a}$=2.1, $J_{5,6b}$=5.5, $J_{5,4}$=10.1 Hz, H-5), 3.48 (dt, 1H, J=6.4, 9.2 Hz, OC$\underline{H}_2CH_2$), 3.41-3.32 (3H, H-5', H-6a', OC$\underline{H}_2CH_2$), 3.31 (dd, 1H, $J_{3',4'}$=2.9, $J_{2',3'}$=9.9 Hz, H-3'), 3.22 (bs, 1H, OH), 1.40-1.32 (2H, $OCH_2C\underline{H}_2$), 1.08-0.95 (10H, CH_2, octyl), 0.88 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.3 (CO, Phth), 138.9, 138.8, 138.3, 137.9, 131.7 (aromatic quat.), 133.6, 130.0, 129.7, 129.5, 127.8, 127.7, 127.6, 127.3, 127.2, 126.7, 123.2, 113.7 (aromatic CH), 103.6 (C-1'), 98.5 (C-1), 82.0 (C-3'), 78.6 (C-4), 78.5 (C-3, C-2'), 74.8 (C-5), 74.6, 74.4, 73.4, 73.2, 72.4 (Ph$\underline{C}H_2$), 73.5 (C-5'), 73.1 (C-4'), 72.4 (C-2'), 69.6 (O$\underline{C}H_2CH_2$), 68.4, 68.1 (C-6, C-6'), 56.0 (C-2), 55.2 (OCH_3),

31.6, 29.3, 29.1, 29.0, 25.8, 22.5 (CH_2, octyl), 14.1 (CH_3, octyl). *Anal.* Calcd for $C_{64}H_{73}NO_{13}$ (1064.26): C, 72.23; H, 6.91. Found: C, 71.62; H, 6.82.

Octyl 3-O-benzyl-4-O-(2,3,4,6-tetra-O-benzyl-β-D-galactopyranosyl)-2-deoxy-6-p-methoxybenzyl-2-phthalimido-β-D-glucopyranoside (**55**)

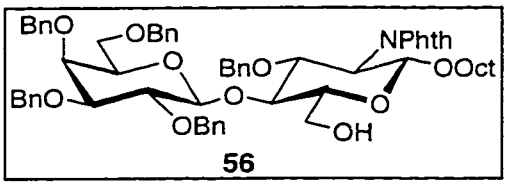


55

Compound **53** (245 mg, 0.023 mmol) was dissolved in diemthylformamide (3 mL) and tetrabutyl ammonium iodide (170 mg, 0.046 mmol) was added. The solution was cooled to 0°C followed by the addition of sodium hydride (13 mg, 60% dispersion in oil, 0.033 mmol). The mixture was stirred for 15 minutes and benzyl bromide (13 μL, 0.12 mmol) was added. Stirring at 0°C was continued for 30 minutes and the reaction was quenched with methanol, diluted with toluene, washed successively with brine and water, dried over sodium sulfate and concentrated under reduced pressure. Column chromatography (5:1 hexane/ethyl aceate) gave **55** (94 mg, 35%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85-7.60 (4H, Phth), 7.40-6.80 (29H, Ph), 5.08 (d, 1H, $J_{1,2}$=8.4 Hz, H-1), 4.92, 4.87, 4.81, 4.70, 4.51, 4.45, 4.35, 4.32, 4.22 (d, 1H, J=11.6 Hz, PhC$\underline{H}_2$), 4.41 (d, 1H, $J_{1',2'}$=7.7 Hz, H-1'), 4.26 (dd, 1H, $J_{3,4}$=8.5, $J_{2,3}$=10.0 Hz, H-3), 4.16 (dd, 1H, $J_{1,2}$=8.4, $J_{2,3}$=9.9 Hz, H-2), 4.02 (dd, 1H, $J_{4,5}$=8.4, $J_{3,4}$=9.9 Hz, H-4) 3.88 (d, 1H, $J_{3',4'}$=2.9 Hz, H-4'), 3.83 (dd, 1H, $J_{5,6a}$=4.1, $J_{6a,6b}$=10.8 Hz, H-6a), 3.79-3.72 (5H, H-2', OC$\underline{H}_2$CH$_2$, OCH$_3$), 3.68 (dd, 1H, $J_{5,6b}$=1.7, $J_{6a,6b}$=11.0 Hz, H-6b), 3.54 (ddd, 1H, $J_{5,6b}$=1.7, $J_{5,6a}$=3.9, $J_{5,4}$=10.1 Hz, H-5), 3.47-3.37 (4H, H-3', H-5', H-6a', H-6b'), 3.34 (dt, 1H, J=6.2, 9.0 Hz, OC$\underline{H}_2$CH$_2$), 1.44-1.30 (2H, OCH$_2$C$\underline{H}_2$), 1.10-0.90 (10H, CH$_2$, octyl),

0.88 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.7 (CO, Phth), 139.8, 139.7, 139.5, 139.3, 138.8, 130.0 (aromatic quat.), 131.2, 129.1, 129.0, 128.9, 128.8, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 127.9, 127.4, 113.7 (aromatic CH), 103.7 (C-1'), 99.0 (C-1), 83.1 (C-3'), 80.8 (C-2'), 78.7 (C-4), 77.9 (C-3), 76.0, 75.2, 75.0, 74.5, 74.1, 73.7, 73.5, 73.4 (C-4', C-5, C-5', $PhCH_2x5$), 70.2 (OCH_2CH_2), 69.0 (C-6'), 68.5 (C-6), 56.5 (C-2), 55.9 (OCH_3), 32.3, 30.0, 29.9, 29.8, 26.5, 23.3 (CH_2, octyl), 14.7 (CH_3, octyl). HR-ESMS calcd for $C_{71}H_{79}NO_{13}Na$ 1176.5449, found 1176.5445.

Octyl 3-O-benzyl-4-O-(2,3,4,6-tetra-O-benzyl-β-D-galactopyranosyl)-2-deoxy-2-phthalimido-β-D-glucopyranoside (**56**)

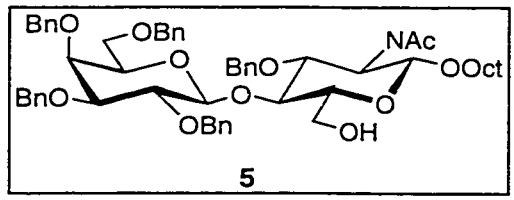


56

Compound **55** (95 mg, 0.082 mmol) was dissolved in DCM (10 mL) and DDQ (29 mg, 0.13 mmol) was added. The solution was stirred at room temperature for 2 hours, and the reaction was quenched with 1,4-cyclohexadiene, followed by successive washes of sodium bicarbonate and water. The solution was dried over sodium sulfate and concentrated under reduced pressure. Column chromatography (8:1 toluene/acetone) resulted in **56** (49 mg, 59%): ^1H NMR (600 MHz, $CDCl_3$) δ 7.88-7.64 (4H, Phth), 7.38-6.80 (25H, Ph), 5.13 (d, 1H, $J_{1,2}$=8.5 Hz, H-1), 4.93, 4.88, 4.85, 4.82, 4.70, 4.52, 4.46, 4.34, 4,24 (d, 1H, J=11.6 Hz, $PhCH_2$), 4.51 (d, 1H, $J_{1',2'}$=7.6 Hz, H-1'), 4.27 (dd, 1H, $J_{3,4}$=8.5, $J_{2,3}$=10.8 Hz, H-3), 4.11 (dd, 1H, $J_{1,2}$=8.5, $J_{2,3}$=10.8 Hz, H-2), 3.91 (dd, 1H, $J_{3,4}$=8.7, $H_{4,5}$=9.6 Hz, H-4), 3.90-3.83 (3H, H-4', H-6a', H-6b'), 3.81 (dd, 1H, $J_{1',2'}$=7.7, $J_{2',3'}$=9.7 Hz, H-2'), 3.73 (dt, 1H, J=6.1, 9.8 Hz, OCH_2CH_2), 3.56-6.52

(2H, H-3', H-5), 3.48-3.38 (3H, H-5', H-6a, H-6b), 3.34 (dt, 1H, J=6.4, 9.8 Hz, $OC\underline{H}_2CH_2$), 1.40-1.28 (2H, $OCH_2C\underline{H}_2$), 1.18-0.88 (10H, CH_2, octyl), 0.79 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.1, 139.0, 138.6, 138.5, 138.1, 133.7 (aromatic quat.), 131.7, 128.5, 128.4, 128.3, 128.2, 128.0, 127.8, 127.7, 127.6, 127.3, 126.8, 123.2 (aromatic CH), 103.4 (C-1'), 98.4 (C-1), 82.5 (C-3'), 80.1 (C-2'), 78.2 (C-4) 77.3 (C-3), 75.6, 74.5, 74.4, 73.8, 73.3 ($Ph\underline{C}H_2$), 75.5 (C-5'), 73.9 (C-4'), 72.8 (C-5), 69.9 ($O\underline{C}H_2CH_2$), 68.7, 68.4 (C-6, C-6'), 56.3 (C-2) 31.6, 29.3, 29.2, 29.1, 25.8, 22.6 (CH_2, octyl), 14.1 (CH_3, octyl). HR-ESMS calcd for $C_{63}H_{71}NO_{12}Na$ 1056.4874, found 1056.4877.

Octyl 2-acetamido-3-O-benzyl-4-O-(2,3,4,6-tetra-O-benzyl-β-D-galactopyranosyl)-2-deoxy-β-D-glucopyranoside (**5**)

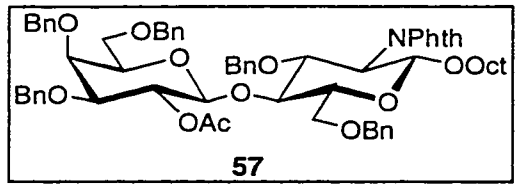


5

Compound **56** (98 mg, 0.095 mmol) was dissolved in *t*-butanol (5 mL) and ethylenediamine (2 mL), heated to 90 °C, and stirred for 30 hours. The solution was cooled to room temperature and co-concentrated with toluene. The resulting oil was dissolved in methanol (5 mL) and acetic anhydride (2 mL) and triethylamine (0.1 mL) added. The solution was stirred at room temperature for 2 hours followed by the addition of ethanol (10 ml) and water (2 mL). The solution was stirred for 15 minutes, washed successively with sodium bicarbonate and water, dried over magnesium sulfate and concentrated under reduced pressure. Column chromatography (6:1 toluene/ethyl acetate) gave **5** (70 mg, 82%) as a colorless oil: ^1H NMR (600 MHz, $CDCl_3$) δ 7.35-7.18

(25H, Ph), 5.59 (d, 1H, J=7.6 Hz, NHAc), 4.95, 4.94, 4.81, 4.79, 4.70, 4.54, 4.52, 4.35, 4.25 (d, 1H, J=11.6 Hz, PhCH$_2$), 4.91 (d, 1H, $J_{1,2}$=7.7 Hz, H-1), 4.47 (d, 1H, $J_{1',2'}$=7.7 Hz, H-1'), 4.10 (dd, 1H, $J_{2,3}$=$J_{3,4}$=9.0 Hz, H-3), 3.92 (d, 1H, $J_{3',4'}$=2.5 Hz, H-4'), 3.86-3.74 (5H, H-2', H-4, H-6a', H-6b', OCH$_2$CH$_2$), 3.54-3.48 (3H, H-3', H-6a, H-5), 3.46-3.38 (3H, H-5', H-6b, OCH$_2$CH$_2$), 3.25 (ddd, 1H, $J_{1,2}$=$J_{2,NHAc}$=7.7, $J_{2,3}$=9.2 Hz, H-2) 1.84 (s, 3H, CH_3 NHAc), 1.56-1.48 (2H, OCH$_2$CH$_2$), 1.32-1.18 (10H, CH_2, octyl), 0.85 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.9 (CO, acetate), 139.7, 139.6, 139.2, 139.1, 138.3 (aromatic quat.), 129.1, 129.0, 128.9, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1 (aromatic CH), 104.0 (C-1'), 100.5 (C-1), 83.1 (C-3'), 80.7 (C-4), 78.4 (C-3), 76.4 (C-2'), 76.1, 75.4, 75.0, 74.5, 74.2, 73.9, 73.5 (C-4', C-5, C-5', PhCH$_2$x5), 70.7 (OCH$_2$CH$_2$), 68.9 (C-6), 62.1 (C-6'), 57.8 (C-2) 32.5, 30.3, 30.0, 29.9, 26.7, 24.5 (CH_2, octyl), 23.4 (CH_3, acetate), 14.8 (CH_3, octyl). HR-ESMS calcd for $C_{57}H_{71}NO_{11}Na$ 968.4925, found 968.4925.

Octyl 4-O-(2-O-acetyl-3,4,6-tri-O-benzyl-β-D-galactopyranosyl)-3,6,-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (**57**)

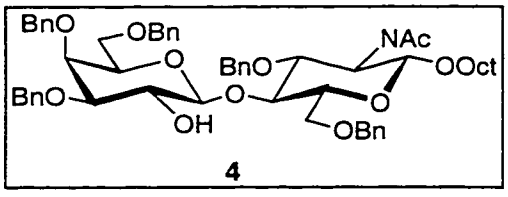


57

Compound **57** (1.38 g, 81% based on the acceptor) was synthesized from *Octyl 3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside* [62] (965 mg, 1.6 mmol), donor **45** (1.65 g, 3.1 mmol), N-iodosuccinimide (765 mg, 3.1 mmol), catalytic silver triflate and dry DCM (30 mL) containing crushed 4 Å molecular sieves as described for the preparation of **52**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80-7.60

(4H, Phth), 7.38-6.78 (25H, Ph), 5.34 (dd, 1H, $J_{1',2'}$=8.0, $J_{2',3'}$=10.1 Hz, H-2'), 5.06 (d, 1H, $J_{1,2}$=8.4 Hz, H-1), 5.06, 4.90, 4.84, 4.73, 4.63, 4.49, 4.45, 4.41, 4.33, 4.25 (d, 1H, J=12.1 Hz, PhC$\underline{H}_2$), 4.47 (d, 1H, $J_{1',2'}$=7.8 Hz, H-1'), 4.24 (dd, 1H, $J_{2,3}$=$J_{3,4}$=8.7 Hz, H-3), 4.13 (dd, 1H, $J_{1,2}$=8.4, $J_{2,3}$=1.08 Hz, H-2), 3.97 (d, 1H, $J_{3',4'}$=3.9 Hz, H-4'), 3.78-3.73 (3H, H-6a, H-6b, OC$\underline{H}_2$CH_2), 3.52 (ddd, 1H, $J_{5,6a}$=$J_{5,6b}$=3.1, $J_{4,5}$=9.9 Hz, H-5), 3.48-3.37 (4H, H-5', H-6a',H-6b', OC$\underline{H}_2$CH_2), 3.34 (dd, $J_{3',4'}$=3.6, $J_{2',3'}$=10.2 Hz, H-3'), 1.98 (s, 3H, CH3, acetate), 1.42-1.36 (2H, OCH_2C$\underline{H}_2$), 1.10-0.90 (10H, CH_2, octyl), 0.78 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.0 (CO, acetate), 139.6, 139.5, 138.9, 138.8, 138.7 (aromatic quat.), 134.3, 129.1, 128.8, 128.6, 128.5, 128.0, 127.4 (aromatic CH), 101.5 (C-1'), 99.1 (C-1), 80.4 (C-3'), 78.0 (C-4), 77.1 (C-3), 75.1 (C-5), 74.6, 74.4, 73.5, 73.4 (Ph$\underline{C}H_2$), 73.3 (C-5'), 72.7 (C-4'), 71.7 (C-2'), 69.6 (O$\underline{C}H_2$CH_2), 68.1, 68.0 (C-6, C-6'), 55.8 (C-2) 31.6, 29.3, 29.1, 25.8, 22.6 (CH_2, octyl), 21.1 (CH_3, acetate), 14.1 (CH_3, octyl). *Anal.* Calcd for $C_{65}H_{73}NO_{13}$ (1076.27): C, 72.54; H, 6.84. Found: C, 72.91; H, 6.86.

*Octyl 2-acetamido-3,6-di-*O*-benzyl-4-*O*-(3,4,6-tri-*O*-benzyl-β-*D*-galactopyranosyl)-2-deoxy-β-*D*-glucopyranoside* (**4**)

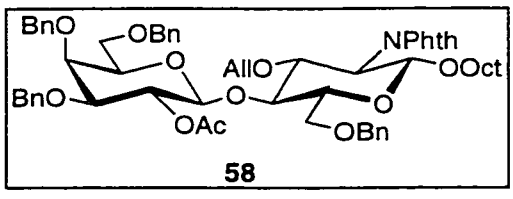


4

Compound **4** (1.10 g, 92%) was synthesized from compound **57** (1.37 g, 1.23 mmol), *t*-butanol (50mL), ethylenediamine (20 mL) followed by acetic anhydride (10 mL), methanol (40 mL) and triethylamine (0.5 mL) as described for the preparation of **5**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18-7.10 (25H, Ph), 5.69 (d, 1H,

J=7.7 Hz, NHAc), 4.87, 4.69, 4.64, 4.62, 4.59, 4.53, 4.51, 4.33, 4.26 (d, 1H, J=12.1 Hz, PhCH$_2$), 4.77 (d, 1H, $J_{1,2}$=7.5 Hz, H-1), 4.48 (d, 1H, $J_{1',2'}$=7.6 Hz, H-1'), 4.09 (dd, 1H, $J_{2,3}$=$J_{3,4}$=8.7 Hz, H-3), 3.98 (dd, 1H, $J_{3,4}$=$J_{4,5}$=8.3 Hz, H-4), 3.95-3.87 (2H, H-2', H-6a), 3.86 (d, 1H, $J_{3',4'}$=2.5 Hz, H-4'), 3.83-3.76 (2H, H-6b, OCH$_2$CH$_2$), 3.59 (ddd, 1H, $J_{5,6a}$=$J_{5,6b}$=3.1, $J_{4,5}$=8.7 Hz, H-5), 3.53 (d, 1H, $J_{5',6a'}$=$J_{6a',6b'}$=7.5 Hz, H-6a'), 3.44-3.32 (4H, H-2, H-5', H-6b', OCH$_2$CH$_2$), 3.34 (dd, $J_{3',4'}$=2.9, $J_{2',3'}$=9.8 Hz, H-3'), 1.82 (s, 3H, CH$_3$, acetate), 1.56-1.49 (2H, OCH$_2$CH$_2$), 1.32-1.12 (10H, CH$_2$, octyl), 0.87 (t, 3H, J=7.0 Hz, CH$_3$, octyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.4 (CO, acetate), 139.0, 138.8, 138.2, 138.0, 137.9 (aromatic quat.), 128.5, 128.4, 128.3, 128.2, 127.9, 127.8, 127.7, 127.6, 127.5, 127.4, 127.3 (aromatic CH), 103.3 (C-1'), 100.0 (C-1), 81.9 (C-3'), 78.8 (C-3), 77.4 (C-4), 74.6, 73.8, 73.4, 72.3 (PhCH$_2$), 74.5 (C-5), 73.5 (C-4'), 72.9 (C-5'), 72.1 (C-2'), 69.6 (OCH$_2$CH$_2$), 68.9 (C-6), 68.2 (C-6'), 55.0 (C-2) 31.9, 29.5, 26.3, 26.0, 24.7, 21.6 (CH$_2$, octyl), 20.8 (CH$_3$, acetate), 14.1 (CH$_3$, octyl). *Anal.* Calcd for $C_{57}H_{71}NO_{11}$ (945.17): C, 72.36; H, 7.56. Found: C, 72.36; H, 7.71.

Octyl 4-O-(2-O-acetyl-3,4,6-tri-O-benzyl-β-D-galactosyl)-3-O-allyl-6-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (**58**)

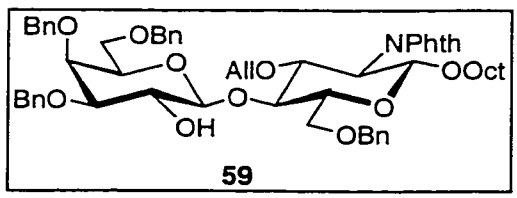


58

Compound **58** (1.85 g, 80% based on the acceptor) was synthesized from acceptor **41** (2.14 g, 2.3 mmol), donor **45** (2.33 g, 4.3 mmol), N-iodosuccinimide (990 mg, 4.0 mmol), catalytic silver triflate and dry DCM (40 mL) containing crushed 4 Å molecular sieves as described for the preparation of **52**: ^{1}H NMR

(500 MHz, $CDCl_3$) δ 7.80-7.70 (4H, Phth), 7.38-7.18 (20H, Ph), 5.44 (1H, H_c allyl), 5.26 (dd, 1H, $J_{1',2'}$=7.9, $J_{2',3'}$=10.2 Hz, H-2'), 5.08 (d, 1H, $J_{1,2}$=8.1 Hz, H-1), 4.91-4.86 (2H, PhC$\underline{H}_2$, H_a allyl), 4.72 (d, 1H, J=12.2 Hz, PhC$\underline{H}_2$), 4.68 (2H, PhC$\underline{H}_2$, H_b allyl), 4.55-4.37 (6H, H-1', PhC$\underline{H}_2$x5), 4.31 (1H, H_d allyl), 4.14 (2H, H-2, H-3), 3.91 (d, 1H, $J_{3',4'}$=2.3 Hz, H-4'), 3.87 (dd, 1H, $J_{3,4}$=8.1, $J_{4,5}$=9.9 Hz, H-4), 3.83-3.72 (4H, H-6a, H-6b, OC$\underline{H}_2$$CH_2$, H_e allyl), 3.61 (dd, 1H, $J_{6a',5'}$=$J_{6a',6b'}$=9.0 Hz, H-6a'), 3.55 (dd, 1H, $J_{6b',5'}$=5.2, $J_{6a',6b'}$=9.2 Hz, H-6b'), 3.51 (ddd, 1H J=2.9, 5.0, 9.9 Hz, H-5), 3.42 (dd, 1H, $J_{5',6b'}$=5.9, $J_{5',6a'}$= 8.9 Hz, H-5'), 3.36 (dt, 1H, J=6.4, 9.0 Hz, OC$\underline{H}_2$$CH_2$), 3.33 (dd, $J_{3',4'}$=2.9, $J_{2',3'}$=10.0 Hz, H-3'), 1.96 (s, 3H, CH3, acetate), 1.42-1.32 (2H, $OCH_2C\underline{H}_2$), 1.18-0.90 (10H, CH_2, octyl), 0.88 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.3 (CO, acetate), 138.8, 138.2, 138.1, 138.0 (aromatic quat.), 135.1 (CH_2=$\underline{C}$$HCH_2O$), 133.9, 131.8, 128.5, 128.4, 128.3, 128.1, 127.9, 127.8, 127.7, 127.6, 127.4, 127.3 (aromatic CH), 116.2 ($\underline{C}H_2$=$CHCH_2O$), 100.8 (C-1'), 98.4 (C-1), 80.4, 77.8, 77.6, 75.1, 74.3 (C-2', C-3, C-3', C-4, C-4'), 73.7, 73.6, 73.5, 72.6, 71.7 (C-5, C-5', Ph$\underline{C}H_2$, CH_2=$CH\underline{C}H_2O$), 69.6 (O$\underline{C}H_2CH_2$), 68.2, 68.1 (C-6, C-6'), 56.0 (C-2) 31.6, 29.3, 29.2, 29.1, 25.9, 22.6 (CH_2, octyl), 21.1 (CH_3, acetate), 14.1 (CH_3, octyl). *Anal.* Calcd for $C_{61}H_{71}NO_{13}$ (1026.22): C, 71.39; H, 6.97. Found: C, 71.13; H, 7.00.

Octyl 3-O-allyl-6-O-benzyl-4-O-(3,4,6-tri-O-benzyl-β-D-galactosyl)-2-deoxy-2-phthalimido-β-D-glucopyranoside (**59**)

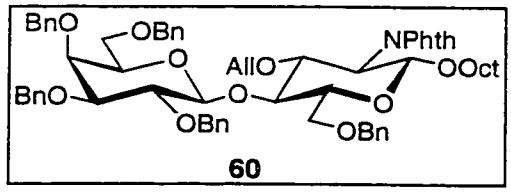


59

Compound **59** (1.31 g 78% mg, 77%) was synthesized from **58** (1.76 g, 1.74 mmol),

methanol (50 mL), and sodium (12mg) as described for the preparation of **53**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88-7.70 (4H, Phth), 7.38-7.20 (20H, Ph), 5.44 (1H, H_c allyl), 5.07 (d, 1H, $J_{1,2}$=8.6 Hz, H-1), 4.90-4.84 (2H, PhC$\underline{H}_2$, H_a allyl), 4.72-4.52 (7H, H-1', PhC$\underline{H}_2$x5, H_b allyl), 4.39, 4.35 (d, 1H, J=11.9 Hz, PhC$\underline{H}_2$), 4.28 (1H, H_d allyl), 4.24 (dd, 1H, $J_{3,4}$=8.5, $J_{2,3}$=10.7 Hz, H-3), 4.13 (dd, 1H, $J_{1,2}$=8.6, $J_{2,3}$=10.9 Hz, H-2), 4.02-3.97 (2H, H-4, H-6a), 3.87-3.74 (4H, H-2', H-6b, OC$\underline{H}_2$CH$_2$, H_e allyl), 3.62-3.56 (2H, H-5, H-6a'), 3.52-3.44 (2H, H-5', H-6b'), 3.35 (dt, 1H, J=6.4, 9.2 Hz, OC$\underline{H}_2$CH$_2$), 3.31 (dd, $J_{3',4'}$=2.9, $J_{2',3'}$=9.7 Hz, H-3'), 3.27 (d, 1H, $J_{3',4'}$=1.2 Hz, H-4'), 1.44-1.30 (2H, OCH$_2$C$\underline{H}_2$), 1.18-0.90 (10H, CH_2, octyl), 0.78 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.5, 139.0, 138.6, 138.5 (aromatic quat.), 135.6 (CH$_2$=$\underline{C}$HCH$_2$O), 134.7, 132.5, 129.1, 129.0, 128.8, 128.7, 128.5, 128.4, 128.3, 128.0 (aromatic CH), 116.7 ($\underline{C}$H$_2$=CHCH$_2$O), 104.5 (C-1'), 99.2 (C-1), 82.5 (C-3', C-4'), 79.3 (C-3), 78.9 (C-4), 75.4 (C-5), 75.0, 74.2, 74.1, 73.7, 73.1 (C-5', Ph$\underline{C}$H$_2$x4, CH$_2$=CH$\underline{C}$H$_2$O), 70.3 (O$\underline{C}$H$_2$CH$_2$), 69.2, 69.1 (C-6, C-6'), 56.8 (C-2) 32.4, 30.0, 29.9, 29.8, 26.5, 23.3 (CH_2, octyl), 14.7 (CH_3, octyl). *Anal.* Calcd for $C_{59}H_{69}NO_{12}$ (983.48): C, 72.00; H, 7.07. Found: C, 71.69; H, 7.14.

Octyl 3-O-allyl-6-O-benzyl-4-O-(2,3,4,6-tetra-O-benzyl-β-D-galactopyranosyl)-2-deoxy-2-phthalimido-β-D-glucopyranoside (**60**)

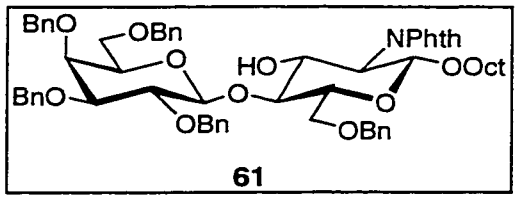


60

Compound **60** (94 mg, 35%, 30% unreacted starting material **59**) was synthesized from compound **59** (115 mg, 0.12 mmol), DMF (2 mL),

tetrabutyl ammonium iodide (90 mg, 0.24 mmol), benzyl bromide (26 μL, 0.24 mmol) and sodium hydride (10 mg, 60% dispersion in oil, 0.25 mmol) as described for the preparation of **55**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88-7.70 (4H, Phth), 7.40-7.18 (25H, Ph), 5.47 (1H, H_c allyl), 5.10 (d, 1H, $J_{1,2}$=8.1 Hz, H-1), 4.89 (H_a allyl), 4.91, 4.78, 4.76, 4.53, 4.52, 4.44 (d, 1H, J=11.2 Hz, PhC$\underline{H}_2$), 4.70-4.65 (4H, H-1', PhC$\underline{H}_2$x2, H_b allyl), 4.40-4.32 (PhC$\underline{H}_2$x2, H_d allyl), 4.20-4.12 (2H, H-2, H-3), 3.93 (dd, 1H, $J_{3,4}$=8.2, $J_{4,5}$=9.9 Hz, H-4), 3.88-3.84 (2H, H-4', H_e allyl), 3.81 (dd, 1H, $J_{5,6a}$=4.4, $J_{6a,6b}$=10.8 Hz, H-6a), 3.77 (dt, 1H, J=6.7, 9.9 Hz, OC$\underline{H}_2$CH$_2$), 3.71 (dd, 1H, $J_{5,6b}$=1.7, $J_{6a,6b}$=10.9 Hz, H-6b), 3.68 (dd, 1H, $J_{1',2'}$=7.7, $J_{2',3'}$=9.7 Hz, H-2'), 3.59 (dd, 1H, $J_{6a',5'}$=$J_{6a',6b'}$=8.2 Hz, H-6a'), 3.56-3.50 (2H, H-5', H-6b'), 3.40-3.32 (3H, H-3', H-5, OC$\underline{H}_2$CH$_2$), 1.42-1.34 (2H, OCH$_2$C$\underline{H}_2$), 1.18-0.90 (10H, CH_2, octyl), 0.78 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.8, 139.5, 139.3, 139.2, 138.8 (aromatic quat.), 136.1 (CH$_2$=$\underline{C}$HCH$_2$O), 134.6, 132.5, 129.1, 129.0, 128.9, 128.8, 128.6, 128.5, 128.4, 128.2, 128.1, 127.9 (aromatic CH), 116.7 ($\underline{C}$H$_2$=CHCH$_2$O), 103.6 (C-1'), 99.1 (C-1), 83.1 (C-3'), 80.7 (C-2'), 78.4 (C-4), 78.2 (C-2, C-3), 76.1, 76.0, 75.1, 74.4, 74.3, 73.8, 73.3 (C-4', C-5, C-5', Ph$\underline{C}$H$_2$x5, CH$_2$=CH$\underline{C}$H$_2$O), 70.2 (O$\underline{C}$H$_2$CH$_2$), 69.1, 69.0 (C-6, C-6'), 56.8 (C-2) 32.4, 30.0, 29.9, 29.8, 26.5, 23.3 (CH_2, octyl), 14.7 (CH_3, octyl). *Anal.* Calcd for $C_{66}H_{75}NO_{12}$ (1074.30): C, 73.79; H, 7.04. Found: C, 73.79; H, 7.20.

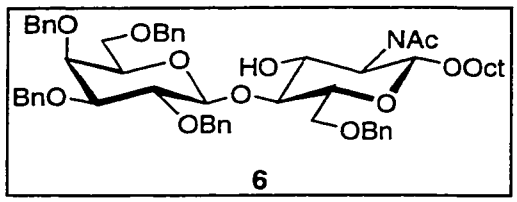
Octyl 6-O-benzyl-4-O-(2,3,4,6-tetra-O-benzyl-β-D-galactopyanosyl)-2-deoxy-2-phthalimido-β-D-glucopyranoside (**61**)



61

Compound **60** (1.03 g, 0.91 mmol) was dissolved in dry methanol (50 mL) and palladium chloride (25 mg, 0.14 mmol) was added. The solution was stirred at room temperature for 3 hours. The solvent was concentrated and the crude was purified without further workup. Column chromatography (10:1 toluene/ethyl acetate) resulted in **61** (781 mg, 95%) as a colorless oil: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.88-7.70 (4H, Phth), 7.38-7.20 (25H, Ph), 5.16 (d, 1H, $J_{1,2}$=8.5 Hz, H-1), 4.88, 4.84, 4.76, 4.69, 4.51(d, 1H, J=11.6 Hz, PhC$\underline{H}_2$), 4.43 (dd, 1H, $J_{3,4}$=8.2, $J_{2,3}$=10.8 Hz, H-3), 4.39-4.25 (6H, H-1', PhC$\underline{H}_2$x5), 4.16 (dd, 1H, $J_{1,2}$=8.6, $J_{2,3}$=10.9 Hz, H-2), 3.82-3.74 (4H, H-2', H-4', H-6a, OC$\underline{H}_2CH_2$), 3.71-6.64 (2H, H-5, H-6), 3.59 (dd, 1H, $J_{3,4}$=$J_{4,5}$=8.3 Hz, H-4), 3.55-3.51 (2H, H-5', H-6a'), 3.48-3.42 (2H, H-3', H-6b'), 3.39 (dt, 1H, J=6.4, 9.8 Hz, OC$\underline{H}_2CH_2$), 1.45-1.18 (2H, $OCH_2C\underline{H}_2$), 1.15-0.82 (10H, CH_2, octyl), 0.80 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.6, 138.5, 138.4, 138.2, 137.5, 133.8 (aromatic quat.), 132.0, 128.5, 128.4, 128.3, 128.1, 128.0, 127.9, 127.8, 127.6, 127.4 (aromatic CH), 82.4 (C-1'), 82.2 (C-1), 79.0 (C-3', C-4), 77.4 (C-2'), 75.5, 74.8, 74.7, 73.6, 73.3, 73.1, 73.0 (C-4', C-5, C-5', Ph$\underline{C}H_2$x5), 69.8 (C-3), 69.7 (O$\underline{C}H_2CH_2$), 68.7, 68.4 (C-6, C-6'), 56.3 (C-2) 31.7, 29.3, 29.2, 25.9, 22.6 (CH_2, octyl), 14.1 (CH_3, octyl).

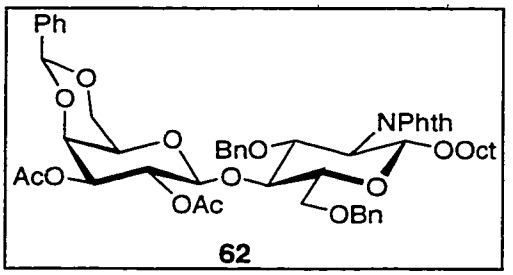
Octyl 2-acetamido-6-O-benzyl-4-O-(2,3,4,6-tetra-O-benzyl-β-D-galactopyranosyl)-2-deoxy-β-D-glucopyranoside (**6**)



6

Compound **6** (615 mg, 96%) was synthesized from compound **61** (700 mg, 0.68 mmol), *t*-butanol (35 mL) and ethylenediamine (10 mL) followed by acetic anhydride (15 mL), methanol (35 mL) and triethylamine (0.5 mL) as described for the preparation of **5**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38-7.20 (25H, Ph), 5.53 (d, 1H, J=7.5 Hz, NHAc), 4.90, 4.82, 4.73, 4.70, 4.54, 4.42, 4.35, 4.28 (d, 1H, J=11.5 Hz, PhCH_2), 4.85 (d, 1H, $J_{1,2}$=8.2 Hz, H-1), 4.29 (d, 1H, $J_{1',2'}$=7.9 Hz, H-1'), 4.27 (dd, 1H, $J_{2,3}$=$J_{3,4}$=9.0 Hz, H-3), 3.85 (d, 1H, $J_{3',4'}$=2.5 Hz, H-4'), 3.83 (dt, 1H, J=6.4, 9.0 Hz, OC$H_2$$CH_2$), 3.76 (dd, 1H, $J_{1',2'}$=7.9, $J_{2',3'}$=9.7 Hz, H-2'), 3.69 (d, 1H, $J_{5,6a}$=1.5, $J_{6a,6b}$=10.7 Hz, H-6a), 3.61 (d, 1H, $J_{5,6b}$=5.0, $J_{6a,6b}$=10.7 Hz, H-6b), 3.58-3.45 (6H, H-4, H-5, H-5', H-6a', H-6b', OC$H_2$$CH_2$), 3.44 (dd, $J_{3',4'}$=2.5, $J_{2',3'}$=9.7 Hz, H-3'), 3.25 (ddd, 1H, $J_{1,2}$=$J_{2,NHAc}$=7.1, $J_{2,3}$=10.1 Hz, H-2) 1.98 (s, 3H, CH_3 NHAc), 1.60-1.50 (2H, OCH_2CH_2), 1.35-1.20 (10H, CH_2, octyl), 0.85 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.9 (CO, acetate), 139.2, 139.1, 138.9, 138.3 (aromatic quat.), 129.2, 129.1, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 128.0 (aromatic CH), 104.4 (C-1'), 100.5 (C-1), 83.0 (C-3'), 82.4 (C-4), 79.7 (C-2'), 76.1, 75.3, 75.1, 74.3, 74.2, 74.0, 73.9, 73.6 (C-4', C-5, C-5', PhCH_2x5), 72.0 (C-3), 70.4 (OC$H_2$$CH_2$), 69.4, 68.9 (C-6, C-6'), 58.5 (C-2) 32.5, 30.3, 30.0, 26.7, 24.5 (CH_2, octyl), 23.4 (CH_3, acetate), 14.8 (CH_3, octyl). *Anal.* Calcd for $C_{57}H_{71}NO_{11}$ (945.17): C, 72.36; H, 7.56. Found: C, 72.59; H, 7.65.

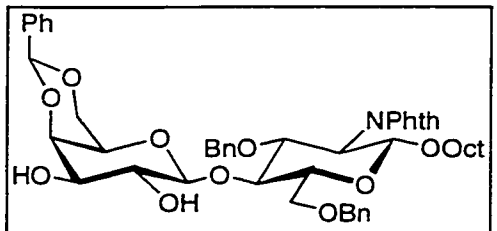
Octyl 4-O-(2,3-di-O-acetyl-4,6,-O-benzylidine-β-D-galactopyranosyl)-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (**62**)



62

Compound **62** (610 mg, 61%) was synthesized from *Octyl 3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside* [62] (612 mg, 1.14 mmol), compound **48** (1.066 g, 1.26 mmol), N-iodosuccinimide (513 mg, 1.28 mmol), catalytic silver triflate, dry DCM (40 mL) and 4 Å sieves as described for the preparation of **52**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80-7.60 (4H, Phth), 7.40-6.82 (25H, Ph), 5.40 (s, 1H, PhC<u>H</u>O_2), 5.34 (dd, 1H, $J_{1',2'}$=7.9, $J_{2',3'}$=10.2 Hz, H-2'), 5.06 (d, 1H, $J_{1,2}$=8.6 Hz, H-1), 4.97, 4.79, 4.52, 4.50 (d, 1H, J=11.5 Hz, PhC<u>H</u>$_2$), 4.77 (dd, 1H, $J_{3',4'}$=3.6, $J_{2',3'}$=10.2 Hz, H-3'), 4.62 (d, 1H, $J_{1',2'}$=8.0 Hz, H-1'), 4.28-4.22 (2H, H-4', H-6a'), 4.12-4.06 (3H, H-2, H-6a, H-6b), 3.90 (dd, 1H, $J_{5',6b'}$=1.6, $J_{6a',6b'}$=12.3 Hz, H-6b'), 3.84-3.72 (3H, H-3, H-4, OC<u>H</u>$_2$CH$_2$), 3.52 (1H, H-5), 3.33 (dt, 1H, J=7.0, 9.4 Hz, OC<u>H</u>$_2$CH$_2$), 3.21 (d, 1H, J=1.1Hz, H-5'), 2.03 (s, 6H, CH_3, acetate), 1.42-1.30 (2H, OCH$_2$C<u>H</u>$_2$), 1.28-0.92 (10H, CH_2, octyl), 0.88 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.7, 139.5, 139.4, 133.8 (aromatic quat.), 129.1, 128.4, 128.3, 128.2, 128.0, 124.3 (aromatic CH), 101.8 (Ph<u>C</u>HO_2), 100.3 (C-1'), 98.1 (C-1), 78.2 (C-2'), 77.0 (C-3), 75.1, 73.1 (Ph<u>C</u>H$_2$), 73.8 (C-5), 72.6 (C-4'), 71.3 (C-3'), 69.8 (O<u>C</u>H$_2$CH$_2$), 69.2 (C-2'), 68.8 (C-6'), 68.0 (C-6), 66.1 (C-5'), 55.6 (C-2) 31.5, 29.3, 29.2, 29.1, 25.8, 22.6 (CH_2, octyl), 14.1 (CH_3, octyl). HR-ESMS calcd for $C_{53}H_{61}NO_{14}Na$ 958.3990, found 958.3997.

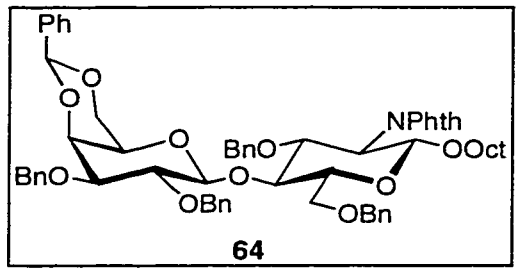
Octyl 3,6-di-O-benzyl-4-O-(4,6-benzylidene-β-D-galactopyranosyl)-2-deoxy-2-phthalimido-β-D-glucopyranoside (**63**)



63

Compound **63** (43 mg, 70%) was synthesized from compound **62** (67 mg, 0.072 mmol), catalytic sodium and methanol (2 mL) as described for the preparation of **53**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80-7.60 (4H, Phth), 7.32-7.20 (15H, Ph), 5.44 (s, 1H, PhC$\underline{H}O_2$), 5.01, 4.69, 4.67, 4.53 (d, 1H, J=11.6 Hz, PhC$\underline{H}_2$), 4.83 (d, 1H, $J_{1,2}$=7.9 Hz, H-1), 4.49 (d, 1H, $J_{1',2'}$=7.6 Hz, H-1'), 4.18 (dd, 1H, $J_{2,3}$=$J_{3,4}$=9.0 Hz, H-3), 4.10 (dd, 1H, $J_{6a',5'}$=1.1, $J_{6a',6b'}$=9.3 Hz, H-6a'), 4.04-3.96 (3H, H-2, H-6a, H-6b), 3.65 (dd, 1H, $J_{1',2'}$=7.8, $J_{2',3'}$=9.6 Hz, H-2'), 3.55 (ddd, 1H, $J_{5,6a}$=$J_{5,6b}$=3.0, $J_{4,5}$=11.1 Hz, H-5), 3.32 (1H, OC$\underline{H}_2$CH$_2$), 3.47-3.40 (2H, H-3', H-6b'), 3.33 (dt, 1H, J=7.0, 9.4 Hz, OC$\underline{H}_2$CH$_2$), 2.99 (bs, 1H, H-5'), 1.66-1.45 (2H, OCH$_2$C$\underline{H}_2$), 1.36-1.20 (10H, CH_2, octyl), 0.82 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.0, 138.0, 137.7, 134.2 (aromatic quat.), 129.2, 128.5, 128.4, 128.3, 128.2, 128.0, 127.8, 127.5, 126.5,123.5 (aromatic CH), 103.4 (C-1'), 101.4 (Ph$\underline{C}HO_2$), 99.9 (C-1), 79.2, 78.1, 75.3, 75.1, 72.8, 72.3, (C-2', C-3, C-3', C-4, C-4', C-5), 74.7, 73.9 (Ph$\underline{C}H_2$), 69.7 (O$\underline{C}H_2$CH$_2$), 69.0, 68.8 (C-6, C-6'), 66.9 (C-5'), 57.2 (C-2) 31.8, 29.6, 29.4, 26.0, 23.6, 22.7 (CH_2, octyl), 14.1 (CH_3, octyl).

Octyl 4-O-(2,3,-di-O-benzyl-4,6,-O-benzylidene-β-D-galactopyranosyl)-3,6,-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (**64**)

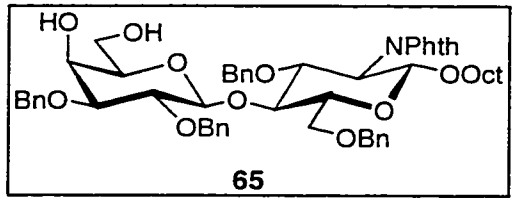


64

Compound **64** (255 mg, 66%) was synthesized from compound **63** (320 mg, 0.38 mmol), sodium hydride (44 mg, 60% dispersion in oil, 1.1 mmol), tetrabutyl ammonium iodide (191 mg, 0.52 mmol), benzyl bromide (100 μL, 0.92 mmol) and DMF (2 mL) as described for the preparation of **55**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82-7.58 (4H, Phth), 7.20-6.75 (25H, Ph), 5.40 (s, 1H, PhC$\underline{H}O_2$), 5.09 (d, 1H, $J_{1,2}$=8.6 Hz, H-1), 5.03, 4.86, 4.83, 4.72, 4.62, 4.59, 4.34 (d, 1H, J=12.7 Hz, PhC$\underline{H}_2$), 4.47 (d, 1H, $J_{1',2'}$=7.6 Hz, H-1'), 4.28 (dd, 1H, $J_{3,4}$=8.4, $J_{2,3}$=10.7 Hz, H-3), 4.26 (dd, 1H, $J_{6a',5'}$=1.2, $J_{6a',6b'}$=12.2 Hz, H-6a'), 4.17 (dd, 1H, $J_{1,2}$=8.5, $J_{2,3}$=10.8 Hz, H-2), 4.08 (dd, 1H, $J_{4,5}$=8.5, $J_{3,4}$=9.9 Hz, H-4), 4.01 (d, 1H, $J_{3',4'}$=3.7 Hz, H-4'), 3.91 (dd, 1H, $J_{5,6a}$=3.8, $J_{6a,6b}$=12.0 Hz, H-6a), 3.85 (dd, 1H, $J_{5,6b}$=1.7, $J_{6a,6b}$=12.4 Hz, H-6b), 3.80-3.69 (3H, H-2', H-6b', OC$\underline{H}_2$CH$_2$), 3.53 (1H, H-5), 3.40 (dd, 1H, $J_{3',4'}$=3.5, $J_{2',3'}$=9.6 Hz, H-3'), 3.32 (dt, 1H, J=6.1, 9.3 Hz, OC$\underline{H}_2$CH$_2$), 3.14 (bs, 1H, H-5'), 1.40-1.25 (2H, OCH$_2$C$\underline{H}_2$), 1.15-0.90 (10H, CH_2, octyl), 0.78 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.7, 138.3, 138.1, 137.9, 134.2 (aromatic quat.), 128.9, 128.7, 128.5, 128.4, 128.3, 127.9, 127.6, 127.4, 125.3, 123.4 (aromatic CH), 102.3 (C-1'), 101.1 (Ph$\underline{C}$HO$_2$), 97.0 (C-1), 79.4 (C-3'), 78.8 (C-2'), 78.4 (C-4), 76.9 (C-3), 74.3 (C-5), 75.1, 74.7, 72.5 71.6 (PhCH$_2$), 71.2 (C-4'), 69.2 (O$\underline{C}$H$_2$CH$_2$), 68.1 (C-6'), 67.5 (C-6), 64.7 (C-5'), 55.0 (C-2) 31.2, 29.9, 29.4, 29.0, 23.6, 22.7 (CH_2, octyl), 14.7 (CH_3,

octyl). *Anal.* Calcd for $C_{63}H_{69}NO_{12}$ (1031.48): C, 73.31; H, 6.74. Found: C, 73.23; H, 6.61.

Octyl 3,6-di-O-benzyl-4-O-(2,3-di-O-benzyl-β-D-galactopyranosyl)-2-deoxy-2-phthalimido-β-D-glucopyranoside (**65**)

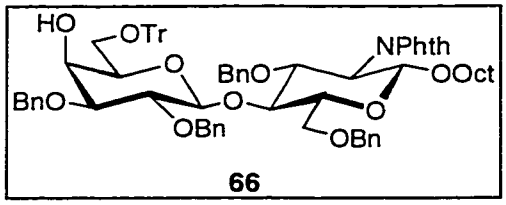


65

Compound **64** (549 mg, 0.52 mmol) was dissolved in 80% acetic acid (50 mL). The solution was heated to 80°C, stirred for 4 hours, cooled to room temperature and co-concentrated with toluene. Column chromatography (5:1 toluene/ethyl acetate) of the crude resulted in **65** (449 mg, 92%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82-7.60 (4H, Phth), 7.38-6.82 (20H, Ph), 5.09 (d, 1H, $J_{1,2}$=8.6 Hz, H-1), 4.87, 4.84, 4.79, 4.69, 4.46, 4.39 (d, 1H, J=12.0 Hz, $PhC\underline{H}_2$), 4.41 (d, 1H, $J_{1',2'}$=8.4 Hz, H-1'), 4.28 (dd, 1H, $J_{3,4}$=8.6, $J_{2,3}$=10.8 Hz, H-3), 4.15 (dd, 1H, $J_{1,2}$=8.4, $J_{2,3}$=10.8 Hz, H-2), 4.03 (dd, 1H, $J_{3,4}$=$J_{4,5}$=9.6 Hz, H-4), 3.88 (d, 1H, $J_{3',4'}$=3.0 Hz, H-4'), 3.85 (dd, 1H, $J_{5,6a}$=4.0, $J_{6a,6b}$=10.8 Hz, H-6a), 3.76 (dt, 1H, J=6.4, 9.4 Hz, $OC\underline{H}_2CH_2$), 3.74-3.68 (2H, H-6a', H6b), 3.62-3.54 (3H, H-2', H-5, H-6b'), 3.38-3.34 (2H, H-3',$OC\underline{H}_2CH_2$), 3.20 (dd, 1H, J=4.1, 5.7 Hz, H-5'), 2.60 (bs, 1H, OH), 2.05 (bs, 1H, OH), 1.42-1.30 (2H, $OCH_2C\underline{H}_2$), 1.20-0.90 (10H, CH_2, octyl), 0.78 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.3, 139.2, 139.1, 138.6, 134.3 (aromatic quat.), 129.2, 129.0, 128.7, 128.6, 128.4, 128.3, 128.2, 127.8, 124.0 (aromatic CH), 103.5 (C-1'), 99.0 (C-1), 81.6 (C-3'), 80.0 (C-2'), 79.2 (C-4), 77.9 (C-3), 76.1, 75.9, 75.4, 74.6, 73.9, 72.9 (C-5, C-5', $Ph\underline{C}H_2$x4), 70.2 ($O\underline{C}H_2CH_2$), 68.7 (C-6, C-4'), 68.0 (C-6'), 63.2

(C-2) 32.3, 30.0, 29.8, 29.7, 26.5, 23.3 (CH_2, octyl), 14.7 (CH_3, octyl). *Anal.* Calcd for $C_{56}H_{65}NO_{12}$ (943.45): C, 71.24; H, 6.94. Found: C, 71.02; H, 6.94.

Octyl 3,6-di-O-benzyl-4-O-(2,3-di-O-benzyl-6-O-trityl-β-D-galactopyranosyl)-2-deoxy-2-phthalimido-β-D-glucopyranoside (**66**)

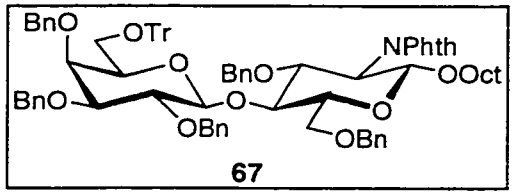


66

Compound **65** (428 mg, 0.45 mmol) was dissolved in dry DCM (15 mL) and trityl chloride (184 mg, 0.65 mmol) and diisopropylethylamine (115 μL, 0.64 mmol) were added. The solution was stirred at room temperature for 8 hours, diluted with toluene and concentrated under reduced pressure. Column chromatography (10:1 toluen:ethyl acetate) of the crude material afforded **66** (556 mg, quant.): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80-7.60 (4H, Phth), 7.40-6.85 (35H, Ph), 5.07 (d, 1H, $J_{1,2}$=8.2 Hz, H-1), 4.82, 4.79, 4.74, 4,71, 4.68, 4.60, 4.46, 4.40 (d, 1H, J=12.2 Hz, PhC$\underline{H}_2$), 4.38 (d, 1H, $J_{1',2'}$=7.9 Hz, H-1'), 4.21 (dd, 1H, $J_{3,4}$=8.3, $J_{2,3}$=10.7 Hz, H-3), 4.16 (dd, 1H, $J_{1,2}$=8.3, $J_{2,3}$=10.7 Hz, H-2), 4.09 (dd, 1H, $J_{3,4}$=8.4, $J_{4,5}$=9.9 Hz, H-4), 3.97 (d, 1H, $J_{3',4'}$=2.9 Hz, H-4'), 3.86 (dd, 1H, $J_{5,6a}$=4.0, $J_{6a,6b}$=11.0 Hz, H-6a), 3.75 (dt, 1H, J=6.4, 9.2 Hz, OC$\underline{H}_2$CH$_2$), 3.71 (dd, 1H, $J_{5,6b}$=1.5, $J_{6a,6b}$=11.0 Hz, H-6b), 3.64 (dd, 1H, $J_{1',2'}$=7.8, $J_{2',3'}$=9.3 Hz, H-2'), 3.51 (ddd, 1H, $J_{5,6b}$=1.7, $J_{5,6a}$=3.0, $J_{5,4}$=9.9 Hz, H-5), 3.42 (dd, 1H, $J_{6a',5'}$=6.4, $J_{6a',6b'}$=9.6 Hz, H-6a'), 3.33 (dt, 1H, J=6.2, 9.0 Hz, OC$\underline{H}_2$CH$_2$), 3.31 (dd, 1H, $J_{3',4'}$=3.3, $J_{2',3'}$=9.3 Hz, H-3'), 3.21 (dd, 1H, $J_{5',6b'}$=4.6, $J_{6a',6b'}$=9.4 Hz, H-6b'), 3.09 (dd, 1H, $J_{5',6a'}$=$J_{5',6b'}$=5.5 Hz, H-5'), 2.60 (bs, 1H, OH), 1.40-1.30 (2H, OCH$_2$C$\underline{H}_2$), 1.25-0.90 (10H, CH_2, octyl), 0.80 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (75 MHz, $CDCl_3$) δ

144.7, 139.4, 139.3, 139.1, 138.9, 134.3 (aromatic quat.), 129.7, 129.4, 129.1, 129.0, 128.9, 128.8, 128.6, 128.5, 128.4, 128.3, 128.2, 127.8, 127.5, 123.8 (aromatic CH), 103.4 (C-1'), 99.1 (C-1), 87.6 ($Ph_3\underline{C}$), 81.7 (C-3'), 80.3 (C-2'), 78.4 (C-4), 77.7 (C-3), 76.0 (C-5), 73.3 (C-5'), 76.1, 74.9, 73.9, 72.7 ($Ph\underline{C}H_2$), 70.2 ($O\underline{C}H_2CH_2$), 68.7 (C-6), 67.9 (C-4'), 63.5 (C-6'), 56.2 (C-2) 32.3, 30.0, 29.9, 29.8, 26.5, 23.3 (CH_2, octyl), 14.7 (CH_3, octyl).

*Octyl 3,6-di-*O*-benzyl-4-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-trityl-β-*D*-galactopyranosyl)-2-deoxy-2-phthalimido-β-*D*-glucopyranoside* (**67**)

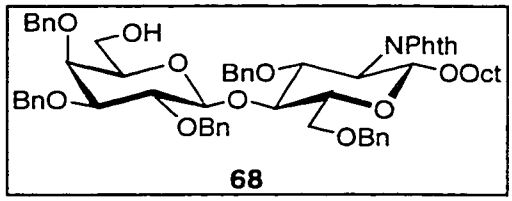


67

Compound **67** (477 mg, 84%) was synthesized from **66** (521 mg, 0.45 mmol), sodium hydride (31mg, 60% dispersion in oil, 0.68 mmol), benzyl bromide (150 μL, 1.35 mmol), tetrabutylammonium iodide (550 mg, 1.35 mmol) and DMF (5 ml) as described for the preparation of **55**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.80-7.60 (4H, Phth), 7.38-6.70 (40H, Ph), 5.02 (d, 1H, $J_{1,2}$=8.6 Hz, H-1), 4.84, 4.78, 4.75, 4,70, 4.69, 4.58, 4.43, 4.41, 4.37 (d, 1H, J=11.5 Hz, $PhC\underline{H}_2$), 4.36 (d, 1H, $J_{1',2'}$=7.7 Hz, H-1'), 4.20 (dd, 1H, $J_{3,4}$=8.3, $J_{2,3}$=10.8 Hz, H-3), 4.11 (dd, 1H, $J_{1,2}$=8.4, $J_{2,3}$=10.8 Hz, H-2), 3.98 (dd, 1H, $J_{3,4}$=8.4, $J_{4,5}$=9.9 Hz, H-4), 3.96 (d, 1H, $J_{3',4'}$=2.9 Hz, H-4'), 3.84 (dd, 1H, $J_{5,6a}$=4.2, $J_{6a,6b}$=10.8 Hz, H-6a), 3.75-3.68 (3H, H-2', H-6b, $OC\underline{H}_2CH_2$), 3.49 (ddd, 1H, $J_{5,6b}$=1.9, $J_{5,6a}$=4.3, $J_{5,4}$=9.9 Hz, H-5), 3.37-3.30 (3H, H-3', H-6a', $OC\underline{H}_2CH_2$), 3.21 (dd, 1H, $J_{5',6b'}=J_{6a',6b'}$=9.1 Hz, H-6b'), 3.11 (dd, 1H, $J_{5',6a'}$=5.9, $J_{5',6b'}$=8.3 Hz, H-5'), 1.40-1.25 (2H, $OCH_2C\underline{H}_2$), 1.08-0.92 (10H, CH_2, octyl), 0.80 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.9, 139.9, 139.6, 139.4, 139.3, 139.2, 134.2 (aromatic quat.),

129.3, 129.1, 128.9, 129.0, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 127.8, 127.7, 127.6, 123.4 (aromatic CH), 103.6 (C-1'), 99.0 (C-1), 87.5 ($Ph_3\underline{C}$), 83.0 (C-3'), 80.9 (C-2'), 78.6 (C-4), 78.6 (C-3), 77.9 (C-5), 76.1, 74.9, 74.7, 73.8, 74.5 ($Ph\underline{C}H_2$), 74.8 (C-4'), 73.9 (C-5'), 70.1 ($O\underline{C}H_2CH_2$), 68.8 (C-6), 62.4 (C-6'), 56.4 (C-2) 32.3, 30.0, 29.9, 29.8, 26.5, 23.3 (CH_2, octyl), 14.7 (CH_3, octyl). *Anal.* Calcd for $C_{82}H_{85}NO_{12}$ (1276.55): C, 77.15; H, 6.71. Found: C, 76.92; H, 6.84.

Octyl 3,6-di-O-benzyl-4-O-(2,3,4-tri-O-benzyl-β-D-galactopyranosyl)-2-deoxy-2-phthalimido-β-D-glucopyranoside (**68**)

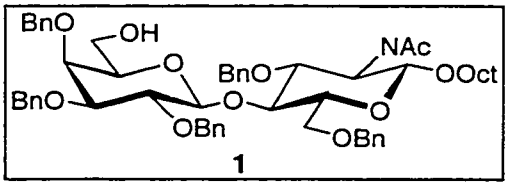


68

Compound **67** (456 mg, 0.36 mmol) was dissolved in a solution of 5% trifluoroacetic acid and 5% triisopropyl silane in DCM (20 mL). The reaction mixture was stirred at room temperature for 2 hours and concentrated with toluene as a co-solvent. Column chromatography (7:1 toluene/ethyl acetate) resulted in **68** (330 mg, 97%) as a colorless oil: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.80-7.60 (4H, Phth), 7.38-6.85 (25H, Ph), 5.08 (d, 1H, $J_{1,2}$=8.4 Hz, H-1), 4.89, 4.88, 4.84, 4,82, 4.56, 4.52, 4.45, 4.38 (d, 1H, J=11.9 Hz, $PhC\underline{H}_2$), 4.41 (d, 1H, $J_{1',2'}$=8.5 Hz, H-1'), 4.28 (dd, 1H, $J_{3,4}$=9.3, $J_{2,3}$=10.8 Hz, H-3), 4.14 (dd, 1H, $J_{1,2}$=8.4, $J_{2,3}$=10.9 Hz, H-2), 3.98 (dd, 1H, $J_{3,4}$=$J_{4,5}$=8.9 Hz, H-4), 3.84 (dd, 1H, $J_{5,6a}$=4.2, $J_{6a,6b}$=10.8 Hz, H-6a), 3.78-3.72 (3H, H-2', H-6b, $OC\underline{H}_2CH_2$), 3.66 (d, 1H, $J_{3',4'}$=3.9 Hz, H-4'), 3.58-3.52 (2H, H-5, H-6a'), 3.39 (dd, 1H, $J_{3',4'}$=2.9, $J_{2',3'}$=9.3 Hz, H-3'), 3.34 (dt, 1H, J=6.1, 9.5 Hz, $OC\underline{H}_2CH_2$), 3.29 (dd, 1H, $J_{5',6b'}$=4.5, $J_{6a',6b'}$=12.0 Hz, H-6b'), 3.20 (dd, 1H, $J_{5',6a'}$=4.6, $J_{5',6b'}$=7.7 Hz, H-5'), 2.34 (bs, 1H, OH),

1.40-1.20 (2H, $OCH_2C\underline{H}_2$), 1.15-0.92 (10H, CH_2, octyl), 0.80 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.8, 138.7, 138.6, 138.5, 133.7 (aromatic quat.), 131.8, 128.5, 128.3, 127.9, 127.6, 127.5, 127.0, 123.2 (aromatic CH), 103.1 (C-1'), 98.4 (C-1), 82.6 (C-3'), 80.0 (C-2'), 78.6 (C-4), 77.3 (C-3), 75.4 (C-5), 75.3, 74.9, 74.7, 74.3, 73.8, 73.2, 73.1 (C-4', C-5', $Ph\underline{C}H_2$x5), 69.5 ($O\underline{C}H_2CH_2$), 68.1 (C-6), 62.0 (C-6'), 55.9 (C-2) 31.7, 29.3, 29.2, 29.1, 25.9, 22.6 (CH_2, octyl), 14.7 (CH_3, octyl). *Anal.* Calcd for $C_{63}H_{71}NO_{12}$ (1034.24): C, 73.16; H, 6.92. Found: C, 72.90; H, 6.85.

*Octyl 2-acetamido-3,6-di-*O*-benzyl-4-*O*-(2,3,4-tri-*O*-benzyl-β-*D*-galactopyranosyl)-2-deoxy-β-*D*-glucopyranoside* (**1**)

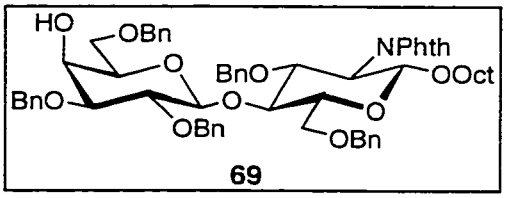


1

Compound **1** (255 mg, 86%) was synthesized from compound **68** (311 mg, 0.30 mmol), *t*-butanol (15 mL) and ethylenediamine (5 mL) followed by acetic anhydride (4 mL), methanol (10 mL) and triethylamine (0.1 mL) as described for the preparation of **5**: ^1H NMR (600 MHz, $CDCl_3$) δ 7.38-7.20 (25H, Ph), 5.65 (d, 1H, J=7.7 Hz, N$\underline{H}$Ac), 4.98, 4.92, 4.82, 4.79, 4.74, 4.72, 4.58, 4.56, 4.53, 4.41 (d, 1H, J=11.2 Hz, $PhC\underline{H}_2$), 4.90 (d, 1H, $J_{1,2}$=7.3 Hz, H-1), 4.39 (d, 1H, $J_{1',2'}$=7.9 Hz, H-1'), 4.17 (dd, 1H, $J_{2,3}=J_{3,4}$=8.8 Hz, H-3), 3.89 (dd, 1H, $J_{3,4}=J_{4,5}$=8.2 Hz, H-4), 3.83-3.74 (4H, H-2', H-6a, H-6b, $OC\underline{H}_2CH_2$), 3.70 (d, 1H, $J_{3',4'}$=2.7 Hz, H-4'), 3.62 (ddd, 1H, J=3.3, 7.9 Hz, H-5), 3.58 (dd, 1H, J=3.5, 7.7, H-6a'), 3.44 (dt, 1H, J=6.2, 9.0 Hz, $OC\underline{H}_2CH_2$), 3.39 (dd, 1H, $J_{3',4'}$=2.9, $J_{2',3'}$=10.7 Hz, H-3'), 3.35 (m, 1H, H-6b'), 3.29 (ddd, 1H, $J_{1,2}=J_{2,NHAc}$=8.5, $J_{2,3}$=9.1 Hz, H-2), 3.19 (dd, 1H, J=5.1, 8.5 Hz, H-5'), 2.40 (bs, 1H, OH), 1.84 (s, 3H, CH_3

NHAc), 1.62-1.45 (2H, $OCH_2C\underline{H}_2$), 1.35-1.20 (10H, CH_2, octyl), 0.84 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0 (CO, acetate), 139.6, 139.3, 139.2, 139.1, 139.0 (aromatic quat.), 129.1, 129.0, 128.9, 128.8, 128.6, 128.4, 128.2, 128.1 (aromatic CH), 103.9 (C-1'), 100.2 (C-1), 83.2 (C-3'), 80.6 (C-2'), 78.2 (C-4), 78.1 (C-3), 76.0, 75.7, 75.5, 75.1, 74.4, 73.9, 73.8, (C-4', C-5, C-5', $Ph\underline{C}H_2x5$), 70.3 ($O\underline{C}H_2CH_2$), 69.4 (C-6), 62.5 (C-6'), 57.1 (C-2) 32.5, 30.3, 30.1, 30.0, 26.7, 24.3 (CH_2, octyl), 23.3 (CH_3, acetate), 14.7 (CH_3, octyl). *Anal.* Calcd for $C_{57}H_{71}NO_{11}$ (945.17): C, 72.36; H, 7.56. Found: C, 72.16; H, 7.71.

Octyl 3,6-di-O-benzyl-4-O-(2,3,6-tri-O-benzyl-β-D-galactopyranosyl)-2-deoxy-2-phthalimido-β-D-glucopyranoside (**69**)

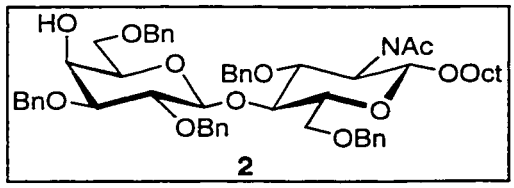


69

Compound **64** (214 mg, 0.21 mmol), sodium cyanoborohydride (64 mg, 1.01 mmol), and methyl orange indicator were dissolved in dry THF (5 mL) containing crushed 4 Å molecular sieves. The solution was cooled to 0°C followed by the addition of ethereal hydrogen chloride until the red color of the solution persisted. After 3 hours the reaction was quenched with sodium bicarbonate, filtered through celite, diluted with DCM, washed with water and concentrated under reduced pressure. Column chromatography (7:1 toluene/ethyl acetate) of the residue gave **69** (124 mg, 57%) as a colorless oil: ^1H NMR (500 MHz, $CDCl_3$) δ 7.80-7.60 (4H, Phth), 7.38-6.80 (25H, Ph), 5.07 (d, 1H, $J_{1,2}$=8.4 Hz, H-1), 4.83, 4.82, 4.78, 4,70, 4.66, 4.57, 4.46, 4.42, 4.37 (d, 1H, J=12.1 Hz, $PhC\underline{H}_2$), 4.41 (d, 1H, $J_{1',2'}$=8.0 Hz, H-1'), 4.26 (dd, 1H, $J_{3,4}$=8.6, $J_{2,3}$=10.9 Hz,

H-3), 4.15 (dd, 1H, $J_{1,2}$=8.4, $J_{2,3}$=10.8 Hz, H-2), 4.04 (dd, 1H, $J_{3,4}$=$J_{4,5}$=8.7 Hz, H-4), 3.99 (s, 1H, H-4'), 3.85 (dd, 1H, $J_{5,6a}$=4.1, $J_{6a,6b}$=11.0 Hz, H-6a), 3.75 (dt, 1H, J=6.0, 9.5 Hz, OC$\underline{H}_2$CH$_2$), 3.71 (dd, 1H, $J_{5,6b}$=1.2, $J_{6a,6b}$=10.9 Hz, H-6b), 3.65 (dd, 1H, $J_{5',6a'}$=6.8, $J_{6a',6b'}$=10.0 Hz, H-6a'), 3.60 (dd, 1H, $J_{1',2'}$=$J_{2',3'}$=7.9 Hz, H-2'), 3.56-3.50 (2H, H-5, H-6b'), 3.37-3.30 (3H, H-3', H-5', OC$\underline{H}_2$CH$_2$), 1.40-1.30 (2H, OCH$_2$C$\underline{H}_2$), 1.18-0.88 (10H, CH$_2$, octyl), 0.78 (t, 3H, J=7.0 Hz, CH$_3$, octyl); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.6, 139.3, 139.1, 138.8, 138.7, 134.3 (aromatic quat.), 132.4, 129.2, 129.1, 129.0, 128.9, 128.7, 128.6, 128.5, 128.4, 128.3, 128.1, 127.6 (aromatic CH), 103.9 (C-1'), 99.0 (C-1), 81.7 (C-3'), 80.1 (C-2'), 78.9 (C-4), 77.8 (C-3), 76.1, 75.1, 74.3, 73.8, 73.5 (Ph$\underline{C}$H$_2$), 75.0 (C-5), 72.8 (C-5'), 70.2 (O$\underline{C}$H$_2$CH$_2$), 69.5 (C-6'), 68.7 (C-6), 67.2 (C-4'), 56.5 (C-2) 32.3, 30.0, 29.9, 29.8, 26.5, 23.3 (CH$_2$, octyl), 14.7 (CH$_3$, octyl). *Anal.* Calcd for $C_{63}H_{71}NO_{12}$ (1034.24): C, 73.16; H, 6.92. Found: C, 73.32; H, 6.87.

*Octyl 2-acetamido-3,6-di-*O*-benzyl-4-*O*-(2,3,6-tri-*O*-benzyl-β-*D*-galactosyl)-2-deoxy-β-*D*-glucopyranoside* (**2**)

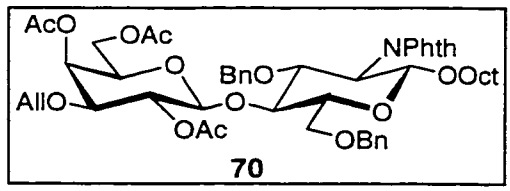


2

Compound **2** (91 mg, 90%) was synthesized from compound **69** (110 mg, 0.11 mmol), *t*-butanol (5 mL) and ethylenediamine (2 mL) followed by acetic anhydride (2 mL), methanol (5 mL) and triethylamine (0.1 mL) as described for the preparation of **5**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35-7.20 (25H, Ph), 5.68 (s, 1H NH$\underline{A}$c), 4.89 (d, 1H, $J_{1,2}$=7.0 Hz, H-1), 4.88, 4.81, 4.74, 4,70, 4.66, 4.58, 4.54, 4.47, 4.43, 4.37 (d, 1H, J=11.3 Hz, PhC$\underline{H}_2$), 4.41 (d, 1H, $J_{1',2'}$=7.8 Hz, H-1'), 4.12 (dd, 1H,

$J_{2,3}$=$J_{3,4}$=8.4 Hz, H-3), 4.00 (d, 1H, $J_{3',4'}$=3.5 Hz, H-4'), 3.96 (dd, 1H, $J_{3,4}$=$J_{4,5}$=7.8 Hz, H-4), 3.83-3.78 (2H, H-6a, OC<u>H</u>$_2$CH$_2$), 3.73 (dd, 1H, $J_{5',6a'}$=3.0, $J_{6a',6b'}$=10.6 Hz, H-6a'), 3.68 (dd, 1H, $J_{5,6b}$=6.8, $J_{6a,6b}$=9.7 Hz, H-6b), 3.61-3.56 (2H, H-2', H-5), 3.53 (dd, 1H, $J_{5',6b'}$=5.3, $J_{6a',6b'}$=9.7 Hz, H-6b'), 3.43 (dt, 1H, J=6.4, 9.1 Hz, OC<u>H</u>$_2$CH$_2$), 3.38-3.30 (3H, H-2, H-3', H-5'), 2.42 (bs, 1H, OH), 1.84 (s, 3H, CH_3, acetate), 1.60-1.48 (2H, OCH$_2$C<u>H</u>$_2$), 1.35-1.20 (10H, CH_2, octyl), 0.85 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.2, 139.1, 138.3, 138.2, 138.0 (aromatic quat.), 128.9, 128.7, 128.6, 128.4, 128.3, 127.4, 127.1, 125.3 (aromatic CH), 102.5 (C-1'), 99.1 (C-1), 81.3 (C-3'), 78.7 (C-2'), 77.3 (C-3), 76.4 (C-4), 74.9, 73.8, 73.1, 72.2, 71.8 (Ph<u>C</u>H$_2$), 74.0 (C-5), 72.1 (C-5'), 69.0 (O<u>C</u>H$_2$CH$_2$), 62.9, 62.8 (C-6, C-6'), 65.2 (C-4'), 54.7 (C-2) 34.8, 32.8, 32.7, 28.9, 22.3 (CH_2, octyl), 23.3 (CH_3, acetate), 14.7 (CH3, octyl). *Anal.* Calcd for $C_{57}H_{71}NO_{11}$ (945.17): C, 72.36; H, 7.56. Found: C, 71.87; H, 7.58.

Octyl 4-O-(2,4,6-tri-O-acetyl-3-O-allyl-β-D-galactopyranosyl)-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (**70**)

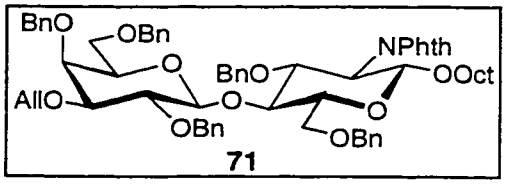


70

Compound **70** (447 mg, 81%) was synthesized from *Octyl 3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside* [62] (343 mg, 0.64 mmol), donor **51** (381 mg, 0.98 mmol), N-iodosuccinimide (247 mg, 0.99 mmol), catalytic silver triflate, and dry DCM (20 mL) as described for compound **52**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80-7.60 (4H, Phth), 7.38-6.80 (10H, Ph), 5.76 (1H, H_c allyl), 5.28 (dd, 1H, $J_{4',5'}$=1.1, $J_{3',4'}$=3.3 Hz, H-4'), 5.22 (1H, H_a allyl), 5.15 (1H H_b allyl), 5.05 (d, 1H, $J_{1,2}$=8.6

Hz, H-1), 5.03 (dd, 1H, $J_{1',2'}$=8.1, $J_{2',3'}$=10.0 Hz, H-2'), 4.79, 4.77, 4.50, 4.42 (d, 1H, J=12.3 Hz, PhC$\underline{H}_2$), 4.54 (d, 1H, $J_{1',2'}$=8.1 Hz, H-1'), 4.22 (dd, 1H, $J_{3,4}$=8.6, $J_{2,3}$=10.9 Hz, H-3), 4.10 (dd, 1H, $J_{1,2}$=8.4, $J_{2,3}$=10.8 Hz, H-2), 4.08 (1H, H_d allyl), 4.00 (dd, 1H, $J_{3,4}$=8.6, $J_{4,5}$=9.9 Hz, H-4), 3.94 (dd, 1H, $J_{5',6a'}$=1.7, $J_{6a',6b'}$=6.7 Hz, H-6a'), 3.84 (1H, H_e allyl), 3.79-3.76 (3H, H-6a, H-6b, H-6b'), 3.73 (dt, 1H, J=6.4, 9.5 Hz, OC$\underline{H}_2$CH$_2$), 3.56 (ddd, 1H, $J_{4',5'}$=1.2, $J_{5',6a'}$=$J_{5',6b'}$=5.5 Hz, H-5'), 3.52 (1H, H-5), 3.32 (dt, 1H, J=6.2, 9.4 Hz, OC$\underline{H}_2$CH$_2$), 3.27 (dd, 1H, $J_{3',4'}$=3.5, $J_{2',3'}$=10.0 Hz, H-3'), 2.02 (s, 9H, CH$_3$, acetate), 1.42-1.34 (2H, OCH$_2$C$\underline{H}_2$), 1.18-0.90 (10H, CH$_2$, octyl), 0.78 (t, 3H, J=7.0 Hz, CH$_3$, octyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.5, 170.3, 169.3 (CO, acetate), 138.8, 138.3 (aromatic quat.), 134.2 (CH$_2$=$\underline{C}$HCH$_2$O), 128.5, 128.0, 127.9, 127.8, 127.0, 123.2 (aromatic CH), 117.1 ($\underline{C}$H$_2$=CHCH$_2$O), 100.6 (C-1'), 98.4 (C-1), 78.3 (C-4), 77.0 76.9 (C-3, C-3'), 75.0 (C-5), 74.4, 73.6 (Ph$\underline{C}$H$_2$), 71.1 (C-2'), 70.7 (C-5'), 70.5 (CH$_2$=CH$\underline{C}$H$_2$O), 69.6 (O$\underline{C}$H$_2$CH$_2$), 67.9 (C-6), 65.9 (C-4'), 61.4 (C-6'), 55.8 (C-2) 31.7, 29.2, 29.1, 25.8, 22.6 (CH$_2$, octyl), 21.0, 20.8 (CH$_3$, acetate), 14.7 (CH$_3$, octyl). HR-ESMS calcd for $C_{51}H_{63}NO_{15}Na$ 952.4095, found 952.4094.

*Octyl 4-O-(3-O-allyl-2,4,6-tri-*O*-benzyl-β-*D*-galactopyranosyl)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-*D*-glucopyranoside* (**71**)

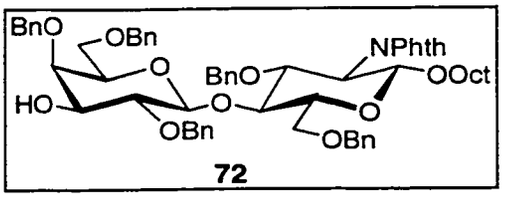


71

Compound **71** (142 mg, 27%) was synthesized through an initial deacetylation of **70** (446 mg, 0.52 mmol) with sodium and methanol as described for compound **53**. The crude was redissolved in DMF (5 mL) with sodium hydride (32 mg,

60% dispersion in oil, 0.80 mmol), tetrabutylammonium iodide (87 mg, 2.4 mmol) and benzyl bromide (250 μL, 2.3 mmol) as described for the preparation of **55**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.80-7.60 (4H, Phth), 7.38-6.80 (25H, Ph), 5.91 (1H, H_c allyl), 5.31 (1H, H_a allyl), 5.15 (1H H_b allyl), 5.08 (d, 1H, $J_{1,2}$=8.4 Hz, H-1), 4.91, 4.86, 4.80, 4.76, 4.55, 4.50, 4.34 (d, 1H, J=11.7 Hz, PhC$\underline{H}_2$), 4.45-4.38 (4H, H-1', PhC$\underline{H}_2$x3), 4.27-4.22 (3H, H-3, H-6a, PhC$\underline{H}_2$), 4.27-4.13 (2H, H-2, H_d allyl), 4.00 (dd, 1H, $J_{3,4}$=8.6, $J_{4,5}$=10.0 Hz, H-4), 3.82-3.66 (6H, H-2', H-4', H-6a', H-6b, OC$\underline{H}_2$CH$_2$, H_e allyl), 3.54 (ddd, 1H, J=1.6, 2.2, 11.5 Hz, H-5), 3.44-3.38 (2H, H-5', H-6b'), 3.36 (dt, 1H, J=6.5, 9.5 Hz, OC$\underline{H}_2$CH$_2$), 3.28 (dd, 1H, $J_{3',4'}$=3.1, $J_{2',3'}$=9.7 Hz, H-3'), 1.40-1.30 (2H, OCH$_2$C$\underline{H}_2$), 1.24-0.90 (10H, CH2, octyl), 0.78 (t, 3H, J=7.0 Hz, CH3, octyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.2, 139.1, 138.9, 138.5, 138.1, 133.3 (aromatic quat.), 135.0 (CH$_2$=$\underline{C}$HCH$_2$O), 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 127.4, 127.3, 126.8 (aromatic CH), 116.5 ($\underline{C}$H$_2$=CHCH$_2$O), 103.0 (C-1'), 98.4 (C-1), 82.2 (C-3'), 80.0 (C-5'),78.2 (C-2'), 77.5 (C-4), 77.3 (C-3), 75.4 (C-5), 74.5, 74.4, 73.5, 73.3, 73.1 (Ph$\underline{C}$H$_2$x5, CH$_2$=CH$\underline{C}$H$_2$O), 69.5 (O$\underline{C}$H$_2$CH$_2$), 68.3, 68.2 (C-4', C-6, C-6'), 55.8 (C-2) 31.7, 29.3, 29.2, 29.1, 25.9, 22.6 (CH$_2$, octyl), 14.1 (CH$_3$, octyl). *Anal.* Calcd for $C_{66}H_{75}NO_{12}$ (1074.30): C, 73.79; H, 7.04. Found: C, 73.43; H, 6.74.

*Octyl 3,6-di-*O*-benzyl-4-*O*-(2,4,6-tri-*O*-benzyl-β-*D*-galactopyranosyl)-2-deoxy-2-phthalimido-β-*D*-glucopyranoside* (**72**)

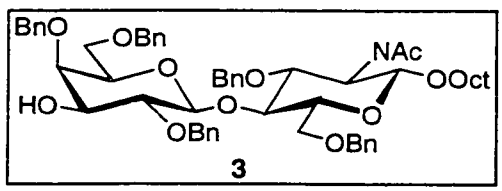


72

Compound **72** (204 mg, 88%) was synthesized from compound **71** (241 mg, 0.25 mmol), palladium

chloride (6 mg, 0.026 mmol), and methanol (5 mL) as described for the preparation of **61**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80-7.60 (4H, Phth), 7.38-6.80 (25H, Ph), 5.09 (d, 1H, $J_{1,2}$=8.5 Hz, H-1), 4.86, 4.72, 4.68, 4.59, 4.56 (d, 1H, J=11.8 Hz, PhC$\underline{H}_2$), 4.48-4.36 (4H, H-1', PhC$\underline{H}_2$x3), 4.30-4.24 (2H, H-3, PhC$\underline{H}_2$), 4.17 (dd, 1H, $J_{1,2}$=8.6, $J_{2,3}$=10.9 Hz, H-2), 3.84 (dd, 1H, $J_{3,4}$=$J_{4,5}$=8.7 Hz, H-4), 3.84 (dd, 1H, $J_{5,6a}$=4.1, $J_{6a,6b}$=11.0 Hz, H-6a), 3.81 (d, 1H, $J_{3',4'}$=2.2 Hz, H-4'), 3.78-3.73 (2H, H6b, OC$\underline{H}_2$CH$_2$), 3.56 (m, 1H, H-5), 3.51-3.42 (5H, H-2', H-3', H-5', H-6a', H-6b'), 3.35 (dt, 1H, J=6.2, 9.0 Hz, OC$\underline{H}_2$CH$_2$), 2.16 (bs, 1H, OH), 1.50-1.40 (2H, OCH$_2$C$\underline{H}_2$), 1.34-0.90 (10H, CH$_2$, octyl), 0.80 (t, 3H, J=7.0 Hz, CH$_3$, octyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.7, 139.4, 139.1, 139.0, 138.7, 134.4 (aromatic quat.), 132.4, 129.2, 129.1, 129.0, 128.7, 128.5, 128.4, 128.3, 128.2, 127.5 (aromatic CH), 103.7 (C-1'), 99.1 (C-1), 81.4 (C-3'), 78.9 (C-4),77.2 (C-3), 76.6 (C-4'), 77.3 (C-3), 76.0 (C-5), 75.8, 75.6, 75.0, 74.7, 74.1, 74.0, 73.9 (C-2', C-5', Ph$\underline{C}$H$_2$x5), 70.2 (O$\underline{C}$H$_2$CH$_2$), 68.8 (C-6, C-6'), 56.5 (C-2) 32.4, 32.0, 29.9, 29.8, 25.5, 23.3 (CH$_2$, octyl), 14.7 (CH$_3$, octyl). HR-ESMS calcd for $C_{63}H_{71}NO_{12}Na$ 1056.4874, found 1056.4868.

*Octyl 2-acetamido-3,6-di-*O*-benzyl-4-*O*-(2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-2-deoxy-β-*D*-glucopyranoside* (**3**)

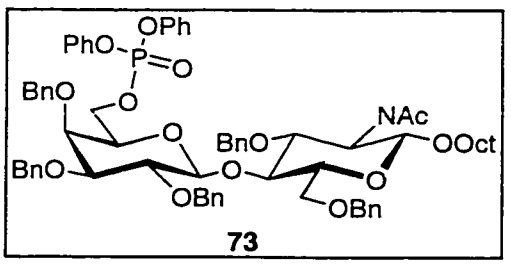


3

Compound **3** (162 mg, 94%) was synthesized from compound **72** (191 mg, 0.18 mmol), *t*-butanol (10mL) and ethylenediamine (4mL) followed by acetic anhydride (4 mL), methanol (10 mL) and triethylamine (0.2 mL) as described for

the preparation of **5**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35-7.20 (25H, Ph), 5.70 (d, 1H, J=7.5 Hz, NHAc), 4.91 (d, 1H, $J_{1,2}$=7.4 Hz, H-1), 4.85, 4.83, 4.76, 4.57, 4.56, 4.54, 4.42, 4.38, 4.30 (d, 1H, J=11.6 Hz, PhC$\underline{H}_2$), 4.14 (d, 1H, $J_{1',2'}$=7.3 Hz, H-1'), 4.14 (dd, 1H, $J_{2,3}$=$J_{3,4}$=8.8 Hz, H-3), 3.94 (dd, 1H, $J_{3,4}$=$J_{4,5}$=8.0 Hz, H-4), 3.83 (d, 1H, $J_{3',4'}$=2.8 Hz, H-4'), 3.81-3.74 (3H, H-6a, H-6b, OC$\underline{H}_2$CH_2), 3.60 (ddd, 1H, $J_{5,6a}$=$J_{5,6b}$=3.3, $J_{5,4}$=7.9 Hz, H-5), 3.54 (dd, 1H, $J_{5',6a'}$=$J_{5',6b'}$=6.4 Hz, H-5'), 3.52-3.40 (5H, H-2', H-3', H-6a', H-6b', OC$\underline{H}_2$CH_2), 3.31 (ddd, 1H, $J_{1,2}$=$J_{2,NHAc}$=7.5, $J_{2,3}$=8.8 Hz, H-2), 2.18 (bs, 1H, OH), 1.92 (s, 3H, CH_3, acetate), 1.60-1.50 (2H, OCH_2C$\underline{H}_2$), 1.34-1.20 (10H, CH_2, octyl), 0.84 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.9 (CO, acetate), 139.7, 139.7, 139.1, 139.0, 138.6 (aromatic quat.), 129.2, 129.1, 129.0, 128.9, 128.7, 128.5, 128.4, 128.3, 128.2, 128.1 (aromatic CH), 103.7 (C-1'), 100.1 (C-1), 81.4 (C-3'), 78.1 (C-3), 77.8 (C-4), 76.5 (C-4'), 75.9 (C-5), 75.8, 75.7, 75.6, 74.7, 74.1, 74.0, 73.9 (C-2', C-5', Ph$\underline{C}$H$_2$x5), 70.4 (O$\underline{C}$H$_2$CH$_2$), 69.3, 68.8 (C-6, C-6'), 57.0 (C-2) 32.4, 32.0, 30.1, 30.0, 26.7, 24.3 (CH_2, octyl), 23.4 (CH_3, acetate), 14.8 (CH_3, octyl). *Anal.* Calcd for $C_{57}H_{71}NO_{11}$ (945.17): C, 72.36; H, 7.56. Found: C, 72.37; H, 7.69.

*Octyl 2-acetamido-3,6-di-*O*-benzyl-4-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-diphenoxyphosphoryl-β-*D*-galactopyranosyl)-2-deoxy-β-*D*-glucopyranoside* (**73**)

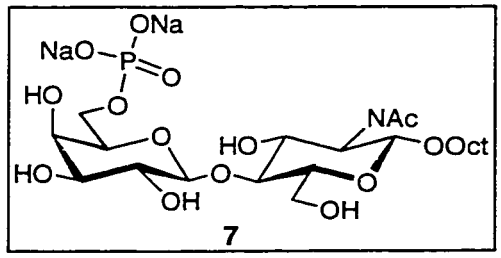


73

Compound **1** (30 mg, 0.32 mmol) was dissolved in pyridine (1 mL) and the solution was cooled to 0°C. To the cooled solution, catalytic 4-dimethylamino pyridine, and diphenyl phosphorochloridate (30 μL,

0.14 mmol) were added and the mixture was allowed to warm to room temperature. The solution was stirred for 24 hours, diluted with DCM, washed sequentially with water, sodium bicarbonate, and water and concentrated under reduced pressure. Column chromatography (5:1 toluene:acetone) gave unreacted starting material (5 mg, 16%) and **73** (27 mg, 72%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38-7.10 (35H, Ph), 5.67 (d, 1H, J=7.5 Hz, N<u>H</u>Ac), 4.94, 4.85, 4.80, 4.77, 4.68, 4.55, 4.53, 4.46, 4.36 (d, 1H, J=11.2 Hz, PhC<u>H</u>$_2$), 4.89 (d, 1H, $J_{1,2}$=7.3 Hz, H-1), 4.39 (d, 1H, $J_{1',2'}$=7.7 Hz, H-1'), 4.19-4.09 (3H, H-3, H-6a', H6b'), (dd, 1H, $J_{3,4}$=$J_{4,5}$=8.2 Hz, H-4), 3.83-3.78 (3H, H-4', H-6a, OC<u>H</u>$_2$CH$_2$), 3.74-3.70 (2H, H-2', H-6b), 3.56 (ddd, 1H, $J_{5,6a}$=$J_{5,6b}$=4.0, $J_{5,4}$=8.4 Hz, H-5), 3.43 (dt, 1H, J=6.8, 9.7 Hz, OC<u>H</u>$_2$CH$_2$), 3.38 (dd, 1H, $J_{5',6a'}$=$J_{5',6b'}$=7.1 Hz, H-5'), 3.33-3.28 (2H, H-2, H-3'), 1.84 (s, 3H, CH_3, acetate), 1.60-1.50 (2H, OCH$_2$C<u>H</u>$_2$), 1.34-1.20 (10H, CH_2, octyl), 0.85 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.9, 138.6, 138.5, 138.4, 138.3 (aromatic quat.), 130.0, 128.4, 128.3, 128.2, 128.1, 128.0, 127.7, 127.6, 127.4, 125.5, 120.1 (aromatic CH), 102.9 (C-1'), 99.7 (C-1), 82.0 (C-3'), 79.6 (C-2'), 77.5 (C-3), 77.3 (C-4), 75.3, 74.7, 74.0, 73.1, 72.9 (Ph<u>C</u>H$_2$), 75.1 (C-5), 73.0 (C-4'), 72.2 (d, $J_{5',P}$=8.4 Hz, C-5'), 69.7 (O<u>C</u>H$_2$CH$_2$), 68.5 (C-6), 66.0 (d, $J_{6',P}$=5.4 Hz, C-6'), 56.4 (C-2) 31.8, 29.6, 29.4, 29.3, 26.0, 23.6 (CH_2, octyl), 22.7 (CH_3, acetate), 14.1 (CH_3, octyl). HR-ESMS calcd for $C_{69}H_{80}NO_{14}NaP$ 1200.5214, found 1200.5230.

Octyl 2-acetamido-2-deoxy-4-O-(6-O-disodiumphosphate-β-D-galactopyanosyl)-β-D-glucopyranoside (**7**)

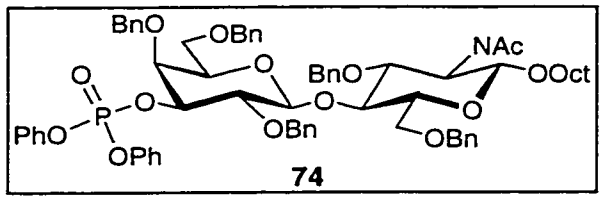


7

Compound **73** (25 mg, 0.021 mmol) was dissolved in 95% ethanol (2 mL) containing 5% palladium on activated charcoal (12 mg) and the mixture was stirred under hydrogen gas at ambient pressure for 15 hours. The catalyst was removed by filtration, the solvent evaporated and the residue was redissolved in 95% ethanol (2 mL). Adams' catalyst (PtO_2) was added and the mixture was stirred under hydrogen gas at ambient pressure for 15 hours. The catalyst was removed by filtration and the solvent concentrated. The resulting residue was redissolved in water and purified using a C-18 Sep-Pak cartridge. The carbohydrate containing fractions were pooled, concentrated and converted to the sodium salt by passage through Dowex 50-X8 (Na^+) cation exchange resin. Lyophilization of the eluent provided **7** (8 mg, 65%): ^{1}H NMR (600 MHz, D_2O (0.05 M $NaDCO_3$, 0.045 M NaOD)) δ 4.50 (d, 1H, $J_{1,2}$=7.7Hz, H-1), 4.47 (d, 1H, $J_{1',2'}$=7.9Hz, H-1'), 4.03 (d, 1H, $J_{3',4'}$=3.6 Hz, H-4'), 3.97 (dd, 1H, $J_{5,6a}$=2.3, $J_{6a,6b}$=12.2 Hz, H-6a), 3.88 (1H, H-6a'), 3.87 (1H, $OC\underline{H}_2CH_2$), 3.86 (1H, H-6b'), 3.81 (2H, H-5, H-6b), 3.70 (1H, H-3), 3.69 (1H, H-4), 3.68 (1H, H-2), 3.67 (1H, H-3'), 3.57 (1H, $OC\underline{H}_2CH_2$), 3.56 (1H, H-5'), 3.52 (dd, 1H, $J_{1',2'}$=7.8, $J_{2',3'}$=10.0 Hz, H-2'), 2.05 (s, 3H, CH3, acetate), 1.56-1.50 (2H, $OCH_2C\underline{H}_2$), 1.62-1.46 (10H, CH_2, octyl), 0.85 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (125 MHz, D_2O (0.05M $NaDCO_3$, 0.045M NaOD)) δ 102.6 (C-1'), 101.9 (C-1), 76.2 (C-5), 76.0 (C-5'), 74.8 (C-4), 73.8 (C-3'), 73.3 (C-3), 71.2 ($OC\underline{H}_2CH_2$), 70.9 (C-2'), 69.4 (C-4'), 61.6,

61.7 (C-6, C-6'), 56.8 (C-2), 32.1, 29.4, 29.3, 29.1, 25.5, 22.3 (CH_2, octyl), 29.2 (CH_3, acetate). HR-ESMS calcd for $C_{22}H_{41}NO_{14}Na_2P$ 620.2060, found 620.2057.

*Octyl 2-acetamido-3,6-di-*O*-benzyl-4-*O*-(2,4,6-tri-*O*-benzyl-3-*O*-diphenoxyphosphoryl-β-D-galactopyranosyl)-2-deoxy-β-*D*-glucopyranoside* (**74**)

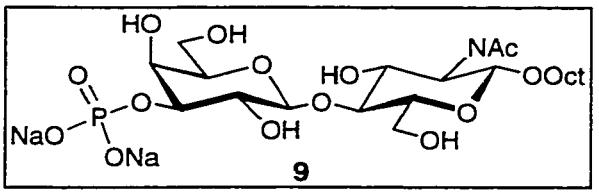


74

Compound **74** (22 mg, 80%) was synthesized from **3** (23 mg, 0.024 mmol), catalytic 4-dimethylamino pyridine, diphenyl phosphorochloridate (30 μL, 0.14 mmol) and pyridine (1 mL) as described for the preparation of **73**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38-7.10 (35H, Ph), 5.67 (d, 1H, J=7.3 Hz, NHAc), 4.89 (d, 1H, $J_{1,2}$=7.5 Hz, H-1), 4.88, 4.76, 4.68, 4.64, 4.53, 4.37, 4.34, 4.24 (d, 1H, J=11.2 Hz, PhCH_2), 4.56 (ddd, 1H, $J_{3',4'}$=3.3, $J_{2',3'}$=$J_{3',P}$=8.6, H-3'), 4.43 (d, 1H, $J_{1',2'}$=7.7 Hz, H-1'), 4.12 (dd, 1H, $J_{2,3}$=$J_{3,4}$=8.0 Hz, H-3), 4.06 (d, 1H, $J_{3',4'}$=3.3 Hz, H-4'), 3.93 (dd, 1H, $J_{3,4}$=$J_{4,5}$=8.2 Hz, H-4), 3.81-3.72 (3H, H-2', H-6a, OC$H_2$$CH_2$), 3.63 (dd, 1H, $J_{5,6b}$=2.8, $J_{6a,6b}$=10.6 Hz, H-6b), 3.49-3.36 (5H, H-5, H-5', H-6a', H-6b', OC$H_2$$CH_2$), 3.24 (ddd, 1H, $J_{1,2}$=$J_{2,NHAc}$=7.5, $J_{2,3}$=8.0 Hz, H-2), 1.82 (s, 3H, CH_3, acetate), 1.56-1.50 (2H, OCH_2CH_2), 1.30-1.20 (10H, CH_2, octyl), 0.88 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.8 (CO, acetate), 152.1, 140.4, 140.0, 139.7, 139.6, 139.4 (aromatic quat.), 131.2, 129.8, 129.7, 129.4, 129.3, 129.1, 129.0, 128.8, 126.8, 121.1 (aromatic CH), 103.9 (C-1'), 100.8 (C-1), 82.4 (d, $J_{3',P}$=6.7 Hz, C-3'), 79.2 (d, $J_{2',P}$=5.5 Hz, C-2'), 77.3 (C-3), 76.8 (C-4), 76.5 (C-4'), 76.2, 76.1, 75.3, 74.4, 74.2 (PhCH_2), 76.0 (C-5), 73.5 (C-5'), 70.7 (OC$H_2$$CH_2$), 69.4 (C-6), 68.7 (C-6'), 57.7 (C-2) 32.7, 30.4, 30.3,

30.2, 26.8, 23.5 (CH_2, octyl), 24.9 (CH_3, acetate), 14.9 (CH_3, octyl). HR-ESMS calcd for $C_{69}H_{80}NO_{14}NaP$ 1200.5214, found 1200.5235.

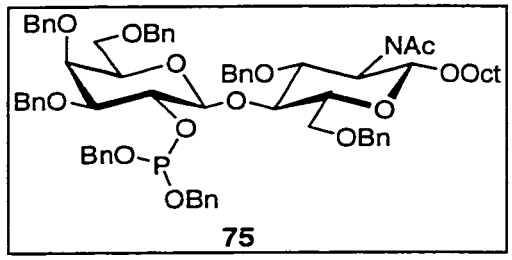
Octyl 2-acetamido-2-deoxy-4-O-(3-O-disodiumphosphate-β-D-galactopyranosyl)-β-D-glucopyranoside (**9**)



9

Compound **9** (6 mg, 56%) was synthesized from **74** (20 mg, 0.017 mmol) as described for the deprotection of **7**: ^{1}H NMR (600 MHz, D_2O (0.05 M $NaDCO_3$, 0.045 M NaOD)) δ 4.54 (d, 1H, $J_{1',2'}$=7.9 Hz, H-1'), 4.50 (d, 1H, $J_{1,2}$=8.1 Hz, H-1), 4.03 (d, 1H, $J_{3',4'}$=3.3 Hz, H-4'), 4.23 (ddd, 1H, $J_{3',4'}$=3.3, $J_{2',3'}$=$J_{3',P}$=8.4 Hz, H-3'), 3.97 (dd, 1H, $J_{5,6a}$=2.0, $J_{6a,6b}$=12.1 Hz, H-6a), 3.87 (dt, 1H, J=6.0, 10.5 Hz, OC$\underline{H}_2$$CH_2$), 3.76 (2H, H-6a', H-6b'), 3.73 (1H, H-3), 3.74 (1H, H-4), 3.71 (1H, H-2), 3.69 (1H, H-5'), 3.66 (dd, 1H, $J_{1',2'}$=7.9, $J_{2',3'}$=9.5 Hz, H-2'), 3.67 (1H, H-3), 3.57 (1H, OC$\underline{H}_2$$CH_2$), 3.56 (1H, H-5), 3.52 (dd, 1H, $J_{1',2'}$=7.8, $J_{2',3'}$=10.0 Hz, H-2'), 2.05 (s, 3H, CH_3, acetate), 1.56-1.50 (2H, $OCH_2C\underline{H}_2$), 1.32-1.26 (10H, CH_2, octyl), 0.85 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (125 MHz, D_2O (0.05M $NaDCO_3$, 0.045M NaOD)) δ 103.8 (C-1'), 102.1 (C-1), 79.3 (C-5'), 78.2 (C-4), 77.6 (C-3'), 76.5 (C-2'), 75.7 (C-5), 73.2 (C-3), 71.8 (C-2'), 71.2 (O$\underline{C}H_2CH_2$), 69.1 (C-4'), 62.9 (C-6'), 60.8 (C-6), 56.5 (C-2), 31.7, 29.3, 29.1, 29.0, 25.6, 22.4 (CH_2, octyl), 23.3 (CH_3, acetate), 14.8 (CH_3, octyl). HR-ESMS calcd for $C_{22}H_{41}NO_{14}Na_2P$ 620.2060, found 620.2067.

Octyl 2-acetamido-3,6-di-O-benzyl-4-O-(3,4,6-tri-O-benzyl-2-O-dibenzylphosphityl-β-D-galactopyranosyl)-2-deoxy-β-D-glucopyranoside (**75**)

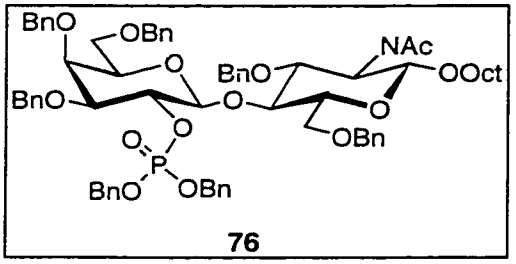


75

Compound **4** (34 mg, 0.036 mmol) was dissolved in dry DCM (500 µL) and 1,2,4 triazole (8 mg) and dibenzyl N,N-diethyl phosphoramidite (30 µL, 0.093 mmol) were added. The mixture was stirred for 15 hours, diluted with DCM, washed successively with sodium bicarbonate, brine, and water, dried over sodium sulfate and concentrated under reduced pressure. Column chromatography (10:1 toluene:acetone) resulted in **75** (38 mg, 89%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38-7.10 (35H, Ph), 5.77 (d, 1H, J=8.1 Hz, NHAc), 5.60-4.79 (9H, $PhCH_2$), 4.70-4.58 (5H, H-1, $PhCH_2x4$), 4.50, 4.42 (d, 1H, J=11.3 Hz, $PhCH_2$), 4.45 (d, 1H, $J_{1',2'}$=8.7 Hz, H-1'), 4.42-4.35 (2H, H-2', $PhCH_2$), 4.01 (dd, 1H, $J_{3,4}=J_{4,5}$=7.3 Hz, H-4), 3.94 (d, 1H, $J_{3',4'}$=2.8 Hz, H-4'), 3.91 (dd, 1H, $J_{2,3}=J_{3,4}$=7.3 Hz, H-3), 3.85 (dd, 1H, $J_{5,6a}$=3.9, $J_{6a,6b}$=10.5 Hz, H-6a), 3.74 (dt, 1H, J=6.7, 9.6 Hz, OCH_2CH_2), 3.66 (dd, 1H, $J_{5,6b}$=3.9, $J_{6a,6b}$=10.6 Hz, H-6b), 3.58-3.52 (2H, H-2, H-6a'), 3.44-3.38 (4H, H-3', H-5, H-5', H-6b'), 3.36 (dt, 1H, J=6.8, 9.7 Hz, OCH_2CH_2), 1.84 (s, 3H, CH_3, acetate), 1.60-1.50 (2H, OCH_2CH_2), 1.30-1.20 (10H, CH_2, octyl), 0.84 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.6 (CO, acetate), 139.6, 139.4, 139.2, 138.7, 138.6 (aromatic quat.), 139.1, 139.0 (d, J=4.8 Hz, aromatic quat.), 129.4, 129.1, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 128.3, 128.2, 128.1, 128.0 (aromatic CH), 101.9 (C-1'), 100.5 (C-1), 82.5 (C-3'), 78.1 (C-3), 76.2 (C-4), 76.1, 75.4, 75.2, 74.9, 74.8, 74.2, 73.9, 73.7, 73.0 (C-2', C-5, C-5', $PhCH_2x5$), 70.1 (OCH_2CH_2), 69.7 (C-6), 68.8 (C-6'), 64.6, 64.1 (d,

J=8.5 Hz, PhCH$_2$), 55.1 (C-2) 32.6, 30.3, 30.1, 30.0, 26.7, 23.4 (CH2, octyl), 24.2 (CH$_3$, acetate), 14.8 (CH$_3$, octyl). HR-ESMS calcd for $C_{71}H_{84}NO_{13}NaP$ 1212.5578, found 1212.5578.

Octyl 2-acetamido-3,6-di-O-benzyl-4-O-(3,4,6-tri-O-benzyl-2-O-dibenzylphosphoryl-β-D-galactopyranosyl)-2-deoxy-β-D-glucopyranoside (**76**)

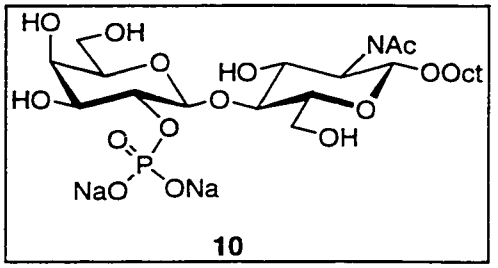


76

Compound **75** (34 mg, 0.029 mmol) was dissolved in THF (2 mL) and cooled to -78°C. To the cooled solution, 30% hydrogen peroxide (0.5 mL) was added dropwise. The mixture was warmed to room temperature, stirred for 2 hours, diluted with DCM, washed successively with sodium thiosulfate, sodium bicarbonate, and water, dried over sodium sulfate and concentrated under reduced pressure. Column chromatography (10:1 toluene/acetone) resulted in **76** (30 mg, 87%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38-7.20 (35H, Ph), 6.60 (bs, 1H, NHAc), 5.02-4.86 (6H, PhCH$_2$), 4.70-4.52 (7H, H-1, H-2', PhCH$_2$x5), 4.44-4.32 (4H, H-1', PhCH$_2$x3), 4.03 (dd, 1H, $J_{3,4}$=$J_{4,5}$=5.9 Hz, H-4), 3.94 (d, 1H, $J_{3',4'}$=2.8 Hz, H-4'), 3.81 (1H, H-3), 3.77 (dd, 1H, $J_{5,6a}$=4.2, $J_{6a,6b}$=10.1 Hz, H-6a), 3.74 (dt, 1H, J=6.6, 9.2 Hz, OCH$_2$CH$_2$), 3.66 (dd, 1H, $J_{5,6b}$=5.5, $J_{6a,6b}$=10.1 Hz, H-6b), 3.56-3.52 (2H, H-5, H-6a'), 3.45-3.42 (2H, H-3', H-6b'), 3.38 (dd, 1H, J=5.5, 7.9 Hz, H-5'), 3.31 (dt, 1H, J=6.8, 9.5 Hz, OCH$_2$CH$_2$), 1.92 (s, 3H, CH$_3$, acetate), 1.54-1.46 (2H, OCH$_2$CH$_2$), 1.30-1.20 (10H, CH$_2$, octyl), 0.87 (t, 3H, J=7.0 Hz, CH$_3$, octyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.9 (CO, acetate), 139.6, 139.2, 139.1, 138.5, 138.4 (aromatic quat.), 136.8, 136.7 (d, J=7.9

Hz, aromatic quat.), 129.2, 129.1, 129.0, 128.9, 128.8, 128.6, 128.5, 128.4, 128.3, 128.2, 127.9 (aromatic CH), 100.8 (C-1), 100.3 (d, $J_{1'\text{-}P}$=3.7 Hz, C-1'), 81.6 (d, $J_{3'\text{-}P}$=3.6 Hz, C-3'), 78.5 (C-3), 78.1 (d, $J_{2'\text{-}P}$=6.0 Hz, C-2'), 75.5, 74.2, 74.0, 73.4, 73.0 (Ph$\underline{C}H_2$), 75.4 (C-5), 74.4 (C-4), 73.9 (C-5'), 73.7 (C-4'), 70.2 (C-6), 70.1 (O$\underline{C}H_2CH_2$), 70.0, 69.9 (d, J=5.4 Hz, Ph$\underline{C}H_2$), 68.6 (C-6'), 52.1 (C-2) 32.6, 30.3, 30.1, 30.0, 26.7, 23.4 (CH_2, octyl), 24.0 (CH3, acetate), 14.8 (CH_3, octyl). HR-ESMS calcd for $C_{71}H_{84}NO_{14}NaP$ 1228.5527, found 1228.5528.

*Octyl 2-acetamido-2-deoxy-4-*O*-(2-*O*-disodiumphosphate-β-*D*-galactopyanosyl)-β-*D*-glucopyranoside* (**10**)

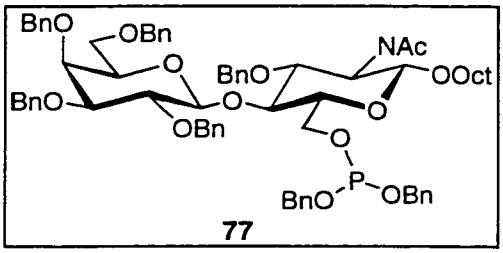


10

Compound **76** (30 mg, 0.025 mmol) was dissolved in 95% ethanol (2 mL) and 5% palladium on charcoal (12 mg) added. The mixture was stirred under hydrogen gas for 24 hours under ambient pressure, filtered, concentrated, dissolved in water and lyophylized to give **10** (10 mg 67%): ^{1}H NMR (600 MHz, D_2O (0.05 M $NaDCO_3$, 0.045 M NaOD)) δ 4.53 (d, 1H, $J_{1',2'}$=7.7 Hz, H-1'), 4.50 (d, 1H, $J_{1,2}$=8.0 Hz, H-1), 4.05 (dd, 1H, $J_{5,6a}$=1.5, $J_{6a,6b}$=12.7 Hz, H-6a), 3.95 (ddd, 1H, $J_{1',2'}$=7.9, $J_{2',3'}$=J=$_{2',P}$=9.2 Hz, H-2'), 3.90 (d, 1H, $J_{3',4'}$=3.5 Hz, H-4'), 3.88 (1H, H-6b), 3.87 (dt, 1H, J=6.1, 10.2 Hz, OC$\underline{H}_2CH_2$), 3.78 (dd, 1H, $J_{3',4'}$=3.1, $J_{2',3'}$=9.5 Hz, H-3'), 3.74 (2H, H-6a', H-6b'), 3.73 (1H, H-3), 3.71 (1H, H-2), 3.70 (1H, H-4), 3.62 (1H, H-5), 3.61 (1H, H-5), 3.58 (dt, 1H, J=6.5, 10.3 Hz, OC$\underline{H}_2CH_2$), 2.05 (s, 3H, CH_3, acetate), 1.55-1.50 (2H, $OCH_2C\underline{H}_2$), 1.32-1.20 (10H, CH_2, octyl), 0.85 (t, 3H,

J=7.0 Hz, CH_3, octyl); ^{13}C NMR (125 MHz, D_2O (0.05M $NaDCO_3$, 0.045M NaOD)) δ 103.5 (C-1'), 102.1 (C-1), 80.6 (C-5'), 75.9 (C-3), 75.7 (C-5), 74.5 (C-2'), 74.4 (C-3'), 73.3 (C-4), 71.2 ($O\underline{C}H_2CH_2$), 68.8 (C-4'), 61.7 (C-6'), 60.6 (C-6), 55.2 (C-2), 31.9, 29.6, 29.4, 29.3, 26.0, 22.7 (CH_2, octyl), 23.3 (CH_3, acetate), 14.8 (CH_3, octyl). HR-ESMS calcd for $C_{22}H_{41}NO_{14}Na_2P$ 620.2060, found 620.2057.

Octyl 2-acetamido-3-O-benzyl-4-O-(2,3,4,6-tetra-O-benzyl-β-D-galactosyl)-6-O-dibenzylphosphityl-2-deoxy-β-D-glucopyranoside (**77**)

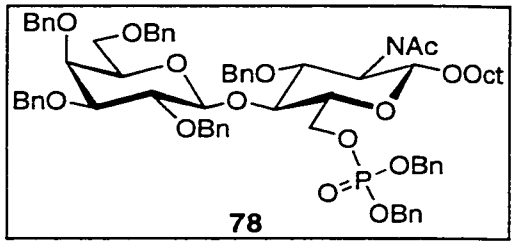


77

Compound **77** (16 mg, 98%) was synthesized from compound **5** (12 mg, 0.013 mmol), 1,2,4 triazole (10 mg), dibenzyl N,N-diethyl phosphoramidite, (30 μL, 0.093 mmol) and DCM (2 mL), as described for the preparation of **75**: ^1H NMR (600 MHz, $CDCl_3$) δ 7.38-7.20 (35H, Ph), 5.77 (d, 1H, J=7.7 Hz, N$\underline{H}$Ac), 5.02-4.59 (9H, PhC$\underline{H}_2$), 4.88 (1H, $J_{1,2}$=6.8 Hz, H-1), 4.65 (s, 2H, PhC$\underline{H}_2$), 4.58, 4.51, 4.35 (d, 1H, J=11.2 Hz, PhC$\underline{H}_2$), 4.50 (d, 1H, $J_{1',2'}$=7.7 Hz, H-1'), 4.38-4.34 (2H, H-6a, PhC$\underline{H}_2$), 4.13 (m, 1H, H-6b), 4.08 (dd, 1H, $J_{2,3}$=$J_{3,4}$=7.8 Hz, H-3), 3.90-3.88 (2H, H-4, H-4'), 3.78-3.74 (2H, H-2', O$\underline{C}H_2CH_2$), 3.64 (ddd, 1H, $J_{5,6b}$=$J_{5,6a}$=4.2, $J_{4,5}$=7.4 Hz, H-5), 3.52 (dd, 1H, $J_{6a',5'}$=$J_{6a',6b'}$=8.2 Hz, H-6a'), 3.44-3.36 (5H, H-2, H-3', H-5', H-6b', O$\underline{C}H_2CH_2$), 1.82 (s, 3H, CH_3, acetate), 1.55-1.45 (2H, $OCH_2C\underline{H}_2$), 1.30-1.20 (10H, CH_2, octyl), 0.85 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.8 (CO, acetate), 139.6, 139.5, 139.3, 139.2, 138.6 (aromatic quat.), 139.0, 136.3 (d, J=6.7 Hz, aromatic quat.), 129.1, 129.0, 128.9, 128.8, 128.7,

128.6, 128.5, 128.4, 128.3, 128.2, 128.1 (aromatic CH), 104.0 (C-1'), 100.2 (C-1), 83.1 (C-3'), 80.7 (C-2'), 77.8 (C-3), 77.4 (C-4), 76.2, 75.4, 74.4, 74.2, 73.9, 73.5 (C-4', C-5', Ph$\underline{C}H_2$x5), 75.7 (d, J_{5P}=4.9 Hz, C-5), 70.2 (O$\underline{C}H_2CH_2$), 68.9 (C-6'), 64.8, 64.7 (d, J=11.0 Hz, Ph$\underline{C}H_2$), 62.4 (d, J_{6P}=10.9 Hz, C-6), 55.9 (C-2) 32.5, 30.2, 30.1, 30.0, 26.7, 23.4 (CH_2, octyl), 24.2 (CH_3, acetate), 14.8 (CH_3, octyl).

*Octyl 2-acetamido-3-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-*D*-galactopyranosyl)-6-*O*-dibenzylphosphoryl-2-deoxy-β-*D*-glucopyranoside* (**78**)

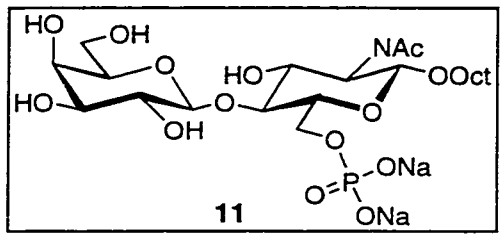


78

Compound **78** (13 mg, 85%) was synthesized from compound **77** (16 mg, 0.013 mmol), 30% hydrogen peroxide (0.5 mL) and tetrahyrofuran (2 mL) as described for the preparation of **76**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38-7.20 (35H, Ph), 5.80 (d, 1H, J=7.9 Hz, N$\underline{H}$Ac), 5.02-5.00 (5H, PhC$\underline{H}_2$), 4.84 (1H, $J_{1,2}$=6.5 Hz, H-1), 4.78, 4.77, 4.67, 4.64, 4.55, 4.51, 4.27 (d, 1H, J=11.4 Hz, PhC$\underline{H}_2$), 4.43-4.40 (2H, H-1', H-6a), 4.36-4.33 (2H, H-6b, PhC$\underline{H}_2$), 4.05 (dd, 1H, $J_{2,3}$=$J_{3,4}$=7.4 Hz, H-3), 3.88 (d, 1H, $J_{3',4'}$=2.9 Hz, H-4'), 3.83 (dd, 1H, $J_{3,4}$=$J_{4,5}$=7.2 Hz, H-4), 3.78-3.72 (2H, H-2', OC$\underline{H}_2CH_2$), 3.66 (1H, H-5), 3.52-3.34 (6H, H-2, H-3', H-5', H-6a', H-6b', OC$\underline{H}_2CH_2$), 1.81 (s, 3H, CH_3, acetate), 1.55-1.42 (2H, $OCH_2C\underline{H}_2$), 1.28-1.18 (10H, CH_2, octyl), 0.86 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.8 (CO, acetate), 139.6, 139.5, 139.3, 139.2, 138.6 (aromatic quat.), 136.6, 136.3 (d, $J_{C,P}$=6.1 Hz, aromatic quat.), 129.4, 129.1, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1 (aromatic CH), 104.0 (C-1'), 100.2 (C-1), 83.1 (C-3'), 80.5

(C-2'), 77.3 (C-3), 77.0 (C-4), 76.1, 75.4, 74.3, 74.2, 74.1, 73.8, 73.5 (C-4', C-5', Ph$\underline{C}H_2$x5), 74.7 (d, J_{5P}=8.5 Hz, C-5), 70.3 (O$\underline{C}H_2CH_2$), 69.9, 69.7 (d, J=5.4 Hz, Ph$\underline{C}H_2$), 68.8 (C-6'), 67.1 (d, J_{6P}=4.9 Hz, C-6), 55.1 (C-2) 32.5, 30.2, 30.1, 30.0, 26.7, 23.4 (CH_2, octyl), 24.2 (CH_3, acetate), 14.8 (CH_3, octyl). HR-ESMS calcd for $C_{71}H_{84}NO_{14}NaP$ 1228.5527, found 1228.5516.

*Octyl 2-acetamido-4-*O*-(β-*D*-galactopyranosyl)-2-deoxy-6-*O*-disodiumphosphate-β-*D*-glucopyranoside* (**11**)

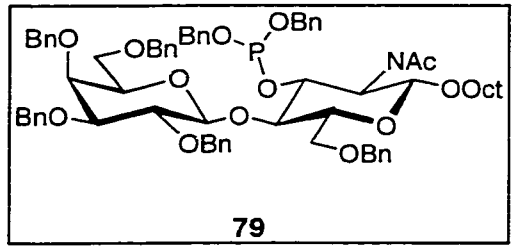


11

Compound **11** (3 mg, 73%) was synthesized from compound **78** (8 mg, $6.6x10^{-3}$ mmol), 5% palladium on charcoal (9 mg), and 95% ethanol as described for **10**: ^{1}H NMR (600 MHz, D_2O (0.05 M $NaDCO_3$, 0.045 M NaOD)) δ 4.66 (d, 1H, $J_{1',2'}$=8.0 Hz, H-1'), 4.52 (d, 1H, $J_{1,2}$=8.4 Hz, H-1), 4.04 (2H, H-6a, H-6b), 3.91 (d, 1H, $J_{3',4'}$=3.5 Hz, H-4'), 3.88 (dt, 1H, J=5.8, 10.3 Hz, OC$\underline{H}_2CH_2$), 3.81 (dd, 1H, $J_{3,4}$=$J_{4,5}$=9.2 Hz, H-4), 3.79 (1H, H-3), 3.74 (2H, H-6a', H-6b'), 3.71 (1H, H-2), 3.70 (1H, H-3'), 3.66 (1H, H-5'), 3.65 (1H, H-5), 3.57 (dt, 1H, J=6.2, 10.2 Hz, OC$\underline{H}_2CH_2$), 3.44 (dd, $J_{1',2'}$=8.1, $J_{2',3'}$=10.2 Hz, H-2'), 2.05 (s, 3H, CH_3, acetate), 1.55-1.50 (2H, $OCH_2C\underline{H}_2$), 1.32-1.20 (10H, CH_2, octyl), 0.85 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (125 MHz, D_2O (0.05M $NaDCO_3$, 0.045M NaOD)) δ 103.5 (C-1'), 102.0 (C-1), 79.0, C-4), 76.2 (C-3), 75.3 (C-5), 74.4 (C-3'), 74.3 (C-5'), 71.8 (C-2'), 71.2 (O$\underline{C}H_2CH_2$), 69.5 (C-4'), 62.9 (C-6), 61.9 (C-6'), 55.9 (C-2), 32.5, 30.2, 30.1, 30.0, 26.7,

23.4 (CH_2, octyl), 24.2 (CH3, acetate), 14.8 (CH_3, octyl). HR-ESMS calcd for $C_{22}H_{41}NO_{14}Na_2P$ 620.2060, found 620.2059.

Octyl 2-acetamido-6-O-benzyl-4-O-(2,3,4,6-tetra-O-benzyl-β-D-galactosyl)-3-O-dibenzylphosphityl-2-deoxy-β-D-glucopyranoside (**79**)

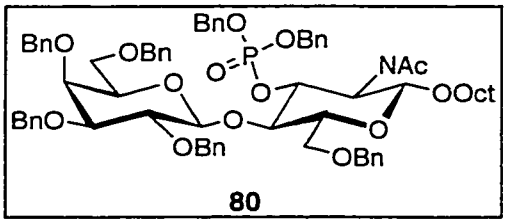


79

Compound **79** (15 mg, 45%) was synthesized from compound **6** (27 mg, 0.029 mmol), 1,2,4 triazole (8 mg), dibenzyl N,N-diethyl phosphoramidite, (27 μL, 0.083 mmol) and DCM (2 mL) as described for the preparation of **75**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38-7.15 (35H, Ph), 5.60 (bs, 1H, NHAc), 4.88-4.62 (10H, H-1, PhCH_2x9), 4.58-4.44 (3H, H-3, PhCH_2x2), 4.40-4.25 (4H, H-1', PhCH_2x3), 3.92 (dd, 1H, $J_{3,4}$=$J_{4,5}$=8.3 Hz, H-4), 3.83 (dd, 1H, $J_{5,6a}$=4.3, $J_{6a,6b}$=10.9 Hz, H-6a), 3.81 (d, 1H, $J_{3',4'}$=3.3 Hz, H-4'), 3.78 (dt, 1H, J=6.6, 9.5 Hz, OC$H_2$$CH_2$), 3.72 (dd, 1H, $J_{5,6b}$=2.7, $J_{6a,6b}$=10.8 Hz, H-6b), 3.67 (dd, 1H, $J_{1',2'}$=7.7, $J_{2',3'}$=9.5 Hz, H-2'), 3.55-3.51 (2H, H-5, H-6a'), 3.49 (dd, 1H, $J_{5',6b'}$=5.3, $J_{6a',6b'}$=9.0 Hz, H-6b'), 3.46-3.38 (2H, H-2, OC$H_2$$CH_2$), 3.35 (dd, 1H, $J_{5',6b'}$=5.8, $J_{5',6a'}$=7.9 Hz, H-5'), 3.32 (dd, 1H, $J_{3',4'}$=3.1, $J_{2',3'}$=9.8 Hz, H-3'), 1.84 (s, 3H, CH_3, acetate), 1.60-1.50 (2H, OCH_2CH_2), 1.30-1.20 (10H, CH_2, octyl), 0.84 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.0 (CO, acetate), 139.5, 139.4, 139.2, 139.1, 138.8 (aromatic quat.), 129.1, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1 (aromatic CH), 103.7 (C-1'), 100.7 (C-1), 83.1 (C-3'), 80.3 (C-2'), 77.8 (C-4), 76.8 (C-5), 75.9, 75.8, 75.3, 74.1, 74.0, 73.8 (C-4', C-5, PhCH_2x5), 73.4 (C-3), 70.1 (OC$H_2$$CH_2$), 69.3 (C-6), 69.1 (C-

6'), 65.1, 65.0 (Ph$\underline{C}H_2$), 57.3 (C-2) 32.5, 30.2, 30.1, 30.0, 26.7, 23.4 (CH_2, octyl), 24.1 (CH_3, acetate), 14.8 (CH_3, octyl). HR-ESMS calcd for $C_{71}H_{84}NO_{13}NaP$ 1212.5578, found 1212.5552.

*Octyl 2-acetamido-6-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-*D*-galactopyranosyl)-3-*O*-dibenzylphosphoryl-2-deoxy-β-*D*-glucopyranoside* (**80**)

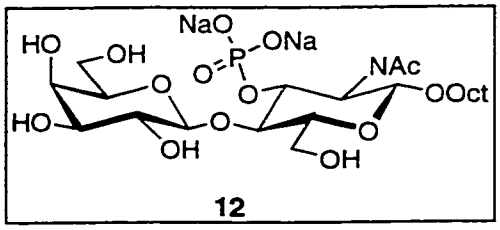


80

Compound **80** (4 mg, 66%) was synthesized from compound **79** (6 mg, $5.0x10^{-3}$ mmol), 30% hydrogen peroxide (0.5 mL) and tetrahyrofuran (2 mL) as described for the preparation of **76**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38-7.05 (35H, Ph), 5.99 (d, 1H, J=8.4 Hz, N$\underline{H}$Ac), 5.10-5.02 (2H, PhC$\underline{H}_2$), 4.96-4.84 (2H, PhC$\underline{H}_2$), 4.68-4.53 (7H, H-1, H-3, PhC$\underline{H}_2$x5), 4.48-4.30 (6H, H-1', PhC$\underline{H}_2$x5), 4.03 (dd, 1H, $J_{3,4}$=$J_{4,5}$=9.2 Hz, H-4), 3.91 (ddd, 1H, $J_{1,2}$=$J_{2,NHAc}$=8.2, $J_{2,3}$=10.3 Hz, H-2), 3.88 (dd, 1H, $J_{5,6a}$=3.6, $J_{6a,6b}$=11.0 Hz, H-6a), 3.83-3.79 (2H, H-4', OC$\underline{H}_2$CH$_2$), 3.66 (dd, 1H, $J_{5,6b}$=2.0, $J_{6a,6b}$=11.2 Hz, H-6b), 3.62 (dd, 1H, $J_{1',2'}$=7.9, $J_{2',3'}$=9.4 Hz, H-2'), 3.50-3.48 (2H, H-6a', H-6b'), 3.42 (dt, 1H, J=6.7, 9.3 Hz, OC$\underline{H}_2$CH$_2$), 3.39 (ddd, 1H, $J_{5,6b}$=2.1, $J_{5,6a}$=3.7, $J_{5,4}$=9.5 Hz, H-5), 3.35-3.30 (2H, H-3'. H-5'), 1.80 (s, 3H, CH_3, acetate), 1.60-1.50 (2H, OCH$_2$C$\underline{H}_2$), 1.35-1.20 (10H, CH_2, octyl), 0.84 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.4 (CO, acetate), 139.3, 139.2, 139.1, 139.0, 138.7 (aromatic quat.), 137.2, 136.5 (d, J=6.1 Hz, aromatic quat.), 129.1, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1 (aromatic CH), 103.5 (C-1'), 101.8 (C-1), 83.1 (C-3'), 80.1 (C-2'), 78.5 (d, J_{3P}=6.1 Hz, C-3), 75.9 (C-5), 75.5 (d, J_{4P}=5.5 Hz, C-4),

75.3, 74.2, 74.1, 74.0, 73.9, 73.5 (C-4', C-5, Ph$\underline{C}H_2$x5), 70.3, 70.2 (d, J=4.3, Ph$\underline{C}H_2$), 70.1 (O$\underline{C}H_2CH_2$), 69.0 (C-6'), 68.6 (C-6), 56.0 (C-2) 32.5, 30.2, 30.1, 30.0, 26.6, 23.3 (CH_2, octyl), 24.1 (CH_3, acetate), 14.8 (CH_3, octyl).

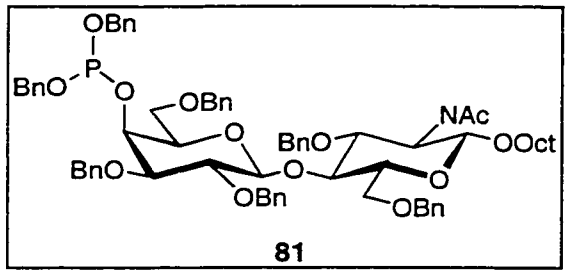
Octyl 2-acetamido-4-O-(β-D-galactopyranosyl)-2-deoxy-3-O-disodiumphosphate-β-D-glucopyranoside (**12**)



12

Compound **12** (1.4 mg, 71%) was synthesized from compound **80** (4 mg, $3.3x10^{-3}$ mmol), 5% palladium on charcoal (11 mg) and 95% ethanol as described for the preparation of **10**: ^{1}H NMR (600 MHz, D_2O (0.05 M $NaDCO_3$, 0.045 M NaOD)) δ 4.60 (d, 1H, $J_{1',2'}$=7.5 Hz, H-1'),4.48 (d, 1H, $J_{1,2}$=8.3 Hz, H-1), 4.19 (ddd, 1H, $J_{2,3}=J_{3,4}=J_{3,P}$=9.4 Hz, H-3), 3.98 (dd, 1H, $J_{5,6a}$=2.6, $J_{6a,6b}$=12.3 Hz, H-6a), 3.91 (dd, 1H, $J_{3,4}=J_{4,5}$=9.2 Hz, H-4), 3.86 (d, 1H, $J_{3',4'}$=3.5 Hz, H-4'), 3.85 (1H, O$\underline{C}H_2CH_2$), 3.81 (2H, H-6a', H-6b'), 3.71 (1H, H-6b), 3.69 (1H, H-5'), 3.68 (1H, H-2), 3.63 (1H, H-2'), 3.62 (1H, H-5), 3.59 (dd, 1H, $J_{3',4'}$=3.3, $H_{3',2'}$=9.9 Hz, H-3'), 3.55 (dt, 1H, J=6.6, 10.3 Hz, O$\underline{C}H_2CH_2$), 2.05 (s, 3H, CH_3, acetate), 1.55-1.50 (2H, $OCH_2\underline{C}H_2$), 1.32-1.20 (10H, CH_2, octyl), 0.85 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (125 MHz, D_2O (0.05M $NaDCO_3$, 0.045M NaOD)) δ 102.7 (C-1), 102.0 (C-1'), 76.6 (C-5), 76.0 (C-5'), 74.7 (C-4), 73.6 (C-3'), 73.5 (C-3), 71.3 (O$\underline{C}H_2CH_2$), 69.7 (C-4'), 61.8 61.7 (C-6, C-6'), 56.3 (C-2), 31.9, 29.6, 29.4, 29.3, 26.0, 22.7 (CH_2, octyl), 23.3 (CH_3, acetate), 14.8 (CH_3, octyl). HR-ESMS calcd for $C_{22}H_{41}NO_{14}Na_2P$ 620.2060, found 620.2064.

Octyl 2-acetamido-3,6-di-O-benzyl-4-O-(2,3,6-tri-O-benzyl-4-O-dibenzylphosphityl-β-D-galactopyranosyl)-2-deoxy-β-D-glucopyranoside (**81**)

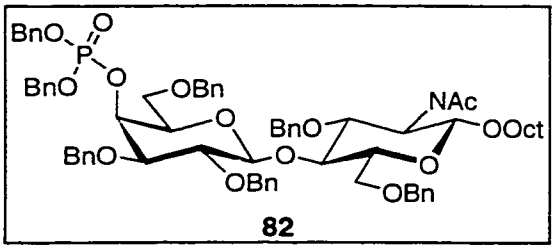


81

Compound **81** (11 mg, 58%) was synthesized from compound **2** (15 mg, 0.016 mmol), 1,2,4 triazole (8 mg), dibenzyl N,N-diethyl phosphoramidite, (10 μL, 0.031 mmol) and DCM as described for the preparation of **75**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38-7.10 (35H, Ph), 5.64 (d, 1H, J=7.3 Hz, NHAc), 5.10-5.05, 4.94-4.84 (5H, PhCH_2), 4.79-4.75 (4H, H-1, PhCH_2x3), 4.68-4.52 (7H, PhCH_2), 4.43 (d, 1H, $J_{1',2'}$=7.9 Hz, H-1'), 4.36, 4.34, 4.28 (d, 1H, J=11.2 Hz, PhCH_2), 4.10 (dd, 1H, $J_{2,3}$=$J_{3,4}$=8.2 Hz, H-3), 3.92 (dd, 1H, $J_{3,4}$=$J_{4,5}$=8.3 Hz, H-4), 3.82-3.77 (2H, H-6a, OCH_2CH_2), 3.71 (dd, 1H, $J_{5,6b}$=2.7, $J_{6a,6b}$=10.6 Hz, H-6b), 3.59-3.54 (3H, H-4', H-5, H-6a'), 3.48-3.40 (3H, H-5', H-6b', OCH_2CH_2), 3.35 (dd, 1H, $J_{3',4'}$=3.1, $J_{2',3'}$=9.7 Hz, H-3'), 3.27 (ddd, 1H, $J_{1,2}$=$J_{2,NHAc}$=7.5, $J_{2,3}$=8.8 Hz, H-2), 1.83 (s, 3H, CH_3, acetate), 1.56-1.48 (2H, OCH_2CH_2), 1.30-1.20 (10H, CH_2, octyl), 0.85 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.8 (CO, acetate), 139.7, 139.3, 139.2, 139.1, 139.0, 138.7, 138.6 (aromatic quat.), 129.4, 129.3, 129.2, 129.1, 129.0, 128.9, 128.7, 128.6, 128.4, 128.3, 128.2, 128.1, 127.9 (aromatic CH), 103.7 (C-1'), 100.2 (C-1), 81.4 (C-3'), 79.8 (C-4', C-2'), 78.3 (C-3), 77.9 (C-4), 75.9 (C-5), 75.8, 74.8, 74.1, 73.8, 73.3, 72.9 (c-5', PhCH$_2$x5), 70.4 (OCH$_2$CH$_2$), 69.4 (PhCH$_2$), 69.2 (C-6), 68.7 (C-6'), 64.6, 64.1 (PhCH$_2$), 57.2 (C-2) 32.3, 30.2, 30.1,

30.0, 26.7, 23.5 (CH_2, octyl), 24.3 (CH_3, acetate), 14.8 (CH_3, octyl). HR-ESMS calcd for $C_{71}H_{84}NO_{13}NaP$ 1212.5578, found 1212.5587.

Octyl 2-acetamido-3,6-di-O-benzyl-4-O-(2,3,6-tri-O-benzyl-4-O-dibenzylphosphoryl-β-D-galactopyranosyl)-2-deoxy-β-D-glucopyranoside (**82**)

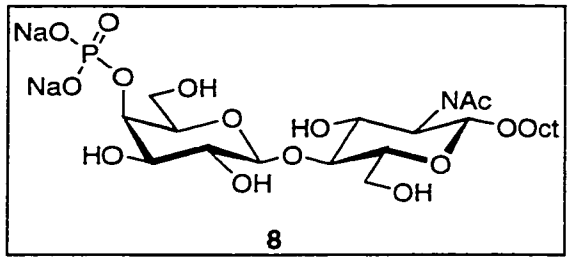


82

Compound **82** (8 mg, 79%) was synthesized from compound **81** (10 mg, $8.4x10^{-3}$ mmol), 30% hydrogen peroxide (0.5 mL) and tetrahyrofuran (2 mL) as described for the preparation of **76**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.41-7.05 (35H, Ph), 5.63 (d, 1H, J=7.6 Hz, NHAc), 5.07 (dd, 1H, $J_{3',4'}$=2.9 Hz, H-4'), 4.98-4.84 (7H, H-1, PhCH_2x6), 4.66, 4.62, 4.35, 4.24 (d, 1H, J=11.7 Hz, PhCH_2), 4.56-4.50 (3H, PhCH_2), 4.40 (d, 1H, $J_{1',2'}$=7.7 Hz, H-1'), 4.14 (dd, 1H, $J_{2,3}$=$J_{3,4}$=8.2 Hz, H-3), 3.92 (dd, 1H, $J_{3,4}$=$J_{4,5}$=8.4 Hz, H-4), 3.82-3.78 (2H, H-6a, OCH_2CH_2), 3.69 (dd, 1H, $J_{5,6b}$=2.6, $J_{6a,6b}$=10.7 Hz, H-6b), 3.59 (dd, 1H, $J_{6a',5'}$=$J_{6a',6b'}$=8.4 Hz, H-6a'), 3.53 (ddd, 1H, $J_{5,6b}$=3.1, $J_{5,6a}$=4.7, $J_{5,4}$=8.4 Hz, H-5), 3.46-3.34 (5H, H-2', H-3', H-5', H-6b', OCH_2CH_2), 3.21 (ddd, 1H, $J_{1,2}$=$J_{2,NHAc}$=7.7, $J_{2,3}$=8.7 Hz, H-2), 1.85 (s, 3H, CH_3, acetate), 1.60-1.50 (2H, OCH_2CH_2), 1.30-1.20 (10H, CH_2, octyl), 0.85 (t, 3H, J=7.0 Hz, CH3, octyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.9 (CO, acetate), 139.5, 139.1, 139.0, 138.7, 138.6 (aromatic quat.), 137.0, 136.7 (d, J=7.9 Hz, aromatic quat.), 129.1, 129.0, 128.9, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 128.0 (aromatic CH), 103.4 (C-1'), 100.2 (C-1), 80.6 (d, $J_{3',P}$=1.3 Hz, C-3'), 79.3 (C-2'), 78.3 (C-3), 77.8 (C-4), 76.0 (C-5), 75.3, 75.0, 74.1, 74.0, 73.0 (c-5', PhCH_2x5), 73.5 (d,

$J_{4',P}$=5.5 Hz, C-4'), 72.8 (d, $J_{5',P}$=4.7 Hz, C-5'), 70.4 (OCH_2CH_2), 69.8, 69.7 (d, J=2.4 Hz, $PhCH_2$), 69.1 (C-6), 68.4 (C-6'), 57.6 (C-2) 32.3, 30.2, 30.1, 30.0, 26.7, 23.4 (CH_2, octyl), 24.3 (CH_3, acetate), 14.8 (CH_3, octyl). HR-ESMS calcd for $C_{71}H_{84}NO_{14}NaP$ 1228.5527, found 1228.5535.

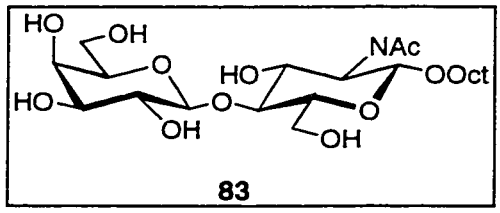
Octyl 2-acetamido-2-deoxy-4-O-(4-O-disodiumphosphate-β-D-galactopyanosyl)-β-D-glucopyranoside (**8**)



8

Compound **8** (3 mg, 73%) was synthesized from compound **82** (8 mg, $6.6x10^{-3}$ mmol), 5% palladium on charcoal (9 mg) and 95% ethanol (1 mL) as described for the preparation of **10**: ^1H NMR (600 MHz, D_2O (0.05 M $NaDCO_3$, 0.045 M NaOD)) δ 4.50 (d, 1H, $J_{1,2}$=7.1 Hz, H-1), 4.47 (d, 1H, $J_{1',2'}$=7.6 Hz, H-1'), 4.38 (dd, 1H, $J_{3',4'}$=1.1, $J_{4',P}$=9.0 Hz, H-4'), 3.96 (dd, 1H, $J_{5,6a}$=2.2, $J_{6a,6b}$=12.2 Hz, H-6a), 3.87 (dt, 1H, J=5.9, 10.2 Hz, OCH_2CH_2), 3.82 (dd, 1H, $J_{5,6b}$=5.1, $J_{=6b,6a}$=12.2 Hz, H-6b), 3.79 (1H, H-5'), 3.75 (2H, H-6a', H-6b'), 3.69 (1H, H-2), 3.68 (1H, H-3), 3.66 (1H, H-4), 3.73 (2H, H-2', H-3)', 3.58 (1H, OCH_2CH_2), 3.56 (1H, H-5), 2.05 (s, 3H, CH_3, acetate), 1.62-1.50 (2H, OCH_2CH_2), 1.32-1.20 (10H, CH_2, octyl), 0.85 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (125 MHz, D_2O (0.05M $NaDCO_3$, 0.045M NaOD)) δ 104.0 (C-1'), 101.6 (C-1), 79.7 (C-4), 75.6 (C-5'), 75.5 (C-5), 73.8 (C-3'), 73.1 (C-3), 72.4 (C-2'), 71.7 (C-4'), 71.4 (OCH_2CH_2), 61.4 (C-6'), 61.1 (C-6), 56.2 (C-2), 33.1, 29.2, 29.0, 28.9, 25.8, 22.4 (CH_2, octyl), 23.4 (CH_3, acetate), 14.8 (CH_3, octyl). HR-ESMS calcd for $C_{22}H_{41}NO_{14}Na_2P$ 620.2060, found 620.2061.

Octyl 2-acetamido-2-deoxy-4-O-(β-D-galactopyanosyl)-β-D-glucopyranoside (**83**)



83

Compound **83** (17 mg, 74%) was synthesized from compound **2** (50 mg, 0.047 mmol), 5% palladium on charcoal (10 mg) and 95% ethanol (5 mL) as described for the preparation of **10**: ^{1}H NMR (600 MHz, D_2O (0.05 M $NaDCO_3$, 0.045 M NaOD)) δ 4.64 (d, 1H, $J_{1,2}$=7.9 Hz, H-1), 4.45 (d, 1H, $J_{1',2'}$=7.8 Hz, H-1'), 3.97 (dd, 1H, $J_{5,6a}$=2.4, $J_{6a,6b}$=12.5 Hz, H-6a), 3.91 (2H, H-2, H-4'), 3.87 (dt, 1H, J=5.9, 10.2 Hz, $OC\underline{H}_2CH_2$), 3.82 (1H, dd, $J_{5,6b}$=5.2, $J_{6a,6b}$=12.3 Hz, H-6b), 3.75 (1H, H-3), 3.71 (1H, H-4), 3.69 (2H, H-6a', H-6b'), 3.67 (1H, H-5'), 3.64 (dd, 1H, $J_{3',4'}$=3.3, $J_{3',2'}$= 10.0 Hz, H-3'), 3.56 (1H, H-5) 3.58 (1H, $OC\underline{H}_2CH_2$), 3.53 (dd, 1H, $J_{1',2'}$=7.8, $J_{2',3'}$= 10.0 Hz, H-2'), 2.05 (s, 3H, CH_3, acetate), 1.62-1.50 (2H, $OCH_2C\underline{H}_2$), 1.32-1.20 (10H, CH_2, octyl), 0.85 (t, 3H, J=7.0 Hz, CH_3, octyl); ^{13}C NMR (125 MHz, D_2O (0.05M $NaDCO_3$, 0.045M NaOD)) δ 105.9 (C-1'), 103.5 (C-1), 81.9 (C-4), 77.9 (C-5'), 77.3 (C-5), 75.6 (C-3'), 75.0 (C-3), 73.4 (C-2'), 71.0 (C-4'), 71.4 ($O\underline{C}H_2CH_2$), 62.8 (C-6, C-6'), 57.6 (C-2), 33.1, 29.2, 29.0, 28.9, 25.8, 22.4 (CH_2, octyl), 23.4 (CH_3, acetate), 14.8 (CH_3, octyl).

Chapter 4

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