SYNTHESIS TOWARDS DEFINED OLIGOSACCHARIDES FOR FUNCTIONAL GENOMIC STUDIES OF THE PRIMARY PLANT CELL WALL

by

JAMES EDWARD NEVES, JR

(Under the Direction of Geert-Jan Boons)

ABSTRACT

This thesis describes the synthetic preparation of a set of oligosaccharides found in the glycostructures of the primary plant cell wall. These oligosaccharides will be used in immunocompetition assays in order to characterize the binding specificities of monoclonal antibodies generated against cell wall extracts. Additionally, these compounds can be used for the generation of monoclonal antibodies.

An orthogonally protected trisaccharide **24** was prepared that allowed direct access to target **1** and for the selective deprotection of the C-2, C-3, and C-6 hydroxyl moieties of the non-reducing terminal galactoside, providing an efficient route to the tetrasaccharide targets **2**, **3**, and **4**. However, an alternate, less convergent route using three different trisaccharides was found to be necessary. The orthogonal Fmoc, levulinoyl, and benzylidene acetal protecting groups were utilized. Also, Ph_2SO/Tf_2O was used as a powerful promoter system in glycosylation reactions.

INDEX WORDS: oligosaccharide synthesis, orthogonal protecting groups, pectin, primary plant cell wall, monoclonal antibodies

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JAMES EDWARD NEVES, JR

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JAMES EDWARD NEVES, JR

Major Professor:	Geert-Jan Boons
Committee:	Michael Hahn
	Robert Woods

Electronic Version Approved:

Maureen Grasso
Dean of the Graduate School
The University of Georgia
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DEDICATION

To my wife, Lori, who has never doubted my intelligence or abilities, has supported me during times of struggle, and has always shown me true love.

To my parents, who taught me that to live is to learn and that to learn is to live.

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I would like to thank Professor Geert-Jan Boons for allowing me the opportunity to pursue a Masters in his group, an environment where the highest levels of research and scholarly pursuit can be accomplished. Also, I would like to thank him for his kindness and patience when neither my research nor my life seemed to be moving in a positive direction.

Dr. Rao Yu deserves special thanks for advice and contributions of his time and effort for the advancement of my research. Rao, you are a good friend, a noble ambassador for China, and a stimulating conversationalist on topics not always limited to chemistry but always dedicated to lofty ideas and ideals.

Dr. Andre P. Venot is an irreplaceable asset to the Boons Group. His guidance and organization have aided me more than I can accurately fathom.

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LIST OF ABBREVIATIONS

$CDCl_3$ .....deuterochloroform

CD_3OD ..... methanol-d_4

CH_2Cl_2 .....dichloromethane

DCC .....*N,N'*-dicyclohexylcarbodiimide

DCU ..... 1,3-bis(1-hydroxy-2,2,2-trichloroethyl) urea

DMAP ..... *N,N*-dimethylaminopyridine

DMF ..... *N,N*-dimethylaminoformamide

Et .....ethyl

Gal .....galactose

h .....Hours

Hz .....Hertz

MALDI .....Matrix Assisted Laser Disorption Ionization

m/z ..... mass to charge ratio

mmol .....millimole

NMR .....Nuclear Magnetic Reasonance

Ph .....phenyl

Tf_2O .....trifluoromethane sulfonic anhydride

TMSOTf ..... trimethylsilyl triflouromethane sulfonate

p-TsOH .....*p*-tolunesulfonic acid

CHAPTER 1

INTRODUCTION

1. Insights into the Plant Cell Wall Structure and Function

The polysaccharide-rich primary cell wall that surrounds all growing plant cells is a complex, dynamic structure that provides structural support, mediates plant growth and development, and determines how plants interact with their environment.[1-7] Considering this complexity in structure and function, it is not surprising that recent estimates predict that in excess of 2000 genes encode the proteins that are involved in the synthesis and modification of plant cell walls,[8] consequently substantiating the belief that plants invest considerable quantities of energy and nutrients towards the growth and maintenance of their cell wall components.[9, 10] Knowledge of how these components are synthesized and combined to form a functional cell wall is limited, as the functions of the majority of the genes involved are unknown.[11, 12] However, very recently insights into the growth and expansion of plant cell walls have transpired.[7]

1.1 Basic Properties of the Plant Cell Wall

The shape and structure of plant cells, tissues, and organs are established by primary cell walls, which are sufficiently robust to maintain the integrity of the cell, yet are plastic to accommodate development.[1] Other roles of the primary cell wall include regulating diffusion of water and nutrients through the cell, storing carbohydrates, protecting against pathogens and dehydration, providing biologically active signaling molecules, and participating in cell-cell

interactions.[7] The primary cell wall is organized into interconnected matrices of polysaccharides and glycoproteins (Figure 1.1)[13] including cellulose, hemicelluloses such as xyloglucan, and the pectic matrix comprised of homogalacturonan, rhamnogalacturonans I and II, other substituted galacturonans, arabinans, galactans, and other polysaccharides.[6, 7]

The vast majority of the primary cell wall is comprised of crystalline microfibrils of the linear polysaccharide cellulose, the most abundant biopolymer on earth.[6, 7] Cellulose is comprised of repeating 1,4-linked β-D-glucose residues arranged in a flip-flop pattern that imposes linearity and rigidity to the molecule; as a result, the linear polymers can orient in parallel fashion, allowing for extensive hydrophobic interactions between cellulose chains. The outcome is the formation of stiff, elongated microfibrils, which provide an excellent structural lattice for the primary cell wall.

Hemicelluloses are matrix polysaccharides that, like cellulose, consist of 1,4-linked β-hexosyl residues, but regular branching prevents them from forming microfibrils. Hemicelluloses form strong, noncovalent associations with cellulose microfibrils to form the rigid, loadbearing structure of the cell wall network.[6, 7] Xyloglucan (XG) is one of the most common hemicelluloses found in the primary cell wall; its backbone is similar to cellulose, but three out of four glucose (Glu) residues are appended with a xylose (Xyl) residue that can be further extended with galactose (Gal) or fucose (Fuc). Xyloglucan is believed to cross-link microfibrils through a direct tether [14-16] or an indirect link.[17]

The pectins are a family of complex, heterogeneous polysaccharides found in distinctive domains, which are believed to be covalently linked together.[18-20] Current structural models describe the pectic network as an independent of and non-covalently bound to the cellulose/hemicellulose network. The distribution of specific pectins in the makeup of primary

cell walls can vary widely between species and even between different tissues in the same species.[6, 18] Homogalacturonan (HG), also called polygalacturonic acid because it is comprised of a linear chain of 1,4-linked α-D-galacturonic acid residues, may make up as much as 60 % of the pectin in a primary cell wall.[6] It forms stiff gels by crosslinking its carboxyl moieties through ionic bonds with Ca^{2+}.[7] Natural methyl esterification of the carboxyl groups negates the ability of HG to form these crosslinks, while pectin methylesterases can liberate the carboxyl moieties regenerating the stiff gels. This process has been implicated in cell growth cycles.[1, 7]

Rhamnogalacturonan I (RG-I) contains a backbone of the repeating disaccharide →4)-α-D-Gal*p*A-(1→2)-α-L-Rha*p*-(1→.[18, 20] In many cases, the C-4 position of the Rha*p* is modified with linear and branched neutral oligosaccharide components that contain α-L-Ara*f* and β-D-Gal*p* residues; these residues may be terminated with α-L-Fuc*p*, β-D-Glu*p*A, and 4-*O*-methyl β-D-Glu*p*A residues.[6, 21] Rhamnogalacturonan II (RG-II) is an unusual polysaccharide containing eleven different sugar residues and four different side chains, and its ability to form borate-ester dimers has received considerable attention.[5, 6, 14] The core structure of RG-II contains at least eight 1,4-linked α-D-Gal*p*A residues. [6] Current models of the organization of the macromolecular structure of the pectic network suggest that HG, RG-I, and RG-II are linked covalently, but further study is necessary to provide evidence for these linkages and to elucidate the structure of the proposed oligosaccharide fragments thought to make up the linkages.

1.2 Monoclonal Antibodies[22]

The production of monoclonal antibodies and their subsequent analysis by immunocompetition assay is a proven strategy to determine the structure of plant cell wall glycoconjugates. Monoclonal antibodies are a single species of antibody that are structurally and functionally identical because they are produced by cells that are clones of a single parent

antibody-producing cell. An antigen is injected into a vertebrate host to stimulate its immune system's B-cells to become plasma cells, which produce antibodies that recognize the injected antigen. Each plasma cell produces only one kind of antibody, but different plasma cells produce antibodies that have different epitope binding specificities and affinities to the antigen. This mixture of polyclonal antibodies is found in the serum of the injected host. To produce monoclonal antibodies, the B-cells from spleen (splenocytes) or lymph nodes (lymphocytes) are removed from an animal that has been challenged several times with an antigen of interest. Monoclonal antibodies cannot be obtained in sufficient quantities by cloning a single antibody-producing cell because the cells die after only a few cell divisions. However, B-cells can be fused with myeloma tumor cells to produce a hybridoma cell that can divide indefinitely and produce large quantities of monoclonal antibodies in culture. (Myeloma cells are immune system cancer cells and have lost the ability to produce antibodies). The binding specificities and affinities of the monoclonal antibodies secreted by different hybridoma cell lines can be determined by immunocompetition assay and other bind assays. Such fully characterized antibodies are valuable reagents of functional studies of plant cell walls.

1.3 Monoclonal Antibodies as Tools for Cell Wall Characterization

Monoclonal antibodies are ideal tools for elucidating the the intricacies of the biosynthesis, structure, and metabolism of the primary plant cell wall at the cellular and sub-cellular level.[21, 23-25] Monoclonal antibodies have been used to determine the localization of differenct glycoconjugates found within the cell wall. It has been shown that the epitope distribution patterns can vary among cell types,[24, 26-29] among the walls surrounding a single cell,[24, 26, 28] in sub-domains of a single cell wall,[23, 24, 26, 27] and at different developmental

stages.[24, 26, 29] Monoclonal antibodies can also be used to determine the consequences of specific gene mutations on the overall structure and composition of walls.[24]

1.4 The Role of Oligosaccharide Synthesis in Plant Cell Wall Functional Genomics

The number of antibodies for which the epitope binding specificity has been characterized in detail is currently too limited to study the vast structural diversity and complexity of the glycoproteins and polysaccharides found within the plant cell wall. Synthetic oligosaccharides can be used to probe the epitope binding specificities of monoclonal antibodies by immunocompetition assays. The basic structural features of some cell wall polysaccharides have been determined [5, 6, 14, 18] and used as paradigms for synthetic oligosaccharides to be used in the determination of monoclonal antibody binding specificities.[30, 31]

Zhu and co-workers [31] successfully synthesized a pentasaccharide fragment of arabinogalactans (Figure 1.2), which contained synthetically challenging β-arabinofuranosides. The synthesis employed a novel glycosyl donor containing a 3,5-*O*-di-*tert*butylsilane protecting group, which locked the corresponding oxacarbenium ion in a conformation in which nucleophilic attack from the β-face is favored. A range of glycosylations of the novel arabinofuranosyl donor with primary and secondary glycosyl acceptors gave the corresponding glycosides with excellent β-selectivities and yields, and ultimately was used in the preparation of the arabinogalactan fragment. The results demonstrated that the preparation of structurally complex plant cell wall oligosaccharides provides opportunity for the development of new methodologies for carbohydrate sythesis.

Rao and Boons [32] prepared oligosaccharide components of side chain B of the structurally complex RG-II (Figure 1.3), which also employed the building block containing the 3,5-*O*-di-*tert*butylsilane protecting group. Careful examination of the chemical shifts and

coupling constants in the ^{1}H and ^{13}C NMR spectra of the synthesized fragments revealed conformational epitopes of the arabinopyranosyl moiety (Figure 1.4). The data indicated that the arabinopyranoside ring in the hexasaccharide adopts a distorted $^{1}C_4$ conformation. Unfavorable steric interactions of the trisubstituted arabinopyranosyl moiety are probably alleviated somewhat in this conformation. The difference in the conformation of a disubstituted (tetrasaccharide) and a trisubstituted (hexasaccharide) arabinopyranosyl moiety of the B side chain of RGII may be biologically significant, as available data suggest that there is considerable structural variability among the RG-II B side chains of different plants as a result of the presence or absence of substituents linked to C-2 and/or C-3 of the Ara*p* moiety.[33] It may well be possible that the conformation of the Ara*p* moiety affects the cross-linking of RG-II by borate esters, which is an essential process for normal plant growth. Additional research will be required to determine the importance of the conformational flexibility of the RG-II side chain to the cross-linking process.

2. Current Techniques in Oligosaccharide Synthesis

Successful formation of glycosidic linkages in oligosaccharide synthesis requires the condensation of a glycosyl acceptor with a compatible glycosyl donor.[34-38] Acceptors either must be suitably protected so that the hydroxyl group(s) of interest can be selectively liberated prior to glycosidic bond formation or the acceptor's free hydroxyl groups must be able to be glycosylated regioselectively due to a greater reactivity or greater steric accessibility. Glycosyl donors also must be suitably protected, as free hydroxyls of the donor can also act as acceptors. The anomeric center must contain a potential leaving group that can be activated under conditions that permit the formation of the glycosidic linkage but will not affect other protecting groups on either the donor or acceptor. The nature of the C-2 protecting group of glycosyl

donors determines the stereochemical outcome of glycosylations. For example, participating functionalities, generally ester groups, lead to 1,2-*trans*-linkages, while non-participating groups such as ethers, lead to a mixture of anomers.[34, 36, 37] The nature of the solvent can have marked influence on the stereochemical outcome of glycosylation reactions with a non-participating protecting group at C-2.[38]

2.1 Thioglycosides in Oligosaccharide Synthesis

Thioglycosides are versatile, conveniently prepared building blocks for oligosaccharide synthesis.[39-41] Anomeric alkyl and aryl thio groups can be activated for glycosylations under mild conditions using soft electrophiles. The exceptional chemical stability of anomeric thio groups allows for the utilization and manipulation of a wide range of protecting groups and makes thioglycosides amenable glycosyl acceptors under appropriate glycoslyating conditions. Anomeric thio groups can also be readily converted into a number of different leaving groups, allowing access to other types of glycosyl donors. Taken together, these qualities contribute to the proclivity of thioglycosides for use in chemoselective, iterative, and orthogonal glycosylations.[42]

The most commonly employed preparation of thioglycosides is (Lewis) acid-catalyzed reaction of peracetylated glycopyranosides with mercaptans (Scheme 1.1), a method popularized by Lemieux and co-workers.[43, 44] A number of catalysts have been reported such as trimethylsilyl triflouromethane sulfonate (TMSOTf),[45] boron trifluoride diethyl etherate ($BF_3 \cdot Et_2O$),[45-50] tin (IV) chloride,[51] titanium tetrachloride,[52-54] indium (III) chloride,[55] MoO_2Cl_2,[56] and *p*-toluenesulfonic acid (*p*TSOH).[47] Nucleophilic substitution of acylated glycosyl halides with thiols[57-66] and disulfides[67] provides *trans*-thioglycosides in high yield. Unprotected sugars have been converted into acetylated 1-thioglycosides in an efficient one-pot

method by sequential per-*O*-acetylation and thioglycosidation reactions catalyzed by $BF_3 \cdot Et_2O$[68, 69] or $HClO_4$.[70]

A range of different anomeric leaving groups can be accessed from thioglycosides (Scheme 1.2), an attractive feature allowing for great flexibility in convergent oligosaccharide synthesis. Glycosyl halides can be obtained through a number of methods. Treatment of a thioglycoside with bromine supplies a glycosyl bromide, which, after workup, can be employed in Hg(II), Ag(I),[71] or phosphine oxide[72] promoted glycosylations. Glycosyl bromides also can be obtained from both activated and deactivated thioglycosides by reaction with iodine bromide, which has enough potency as an iodonium ion source to permit glycosylation by deactivated glycosyl bromides and thioglycosides.[73] A glycosyl fluoride will result from the treatment of a thioglycoside with *N*-bromosuccinimide/(diethylamino)sulfur trifluoride (NBS/DAST).[74-76] Anomeric thio groups can be hydrolyzed under a wide range of conditions, most commonly by reaction in wet acetone with NBS or *N*-iodosuccinimide (NIS)[77-79] or with silver nitrate ($AgNO_3$).[80, 81] The resulting lactol can be converted into a trichloroacetimidate donor in a base-catalyzed reaction with trichloroacetonitrile.[82-84] Finally, thioglycosides can be oxidized to the corresponding sulfoxides by reaction with mCPBA and then activated by triflic anhydride for glycosylations at low temperature.[85, 86]

The most commonly used promoters for the activation of thioglycosides (Scheme 1.3) include dimethyl(methylthio)sulfonium triflate (DMTST),[87] *N*-iodosuccinimide – triflic acid (NIS-TfOH),[88, 89] iodonium dicollidine perchlorate (IDCP),[90, 91] or phenylselenyl triflate (PhSeOTf).[92, 93] The electrophilic species provided by these activators react with the lone-pair of electrons of the sulfur atom forming a sulfonium ion intermediate, which is an excellent leaving-group that is easily displaced by a sugar hydroxyl. Recently, a number of more powerful

thiophilic activators have been described. Thiophilic promoter systems such as diphenylsulfoxide,[94, 95] *S*-(4-methoxyphenyl) benzenethiosulfinate (MPBT),[96] benzenesulfinyl morpholine (BSM)[97] or 1-benzenesulfinyl piperidine/2,4,6-tri-*tert*butylpyrimidine (BSP/TTBP)[98] in combination with triflic anhydride (Tf_2O) can activate thioglycosides at low temperature and have provided high yields of products for difficult glycosylations. Anomeric thio protecting groups can also be activated to an S-glycosyl radical cation intermediate in a single-electron transfer from sulfur to tris-(4-bromophenyl)ammonium hexachloroantimonate ($TBPA^{+\cdot}$).[99, 100]

2.2 Orthogonal Protecting Group Strategies in Oligosaccharide Synthesis

Carbohydrates contain multiple reactive functionalities that must be protected and liberated in a controlled fashion during oligosaccharide synthesis. A number of issues must be considered during the choice of protecting groups.[101-106] The reaction conditions used for their installation and removal should be compatible with other reactive moieties in the compound and should give high yields. Likewise, protecting groups should be able to withstand subsequent synthetic steps. Protecting groups may influence the reactivity of other functionalities through electronic or steric effects. Generally, electron-withdrawing protecting groups (*e.g.* esters) will decrease the reactivity of the other carbohydrate functionalities, while more electron-donating species (*e.g.* benzyl ethers) will have the opposite effect. Ultimately, the cost and availability of the reagents required for both installation and manipulation/removal of the protecting groups should be considered.

Protecting groups should also be chosen based upon the need of further chemical modification or lack-there-of.[107] Permanent (or persistent) protecting groups, which block functionalities that do not require further functionalization, should be robust and stable to a wide

range of chemical conditions. However, it is also paramount that they can be effectively removed in a limited number of chemical operations at the end of a synthetic sequence. Most commonly, acetyl and benzoyl esters are removed by treatment with a strong, nucleophilic base such as sodium methoxide, and then benzyl ethers are reduced by catalytic hydrogenation. Functionalities that are to be glycosylated or further modified during the synthetic sequence are blocked by temporary protecting groups. Even in the most routine oligosaccharide syntheses, multiple positions often require differential functionalization. This requires the use of orthogonal protecting groups, which can be selectively removed in any order, without affecting the other functionalities in the molecule. However, no universally applicable set of orthogonal protecting groups for carbohydrate synthesis has been developed.

Orthogonal protecting groups are invaluable in combinatorial syntheses. Wong and co-workers[108] demonstrated that a single orthogonally protected monosaccharide building block (Scheme 1.4) can be utilized to access a large number of di- and trisaccharides. The four orthogonal protecting groups, chloroacetyl (ClAc), *p*-methoxybenzyl (PMB), levulinoyl (Lev),[109] and *tert*-butyldiphenyl silyl (TBDPS), can be selectively removed in high yields using sodium bicarbonate,[110] trifluoroacetic acid,[111, 112] hydrazine,[109, 113] and hydrogen fluoride—pyridine,[114, 115] respectively. While these reactions were carried out in the solution phase, the authors noted that the strategy was also amenable to polymer-supported synthesis.

Zhu and Boons[116] developed a set of orthogonal protecting groups (Scheme 1.5) compatible with methylpolyethyleneglycol (MPEG) polymer-supported oligosaccharide synthesis using a *p*-alkyloxylbenzyl-type linker. The hydroxyl-protecting groups 9-fluorenylmethoxycarbonyl (Fmoc) and Lev and the amino-protecting group 2,2,2-trichloroethoxycarbonyl (Troc) were employed. The more commonly used phthalimido amino-

protecting group is removed under relatively harsh, basic conditions,[117] which would also result in cleavage of the Fmoc group. Alternatively, the Troc group can be removed under mild conditions,[118] using Zn in acetic acid. Also, glycosyl donors containing *N*-Troc are generally more reactive than those protected with a phthalimido group.[119] The almost neutral conditions used to remove Lev [109] did not affect either the Troc or the Fmoc group. The Fmoc group was found to be removed selectively and in high yield by use of the non-nucleophilic base triethylamine in CH_2Cl_2. These orthogonal protecting groups were also shown to be stable under standard glycosylating conditions and cleavage of allyloxyl carbonyl protecting groups and a *p*-alkyloxylbenzyl-type linker.[116]

In an effort to synthesize a set of disaccharide fragments found in heparan sulfate, Prabhu and co-workers[120] utilized six similarly protected monosaccharide building blocks containing Lev, Fmoc, TBDPS, and an anomeric allyl ether (All) as a set of orthogonal protecting groups (Figure 1.5). Anomeric allyl ethers can be easily isomerized to the vinyl ether, which subsequently can be hydrolyzed to the hemiacetal, an appropriate substrate for conversion to a trichloroacetimidate donor.[37] Of special interest was the use of the Lev protecting group. As heparin sulfate is highly sulfated in varying patterns at the C-2, C-3, and C-6 positions, Lev was used to block these positions in an appropriate pattern, allowing for selective deprotection of these sites once the target disaccharides could be obtained. It was also critical that the Lev group act as a C-2 participating functionality to provide 1,2-*trans*-glycosyl linkages. In cases where the C-2 functionality did not need sulfation, acetyl groups were employed as the permanent protecting group.

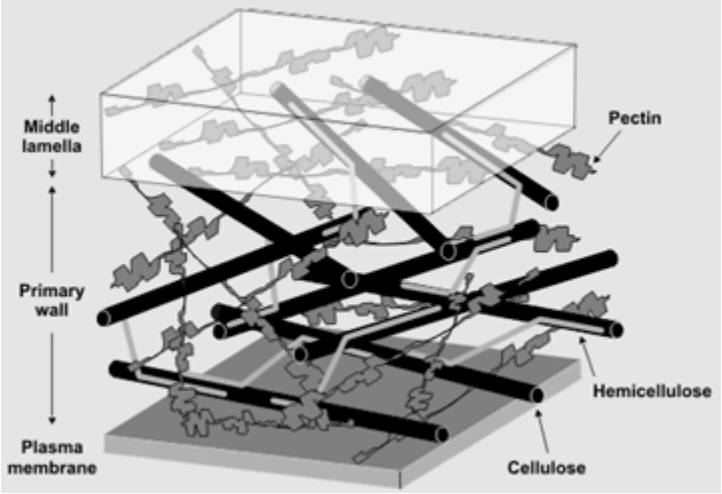
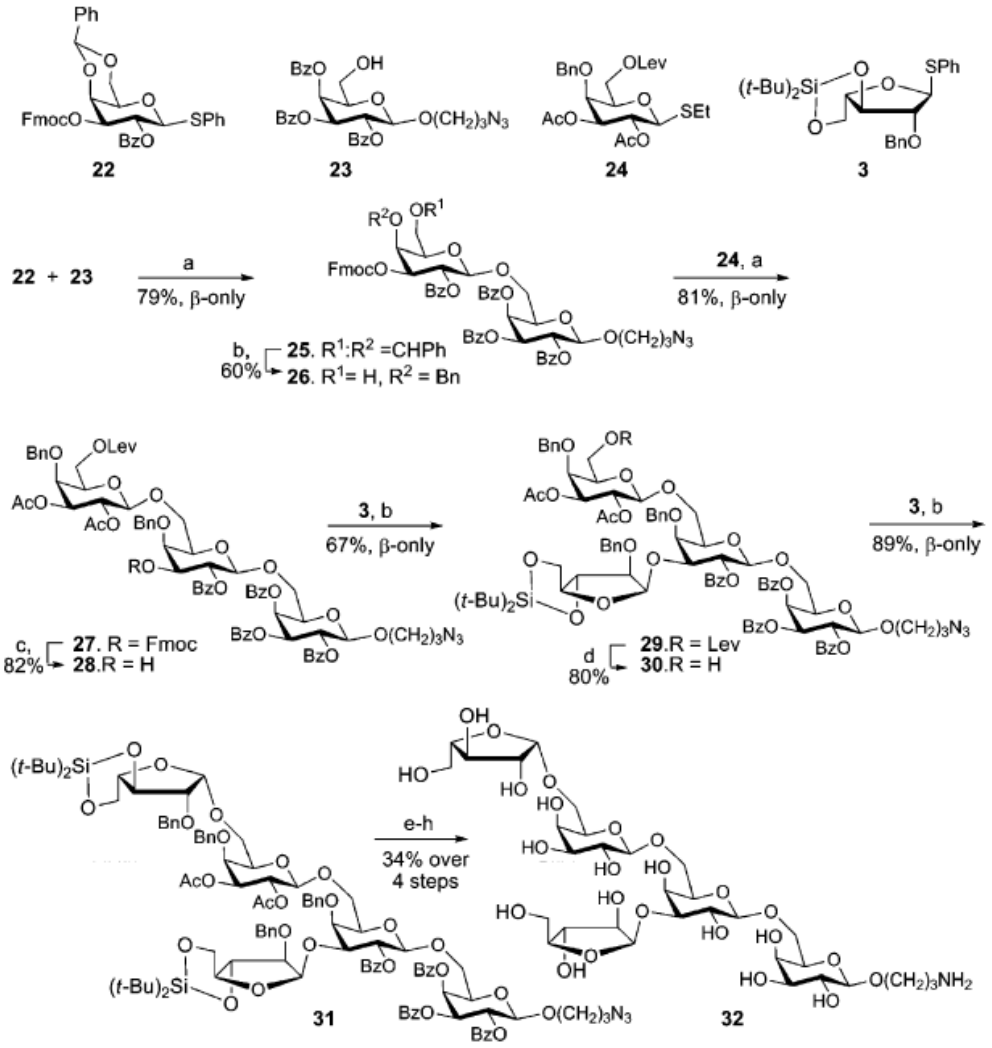
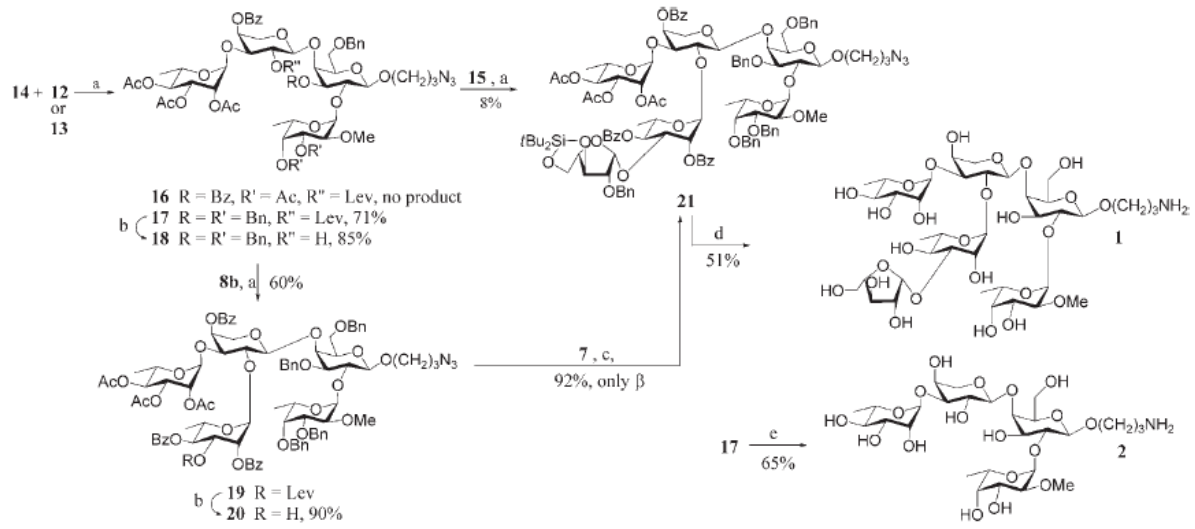


Figure 1.1: The architecture of the primary plant cell wall[121].



[a] Reagents and conditions: (a) NIS, AgOTf, DCM, MS 4A, −20 °C; (b) Bu_2BOTf, BH_3, THF, DCM, 0 °C; (c) Et_3N, DCM; (d) H_2NNH_2, DCM/MeOH; (e) TBAF, THF; (f) NaOMa, MeOH, 50 °C; (g) Pd/C, H_2, pyridine; (h) $Pd(OH)_2$, H_2, AcOH, H_2O.

Figure 1.2: X. Zhu's synthesis of a pentasaccharide fragment of arabinogalactan.



Reagents and conditions: a) NIS, TfOH, 4-Å MS, CH_2Cl_2, −20°C; b) NH_2NH_2·AcOH, CH_2Cl_2/MeOH, RT; c) TMSOTf, 4-Å MS, CH_2Cl_2, −70°C; d) 1. TBAF, THF, RT; 2. NaOMe/MeOH, RT; 3. Pd/C, *t*BuOH/AcOH/H_2O, RT; e) 1. NaOMe/MeOH, RT; 2. Pd/C, *t*BuOH/AcOH/H_2O, RT. TBAF = tetrabutylammonium fluoride.

Figure 1.3: Yu Rao's synthesis of oligosaccharide fragments of the B side chain of RG-II.

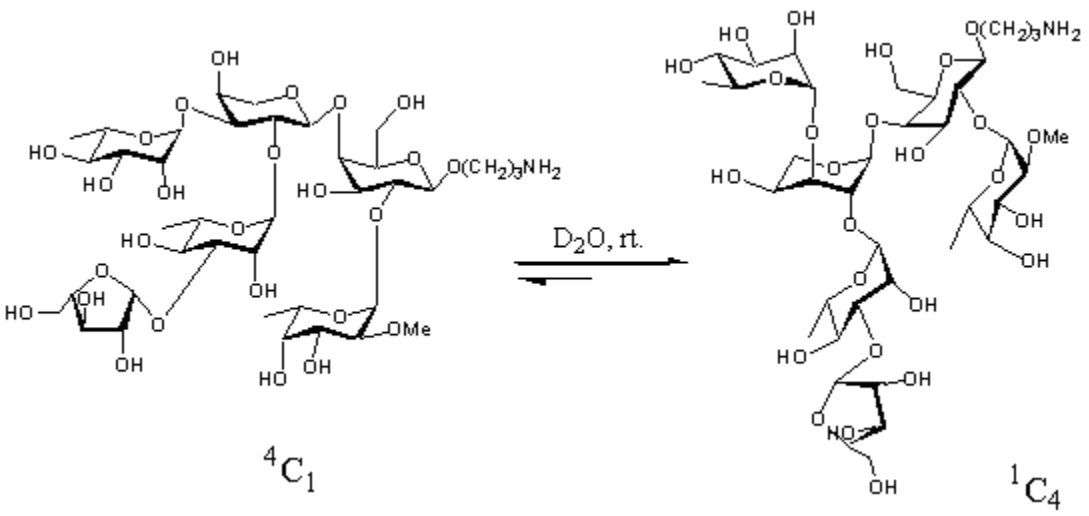
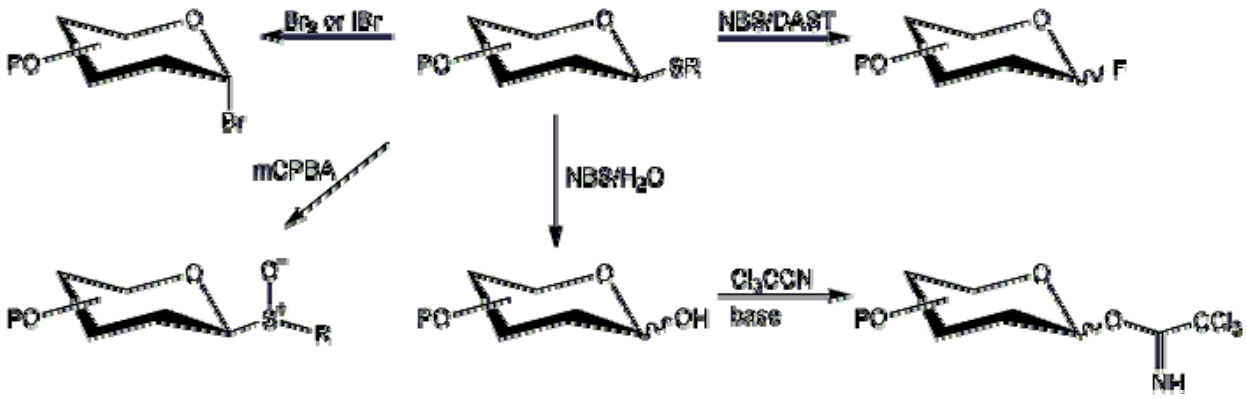
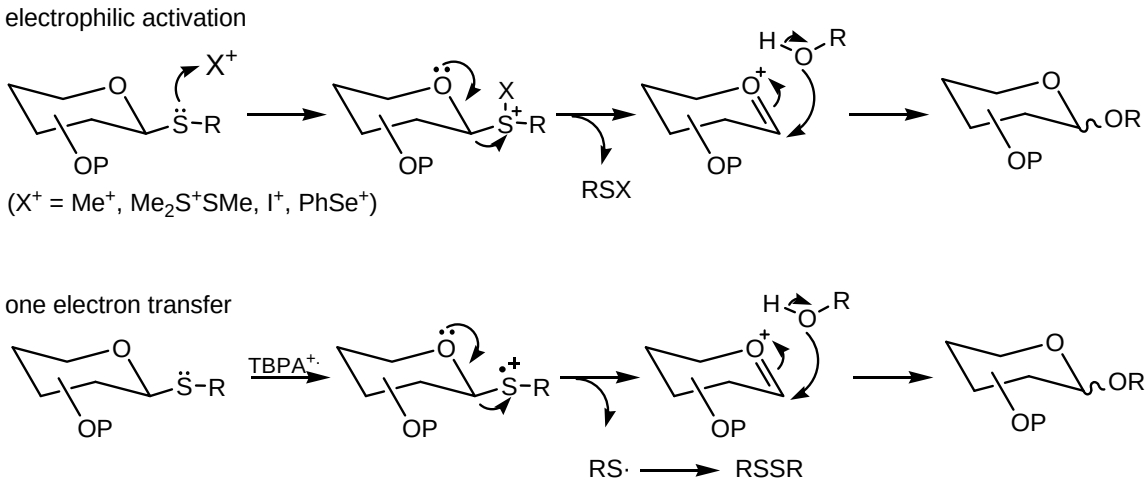


Figure 1.4: Conformations of a hexasaccharide fragment of the B side chain of RG-II.

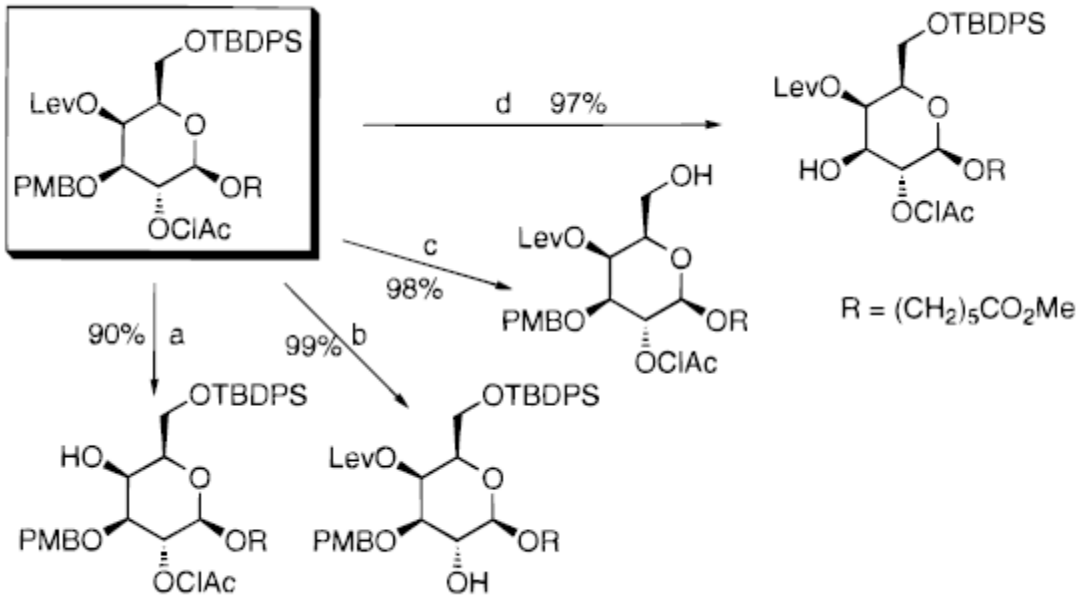
Scheme 1.1: Preparation of thioglycosides.



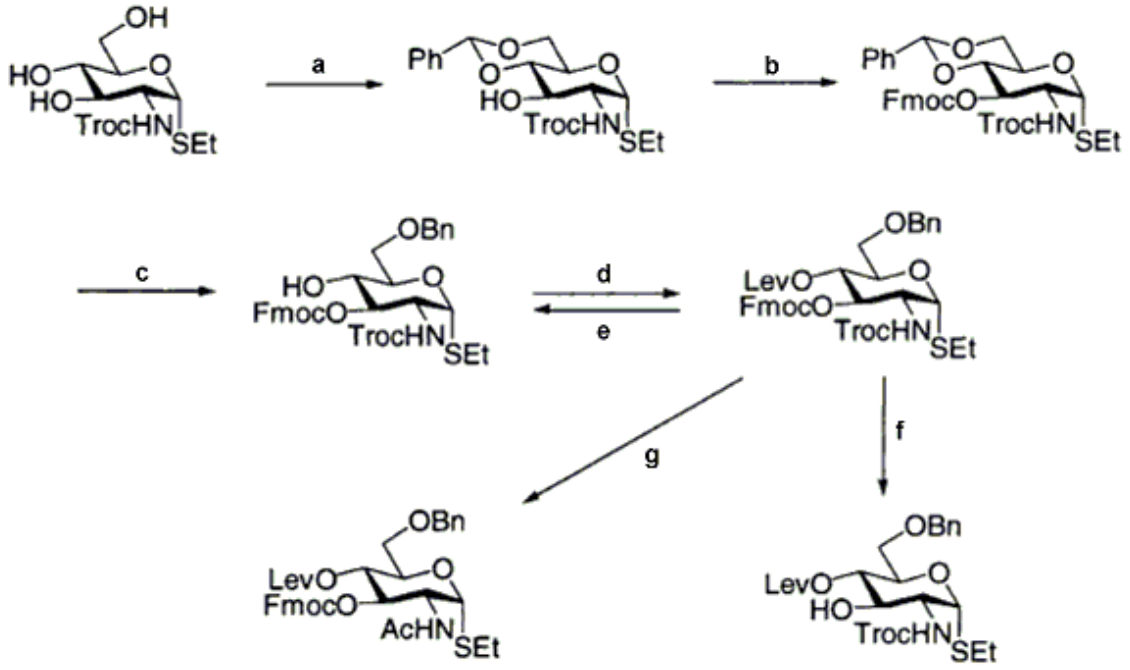
Scheme 1.2: Leaving group interconversions of thioglycosides**.**



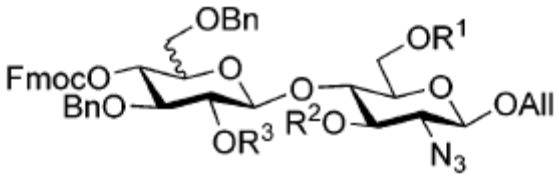
Scheme 1.3: Direct activation of thioglycosides.



Scheme 1.4: Utility of an orthogonally protected monosaccharide. Reagents and conditions: (a) NH_2NH_2/AcOH, THF/MeOH (10:1); (b) $NaHCO_3$, MeOH/H_2O (5:1), 60 °C; (c) HF-pyridine, HOAc/THF (1:4); (d) trifluoroacetic acid, CH_2Cl_2, -20 °C.



Scheme 1.5: The implementation of Fmoc, Lev, and Troc as orthogonal protection groups that is compatible with polymer-supported oligosaccharide synthesis. Reagents and conditions: (a) dimethyl benzaldehyde acetal, CSA, MeCN, 87%; (b) FmocCl, pyridine, 94%; (c) $NaCNBH_3$, HCl/Et_2O, THF, MS 3 Å, 94%; (d) LevOH, DCC, cat. DMAP, CH_2Cl_2, 98%; (e) NH_2NH_2/AcOH, THF/MeOH (10:1), 99%; (f) 20 % Et_3N, CH_2Cl_2, 99%; (g) Zn, AcOH then Ac_2O, pyridine, 86%.



Sulfonated	Unsulfonated
R^1 = Lev	R^1 = TBDPS
R^2 = Lev	R^2 = Bn
R^3 = Lev	R^3 = Ac

Figure 1.5: Orthogonal protecting groups for disaccharide building blocks of heparan sulfate.

CHAPTER 2

DESCRIPTION OF PROJECT

1. Objective

While the primary plant cell wall controls the morphology of plant cells, it is has also been implicated in the development and differentiation of plant cells.[122] Monoclonal antibodies show promise as useful tools to study the localization of particular saccharide motifs during plant growth and development because they are highly specific and sensitive enough to monitor changes at the cellular level.[123] Synthetic oligosaccharides provide structurally-defined antigens for the generation of monoclonal antibodies and potential ligands for mapping the binding speficities of monoclonal antibodies generatated from isolated cell wall oligosaccharides. Putative primary cell wall oligosaccharide moieties **1**-**4** (Figure 2.1) were chosen for synthetic preparation.

It was envisioned that the orthogonally protected trisaccharide **24** would allow access to target **1** and permit selective deprotection of the C-2, C-3, and C-6 hydroxyl moieties of the non-reducing terminal galactoside, providing an efficient route to tetrasaccharide targets **2**, **3**, and **4**. As our group has pioneered the use of the orthogonal 9-fluorenylmethoxycarbonyl (Fmoc) and levulinoyl (Lev) protecting groups in carbohydrate synthesis,[120] the C-2 hydroxyl could be protected with the Lev ester to provide the β-directing neighboring group participation required for the formation of the 1,6-β-galactosyl backbone. The C-3 hydroxyl could be regioselectively blocked in the presence of a free C-2 hydroxyl with the base labile Fmoc group by using one

equivalent of FmocCl in pyridine. Furthermore, a 4,6-*O*-benzylidine acetal of **24** could be selectively opened under Lewis acid conditions to give a C-6 hydroxyl by using triethylsilane (Et_3SiH) and dichlorophenyl borane ($PhBCl_2$).[124]

2. Results and Discussion

2.1 Synthesis of Core Trisaccharides

Installation of the linker of acceptor **8** was achieved by reaction of 1,2,3,4,6-penta-*O*-acetyl-β-D-galactose with 3-bromo-1-propanol in the presence of boron trifluoride diethyl etherate ($BF_3 \cdot Et_2O$) (Scheme 2.1). An approximately 2:1 mixture of product and starting galactoside, respectively, was isolated before purification. Purification of the crude mixture afforded intermediate **5** (53%). The bromide of **5** was displaced by an azido group to give **6** by heating under reflux in a 2:1 mixture of acetone and water in the presence of NaN_3 (98%). Compound **6** was treated under Zemplen conditions (sodium methoxide/methanol) to remove the acetyl esters. The C-6 hydroxyl of the resulting compound was regioselectively protected using *tert*-butyldiphenylsilyl chloride (TBDPSCl) in pyridine, and subsequently the C-2, C-3, and C-4 hydroxyl groups were converted into benzoyl (Bz) esters by treatment with benzoyl chloride (BzCl) in pyridine to give **7** (94%, 3 steps). The *tert*-butyldiphenylsilyl (TBDPS) group of **7** was then removed by reaction with hydrogen fluoride (HF) in pyridine to give **8** (93%).

The preparation of thiogalactosyl donors **11**, **13-15**, and **17** began with the installation of the thiophenyl glycoside by reaction of 1,2,3,4,6-penta-*O*-acetyl-β-D-galactose with thiophenol in the presence of $BF_3 \cdot Et_2O$ (Scheme 2.2). Subsequent removal of the acetyl esters under Zemplen conditions gave thioglycoside **9** (98%, 2 steps). A 4,6-*O*-benzylidene acetal protecting group was installed by a *para*-toluenesulfonic acid- (*p*-TsOH) catalyzed reaction of **9** with

benzaldehyde dimethylacetal to give **10** (66%). Glycosyl donor **11** (99.8%) was obtained by reaction with BzCl in pyridine.

Regioselective protection of the C-3 hydroxyl group of **10** over the less-reactive hydroxyl at the C-2 position was achieved by using one equivalent of a soft chloride electrophile; the use of more than one equivalent in the reaction can result in blocking both the C-2 and C-3 positions. Treatment of **10** with 9-fluorenylmethoxycarbonyl chloroformate (FmocCl, 1.1 equiv.) in pyridine gave **12** (83%), and preparation of **16** (34%) was carried out by reaction of **10** with *tert*-butyldimethylsilyl chloride (TBSCl) in pyridine. Acylation of **12** and **16** with benzoyl chloride in pyridine gave glycosyl donors **13** (85%) and **17** (53%), respectively. Glycosyl donor **14** (79%) was obtained by reaction of **12** with levulinic acid in the presence of *N,N'*-dicyclohexylcarbodiimide (DCC) and *N,N*-dimethylaminopyridine (DMAP). Removal of the 1,3-bis(1-hydroxy-2,2,2-trichloroethyl) urea (DCU) byproduct proved problematic but could be achieved by dissolving the crude reaction residue in ethyl acetate (EtOAc) and filtering off the DCU crystals several times. This procedure was followed by careful flash silica gel column chromatography to give pure **14**. Removal of the Fmoc protecting group of **14** by treatment with triethylamine in dichloromethane followed by benzoylation under standard conditions afforded glycosyl donor **15** (43%, 2 steps).

The reaction of glycosyl donor **11** with acceptor **8** (Scheme 2.3) using *N*-iodosuccinimide/trimethylsilyl triflouromethane sulfonate (NIS/TMSOTf) as the promoter system gave disaccharide **18** (79%). Access to the C-6' hydroxyl for further galactosylation was achieved by two methods. Hydrolysis of the benzylidene acetal of **18** in 80% acetic acid (AcOH) at 60 °C gave **19** (87%). Alternatively, chemoselective opening of the benzylidene acetal[124] of **18** using Et_3SiH and $PhBCl_2$ gave **20** (86%). The selectivity of this reaction was

confirmed by first acetylating **20** and comparing the ^{1}H NMR spectra of the acetylated compound with **20**. The chemical shift of the C-6' protons in the ^{1}H NMR was observed to change from 3.5 ppm and 3.8 ppm for **20** to about 4.1 ppm and 4.3 ppm in the acetylated compound. Also, no downfield shift was observed for the C-4' proton, which was observed in both compounds at about 3.9 ppm, and the benzyl ether methylene protons from C-4' were observed at 4.6 ppm and 5.0 ppm.

The preparation of trisaccharides **21**-**23** (Scheme 2.4) was carried out in an effort towards the synthesis of target compound **4** (Figure 2.1). Also, compounds **21**-**23** provided easy access to target trisaccharide **1**. Glycosyl donor **11** was activated with NIS/TMSOTf and reacted with acceptor **19** to give **22** (52%). Glycosyl donor **11** and acceptor **20** were coupled under the same conditions to give **21** (88%). The free C-4'hydroxyl of **22** was readily acetylated to give the fully-protected trisaccharide **23** (76%).

Compounds **24**-**28** (Scheme 2.4) were formed as intermediates leading to **3**. Coupling glycosyl donor **14** with acceptor **19** using NIS/TMSOTf as the promoter system gave a low yield of compound **24**. No definitive explanation for this result has been determined; however, the reactivity of donor **14** may not be suitably reactive for using NIS/TMSOTf as the promoter system. Thus, using the more powerful phenylsulfoxide/triflouromethane sulfonatic anhydride (Ph_2SO/Tf_2O) as the promoter system[94] afforded target trisaccharide **24** in an improved yield of 66%. Similarly, the glycosylation of glycosyl donor **15** with acceptor **19** afforded trisaccharide **27** (33%) when Ph_2SO/Tf_2O was used as the promoter system. Acetylation of the C-4' hydroxyl of **24** and **27** using acetic anhydride (Ac_2O), pyridine, and DMAP gave **25** (90%) and **28** (74%), respectively.

It may be that use of the powerful Ph_2SO/Tf_2O promoter system is not compatible with glycosyl acceptors such as **19**, which contain multiple possible glycosylation sites. It should be noted that glycosylation at the C-6 position of a galactose is much more likely to occur than glycosylation at the C-4 hydroxyl. The nucleophilicity of the C-4 hydroxyl of galactose is known to be much lower than that of the C-6 hydroxyl, and the exo-anomeric effect and torsional freedom are much more favorable for 1,6-linked galactosides.[107]

It is anticipated that trisaccharide **26** can be prepared by coupling **15** with **20** in a yield superior to that obtained for **27**, however, efforts to isolate this compound from crude mixtures proved unsuccessful. Purification of the galactosyl trisaccharides containing a C-3 Fmoc protecting group apparently requires very exacting conditions that have yet to be solved.

Including the previously described compounds **24** and **25**, trisaccharide intermediate **30** (Scheme 2.4) was appropriately protected for the preparation of targeted compound **2**. The glycosylation of acceptor **20** with glycosyl donor **17** resulted in the formation of **30** (37%).

2.2 Synthesis of Fucosyl Donor

1-thio-L-fucoside **31** (65%, 2 steps) was obtained by acetylation of L-fucose using Ac_2O and pyridine followed by installment of the anomeric thioethyl moiety by treatment with ethanethiol and $BF_3 \cdot Et_2O$ as the promoter (Scheme 2.5). In a case of serendipity, pure crystals of compound **31** were isolated from a vented vessel containing a syrupy, post-purification mixture of **31** and partially inseparable side-products. The clear, colorless crystals were washed with a small amount of hexanes to remove the residual yellow-brown syrup. Removal of the acetyl esters of **31** using Zemplen conditions, followed by 3,4-*O*-isopropylidene acetal formation employing 2,2-dimethoxypropane and *p*-TsOH in *N,N*-dimethylaminoformamide (DMF) resulted in the formation of **32** (85%, 2 steps). The free C-2 hydroxyl of **32** was readily benzylated using

NaH, BnBr, and a catalytic amount of tetrabutylamonium iodide (TBAI) in DMF to afford **33** (99%). Subsequently, fucosyl donor **34** (91%) was easily obtained by first removing the isopropylidine acetal using Zemplen conditions and then protecting the resulting free hydroxyls as acetyl esters using Ac_2O and pyridine.

2.3 Synthesis of a 2-*O*-Fucosyl Containing Tetrasaccharide

As previously mentioned, it was originally envisioned that a common orthogonally protected trisaccharide **24** (Scheme 2.6) could be prepared that would provide an efficient route to trisaccharide **1** and tetrasaccharide targets **2**, **3**, and **4** (Figure 2.1). As described in the synthesis of glycosyl donor **14**, the C-3 hydroxyl of the 4,6-*O*-benzylidene protected thiogalactoside **10** can be regioselectively blocked in the presence of a free C-2 hydroxyl using 1 equivalent of FmocCl in pyridine. The Fmoc group can be selectively removed in high yield by using triethylamine in CH_2Cl_2, while the Lev ester can be selectively removed using hydrazine acetate in the presence of other ester protecting groups such as acetyl and benzoyl esters.[120] Also, the 4,6-*O*-benzylidine acetal of **24** can be regioselectively opened to give a C-6 hydroxyl by treatment with Et_3SiH and $PhBCl_2$,[124] as previously described in the preparation of disaccharide **20**.

In an effort towards the preparation of target compound **3**, the levulinoyl esters of **24** and **25** were removed using AcOH-buffered hydrazine in pyridine (Scheme 2.6) to give **35** (96%) and **36** (42%), respectively. The coupling of fucosyl donor **34** with acceptor **35** using NIS/TMSOTf as the promoter gave tetrasaccharide **49** (38%). A homologous glycosyl acceptor **36** was prepared from **25** (42%); glycosylation of this acceptor using **34** and NIS/TMSOTf as the promoter system in CH_2Cl_2 gave tetrasacchride **50** (23%). Attempts to repeat these glycosylations under a number of different conditions gave unsatisfactory results (Table 2.2).

It was hypothesized that the neighboring bulky 3-*O*-Fmoc protecting group would sterically block the C-2 hydroxyl preventing fucosylation with **34**. In an effort to test this hypothesis (Scheme 2.7), the anomeric thioether of **14** was converted into a methyl galactoside under standard NIS/TMSOTf promoted glycosylation conditions in the presence of methanol to give **46** (86%). The C-2 levulinoyl protecting group was subsequently removed using AcOH-buffered hydrazine in pyridine to afford glycosyl acceptor **47** (70%). Glycosylation of this acceptor with fucosyl donor **34** was readily carried out to give **48** exclusively as the α-anomer (^{1}H NMR, 300 MHz, $CDCl_3$: δ 4.5 ppm, $J_{1,2}$ = 4.0 Hz, 1H, H-1') in a 79% yield, a result which suggests that the presence of a C-3 Fmoc protecting group alone did not determine the failure of the fucosylations at the C-2 hydroxyl.

Nonetheless, further use of a C-3 Fmoc protecting group in the preparation of tetrasaccharide **3** was avoided. Trisaccharide **28** was converted to acceptor **38** (80%) using AcOH-buffered hydrazine, as previously described. The subsequent fucosylation using glycosyl donor **34** and NIS/trifluoromethane sulfonic acid (TfOH) as the promoter system easily afforded **51** (70%). It was predicted that glycosyl acceptor **37** could be utilized in a similar approach.

Target tetrasacchride **3** was obtained by first removing the ester protecting groups of **51** by using Zemplen conditions; catalytic hydrogenation of the isolated intermediate using H_2 and Pd/C in a 20:2:1 mixture of isopropanol/AcOH/water provided **3** in a yield of 52% in two steps.

2.4 Synthesis of a 3-*O*-Fucosyl Containing Tetrasaccharide

The Fmoc group of **24** (Scheme 8) was readily removed using triethylamine in CH_2Cl_2 to afford **40** (87%). However, fucosylation using glycosyl donor **34** and NIS/TMSOTf as the promoter system proved difficult. While some of the desired tetrasaccharide **53** (28%) was isolated, pentasaccharide (5%), a result of fucosylation of the unprotected C-4' hydroxyl, was

also isolated and identified by MALDI-MS. In order to avoid multiple fucosylations, glycosyl acceptor **42**, having only a free C-3'' hydroxyl, was prepared. Compound **39** was obtained by using Ac_2O in pyridine to acetylate a mixture of compounds **35** and **36**. The C-3'' Fmoc protecting group of **39** was removed by treatment with triethylamine in CH_2Cl_2 to give glycosyl acceptor **42** (64%). Subsequent condesation of **42** with fucosyl donor **34** using NIS/TMSOTf as the promoter system gave **55** (70%). In comparison to **42**, trisaccharide acceptor **41** was obtained in a more linear approach by removing the C-3 TBS protecting group of **30** using 70% HF/pyridine in a yield of 96%; it is expected that **41** can also be prepared by the removal of the C-3'' Fmoc group of **29** using triethylamine in CH_2Cl_2. Condensation of **41** with fucosyl donor **34** using NIS/TMSOTf as the promoter system gave **54** (70%).

2.5 Synthesis of a 6-*O*-Fucosyl Containing Tetrasaccharide

Hydrolysis of the benzylidene acetal of **22** (Scheme 2.9) in 80% AcOH at 60 °C gave **44** (70%). Like the fucosylation of the C-3'' glycosyl acceptor **40**, the result of the subsequent fucosylation of **44** gave a low yield of desired tetrasaccharide **57** (2.4%). Additionally, a pentasaccharide side product (2.6%), a result of an additional fucosylation at either the free C-4' or C-4'' hydroxyl, was also isolated and identified by MALDI-MS. No hexasaccharide was isolated. In order to avoid the possibility of multiple fucosylations, the benzylidene acetal of **23** was chemoselectively opened using Et_3SiH and $PhBCl_2$ to liberate the C-6'' hydroxyl, as previously described,[124] to give **45** (65%). The coupling between fucosyl donor **34** and **45** using NIS/TMSOTf as the promoter system in 4:1 Et_2O/CH_2Cl_2 gave target tetrasaccharide **58** (72%) as a 4:1 mixture of α and β anomers, as determined by ^1H NMR and MALDI-TOF mass spectrometry.

A singlet arising from the α fucosyl H-1''' and one of the C-4'' benzyl ether methylene protons was found at 4.82 ppm; the C-1''' carbon of the α anomer was identified at 97.9 ppm. The β H-1''' peak could not be identified in order to measure its coupling with H-2'''; further analysis by ^{13}C NMR should provide evidence of the β anomer by the identification of the C-1''' peak at approximately 100 ppm. The presence of the β anomer is proposed because further analysis of the ^{1}H NMR spectrum revealed a peak at 1.10 ppm (d, $J_{5,6}$ = 6.3 Hz), which was clearly analogous to the peak at 0.90 ppm (d, $J_{5,6}$ = 6.3 Hz) arising from the fucose C-6''' protons. The relative abundance of the two anomers was determined to be 4:1 (α/β) by comparing the integration of the two peaks. Also, two sets of peaks arising from the methyl protons of the C-3'', C-4', and C-4'' acetyl esters of the two isomers showed similar disparity in abundance by integration. The presence of regioisomers was not considered, as only the C-6'' hydroxyl was available for fucosylation. High-resolution MALDI-TOF mass spectrometry identified only one product (1790.7355 $[M + Na]^+$; 1767.5844 Calcd. for $C_{96}H_{93}N_3O_{30}$).

3. Conclusion

Protected oligosaccharides amenable to deprotection leading to target compounds **1-4** (Figure 2.4) were successfully synthesized. Also, target compound **3** was isolated as pure product. Once all targets are isolated, they will be conjugated to a protein for analysis via ELISA to determine the epitope binding specifity of antibodies which recognize primary plant cell wall epitopes. Isolated targets may also be conjugated with a carrier protein for the immunization of BALB/c mice to provide serum for generation monoclonal antibodies from hybridoma cell lines. The information garnered from this research should aid in the identification of the carbohydrate processing enzymes involved in the formation of pectic polysaccharides such as arabinogalactan and rhamnogalacturonan-I (RG-1) and the

hemicellulose xyloglucan. Ultimately, these studies will allow for identification of the genes encoded for the production of the identified proteins.

The use of the orthogonal Fmoc and levulinoyl protecting groups in a common trisaccharide leading to target compounds **1**-**4** proved unsuccessful, yet this result cannot be used to dispute the utility of these protecting groups in carbohydrate synthesis. It is clear that the use of the bulky Fmoc group on glycosyl acceptors may prove unwise in cases where steric bulk may prevent coupling between glycosyl donor and acceptor. Also, the use of these protecting groups on glycosyl donors may require the use of more powerful promoter systems such as Ph_2SO/Tf_2O, especially in cases where the levulinoyl group is used as a neighboring group participating functionality.

The reactivity of alkyl 1-thio-fucoside donors should not be underestimated. Despite the low reactivity of the C-4 hydroxyl of galactose, it was still found reactive, even in cases when only one equivalent of fucosyl donor was used to target the primary C-6 hydroxyl. While it is possible to regioselectively fucosylate the C-6 hydroxyl of galactose with absolutely no reaction with the C-4 hydroxyl of the same galactosyl unit, it appears that in some cases it is advantageous to protect the C-4 hydroxyls of other galactosyl units in the same oligosaccharide acceptor.

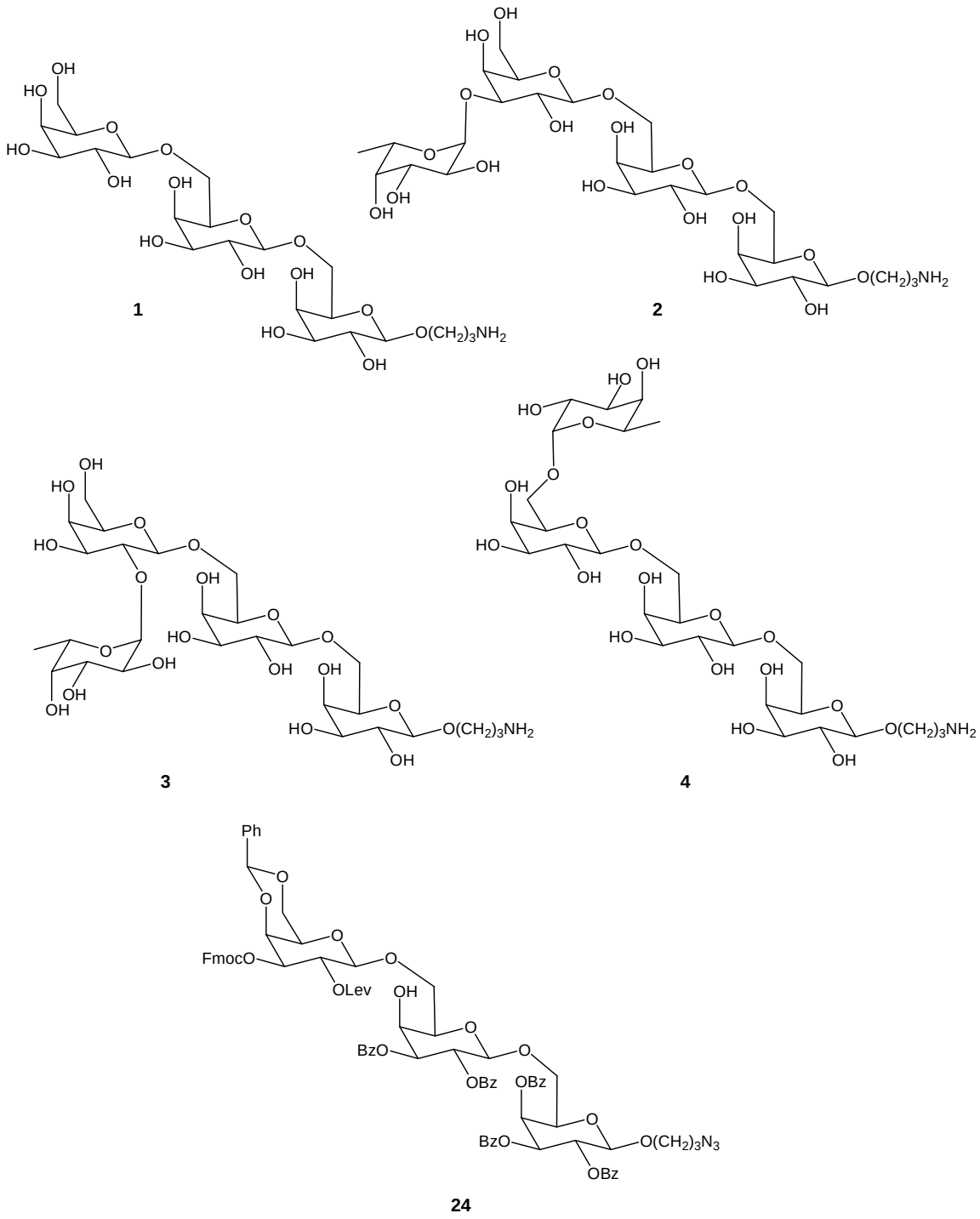
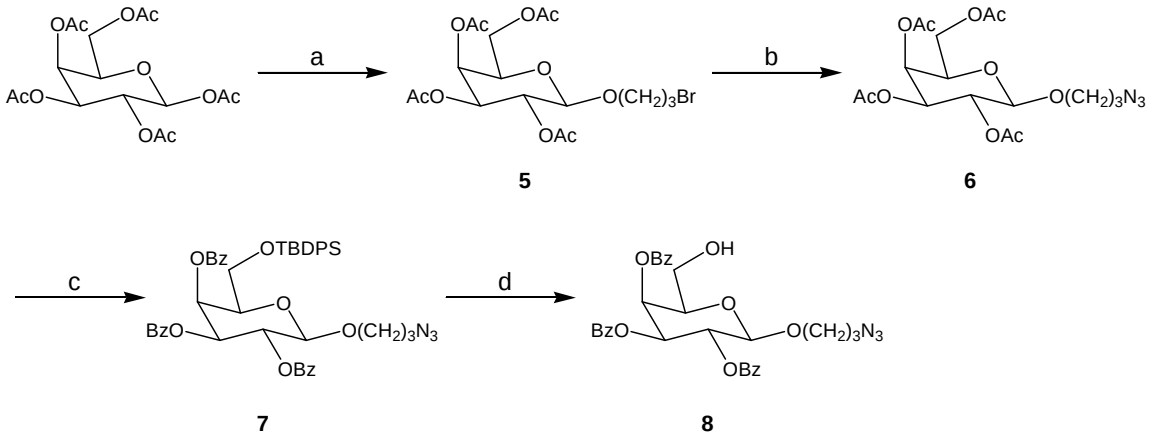
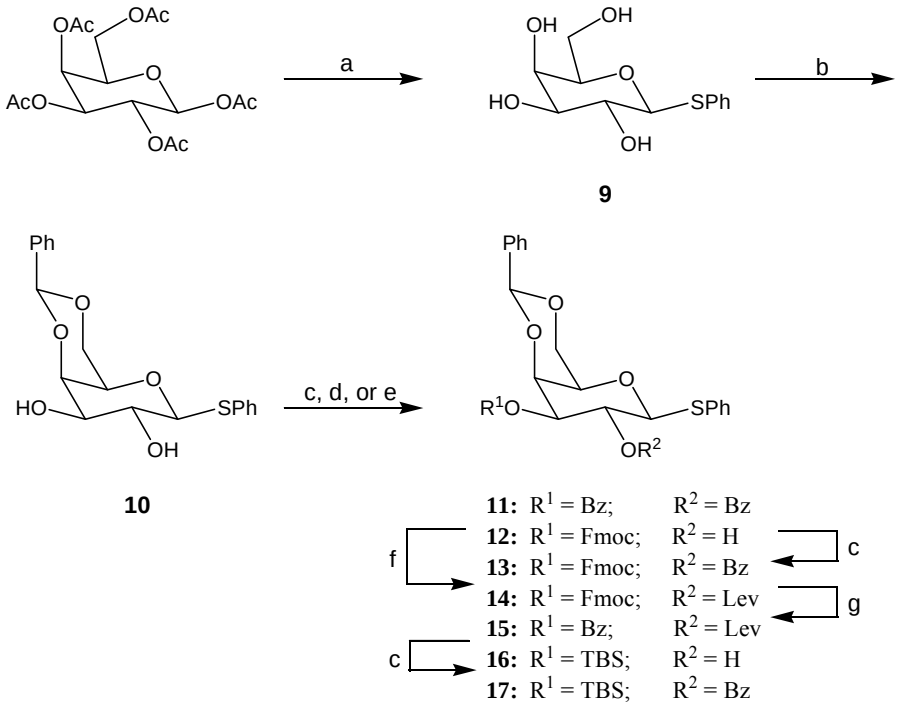


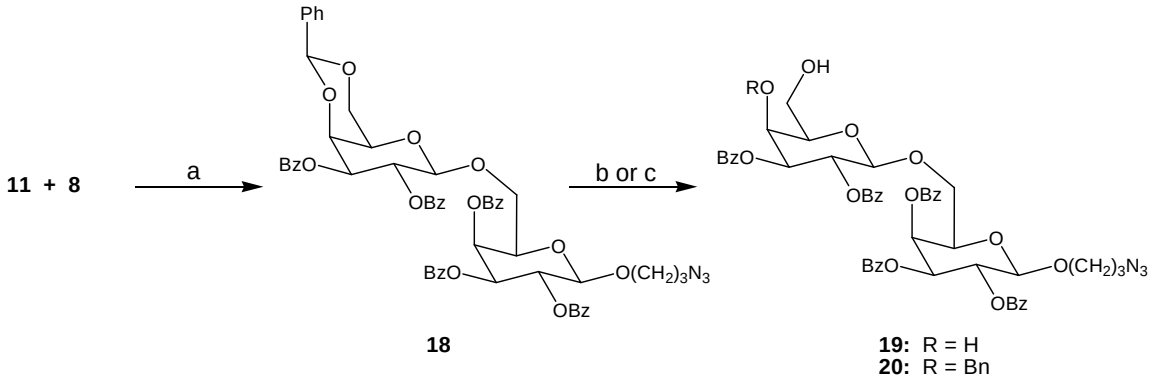
Figure 2.1: Targets **1**-**4** for epitope characterization studies and **24** as the common trisaccharide building block.



Scheme 2.1: Reagents and conditions: (a) 3-bromo-1-propanol, $BF_3 \cdot Et_2O$, CH_2Cl_2 (53%); (b) NaN_3, acetone/water, 80 °C (98%); (c) i. NaOMe/MeOH, MeOH; ii. TBDPSCl, pyridine; iii. BzCl, pyridine; (94%); (d) HF/pyridine, THF, (93%).



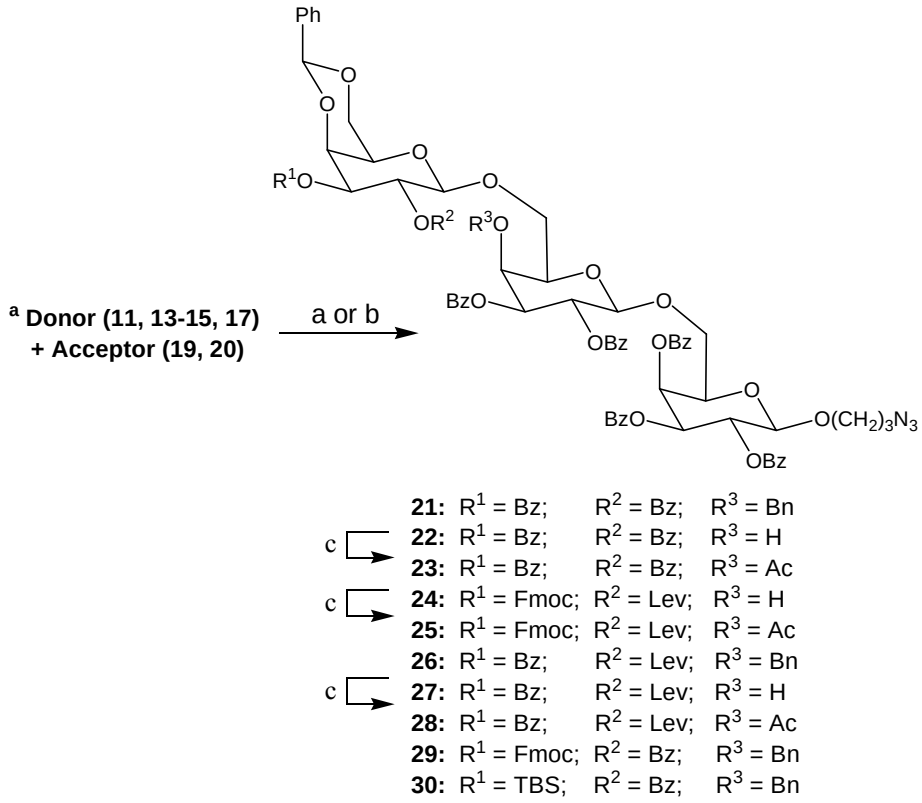
Scheme 2.2: Reagents and conditions: (a) i. PhSH, $BF_3 \cdot Et_2O$, CH_2Cl_2, 0°C → RT, (98%); (b) $PhCH(OMe)_2$, *p*TSOH, DMF, (66%); (c) BzCl, pyridine; **11** (quant.); **13** (85%); **17** (53%); (d) FmocCl, pyridine, **12** (83%); (e) TBSCl, pyridine, **16** (34%); (f) levulinic acid, DCC, DMAP, CH_2Cl_2, **14** (79%); (g) i. NEt_3, CH_2Cl_2; ii. BzCl, pyridine; **15** (45%).



18

19: R = H
20: R = Bn

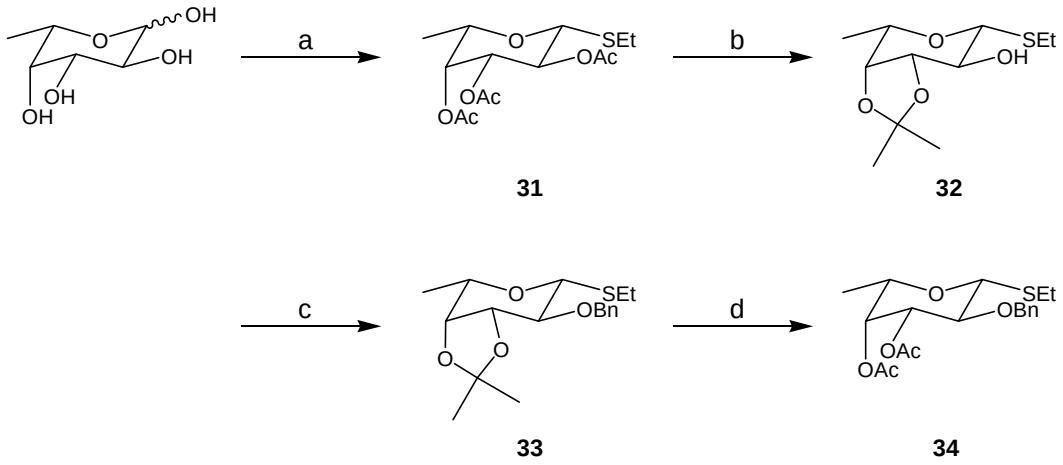
Scheme 2.3: Reagents and conditions: (a) NIS, TMSOTf, CH_2Cl_2, MS 4Å, 0 °C, (80%); (b) 80% AcOH, 60 °C, **19** (87%); (c) Et_3SiH, $PhBCl_2$, CH_2Cl_2, MS 4Å, -78 °C, **20** (86%).



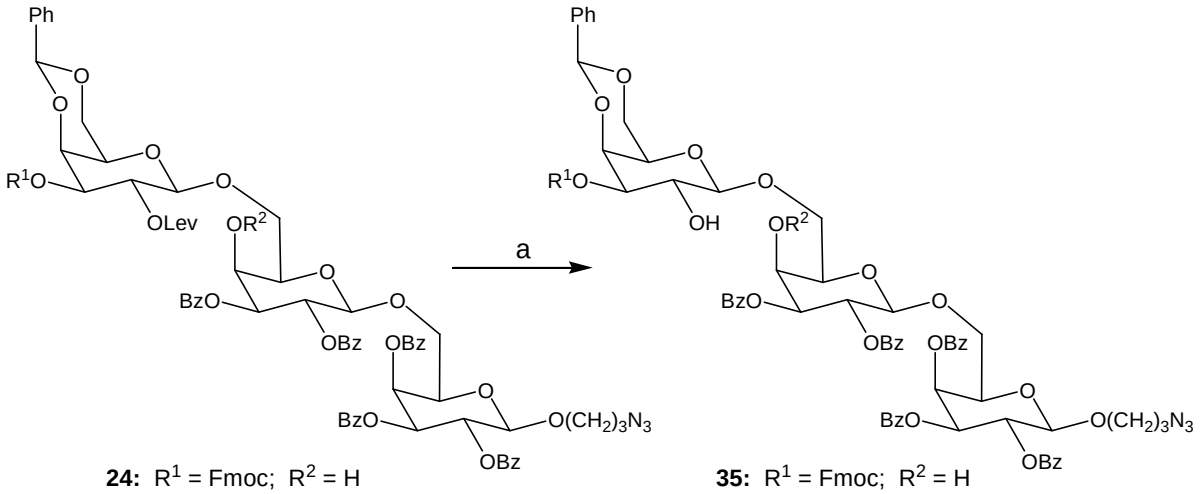
Scheme 2.4: Reagents and conditions: (a) NIS, TMSOTf, CH_2Cl_2, MS 4Å, 0 °C; (b) Ph_2SO, Tf_2O, CH_2Cl_2, MS 4Å, -60 °C → RT; (c) Ac_2O, pyridine; **23** (76%); **25** (65%); **28** (74%). [a] For donor and acceptor coupling conditions, see Table 2.1.

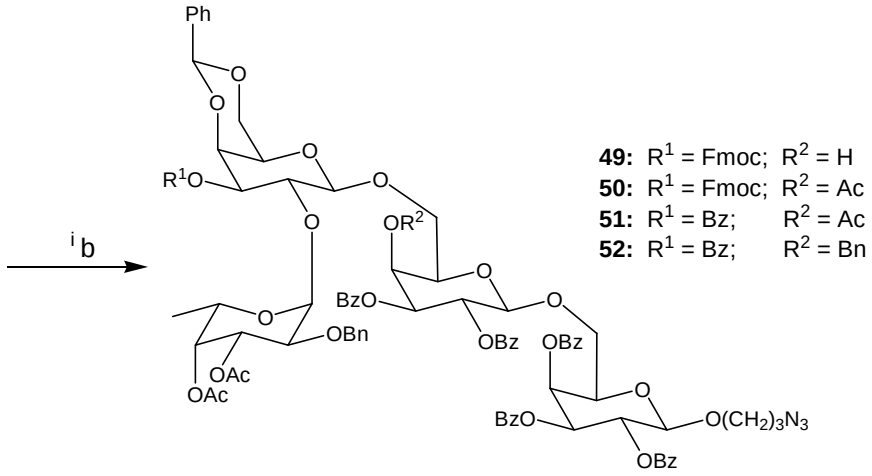
Table 2.1. Formation of core galactosyl trisaccharides. [a] Reagents and conditions: (a) NIS, TMSOTf, CH_2Cl_2, MS 4Å, 0 °C; (b) Ph_2SO, Tf_2O, CH_2Cl_2, MS 4Å, -60 °C → RT.

Donor	Acceptor	[a] Conditions	Product	Yield
11	**20**	a	**21**	88 %
11	**19**	a	**22**	52 %
14	**19**	b	**24**	66 %
15	**20**	b	**26**	proposed
15	**19**	b	**27**	33 %
13	**20**	a	**29**	---
17	**20**	a	**30**	37 %



Scheme 2.5: Reagents and conditions: (a) i. Ac_2O, pyridine; ii. EtSH, $BF_3 \cdot Et_2O$, CH_2Cl_2, MS 4Å, 0 °C, (65%); (b) i. NaOMe/MeOH, MeOH; ii. 2,2-dimethoxypropane, *p*TSOH, DCM, (85%); (c) NaH, BnBr, TBAI, DMF, 0 °C → RT, (99%); (d) i. 80% AcOH, 60 °C; ii. Ac_2O, pyridine, (91%).

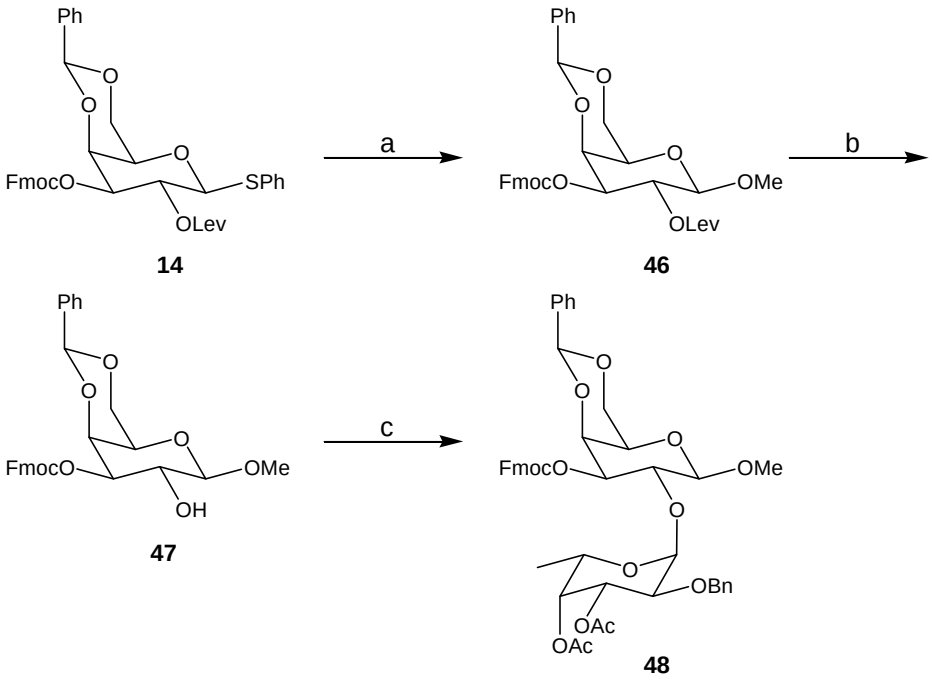




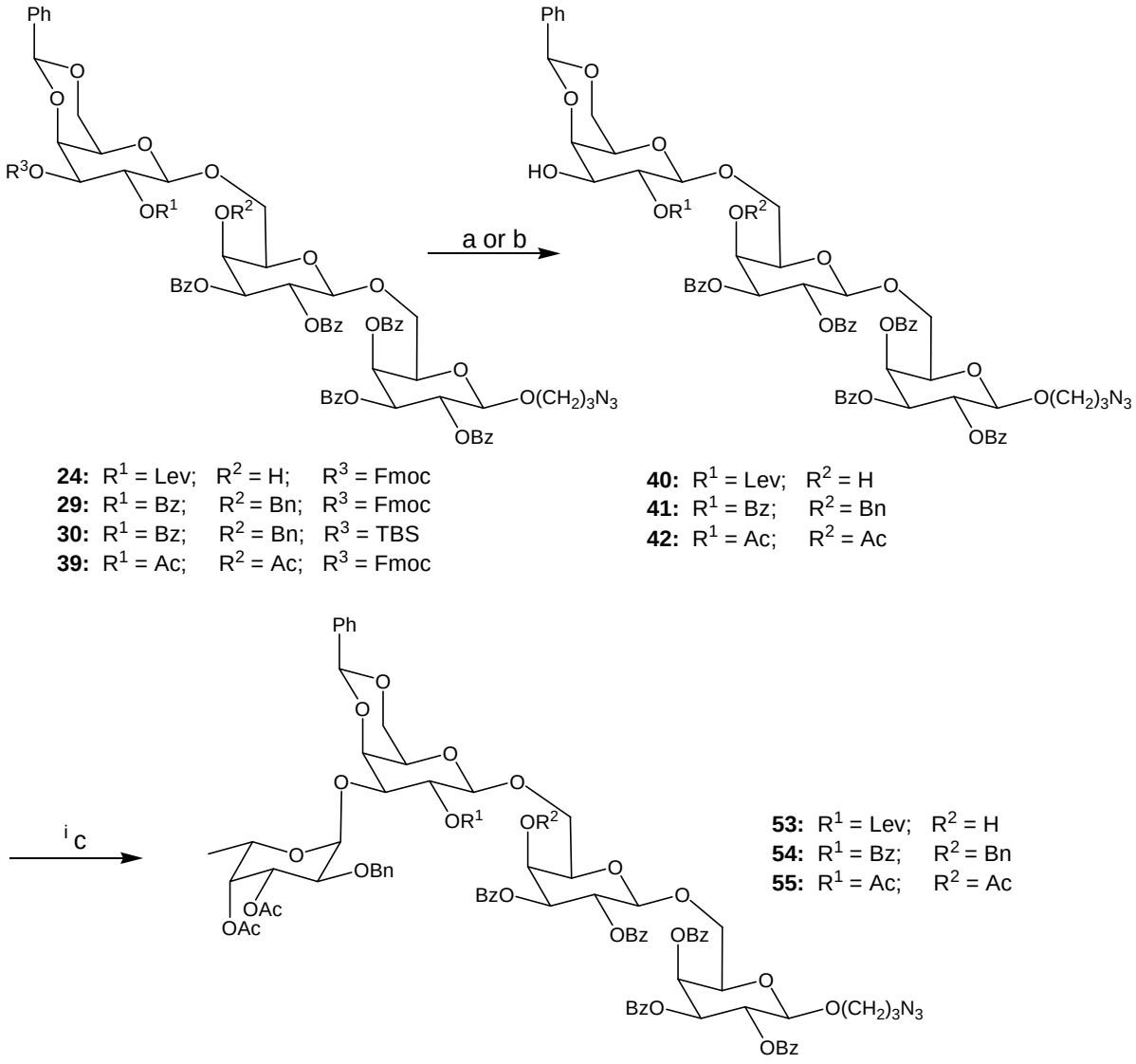
Scheme 2.6: Reagents and conditions: (a) AcOH, pyridine, $H_2NNH_2 \cdot H_2O$, acetone; **35** (96%); **36** (42%); **37** (--%); **38** (80%); (b) **34**, NIS, TMSOTf or TfOH, CH_2Cl_2, MS 4Å. [i] For further information see Table 2.2.

Table 2.2: Formation of 2-O-fucosyl tetrasaccharides

Acceptor	Donor	Promoter	Solvent	Time	Temp.	4Å MS	Product	Result
35	1.1 equiv	1.3 equiv NIS, 0.2 equiv TMSOTf	1:1 CH_2Cl_2/Et_2O	1 h	0 °C	Yes	**49**	38%
35	3 equiv	3.3 equiv NIS, 0.3 equiv TMSOTf	1:1 CH_2Cl_2/Et_2O	1.5 h	0 °C	Yes	**49**	8%
35	1.5 equiv	1.5 equiv NIS, 0.2 equiv TMSOTf	1:1 CH_2Cl_2/Et_2O	1 h	0 °C	Yes	**49**	--
35	1.5 equiv	1.5 equiv NIS, 0.2 equiv TMSOTf	CH_2Cl_2	1 h	-20 °C	No	**49**	--
36	1.1 equiv	1.3 equiv NIS, 0.05 equiv TMSOTf	CH_2Cl_2	1 h	0 °C	Yes	**50**	23%
38	2 equiv	1.3 equiv NIS, 0.2 equiv TfOH	CH_2Cl_2	1 h	-20 °C	Yes	**51**	70%



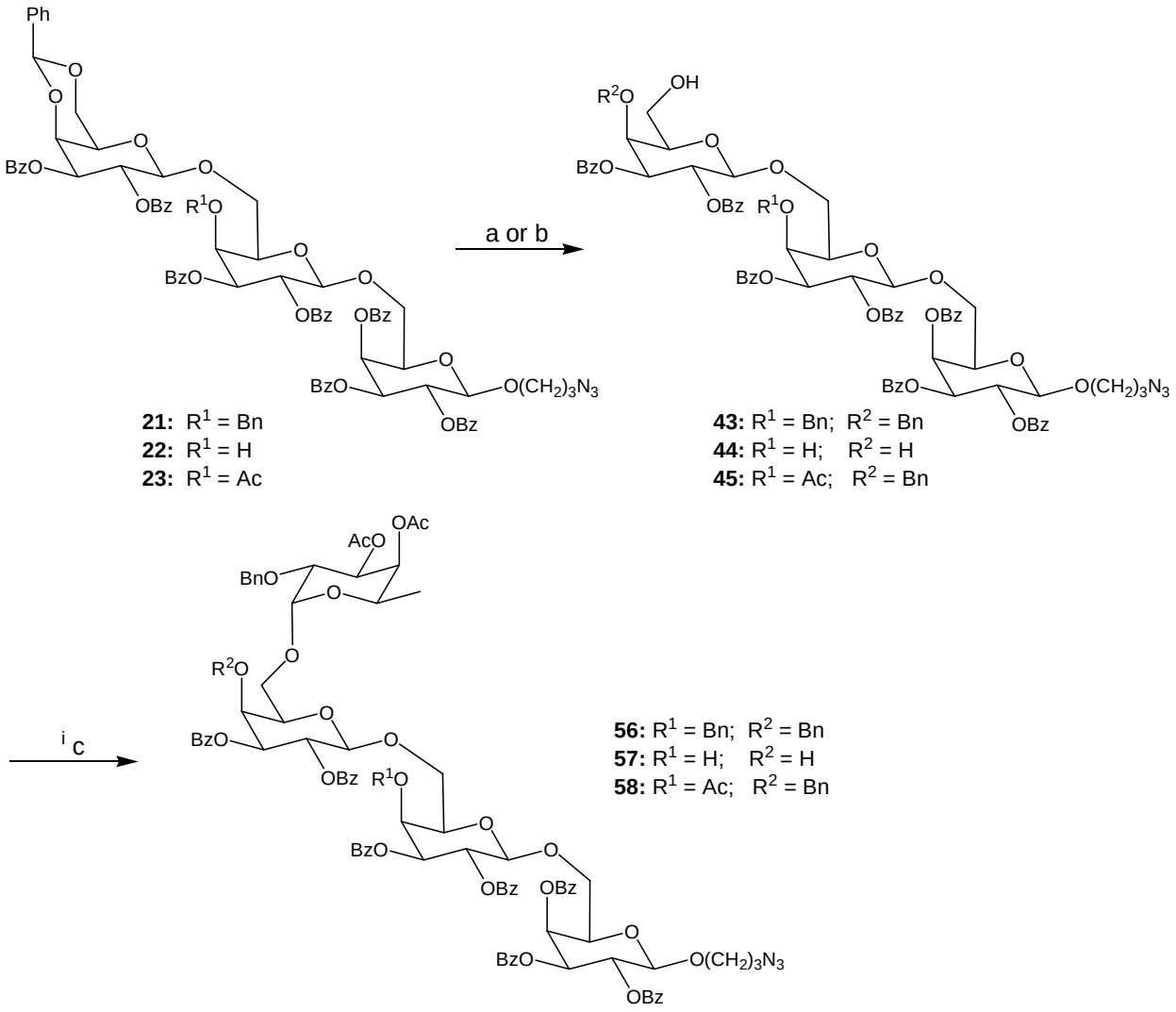
Scheme 2.7: Reagents and conditions: (a) NIS, TMSOTf, MeOH, CH_2Cl_2, MS 4Å, 0 °C, (86%); (b) AcOH, pyridine, $H_2NNH_2 \cdot H_2O$, acetone, (70%); (c) **34**, NIS, TMSOTf, CH_2Cl_2, MS 4Å, 0 °C, (79%).



Scheme 2.8: Reagents and conditions: (a) NEt_3, CH_2Cl_2; **40** (87%); **41** (--%); **42** (64%); (b) HF/pyridine, THF, **41** (96%); (c) **34**, NIS, TMSOTf, CH_2Cl_2, MS 4Å, 0 °C. [i] For further information see Table 2.3.

Table 2.3: Formation of 3-O-fucosyl tetrasaccharides

Acceptor	Donor	Promoter	Solvent	Time	Temp.	4Å MS	Product	Result
40	1.1 equiv	1.3 equiv NIS, 0.1 equiv TMSOTf	CH_2Cl_2	1 h	0 °C	Yes	**53** (pentasacch).	28% (5%)
41	5 equiv	5.5 equiv NIS, 0.8 equiv TMSOTf	CH_2Cl_2	0.5 h	0 °C	Yes	**54**	70%
42	1.1 equiv	1.3 equiv NIS, 0.15 equiv TMSOTf	CH_2Cl_2	1 h	0 °C	Yes	**55**	70%



Scheme 2.9: Reagents and conditions: (a) Et_3SiH, $PhBCl_2$, CH_2Cl_2, MS 4Å, -78 °C; **43** (--%); **45** (65%); (b) 80% AcOH, 60 °C, **44** (70%); (c) **34**, NIS, TMSOTf, CH_2Cl_2, MS 4Å, 0 °C. [i] For further information see Table 2.4.

Table 2.4: Formation of 6-O-fucosyl tetrasaccharides

Acceptor	Donor	Promoter	Solvent	Time	Temp.	4Å MS	Product	Result
43	2 equiv	1.5 equiv NIS, 0.15 equiv TMSOTf	4:1 CH_2Cl_2/Et_2O	1 h	-20 °C	Yes	**56**	proposed
44	1.1 equiv	1.3 equiv NIS, 0.1 equiv TMSOTf	CH_2Cl_2	1 h	0 °C	Yes	**57** (pentasacch)	8% (3%)
45	1.1 equiv	1.5 equiv NIS, 0.15 equiv TMSOTf	4:1 CH_2Cl_2/Et_2O	1 h	0 °C	Yes	**58**	72% α/β (4:1)

CHAPTER 3

EXPERIMENTAL

General Methods and Materials

Solvents were purified according to standard procedures. Reactions were performed under argon unless stated otherwise. Reactions were monitored by thin-layer chromatography (TLC) using silica gel 60 F_{254}, and the compounds were visualized with UV light (254 nm) or by treatment with a solution of 10% H_2SO_4 in ethanol. Flash chromatography was performed on 70-230 mesh silica gel. Solvents were evaporated under reduced pressure while bath temperature was maintained below 40°C. NMR spectra were recorded on Varian spectrometers (Models Inova300, Inova500, and Inova600) equipped with Sun workstations. ^{1}H NMR spectra were recorded in $CDCl_3$ or CD_3OD and referenced to $CHCl_3$ at 7.26 ppm or CH_3OH at 4.78 ppm, respectively; ^{13}C NMR spectra were referenced to the central peak of $CDCl_3$ at 77.0 ppm or to the central peak of CD_3OD at 49.15 ppm. MS spectra were recorded on a VOYAGER-DE Applied Biosystems instrument in the positive mode by using 2,5-dihydroxylbenzoic acid in THF as matrix.

3-Bromopropyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside (5)

To a solution of β-D-galactose pentaacetate (4.00 g, 10.25 mmol) in CH_2Cl_2 (11 mL), 3-bromo-1-propanol (1.02 mL, 11.27 mmol) was added. The solution was cooled (0°C), and $BF_3 \cdot Et_2O$ (1.42 mL, 11.27 mmol) was added dropwise. The solution was allowed to warm to room temperature and was stirred for 18 h. The solution was diluted with CH_2Cl_2 (40 mL) washed

successively with 1M HCl (aq) (20 mL), saturated aqueous NaHCO3 (20 mL), and brine (20 mL). The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo*. The residue was purified using flash silica gel column chromatography (hexanes:EtOAc, 3:1 → 2:1, v/v) to afford **5** (2.53 g, 53%) as a clear, colorless syrup: TLC R_f = 0.62 (hexane/EtOAc, 2:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.40 (d, $J_{3,4}$ = 3.3 Hz, 1H, H-4), 5.20 (dd, $J_{1,2}$ = 7.8 Hz, $J_{2,3}$ = 10.5 Hz, 1H, H-2), 5.03 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3), 4.48 (d, $J_{1,2}$ = 7.8 Hz, 1H, H-1), 4.12 (m, 2H, OC*H*$_2$CH$_2$CH$_2$Br), 3.99 (*A*B, $J_{A,B}$ = 6.3 Hz, 1H, H-6), 3.92 (A*B*, $J_{A,B}$ = 6.3, 1H, H-6), 3.69 (s, 1H, H-5), 3.48 (m, *J* = 5.7 Hz, OCH$_2$CH$_2$C*H*$_2$Br), 2.15 (s, 3H, COC*H*$_3$), 2.08 (s, 3H, COC*H*$_3$), 2.05 (s, 3H, COC*H*$_3$), 2.00 (m, 2H, CH$_2$C*H*$_2$CH$_2$Br), 1.98 (s, 3H, COC*H*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.48, 170.33, 170.21, 169.69, 101.64, 70.92, 70.76, 68.93, 67.40, 67.11, 62.37, 32.32, 30.26, 20.90, 20.77, 20.74, 20.67. $C_{30}H_{29}N_3O_5$ (491.04): MS (MALDI) *m/z* = 491.11 $[M + Na]^+$.

3-Azidopropyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside (6)

Sodium azide (3.95 g, 60.7 mmol) was added to a solution of **5** (5.70 g, 12.1 mmol) in a mixture of acetone (65 mL) and water (35 mL). The mixture was heated under reflux 18 h. Acetone was removed *in vacuo*, and the resulting aqueous solution was diluted with water (20 mL). The water layer was extracted with CH_2Cl_2 (3 x 25 mL). The organic layer was then washed successively with 1M HCl (25 mL), saturated aqueous $NaHCO_3$ (25 mL), and brine (25 mL). The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo* to give **6** (5.54 g, 98%) as a clear, colorless syrup without purification: TLC R_f = 0.62 (hexane/EtOAc, 2:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.79 (m, 2H, OCH$_2$C*H*$_2$CH$_2$N$_3$), 1.92 (s, 3H, COC*H*$_3$), 1.98 (s, 3H, COC*H*$_3$), 2.00 (s, 3H, COC*H*$_3$), 2.09 (s, 3H, COC*H*$_3$), 3.31 (t, *J* = 6.8 Hz, 2H, OCH$_2$CH$_2$C*H*$_2$N$_3$), 3.54 and 3.90 (2 m, 2H, OC*H*$_2$CH$_2$CH$_2$N$_3$), 3.85 (t, $J_{5,6}$ = 6.6 Hz, 1H, H-5), 4.09 (m, 2H, H-6, H-

6), 4.41 (d, $J_{1,2}$ = 8.1 Hz, 1H, H-1), 4.95 (dd, $J_{2,3}$ = 10.8 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3), 5.13 (dd, $J_{1,2}$ = 8.1 Hz, $J_{2,3}$ = 10.8 Hz, 1H, H-2), 5.32 (d, $J_{3,4}$ = 3.3 Hz, 1H, H-4). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.48, 170.33, 170.21, 169.69, 101.64, 70.92, 70.76, 68.93, 67.40, 67.11, 62.37, 32.32, 30.26, 20.90, 20.77, 20.74, 20.67. $C_{17}H_{25}N_3O_{10}$ (431.15399): MS (MALDI) *m/z* = 594.59257 [M + Na]$^+$, 470.53338 [M + K]$^+$.

3-Azidopropyl 2,3,4-tri-*O*-benzoyl-6-*O*-*tert*-butyldiphenylsilyl-β-D-galactopyranoside (7)

Compound **6** (1.04 g, 2.41 mmol) was dissolved in MeOH (25 mL), and sodium methoxide (1M) was added until pH 9. This solution was stirred until TLC analysis (hexanes:EtOAc, 1:1, v/v) showed the reaction to be complete (~3 h). The solution was then neutralized using weakly acidic (pH 5) Amberlite resin and concentrated *in vacuo* to give an intermediate (0.634 g) as a clear, colorless syrup. This syrup and DMAP (0.0883 g, 0.723 mmol) were dissolved in pyridine (15 mL). The solution was cooled (0 °C), and *tert*-butyldimethylsilyl chloride (0.68 mL, 2.65 mmol) was added. The reaction mixture was allowed to warm to room temperature and stirred for 18 h. The reaction was quenched by the addition of MeOH (2 mL). The resulting solvents were removed *in vacuo*, and the residue was dissolved in CH_2Cl_2 (25 mL), which was subsequently washed with 1M HCl (10 mL), saturated aqueous $NaHCO_3$ (10 mL), and brine (10 mL). The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo*. The residue was purified by passing it through a short plug of silica gel (EtOAc) to afford a clear, colorless syrup (1.24g). The isolated intermediate was dissolved in pyridine (10 mL), cooled to 0 °C, and benzoyl chloride (1.68 mL, 14.5 mmol) was then added. The reaction was stirred at room temperature for 18 h. The reaction was quenched by the addition of MeOH (2 mL). The resulting solvents were removed in vacuo, and the residue was dissolved in CH_2Cl_2 (25 mL), which was subsequently washed with 1M HCl (10 mL), saturated aqueous $NaHCO_3$ (10

mL), and brine (10 mL). The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo*. The residue was purified using flash silica gel column chromatography (hexanes:EtOAc, 6:1, v/v) to afford **7** (1.834 g, 94%) as a clear, colorless syrup: TLC R_f = 0.55 (hexane/EtOAc, 6:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.92 (s, 9H, SiC(CH_3)$_3$), 1.70 (m, 2 H, $OCH_2CH_2CH_2N_3$), 3.14 (t, J = 6.3 Hz, 2H, $OCH_2CH_2CH_2N_3$), 3.51 and 3.88 (2 m, 2H, $OCH_2CH_2CH_2N_3$), 3.75 (d, $J_{5,6}$ = 6.6 Hz, 2H, H-6, H-6), 3.99 (t, $J_{5,6}$ = 6.6 Hz, 1H, H-5), 4.66 (d, $J_{1,2}$ = 7.8 Hz, 1H, H-1), 5.54 (dd, $J_{2,3}$ = 10.4 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3), 5.62 (dd, $J_{1,2}$ = 7.8 Hz, $J_{2,3}$ = 10.4 Hz, 1H, H-2), 5.96 (d, $J_{3,4}$ = 3.3 Hz, 1H, H-4), 7.04 (t, J = 7.5 Hz, 2H, Ar), 7.17 (t, J = 7.5 Hz, 4H, Ar), 7.34 (m, 13H, Ar), 7.60 (m, 6H, Ar), 7.73 (d, J = 7.5 Hz, 2H, Ar), 7.88 (d, J = 7.5 Hz, 2H, Ar), 7.96 (d, J = 7.5 Hz, 2H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ 18.98 (SiC(CH_3)$_3$), 26.54 (SiC(CH$_3$)$_3$), 26.63 (SiC(CH$_3$)$_3$), 26.95 (SiC(CH$_3$)$_3$), 28.92 ($OCH_2CH_2CH_2N_3$), 47.86 ($OCH_2CH_2CH_2N_3$), 52.07 ($OCH_2CH_2CH_2N_3$), 61.32 (C-6), 67.83 (C-4), 70.03 (C-2), 71.85 (C-3), 73.90 (C-5), 101.64 (C-1), 127.59, 127.65, 127.69, 127.75, 128.21, 128.33, 128.42, 128.50, 128.99, 129.33, 129.47 129.55 129.57, 129.64 129.77 129.81 129.97 130.14, 132.52, 132.88, 132.92, 133.10, 133.24 134.78 135.44, 135.49 135.55, 165.26, 165.60, 167.10. $C_{46}H_{47}N_3O_9Si$ (813.31): MS (MALDI) m/z = 836.35 $[M + Na]^+$, 852.35 $[M + K]^+$.

3-Azidopropyl 2,3,4-tri-*O*-benzoyl-β-D-galactopyranoside (8)

A solution of 70 % HF in pyridine (3 mL, 117 mmol) was added to a solution of **7** (4.77 g, 5.86 mmol) in THF (30 mL), and the reaction mixture was stirred for 18 h. The reaction mixture was diluted with CH_2Cl_2 (20 mL), transferred to a large Erlenmeyer flask, and stirred in an ice bath. Saturated aqueous $NaHCO_3$ was added slowly until evolution of CO_2 had ceased. The biphasic mixture was then transferred to a separatory funnel, and the organic layer was washed subsequently with saturated aqueous $NaHCO_3$ (25 mL) and brine (25 mL). The organic layer

was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo* to give **8** (3.14 g, 93%) as a white, amorphous solid: TLC R_f = 0.24 (hexane/EtOAc, 2:1). $[\alpha]^{25}_D$ +5.9° (*c* 0.9, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.70 (m, 2 H, $OCH_2CH_2CH_2N_3$), 3.16 (m, 2 H, $OCH_2CH_2CH_2N_3$), 3.58 (m, 2H, H-6, H-6), 3.76 and 3.97 (2 m, 2H, $OCH_2CH_2CH_2N_3$), 3.99 (m, 1H, H-5), 4.74 (d, $J_{1,2}$ = 8.1 Hz, 1H, H-1), 5.54 (dd, $J_{2,3}$ = 8.1 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3), 5.78 (dd, $J_{1,2}$ = 8.1 Hz, $J_{2,3}$ = 8.1 Hz, 1H, H-2), 5.79 (d, $J_{3,4}$ = 3.3 Hz, 1H, H-4), 7.19 (t, *J* = 7.5 Hz, 2H, Ar), 7.35 (m, 3 H, Ar), 7.45 (m, 3H, Ar), 7.56 (t, *J* = 7.5 Hz, 1H, Ar), 7.74 (d, *J* = 7.2 Hz, 2H, Ar), 7.92 (d, *J* = 7.2 Hz, 2H, Ar), 8.04 (d, *J* = 7.5 Hz, 2H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.81 ($OCH_2CH_2CH_2N_3$), 47.68 ($OCH_2CH_2CH_2N_3$), 60.45, 66.53, 68.75, 69.88, 71.73, 73.99, 101.51 (C-1), 128.17, 128.33, 128.49, 128.65, 128.70, 129.51, 129.57, 129.91, 133.17, 133.21, 133.60, 165.25, 165.42, 166.45. $C_{30}H_{29}N_3O_5$ (575.1904): MS (MALDI) *m/z* = 598.1057 $[M + Na]^+$.

Phenyl 1-thio-β-D-galactoside (9)

A solution of 1,2,3,4,6-penta-*O*-acetyl-β-D-galactopyranose (20.00 g, 51.2 mmol) in CH_2Cl_2 (100 mL) was stirred at 0 °C. Phenyl thiol (9.67 mL, 76.9 mmol) was added to the solution, followed by the slow addition of $BF_3 \cdot Et_2O$ (13.2 mL, 128 mmol). The solution was stirred at 0 °C for 1 h and for another 1 h at room temperature. The reaction was quenched by the addition of triethylamine and washed subsequently with saturated aqueous $NaHCO_3$ (30 mL) and brine (30 mL). The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo* to give a thick, clear syrup. Purification was carried out using flash silica gel column chromatography (hexanes:EtOAc, 2:1, v/v) to afford an intermediate as a white, amorphous solid: TLC R_f = 0.33 (hexane/EtOAc, 2:1). The intermediate was dissolved in MeOH (35 mL), and sodium methoxide (1M) was added until pH 9. The solution was stirred stirred until TLC

analysis (3:2 hexanes:EtOAc, v/v) showed the reaction to be complete (~3 h). The solution was neutralized using weakly acidic (pH 5) Amberlite resin, filtered, and the filtrate was concentrated *in vacuo* to give **9** (13.69 g, 98%) as clear syrup: TLC R_f = 0.00 (hexane/EtOAc, 1:1). ^{1}H NMR (300 MHz, CD_3OD): δ 3.44 (dd, $J_{2,3}$ = 9.6 Hz, $J_{3,4}$ = 3.0 Hz, 1H, H-3), 3.50 (ABX, $J_{AB,X}$ = 5.4 Hz, 1H, H-5), 3.55 (d, $J_{1,2}$ = 9.1 Hz, s, 1H, H-2), 3.67 (*AB*X, $J_{AB,X}$ = 5.4 Hz, $J_{A,B}$ = 11.4 Hz, 2H, H-6, H-6), 3.84 (d, $J_{3,4}$ = 3.0 Hz, 1H, H-4), 4.52 (d, $J_{1,2}$ = 9.6 Hz, 1H, H-1), 7.13-7.25 (m, 3H, Ar), 7.49 (d, J = 7.8 Hz, 2H, Ar). ^{13}C NMR (75 MHz, CD_3OD): δ 62.58 (C-6), 70.38 (C-4), 70.98 (C-2), 76.29 (C-3), 80.56 (C-5), 90.24 (C-1), 127.98, 129.83, 132.05, 136.03. $C_{12}H_{16}O_5S$ (272.07): MS (MALDI) *m/z* = 295.0458 $[M + Na]^+$.

Phenyl 4,6-*O*-benzylidene-1-thio-β-D-galactoside (10)

Compound **9** (0.736 g, 2.70 mmol) was dissolved in DMF (13.5 mL), and *p*-toluenesulfonic acid monohydrate (*p*-TsOH) was added until pH 3. Benzaldehyde dimethylacetal (0.475 mL, 3.24 mmol) was added, and the reaction was stirred under slight vacuum 18 h. The reaction was neutralized by the addition of triethylamine, diluted with toluene, and concentrated *in vacuo*. The residue was dissolved in CH_2Cl_2 and washed subsequently with 1M HCl, saturated aqueous $NaHCO_3$, and brine. The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo*. The residue was purified using flash silica gel column chromatography (hexane/EtOAc, 2:1 → 1:4, v/v) to afford **10** (0.641 g, 66%) as a white, amorphous solid: TLC R_f = 0.38 (hexane/EtOAc, 1:4). ^{1}H NMR (300 MHz, $CDCl_3/CD_3OD$): δ 3.48 (s, 1H, H-5), 3.58 (dd, $J_{2,3}$ = 9.0 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3), 3.65 (dd, $J_{1,2} = J_{2,3}$ = 9.0 Hz, 1H, H-2), 3.99 and 4.28 (AB, $J_{A,B}$ = 12.5 Hz, 2 H, H-6, H-6), 4.15 (d, $J_{3,4}$ = 3.3 Hz, 1H, H-4), 4.50 (d, $J_{1,2}$ = 9.0 Hz, 1H, H-1), 5.40 (s, 1H, PhC*H*), 7.24 (m, 3H, Ar), 7.40 (m, 2H, Ar), 7.64 (m, 2H, Ar). ^{13}C NMR (75 MHz, $CDCl_3/CD_3OD$): δ 68.00 (C-2), 68.97 (C-6), 69.62 (C-5), 73.45 (C-3), 75.58 (C-4), 86.93

(C-1), 100.99 (Ph*C*H), 126.21, 127.43, 127.79, 128.45, 128.86, 131.50, 132.88, 137.45. $C_{19}H_{20}O_5S$ (360.10): HR-MS (MALDI) *m/z* = 383.0246 $[M + Na]^+$, 399.0097 $[M + K]^+$.

Phenyl 2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-1-thio-β-D-galactoside (11)

A solution of **10** (1.5 g, 4.16 mmol) in pyridine (40 mL) was stirred at 0 °C. Benzoyl chloride (1.9 mL, 16.6 mmol) was added, and the reaction was stirred at room temperature for 18 h. The reaction was quenched by the addition of MeOH (5 mL), diluted with toluene, and concentrated *in vacuo*. The resulting residue was dissolved in CH_2Cl_2 (20 mL) and washed subsequently with 1M HCl (10 mL), saturated aqueous $NaHCO_3$ (10 mL), and brine (10 mL). The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo*. The product was purified using flash silica gel column chromatography (hexanes:EtOAc, 4:1 → 2:1, v/v) to afford **11** (2.36 g, quantitative) as a white, amorphous solid: TLC R_f = 0.50 (hexane/EtOAc, 2:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.66 (s, 1H, H-5), 3.99 and 4.35 (AB, $J_{A,B}$ = 12.4 Hz, 2H, H-6, H-6), 4.50 (d, $J_{3,4}$ = 3.3 Hz, 1H, H-4), 4.88 (d, $J_{1,2}$ = 9.9 Hz, 1H, H-1), 5.29 (dd, $J_{2,3}$ = 9.9 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3), 5.42 (s, 1H, PhC*H*), 5.73 (dd, $J_{1,2}$ = 9.9 Hz, $J_{2,3}$ = 9.9 Hz, 1H, H-2), 7.13-7.44 (m, 14H, Ar), 7.53 (d, *J* = 7.5 Hz, 2H, Ar), 7.84 (d, *J* = 7.8 Hz, 2H, Ar), 7.89 (d, *J* = 7.5 Hz, 2H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ 67.01 (C-2), 69.06 (C-6), 69.84 (C-5), 73.59 (C-4), 74.02 (C-3), 85.23 (C-1), 100.83 (Ph*C*H), 126.37, 128.04, 128.18, 128.29, 128.73, 128.97, 129.00, 129.58, 129.68, 129.88, 131.00, 133.08, 133.26, 133.77, 137.50, 164.87, 166.08. $C_{33}H_{28}O_7S$ (568.16): HR-MS (MALDI) *m/z* = 591.1250 $[M + Na]^+$, 607.1158 $[M + K]^+$.

Phenyl 4,6-*O*-benzylidene-3-*O*-(9-fluorenylmethoxycarbonyl)-1-thio-β-D-galactoside (12)

A solution of **10** (2.5 g, 6.94 mmol) in pyridine (70 mL) was stirred at 0°C. A portion of 9-fluorenylmethoxycarbonyl chloride (1.97 mL, 7.63 mmol) was added, and the reaction was stirred at room temperature for 18 h. The reaction was quenched by the addition of MeOH (5

mL), diluted with toluene, and concentrated *in vacuo*. The resulting residue was dissolved in CH_2Cl_2 (50 mL) and washed subsequently with 1M HCl (20 mL), saturated aqueous $NaHCO_3$ (20 mL), and brine (20 mL). The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo*. The residue was purified using flash silica gel column chromatography (hexanes:EtOAc, 4:1 → 1:1, v/v) to afford **12** (3.34 g, 83%) as a white, amorphous solid: TLC R_f = 0.48 (hexane/EtOAc, 2:1). $[\alpha]^{25}_D$ -85.6° (*c* 1.8, CH_2Cl_2); ^{1}H NMR (300MHz, $CDCl_3$): δ 3.52 (s, 1H, H-5), 3.96 (A*B*, $J_{A,B}$ = 12.1 Hz, 1H, H-6), 3.98 (dd, $J_{1,2}$ = 9.6 Hz, $J_{2,3}$ = 9.6 Hz, 1H, H-2), 4.18 (t, 1H, *J* = 7.5 Hz, OCH_2CH), 4.32 (*A*B, $J_{A,B}$ = 12.1 Hz, 1H, H-6), 4.35 (m, 3H, OCH_2CH, H-4), 4.52 (d, $J_{1,2}$ = 9.3 Hz, 1H, H-1), 4.69 (dd, $J_{2,3}$ = 9.3 Hz, $J_{3,4}$ = 9.6 Hz, 1H, H-3), 5.42 (s, 1H, PhC*H*), 7.10-7.35 (m, 12H, Ar), 7.48 (t, *J* = 5.5, 7.1 Hz, 2H, Ar), 7.64 (m, 4H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ 46.87, 65.81, 69.36, 69.93, 70.42, 73.54, 78.81, 87.51 (C-1), 101.09, 120.29, 125.44, 125.47, 126.72, 127.41, 127.45, 128.14, 128.39, 128.54, 129.30, 129.37, 130.62, 133.95, 137.93, 141.49, 141.50, 143.31, 143.58, 154.84. $C_{34}H_{30}O_7S$ (582.17): MS (MALDI) *m/z* = 605.67 $[M + Na]^+$, 621.62 $[M + K]^+$.

Phenyl 4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-1-thio-β-D-galactoside (16)

A solution of **10** (0.150 g, 0.416 mmol) in pyridine (3 mL) was stirred at 0 °C. The compound *tert*-butyldimethylsilyl chloride (0.069 mL, 0.458 mmol) was added, and the reaction was stirred at room temperature for 18 h. The reaction was quenched by the addition of MeOH (0.5 mL), diluted with toluene, and concentrated *in vacuo*. The resulting residue was dissolved in CH_2Cl_2 (20 mL) and washed subsequently with 1M HCl (5 mL), saturated aqueous $NaHCO_3$ (5 mL), and brine (5 mL). The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo*. The product was purified using flash silica gel column chromatography (hexanes:EtOAc, 1:1 → 1:2, v/v) to afford **16** (0.068 g, 34%) as a white, amorphous solid: TLC R_f = 0.19

(hexane/EtOAc, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ -0.13 (s, 3H, Si(CH_3)$_2$C(CH$_3$)$_3$), 0.03 (s, 3H, Si(CH_3)$_2$C(CH$_3$)$_3$), 0.80 (s, 9 H, Si(CH$_3$)$_2$C(CH_3)$_3$), 3.39 (s, 1H, H-5), 3.64 (dd, $J_{2,3}$ = 9.0 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3), 3.75 (dd, $J_{1,2}$ = 9.0 Hz, $J_{2,3}$ = 9.0 Hz, 1H, H-2), 3.90 and 4.27 (AB, $J_{A,B}$ = 12.3 Hz, 2H, H-6, H-6), 3.95 (d, $J_{3,4}$ = 3.3 Hz, 1H, H-4), 4.45 (d, $J_{1,2}$ = 9.0 Hz, 1H, H-1), 5.39 (s, 1H, PhC*H*), 7.08-7.15 (m, 3H, Ar), 7.25-7.28 (m, 3H, Ar), 7.35-7.39 (m, 2H, Ar), 7.55-7.58 (m, 2H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ -4.79 (Si(*C*H$_3$)$_2$C(CH$_3$)$_3$), -4.43 (Si(*C*H$_3$)$_2$C(CH$_3$)$_3$), 18.10 (Si(CH$_3$)$_2$*C*(CH$_3$)$_3$), 25.70 (Si(CH$_3$)$_2$C(*C*H$_3$)$_3$), 68.01 (C-2), 69.24 (C-6), 69.98 (C-5), 75.35 (C-3), 76.47 (C-4), 87.33 (C-1), 100.67 (Ph*C*H), 126.15, 127.55, 127.89, 128.66, 128.68, 131.69, 132.76, 137.92. $C_{25}H_{35}O_5SSi$ (474.1896): HR-MS (MALDI) *m/z* = 497.1237 $[M + Na]^+$, 513.0984 $[M + K]^+$.

Phenyl 4,6-*O*-benzylidene-3-*O*-(9-fluorenylmethoxycarbonyl)-2-levulinoyl-1-thio-β-D-galactoside (14)

Levulinic acid (0.66 mL, 7.43 mmol) was added to a stirring solution of **12** (0.433 g, 0.743 mmol) in CH_2Cl_2 (20 mL). A solution of DCC (0.77 g, 3.72 mmol) and DMAP (0.0136 g, 0.111 mmol) in CH_2Cl_2 (5 mL) was added, and the reaction was stirred for 18 h. The DCU precipitate was removed by filtration through a pad of Celite, and the filtrate was the concentrated *in vacuo*. The resulting residue was dissolved in EtOAc, and the remaining solid DCU was again removed by filtration through a pad of Celite. The filtrate was concentrated *in vacuo*. This process was repeated as necessary until the major portion of DCU had been removed. The residue was dissolved in CH_2Cl_2 (30 mL) and washed subsequently with 1M HCl (15 mL), saturated aqueous NaHCO3 (15 mL), and brine (15 mL). The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo*. The residue was purified using flash silica gel column chromatography (hexanes:EtOAc, 3:1 → 2:1, v/v) to afford **14** (0.398 g, 79%) as a white,

amorphous solid: TLC R_f = 0.41 (hexane/EtOAc, 2:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.02 (s, 3 H, $COCH_2CH_2COCH_3$), 2.50 and 2.63 (ABXY, 4H, $COCH_2CH_2COCH_3$), 3.49 (s, 1H, H-5), 3.93 and 4.25 (AB, $J_{A,B}$ = 11.1 Hz, 2H, H-6, H-6), 4.16 (t, J = 7.2 Hz, 1H, OCH_2CH), 4.25-4.37 (m, 3H, OCH_2CH, H-4), 4.66 (d, $J_{1,2}$ = 9.6 Hz, 1H, H-1), 5.11 (dd, $J_{2,3}$ = 9.6 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3), 5.34 (dd, $J_{1,2}$ = 9.9 Hz, $J_{2,3}$ = 9.9 Hz, 1H, H-2), 5.41 (s, 1H, PhCH), 7.16 (m, 5H, Ar), 7.30 (m, 7H, Ar), 7.47 (d, J = 7.8 Hz, 2H, Ar), 7.53 (d, J = 6.6 Hz, 2H, Ar), 7.64 (d, J = 7.2 Hz, 2H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ 27.94 ($COCH_2CH_2COCH_3$), 29.71 ($COCH_2CH_2COCH_3$), 37.78 ($COCH_2CH_2COCH_3$), 46.43 (OCH_2CH), 66.73 (C-2), 68.94 (C-6), 69.53 (C-5), 70.10 (OCH_2CH), 73.43 (C-4), 76.51 (C-3), 84.96 (C-1), 100.91 (PhCH), 119.91 (OC(O)O), 125.19, 125.25, 126.41, 127.07, 127.78, 128.05, 128.09, 128.73, 129.04, 131.15, 133.58, 137.49, 140.95, 143.13, 143.44, 154.09, 170.33, 205.39. $C_{39}H_{36}O_9S$ (680.21): MS (MALDI) *m/z* = 703.33 [M + Na]$^+$, 719.33 [M + K]$^+$.

Phenyl 2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-(9-fluorenylmethoxycarbonyl)-1-thio-β-D-galactoside (13)

A solution of **12** (1.2 g, 2.09 mmol) in pyridine (20 mL) was stirred at 0 °C. Benzoyl chloride (0.87 mL, 7.5 mmol) was added, and the reaction was stirred at room temperature for 18 h. The reaction was quenched by the addition of MeOH (2 mL), diluted with toluene, and concentrated *in vacuo*. The resulting residue was dissolved in CH_2Cl_2 and washed subsequently with 1M HCl, saturated aqueous NaHCO3, and brine. The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo*. The residue was purified using flash silica gel column chromatography (hexanes:EtOAc, 4:1 → 1:1, v/v) to afford **13** (1.4 g, 85%) as white foam: TLC R_f = 0.33 (hexane/EtOAc, 3:1). $[\alpha]^{25}_D$ -58.1° (*c* 2.1, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.13 (s, 1H, H-5), 4.18 (t, J = 7.2 Hz, 1H, OCH_2CH), 4.27 (d, $J_{3,4}$ = 6.3 Hz, 1H, H-4), 4.32-4.44

(m, 3H, OCH_2CH, H-6), 4.50 (m, 2H, H-3, H-6), 4.83 (d, $J_{1,2}$ = 9.3 Hz, 1H, H-1), 5.27 (dd, $J_{1,2}$ = 9.3 Hz, $J_{2,3}$ = 6.5 Hz, 1H, H-2), 5.83 (s, 1H, PhC*H*), 7.17 (m, 3H, Ar), 7.23 (t, *J* = 5.4, 7.8 Hz, 2H, Ar), 7.34 (m, 6H, Ar), 7.39-7.49 (m, 6H, Ar), 7.54 (d, *J* = 7.8 Hz, 2H, Ar), 7.69 (d, *J* = 7.5 Hz, 2H, Ar), 7.98 (d, *J* = 7.5 Hz, 2H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ 46.74 (OCH_2*C*H), 66.71 (C-6), 69.94 (O*C*H_2CH), 72.55 (C-2), 73.92 (C-5), 75.19 (C-4), 76.58 (C-3), 84.96 (C-1), 105.44 (Ph*C*H), 120.05 (O*C*(O)O), 125.08, 125.11, 127.11, 127.17, 127.86, 127.91, 128.38, 128.45, 128.84, 129.63, 129.72, 129.88, 132.37, 133.06, 133.26, 136.06, 141.28, 143.20, 143.24, 154.87, 165.07. $C_{41}H_{34}O_8S$ (686.20): MS (MALDI) *m/z* = 708.39 $[M + Na]^+$, 724.26 $[M + K]^+$; HR-MS (MALDI) *m/z* = 709.2122 $[M + Na]^+$.

Phenyl 3-*O*-benzoyl-4,6-*O*-benzylidene-2-*O*-levulinoyl-1-thio-β-D-galactoside (15)

An excess of triethylamine (0.7 mL) was added to a solution of **14** (203 mg, 0.299 mmol) in CH_2Cl_2 (3 mL) and was stirred 3 h. The reaction mixture was diluted with CH_2Cl_2 and washed subsequently with 1M HCl, saturated aqueous NaHCO3, and brine. The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo* afford the desired intermediate as a white, amorphous solid: $C_{24}H_{26}O_7S$ (458.14): MS (MALDI) *m/z* = 481.71 $[M + Na]^+$, 497.55 $[M + K]^+$. The intermediate was dissolved in pyridine and stirred at 0°C. Benzoyl chloride (0.052 mL, 0.448 mmol) was added, and the reaction was stirred at room temperature for 18 h. The reaction was quenched by the addition of MeOH (0.1 mL), diluted with toluene, and concentrated *in vacuo*. The resulting residue was dissolved in CH_2Cl_2 and washed subsequently with 1M HCl, $NaHCO_3$, and brine. The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo*. The residue was purified using flash silica gel column chromatography (hexanes:EtOAc, 3:2 → 1:2, v/v) to afford **15** (76 mg, 45%) as a white, amorphous solid: TLC R_f = 0.68 (hexane/EtOAc, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.77 (s,

3H, $COCH_2CH_2COCH_3$), 2.32 and 2.44 (ABXY, 4H, $COCH_2CH_2COCH_3$), 3.54 (s, 1H, H-5), 3.94 and 4.29 (AB, $J_{A,B}$ = 8.7 Hz, 2H, H-6, H-6), 4.30 (d, $J_{3,4}$ = 3.3 Hz, 1H, H-4), 4.78 (d, $J_{1,2}$ = 9.9 Hz, 1H, H-1), 5.11 (dd, $J_{2,3}$ = 9.9 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3), 5.41 (s, 1H, PhC*H*), 5.51 (dd, $J_{1,2}$ = 9.9 Hz, $J_{2,3}$ = 9.9 Hz, 1H, H-2), 7.13-7.22 (m, 3H, Ar), 7. 28 (m, 3H, Ar), 7.32-7.39 (m, 4H, Ar), 7.49 (m, 3H, Ar), 7.94 (d, J = 8.1 Hz, 2H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.13 ($COCH_2CH_2COCH_3$), 29.28 ($COCH_2CH_2COCH_3$), 37.63 ($C(O)CH_2CH_2C(O)CH_3$), 67.18 (C-2), 68.94 (C-6), 69.61 (C-5), 73.08 (C-3), 73.43 (C-4), 85.16 (C-1), 100.95 (PhCH), 126.46, 128.01, 128.36, 128.66, 129.02, 129.51, 129.73, 131.15, 133.17, 133.59, 137.49, 164.81, 171.89, 206.05. $C_{31}H_{30}O_8S$ (562.17): MS (MALDI) *m/z* = 586.13 $[M + Na]^+$, 601.88 $[M + K]^+$.

Phenyl 2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-1-thio-β-D-galactoside (17)

A solution of **16** (0.068 g, 0.143 mmol) in pyridine (5 mL) was stirred at 0 °C. Benzoyl chloride (0.050 mL, 0.430 mmol) was added, and the reaction was stirred at room temperature for 18 h. The reaction was quenched by the addition of MeOH (0.1 mL), diluted with toluene, and concentrated *in vacuo*. The resulting residue was dissolved in CH_2Cl_2 and washed subsequently with 1M HCl, saturated aqueous NaHCO3, and brine. The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo*. The product was purified using flash silica gel column chromatography (hexanes:EtOAc, 6:1, v/v) to afford **17** (0.0435 g, 53%) as a white, amorphous solid: TLC R_f = 0.35 (hexane/EtOAc, 4:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ -0.13 and 0.03 (2 s, each 3 H, $Si(CH_3)_2C(CH_3)_3$), 0.75 (s, 9 H, $Si(CH_3)_2C(CH_3)_3$), 3.58 (s, 1H, H-5), 4.07 (m, 1H, H-3), 4.14 (d, $J_{3,4}$ = 3.3 Hz, 1H, H-4), 4.07 and 4.43 (AB, $J_{A,B}$ = 12.0 Hz, 2H, H-6, H-6), 4.85 (d, $J_{1,2}$ = 9.6 Hz, 1H, H-1), 5.53 (m, 1H, H-2), 5.54 (s, 1H, PhC*H*), 7.23 (m, 3H, Ar), 7.40-7.51 (m, 7H, Ar), 7.58 (m, 3H, Ar), 8.06 (d, J = 7.5 Hz, 2H, Ar). ^{13}C NMR (75 MHz,

$CDCl_3$): δ -4.79 ($Si(CH_3)_2C(CH_3)_3$), -4.69 ($Si(CH_3)_2C(CH_3)_3$), 18.12 ($Si(CH_3)_2C(CH_3)_3$), 25.37 ($Si(CH_3)_2C(CH_3)_3$), 69.22 (C-2), 70.07 (C-6), 70.16 (C-5), 73.55 (C-3), 76.53 (C-4), 85.63 (C-1), 100.86 (PhCH), 126.28, 127.67, 128.00, 128.24, 128.61, 128.77, 129.66, 132.82, 132.87, 132.98, 137.79, 164.84. $C_{32}H_{38}O_6SSi$ (578.22): MS (MALDI) *m/z* = 600.48 $[M + Na]^+$, 616.52 $[M + K]^+$.

Ethyl 2,3,4-tri-*O*-acetyl-1-thio-β-L-fucopyranoside (31)

L-fucose (5 g, 30.5 mmol) was dissolved in pyridine (80 mL) and stirred at 0 °C. Acetic anhydride (28.6 mL, 305 mmol) was added, and the reaction was stirred at room temperature for 18 h. The reaction was quenched by the addition of MeOH (0.1 mL), diluted with toluene, and concentrated *in vacuo*. The resulting residue was dissolved in CH_2Cl_2 and washed subsequently with 1M HCl, saturated aqueous NaHCO3, and brine. The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo* to afford the desired intermediate (10.13 g) as a clear, colorless syrup. $C_{14}H_{20}O_9$ (332.11): MS (MALDI) *m/z* = 355.17 $[M + Na]^+$, 371.13 $[M + K]^+$. A portion of the syrup (0.997 g, 2.94 mmol) was dissolved in CH_2Cl_2 (5 mL) and stirred at 0 °C. Ethane thiol (0.550 mL, 7.35 mmol) was added to the solution, followed by the slow addition of $BF_3 \cdot Et_2O$ (0.554 mL, 4.41 mmol). The reaction mixutre was stirred at 0 °C for 1 h, then at room temperature for 18 h. The reaction was quenched by the addition of triethylamine and washed subsequently with saturated aqueous $NaHCO_3$ and water. The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo*. The residue was purified using flash silica gel column chromatography (hexanes:EtOAc, 5:1, v/v) to afford **31** (0.637 g, 65%) as a clear, colorless syrup. Mixed fractions were combined and concentrated *in vacuo* into thick, yellow-brown syrup. Pure, colorless crystals of the desired product **31** could be obtained by allowing the syrup to sit undisturbed for at least one week in a flask fitted with a rubber

septum with a small syringe needle providing a small vent. Crystals were washed with a small amount of hexanes to remove the residual yellow-brown syrup: TLC R_f = 0.32 (hexane/EtOAc, 4:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.18 (d, $J_{5,6}$ = 6.3 Hz, 3H, H-6, H-6, H-6), 1.24 (t, J = 7.5 Hz, 3H, SCH_2CH_3) , 1.95 (s, 3H, , 1.997, $COCH_3$), 2.00 (s, 3H, $COCH_3$), 2.14 (s, 3H, $COCH_3$), 2.70 (ABX, 2H, SCH_2CH_3), 3.79 (qd, $J_{4,5}$ = 1.0 Hz, $J_{5,6}$ = 6.6 Hz, 1H, H-5), 4.42 (d, $J_{1,2}$ = 9.9 Hz, 1H, H-1), 5.01 (dd, $J_{2,3}$ = 9.9 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3), 5.19 (dd, $J_{1,2}$ = 9.9 Hz, $J_{2,3}$ = 9.9 Hz, 1H, H-2), 5.23 (dd, $J_{3,4}$ = 3.3 Hz, $J_{4,5}$ = 1.0 Hz, 1H, H-4). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.71 (C-6), 16.40 (SCH_2CH_3), 20.60 ($COCH_3$), 20.66 ($COCH_3$), 20.82 ($COCH_3$), 24.08 (SCH_2CH_3), 67.30 (C-2), 70.43 (C-4), 72.33 (C-3), 73.15 (C-5), 83.49 (C-1), 169.62 ($COCH_3$), 170.09 ($COCH_3$), 170.61 ($COCH_3$). $C_{14}H_{22}O_7S$ (334.11): HR-MS (MALDI) *m/z* = 357.0947 [M + Na]$^+$, 373.0671 [M + K]$^+$.

Ethyl 3,4-*O*-dimethylacetal-1-thio-β-L-fucopyranoside (32)

Compound **31** (2.25 g, 6.70 mmol) was dissolved in MeOH (50 mL), and sodium methoxide (1M) was added until pH 9 and stirred 3 h. The solution was neutralized using weakly acidic (pH 5) Amberlite resin. Concentration *in vacuo* gave clear syrup, which was subjected to high vacuum (5 torr) to remove all residual MeOH. The syrup was dissolved in CH_2Cl_2 (15 mL), and *p*-TsOH was added until pH 3. A portion of 2,2'-dimethoxypropane (12.4 mL, 101 mmol) was added, and the reaction was stirred under slight vacuum 18 h. The reaction was neutralized by the addition of triethylamine, diluted with toluene, and concentrated *in vacuo*. The residue was dissolved in CH_2Cl_2 and washed subsequently with 1M HCl, saturated aqueous NaHCO3, and brine. The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo*. The residue was purified using flash silica gel column chromatography (hexanes:EtOAc, 2:1 → 1:4, v/v) to afford **32** (1.41 g, 85%) as clear syrup: TLC R_f = 0.38 (hexane/EtOAc, 2:1). ^{1}H

NMR (300 MHz, $CDCl_3$): δ 1.33 (t, J = 7.5 Hz, 3H, SCH_2CH_3), 1.35 and 1.52 (2 s, each 3H, $C(CH_3)_2$), 1.40 (d, $J_{5,6}$ = 6.6 Hz, 3H, H-6, H-6, H-6), 2.73 (ABX_3, $J_{A,B}$ = 2.4 Hz, $J_{AB,X}$ = 7.5 Hz, 2H, SCH_2CH_3), 3.53 (dd, $J_{1,2}$ = 10.2 Hz, $J_{2,3}$ = 6.3 Hz, 1H, H-2), 3.86 (dd, $J_{4,5}$ = 2.4 Hz, $J_{5,6}$ = 6.6 Hz, 1H, H-5), 4.03 (d, $J_{2,3}$ = 6.3 Hz, 1H, H-3), 4.04 (d, $J_{4,5}$ = 2.4 Hz, 1H, H-4), 4.20 (d, $J_{1,2}$ = 10.2 Hz, 1H, H-1). ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.25 (SCH_2CH_3), 16.88 (C-6), 24.22 (SCH_2CH_3), 26.29 ($(O)_2C(CH_3)_2$), 28.25 ($(O)_2C(CH_3)_2$), 71.92 (C-4), 72.84 (C-5), 76.38 (C-3), 79.00 (C-2), 85.18 (C-1), 109.78 ($(O)_2C(CH_3)_2$). $C_{11}H_{20}O_4S$ (248.11): MS (MALDI) *m/z* = 271.74 $[M + Na]^+$, 287.74 $[M + K]^+$.

Ethyl 2-*O*-benzyl-3,4-*O*-dimethylacetal-1-thio-β-L-fucopyranoside (33)

Sodium hydroxide (0.272 g, 6.79 mmol) was added slowly to a solution of **32** (1.41 g, 5.66 mmol) in DMF (40 mL) at 0 °C. The solution was left to stir until hydrogen gas evolution ceased. Then benzyl bromide (0.808 mL, 6.79 mmol) and tetrabutylammonium iodide (0.105 g, 0.283 mmol) were added, and the solution was allowed to slowly return to room temperature, where it was left to stir for 1 h. The mixture was diluted with MeOH and EtOAc, and the organic layer was washed with brine (2 times) and water (2 times). The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo*. The residue was purified using flash silica gel column chromatography (hexanes:EtOAc, 5:1, v/v) to afford **33** (1.90 g, 99%) as clear syrup: TLC R_f = 0.76 (hexane/EtOAc, 3:1). $C_{18}H_{26}O_4S$ (338.16): MS (MALDI) *m/z* = 360.63 $[M + Na]^+$, 376.58 $[M + K]^+$.

Ethyl 3,4-di-*O*-acetyl-2-*O*-benzyl-1-thio-β-L-fucopyranoside (34)

A solution of **33** (1.90 g, 5.60 mmol) in 80% acetic acid was stirred at 60 °C for 4 h. The reaction mixture was diluted with toluene and concentrated *in vacuo*. The residue was the dissolved in pyridine and in excess acetic anhydride and stirred at room temperature for 18 h.

The reaction was quenched by the addition of MeOH (10 mL), diluted with toluene, and concentrated *in vacuo*. The resulting residue was dissolved in CH_2Cl_2 and washed subsequently with 1M HCl, saturated aqueous NaHCO3, and brine. The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo*. The residue was purified using flash silica gel column chromatography (hexanes:EtOAc, 5:1, v/v) to afford **34** (1.95 g, 91%) as clear syrup: TLC R_f = 0.44 (hexane/EtOAc, 3:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.13 (d, $J_{5,6}$ = 6.5 Hz, 3H, H-6, H-6, H-6), 1.26 (t, J = 7.5 Hz, 3H, SCH_2CH_3), 1.87 (s, 3H, $COCH_3$), 2.08 (s, 3H, $COCH_3$), 2.72 (q, J = 7.5 Hz, 2H, SCH_2CH_3), 3.57 (dd, $J_{1,2}$ = 9.5 Hz, $J_{2,3}$ = 9.5 Hz, 1H, H-2), 3.71 (q, $J_{5,6}$ = 6.5 Hz, 1H, H-5), 4.45 (d, $J_{1,2}$ = 9.7 Hz, 1H, H-1), 4.53 and 4.80 (AB, J = 10.9 Hz, 2H, CH_2Ph), 4.94 (dd, $J_{2,3}$ = 9.5 Hz, $J_{3,4}$ = 3.4 Hz, 1H, H-3), 5.19 (d, $J_{3,4}$ = 3.4 Hz, 1H, H-4), 7.25 (m, 5H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.89 (SCH_2CH_3), 16.42 (C-6), 20.71 ($COCH_3$), 20.73 ($COCH_3$), 25.20 (SCH_2CH_3), 70.89 (C-4), 72.74 (C-5), 74.41 (C-3), 75.45 (CH_2Ph), 76.12 (C-2), 85.10 (C-1), 127.78, 127.89, 128.31, 137.90, 170.03 ($COCH_3$), 170.63 ($COCH_3$). $C_{19}H_{26}O_6S$ (382.15): HR-MS (MALDI) *m/z* = 405.2562 $[M + Na]^+$, 421.1918 $[M + K]^+$.

3-Azidopropyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-β-D-galactopyranosyl)-β-D-galactopyranoside (18)

A mixture of the glycosyl donor **11** (1.00 g, 1.74 mmol), the acceptor **8** (1.09 g, 1.91 mmol), and powdered 4 Å molecular sieves (2 g) in CH_2Cl_2 (30 mL) was stirred at room temperature for 30 min and then cooled to 0 °C. NIS (508 mg, 2.26 mmol), followed by TMSOTf (0.064 mL, 0.347 mmol), was added. The reaction mixture was stirred for 30 min and then quenched by the addition of triethylamine. The suspension was diluted with CH_2Cl_2 (50 mL) and filtered through a pad of Celite, and the filtrate was washed successively with 10% $Na_2S_2O_3$ and brine. The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo* to give a

residue, which was purified using flash silica gel column chromatography (hexane/EtOAc, 2:1, v/v) to give **18** (1.423 g, 79%) as a white foam: TLC R_f = 0.28 (hexane/EtOAc, 2:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.45 (m, 2H, $OCH_2CH_2CH_2N_3$), 3.16 (t, J = 6.8 Hz, 2H, $OCH_2CH_2CH_2N_3$), 3.21 and 3.55 (2 m, 2H, $OCH_2CH_2CH_2N_3$), 3.62 (s, 1H, H-5'), 3.79 (m, 1H, H-6), 4.03 (m, 1H, H-6), 4.04 and 4.37 (AB, $J_{A,B}$ = 11.1 Hz, 2H, H-6', H-6'), 4.14 (m, 1H, H-5), 4.51 (d, $J_{1,2}$ = 7.8 Hz, 1H, H-1'), 4.51 (d, $J_{3,4}$ = 3.9 Hz, 1H, H-4'), 4.75 (d, $J_{1,2}$ = 7.8 Hz, 1H, H-1), 5.29 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.9 Hz, 1H, H-3'), 5.42 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3), 5.48 (s, 1H, PhC*H*), 5.59 (dd, $J_{1,2}$ = 7.8 Hz, $J_{2,3}$ = 10.5 Hz, 1H, H-2), 5.79 (d, $J_{3,4}$ = 3.3 Hz, 1H, H-4), 5.84 (dd, $J_{1,2}$ = 7.8 Hz, $J_{2,3}$ = 10.5 Hz, 1H, H-2'), 7.14 (t, J = 7.5 Hz, 3H, Ar), 7.29 (m, 9H, Ar), 7.42 (m, 7H, Ar), 7.53 (t, J = 7.5 Hz, 2H, Ar), 7.68 (d, J = 7.5 Hz, 2H, Ar), 7.88 (m, 5H, Ar), 7.98 (d, J = 7.5 Hz, 2H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.58 ($OCH_2CH_2CH_2N_3$), 47.79 ($OCH_2CH_2CH_2N_3$), 66.25, 66.50, 68.28, 68.80, 68.962, 69.85, 71.73, 72.59, 73.45, 100.76, 101.28, 126.10, 126.22, 128.12, 128.20, 128.34, 128.39, 128.53, 128.85, 128.94, 129.06, 129.09, 129.27, 129.35, 129.53, 129.62, 129.67, 129.71, 129.90, 129.95, 130.02, 132.40, 133.13, 133.25, 133.36, 133.47, 137.49, 165.12, 165.27, 165.41, 165.56, 166.14, 176.35. $C_{57}H_{51}N_3O_{16}$ (1033.33): MS (MALDI) *m/z* = 1056.07435 $[M + Na]^+$, 1071.76002 $[M + K]^+$.

3-Azidopropyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,3-di-*O*-benzoyl-β-D-galactopyranosyl)-β-D-galactopyranoside (19)

A solution of **18** (1.04 g, 1.00 mmol) in 80% AcOH was stirred at 80 °C for 3 h. The reaction mixture was diluted with toluene and concentrated *in vacuo*. The residue was purified using flash silica gel column chromatography (hexanes/EtOAc, 3:2, v/v) to afford **19** (0.825 g, 87%) as white foam: TLC R_f = 0.33 (hexane/EtOAc, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.58 (m, 2H, $OCH_2CH_2CH_2N_3$), 3.08 (t, J = 6.6 Hz, 2H, $OCH_2CH_2CH_2N_3$), 3.38 and 3.60 (2 m, 2H,

OC*H*$_2$CH$_2$CH$_2$N$_3$), 3.52 (AB*X*, $J_{AB,X}$ = 4.1 Hz, 1H, H-5'), 3.60-3.82 (m, 3H, H-6, H-6', H-6'), 4.00 (m, 1H, H-6), 4.09 (m, 1H, H-5), 4.31 (d, $J_{3,4}$ = 3.0 Hz, 1H, H-4), 4.51 (d, $J_{3,4}$ = 3.3 Hz, 1H, H-4'), 4.62 (d, $J_{1,2}$ = 8.1 Hz, 1H, H-1), 4.65 (d, $J_{1,2}$ = 8.1 Hz, 1H, H-1'), 5.16 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3'), 5.49 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3), 5.61 (dd, $J_{1,2}$ = 8.1 Hz, $J_{2,3}$ = 10.5 Hz, 1H, H-2), 5.73 (dd, $J_{1,2}$ = 8.1 Hz, $J_{2,3}$ = 10.5 Hz, 1H, H-2'), 5.95 (d, $J_{3,4}$ = 3.3 Hz, 1H, H-4), 7.16 (t, *J* = 7.8 Hz, 3H, Ar), 7.24-7.35 (m, 7H, Ar), 7.37-7.46 (m, 4H, Ar), 7.58 (t, *J* = 7.5 Hz, 1H, Ar), 7.69 (d, *J* = 7.5 Hz, 2H, Ar), 7.88 (m, 6H, Ar), 8.01 (d, *J* = 7.8 Hz, 2H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.817 (OCH$_2$*C*H$_2$CH$_2$N$_3$), 47.801 (OCH$_2$CH$_2$*C*H$_2$N$_3$), 62.98 (C-6'), 66.48 (O*C*H$_2$CH$_2$CH$_2$N$_3$), 67.37 (C-6), 68.58 (C-4), 68.93 (C-4'), 69.60 (C-2'), 69.83 (C-2), 71.76 (C-3), 72.71 (C-5), 73.55 (C-5'), 74.23 (C-3'), 101.21 (C-1'), 101.58 (C-1), 128.25, 128.36, 128.39, 128.43, 128.77, 128.80, 129.05, 129.15, 129.22, 129.54, 129.65, 129.71, 129.75, 129.85, 129.97, 130.13, 132.23, 133.30, 133.80, 165.27, 165.54, 165.97, 166.25. $C_{50}H_{47}N_3O_{16}$ (945.30): MS (MALDI) *m/z* = 968.20858 $[M + Na]^+$, 984.18358 $[M + K]^+$.

3-Azidopropyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,3-di-*O*-benzoyl-4-*O*-benzyl-β-D-galactopyranosyl)-β-D-galactopyranoside (20)

A mixture of disaccharide **18** (0.400 g, 0.387 mmol) and powdered 4 Å molecular sieves (1 g) in CH_2Cl_2 (3 mL) was stirred at room temperature for 30 min and then cooled to -78 °C. Et_3SiH (0.163 mL, 1.26 mmol), followed by $PhBCl_2$ (0.178 mL, 1.11 mmol), was added. The reaction mixture was stirred for 1 h and then quenched by the addition of triethylamine (0.092 mL). The suspension was diluted with CH_2Cl_2 (20 mL) and filtered through a pad of Celite, and the filtrate was washed successively with saturated aqueous $NaHCO_3$ and brine. The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo* to give a residue, which was purified using flash silica gel column chromatography (hexane/EtOAc, 2:1, v/v) to give **20**

(0.345 g, 86%) as a white foam: TLC R_f = 0.44 (hexane/EtOAc, 2:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.54 (m, 2H, $OCH_2CH_2CH_2N_3$), 3.03 (t, J = 6.6 Hz, 2H, $OCH_2CH_2CH_2N_3$), 3.36 and 3.60 (2 m, 2H, $OCH_2CH_2CH_2N_3$), 3.48 and 3.74 (AB, $J_{A,B}$ = 11.1 Hz, 2H, H-6'), 3.62 (m, 1H, H-5'), 3.77 and 4.00 (AB, $J_{A,B}$ = 11.1 Hz, 1H, H-6), 3.94-4.06 (m, 2H, H-4', H-5), 4.42 and 4.71 (AB, $J_{A,B}$ = 11.7 Hz, 2H, $PhCH_2$), 4.55 (d, $J_{1,2}$ = 8.0 Hz, 1H, H-1), 4.64 (d, $J_{1,2}$ = 8.0 Hz, 1H, H-1'), 5.24 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.0 Hz, 1H, H-3'), 5.42 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3), 5.59 (dd, $J_{1,2}$ = 8.0 Hz, $J_{2,3}$ = 10.5 Hz, 1H, H-2), 5.78 (dd, $J_{1,2}$ = 8.0 Hz, $J_{2,3}$ = 10.5 Hz, 1H, H-2'), 5.82 (d, $J_{3,4}$ = 3.3 Hz, 1H, H-4), 7.17 (m, 7H, Ar), 7.27-7.37 (m, 7H, Ar), 7.40-7.46 (m, 5H, Ar), 7.54 (t, J = 7.5 Hz, 1H, Ar), 7.68 (d, J = 7.5 Hz, 2H, Ar), 7.87 (m, 6H, Ar), 7.98 (d, J = 7.2 Hz, 2H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.69 ($OCH_2CH_2CH_2N_3$), 47.73 ($OCH_2CH_2CH_2N_3$), 61.61 (C-6'), 66.21 ($OCH_2CH_2CH_2N_3$), 68.52 (C-6), 68.87 (C-4), 69.79 (C-2), 69.99 (C-2'), 71.66 (C-3), 73.32 (C-4', C-5), 74.58 (C-3'), 74.71 (CH_2Ph), 75.18 (C-5'), 101.26 (C-1), 101.49 (C-1'), 126.19, 127.74, 128.02, 128.17, 128.31, 128.36, 128.40, 128.46, 128.54, 128.74, 128.84, 128.95, 129.18, 129.49, 129.56, 129.60, 129.66, 129.78, 129.96, 133.07, 133.13, 133.22, 133.42, 133.52, 137.22, 165.19, 165.41, 165.67, 165.90. $C_{57}H_{53}N_3O_{16}$ (1035.34): HR-MS (MALDI) m/z = 1058.3589 $[M + Na]^+$, 1074.3395 $[M + K]^+$.

3-Azidopropyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,3-di-*O*-benzoyl-4-*O*-benzyl-6-*O*-(2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-β-D-galactopyranosyl)-β-D-galactopyranosyl)-β-D-galactopyranoside (21)

A mixture of the glycosyl donor **11** (47 mg, 0.0828 mmol), the acceptor **20** (78 mg, 0.0753 mmol), and powdered 4 Å molecular sieves (125 mg) in CH_2Cl_2 (1.6 mL) was stirred at room temperature for 30 min and then cooled to 0 °C. NIS (22 mg, 2.26 mmol), followed by TMSOTf (0.0028 mL, 0.0152 mmol), was added. The reaction mixture was stirred for 30 min and then

quenched by the addition of triethylamine. The suspension was diluted with CH_2Cl_2 (10 mL) and filtered through a pad of Celite, and the filtrate was washed successively with 10% $Na_2S_2O_3$ and brine. The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo* to give a residue, which was purified using LH-20 column chromatography (MeOH/CH_2Cl_2, 2:1, v/v) to give **21** (108.7 mg, 88 %) as a white, amorphous solid: TLC R_f = 0.29 (hexane/EtOAc, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.44 (m, 2H, $OCH_2CH_2CH_2CH_2N_3$), 2.97 (t, J = 6.8 Hz, 2H, $OCH_2CH_2CH_2N_3$), 3.20 and 3.50 (2 m, 2H, $OCH_2CH_2CH_2N_3$), 3.60 (s, 1H, H-5''), 3.65 (m, 1H, H-6), 3.36 (m, 2H, H-5', H-6'), 3.92 (m, 1H, H-6), 4.03 (m, 3H, H-4'', H-5, H-6'), 4.04 and 4.37 (AB, $J_{A,B}$ = 12.3 Hz, 2H, H-6'', H-6''), 4.50 (d, $J_{1,2}$ = 7.8 Hz, 1H, H-1''), 4.51 (d, $J_{1,2}$ = 7.8 Hz, 1H, H-1), 4.60 (d, $J_{3,4}$ = 3.6 Hz, 1H, H-4'), 4.75 (d, $J_{1,2}$ = 7.8 Hz, 1H, H-1'), 5.19 (dd, $J_{2,3}$ = 10.8 Hz, $J_{3,4}$ = 3.0 Hz, 1H, H-3''), 5.30 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.6 Hz, 1H, H-3'), 5.39 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3), 5.46 (s, 1H, PhC*H*), 5.57 (dd, $J_{1,2}$ = 7.8 Hz, $J_{2,3}$ = 10.5 Hz, 1H, H-2), 5.70 (m, 2H, H-2'', H-2'), 5.77 (d, $J_{3,4}$ = 3.3 Hz, 1H, H-4), 7.14 (t, J = 7.5 Hz, 3H, Ar), 7.20-7.31 (m, 19H, Ar), 7.33-7.47 (m, 8H, Ar), 7.68 (d, J = 7.5 Hz, 2H, Ar), 7.76-7.93 (m, 12H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.66 , 47.76, 66.25, 66.50, 68.28, 68.80, 68.96, 69.85, 71.73, 72.59, 73.45, 100.76, 101.28, 126.10, 126.22, 128.12, 128.20, 128.34, 128.39, 128.53, 128.85, 128.94, 129.06, 129.09, 129.27, 129.35, 129.53, 129.62, 129.67, 129.71, 129.90, 129.95, 130.02, 132.40, 133.13, 133.25, 133.36, 133.47, 137.49, 165.12, 165.27, 165.41, 165.56, 166.14, 176.35. $C_{57}H_{51}N_3O_{16}$ (1493.48): MS (MALDI) *m/z* = 1515.175 $[M + Na]^+$, 1531.973 $[M + K]^+$.

3-Azidopropyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,3-di-*O*-benzoyl-6-*O*-(2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-β-D-galactopyranosyl)-β-D-galactopyranosyl)-β-D-galactopyranoside (22)

A mixture of the glycosyl donor **11** (0.227 g, 0.399 mmol), the acceptor **19** (0.314 g, 0.332 mmol), and powdered 4 Å molecular sieves (250 mg) in CH_2Cl_2 (7 mL) was stirred at room temperature for 30 min and then cooled to 0 °C. NIS (22 mg, 0.0978 mmol), followed by TMSOTf (0.0061 mL, 0.0332 mmol), was added. The reaction mixture was stirred for 30 min and then quenched by the addition of triethylamine. The suspension was diluted with CH_2Cl_2 (20 mL) and filtered through a pad of Celite, and the filtrate was washed successively with 10% $Na_2S_2O_3$ and brine. The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo* to give a residue, which was purified using flash silica gel column chromatography (hexanes:EtOAc, 3:1 → 3:2, v/v) to give **22** (245 mg, 52%) as a white, amorphous solid: TLC R_f = 0.59 (hexane/EtOAc, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.47 (m, 2H, $OCH_2CH_2CH_2N_3$), 3.00 (t, J = 6.8 Hz, 2H, $OCH_2CH_2CH_2N_3$), 3.24 and 3.57 (2 m, 2H, $OCH_2CH_2CH_2N_3$), 3.63 (s, 1H, H-5''), 3.63-3.76 (m, 2H, H-6, H-6'), 3.71 (s, 1H, H-5'), 3.91-4.08 (m, 3H, H-5, H-6, H-6'), 4.10 and 4.33 (AB, $J_{A,B}$ = 12.3 Hz, 2H, H-6'', H-6''), 4.21 (d, $J_{3,4}$ = 3.3 Hz, 1H, H-4'), 4.52 (d, $J_{3,4}$ = 3.3 Hz, 1H, H-4''), 4.53 (d, $J_{1,2}$ = 7.8 Hz, 1H, H-1''), 4.54 (d, $J_{1,2}$ = 7.8 Hz, 1H, H-1), 4.73 (d, $J_{1,2}$ = 7.8 Hz, 1H, H-1), 5.13 (dd, $J_{2,3}$ = 10.2 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3''), 5.30 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3'), 5.42 (dd, $J_{2,3}$ = 10.2 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3), 5.46 (s, 1H, PhC*H*), 5.58 (dd, $J_{1,2}$ = 7.8 Hz, $J_{2,3}$ = 10.2 Hz, 1H, H-2), 5.63 (dd, $J_{1,2}$ = 7.8 Hz, $J_{2,3}$ = 10.2 Hz, 1H, H-2''), 5.74 (d, $J_{3,4}$ = 3.3 Hz, 1H, H-4), 5.74 (dd, $J_{1,2}$ = 7.8 Hz, $J_{2,3}$ = 10.5 Hz, 1H, H-2'), 7.14 (t, J = 7.5 Hz, 3H, Ar), 7.19-7.32 (m, 16H, Ar), 7.35-7.47 (m, 9H, Ar), 7.68 (d, J = 7.5 Hz, 2H, Ar), 7.89 (m, 10H, Ar), 7.95 (d, J = 7.5 Hz, 2H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ 29.52 ($OCH_2CH_2CH_2N_3$), 47.78 ($OCH_2CH_2CH_2N_3$), 65.97 (C-6'), 66.25 ($OCH_2CH_2CH_2N_3$), 66.66 (C-4''), 66.75 (C-5''), 67.82 (C-6), 68.82 (C-2', C-4, C-6''), 69.76 (C-2''), 69.88 (C-2), 71.61 (C-3), 72.62 (C-3'), 73.17 (C-5), 73.34 (C-5'), 73.39 (C-4'), 73.59 (C-

3''), 100.78 (C-1', Ph*C*H), 101.12 (C-1''), 101.27 (C-1), 126.17, 128.11, 128.20, 128.30, 128.39, 128.50, 128.84, 128.92, 129.07, 129.13, 129.249, 129.40, 129.60, 129.65, 129.71, 129.84, 129.91, 130.00, 130.02, 130.15, 133.24, 133.35, 137.38, 165.08, 165.36, 165.58, 165.63, 166.12, 177.16. $C_{77}H_{69}N_3O_{23}$ (1403.43): MS (MALDI) *m/z* = 1426.11 $[M + Na]^+$, 1442.08 $[M + K]^+$.

3-Azidopropyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,3-di-*O*-benzoyl-4-*O*-benzyl-6-*O*-(2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-(9-fluorenylmethoxycarbonyl)-β-D-galactopyranosyl)-β-D-galactopyranosyl)-β-D-galactopyranoside (29)

A mixture of the glycosyl donor **13** (37 mg, 0.053 mmol), the acceptor **20** (50 mg, 0.048 mmol), and powdered 4 Å molecular sieves (75 mg) in CH_2Cl_2 (0.8 mL) was stirred at room temperature for 30 min and then cooled to 0 °C. NIS (14 mg, 0.063 mmol), followed by TMSOTf (0.0013 mL, 0.0072 mmol), was added. The reaction mixture was stirred for 30 min and then quenched by the addition of triethylamine. The suspension was diluted with CH_2Cl_2 (10 mL) and filtered through a pad of Celite, and the filtrate was washed successively with 10% $Na_2S_2O_3$ and brine. The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo* to give a residue, which was purified using flash silica gel column chromatography (hexanes:EtOAc, 8:1 → 2:1, v/v) to give **29** (yield unavailable) as only a partially purified compound: TLC R_f = 0.72 (hexane/EtOAc, 3:2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.43 (m, 2H, $OCH_2CH_2CH_2N_3$), 2.97 (t, *J* = 6.6 Hz, 2H, $OCH_2CH_2CH_2N_3$), 3.21 and 3.62 (2 m, 2H, $OCH_2CH_2CH_2N_3$), 3.52 (s, 1H, H-5''), 3.62 (m, 1H, H-6), 3.73 (m, 2H, H-5', H-6'), 3.88-4.06 (m, 5H, H-5, H-6, H-6', H-6'', CH_2CH), 4.20 (m, 3H, H-6'', OCH_2CH), 4.28 (m, 1H, H-6''), 4.44 (s, 1H, H-4''), 4.50 (d, $J_{1,2}$ = 7.8 Hz, 1H, H-1''), 4.51 (d, $J_{1,2}$ = 7.8 Hz, 1H, H-1), 4.60 (s, 1H, H-4'), 4.69 (d, $J_{1,2}$ = 7.8 Hz, 1H, H-1'), 5.00 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3''), 5.19 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3'), 5.38 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3), 5.48 (s, 1H, C*H*Ph), 5.57 (dd, $J_{1,2}$ = 7.8 Hz,

$J_{2,3}$ = 10.5 Hz, 1H, H-2), 5.62-5.72 (m, 2H, H-2', H-2''), 5.80 (d, $J_{3,4}$ = 3.3 Hz, 1H, H-4), 6.94-7.98 (m, 48H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.66 ($OCH_2CH_2CH_2N_3$), 46.36 (OCH_2CH), 47.75 ($OCH_2CH_2CH_2N_3$), 66.20 ($OCH_2CH_2CH_2N_3$), 66.18, 66.36, 68.47, 68.99, 69.09, 69.83, 70.13, 70.27, 71.66, 71.91, 77.16, 73.23, 73.43, 73.75, 73.83, 75.10, 75.50, 100.59 (PhCH), 100.95 (C-1'), 101.20 (C-1), 101.33 (C-1''), 119.85, 125.07, 126.30, 127.05, 127.75, 128.11, 128.39, 128.57, 129.22, 129.44, 129.59, 129.68, 129.77, 129.99, 133.00, 133.38, 137.86, 141.08, 142.97, 143.07, 154.38, 164.89, 165.12, 165.24, 165.38, 165.56.

3-Azidopropyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,3-di-*O*-benzoyl-4-*O*-benzyl-6-*O*-(2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-β-D-galactopyranosyl)-β-D-galactopyranosyl)-β-D-galactopyranoside (30)

A mixture of the glycosyl donor **17** (42 mg, 0.0726 mmol), the acceptor **20** (68 mg, 0.066 mmol), and powdered 4 Å molecular sieves (100 mg) in CH_2Cl_2 (1.4 mL) was stirred at room temperature for 30 min and then cooled to 0 °C. NIS (19 mg, 0.086 mmol), followed by TMSOTf (0.0018 mL, 0.0099 mmol), was added. The reaction mixture was stirred for 30 min and then quenched by the addition of triethylamine. The suspension was diluted with CH_2Cl_2 (10 mL) and filtered through a pad of Celite, and the filtrate was washed successively with 10% $Na_2S_2O_3$ and brine. The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo* to give a residue, which was purified using flash silica gel column chromatography (hexanes:EtOAc, 8:1 → 2:1, v/v) to give **30** (37 mg, 37%) as a white, amorphous solid: TLC R_f = 0.72 (hexane/EtOAc, 3:2). $C_{83}H_{85}N_3O_{22}Si$ (1503.54): MS (MALDI) *m/z* = 1526.72 $[M + Na]^+$, 1542.54 $[M + K]^+$.

3-Azidopropyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,3-di-*O*-benzoyl-6-*O*-(4,6-*O*-benzylidene-3-*O*-(9-fluorenylmethoxycarbonyl)-2-*O*-levulinoyl-β-D-galactopyranosyl)-β-D-galactopyranosyl)-β-D-galactopyranoside (24)

A mixture of the glycosyl donor **14** (0.147 g, 0.215 mmol), Ph_2SO (0.122 g, 0.603 mmol), and powdered 4 Å molecular sieves (0.36 g) in CH_2Cl_2 (2.9 mL) was stirred at room temperature for 15 min and then cooled to -60 °C (15 min). Tf_2O (0.051 mL, 0.301 mmol) was added, and the reaction mixture was left to stir for 5 min. A solution of glycosyl acceptor **19** (214 g, 0.226 mmol) in CH_2Cl_2 (1.5 mL) was then added. The reaction mixture was stirred for 1 h at -60 °C and then allowed to slowly reach room temperature (1 h). The suspension was diluted with CH_2Cl_2 (10 mL) and filtered through a pad of Celite into saturated aqueous $NaHCO_3$, and the filtrate was washed successively with saturated aqueous $NaHCO_3$ and brine. The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo* to give a residue, which was purified using flash silica gel column chromatography (hexane/EtOAc, 3:1 → 1:1, v/v) to give **24** (0.214 g, 66%) as a white, amorphous solid: TLC R_f = 0.53 (hexane/EtOAc, 4:5). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.45 (m, 2H, $OCH_2CH_2CH_2N_3$), 1.58 (s, 3H, $COCH_2CH_2COCH_3$), 2.22-2.72 (ABXY, 4H, $COCH_2CH_2COCH_3$), 2.99 (t, J = 6.6 Hz, 2H, $OCH_2CH_2CH_2N_3$), 3.23 and 3.52 (2 m, 2H, $OCH_2CH_2CH_2N_3$), 3.46 (s, 1H, H-5''), 3.73 and 4.02 (*AB*X, $J_{AB,X}$ = 7.5 Hz, $J_{A,B}$ = 10.5 Hz, 1H, H-6, H-6), 3.86 (m, 2H, H-5', H-6'), 4.02 (m, 3H, H-5, H-6', H-6''), 4.17 (t, J = 7.2 Hz, 1H, OCH_2CH), 4.25-4.33 (m, 5H, H-4', H-4'', H-6'', OCH_2CH), 4.52 (d, $J_{1,2}$ = 8.0 Hz, 1H, H-1''), 4.54 (d, $J_{1,2}$ = 8.0 Hz, 1H, H-1), 4.71 (d, $J_{1,2}$ = 8.0 Hz, 1H, H-1'), 4.76 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3''), 5.24 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3'), 5.34-5.47 (m, 2H, H-2'', H-3), 5.43 (s, 1H, CHPh), 5.58 (dd, $J_{1,2}$ = 8.0 Hz, $J_{2,3}$ = 10.5 Hz, 1H, H-2), 5.72 (dd, $J_{1,2}$ = 8.0 Hz, $J_{2,3}$ = 10.5 Hz, 1H, H-2'), 5.82 (s, 1H, H-4), 7.13 (t, J = 7.5 Hz, 2H, Ar), 7.23-7.32 (m,

13H, Ar), 7.34-7.55 (m, 11H, Ar), 7.66 (d, J = 7.5 Hz, 2H, Ar), 7.87 (m, 6H, Ar), 7.98 (d, J = 8.2 Hz, 2H, Ar). $C_{83}H_{77}N_3O_{25}$ (1515.48): MS (MALDI) m/z = 1528.5587 $[M + Na]^+$, 1554.465 $[M + K]^+$.

3-Azidopropyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,3-di-*O*-benzoyl-6-*O*-(3-*O*-benzoyl-4,6-*O*-benzylidene-2-*O*-levulinoyl-β-D-galactopyranosyl)-β-D-galactopyranosyl)-β-D-galactopyranoside (27)

A mixture of the glycosyl donor **15** (0.076 g, 0.135 mmol), Ph_2SO (0.0695 g, 0.344 mmol), and powdered 4 Å molecular sieves (0.1 g) in CH_2Cl_2 (2.0 mL) was stirred at room temperature for 15 min and then cooled to -60 °C (15 min). Tf_2O (0.029 mL, 0.172 mmol) was added, and the reaction mixture was left to stir for 5 min. A solution of glycosyl acceptor **19** (0.116 g, 0.123 mmol) in CH_2Cl_2 (1.0 mL) was then added. The reaction mixture was stirred for 1 h at -60 °C and then allowed to slowly reach room temperature (1 h). The suspension was diluted with CH_2Cl_2 (10 mL) and filtered through a pad of Celite into saturated aqueous $NaHCO_3$, and the filtrate was washed successively with saturated aqueous $NaHCO_3$ and brine. The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo* to give a residue, which was purified using flash silica gel column chromatography (hexane/EtOAc, 3:2 → 2:3, v/v) to give **27** (63 mg, 33%) as a white, amorphous solid: TLC R_f = 0.68 (hexane/EtOAc, 2:3). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.47 (m, 2H, $OCH_2CH_2CH_2N_3$), 1.82 (s, 3H, $COCH_2CH_2COCH_3$), 2.39 and 2.49 (2 m, 4H, $COCH_2CH_2COCH_3$), 3.00 (t, J = 6.6 Hz, 2H, $OCH_2CH_2CH_2N_3$), 3.46 (s, 1H, H-5''), 3.24 and 3.57 (2 m, 2H, $OCH_2CH_2CH_2N_3$), 3.66 (s, 1H, H-5'), 3.67 (m, 2H, H-6, H-6'), 3.88-4.01 (m, 3H, H-5, H-6, H-6'), 3.90 and 4.22 (AB, $J_{A,B}$ = 12.6 Hz, 2H, H-6''), 4.18 (d, $J_{3,4}$ = 3.0 Hz, H-4'), 4.32 (d, $J_{3,4}$ = 3.0 Hz, 1H, H-4''), 4.52 (d, $J_{1,2}$ = 7.8 Hz, 2H, H-1, H-1''), 4.61 (d, $J_{1,2}$ = 7.8 Hz, 1H, H-1'), 5.09 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.0 Hz, 1H, H-3''), 5.12 (dd, $J_{2,3}$

= 10.5 Hz, $J_{3,4}$ = 3.0 Hz, 1H, H-3'), 5.40 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3), 5.44 (s, 1H, C*H*Ph), 5.49-5.65 (m, 3H, H-2, H-2', H-2''), 5.72 (s, 1H, H-4), 7.13 (t, J = 7.8 Hz, 2H, Ar), 7.23-7.51 (m, 21H, Ar), 7.66 (d, *J* = 7.5 Hz, 2H, Ar), 7.87 (m, 6H, Ar), 7.90 (d, *J* = 7.8 Hz, 2H, Ar), 7.94 (d, *J* = 7.2 Hz, 2H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.13 ($COCH_2CH_2COCH_3$), 28.68 ($OCH_2CH_2CH_2N_3$), 29.37 ($COCH_2CH_2COCH_3$), 37.72 ($COCH_2CH_2COCH_3$), 47.75 ($OCH_2CH_2CH_2N_3$), 66.73 (C-6), 66.20 ($OCH_2CH_2CH_2N_3$), 66.55 (C-5''), 66.64 (C-4'), 67.72 (C-6'), 68.76 (C-2, C-4, C6''), 69.73 (C-2'), 69.85 (C-2''), 71.58 (C-3), 71.77 (C-3''), 73.12 (C-5, C-5'), 73.35 (C-4''), 73.52 (C-3'), 100.65 (C-1'), 100.99 (C-1), 101.07 (C-1''), 101.23 (Ph*C*H), 126.30, 128.14, 128.18, 128.26, 128.37, 128.46, 128.51, 128.81, 129.04, 129.12, 129.22, 129.38, 129.57, 129.61, 129.67, 129.73, 129.80, 129.98, 132.99, 133.12, 133.23, 133.28, 133.39, 137.38, 165.06, 165.23, 165.32, 165.49, 165.61, 173.03, 206.08. $C_{75}H_{71}N_3O_{24}$ (1397.44): MS (MALDI) *m/z* = 1419.10 $[M + Na]^+$, 1434.97 $[M + K]^+$.

3-Azidopropyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,3-di-*O*-benzoyl-6-*O*-(2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-β-D-galactopyranosyl)-β-D-galactopyranosyl)-β-D-galactopyranoside (23)

A solution of **22** (0.245 g, 0.174 mmol) in pyridine (2 mL) and in acetic anhydride (0.163 mL, 1.74 mmol) was stirred at room temperature for 18 h. The reaction was quenched by the addition of MeOH (1 mL), diluted with toluene, and concentrated *in vacuo*. The resulting residue was dissolved in CH_2Cl_2 and washed subsequently with 1M HCl, saturated aqueous NaHCO3, and brine. The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo*. The residue was purified using flash silica gel column chromatography (hexanes:EtOAc, 1:1, v/v) to afford **23** (0.191 g, 76%) as a white amorphous solid: TLC R_f = 0.73 (hexane/EtOAc, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.42-1.49 (m, 2H, $OCH_2CH_2CH_2N_3$), 1.99 (s, 3H, $COCH_3$), 3.01 (t, *J* = 6.6 Hz, 2H, $OCH_2CH_2CH_2N_3$), 3.23 and 3.56 (2 m, 2H, $OCH_2CH_2CH_2N_3$), 3.63 (s,

1H, H-5''), 3.06-3.82 (m, 3H, H-6, H-6', H-6'), 3.95 (m, 3H, H-5, H-5', H-6), 4.05 and 4.42 (AB, $J_{A,B}$ = 12.5 Hz, 2H, H-6''), 4.54 (m, 3H, H-1, H-1'', H-4''), 4.73 (d, $J_{1,2}$ = 7.8 Hz, 1H, H-1'), 5.26 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.0 Hz, 1H, H-3''), 5.29 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.0 Hz, 1H, H-3'), 5.41 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.0 Hz, 1H, H-3), 5.47 (s, 1H, PhC*H*), 5.53 (dd, $J_{1,2}$ = 8.1 Hz, $J_{2,3}$ = 10.5 Hz, 1H, H-2''), 5.58 (dd, $J_{1,2}$ = 8.1 Hz, $J_{2,3}$ = 10.5 Hz, 1H, H-2), 5.65 (d, $J_{3,4}$ = 3.0 Hz, 1H, H-4'), 5.69 (d, $J_{3,4}$ = 3.0 Hz, 1H, H-4), 5.76 (dd, $J_{1,2}$ = 8.1 Hz, $J_{2,3}$ = 10.5 Hz, 1H, H-2'), 7.15 (t, *J* = 8.1 Hz, 3H, Ar), 7.25-7.34 (m, 15H, Ar), 7.37-7.45 (m, 8H, Ar), 7.68 (d, *J* = 7.8 Hz, 2H, Ar), 7.76 (d, *J* = 7.8 Hz, 2H, Ar), 7.86 (d, *J* = 7.8 Hz, 8H, Ar), 7.89 (d, *J* = 7.8 Hz, 2H, Ar), 7.93 (d, *J* = 7.8 Hz, 2H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.50 ($CO\mathit{C}H_3$), 28.71 ($OCH_2\mathit{C}H_2CH_2N_3$), 47.75 ($OCH_2CH_2\mathit{C}H_2N_3$), 66.00 (C-6'), 66.12 ($O\mathit{C}H_2CH_2CH_2N_3$), 66.53 (C-5''), 67.79 (C-4'), 68.21 (C-6), 68.43 (C-2'), 68.75 (C-4), 68.83 (C-6''), 69.64 (C-2''), 69.85 (C-2), 71.57 (C-3), 71.70 (C-3''), 72.69 (C-3'), 72.83 (C-5), 73.10 (C-5'), 73.39 (C-4''), 100.80 (C-1, C-1''), 100.96 (C-1'), 101.27 (Ph*C*H), 126.23, 128.11, 128.20, 128.36, 128.45, 128.82, 128.94, 129.02, 129.10, 129.23, 129.38, 129.50, 129.58, 129.65, 129.71, 129.91, 129.97, 133.12, 133.23, 133.30, 137.51, 165.07, 165.23, 165.36, 166.08, 169.80. $C_{79}H_{71}N_3O_{24}$ (1445.44): MS (MALDI) *m/z* = 1468.34 $[M + Na]^+$, 1484.33 $[M + K]^+$.

3-Azidopropyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,3-di-*O*-benzoyl-4-*O*-acetyl-6-*O*-(4,6-*O*-benzylidene-3-*O*-(9-fluorenylmethoxycarbonyl)-2-*O*-levulinoyl-β-D-galactopyranosyl)-β-D-galactopyranosyl)-β-D-galactopyranoside (25)

A solution of **24** (0.146 g, 0.0963 mmol) and a catalytic amount of DMAP in pyridine and in acetic anhydride (0.1 mL, 1.06 mmol) was stirred at room temperature for 18 h. The reaction was quenched by the addition of MeOH (0.5 mL), diluted with toluene, and concentrated *in vacuo*. The resulting residue was dissolved in CH_2Cl_2 and washed subsequently with 1M HCl,

saturated aqueous NaHCO3, and brine. The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo*. The residue was purified using flash silica gel column chromatography (hexanes:EtOAc, 2:1 → 1:1, v/v) to afford **25** (0.135 g, 90%) as a white amorphous, solid: TLC R_f = 0.56 (hexane/EtOAc, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.42 (m, 2H, $OCH_2CH_2CH_2N_3$), 2.02 (s, 3H, $COCH_2CH_2COCH_3$), 2.03 (s, 3H, $COCH_3$), 2.20-2.66 (m, 4H, $COCH_2CH_2COCH_3$), 2.97 (t, J = 6.6 Hz, 2H, $OCH_2CH_2CH_2N_3$), 3.19 and 3.46 (2 m, 2H, $OCH_2CH_2CH_2N_3$), 3.44 (s, 1H, H-5''), 3.75 (m, 2H, H-5', H-6), 4.02 (m, 4H, H-6, H-6', H-6', H-6''), 4.18 (t, J = 7.5 Hz, 1H, OCH_2CH), 4.28 (m, 4H, H-5, H-6'', OCH_2CH), 4.36 (d, $J_{3,4}$ = 3.6 Hz, 1H, H-4''), 4.55 (d, $J_{1,2}$ = 8.0 Hz, 1H, H-1''), 4.55 (d, $J_{1,2}$ = 8.0 Hz, 1H, H-1), 4.74 (m, 1H, H-3''), 4.77 (d, $J_{1,2}$ = 8.0 Hz, 1H, H-1'), 5.24-5.46 (m, 3H, H-2'', H-3, H-3') 5.42 (s, 1H, CHPh), 5.59 (m, 3H, H-2, H-2', H-4'), 5.82 (d, $J_{3,4}$ = 3.3 Hz, 1H, H-4), 7.12 (m, 3H, Ar), 7.22-7.31 (m, 13H, Ar), 7.35-7.52 (m, 10H, Ar), 7.66 (d, J = 7.5 Hz, 4H, Ar), 7.77 (d, J = 7.2 Hz, 2H, Ar), 7.85 (d, J = 8.1 Hz, 2H, Ar), 7.88 (d, J = 7.5 Hz, 2H, Ar), 7.96 (d, J = 7.2 Hz, 2H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.54 ($COCH_2CH_2COCH_3$), 27.62 ($COCH_2CH_2COCH_3$), 28.63 ($OCH_2CH_2CH_2N_3$), 29.74 ($COCH_3$), 37.58 ($COCH_2CH_2COCH_3$), 46.49 (OCH_2CH), 47.68 ($OCH_2CH_2CH_2N_3$), 64.86 (C-5'), 66.06 ($OCH_2CH_2CH_2N_3$), 66.17 (C-5''), 66.71 (C-4'), 68.31 (C-2'') 68.67 (C-6, C-6'), 68.92 (C-4), 69.61 (C-2'), 69.81 (C-2), 70.12 (C-6''), 71.59 (C-3), 71.69 (C-3'), 72.63 (C-5), 72.91 (C-4''), 73.23 (OCH_2CH), 75.24 (C-3''), 100.43 (C-1'), 100.86 (C-1), 100.91 (C-1''), 101.21 (PhCH), 119.68, 119.89, 120.94, 125.17, 125.27, 126.28, 126.99, 127.09, 127.77, 128.09, 128.16, 128.38, 128.55, 128.68, 128.99, 129.08, 129.17, 129.34, 129.55, 129.63, 129.95, 133.18, 133.48, 137.31, 141.16, 143.12, 143.28, 154.18, 165.10, 165.21, 165.36, 169.73, 171.17, 206.38. $C_{85}H_{79}N_3O_{26}$ (1557.50): MS (MALDI) *m/z* = 1579.77292 $[M + Na]^+$, 1595.75589 $[M + K]^+$.

3-Azidopropyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,3-di-*O*-benzoyl-4-*O*-acetyl-6-*O*-(3-*O*-benzoyl-4,6-*O*-benzylidene-2-*O*-levulinoyl-β-D-galactopyranosyl)-β-D-galactopyranosyl)-β-D-galactopyranoside (28)

A solution of **27** (75 mg, 0.054 mmol) and a catalytic amount of DMAP in pyridine and in excess acetic was stirred at room temperature 2 h. The reaction was quenched by the addition of MeOH (1 mL) at 0 °C, diluted with toluene, and concentrated *in vacuo*. The resulting residue was dissolved in CH_2Cl_2 and washed subsequently with 1M HCl, saturated aqueous NaHCO3, and brine. The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo*. The residue was purified using flash silica gel column chromatography (hexanes:EtOAc, 1:1 → 3:4, v/v) to afford **28** (58 mg, 74%) as a white amorphous, solid: TLC R_f = 0.53 (hexane/EtOAc, 1:2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.95 (d, J = 6.9 Hz, 2H, Ar), 7.92 (d, J = 8.1 Hz, 2H, Ar), 7.85 (m, 4H, Ar), 7.75 (d, J = 7.5 Hz, 2H, Ar), 7.67 (d, J = 7.5 Hz, 2H, Ar), 7.50-7.22 (m, 20H, Ar), 7.15 (d, J = 7.8 Hz, 2H, Ar), 5.69 (d, $J_{3,4}$ = 3.3 Hz, 1H, H-4), 5.62 (d, $J_{3,4}$ = 3.3 Hz, 1H, H-4'), 5.57 (d, $J_{1,2}$ = 7.8 Hz, $J_{2,3}$ = 10.5 Hz, 1H, H-2), 5.54 (d, $J_{1,2}$ = 7.8 Hz, $J_{2,3}$ = 10.5 Hz, 1H, H-2), 5.51 (d, $J_{1,2}$ = 7.8 Hz, $J_{2,3}$ = 10.5 Hz, 1H, H-2), 5.45 (s, 1H, PhC*H*), 5.39 (d, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3), 5.24 (d, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3'), 5.09 (d, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3''), 4.60 (d, $J_{1,2}$ = 3.3 Hz, 1H, H-1'), 4.54 (d, $J_{1,2}$ = 3.3 Hz, 1H, H-1''), 4.53 (d, $J_{1,2}$ = 3.3 Hz, 1H, H-1'), 4.36 and 4.00 (AB, $J_{6,6}$ = 12.6 Hz, 2H, H-6'', H-6''), 4.31 (d, $J_{3,4}$ = 3.3 Hz, 1H, H-4'), 3.94 (m, 3H, H-5', H-6, H-6'), 3.72 (m, 2H, H-5, H-6'), 3.63 (ABX, $J_{5,6}$ = 7.5 Hz, $J_{6,6}$ = 10.2 Hz, 1H, H-6), 3.56 and 3.24 (2 m, 2H, OCH_2CH$_2$CH$_2$N$_3$), 3.52 (s, 1H, H-5''), 3.01 (t, J = 6.6 Hz, 1H, OCH$_2$CH$_2$CH_2N$_3$), 2.49-2.38 (m, 4H, COCH_2CH_2COCH$_3$), 1.99 (s, 3H, COCH_3), 1.81 (s, 3H, COCH_3), 1.47 (m, 2H, OCH$_2$CH_2CH$_2$N$_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.00, 169.77, 165.36, 165.31, 165.23, 165.07, 165.00, 137.54, 133.39, 133.25, 133.17, 129.99,

129.78, 129.71, 129.65, 129.59, 129.53, 129.37, 129.24, 129.15, 129.08, 129.02, 128.83, 128.50, 128.44, 128.39, 128.36, 128.31, 128.20, 128.17, 126.41, 101.26, 101.03, 100.95, 100.71, 76.62, 73.28, 73.07, 72.62, 71.88, 71.58, 69.83, 69.64, 68.79, 68.68, 68.41, 68.08, 67.64, 66.45, 66.13, 66.01, 47.75, 38.76, 29.38, 28.71, 28.18, 20.51. $C_{85}H_{79}N_3O_{26}$ (1439.45): MS (MALDI) *m/z* = 1462.36 $[M + Na]^+$.

3-Azidopropyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,3-di-*O*-benzoyl-4-*O*-acetyl-6-*O*-(4,6-*O*-benzylidene-3-*O*-(9-fluorenylmethoxycarbonyl)-β-D-galactopyranosyl)-β-D-galactopyranosyl)-β-D-galactopyranoside (36)

To a solution of **25** (0.135 g, 0.0866 mmol) in CH_2Cl_2 (1 mL) was added a solution of hydrazine acetate (8.8 mg, 0.0953 mmol) in methanol (0.0205 mL). The reaction solution was stirred at room temperature for 4 h. The reaction was then quenched by the addition of acetone. The reaction was diluted with toluene, and concentrated *in vacuo*. The residue was purified using flash silica gel column chromatography (hexanes:EtOAc, 3:1 → 1:1, v/v) to afford **36** (0.053 g, 42%) as a white, amorphous solid: TLC R_f = 0.59 (hexane/EtOAc, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.51 (m, 2H, $OCH_2CH_2CH_2N_3$), 2.06 (s, 3H, $COCH_3$), 3.01 (t, *J* = 6.6 Hz, 2H, $OCH_2CH_2CH_2N_3$), 3.23 and 3.55 (2 m, 2H, $OCH_2CH_2CH_2N_3$), 3.42 (s, 1H, H-5''), 3.71 (m, 2H, H-6, H-6'), 3.85-4.15 (m, 7H, H-2'', H-5, H-5', H-6, H-6', H-6'', CH_2CH), 4.28 (m, 5H, H-1'', H-4'', H-6'', OCH_2CH), 4.57 (d, $J_{1,2}$ = 7.8 Hz, 1H, H-1), 4.62 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.6 Hz, 1H, H-3''), 4.66 (d, $J_{1,2}$ = 7.8 Hz, 1H, H-1'), 5.34 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3') 5.43 (s, 1H, CHPh), 5.43 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3), 5.60 (m, 3H, H-2, H-2', H-4'), 5.74 (d, $J_{3,4}$ = 3.3 Hz, 1H, H-4), 7.12 (t, *J* = 7.5 Hz, 3H, Ar), 7.28 (m, 12H, Ar), 7.36-7.54 (m, 10H, Ar), 7.62 (m, 3H, Ar), 7.66 (d, *J* = 7.5 Hz, 2H, Ar), 7.79 (d, *J* = 7.5 Hz, 2H, Ar), 7.86 (d, *J* = 7.8 Hz, 2H, Ar), 7.89 (d, *J* = 7.8 Hz, 2H, Ar), 8.01 (d, *J* = 6.9 Hz, 2H, Ar). ^{13}C NMR (75

MHz, $CDCl_3$): δ 20.58 ($CO\mathit{C}H_3$), 28.63 ($OCH_2\mathit{C}H_2CH_2N_3$), 46.55 ($OCH_2\mathit{C}H$), 47.69 ($OCH_2CH_2\mathit{C}H_2N_3$), 66.16 ($O\mathit{C}H_2CH_2CH_2N_3$), 66.18 (C-5''), 66.73 (C-6), 67.70 (C-4'), 68.00 (C-5'), 69.15 (C-4), 69.62 (C-6', C-6'') 69.73 ($O\mathit{C}H_2CH$), 69.88 (C-2, C-2'), 71.58 (C-3, C-3'), 72.26 (C-5), 72.94 (C-4''), 73.40 (C-2''), 77.41 (C-3''), 100.76 (Ph*C*H), 101.19 (C-1'), 101.36 (C-1), 102.80 (C-1''), 119.86, 125.13, 126.23, 127.04, 127.73, 128.05, 128.15, 128.36, 128.62, 128.87, 129.17, 129.30, 129.56, 130.00, 133.22, 133.61, 137.49, 141.14, 143.00, 143.31, 154.57, 165.13, 165.44, 165.80, 170.22. $C_{80}H_{73}N_3O_{24}$ (1459.46): MS (MALDI) *m/z* = 1482.80 $[M + Na]^+$, 1498.77 $[M + K]^+$.

3-Azidopropyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,3-di-*O*-benzoyl-4-*O*-acetyl-6-*O*-(3-*O*-benzoyl-4,6-*O*-benzylidene-β-D-galactopyranosyl)-β-D-galactopyranosyl)-β-D-galactopyranoside (38)

To a solution of **28** (58 mg, 0.0403 mmol) in CH_2Cl_2 (0.5 mL) was added a solution of hydrazine acetate (19 mg, 0.206 mmol) in methanol (0.05 mL). The reaction solution was stirred at room temperature for 3 h. The reaction was then quenched by the addition of acetone. The reaction was diluted with toluene, and concentrated *in vacuo*. The residue was purified using flash silica gel column chromatography (hexanes:EtOAc, 1:1 → 1:2, v/v) to afford **38** (0.033 g, 61%) as a white, amorphous solid: TLC R_f = 0.48 (hexane/EtOAc, 1:2). ^{1}H NMR (600 MHz, D_2O): δ 7.90 (d, J = 3.6 Hz, 2H, Ar), 7.84 (d, J = 3.3 Hz, 2H, Ar), 7.81 (d, J = 4.2 Hz, 2H, Ar), 7.80 (d, J = 3.9 Hz, 2H, Ar), 7.69 (d, J = 3.9 Hz, 2H, Ar), 7.61 (d, J = 3.9 Hz, 2H, Ar), 7.41-7.18 (m, 21H, Ar), 7.09 (t, J = 3.9 Hz, 2H, Ar), 5.63 (d, $J_{3,4}$ = 1.5 Hz, 1H, H-4), 5.54 (d, $J_{3,4}$ = 1.5 Hz, 1H, H-4'), 5.54 (dd, $J_{1,2}$ = 4.0 Hz, $J_{2,3}$ = 5.1 Hz, 1H, H-2), 5.49 (dd, $J_{1,2}$ = 4.0 Hz, $J_{2,3}$ = 5.3 Hz, 1H, H-2'), 5.45 (s, 1H, PhC*H*), 5.35 (dd, $J_{2,3}$ = 5.1 Hz, $J_{3,4}$ = 1.5 Hz, 1H, H-3), 5.20 (dd, $J_{2,3}$ = 5.3 Hz, $J_{3,4}$ = 1.5 Hz, 1H, H-3'), 5.63 (dd, $J_{1,2}$ = 4.0 Hz, $J_{2,3}$ = 5.0 Hz, 1H, H-2''), 4.56 (d, $J_{1,2}$ = 4.0 Hz, 1H, H-1''), 4.52 (d, $J_{1,2}$ = 4.0 Hz, 1H, H-1'), 4.48 (d, $J_{1,2}$ = 4.0 Hz, 1H, H-1), 4.30 and 3.98 (AB, $J_{A,B}$ =

6.0 Hz, 2H, H-6'', H-6''), 4.12 (d, $J_{3,4}$ = 1.5 Hz, 1H, H-4''), 3.95 (AB*X*, $J_{5,6}$ = 1.5 Hz, $J_{5,6}$ = 3.9 Hz, 1H, H-5), 3.92 (*A*BX, $J_{5,6}$ = 1.5 Hz, $J_{6,6}$ = 5.3 Hz, 1H, H-6), 3.86 (t, $J_{5,6}$ = 3.0 Hz, 1H, H-5'), 3.80 (dd, $J_{2,3}$ = 5.1 Hz, $J_{3,4}$ = 1.5 Hz, 1H, H-3''), 3.73 and 3.65 (ABX, $J_{5,6}$ = 3.0 Hz, $J_{6,6}$ = 5.7 Hz, 2H, H-6', H-6'), 3.61 (A*B*X, $J_{5,6}$ = 3.9 Hz, $J_{6,6}$ = 5.3 Hz, 1H, H-6), 3.45 and 3.14 (2 m, 2H, OC*H*$_2$CH$_2$CH$_2$N$_3$), 3.44 (s, 1H, H-5''), 2.94 (t, *J* = 3.5 Hz, OCH$_2$CH$_2$C*H*$_2$N$_3$), 1.95 (s, 3H, COC*H*$_3$), 1.42 and 1.32 (2 m, 2H, OCH$_2$C*H*$_2$CH$_2$N$_3$). ^{13}C NMR (75 MHz, CDCl$_3$): δ 169.76, 166.01, 165.55, 165.42, 165.32, 165.25, 165.09, 137.35, 133.47, 133.23, 133.06, 130.01, 129.78, 129.70, 129.67, 129.59, 129.33, 129.27, 129.21, 128.96, 128.91, 128.74, 128.53, 128.41, 128.33, 128.28, 128.23, 126.42, 101.50 (Ph*C*H), 101.27 (C-1), 101.11 (C-1'), 100.49 (C-1''), 75.57 (C-4''), 73.39 (C-5'), 73.24 (C-5), 72.59 (C-2''), 71.58 (C-3), 71.47 (C-3', C-3''), 69.81 (C-2), 69.58 (C-2'), 68.87 (C-4, C-6''), 68.57 (C-6), 67.83 (C-4'), 66.67(C-5''), 66.30 (C-6'), 66.12 (O*C*H$_2$CH$_2$CH$_2$N$_3$), 47.72 (OCH$_2$CH$_2$*C*H$_2$N$_3$), 28.69 (OCH$_2$*C*H$_2$CH$_2$N$_3$), 20.49 (CO*C*H$_3$). $C_{80}H_{73}N_3O_{24}$ (1341.42): HR-MS (MALDI) *m/z* = 1364.80 $[M + Na]^+$, 1380.77 $[M + K]^+$.

3-Azidopropyl 2,3,4-tri-*O*-benzoyl-6-*O*-(4-*O*-acetyl-2,3-di-*O*-benzoyl-6-*O*-(2,3-di-*O*-benzoyl-4-*O*-benzyl-β-D-galactopyranosyl)-β-D-galactopyranosyl)-β-D-galactopyranoside (45)

A mixture of trisaccharide **23** (0.167 g, 0.116 mmol) and powdered 4 Å molecular sieves (0.5 g) in CH_2Cl_2 (1 mL) was stirred at room temperature for 15 min and then cooled to -78 °C. Et_3SiH (0.0487 mL, 0.376 mmol), followed by $PhBCl_2$ (0.0532 mL, 0.332 mmol), was added. The reaction mixture was stirred for 1 h and then quenched by the addition of triethylamine (0.092 mL). The suspension was diluted with CH_2Cl_2 (10 mL) and filtered through a pad of Celite, and the filtrate was washed successively with saturated aqueous $NaHCO_3$ and brine. The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo* to give a residue, which was purified using flash silica gel column chromatography (hexane/EtOAc, 2:1, v/v) to

give **45** (0.109 g, 65 %) as a white foam: TLC R_f = 0.38 (hexane/EtOAc, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ. ^{13}C NMR (75 MHz, $CDCl_3$): δ. $C_{79}H_{73}N_3O_{24}$ (1447.4584): MS (MALDI) *m/z* = 1470.80 $[M + Na]^+$, 1486.77 $[M + K]^+$.

3-Azidopropyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,3-di-*O*-benzoyl-4-*O*-benzyl-6-*O*-(2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-galactopyranosyl)-β-D-galactopyranosyl)-β-D-galactopyranoside (41)

A solution of 70% HF in pyridine (0.032 mL, 1.23 mmol) was added to a solution of trisaccharide **30** (37 mg, 0.0246 mmol) in THF (1 mL), and the reaction solution was stirred at room temperature for 18 h. The solution was diluted with CH_2Cl_2 (10 mL) and washed successively with saturated aqueous $NaHCO_3$ and brine. The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo* to give a residue, which was purified using flash silica gel column chromatography (hexane/EtOAc, 3:1 → 1:1, v/v) to give **41** (0.033 g, 96%) as a white, amorphous solid: TLC R_f = 0.14 (hexane/EtOAc, 3:2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.35 and 1.43 (2 m, 2H, $OCH_2CH_2CH_2N_3$), 2.96 (t, J = 6.8 Hz, 2H, $OCH_2CH_2CH_2N_3$), 3.17 and 3.46 (2 m, 2H, $OCH_2CH_2CH_2N_3$), 3.48 (s, 1H, H-5''), 3.66 (*A*BX, $J_{5,6}$ = 7.8 Hz, $J_{6,6}$ = 10.5 Hz, 1H, H-6), 3.71 (t, $J_{5,6}$ = 6.0 Hz, 1H, H-5'), 3.82 (A*B*X, $J_{5,6}$ = 5.5 Hz, $J_{6,6}$ = 10.5 Hz, 1H, H-6'), 3.88 (dd, $J_{2,3}$ = 10.2 Hz, $J_{3,4}$ = 3.6 Hz, H-3''), 3.99 (m, 5H, H-4', H-5, H-6, H-6', H-6''), 4.21 (d, $J_{3,4}$ = 3.6 Hz, 1H, H-4''), 4.24 (A*B*, $J_{6,6}$ = 13.2 Hz, 1H, H-6''), 4.52 (d, $J_{1,2}$ = 8.0 Hz, 1H, H-1'), 4.53 (d, $J_{1,2}$ = 8.1 Hz, 1H, H-1), 4.59 (s, 2H, OCH_2Ph), 4.64 (d, $J_{1,2}$ = 8.1 Hz, 1H, H-1''), 5.19 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.0 Hz, 1H, H-3'), 5.26 (dd, $J_{1,2}$ = 8.1 Hz, $J_{2,3}$ = 10.2 Hz, 1H, H-2''), 5.39 (dd, $J_{2,3}$ = 10.2 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3), 5.50 (s, 1H, PhC*H*), 5.59 (dd, $J_{1,2}$ = 8.0 Hz, $J_{2,3}$ = 10.2 Hz, 1H, H-2), 5.71 (d, $J_{3,4}$ = 3.2 Hz, 1H, H-4), 5.76 (dd, $J_{1,2}$ = 8.0 Hz, $J_{2,3}$ = 10.5 Hz, 1H, H-2'), 7.15 (m, 4H, Ar), 7.22-7.50 (m, 24H, Ar), 7.67 (d, J = 7.5 Hz, 2H, Ar), 7.79 (d, J = 7.5 Hz, 2H, Ar), 7.84 (d, J = 7.5 Hz, 2H, Ar), 7.86 (d, J = 7.5 Hz, 8H, Ar), 7.89 (d, J = 7.5 Hz,

2H, Ar), 7.95 (d, J = 7.5 Hz, 2H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.64 ($OCH_2CH_2CH_2N_3$), 47.70 ($OCH_2CH_2CH_2N_3$), 65.97 (C-6'), 66.15 ($OCH_2CH_2CH_2N_3$), 66.66 (C-5''), 68.75 (C-6), 68.83 (C-6''), 69.04 (C-4), 69.78 (C-2), 70.03 (C-2'), 71.52 (C-3''), 71.62 (C-3), 72.93 (C-2''), 73.44 (C-4', C-5), 73.78 (C-3'), 73.85 (C-5'), 75.04 (OCH_2Ph), 75.60 (C-4''), 100.26 (C-1''), 101.19 (C-1'), 101.38 (C-1), 101.44 (PhCH), 126.36, 127.58, 128.21, 128.24, 128.34, 128.40, 128.51, 128.70, 128.83, 128.95, 129.17, 129.20, 129.51, 129.59, 128.67, 129.77, 130.02, 133.04, 133.24, 133.50, 137.31, 137.67, 165.12, 165.24, 165.41, 165.61, 165.63, 165.04. $C_{77}H_{71}N_3O_{22}$ (1389.45): MS (MALDI) m/z = 1412.53 $[M + Na]^+$, 1428.68 $[M + K]^+$.

3-Azidopropyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,3-di-*O*-benzoyl-4-*O*-acetyl-6-*O*-(2-*O*-acetyl-4,6-*O*-benzylidene-3-*O*-(9-fluorenylmethoxycarbonyl)-β-D-galactopyranosyl)-β-D-galactopyranosyl)-β-D-galactopyranoside (39)

A solution of a mixture (0.058 g) of **36** and the 4'-OH version of **36** in pyridine and in acetic anhydride (0.1 mL, 1.06 mmol) was stirred at room temperature for 18 h. The reaction was quenched by the addition of MeOH (0.5 mL), diluted with toluene, and concentrated *in vacuo*. The resulting residue was dissolved in CH_2Cl_2 and washed subsequently with 1M HCl, saturated aqueous NaHCO3, and brine. The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo*. The residue was purified using flash silica gel column chromatography (hexanes:EtOAc, 4:1 → 3:2, v/v) to afford **39** (0.035 g) as a white amorphous, solid: TLC R_f = 0.41 (hexane/EtOAc, 1:1). $C_{82}H_{75}N_3O_{25}$ (1501.47): MS (MALDI) m/z = 1525.39 $[M + Na]^+$, 1541.90 $[M + K]^+$.

3-Azidopropyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,3-di-*O*-benzoyl-4-*O*-acetyl-6-*O*-(2-*O*-acetyl-4,6-*O*-benzylidene-β-D-galactopyranosyl)-β-D-galactopyranosyl)-β-D-galactopyranoside (42)

A couple of drops of triethylamine was added to a solution of **39** (0.035 g, 0.0233 mmol) in CH_2Cl_2 (1 mL), and the solution was stirred at room temperature 2 h. The reaction was diluted with toluene, and concentrated *in vacuo*. The resulting residue was dissolved in CH_2Cl_2 and washed subsequently with 1M HCl, saturated aqueous NaHCO3, and brine. The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo*. The residue was purified using flash silica gel column chromatography (hexanes:EtOAc, 3:2 → 1:1, v/v) to afford **42** (0.019 g, 64%) as a white amorphous, solid: TLC R_f = 0.24 (hexane/EtOAc, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.35 and 1.43 (ABXYX'$_2$, 2H, $OCH_2CH_2CH_2N_3$), 1.89 (s, 3H, $COCH_3$), 2.05 (s, 3H, $COCH_3$), 2.98 (t, J = 6.8 Hz, 2H, $OCH_2CH_2CH_2N_3$), 3.17 and 3.46 (ABX_2, 2H, $OCH_2CH_2CH_2N_3$), 3.42 (s, 1H, H-5''), 3.67 (dd, $J_{2,3}$ = 9.9 Hz, $J_{3,4}$ = 3.5 Hz, 1H, H-3''), 3.73 (m, 3H, H-5', H-6, H-6'), 4.00 (m, 4H, H-5, H-6, H-6', H-6''), 4.13 (d, $J_{3,4}$ = 3.5 Hz, 1H, H-4''), 4.30 (AB, $J_{6,6}$ = 12.3 Hz, 1H, H-6''), 4.42 (d, $J_{1,2}$ = 8.0 Hz, 1H, H-1''), 4.55 and 4.67 (2 d, $J_{1,2}$ = 7.8 Hz, each 1H, H-1, H-1'), 4.96 (dd, $J_{1,2}$ = 8.0 Hz, $J_{2,3}$ = 9.9 Hz, 1H, H-2''), 5.33 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.6 Hz, 1H, H-3'), 5.42 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3), 5.47 (s, 1H, PhC*H*), 5.60 (t-like, 3H, H-2, H-2', H-4'), 5.75 (d, $J_{3,4}$ = 3.3 Hz, 1H, H-4), 7.15 (m, 2H, Ar), 7.24-7.34 (m, 10H, Ar), 7.37-7.47 (m, 7H, Ar), 7.54 (t, J = 7.5 Hz, 1H, Ar), 7.67 (d, J = 6.9 Hz, 2H, Ar), 7.79 (d, J = 6.9 Hz, 2H, Ar), 7.86 (d, J = 6.9 Hz, 2H, Ar), 7.90 (d, J = 6.9 Hz, 8H, Ar), 8.01 (d, J = 6.9 Hz, 2H, Ar). $C_{82}H_{75}N_3O_{25}$ (1279.40): MS (MALDI) *m/z* = 1301.81 $[M + Na]^+$, 1317.77 $[M + K]^+$.

3-Azidopropyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,3-di-*O*-benzoyl-4-*O*-acetyl-6-*O*-(4,6-*O*-benzylidene-3-*O*-(9-fluorenylmethoxycarbonyl)-2-*O*-(3,4-di-*O*-acetyl-2-*O*-benzyl-α-L-fucopyranosyl)-β-D-galactopyranosyl)-β-D-galactopyranosyl)-β-D-galactopyranoside (50)

A mixture of the glycosyl donor **34** (15.3 mg, 0.0399 mmol), the acceptor **36** (53.0 mg, 0.0363 mmol), and powdered 4 Å molecular sieves (70 mg) in CH_2Cl_2 (0.75 mL) was stirred at room temperature for 30 min and then cooled to 0 °C. NIS (10.6 mg, 0.0472 mmol), followed by TMSOTf (0.0014 mL, 0.0076 mmol), was added. The reaction mixture was stirred for 30 min and then quenched by the addition of pyridine. The suspension was diluted with CH_2Cl_2 (10 mL) and filtered through a pad of Celite, and the filtrate was washed successively with 10% $Na_2S_2O_3$ and brine. The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo* to give a residue, which was purified using flash silica gel column chromatography (hexanes:EtOAc, 3:2, v/v) to give **50** (15 mg, 23%) as a white, amorphous solid: TLC R_f = 0.59 (hexane/EtOAc, 1:1). $C_{83}H_{85}N_3O_{22}Si$ (1779.58): MS (MALDI) *m/z* = 1802.36 $[M + Na]^+$, 1818.44 $[M + K]^+$.

3-Azidopropyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,3-di-*O*-benzoyl-4-*O*-acetyl-6-*O*-(3-*O*-benzoyl-4,6-*O*-benzylidene-2-*O*-(3,4-di-*O*-acetyl-2-*O*-benzyl-α-L-fucopyranosyl)-β-D-galactopyranosyl)-β-D-galactopyranosyl)-β-D-galactopyranoside (51)

A mixture of the glycosyl donor **34** (13 mg, 0.0342 mmol), the acceptor **38** (23.0 mg, 0.0171 mmol), and powdered 4 Å molecular sieves (30 mg) in CH_2Cl_2 (0.60 mL) was stirred at room temperature for 30 min and then cooled to -20 °C. NIS (3.54 mg, 0.0342 mmol), followed by TfOH (0.001 mL, 0.0017 mmol), was added. The reaction mixture was stirred for 30 min and then quenched by the addition of triethylamine. The suspension was diluted with CH_2Cl_2 (10 mL) and filtered through a pad of Celite, and the filtrate was washed successively with 10% $Na_2S_2O_3$ and brine. The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo* to give a residue, which was purified using flash silica gel column chromatography (hexanes:EtOAc, 2:1 → 1:1, v/v) to give **51** (25.6 mg, 90%) as a white,

amorphous solid: TLC R_f = 0.38 (hexane/EtOAc, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.02 (d, J = 8.4 Hz, 2H, Ar), 7.96 (d, J = 8.4 Hz, 2H, Ar), 7.91 (d, J = 8.4 Hz, 4H, Ar), 7.81 (d, J = 8.4 Hz, 2H, Ar), 7.73 (d, J = 8.4 Hz, 2H, Ar), 7.55-7.11 (m, 28H, Ar), 6.87 (m, 2H, Ar), 5.73 (d, $J_{3,4}$ = 1.5 Hz, 1H, H-4), 5.54 (d, $J_{3,4}$ = 1.5 Hz, 1H, H-4'), 5.54 (dd, $J_{1,2}$ = 4.0 Hz, $J_{2,3}$ = 5.1 Hz, 1H, H-2), 5.49 (dd, $J_{1,2}$ = 4.0 Hz, $J_{2,3}$ = 5.3 Hz, 1H, H-2'), 5.45 (s, 1H, PhC*H*), 5.35 (dd, $J_{2,3}$ = 5.1 Hz, $J_{3,4}$ = 1.5 Hz, 1H, H-3), 5.20 (dd, $J_{2,3}$ = 5.3 Hz, $J_{3,4}$ = 1.5 Hz, 1H, H-3'), 5.63 (dd, $J_{1,2}$ = 4.0 Hz, $J_{2,3}$ = 5.0 Hz, 1H, H-2''), 4.56 (d, $J_{1,2}$ = 4.0 Hz, 1H, H-1''), 4.52 (d, $J_{1,2}$ = 4.0 Hz, 1H, H-1'), 4.48 (d, $J_{1,2}$ = 4.0 Hz, 1H, H-1), 4.30 and 3.98 (AB, $J_{6,6}$ = 6.0 Hz, 2H, H-6'', H-6''), 4.12 (d, $J_{3,4}$ = 1.5 Hz, 1H, H-4''), 3.95 (AB*X*, $J_{5,6}$ = 1.5 Hz, $J_{5,6}$ = 3.9 Hz, 1H, H-5), 3.92 (*A*BX, $J_{5,6}$ = 1.5 Hz, $J_{6,6}$ = 5.3 Hz, 1H, H-6), 3.86 (t, $J_{5,6}$ = 3.0 Hz, 1H, H-5'), 3.80 (dd, $J_{2,3}$ = 5.1 Hz, $J_{3,4}$ = 1.5 Hz, 1H, H-3''), 3.73 and 3.65 (ABX, $J_{5,6}$ = 3.0 Hz, $J_{6,6}$ = 5.7 Hz, 2H, H-6', H-6'), 3.61 (A*B*X, $J_{5,6}$ = 3.9 Hz, $J_{6,6}$ = 5.3 Hz, 1H, H-6), 3.45 and 3.30 (2 m, 2H, OC*H*$_2$CH$_2$CH$_2$N$_3$), 3.54 (s, 1H, H-5''), 3.06 (t, J = 6.8 Hz, OCH$_2$CH$_2$C*H*$_2$N$_3$), 2.03 (s, 3H, COC*H*$_3$), 2.00 (s, 3H, COC*H*$_3$), 1.77 (s, 3H, COC*H*$_3$), 1.55 (m, 2H, OCH$_2$C*H*$_2$CH$_2$N$_3$), 0.90 (d, $J_{5,6}$ = 6.6 Hz, 3H, H-6'''). ^{13}C NMR (75 MHz, $CDCl_3$): δ 177.47, 170.34, 169.93, 169.57, 165.41, 165.37, 165.36, 165.25, 165.09, 164.93, 138.16, 137.34, 133.40, 133.21, 133.14, 132.71, 130.09, 129.98, 129.72, 129.65, 129.58, 129.41, 129.26, 129.21, 129.15, 129.05, 128.85, 128.52, 128.36, 128.30, 128.18, 128.14, 128.00, 127.24, 127.14, 126.20, 101.24 (Ph*C*H), 101.21 (C-1'), 100.83 (C-1), 100.58 (C-1''), 100.02 (C-1'''), 79.88, 77.20, 75.41, 72.99, 72.70, 72.65, 71.85, 71.74, 71.63, 71.42, 69.94, 69.88, 69.67, 69.34, 69.00, 68.70, 68.40, 67.75, 66.50, 66.12, 65.55, 65.08, 47.77 (OCH$_2$CH$_2$*C*H$_2$N$_3$), 28.70 (OCH$_2$*C*H$_2$CH$_2$N$_3$), 20.62(CO*C*H$_3$), 20.51 (CO*C*H$_3$, CO*C*H$_3$), 16.89 (C-6'''). $C_{80}H_{73}N_3O_{24}$ (1661.54): HR-MS (MALDI) *m/z* = 1684.80 $[M + Na]^+$, 1700.77 $[M + K]^+$.

3-Azidopropyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,3-di-*O*-benzoyl-4-*O*-benzyl-6-*O*-(2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-(3,4-di-*O*-acetyl-2-*O*-benzyl-α-L-fucopyranosyl)-β-D-galactopyranosyl)-β-D-galactopyranosyl)-β-D-galactopyranoside (54)

A mixture of the glycosyl donor **34** (36 mg, 0.0935 mmol) and the acceptor **41** (26.0 mg, 0.0187 mmol) was dissolved in toluene and concentrated *in vacuo* three times. The residue was then dried 18 h under high vacuum in a desiccator in the presence of the desiccant P_2O_5. The residue was dissolved in CH_2Cl_2 (0.95 mL) and was stirred at room temperature for 30 min and then cooled to -20 °C. NIS (23 mg, 0.103 mmol), followed by TMSOTf (2.8 μL, 0.015 mmol), was added. The reaction mixture was stirred for 30 min during which time the mixture was allowed to warm to room temperature. The reaction was quenched by the addition of triethylamine (2.1 μL). The reaction solution was diluted with CH_2Cl_2 (10 mL) and was washed successively with 10% $Na_2S_2O_3$ and brine. The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo* to give a residue, which was purified using flash silica gel column chromatography (hexanes:EtOAc, 8:1 → 3:2, v/v) to give **54** (23 mg, 71%) as a white, amorphous solid: TLC R_f = 0.14 (hexane/EtOAc, 4:5). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.07 (d, J = 7.5 Hz, 2H, Ar), 7.95 (d, J = 7.5 Hz, 2H, Ar), 7.91 (d, J = 7.5 Hz, 2H, Ar), 7.87 (d, J = 7.5 Hz, 2H, Ar), 7.82 (d, J = 7.5 Hz, 2H, Ar), 7.73 (d, J = 7.5 Hz, 2H, Ar), 7.5 (d, J = 7.2 Hz, 1H, Ar), 7.51-7.37 (m, 10H, Ar), 7.35-7.28 (m, 11H, Ar), 7.26-7.18 (m, 6H, Ar), 7.15-7.13 (m, 5H, Ar), 6.88 (m, 2H, Ar), 5.75 (d, $J_{3,4}$ = 3.3 Hz, 1H, H-4), 5.73 (dd, $J_{1,2}$ = 7.8 Hz, $J_{2,3}$ = 10.2 Hz, 1H, H-2'), 5.62 (dd, $J_{1,2}$ = 8.1 Hz, $J_{2,3}$ = 10.5 Hz, 1H, H-2), 5.56 (dd, $J_{1,2}$ = 7.8 Hz, $J_{2,3}$ = 10.2 Hz, 1H, H-2'), 5.50 (s, 1H, PhC*H*), 5.43 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3), 5.23 (dd, $J_{2,3}$ = 10.2 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3'), 5.21 (d, $J_{3,4}$ = 3.3 Hz, 1H, H-4'''), 5.16 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3'''), 4.95 (d, $J_{1,2}$ = 3.3 Hz, 1H, H-1'''), 4.77 (d, $J_{1,2}$ = 7.8 Hz, 1H, H-1''), 4.65 (AB,

$J_{A,B}$ = 6.0 Hz, 2H, OCH_2Ph), 4.58 (d, $J_{1,2}$ = 8.1 Hz, 1H, H-1), 4.54 (d, $J_{1,2}$ = 7.8 Hz, 1H, H-1'), 4.39-4.29 (m, 3H, H-4'', H-5''', H-6''), 4.13-4.02 (m, 6H, H-4', H-5, H-6', H-6'', OCH_2Ph), 3.96 (m, 1H, H-6), 3.92 (dd, $J_{2,3}$ = 10.2 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3''), 3.84-3.65 (m, 3H, H-5', H-6, H-6'), 3.60 (dd, $J_{1,2}$ = 3.3 Hz, $J_{2,3}$ = 10.2 Hz, 1H, H-2'''), 3.56 and 3.28 (2 m, 2H, OCH_2CH$_2$CH$_2$N$_3$), 3.52 (s, 1H, H-5''), 3.03 (t, J = 6.9 Hz, OCH$_2$CH$_2$CH_2N$_3$), 2.01 (s, 1H, COCH_3), 1.78 (s, 1H, COCH_3), 1.49 (m, 2H, OCH$_2$CH_2CH$_2$N$_3$), 0.91 (d, $J_{5,6}$ = 6.3 Hz, 3H, H-6'''). ^{13}C NMR (75 MHz, CDCl$_3$): δ 170.31, 169.58, 165.55, 165.52, 165.41, 165.26, 165.12, 164.90, 138.21, 137.89, 137.31, 133.45, 133.25, 133.16, 133.13, 132.97, 132.68, 130.12, 130.02, 129.78, 129.72, 129.68, 129.60, 129.24, 129.14, 129.08, 128.83, 128.53, 128.40, 128.30, 128.28, 128.21, 128.15, 128.12, 128.01, 127.41, 127.23, 127.12, 126.19, 101.39 (Ph*C*H), 101.19 (C-1'), 101.18 (C-1), 100.56 (C-1''), 100.18 (C-1'''), 80.09 (C-3''), 75.59 (C-4''), 75.10 (O*C*H$_2$Ph), 73.87 (C-4'), 73.70 (C-3'), 73.42 (C-5), 73.26 (C-5'), 72.71 (C-2'''), 71.86 (O*C*H$_2$Ph), 71.73 (C-3), 71.42 (C-4'''), 70.33 (C-2''), 70.16 (C-2'), 69.99 (C-3'''), 69.84 (C-2), 69.01 (C-4), 68.96 (C-6''), 68.38 (C-6), 66.57 (C-5), 66.25 (O*C*H$_2$CH$_2$CH$_2$N$_3$), 65.56 (C-6'), 65.06 (C-5'''), 47.78 (OCH$_2$CH$_2$*C*H$_2$N$_3$), 28.70 (OCH$_2$*C*H$_2$CH$_2$N$_3$), 20.09(CO*C*H$_3$), 20.08 (CO*C*H$_3$), 15.97 (C-6'''). C$_{94}$H$_{91}$N$_3$O$_{28}$ (1710.73): HR-MS (MALDI) *m/z* = 1732.8136 [M + Na]$^+$, 1748.7913 [M + K]$^+$.

3-Azidopropyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,3-di-*O*-benzoyl-4-*O*-acetyl-6-*O*-(2-*O*-acetyl-4,6-*O*-benzylidene-3-*O*-(3,4-di-*O*-acetyl-2-*O*-benzyl-α-L-fucopyranosyl)-β-D-galactopyranosyl)-β-D-galactopyranosyl)-β-D-galactopyranoside (55)

A mixture of the glycosyl donor **34** (6.24 mg, 0.0163 mmol) and the acceptor **42** (19.0 mg, 0.0148 mmol) was dissolved in toluene and concentrated *in vacuo* three times. The residue was then dried 18 h under high vacuum in a desiccator in the presence of the desiccant P_2O_5. The residue was dissolved in CH_2Cl_2 (0.75 mL) and was stirred at room temperature for 30 min and

then cooled to 0 °C. NIS (4.34 mg, 0.0193 mmol), followed by TMSOTf (0.41 μL, 0.00223 mmol), was added. The reaction mixture was stirred for 30 min and then quenched by the addition of triethylamine (0.31 μL). The reaction solution was diluted with CH_2Cl_2 (10 mL) and was washed successively with 10% $Na_2S_2O_3$ and brine. The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo* to give a residue, which was purified using flash silica gel column chromatography (hexanes:EtOAc, 8:1 → 3:2, v/v) to give **55** (6.8 mg, 70%) as a white, amorphous solid: TLC R_f = 0.12 (hexane/EtOAc, 1:1). $C_{83}H_{85}N_3O_{22}Si$ (1599.53): MS (MALDI) *m/z* = 1623.73 $[M + Na]^+$, 1640.76 $[M + K]^+$.

3-Azidopropyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,3-di-*O*-benzoyl-4-*O*-acetyl-6-*O*-(2,3-di-*O*-benzoyl-4-*O*-benzyl-6-*O*-(3,4-di-*O*-acetyl-2-*O*-benzyl-α-L-fucopyranosyl)-β-D-galactopyranosyl)-β-D-galactopyranosyl)-β-D-galactopyranoside (58)

A mixture of the glycosyl donor **34** (31.6 mg, 0.0826 mmol), the acceptor **45** (108.8 mg, 0.0751 mmol), and powdered 4 Å molecular sieves (50 mg) in Et_2O (1.2 mL) and CH_2Cl_2 (0.3 mL) was stirred at room temperature for 30 min and then cooled to 0 °C. NIS (22 mg, 0.0976 mmol), followed by TMSOTf (2.1 μL, 0.0113 mmol), was added. The reaction mixture was stirred for 30 min and then quenched by the addition of triethylamine (1.6 μL). The suspension was diluted with CH_2Cl_2 (10 mL) and filtered through a pad of Celite, and the filtrate washed successively with 10% $Na_2S_2O_3$ and brine. The organic layer was dried ($MgSO_4$), filtered, and the filtrate was concentrated *in vacuo* to give a residue, which was purified using flash silica gel column chromatography (hexanes:EtOAc, 3:1 → 3:2, v/v) to give [an α/β mixture (4:1)] of **58** (95 mg, 72%) as a white, amorphous solid: TLC R_f = 0.44 (hexane/EtOAc, 3:2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.88 (d, $J_{5,6}$ = 6.3 Hz, 3H, H-6’’’, H-6’’’, H-6’’’), 1.43 and 1.49 (m, 2H, $OCH_2CH_2CH_2N_3$), 1.90 (s, 3H, $COCH_3$), 1.93 (s, 3H, $COCH_3$), 2.02 (s, 3H, $COCH_3$), 2.98 (t, *J*

= 7.5 Hz, 2H, $OCH_2CH_2CH_2N_3$), 3.24 and 3.57 (ABX_2, 2H, $OCH_2CH_2CH_2N_3$), 3.61-3.87 (m, 9H, H-2’’’, H-5’, H-5’’, H-5’’’, H-6, H-6’, H-6’, H-6’’, H-6’’), 3.96 (m, 2H, H-5, H-6), 4.14 (d, $J_{3,4}$ = 3.0 Hz, 1H, H-4’’), 4.44 and 4.80 (AB, $J_{6,6}$ = 11.7 Hz, 2H, CH_2Ph), 4.480 (m, 5H, H-1, H-1’, H-1’’, CH_2Ph), 4.82 (s, 1H, H-1’’’), 5.11 (d, $J_{3,4}$ = 3.0 Hz, 1H, H-4’’’), 5.18 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.0 Hz, 1H, H-3’’’), 5.23 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.0 Hz, 1H, H-3’’), 5.30 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.0 Hz, 1H, H-3’), 5.41 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.3 Hz, 1H, H-3), 5.52 (dd, $J_{1,2}$ = 7.8 Hz, $J_{2,3}$ = 10.5 Hz, 1H, H-2), 5.52 (d, $J_{3,4}$ = 3.0 Hz, 1H, H-4’), 5.57 (dd, $J_{1,2}$ = 7.8 Hz, $J_{2,3}$ = 10.5 Hz, 1H, H-2’’), 5.68 (d, $J_{3,4}$ = 3.0 Hz, 1H, H-4), 5.69 (dd, $J_{1,2}$ = 7.8 Hz, $J_{2,3}$ = 10.5 Hz, 1H, H-2’), 7.14 (m, 3H, Ar), 7.20-7.33 (m, 20H, Ar), 7.36-7.45 (m, 8H, Ar), 7.67 (d, J = 7.5 Hz, 2H, Ar), 7.74 (d, J = 7.2 Hz, 2H, Ar), 7.85 (m, 8H, Ar), 7.92 (d, J = 6.9 Hz, 8H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.73 (C-6’’’), 20.42 ($COCH_3$), 20.62 ($COCH_3$), 20.81 ($COCH_3$), 28.70 ($OCH_2CH_2CH_2N_3$), 47.75 ($OCH_2CH_2CH_2N_3$), 64.51, 65.98, 66.10, 66.48, 67.64, 68.03, 68.68, 69.57, 69.73, 69.83, 69.90, 71.39, 71.56, 72.64, 72.76, 72.96, 73.07, 73.21, 74.24, 74.30, 74.97, 97.90 (H-1’’’), 100.89 (H-1’’), 101.04 (H-1’), 101.23 (H-1), 127.59, 127.67, 127.78, 127.83, 128.18, 128.31, 128.39, 128.44, 128.85, 129.01, 129.11, 129.26, 129.35, 129.58, 129.65, 129.84, 129.98, 133.01, 133.17, 133.34, 137.82, 138.20, 165.15, 165.26, 165.33, 165.72, 169.59, 170.04, 170.46. $C_{96}H_{93}N_3O_{30}$ (1767.5844): HR-MS (MALDI) *m/z* = 1790.7355 $[M + Na]^+$, 1806.7070 $[M + K]^+$.

3-Aminopropyl 6-*O*-(6-*O*-(2-*O*-(α-L-fucopyranosyl)-β-D-galactopyranosyl)-β-D-galactopyranosyl)-β-D-galactopyranoside (3)

A solution of **51** (36 mg, 0.0217 mmol) in MeOH (10 mL) was adjusted to pH 12 with sodium methoxide solution. The solution was stirred at room temperature for 3 h, and then the solution was returned to neutral pH using weakly acidic (pH 5) Amberlite resin. The reaction solution

was then concentrated *in vacuo*. The residue was purified by passing the materials through a small amount of Iatrobeads (isopropanol:NH_4OH, 8:1 → 4:1, v/v) to give the desired intermediate: $C_{41}H_{57}N_3O_{20}$ (911.35): HR-MS (MALDI) *m/z* = 934.2299 $[M + Na]^+$. Pd/C (10%, 1.5 times the weight of the starting material) was added to a solution of the intermediate a mixture of *t*-BuOH, AcOH, and H_2O (20:2:1, v/v/v, 2-5 mL) under Ar. The mixture was placed under an atmosphere of H_2 and stirred for 18 h. TLC analysis *i*-PrOH/28% NH4OH (1:2, v/v) indicated the presence of a single compound. The solvents were coevaporated with toluene. The residue was dried *in vacuo* for several hours. The recovered materials were passed through a small amount of Iatrobeads (isopropanol:NH_4OH, 1:2, v/v). Fractions containing the products were collected and concentrated *in vacuo*. Acetic acid was added the products until pH 4.5. The products were freeze-dried to afford the fully deprotected tetrasaccharide **3** (8.0 mg, 52%). TLC R_f = 0.28 (isopropanol:NH_4OH, 1:2). ^{1}H NMR (500 MHz, D_2O): δ = 5.05 (d, $J_{1,2}$ = 2.7 Hz, 1H, H-1’’’), 4.39 (d, $J_{1,2}$ = 4.2 Hz, 1H, H-1’’), 4.35 (d, $J_{1,2}$ = 4.5 Hz, 1H, H-1’), 4.33 (d, $J_{1,2}$ = 5.4 Hz, 1H, H-1), 4.07 (d, $J_{5,6}$ = 4.2 Hz, 1H, H-5’’’), 3.91 (m, 4H, ?, ?, ?, $OCH_2CH_2CH_2N_3$), 3.83 (m, 6H, ?, ?, ?, ?, ?, ?), 3.75 (m, 1H, $OCH_2CH_2CH_2N_3$), 3.71 (d, $J_{3,4}$ = 1.8 Hz, 1H, H-4[?]), 3.66 (m, 3H, H-2’’’, ?, ?), 3.59 (m, 3H, H-2’’, ?, ?), 3.54 (dd, $J_{2,3}$ = 6.0 Hz, $J_{3,4}$ = 2.1 Hz, 1H, H-3[?]), 3.41 (m, 3H, H-2, H-2’, ?), 3.23 (s, 1H, ?), 3.06 (t, *J* = 6.8 Hz, $OCH_2CH_2CH_2N_3$), 1.55 (m, 2H, $OCH_2CH_2CH_2N_3$), 0.90 (d, $J_{5,6}$ = 6.6 Hz, 3H, H-6’’’). ^{13}C NMR (75 MHz, $CDCl_3$): δ 177.47, 170.34, 169.93, 169.57, 165.41, 165.37, 165.36, 165.25, 165.09, 164.93, 138.16, 137.34, 133.40, 133.21, 133.14, 132.71, 130.09, 129.98, 129.72, 129.65, 129.58, 129.41, 129.26, 129.21, 129.15, 129.05, 128.85, 128.52, 128.36, 128.30, 128.18, 128.14, 128.00, 127.24, 127.14, 126.20, 101.24 (PhCH), 101.21 (C-1’), 100.83 (C-1), 100.58 (C-1’’), 100.02 (C-1’’’), 79.88, 77.20, 75.41, 72.99, 72.70, 72.65, 71.85, 71.74, 71.63, 71.42, 69.94, 69.88, 69.67, 69.34, 69.00, 68.70, 68.40,

67.75, 66.50, 66.12, 65.55, 65.08, 47.77 ($OCH_2CH_2CH_2N_3$), 28.70 ($OCH_2CH_2CH_2N_3$), 20.62($COCH_3$), 20.51 ($COCH_3$, $COCH_3$), 16.89 (C-6’’’). $C_{27}H_{49}NO_{20}$ (707.28): HR-MS (MALDI) *m/z* = 730.2106 $[M + Na]^+$, 746.2016 $[M + K]^+$.

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