STEREOSELECTIVE GLYCOSYLATIONS VIA CHIRAL AUXILIARIES

by

HAI YANG

(Under the Direction of Geert-Jan Boons)

ABSTRACT

In this study, three generations of chiral auxiliary are synthesized and attached to glucose and galactose. The donors containing these chiral auxiliary are synthesized and glycosylations with a variety of glycosyl acceptors are conducted. The glycosylation results showed that a glycosyl donor substituted with a chiral auxiliary can be employed for the stereoselective introduction of 1, 2-*cis* glycosides such as α-glucosides and α-galactosides. The neighboring group participation by the chiral auxiliary leads to a quasi-stable anomeric sulfonium ion, which due to steric and electronic factors, is formed as a *trans*-decalin ring system. Displacement of the sulfonium ion by a glycosyl acceptor leads to the stereoselective formation of α-glycosides. The use of this new method in combination with traditional neighboring group participation by esters to introduce β-glycosides makes it possible to synthesize a wide variety of complex carbohydrates with complete anomeric control.

INDEX WORDS: Chiral Auxiliary, Glycosylations, 1, 2-*cis* Glycosides, Neighboring Group Participation, Carbohydrate

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"It was the best of times, it was the worst of times."

Charles Dickens

To my family

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LIST OF ABBREVIATIONS

Ac……acetyl

Ac_2O……..acetic anhydride

All……...allyl

Bn……benzyl

Bu_4NBr……..tetrabutyl ammonium bromide

Bz……...benzoyl

CSA……camphor-2-sulphonic acid

DBU…….1,8-diazabicyclo[5.4.0]undec-7-ene

DCM……...methylene chloride

DMAP……. *N*,*N*-dimethylaminopyridine

DMDO…….dimethyl dioxilane

DMF……. *N*,*N*-dimethylformamide

DMTST…..dimethyl(methylthio)sulfonium triflate

DTBMP…..2,6-di-*tert*-butyl-4-methylpyridine

eq……...equivalent

Et……ethyl

EtOH……..ethanol

Fuc……...fucoside

Gal……...galactoside

COSY…….Correlation Homonuclear Spectroscopy

Glc……glucose

h…….hour

IDCP……..……iodonium dicollidine perchlorate

Hz……..hertz

HMBC.....Heteronuclear Multiple Bond Correlation

m……..multiplet

m/z……...…….…….…….mass to charge ratio

Man……..mannoside

MALDI-TOF……..mass assisted laser desorption ionization time of flight

Me……...methyl

MeOH…….methanol

MeOTf…….…..…methyl trifluoromethanesulfonate

Min…….….minute

mM……millimolar

mmol……...millimole

MS……...molecular sieves

Ms…….....methanesulfonyl

NBS……..……*N*-bromosuccinimide

NIS……..*N*-iodosuccinimide

NMR……..…….Nuclear Magnetic Resonance

NOESY……..…. Nuclear Overhauser Enhancement Spectroscopy

NPth……..……...……...*N*-phthalimido

Naph……..……..……2-naphthalenemethanol

Pd/C…….....palladium on charcoal

Ph……..……...……phenyl

Phth……...phthalimidoyl

q……..quartet

Rf…….…..retention factor

RT…….....room temperature

s……...singlet

SE……..2-trimethylsilylethanol

SEt……thioethyl

t……triplet

TBAF……...…….……..tetrabutylammonium fluoride

TBDMS……...…...…...*tert*-butyl dimethylsilyl

TBDPS……...……*tert*-butyldiphenylsilyl

TFA…….……trifluoroacetyl

Tf……trifluoromethanesulfonyl

TfOH…….……...……trifluoromethanesulfonic acid

THF…….…..tetrahydrofuran

TLC……..……thin layer chromatography

TMSOTf…….....……trimethylsilyl trifluoromethanesulfonate

TOCSY…… Total Correlation Spectroscopy Experiment

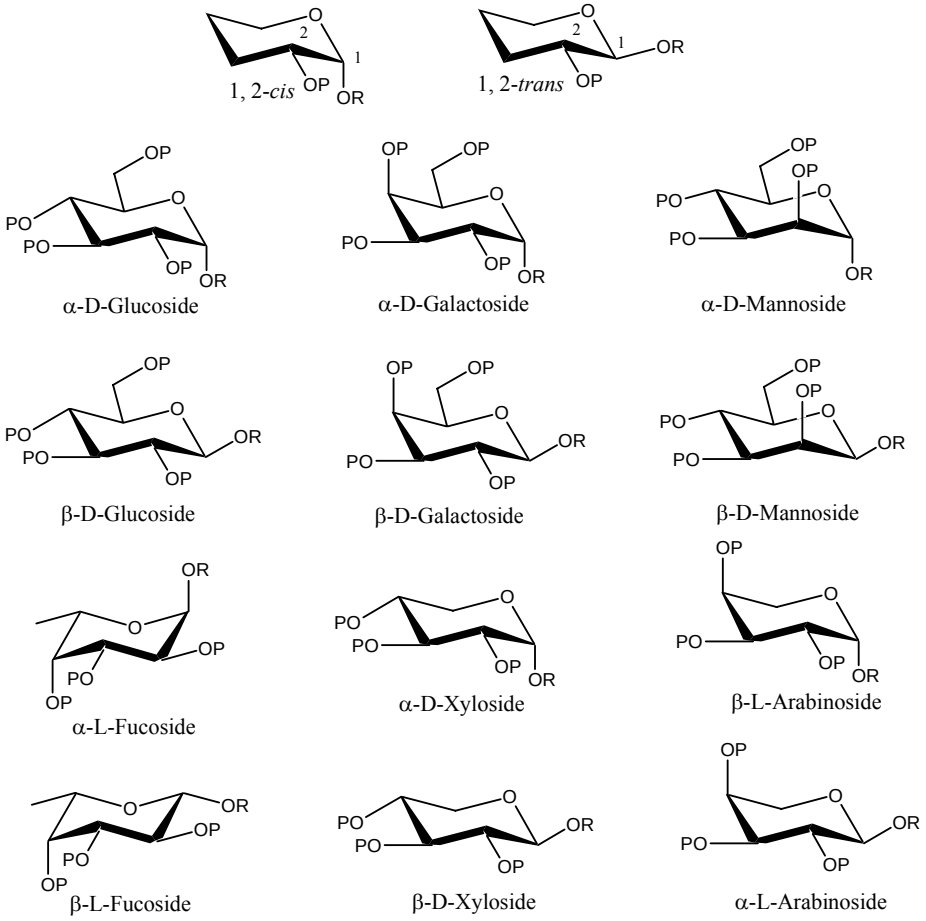
Ts…….…….……*p*-toluenesulfonyl

CHAPTER 1

INTRODUCTION

It is now well established that protein- and lipid- bound saccharides play essential roles in molecular processes such as fertilization, embryogenesis, neuronal development, hormonal activities, the proliferation of cells and their organization of cells into specific tissues.[1-3] Nature uses the glycosylation of peptides to alter their properties as glycosylated proteins behave in a clearly different manner from that of their non-glycosylated counterparts in terms of solubility and stability, for instance.[4] Many glycoproteins and glycolipids are embedded in the outer surface of mammalian cells. The carbohydrate coat surrounding a cell is characteristic of a particular species, the cell type, and its developmental status. The interactions of saccharides with proteins or lipids play roles in the invasion and attachment of pathogens, inflammation, blood-group immunology and xenotransplantation. It has been found that remarkable changes in the cell-surface carbohydrates occur with tumor progression, which often leads to metastasis. One of the major obstacles to advances in glycobiology is the lack of pure and structurally well defined carbohydrates and glycoconjugates. These compounds are often found in low concentrations and in microheterogeneous forms, which renders them difficult to isolate and characterize. In many cases, well defined carbohydrates can only be obtained by organic synthesis.[5]

Although many advances have been made in the synthesis of complex carbohydrates over the past two decades, it should be emphasized that each oligosaccharide synthesis remains an independent challenge, the completion of which requires systematic research. The fact remains that no universal reaction conditions exist for carbohydrate synthesis.[6]



P = Protecting Goup; R = Generic Aglycon Residue

Figure 1

The carbohydrates found in nature mostly exist in the form of polysaccharides, glycoconjugates (glycoproteins or glycolipids) and glycosides. The monosaccharide units of these carbohydrates are linked together or with an aglycon *via O*-glycosidic bonds. There are two major types of *O*-glycosides, which are generally defined as α- and β-, or 1, 2-*cis* and 1, 2-*trans* glycosides. The 1, 2-*cis* glycosyl residues (for example, α-glycosides for D-glucose, D-galactose, L-fucose, D-xylose and β-glycosides for D-mannose, L-arabinose, Figure 1) and their 1, 2-*trans* counterparts (β-glycosides for D-glucose, D-galactose, α-glycosides for D-mannose) are equally

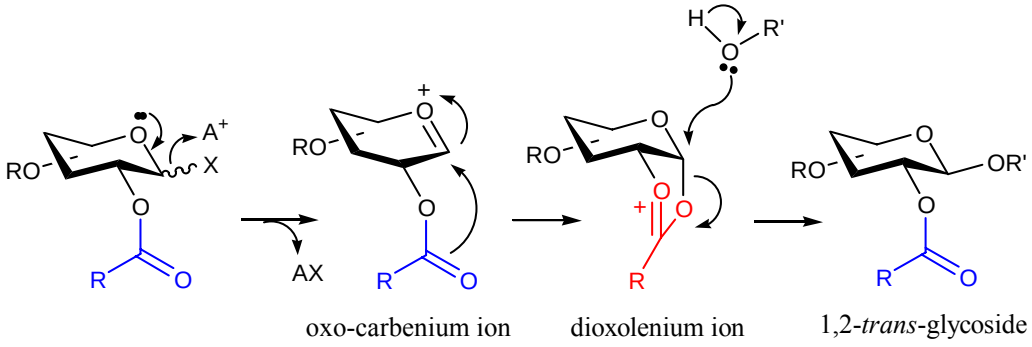
important components of a large variety of natural compounds with biological significance and therapeutic potential.

Although much progress has been made in complex carbohydrate synthesis in the past two decades, the construction of oligosaccharides remains time consuming.[7] Solid phase syntheses[8, 9] and one-pot multi-step glycosylations[10] are two major approaches currently used to simplify the preparation of complex carbohydrates. Despite the inherent simplicity of the two strategies, both suffer from a lack of stereoselectivity during glycosylation. Often the glycosylation reactions give mixtures of the two possible anomers: the 1, 2 *cis* and 1, 2 *trans* glycosides. These anomers must be separated after each glycosylation step. If the anomers are not separated, the final product will be too complicated for analysis and unsuitable for biological studies. As a result, routine carbohydrate synthesis will only be possible when reliable and powerful stereoselective glycosylations become available.

In a natural environment the stereoselectivity of glycosylation is not problematic because specific enzymes are responsible for the selectivity of the glycosylations. There is no general and reliable methodology, however, for the stereoselective chemical synthesis of oligosaccharides. Thus chemical *O*-glycosylation with complete stereoselectivity is regarded as one of the primary challenges associated with carbohydrate synthesis.

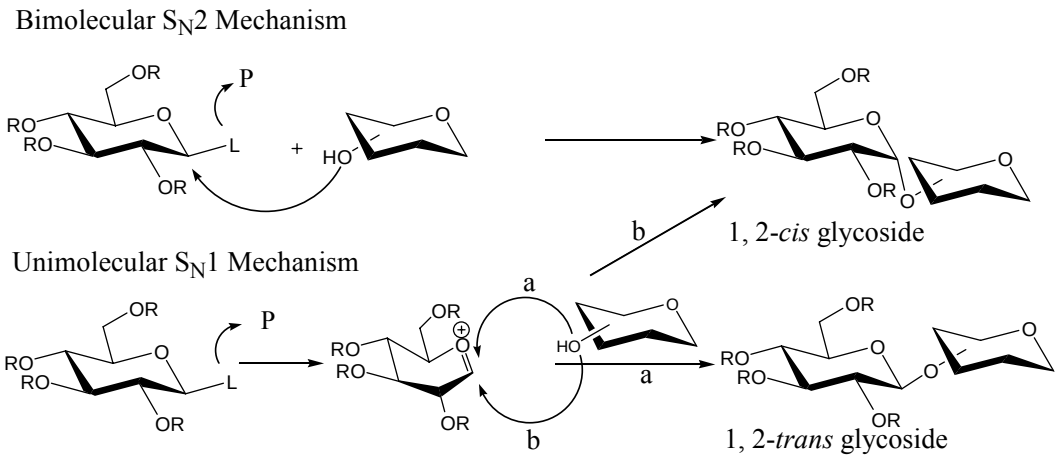
It is well-established that the most reliable method for the generation of 1, 2-*trans*-glycosides (such as α-D-mannose, β-D-glucose and β-D-galactose, *etc.*) is the neighboring group participation of a 2-*O*-acyl moiety such as *O*-acetyl (Ac), *O*-benzoyl (Bz),[11] *N*-phthalimido (Phth),[12] picolyl,[13] *etc.* It has been proven that the mechanism of the glycosylation involves a bicyclic intermediate, specifically the dioxolenium ion (acetoxonium ion in terms of acetyl participation group) formed after the promoter A assisted the departure of leaving group X

followed by the oxo-carbenium ion intermediate (Scheme 1.1). In this case, the nucleophilic attack of the glycosyl acceptor or alcohol is only possible from the upper face of the sugar ring, providing 1, 2-*trans* glycosides stereoselectively. Indeed, a variety of glycosyl donors including halides, thioglycosides, acetates, pentenyl glycosides and trichloroacetimidates give excellent 1, 2-*trans* stereoselectivity and almost quantitative yields.



Scheme 1.1 Neighboring Group Participation to Form 1, 2-*trans* Glycoside

In contrast to the synthesis of 1, 2-*trans* glycosides, a prerequisite for stereoselective synthesis of 1, 2-*cis* glycosides is the installment of a non-participating functionality at C-2 position. In most of cases, the benzyl protecting group is used for neutral sugars and the azide protecting group for 2-amino-2-deoxy sugars. Ideally, 1, 2-*cis* glycosides can be formed stereoselectivelly *via* an S_N2 mechanism from 1, 2-*trans*-oriented glycosyl donors (Scheme 1.2). However, in most cases the glycosyl acceptors are fairly weak nucleophiles. Thus the glycosylation often proceeds through an S_N1 mechanism instead of S_N2 mechanism. Although the α-anomeric product is thermodynamically favorable due to the anomeric effect, a substantial amount of kinetic β-anomeric product is formed and sometimes preferred due to the irreversible character of the glycosylation process.



Scheme 1.2 S_N1 and S_N2 Glycosylation Mechanisms

Factors Influencing the Stereoselectivity of Glycosylation

As mentioned above, the preparation of 1, 2-*cis* glycosides is much more difficult than that of 1, 2-*trans* glycosides. While 1, 2-*trans* glycosides can be formed with the help of C-2 neighboring group participation, the generation of 1, 2-*cis* glycosides is dependent upon anomeric effect. Hence, the general strategy for α glycosylation is to use a non-participating functionality at the C-2 position. However, it must be noted that this does not guarantee the formation of 1, 2-*cis* glycosidic bonds; other factors must also be brought to attention, and are summarized in Figure 2:[14] (a) glycosylation through a S_N2 mechanism; (b) participating solvent effect; (c) glycosyl donor and acceptor structure (d) steric hindrance at C-6; and (e) other factors such as reaction temperature, protection group patterns, pressure, *etc.* Those factors will be discussed in the following sections.

The Leaving Group

After more than one hundred years of research, particularly over the past two decades, many leaving groups are now available to carbohydrate chemists (Scheme 1.3).[15] However,

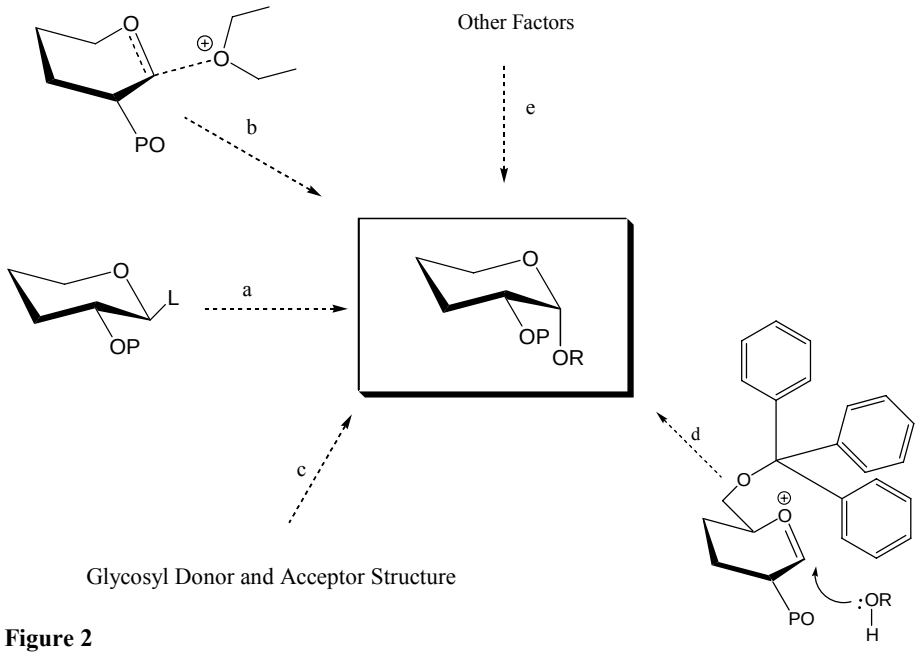
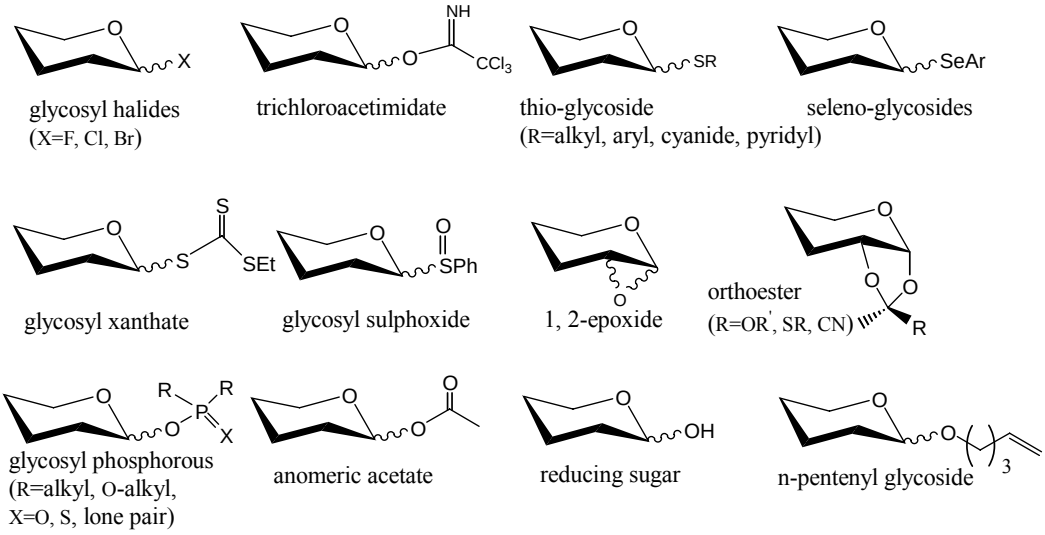


Figure 2



Scheme 1.3 Glycosyl Donors with Different Leaving Groups

only a few of these leaving groups can afford a favorable α/β glycoside ratio, of which the halide leaving group is an example. Early attempts to address the issue of stereoselectivity were primarily directed towards the development of novel promoters and the optimization of reaction

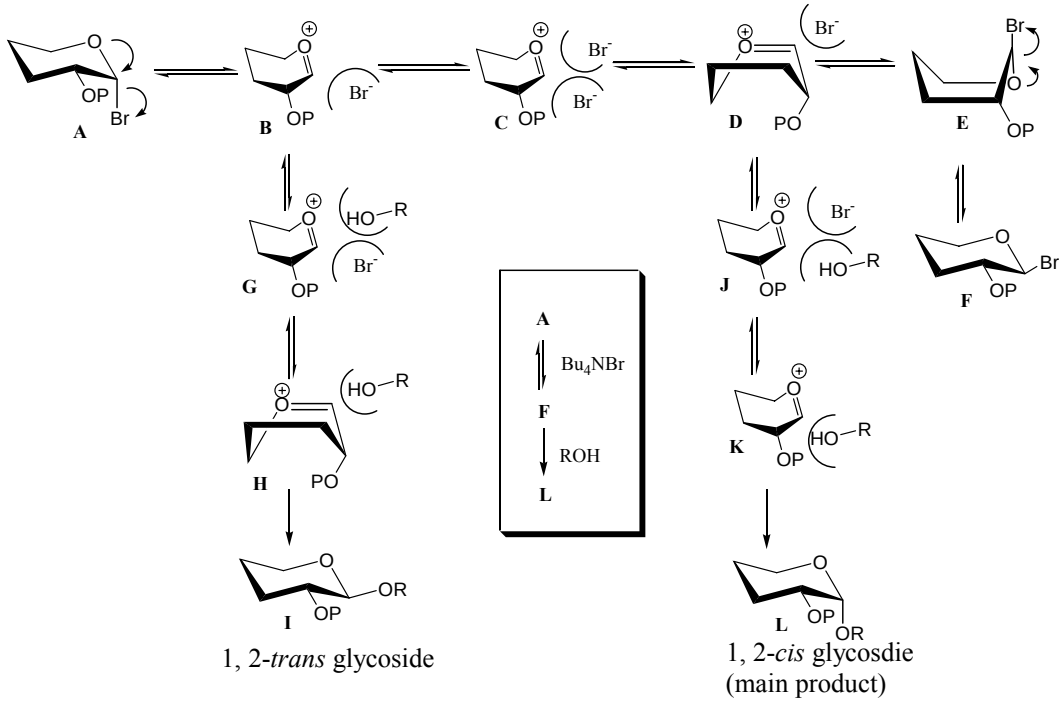
conditions. A major breakthrough occurred when Lemieux and co-workers discovered the *in-situ* anomerization concept; "halide ion catalyzed glycosidation reactions" (Scheme 1.4).[16] For the first time, a rapid equilibrium could be established between a thermodynamically stable α-halide and the more reactive β-halide by the addition of mild catalyst tetrabutyl ammonium bromide (Bu_4NBr) (Scheme 1.4). Since the energy barrier for a nucleophilic reaction of glycosyl bromides with alcohol ROH *via* F→E→D→J→K→L is lower than that for the corresponding reaction A→B→G→H→I, formation of 1, 2-*cis* glycosides is faster than that of 1, 2-*trans* glycosides. If the difference in the energy barrier is sufficient, it would be possible to direct the reaction towards the formation of 1, 2-*cis* glycosides stereoselectively. While the reaction has proven effective in many cases, very reactive glycosyl donors and acceptors as well as long reaction time are required to achieve stereoselectivity, thus reducing the usefulness of this methodology for the synthesis of complex carbohydrates.

Imidatate Donors

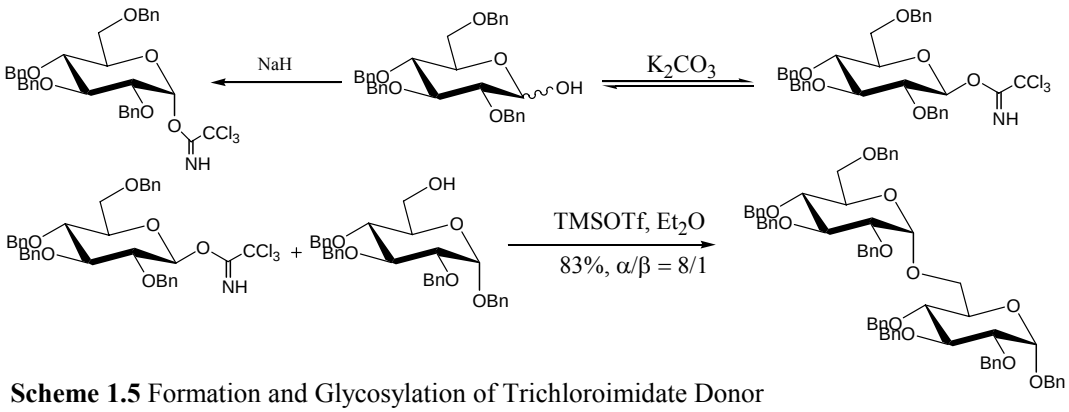
(N-Methyl)acetimidates were first introduced by Sinay as an alternative to the classic Koenigs-Knorr approach for the synthesis of 1, 2-*cis* glycosides.[17, 18] The methodology was further explored by Schmidt, who discovered that trichloroacetimidates are more potent glycosyl donors.[19] Since the paper describing this methodology was published in 1980, it has gained greater popularity among carbohydrate chemists. The principal advantage of this donor is that it requires a catalytic amount of Lewis acid promoter instead of at least an equimolar amount of heavy metal promoter, when compared to the halide ion method.

The basic foundation of the trichloroacetimidate method is a simple base-catalyzed addition of trichloroacetonitrile to the anomeric hydroxyl group to form the *O*-glycosyl trichloroacetimidate, a reaction which is generally high yielding. It is noteworthy that

stereocontrol of the anomeric substitution is strongly influenced by the nature of the base used to catalyze the reactions. A strong base, such as DBU or NaH, affords the mainly thermodynamically stable α-trichloroacetimidate,[20] whereas a weak base such as potassium carbonate affords the kinetic product β-trichloroacetimidate[19] (Scheme 1.5). In the next step, using a mild acid or Lewis acid such as TMSOTf or BF_3-Et_2O as catalyst, glycosylation with various glycosyl acceptors can be readily achieved with high yields in most cases. The anomeric configuration of product is often influenced by the catalyst used in the glycosylation step. The stronger and harder catalyst TMSOTf favors the formation of thermodynamically more stable α products, while the weaker and softer catalyst BF_3-Et_2O favors the formation of kinetic β products. However, most of the time an α/β mixture of product was formed in the glycosylation. The simplicity and efficiency of the trichloroacetimidate method has been employed in the synthesis of many target compounds.[21]



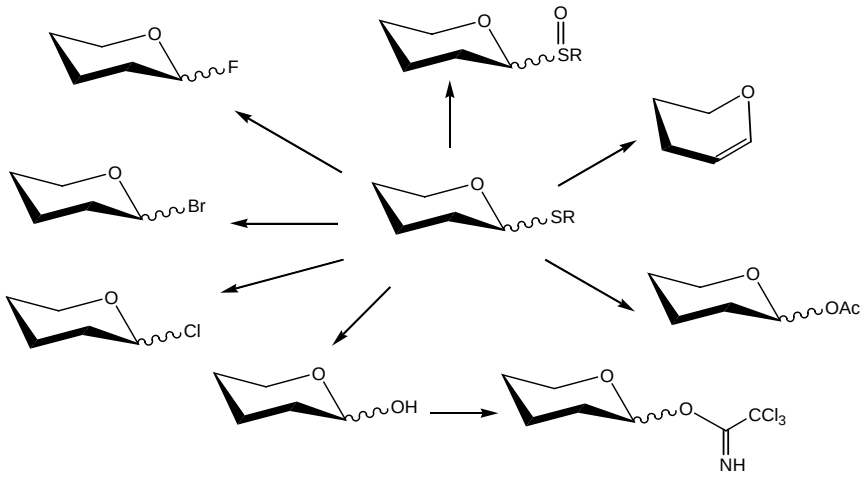
Scheme 1.4 Halide Ion Catalyzed Glycosidation Reactions[16]



Scheme 1.5 Formation and Glycosylation of Trichloroimidate Donor

Thioglycosides

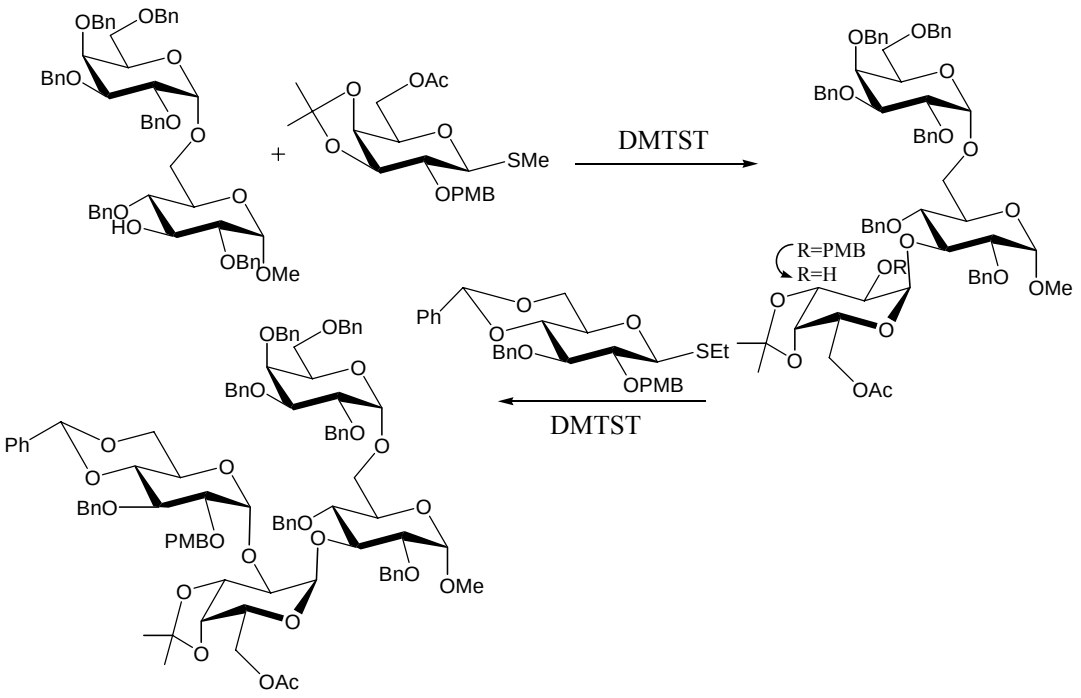
Thioglycosides possess many unique properties, including their facile synthesis, an ability to withstand most reaction conditions used in protecting group manipulations of major classes of functional groups (such as ethers, esters and acetals) and glycosylations, and effective activation with fairly mild electrophilic promoters. Furthermore, thioglycosides are readily transformed into other types of glycosyl donors (Scheme 1.6).[22]



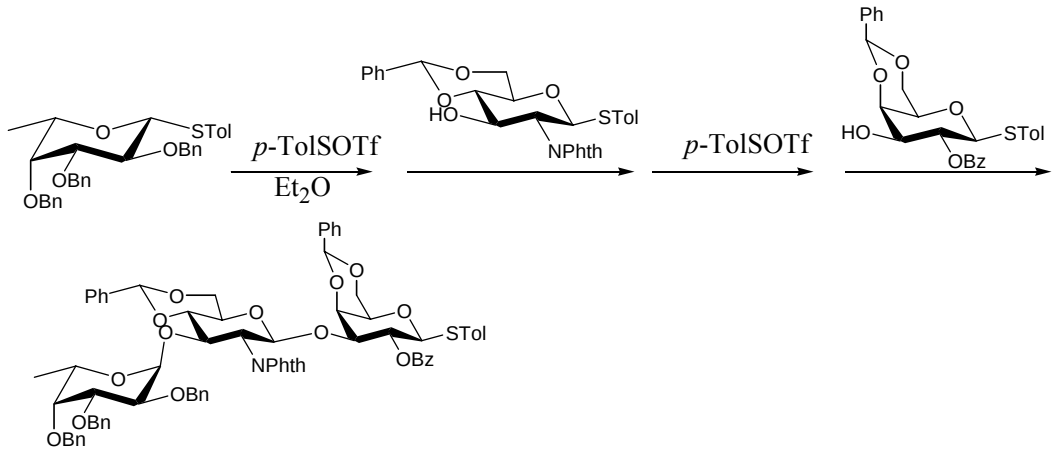
Scheme 1.6 Transformation of Thioglycoside to Other Glycosyl Donors

Initial glycosylation attempts with thioglycosides actually employed harsh reaction conditions, using mercury (II) sulfate,[23] NBS[24] or phenyl mercury triflate,[25] These promoters gave only modest yields and stereoselectivity. Presently, many thiophilic promoters with good 1, 2-*cis* stereoselectivity are available and range from least reactive (IDCP[26] and MeOTf [27-29]) to the moderate (DMTST[30, 31]) to the most reactive (NIS/TfOH[31]). DMTST works well with sterically hindered or weak nucleophiles when other promoters fail. For example, the assembly of a tetrasaccharide consisting of four 1, 2-*cis* linked monosaccharide building blocks was achieved using DMTST (Scheme 1.7).[32] However, these activating conditions as well as other common promoters such as NIS-TfOH, NIS-TMSOTf, and phenyl selenyl triflate (PhSeOTf) are generally too strong to effect the 1, 2-*cis* glycosylation in a stereocontrolled manner.[22] Nevertheless, a few examples of 1, 2-*cis* glycosylations have been achieved successfully with thioglycosides.[33, 34]

It is noteworthy that *p*-tolyl thioglycosides are efficient building blocks for the assembly of oligosaccharides *via* iterative one-pot synthesis.[35-37] In the reactivity-based one-pot method, glycosyl donors with decreasing anomeric reactivities react sequentially in a single reaction flask. The general reaction conditions use *p*-tolyl thioglycosides as building blocks, *p*-toluenesulfenyl triflate (*p*-TolSOTf)[38, 39] formed in *situ* from *p*-toluenesulfenyl chloride (*p*-TolSCl) and AgOTf as the stoichiometric promoter in the presence of dehydrating reagent MS-AW300.[37] It should be noted that assembly of the trisaccharide was achieved with excellent stereoselectivities in terms of both α and β linkages (Scheme 1.8).[37]



Scheme 1.7



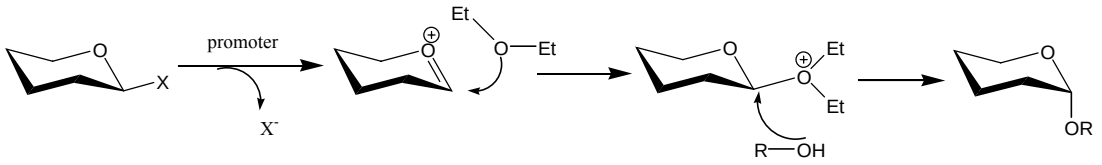
Scheme 1.8 One Pot Synthesis Using Thioglycoside[37]

Solvent Effect

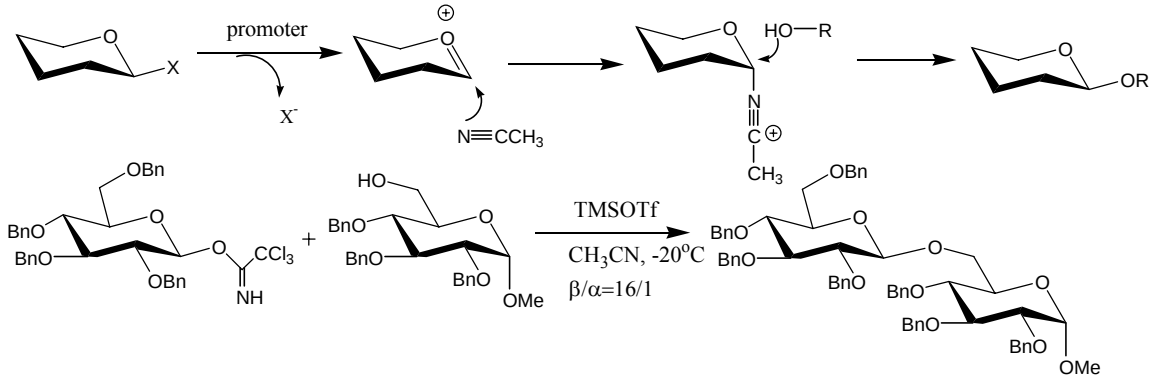
The anomeric outcome of glycosylations with glycosyl donors having a nonparticipating group at the C-2 position is markedly influenced by the nature of the solvent.[15] It has been

shown that some solvents in the reaction media have a stereodirecting effect. In general, solvents of low polarity such as DCM, $ClCH_2CH_2Cl$ or toluene are thought to increase α-selectivity. In these cases, *in situ* anomerization is facilitated and the formation of oxo-carbenium ions suppressed. Solvents of moderate polarity, such as the mixture of toluene and nitromethane, are highly beneficial when glycosyl donors are used with active neighboring group substituents, believed to stabilize the positively charged intermediates. Polar reaction solvents increase the rate of the β-glycoside formation by reducing the anomeric effect *via* charge separation between O-5 and β-O-1. However, a force more powerful than solvolysis is so-called solvent participation. Diethyl ether was found to be helpful to the formation of α-D-glucosides, and acetonitrile was found to be limiting in the preferential formation of β-D-glucosides.[40] The mechanism is believed to be the participation of a solvent to form the diethyl oxonium ion (Scheme 1.9). The β–configuration of this intermediate is favored due to the reverse anomeric effect. Since the upper face is blocked, nucleophilic attack could only be possible from the lower face to form α–glycosides. In the case of acetonitrile, it has been proposed that the reaction proceeds via an α-nitrilium ion which is generated under S_N1 conditions (scheme 1.9).[41] It is not well understood why the nitrilium ion adopts an axial orientation,[42] but the proposed anomeric configuration is supported by spectroscopic studies. Nucleophilic substitution of the intermediate leads to β-glycosides, and it has been shown that different types of glycosyl donors such as fluorides, trichloroacetimidates and thioglycosides feature the ability to form highly reactive nitrilium intermediates in the presence of acetonitrile.[43, 44] The best β–selectivity is obtained with reactive acceptors at low temperatures.

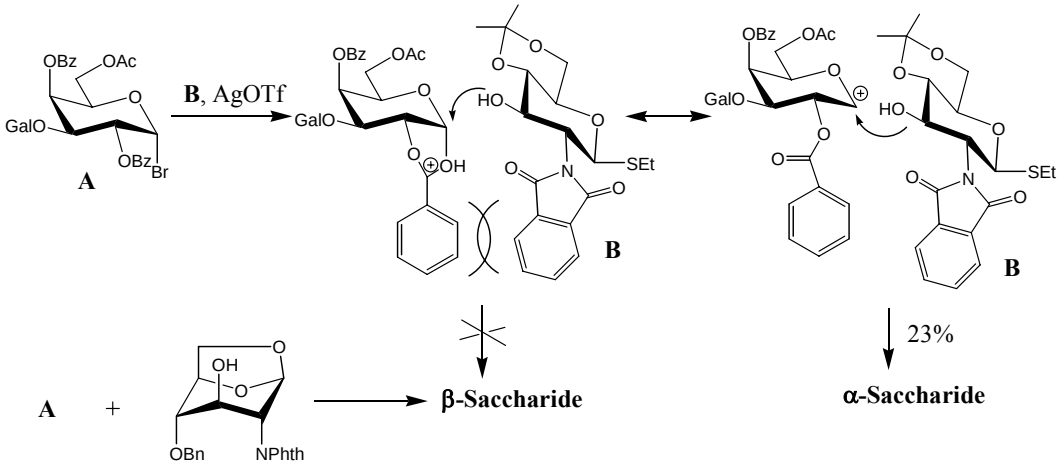
I. Participation of diethyl ether



II. Participation of acetonitrile



Scheme 1.9 Solvent participation effects



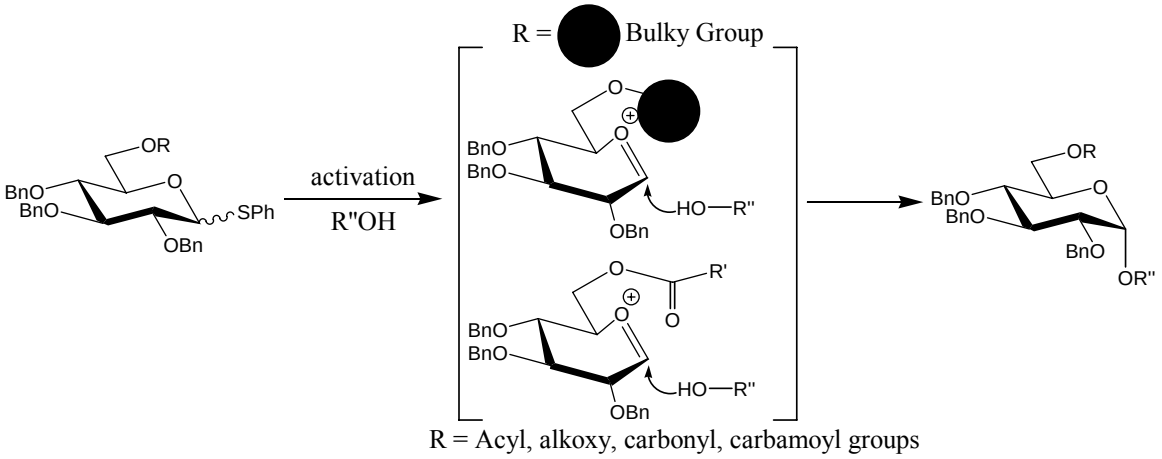
Scheme 1.10 Double Stereodifferentiation Effect[45]

Steric Factors

Unfavorable steric interactions that occur between a glycosyl donor and acceptor in the transition state may direct the stereochemical outcome of glycosylation. One such effects is "double stereodifferentiation" (Scheme 1.10),[45] by which glycosylation between compound A

and B gave exclusively the unexpected α-linked product, whereas coupling of the same glycosyl donor with conformationally modified acceptor C gave a β-linked product. Steric interactions between a glycosyl donor and acceptor may sometimes prevail over the stereodirecting effect of a neighboring participating group.

Another possible strategy that takes advantage of the steric interaction to control the stereochemistry of the anomeric position is to place a bulky group at the C-6 position (Scheme 1.11).[46] A simplified structure of the oxo-carbenium ion intermediate was used for the molecular modeling calculation. It was found that conformation B, which afforded the β-glycoside, was 6.3 KJ less stable than A and hence considered to be a minor conformation (Figure 3).[46]



Scheme 1.11[46] α-Selective Glucosylation by Using the Effects of 6-*O*-Substituents.

Enzymatic Glycosylation

The most efficient methods for stereoglycosylation come from nature. The enzymatic methods bypass the need for protecting groups since the enzymes control both the

regioselectivity and stereoselectivity of glycosylation reactions (Scheme 1.12).[47-49] There are two main types of enzymes for oligosaccharide synthesis: glycosyl transferases and glycosyl hydrolases. Glycosyl transferases can be isolated from milk and serum and are generally purified by affinity column chromatography using immobilized sugar nucleotide diphosphates. Several glycosyl transferases have been cloned and are now available in reasonable quantities. However, there are still not enough commercial available glycosyl transferases. Nature utilizes glycosyl hydrolases for the degradation of oligosaccharides. However, these enzymes could also be used in specific glycosidic bond formation. Glycosyl hydrolases are much more readily available than glycosyl transferases but are typically less stereoselective with lower yield.

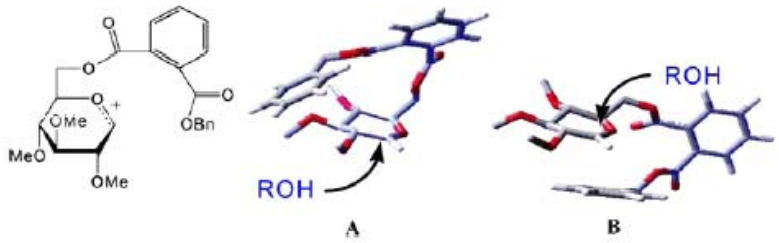
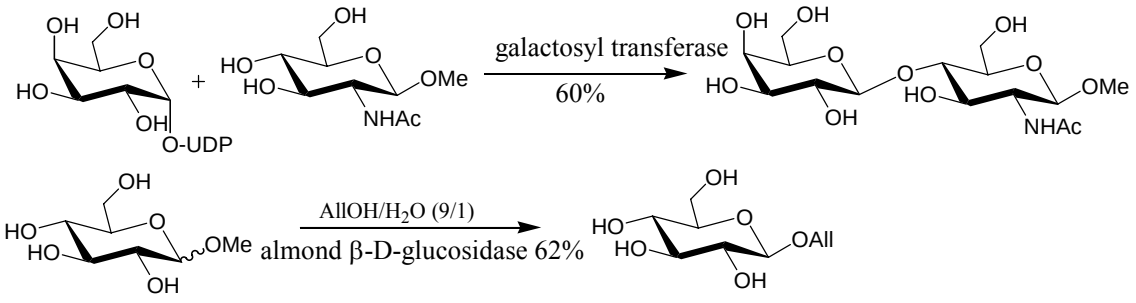


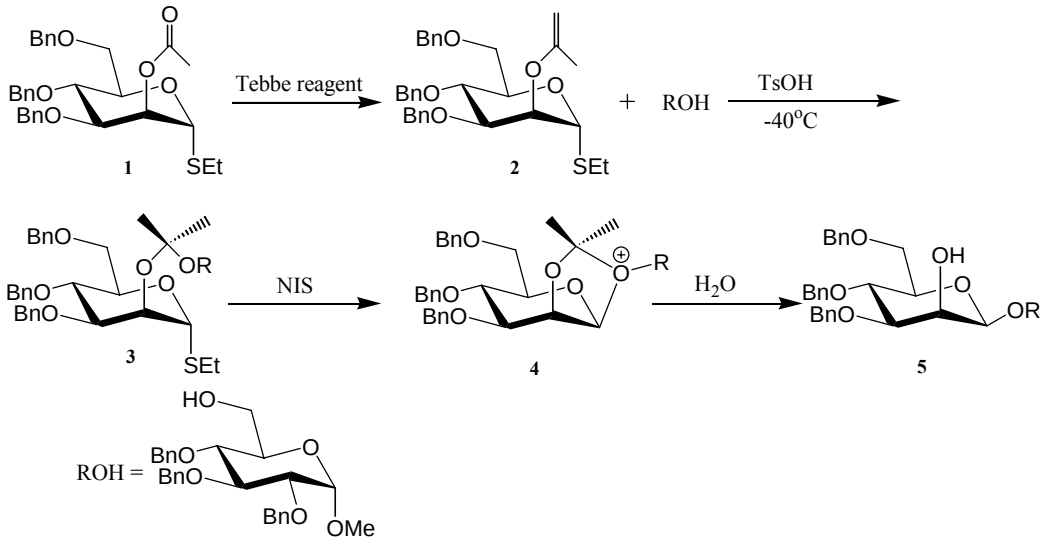
Figure 3[41]. The Lowest Energy Conformation of Oxocarbenium Intermediate (A) and the Conformation that Shields the α-Face (B)



Scheme 1.12 Enzymatic Glycosylations

Intramolecular Aglycon Delivery

Hindsgaul reported the first intramolecular glycosylation procedure in 1991, where a glycosyl acceptor was tethered to a glycosyl donor followed by the formation of 1, 2-*cis* glycosidic bonds.[50] The glycosyl donor was thioglycoside **1** with a 2-*O*-acetate group (Scheme 1.13) and the acetate was converted to methylene derivative **2** with the Tebbe reagent. Treatment of **2** with glycosyl acceptor in the presence of a catalytic amount of TsOH afforded tethered product **3** in a moderate yield. Activation of compound **3** with 5 equiv. NIS resulted in the stereoselective intramolecular glycosidation at the β face, which upon aqueous work-up gave the desired β-mannopyranoside **6**. The stereoselectivity of this method is, however, sometimes compromised by the low yield of the tethering reaction and the following glycosidation reaction.[51, 52]



Scheme 1.13 1, 2-*cis* Glycoside Formation Using Intramolecular Aglycon Delivery

Other Factors

There are other factors that influence the stereoglycosylation, one of which is the position of hydroxyl groups on the acceptors. General principles of acceptor reactivity are inversely

correlated with the 1, 2-*cis* stereoselectivity. Usually the most reactive C-6 primary hydroxyls give the lowest α/β ratios because the stronger the nucleophile, the faster the reaction, and hence the more difficult it is to control the reaction.[53-55] An additional factor is the protecting group pattern on the donors and acceptors. Generally, electron-withdrawing ester substituents reduce the electron density of the hydroxyl group, thus lowering its nucleophilicity and making it easier to control the reaction. While the protecting group pattern may improve stereoselectivity, it may result in a lower yield when the acceptors are protected with all deactivating species.[56-58] Milder promoters are usually beneficial for the formation of 1, 2-*cis* glycosides. While high pressure generally helps the formation of 1, 2-*trans* glycosides. Lower temperature typically favors the 1, 2-*trans* glycosides formation in kinetically controlled glycosylations.[59-61] However, better 1, 2-*cis* stereoselectivities achieved at lower temperature have also been reported.[62, 63]The concentration of the glycosylation also plays a minor role in the stereoselectivity, as dilution slows down the glycosylation yet sometimes improves the 1, 2-*cis* selectivity, thus demonstrating the delicate balance between selectivity and efficiency.[64, 65]

Despite the great progress made in the last decade in synthetic organic chemistry, there is still no general approach for the 1, 2-*cis* glycosylation of a wide range of substrates in high yields and with complete stereoselectivity. Most efforts have been directed towards the development of novel leaving groups and milder promoters. Despite these progresses, problems associated with these methods remain and stereoselective glycosylation remain a great challenge to synthetic organic chemists.

CHAPTER 2

PROJECT OBJECTIVE

In this study, three generations of chiral auxiliary are synthesized and attached to glucose and galactose. The donors containing these chiral auxiliary are synthesized and glycosylations with a variety of glycosyl acceptors are conducted. The central hypothesis is a novel participation pattern of C-2 functionality to facilitate the formation of 1, 2-*cis* glycosidic bonds. Classical C-2 acyl groups participate to form a five-member ring intermediate, blocking the α face of the oxocarbenium ion, hence facilitating the formation of 1, 2-*trans* glycosidic bonds. The proposed participation of novel chiral auxiliaries forms a six-member ring intermediate, blocking the β face of the oxocarbenium ion, hence facilitating the formation of 1, 2-*cis* glycosidic bonds.

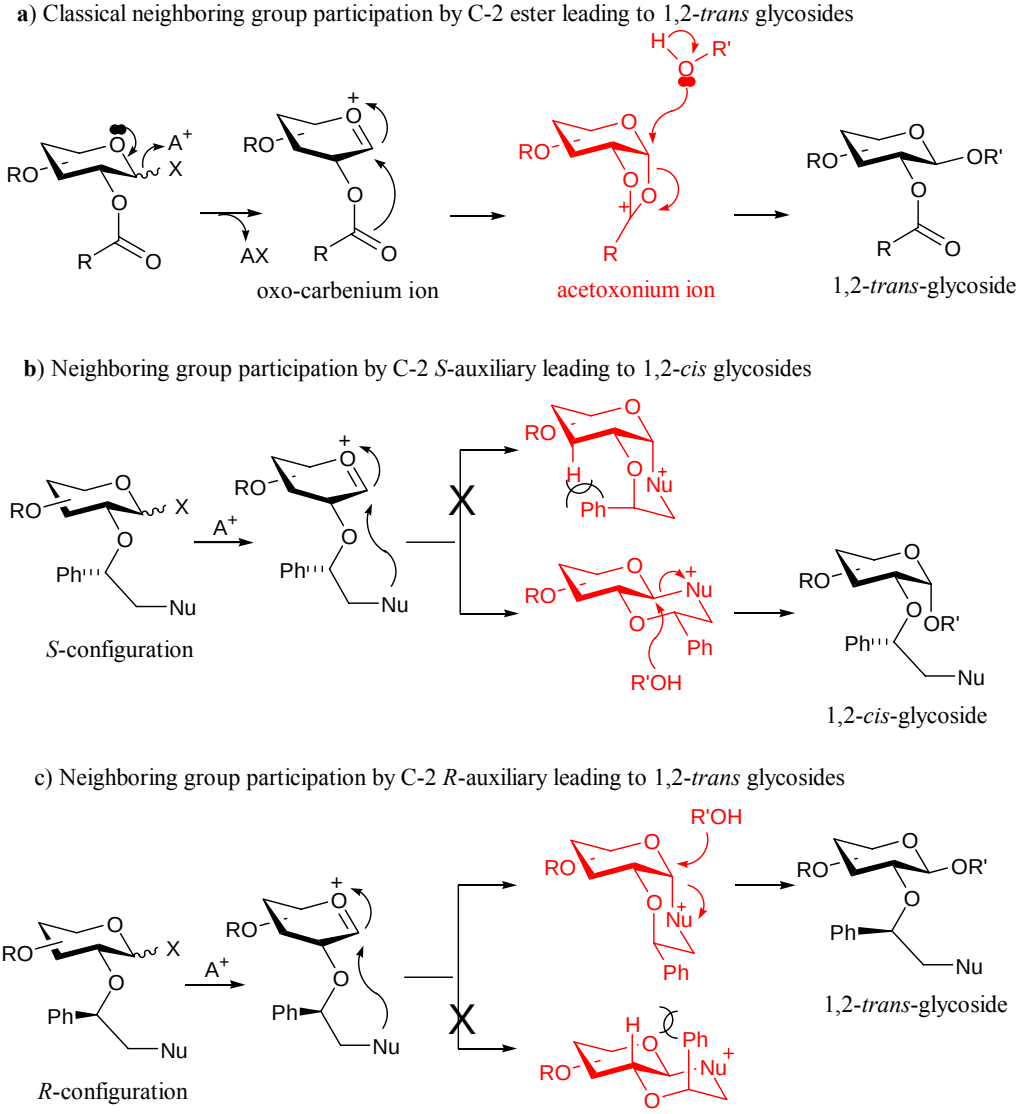
The specific goal of this project is to develop novel chiral auxiliaries for stereoselective glycosylations with improved properties such as improved anomeric selectivities when used for highly reactive glycosyl donors and selectively removal in the presence of acid sensitive protecting group.

The ultimate goal of this project is to develop a general strategy for the introduction of 1, 2-*cis* glycosides *via* using chiral auxiliaries.

FIRST GENERATION CHIRAL AUXILIARY[66-68]

The most reliable method for stereoselective glycosidic bond formation is based on the neighboring-group participation of a 2-*O*-acyl functionality (Scheme 2.1a).[69] In these reactions, a promoter activates an anomeric leaving group, thereby resulting in its departure and the formation of an oxonium ion. Subsequent neighboring-group participation of a 2-*O*-acyl protecting group will give a more stable acetoxonium ion. An alcohol can attack the anomeric center of an acetoxonium ion from only one face, to provide a 1, 2-*trans* glycoside. Thus, β-linked products will be obtained in the case of glucosyl-type donors, whereas mannosides will give α glycosides. The introduction of 1, 2-*cis* glycosidic linkages, such as α-glucosides and α-galactosides, requires glycosyl donors with a non-assisting functionality at the C2 position. Invariably, these glycosylations lead to mixtures of anomers.[70] In general, reasonable anomeric selectivities will only be obtained by extensive optimization of reaction conditions such as solvent, temperature, promoter, leaving group, and protecting-group pattern. Thus, the stereoselective formation of 1, 2-*cis* glycosides is the principal challenge in complex oligosaccharide synthesis.

In this project, we developed a novel strategy for stereoselective glycosylations in which a chiral auxiliary at the 2-position of a glycosyl donor is used (Scheme 2.1b, c). In the design of chiral auxiliary, a substituted ethyl moiety that contains a nucleophilic group was chose. Upon formation of an oxonium ion, participation of the nucleophilic moiety of the auxiliary should lead to the formation of either a *trans*- or a *cis*-decalin system. It was expected that the use of an

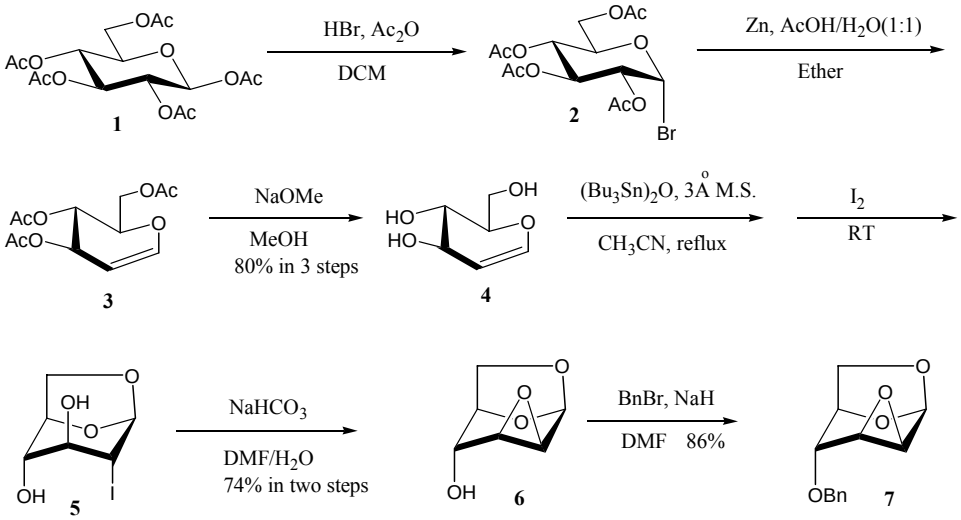


Scheme 2.1 Conventional and New Approaches for Stereoselective Glycosylation.
A=activating group, Nu=nucleophiile, X=leaving group

auxiliary with *S* stereochemistry would lead only to the formation of the *trans* decalin, since the alternate *cis*-fused system would place the phenyl substituent in an axial position and induce unfavorable steric interactions (Scheme 2.1b). Subsequent displacement of the anomeric moiety of the *trans*-decalin intermediate would then lead to the formation of a 1, 2-*cis* glycoside.

Alternatively, the use of an auxiliary with *R* stereochemistry would lead to the formation of a 1, 2-*trans* glycoside, because in this case the trans-decalin system would experience unfavorable steric interactions, and therefore glycosylation would only take place from the cis-decalin intermediate (Scheme 2.1c).

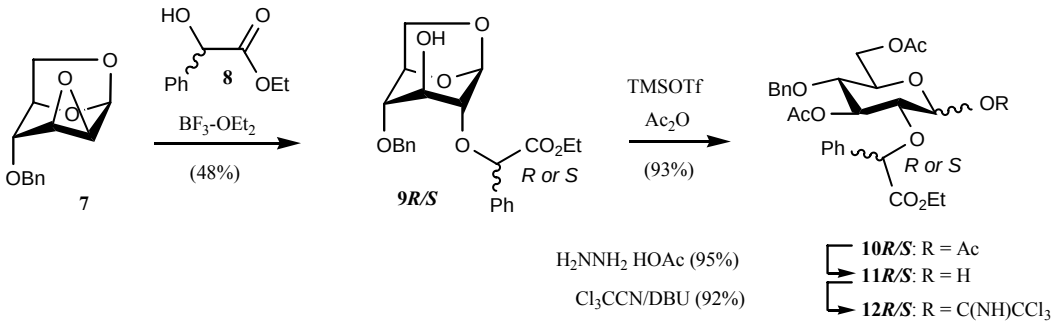
Ethyl mandelate was explored as a first-generation chiral auxiliary (Scheme 2.2 and 2.3). This derivative was deemed attractive because both enantiomers are readily available, esters are well established as appropriate participating functionalities in glycosylations, and the benzylic nature of the auxiliary should make its removal possible under reductive conditions.



Scheme 2.2 Preparation of Cerny Epoxide **7**

We started synthesis of cerny epoxide **7** with transformation of fully acetylated glucopyranose **1** into bromo sugar **2**. Reduction of **2** with zinc and acetic acid afforded acetylated glucal which was deprotected by NaOMe to give D-glucal **4**. After tin mediated 1, 6-iodocyclization, **6** was obtained in 74%. Thereafter, epoxide **6** was readily converted into its benzyl derivative **7** by conventional alkylation in excellent yield (Scheme 2.2).[71]

Thus, the reaction of **7** with ethyl (*R*)-mandelate in the presence of $BF_3 \cdot Et_2O$ led to a trans-diaxial opening of the epoxide to give **9*R*** in a yield of 48%. Next, acetolysis of the 1, 6-anhydro bridge of **9*R*** with acetic anhydride and TMSOTf gave compound **10*R*** in an almost quantitative yield. The anomeric acetyl group of **10*R*** was selectively removed with hydrazine acetate to give hemiacetal **11*R***, which was converted into trichloroacetimidate **12*R*** by using standard conditions.[72] Glycosyl donor **12*S*** was prepared by a similar protocol with ethyl (*S*)-mandelate as the starting material (Scheme 2.3).



Scheme 2.3 Preparation of Glycosyl Donors **12*R/S***. Bn = benzyl, DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene, TMSOTf = trimethylsilyl trifluoromethanesulfonate**.**

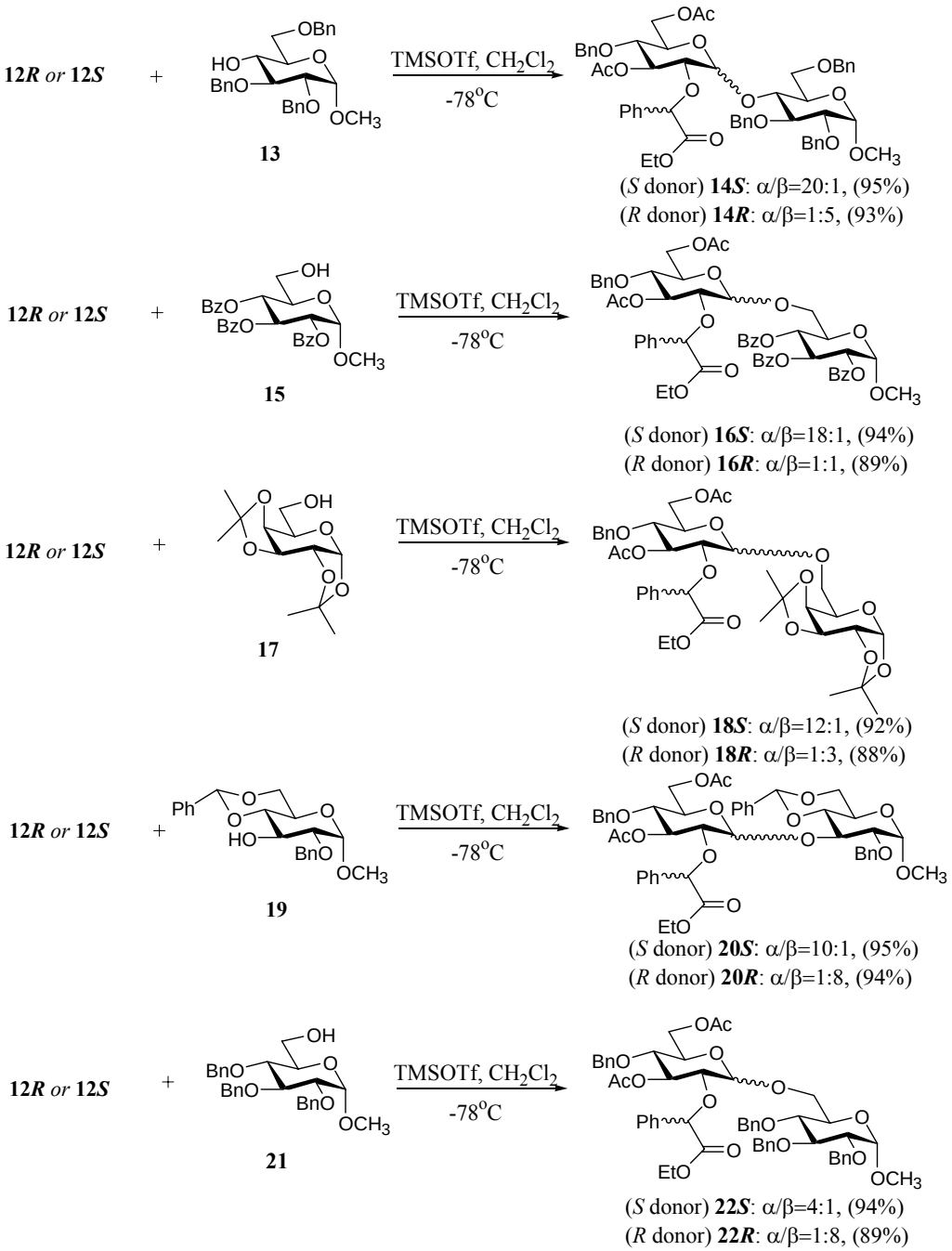
With glycosyl donors **12*R*** and **12*S*** in hand, attention was focused on the glycosylation of a range of different glycosyl acceptors. Thus, coupling of **12*S*** with **13** by using a catalytic amount of TMSOTf in dichloromethane at -78°C gave disaccharide **14*S***, mainly as the α glycoside, in an almost quantitative yield (Scheme 2.4) (Note: disaccharide **14*S/R*** were synthesized by : . At this low temperature, the reaction was completed within 15 minutes, which indicates that the glycosyl donor **12*S*** is highly reactive. Dilution of the reaction mixture led to a

small increase in anomeric selectivity, whereas higher reaction temperatures led to decreases in selectivity. As expected, coupling of **12*R*** with **13** under similar reaction conditions gave **14*R*** mainly as the β anomer.

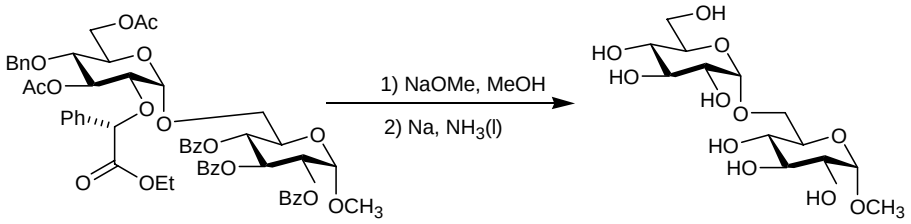
The fact that an inversion of configuration at the asymmetric center of the auxiliary led to a reversal of the stereochemical outcome of the glycosylation provides strong support for the proposed mode of participation as outlined in Scheme 2.1.

To demonstrate the generality of the approach, a range of glycosyl acceptors were glycosylated with **12*R*** and **12*S***. As can be seen in Scheme 2.4, glycosylations of **12*S*** with glycosyl acceptors that have either a primary or a secondary hydroxyl group gave disaccharides with high α-anomeric selectivity. In each case, the use of glycosyl donor **12*R*** led to a reversal of anomeric selectivity and mainly β-linked disaccharides were isolated, albeit with somewhat lower selectivity than that observed with **12*S***.

The results of the glycosylations indicate that the use of ethyl mandelate as an auxiliary at the 2-position provides a reliable approach for the synthesis of α-linked glycosides. To be useful for target synthesis, it is important that the auxiliary can be removed under mild conditions. The auxiliary was designed as a substituted benzyl ether, and thus should be removable by a catalytic hydrogenation over Pd or by Birch reduction. Indeed, saponification of the benzoyl and acetyl esters of **16*S*** by treatment with NaOMe in methanol followed by removal of the benzyl ethers and the auxiliary by using sodium in liquid ammonia led to the clean formation of the deprotected compound **23** (Scheme 2.5).



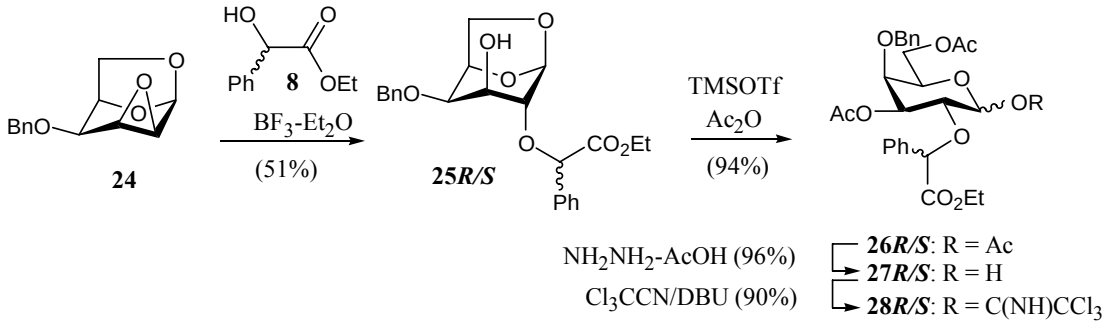
Scheme 2.4 Stereoselective Glycosylation with Glycosyl Donors **12*R*** and **12*S***. Bz=benzoyl



16*S* **23**

Scheme 2.5 Removal of First Generation Chiral Auxiliary

Finally, it was investigated whether the novel methodology can also be applied to galactosyl donors. For this purpose, the galactosyl trichloroacetimidates **28*R/S*** were prepared by starting from the readily available 1,6:2,3-di-anhydro-β-D-talopyranose (**24**). Thus, a trans-diaxial opening of the epoxide of **24** with ethyl *R*-mandelate in the presence of BF_3-OEt_2 gave **25*R*** in a yield of 51%. Treatment of **25*R*** with acetic anhydride and TMSOTf resulted in the opening of the 1, 6-anhydro-bridge to give compound **26*R*** in an almost quantitative yield, which was converted into trichloroacetimidate **28*R*** by selective removal of the anomeric acetyl group using hydrazinium acetate to give hemiacetal **27*R***, followed by treatment with trichloroacetonitrile in the presence of DBU. Glycosyl donor **28*S*** was prepared by a similar protocol using ethyl *S*-mandelate as the starting material (Scheme 2.6).



24 **25*R/S***

Scheme 2.6 Preparation of Glycosyl Donors **28*R/S***

Gratifyingly, TMSOTf mediated glycosylation of **28*S*** with glycosyl acceptors **13** and **15** gave the corresponding disaccharides **29*S*** and **30*S*** with good α-anomeric selectivity whereas the use of the glycosyl donor **29*R***, which has a *R*-mandelate at C-2, gave **29*R*** and **30***R* with modest β-selectivity (Table 2.1).

Table 2.1 Glycosylation of Galactosyl Donor **28S/R** with Glycosul Acceptor **13** and **15**

Entry	Glycosyl Donor	Glycosyl Acceptor	Product	α:β Ratio (% yield)[a]
1	**28*S***	**13**	**29*S***	10/1 (75%)
2	**28*R***		**29*R***	1/4 (79%)
3	**28*S***	**15**	**30*S***	6/1 (78%)
4	**28*R***		**30*R***	1/2 (82%)

[a] Product ratios were determined by ^{1}H NMR analysis of the crude reaction products.

The anomeric selectivities summarized in Scheme 2.4 and Table 2.1 show that glycosylations with glycosyl donors having an (*S*)-ethoxycarbonylbenzyl moiety at C-2 give predominantly α-glycosides whereas the donors containing an auxiliary with opposite stereochemistry give mainly β-glycosides. It was, however, observed that the β-anomeric selectivities are somewhat lower. These glycosylations are proposed to proceed through a *cis*-decalin intermediate, which places the phenyl substituent of the auxiliary in an equatorial orientation (Scheme 2.1c). It is important to note that a *cis*-decalin does experience unfavorable gauche interactions. The (*S*)-ethoxycarbonylbenzyl auxiliary, which reacts through a *trans*-

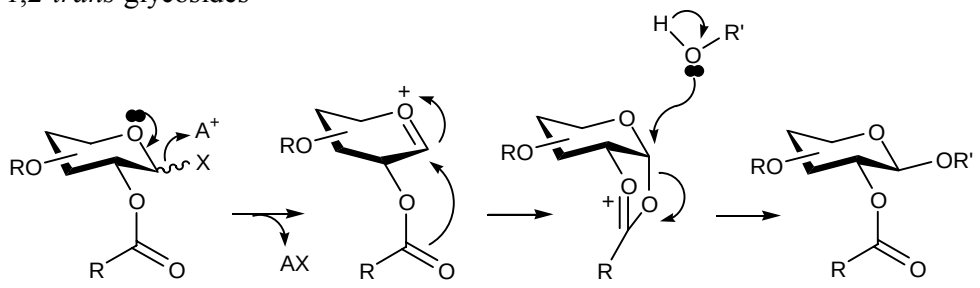
decalin intermediate, does not experience these unfavorable interactions rationalizing its more efficient anomeric control.

Although the glycosylations with **12*S*** and **28*S*** led to disaccharides with high α-anomeric selectivity, the ultimate goal is the development of an auxiliary that gives only one of the two possible anomers in each glycosylation. The small amount of unwanted anomer that is formed probably results from glycosylation of the oxonium ion. In this respect, participation by an ethoxycarbonylbenzyl moiety is probably slower than that of conventional acyl functionality because the formation of the six-membered ring is slower than that of the five membered ring. Thus, it is expected that a second-generation auxiliary could be obtained by improving the nucleophilicity of the auxiliary or reducing the flexibility of the rotatable bonds.

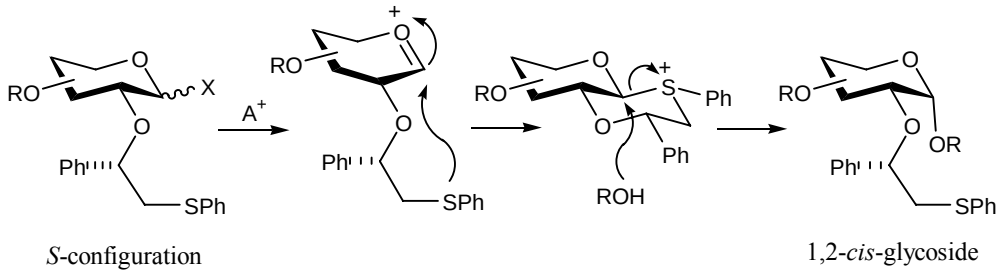
SECOND GENERATION CHIRAL AUXILIARY [73-75]

In the design of the second generation chiral auxiliary, we substitute the ester participating functionality with a more nucleophilic functionality-phenyl sulfide. The glycosylation approach is based on neighboring group participation of a (1*S*)-1-phenyl-2-(phenylthio)ethyl moiety at C-2 of a glycosyl donor (Scheme 2.7 b). Upon formation of an oxocarbenium ion, the nucleophilic phenylsulfanyl moiety of the C-2 functionality will participate, leading to the formation of an intermediate sulfonium ion as either *trans*- or *cis*-decalin. The formation of the *trans*-decalin is expected due to the absence of unfavorable gauche interactions. In addition, the *cis*-decalin system will place the phenyl substituent in an axial position inducing further unfavorable steric interactions. Displacement of the equatorial anomeric sulfonium ion by a sugar alcohol will then lead to the formation of a 1, 2-*cis*-glycoside.

a) Classical neighboring group participation by C-2 ester leading to 1,2-*trans* glycosides



b) Neighboring group participation by C-2 *S*-auxiliary to 1,2-*cis* glycosides

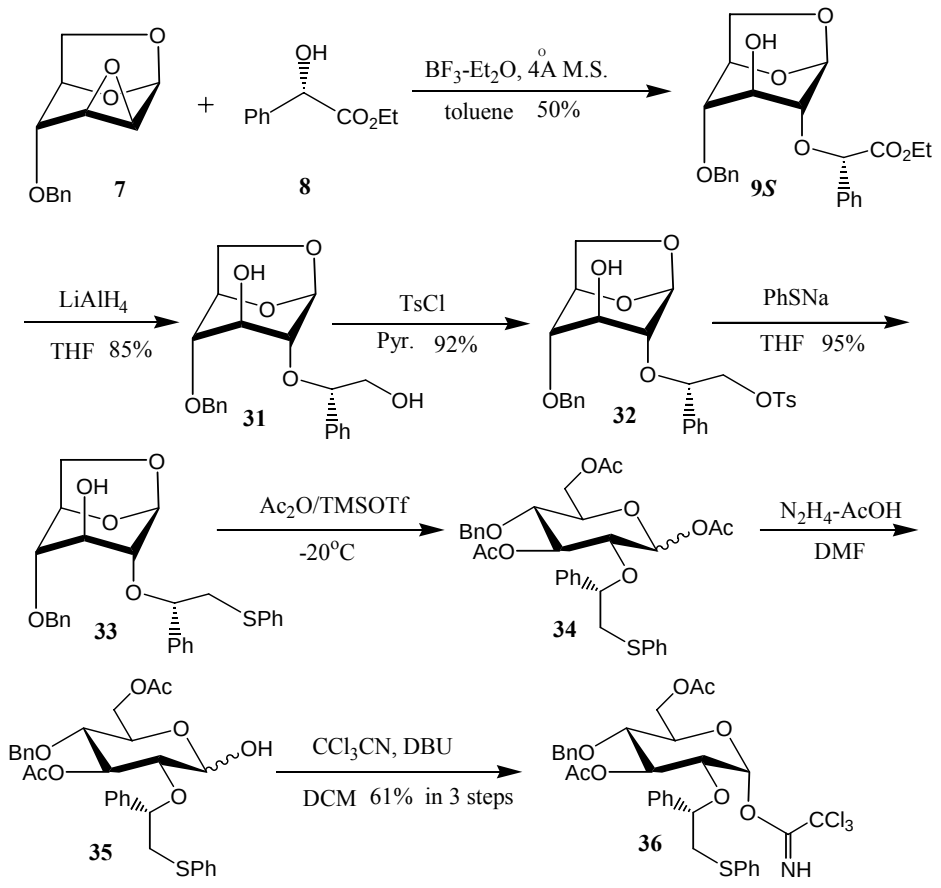


Scheme 2.7 Conventional and New Approach for Stereoselective Glycosylation

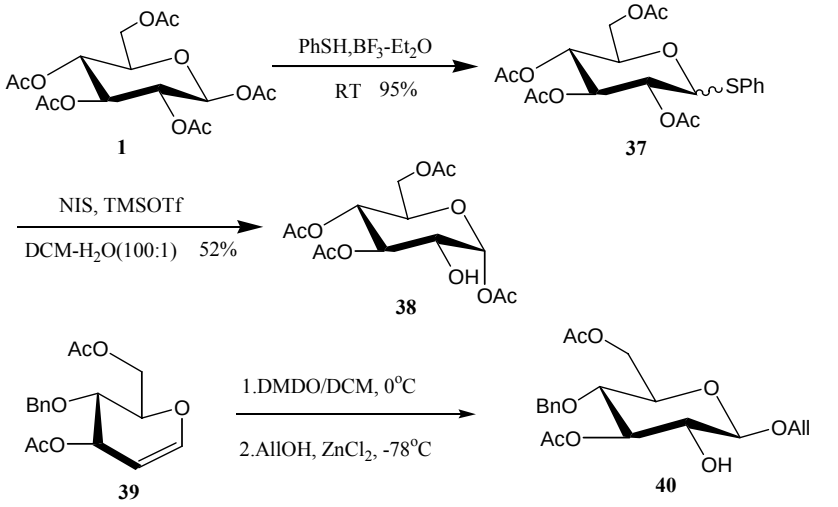
The initial synthesis of Donor **36** containing the (1*S*)-1-phenyl-2-(phenylthio)ethyl moiety started with reduction of **9S** with $LiAlH_4$, subsequent tosylation reaction and substitution with thiophenoxide gave **33**. Opening of 1, 6 anhydro bridge failed at 0^{o}C with cleavage of the chiral auxiliary. However, it was found at -20^{o}C the transformation was complete in excellent yield. Thereafter, Donor **36** was obtained by standard procedure in high yield (Scheme 2.8). However, the synthetic route from fully acetylated glucopyranose to second generation donor involved 13 steps. This laborious route makes it necessary to develop a more efficient one.

It was found that the (1*S*)-1-phenyl-2-(phenylthio)ethyl moiety could easily be installed by reaction with a sugar alcohol, such as **38**[71] and **40,**[76] both of which could be readily synthesized (Scheme 2.9), with acetic acid (1*S*)-1-phenyl-2-(phenylsulfanyl)ethyl ester in the

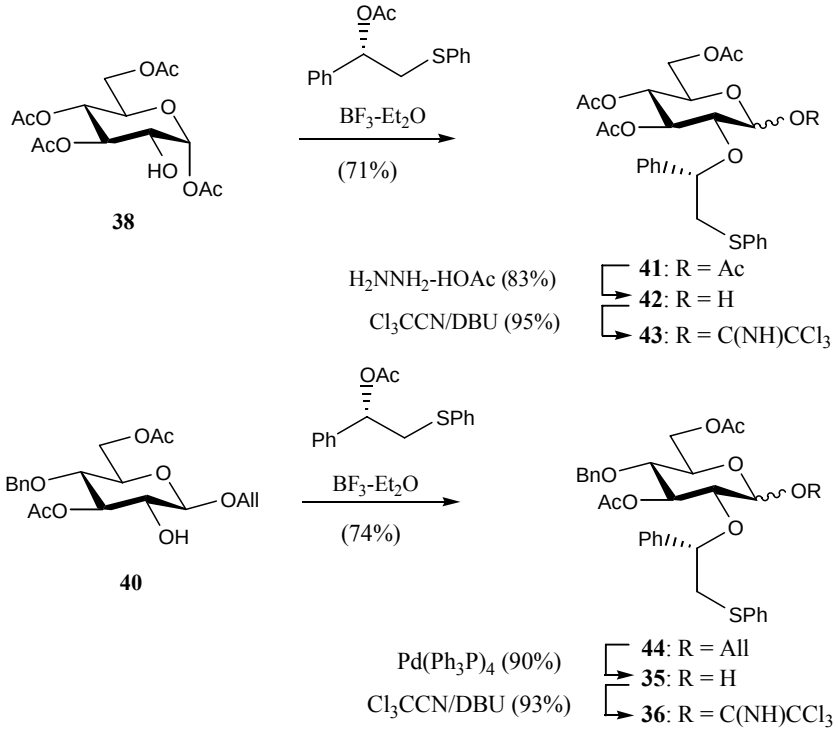
presence of BF_3-OEt_2[77] (Scheme 2.10). This reaction proceeds by a BF_3-OEt_2-promoted departure of the acetate with concomitant formation of an episulfonium ion. Subsequently, nucleophilic attack at the benzylic position of the episulfonium ion by a sugar hydroxyl leads to the required substituted benzyl ether with overall retention of configuration. Detailed NMR analysis of products **41** and **34** revealed that no other regio- or stereoisomers had been formed. Compounds **41** and **34** could be converted into glycosyl donors **43** and **36** by either removal of the anomeric acetyl ester or allyl ether followed by conversion of the hemiacetals into anomeric trichloroacetimidate using standard reaction conditions[78] (Scheme 2.10).



Scheme 2.8 Preparation of Glycosyl Donor **36**



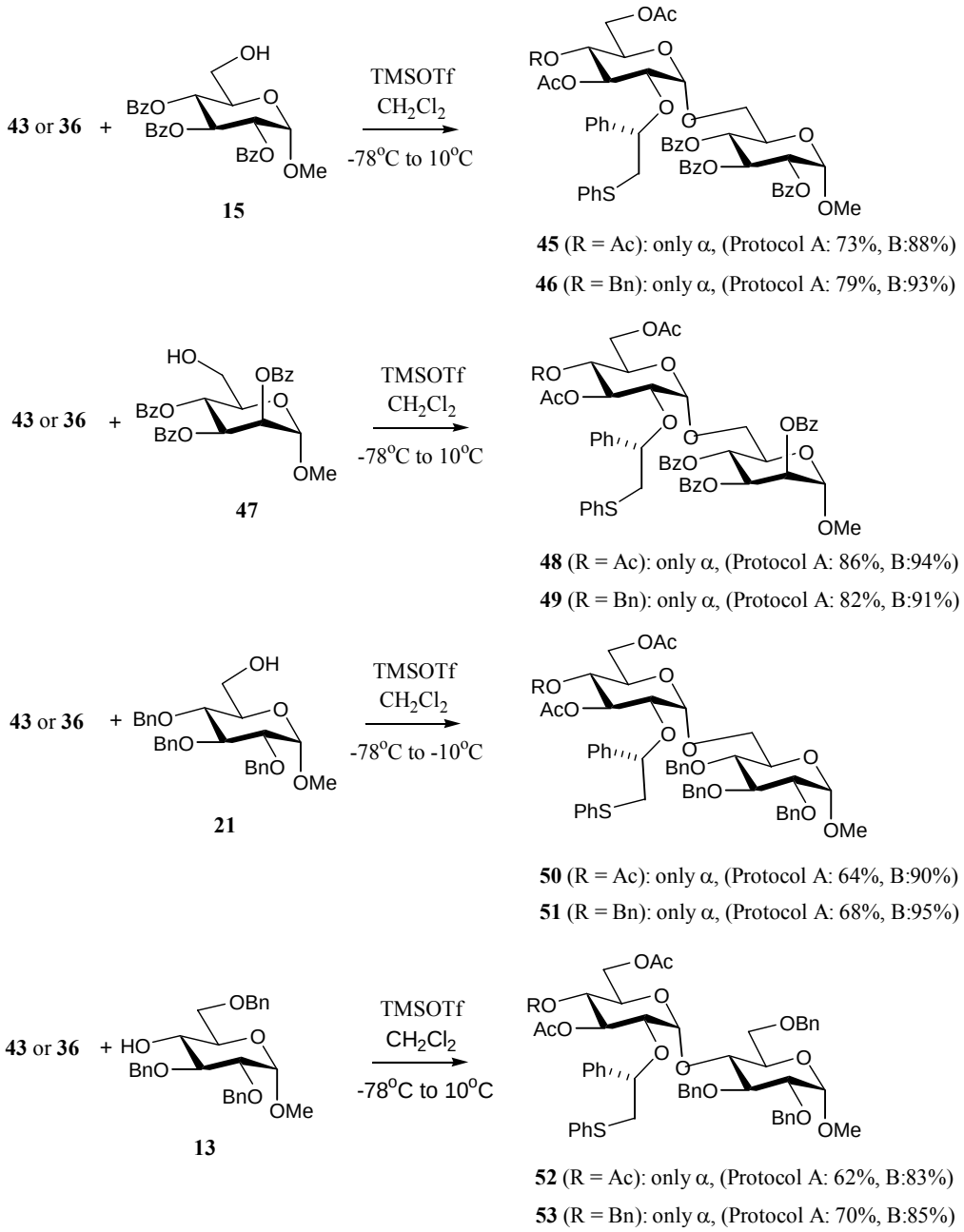
Scheme 2.9



Scheme 2.10 Preparation of Glycosyl Donors **43** and **36**

With glycosyl donors **43** and **36** at hand, attention was focused on the glycosylation of a range of different glycosyl acceptors (Scheme 2.11). Thus, coupling of **43** or **36** with glycosyl acceptor **15** using a catalytic amount of TMSOTf in dichloromethane at -78 ^{o}C followed by

gradual warming to 10 °C gave, after a reaction time of 3 h, disaccharides **45** and **46** as only the α glycosides in good yields (protocol A). To demonstrate the generality of the approach, glycosyl acceptors **13**, **21**, and **47** were also coupled with **43** and **36** as can be seen in Scheme 2.11; in each case, only the expected α anomer was isolated.

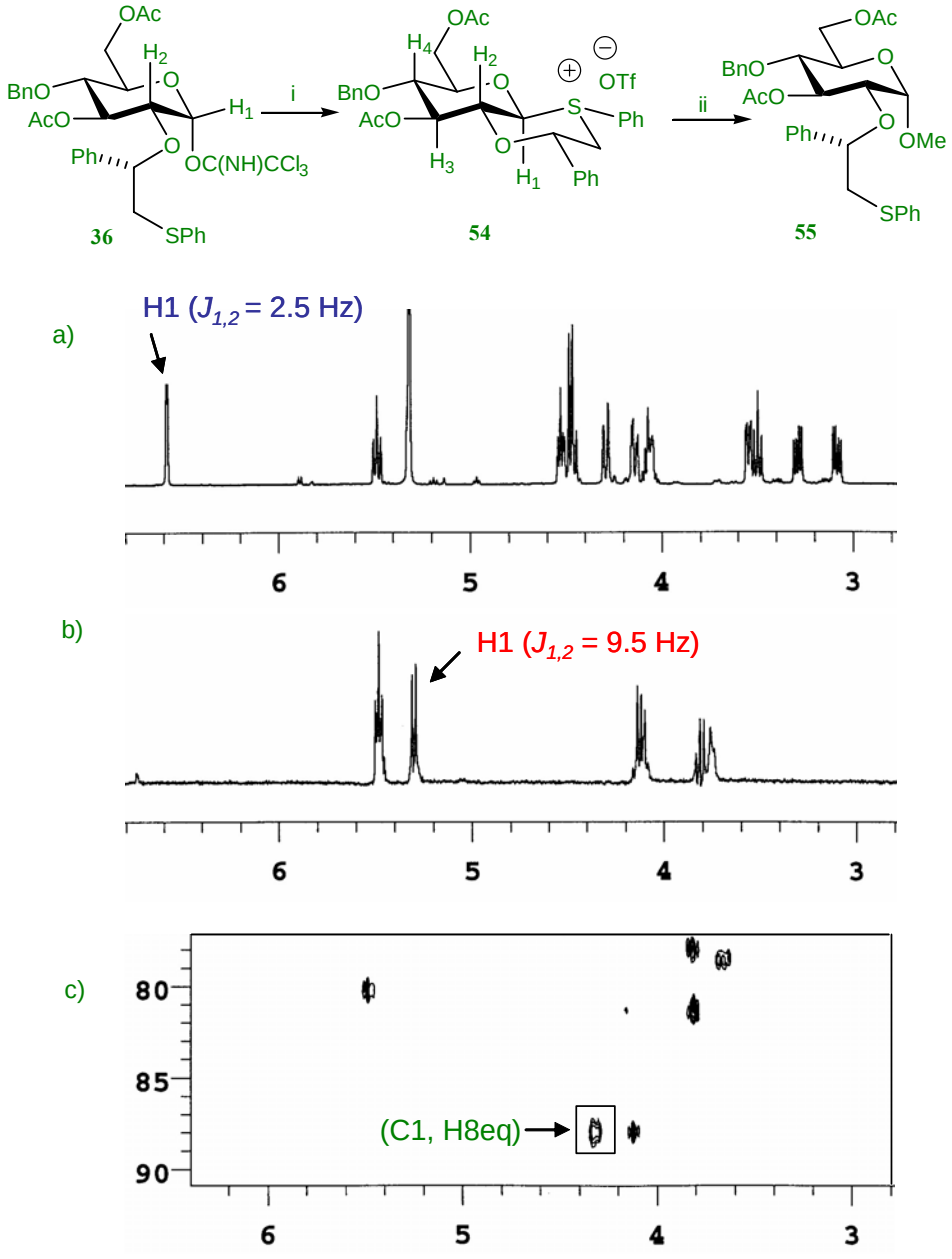


Scheme 2.11 Stereoselective Glycosylations with Glycosyl Donors **43** and **36**

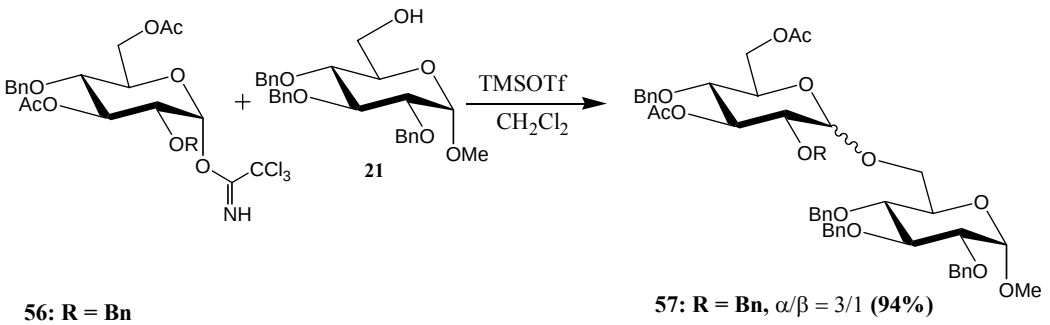
TLC analysis of the reaction mixture indicated that the glycosyl donor had been consumed within 10 min after adding TMSOTf. The glycoside products were, however, formed over a period of 3 h indicating the presence of a quasi-stable intermediate anomeric sulfonium ion. Furthermore, it was observed that some degradation had occurred probably due to the acidic nature of the reaction conditions. To address the latter problem, the glycosylations were performed by an alternative protocol (Scheme 2.11, protocol B) whereby the glycosyl donor was first activated with TMSOTf followed by the addition of the acceptor in the presence of the base 2, 6-di-*tert*-butyl-4-methylpyridine. As expected, under these conditions no degradation was observed and, in each case, the disaccharides were isolated in improved and near quantitative yield.

The fact that the glycosylations lead to the formation of exclusively α–anomers provides strong support that the reactions proceed through an equatorially substituted anomeric sulfonium ion. To confirm the presence of this intermediate, glycosyl donor **36** in CD_2Cl_2 at -50 ^oC was treated with 1 equiv of TMSOTf, and after the temperature was raised to -20 ^oC, 1H, 1H-TOCSY, HSQC, and HMBC NMR spectra were recorded. The collected data showed the formation of a single new compound, which was unambiguously identified as the sulfonium ion **54** (Scheme 2.12). Upon activation, the anomeric proton of **36** (δ 6.58, d, $J_{1,2}$ = 2.5 Hz) shifted upfield (δ 5.30, d, $J_{1,2}$ = 9.5 Hz) and its large vicinal coupling constant established an equatorial orientation of the anomeric substituent. The coupling constants of the other saccharide protons showed that no conformational distortion of the saccharide ring had occurred. The HMBC spectrum, which allows the determination of three-bond proton-carbon couplings, showed a correlation between C-1 and $H8_{eq}$, proving that the trans-decalin system of **54** had been formed. Treatment of **54** with

methanol resulted in the clean formation of the α-methyl glycoside **55**, demonstrating that the glycosylation proceeds by inversion of configuration of the anomeric center.



Scheme 2.12 i) TMSOTf, CD_2Cl_2, -50°C to 0°C ii) MeOH, -20°C to 0°C a) ^{1}H NMR spectrum of glycosyl donor **36** b) ^{1}H TOCSY 1D spectrum on irradiation of H4 of sulfonium ion **53** c) HMBC spectrum of sulfonium ion **53**



56: R = Bn

58: R = (*R*)-CH(Ph)CH_2SPh

36: R = (*S*)-CH(Ph)CH_2SPh

57: R = Bn, α/β = 3/1 **(94%)**

59: R = (*R*)-CH(Ph)CH_2SPh, α/β = 1/1, **(88%)**

50: R = (*S*)-CH(Ph)CH_2SPh, α only, (95%)

Scheme 2.13 Glycosylation with Glycosyl Donors **56, 58** and **36**

A number of experiments established which features of the (1*S*)-1-phenyl-2-(phenylthio)ethyl moiety are important for controlling the α-anomeric selectivity. In this respect, trichloroacetimidates **56** and **58** were coupled with **21** using TMSOTf as a promoter and the results were compared with a similar coupling with glycosyl donor **36** (Scheme 2.13). A standard glycosylation of trichloroacetimidate **56**, which has a C-2 benzyl ether, gave the disaccharide **57** as a 3/1 mixture of α/β anomers. Glycosylations were also performed with glycosyl donor **58**, which has an opposite (1*R*)-stereochemistry. The formation of a β–substituted sulfonium ion will place the (1*R*)-phenyl substituent in an axial orientation thereby inducing unfavorable steric interactions. In the alternative α-substituted sulfonium ion (*cis*-decalin), the (1*R*)-phenyl group will adopt an equatorial orientation; however, this intermediate will experience unfavorable gauche interactions. Displacement of the α-sulfonium ion would lead to the formation of β-glycoside. Thus, a standard glycosylation with **58** resulted in the formation of **59** as an anomeric mixture (α/β = 1/1). These results indicate that a combination of an equatorially oriented (1*S*)-

phenyl substituent and *trans*-decalin formation are important features for controlling the α anomeric selectivity.

Finally, the removal of the (1*S*)-1-phenyl-2-(phenylthio)ethyl group was achieved in the condition of BF_3-OEt_2 in acetic anhydride.[73]

It has been shown that a (1*S*)-1-phenyl-2-(phenylthio)ethyl moiety at C-2 of a glycosyl donor can direct the formation of α–glucosides. These glycosyl donors react through a new reaction mechanism whereby the phenylsulfanyl moiety of the C-2 functionality performs neighboring group participation to give a quasi-stable anomeric sulfonium ion. Due to steric and electronic effects, the sulfonium ion is only formed as a trans-decalin. Displacement of the sulfonium ion by a sugar hydroxyl leads exclusively to the formation of an α-glycoside. The formation of an intermediate cyclic β–linked sulfonium ion was convincingly demonstrated by NMR experiments. This (1*S*)-1-phenyl-2-(phenylthio)ethyl moiety can be introduced and removed under mild reaction conditions by exploiting the high reactivity of an episulfonium ion. A combined use of a new approach to introduce α-glycosides and traditional neighboring group participation by C-2 esters to give β-glycosides provides a general strategy for the synthesis of a wide variety of oligosaccharides.

THIRD GENERATION CHIRAL AUXILIARY

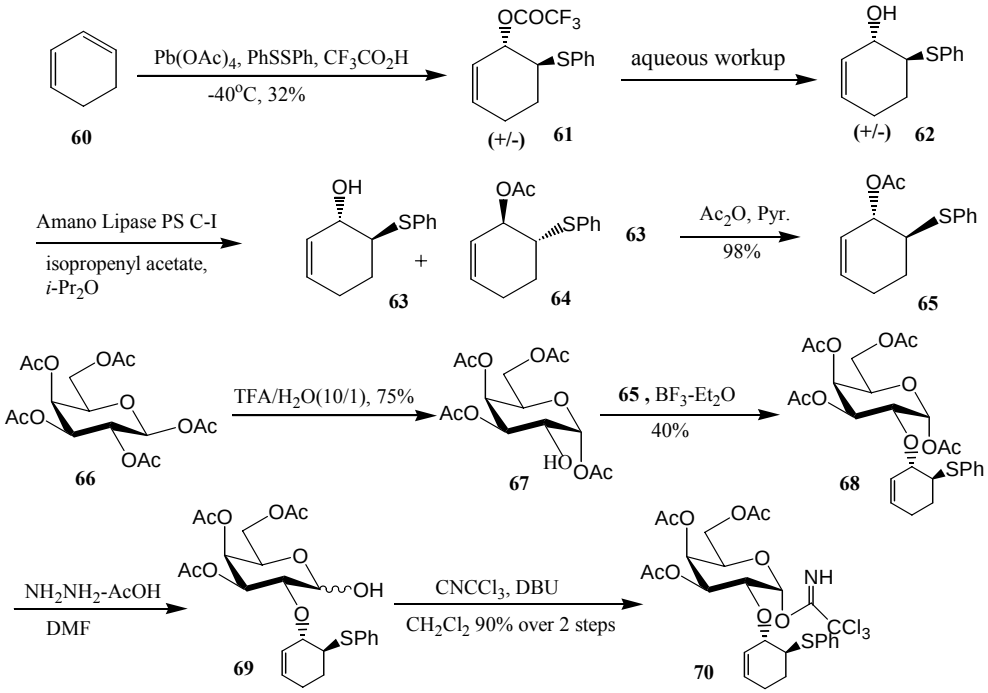
Despite the many attractive features of the second generation chiral auxiliary, there is a need to expand the scope of the methodology. It has been observed that the (*S*)-(phenylthiomethyl)benzyl auxiliary is sensitive to strong acidic conditions, which limits particular protecting group manipulations. Therefore, a third generation chiral auxiliary needed

to be developed with greater chemical stability, which can be cleaved under mild conditions. The third generation chiral auxiliary-(1*S,* 6*R*)-6-(phenylsulfanyl)-cyclohexene-2-yl and (1*S,* 2*R*)-2-phenylsulfanyl-cyclohexanyl was designed based on the rational that the disubstituted additional six-membered ring system can promote the rate of ring formation and stabilization of participating sulfonium intermediate.

The synthesis of donors containing the third generation chiral auxiliary started with 1, 3-cyclohexadiene.[79] Lead tetraacetate and diphenyl disulfide in the presence of trifluoroacetic acid (generating the lead (IV) trifluoroacetate *in situ*) in methylene chloride at -40^{o}C forms a blue solution which rapidly turns yellow. Addition of 1, 3-cyclohexadiene at this stage leads to phenylthiohydrin **62** upon basic work-up of **61**. The racemic *trans*-2-hydroxy-3-cyclohexen-l-yl phenyl sulfide could not be resolved by reaction with single enantiomer camphorsulfonic acid or mandelic acid. Fortunately, it was found that the enzyme Amano Lipase PS C-I could resolve **62** in the presence of isopropenyl acetate and diisopropyl ether.[80] Reaction of **63** with Mosher's acid chloride revealed that **63** remained unreacted with more than 99% *ee* while the enantiomer of **63** was acetylated to give **64**. After acetylation, the chiral auxiliary was attached to sugar **67** using BF_3-Et_2O. However, the yield is not as good as in the attachment of the second generation chiral auxiliary. Donor **70** was obtained after conventional transformation in excellent yield. To our surprise, the donor **70** exists with two rotamers at RT due to perhaps the double bond in the cyclohexene ring reduces flexibility of C-2 functionality.

With glycosyl donor **70** in hand, attention was focused on the glycosylation of different glycosyl acceptors (table 2.2). Thus, coupling of **70** with glycosyl acceptor **47** using 1 equivalent of TMSOTf in dichloromethane at -78 ^{o}C followed by gradual warming to -40 ^{o}C gave, after a reaction time of 1h, disaccharide **71** as only the α-glycoside in 90% yield. Another glycosylation

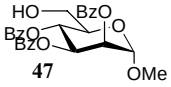
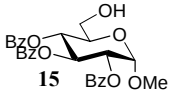
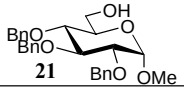
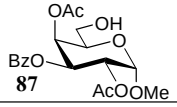
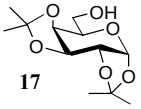
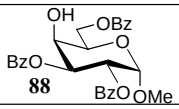
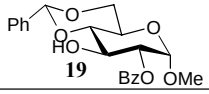
with benzoyl protected glycosyl acceptor **15** was performed and again only the α product **72** was obtained in 92% yield. To our disappointment, the coupling reactions gave α/β glycosides mixtures in the case of glycosyl acceptors with primary hydroxyl groups (**17**, **21** and **87**) and degradation products in the case of glycosyl acceptors with secondary hydroxyl groups (**19** and **88**).



Scheme 2.14 Preparation of Glycosyl Donor **70**

To investigate the reason of low stereoselectivity of the donor containing (1*S*)-(6*R*)-(phenylsulfanyl)-cyclohexene-2-yl, a low temperature NMR experiment in CD_2Cl_2 was performed at -30 ^oC. It was hoped that a participation intermediate could be detected; however, no such species was detected on the NMR time scale. The strain exerted by the double bond in the cyclohexene possibly cause the decomposition of any participation intermediate even at -30 ^oC, so we decided to synthesize donor **78** in which the double bond is reduced and the strain is removed.

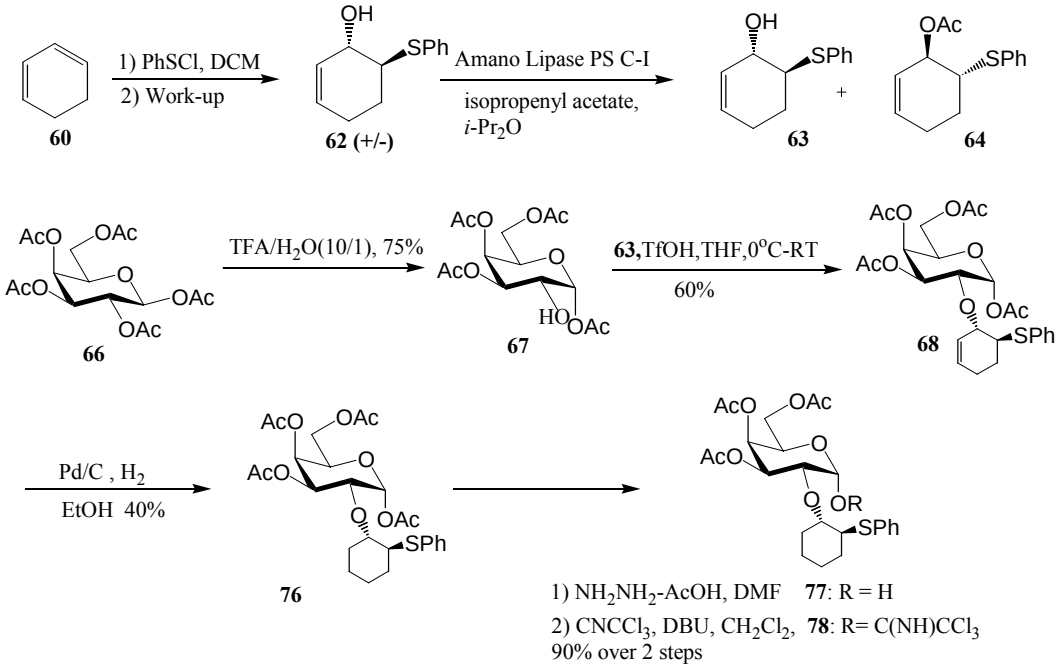
Table 2.2 Stereoselective Glycosylations with Glycosyl Donor **70**

Entry	Glycosyl Donor	Glycosyl Acceptor	Product	α:β Ratio (% yield)[a]
1	**70**	 **47**	**71**	only α, 90%
2	**70**	 **15**	**72**	only α , 92%
3	**70**	 **21**	**73**	5/1, 90%
4	**70**	 **87**	**74**	12/1, 70%
5	**70**	 **17**	**75**	7/1, 65%
6	**70**	 **88**		Donor decompose
7	**70**	 **19**		Donor decompose

[a] Product ratios were determined by ^{1}H NMR analysis of the crude reaction products.

The synthesis of donor containing third generation chiral auxiliary **78** started with 1, 3-cyclohexadiene.[81] This reaction proceeds by the addition of phenylsulfenyl chloride to the double bond in cyclohexadiene with concomitant formation of *trans*-2-chloro-3-cyclohexen-l-yl phenyl sulfide. Subsequent aqueous work-up leads to racemate **62**. After resolution of **62** with enzyme Amano Lipase PS C-1, the chiral auxiliary **63** could be installed to a sugar alcohol, such as **67,** which was formed from fully acetylated galactopyranoside **66**.[82] This installation reaction started with a TfOH-promoted formation of an episulfonium ion. Subsequently, nucleophilic attack at the allylic position of the episulfonium ion by a sugar hydroxyl leads to **68** with the required stereochemistry. The reduction of the double bond in the clyclohexene ring of **68** posed a great challenge due to poisoning of the catalyst. Catalytic hydrogenation with palladium, platinum or diimide generated *in situ* by heating toluenesulfohydrazide[83] failed to generate

reduced product. Fortunately, it was found **68** could be reduced using 3 equivalents of Pd in presence of H_2 atmosphere and ethanol. However, the reduction reaction was compromised by the formation of a large amount of side product from the cleavage of phenylsulfanyl group. Reduced compound **76** could be converted into glycosyl donor **78** using standard reaction conditions (Scheme 2.15). Compared to donor **70** which exists as two rotamers, donor **78** exists as only one compound.



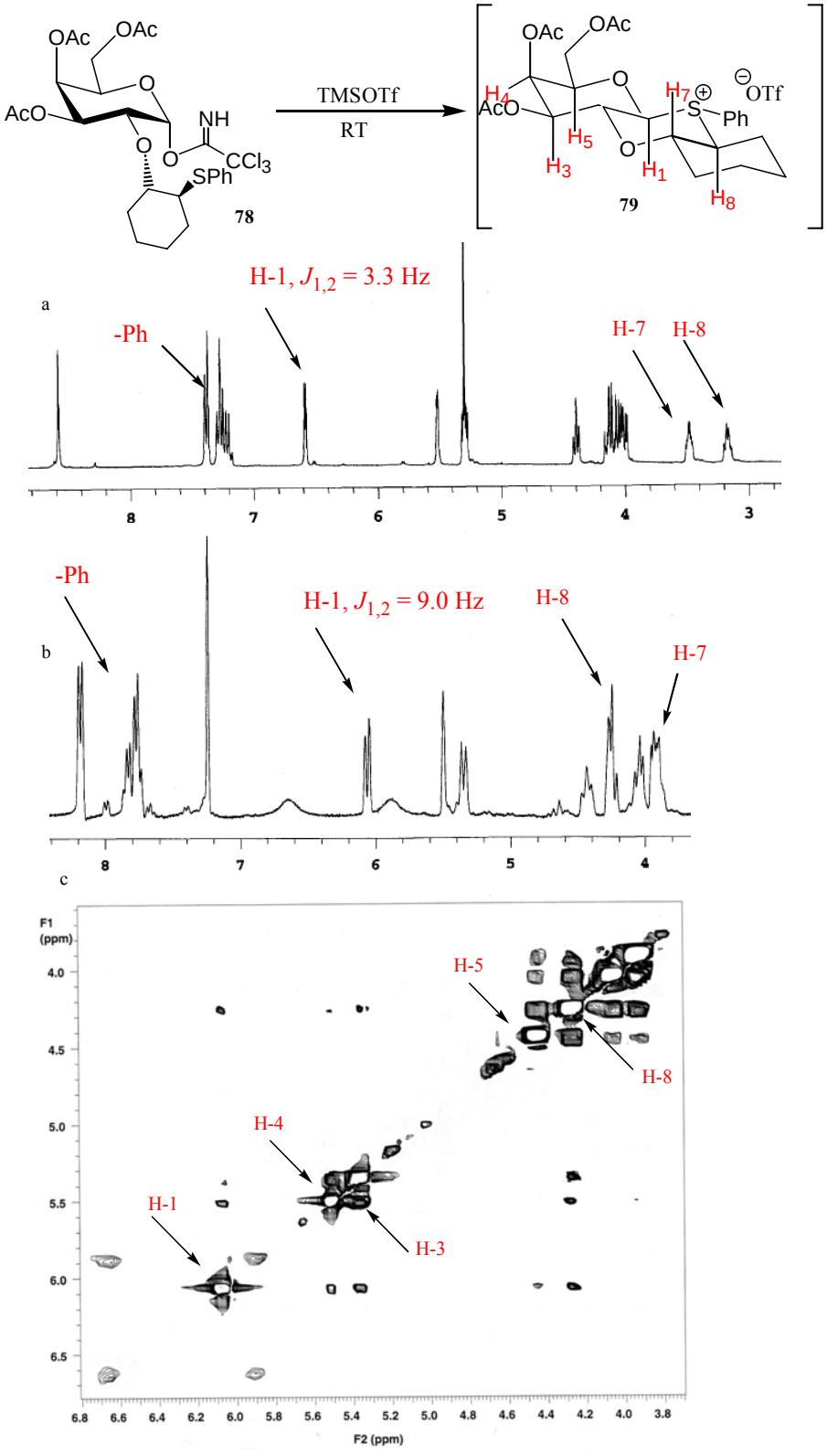
Scheme 2.15 Preparation of Glycosyl Donor **78**

With the reduction of the double bond in the cyclohexene ring, we expected the glycosyl donor **78** would form a stable participation intermediate. Indeed, glycosyl donor **78** in $CDCl_3$ at -20 ^oC was treated with 1 equivalent of TMSOTf, and after the temperature was raised to RT, ^1H, COSY and NOESY NMR spectra were recorded. The collected data showed the formation of a single new compound, which was unambiguously identified as the sulfonium ion **79** (Scheme

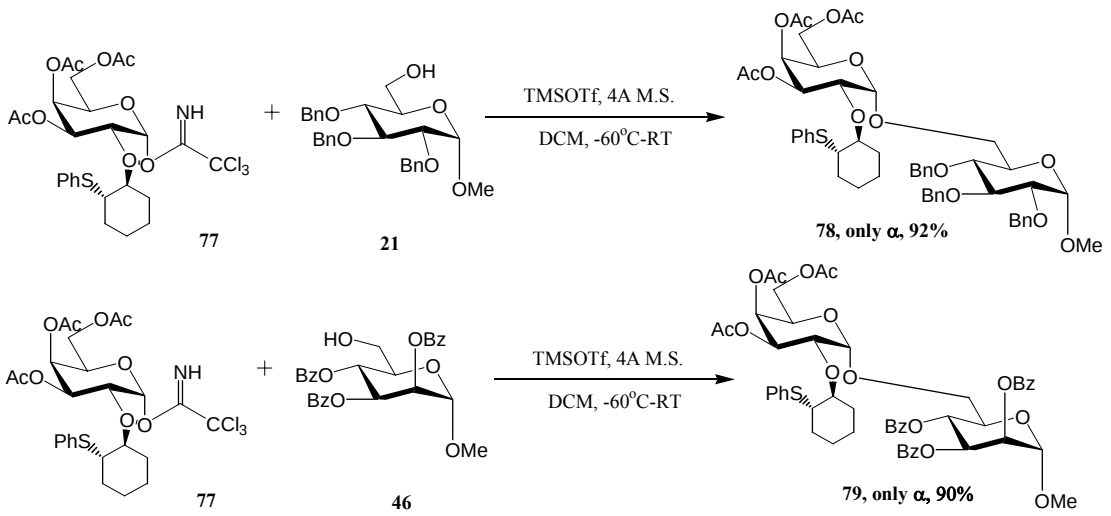
2.16). Upon activation, the aromatic and anomeric proton of **78** (δ 6.58, d, $J_{1,2}$ = 3.3 Hz) shifted upfield (6.07, d, $J_{1,2}$ = 9.0 Hz) and the large vicinal coupling constant of the anomeric proton established an equatorial orientation of the anomeric substituent. The coupling constants of the other saccharide protons showed no conformational distortion of the saccharide ring had occurred. The NOESY spectrum, which allows the determination of through-space interactions for stereochemistry, showed a correlation between H-1 and H-8, proving the tricyclic system **79** had been formed.

The fact that the participation intermediate **79** exists at RT shows that this species is more stable than the second generation participation intermediate starts to decompose after being stable for 5h at 0 ^{o}C. The sterichindrance of tricyclic intermediate structure, however, would make the nucleophilic attack of glycosyl acceptor more difficult. Hence, we revised the glycosylation protocol of the second generation glycosyl donors. Activation of **78** with 1 equivalent of TMSOTf from -78 ^{o}C to - 20 ^{o}C followed by coupling of the participation sulfonium species with glycosyl acceptor **31** and **47** in dichloromethane at -78 ^{o}C, followed by gradual warming to RT gave, after a reaction time of 6 h, disaccharide **80** and **81** as only the α-glycosides in excellent yield (Scheme 2.17).

It is noteworthy that the third generation chiral auxiliary participation intermediate is stable at room temperature for a period of 12h. The stability of the participation intermediate is very helpful for the 1, 2-*cis* stereoselective glycosylation reactions. It is expected that this methodology could be used for the synthesis of oligosaccharide with complete anomeric control.



Scheme 2.16 a. Proton NMR before activation; b. Proton NMR after activation c. NOESY NMR after activation



77 21 46

Scheme 2.17 Stereoselective Glycosylation with Glycosyl Donor **77**

CONCLUSION

In this study, it has been shown that a glycosyl donor substituted with a chiral auxiliary can be employed for the stereoselective introduction of 1, 2-*cis* glycosides such as α-glucosides and α-galactosides. The neighboring group participation by the chiral auxiliary leads to a quasi-stable anomeric sulfonium ion, which due to steric and electronic factors, is formed as a *trans*-decalin ring system. Displacement of the sulfonium ion by a glycosyl acceptor leads to the stereoselective formation of α-glycosides. The use of this new method in combination with traditional neighboring group participation by esters to introduce β-glycosides makes it possible to synthesize a wide variety of complex carbohydrates with complete anomeric control. The future direction of this project would be to apply this methodology to solid phase oligosaccharide synthesis and synthesis of complex oligosaccharides of biological significance.

CHAPTER 3

EXPERIMENTAL

General Procedures. All reactions were carried out under a positive pressure of argon unless otherwise noted. All chemicals were purchased from commercial suppliers and used without further purification unless otherwise noted. Dichloromethane was distilled from calcium hydride under an atmosphere of nitrogen. Toluene was distilled from molten sodium under an atmosphere of nitrogen. *N, N*-Dimethylformamide (DMF) was distilled from barium oxide under an atmosphere of nitrogen. Column chromatography was performed on silica gel 60 (EM Science, 70-230 mesh). Reactions were monitored by TLC on Kieselgel 60 F254 (EM Science) and the compounds were detected by examination under UV light and visualized by dipping the plates in a cerium sulfate-ammonium molybdate solution followed by heating. Organic solutions were concentrated by rotary evaporation below 40 ^{o}C under reduced pressure. Molecular sieves (3Å and 4Å) were crushed and activated in vacuo at 400 °C for 5 h. Optical rotations were measured with a 'Jasco P-1020' polarimeter. 1H NMR and 13C NMR spectra were recorded with a Varian Inova 300 spectrometer and a Varian Inova 500 spectrometer equipped with Sun workstations. Chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane. Data are presented as follow: Chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, dd = double of doublet, m = multiplet and/or multiple resonances), integration, coupling constant in Hertz (Hz). High-resolution mass spectrometry was run in a JMS SX/SX102A tandem mass

spectrometer, equipped with FAB source. The matrix used was DHB and the internal standards ultramark 1621 and PEG.

1,6-Anhydro-4-*O*-benzyl-2-*O*-(*S*)-ethoxycarbonylbenzyl-*β*-D-glucopyranose (9*S*). BF_3-OEt_2 (543 μL, 4.27 mmol) was added dropwise to a mixture of 1,6:2,3-di-anhydro-4-*O*-benzyl-*β*-D-mannopyranose (**7**) (5 g, 21.3 mmol), (*S*)-ethyl mandelate (11.5 g, 63.9 mmol) and activated molecular sieves (4Å, 2 g) in toluene (20 mL) at room temperature. After stirring for 1h, the reaction mixture was quenched with aqueous saturated $NaHCO_3$ solution (30 mL) and then diluted with ethyl acetate (30 mL). The organic phase was dried ($MgSO_4$), filtered and the filtrate was concentrated in vacuo. The residue was purified by silica gel column chromatography (20% ethyl acetate in hexane) to afford **9*S*** (4.23 g, 48%): colorless syrup, R_f = 0.34 (ethyl acetate/hexane, 1/1); $[\alpha]^{20}_D$ = +40.3˚ (c = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25-7.48 (m, 10H, aromatic), 5.54 (s, 1H, H-1), 5.22 (s, 1H, >CHPh), 4.63 (d, 1H, J = 12.3 Hz, C*H*HPh), 4.61 (d, 1H, J = 12.3 Hz, CH*H*Ph), 4.54 (d, 1H, J = 5.4 Hz, H-5), 4.13-4.23 (m, 2H, $COOCH_2CH_3$), 3.88 (t, 1H, J = 4.8 Hz, H-3), 3.73 (d, 1H, J = 7.5 Hz, H-6_a), 3.61 (dd, 1H, J = 5.4, 7.2 Hz, H-6_b), 3.33 (d, 1H, J = 4.8, H-2), 3.29 (d, 1H, J = 4.8, H-4), 2.61 (b, 1H, OH), 1.21 (t, 3H, J = 7.2 Hz, $COOCH_2CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.07, 137.79, 136.01, 128.73, 128.59, 128.43, 127.78, 127.75, 127.50, 101.80, 80.49, 80.17, 80.02, 75.48, 71.80, 71.25, 66.85, 61.43, 14.01; HR MALDI-TOF MS m/z calcd for $C_{23}H_{26}O_7$ $[M+Na]^+$ 437.1577, found 437.1532.

1,6-Anhydro-4-*O*-benzyl-2-*O*-(*R*)-ethoxycarbonylbenzyl-*β*-D-glucopyranose (9*R*). Compound **9*R*** was synthesized from compound **7** and (*R*)-ethyl mandelate according to the procedure described for the synthesis of compound **9*S***: Colorless syrup, R_f = 0.35 (ethyl acetate/hexane, 1/1); $[\alpha]^{20}_D$ = -10.3˚ (c = 1.2, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26-7.45 (m, 10H, aromatic), 5.34 (s, 1H, H-1), 5.11 (s, 1H, >CHPh), 4.83 (d, 1H, J = 12.0 Hz, C*H*HPh),

4.67 (d, 1H, J = 12.0 Hz, CH*H*Ph), 4.51 (d, 1H, J = 5.1 Hz, H-5), 4.06-4.23 (m, 2H, $COOCH_2CH_3$), 3.99 (t, 1H, J = 6.3 Hz, H-3), 3.57-3.65 (m, 2H, H-6_a, H-6_b), 3.34 (d, 1H, J = 6.3 Hz, H-2), 3.24 (d, 1H, J = 6.3 Hz, H-4), 1.17 (t, 1H, J = 7.2 Hz, $COOCH_2CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.84, 138.04, 135.85, 128.65, 128.46, 128.27, 127.70, 127.56, 127.06, 101.78, 83.17, 81.24, 79.89, 76.18, 72.57, 71.81, 67.31, 61.67, 13.82; HR MALDI-TOF MS m/z calcd for $C_{23}H_{26}O_7$ $[M+Na]^+$ 437.1577, found 437.1548.

Acetyl 3,6-di-*O*-acetyl-4-*O*-benzyl-2-*O*-(*S*)-ethoxycarbonylbenzyl-α/β-D-glucopyranose (10*S*). Trimethylsilyl trifluoromethanesulfonate (24 μL, 0.13 mmol) was added to a solution of **9*S*** (6.52 g, 6.52 mmol) in acetic anhydride (10 mL) at 0 °C. After the reaction mixture was stirred at 0 °C for 20 min, it was quenched with an aqueous saturated solution of $NaHCO_3$, and the resulting mixture was extracted with DCM (2 × 30 mL). The organic phase was washed with water (30 mL) and brine (30 mL) and dried ($MgSO_4$), filtered and the filtrate was concentrated in vacuo. The residue was purified by silica gel column chromatography (20% ethyl acetate in hexane) to afford **10*S*(α)** (2.69 g, 74%): colorless syrup, R_f = 0.57 (ethyl acetate/hexane, 1/1); $[\alpha]^{20}_D$ = +164° (c = 2.1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22-7.35 (m,10H, aromatic), 6.44 (d, 1H, J = 3.6 Hz, H-1), 5.57 (t, 1H, J = 9.6 Hz, H-3), 4.96 (s, 1H, >C*H*Ph), 4.55 (d, 1H, J = 11.1 Hz, C*H*HPh), 4.48 (d, 1H, J = 11.1 Hz, C*H*HPh), 4.25 (d, 2H, J = 3.0 Hz, H-6_a, H-6_b), 4.08-4.20 (m, 2H, COOC$H_2$$CH_3$), 3.97-4.02 (m, 1H, H-5), 3.61 (dd, 1H, J = 3.6, 9.9 Hz, H-2), 3.55 (t, 1H, J = 9.6 Hz, H-4) 2.18 (s, 3H, $COCH_3$), 2.05 (s, 3H, $COCH_3$), 1.88 (s, 3H, $COCH_3$), 1.20 (t, 3H, J = 7.2 Hz, $COOCH_2CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.46, 169.93, 169.47, 169.23, 137.02, 135.82, 128.83, 128.54, 128.13, 128.09, 127.22, 89.40, 81.44, 76.27, 75.48, 74.58, 73.21, 70.71, 62.37, 61.48, 20.97, 20.86, 20.77, 13.93; HR MALDI-TOF MS m/z calcd for $C_{29}H_{34}O_{11}$ $[M+Na]^+$ 581.1999, found 581.1983. **10*S*(β)** (0.69 g, 19%):

colorless syrup, R_f = 0.62 (ethyl acetate/hexane, 1/1); $[\alpha]^{20}_D$ = +120° (*c* = 1.2, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.19-7.38 (m,10H, aromatic), 5.73 (d, 1H, *J* = 8.1 Hz, H-1), 5.37 (t, 1H, *J* = 9.0 Hz, H-3), 4.99 (s, 1H, >C*H*Ph), 4.51 (d, 1H, *J* = 11.1 Hz, C*H*HPh), 4.46 (d, 1H, *J* = 11.1 Hz, CH*H*Ph), 4.29 (dd, 1H, *J* = 2.4, 12.3 Hz, H-6a), 4.21 (dd, 1H, *J* = 4.5, 12.3 Hz, H-6b), 4.05-4.17 (m, 2H, COOC*H*$_2$CH$_3$), 3.71-3.76 (m, 1H, H-5), 3.49-3.56 (m, 2H, H-4, H-2), 2.15 (s, 3H, $COCH_3$), 2.04 (s, 3H, $COCH_3$), 1.60 (s, 3H, $COCH_3$), 1.83 (t, 3H, *J* = 7.2 Hz, $COOCH_2CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.51, 170.20, 169.43, 168.53, 137.04, 136.65, 128.71, 128.54, 128.15, 128.07, 127.18, 93.51, 83.08, 80.00, 77.20, 75.47, 74.71, 74.31, 73.50, 62.44, 61.37, 20.97, 20.82, 20.62, 13.98; HR MALDI-TOF MS m/z calcd for $C_{29}H_{34}O_{11}$ [M+Na]+ 581.1999, found 581.1947.

Acetyl 3,6-di-*O*-acetyl-4-*O*-benzyl-2-*O*-(*R*)-ethoxycarbonylbenzyl-*α/β*-D-glucopyranose (10*R*). Compound **10*R*** was synthesized according to the procedure described for the synthesis of compound **10*S***: **10*R*(*α*)**: Colorless syrup, R_f = 0.55 (ethyl acetate/hexane, 1/1); $[\alpha]^{20}_D$ = +99.9° (*c* = 2.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26-7.37 (m,10H, aromatic), 6.29 (d, 1H, *J* = 3.6 Hz, H-1), 5.58 (t, 1H, *J* = 9.9 Hz, H-3), 4.98 (s, 1H, >C*H*Ph), 4.66 (d, 1H, *J* = 10.8 Hz, C*H*HPh), 4.55 (d, 1H, *J* = 10.8 Hz, C*H*HPh), 4.26 (d, 2H, *J* = 2.7 Hz, H-6$_a$, H-6$_b$), 4.09-4.21 (m, 2H, COOC*H*$_2$CH$_3$), 3.96-4.01 (m, 1H, H-5), 3.68 (dd, 1H, *J* = 3.6, 9.9 Hz, H-2), 3.66 (t, 1H, *J* = 9.9 Hz, H-4), 2.18 (s, 3H, $COCH_3$), 2.05 (s, 3H, $COCH_3$), 2.01 (s, 3H, $COCH_3$), 1.20 (t, 3H, *J* = 7.2 Hz, $COOCH_2CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.46, 170.05, 169.94, 169.04, 137.19, 135.85, 128.72, 128.54, 128.49, 128.11, 128.07, 127.01, 88.72, 79.66, 75.89, 75.06, 74.65, 72.95, 70.84, 62.36, 61.25, 21.15, 20.76, 14.00; HR MALDI-TOF MS m/z calcd for $C_{29}H_{34}O_{11}$ $[M+Na]^+$ 581.1999, found 581.1989. **10*R*(*β*)**: colorless syrup, R_f = 0.60 (ethyl acetate/hexane, 1/1); $[\alpha]^{20}_D$ = -38° (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26-

7.34 (m,10H, aromatic), 5.59 (d, 1H, J = 8.1 Hz, H-1), 5.44 (t, 1H, J = 9.3 Hz, H-3), 5.10 (s, 1H, >C*H*Ph), 4.63 (d, 1H, J = 11.1 Hz, C*H*HPh), 4.54 (d, 1H, J = 11.1 Hz, CH*H*Ph), 4.20-4.30 (m, 2H, H-6_a, H-6_b), 4.05-4.21 (m, 2H, COOCH_2CH$_3$), 3.55-3.74 (m, 3H, H-5, H-2, H-4), 2.15 (s, 3H, $COCH_3$), 2.03 (s, 3H, $COCH_3$), 1.85 (s, 3H, $COCH_3$), 1.20 (t, 3H, J = 7.2 Hz, COOCH$_2$CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.51, 170.11, 169.94, 168.45, 137.18, 136.47, 128.61, 128.57, 128.51, 128.15, 128.09, 126.80, 93.57, 82.00, 79.10, 75.33, 75.00, 74.46, 73.65, 62.45, 61.29, 21.19, 20.82, 20.65, 14.06; HR MALDI-TOF MS m/z calcd for $C_{29}H_{34}O_{11}$ $[M+Na]^+$ 581.1999, found 581.1983.

3,6-Di-*O*-acetyl-4-*O*-benzyl-2-*O*-(*S*)-ethoxycarbonylbenzyl-$\tilde{\alpha/\beta}$-D-glucopyranosyl trichloroacetimidate (12*S*). Hydrazinium acetate (254 mg, 2.76 mmol) was added to a solution of **10*S*** (1.40 g, 2.51 mmol) in DMF (10 mL) at room temperature. After stirring the reaction mixture for 18 h, it was quenched with an aqueous saturated solution of $NaHCO_3$. The mixture was extracted with ethyl acetate (30 mL), and the organic phase was washed with an aqueous saturated solution of NH_4Cl (30 mL) and dried (MgSO4), filtered and the filtrate was concentrated in vacuo. The residue was purified by silica gel column chromatography (20% ethyl acetate in hexane) to afford **11*S*** (1.23 g, 95%). Trichloroacetonitrile (2.38 mL) and 1, 8-diazabicyclo[5.4.0]undec-7-ene (DBU) (143 µL) were added to a solution of **11*S*** (1.23 g, 2.38 mmol) in dichloromethane (10 mL) at 0 °C. After stirring the reaction mixture for 1 h, it was concentrated in vacuo. The residue was purified by silica gel column chromatography (20% ethyl acetate in hexane) to afford **12*S*(*α*)** (1.21 g, 77%): R_f = 0.65 (ethyl acetate/hexane, 1/1); $[\alpha]^{20}_D$ = +107.4˚ (c = 2.1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.68 (s, 1H, NH), 7.23-7.38 (m,10H, aromatic), 6.68 (d, 1H, J = 3.6 Hz, H-1), 5.65 (t, 1H, J = 9.6 Hz, H-3), 5.03 (s, 1H, >C*H*Ph), 4.56 (d, 1H, J = 11.1 Hz, C*H*HPh), 4.51 (d, 1H, J = 11.1 Hz, CH*H*Ph), 4.32 (dd, 1H, J = 2.1, 12.0 Hz,

H-6_a), 4.24 (dd, 1H, J = 3.9, 12.0 Hz, H-6_b), 4.08-4.19 (m, 3H, COOCH_2CH$_3$, H-5), 3.72 (dd, 1H, J = 3.6, 9.9 Hz, H-2), 3.61 (t, 1H, J = 9.9 Hz, H-4), 2.04 (s, 3H, $COCH_3$), 1.87 (s, 3H, $COCH_3$), 1.20 (t, 3H, J = 7.2 Hz, $COOCH_2CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.46, 170.25, 169.31, 161.20, 137.01, 135.78, 128.77, 128.57, 128.48, 128.27, 128.20, 127.05, 93.93, 81.80, 76.67, 75.35, 74.47, 73.35, 71.10, 62.35, 61.51, 20.85, 20.78, 14.01. **12*S*(*β*)** (0.24 g, 15%): R_f = 0.69 (ethyl acetate/hexane, 1/1); $[\alpha]^{20}_D$ = +126.7° (c = 1.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.73 (s, 1H, NH), 7.19-7.43 (m,10H, aromatic), 6.03 (d, 1H, J = 6.9 Hz, H-1), 5.32 (t, 1H, J = 8.1 Hz, H-3), 5.32 (s, 1H, >C*H*Ph), 4.52 (d, 1H, J = 11.4 Hz, C*H*HPh), 4.46 (d, 1H, J = 11.4 Hz, CH*H*Ph), 4.32 (dd, 1H, J = 2.1, 12.0 Hz, H-6_a), 4.21 (dd, 1H, J = 3.9, 12.0 Hz, H-6_b), 4.02-4.15 (m, 2H, COOCH_2CH$_3$), 3.78-3.83 (m, 1H, H-5), 3.65-3.71 (m, 2H, H-2, H-4), 2.00 (s, 3H, $COCH_3$), 1.75 (s, 3H, $COCH_3$), 1.14 (t, 3H, J = 7.2 Hz, $COOCH_2CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.49, 169.82, 169.56, 160.26, 137.08, 136.46, 128.86, 128.59, 128.50, 128.10, 127.99, 97.61, 81.06, 75.10, 74.92, 74.04, 72.89, 62.36, 61.24, 20.86, 20.80, 13.95.

3,6-Di-*O*-acetyl-4-*O*-benzyl-2-*O*-(*R*)-ethoxycarbonylbenzyl-$\tilde{\alpha}/\beta$-D-glucopyranosyl trichloroacetimidate (12*R*). Compound **12*R*** was synthesized according to the procedure described for the synthesis of compound **12*S***. R_f = 0.67 (ethyl acetate/hexane, 1/1); $[\alpha]^{20}_D$ = +61.0° (c = 1.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.39 (s, 1H, NH), 7.26-7.37 (m,10H, aromatic), 6.49 (d, 1H, J = 3.3 Hz, H-1), 5.70 (t, 1H, J = 9.6 Hz, H-3), 5.04 (s, 1H, >C*H*Ph), 4.68 (d, 1H, J = 11.1 Hz, C*H*HPh), 4.57 (d, 1H, J = 11.1 Hz, CH*H*Ph), 4.11-4.34 (m, 5H, H-6_a, H-6_b, H-5, COOCH_2CH$_3$), 3.77 (dd, 1H, J = 3.6, 9.9 Hz, H-2), 3.71 (t, 1H, J = 9.9 Hz, H-4), 2.17 (s, 3H, $COCH_3$), 2.03 (s, 3H, $COCH_3$), 1.21 (t, 3H, J = 7.2 Hz, $COOCH_2CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.42, 169.97, 169.90, 160.77, 137.15, 135.91, 128.54, 128.47, 128.29, 128.19, 128.15, 126.81, 92.96, 79.72, 76.37, 74.89, 74.58, 72.74, 71.21, 62.28, 61.25, 21.13, 20.74, 14.03.

The β-anomer of **12*R*** was also identified and isolated: R_f = 0.71 (ethyl acetate/hexane, 1/1); $[\alpha]^{20}_D$ = +47° (*c* = 1.3, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.66 (s, 1H, NH), 7.26-7.37 (m, 10H, aromatic), 5.83 (d, 1H, *J* = 7.5 Hz, H-1), 5.45 (s, 1H, >C*H*Ph), 5.44 (t, 1H, *J* = 9.6 Hz, H-3), 4.68 (d, 1H, *J* = 11.4 Hz, C*H*HPh), 4.58 (d, 1H, *J* = 11.4 Hz, CH*H*Ph), 4.33 (d, 1H, *J* = 12.3 Hz, H-6_a), 4.26 (dd, 1H, *J* = 2.4, 12.3 Hz, H-6_b), 4.08-4.22 (m, 3H, COOCH_2CH$_3$, H-5), 3.73-3.82 (m, 2H, H-2, H-4), 2.19 (s, 3H, $COCH_3$), 2.02 (s, 3H, $COCH_3$), 1.20 (t, 3H, *J* = 7.2 Hz, $COOCH_2CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.54, 170.42, 170.36, 160.30, 137.29, 136.14, 128.76, 128.54, 128.44, 128.13, 126.83, 97.85, 79.90, 77.24, 77.20, 74.96, 74.26, 73.32, 62.41, 61.15, 21.28, 20.82, 14.08.

General Procedure for the Glycosylation Employing 3,6-Di-*O*-acetyl-4-*O*-benzyl-2-*O*-(*S/R*)-ethoxycarbonylbenzyl-α-D-glucopyranosyl trichloroacetimidate (12*S* *or* 12*R*). A mixture of donor **12*S*** *or* **12*R*** (20 mg, 0.03 mmol, 1 equiv), acceptor (0.036 mmol, 1.2 equiv) and activated molecular sieves (4Å) in DCM (10 mL) was stirred for 1 h under an atmosphere of argon at RT, then cooled to -78 °C. After addition of trimethylsilyl trifluoromethanesulfonate (2.2 μL, 0.012 mmol, 0.4 equiv), the reaction mixture was stirred at -78 °C for 1 h and allowed to warm over 1 h to 0 °C. The reaction mixture was quenched with aqueous saturated $NaHCO_3$ (10 mL) and separated. The organic phase was dried ($MgSO_4$), filtered and the filtrate was concentrated *in vacuo*. The residue was purified by silica gel column chromatography (DCM/n-hexane/ethyl acetate = 2/2/1).

Methyl (3,6-Di-*O*-acetyl-4-*O*-benzyl-2-*O*-(*S*)-ethoxycarbonylbenzyl-α-D-glucopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (14*S*α); $[\alpha]^{20}_D$ = +251.9° (*c* = 1.3, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16-7.37 (m, 25H, aromatic), 5.81 (d, 1H, *J* = 3.5 Hz, H-1'), 5.54 (t, 1H, *J* = 9.5 Hz, H-3'), 5.06 (d, 1H, *J* = 11.5 Hz, C*H*HPh), 4.93 (d, 1H, *J* =

11.5 Hz, CH*H*Ph), 4.91 (s, 1H, >C*H*Ph), 4.67 (d, 1H, *J* = 12.5 Hz, C*H*HPh), 4.61 (d, 1H, *J* = 3.5 Hz, H-1), 4.56 (d, 1H, *J* = 12.5 Hz, CH*H*Ph), 4.51 (s, 2H, CH_2Ph), 4.50 (d, 1H, *J* = 11.0 Hz, C*H*HPh), 4.43 (d, 1H, *J* = 11.0 Hz, C*H*HPh), 4.00-4.08 (m, 6H, H-3, H-6_a, H-$6_{a'}$, H-$6_{b'}$, COOC$H_2$$CH_3$), 3.85-3.93 (m, 3H, H-5', H-4, H-6_b), 3.64 (d, 1H, *J* = 10.0 Hz, H-5), 3.59 (dd, 1H, *J* = 4.0, 9.0 Hz, H-2), 3.43 (t, 1H, *J* = 9.5 Hz, H-4'), 3.39 (dd, 1H, *J* = 3.5, 10.0 Hz, H-2'), 3.38 (s, 3H, OCH_3), 1.97 (s, 3H, $COCH_3$), 1.92 (s, 3H, $COCH_3$), 1.12 (t, 3H, *J* = 7.0 Hz, $COOCH_2CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.47, 170.09, 169.52, 139.36, 137.98, 137.54, 135.82, 128.71, 128.47, 128.43, 128.24, 128.17, 128.01, 127.93, 127.89, 127.45, 127.41, 126.92, 97.67, 95.28, 81.60, 80.53, 80.23, 77.21, 76.42, 76.04, 74.15, 73.84, 73.38, 73.26, 73.20, 71.75, 69.28, 68.85, 68.79, 62.75, 61.26, 55.13, 21.04, 20.86, 13.98; HR MALDI-TOF MS m/z calcd for $C_{55}H_{62}O_{15}$ $[M+Na]^+$ 985.3986, found 985.3965.

Methyl (3,6-Di-*O*-acetyl-4-*O*-benzyl-2-*O*-(*R*)-ethoxycarbonylbenzyl-*β*-D-glucopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-*α*-D-glucopyranoside (14*R*β); $[\alpha]^{20}_D$ = +91.6° (*c* = 0.3, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20-7.38 (m, 25H, aromatic), 5.14 (s, 1H, >C*H*Ph), 5.14 (t, 1H, *J* = 9.5 Hz, H-3'), 4.98 (d, 1H, *J* = 11.0 Hz, C*H*HPh), 4.73 (d, 1H, *J* = 11.5 Hz, CH*H*Ph), 4.69 (d, 1H, *J* = 11.0 Hz, C*H*HPh), 4.60 (d, 1H, *J* = 12.0 Hz, CH*H*Ph), 4.57 (d, 1H, *J* = 12.5 Hz, C*H*HPh), 4.53 (d, 1H, *J* = 4.0 Hz, H-1), 4.51 (d, 1H, *J* = 12.0 Hz, CH*H*Ph), 4.49 (d, 1H, *J* = 12.0 Hz, C*H*HPh), 4.14-4.19 (m, 4H, H-$6_{a'}$, H-$6_{b'}$, H-1', CH*H*Ph), 4.03-4.10 (m, 2H, COOC$H_2$$CH_3$), 3.89 (t, 1H, *J* = 10.0 Hz, H-4), 3.77 (t, 1H, *J* = 9.5 Hz, H-3), 3.54 (t, 1H, *J* = 9.5 Hz, H-4'), 3.45 (dd, 1H, *J* = 4.0, 9.5 Hz, H-2), 3.32 (s, 3H, OCH_3), 3.28 (dd, 1H, *J* = 2.0, 11.5 Hz, H-6_a), 3.20-3.26 (m, 2H, H-2', H-5'), 3.16 (d, 1H, *J* = 10.5 Hz, H-5), 2.91 (dd, 1H, *J* = 1.5, 11.0 Hz, H-6_b), 2.17 (s, 3H, $COCH_3$), 1.88 (s, 3H, $COCH_3$), 1.18 (t, 3H, *J* = 7.5 Hz, $COOCH_2CH_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.65, 170.60, 170.30, 139.44, 138.30, 137.59, 137.35, 136.88,

128.64, 128.49, 128.33, 128.30, 128.25, 128.22, 128.13, 128.05, 128.00, 127.95, 127.88, 127.81, 127.73, 127.20, 127.09, 101.93, 98.21, 81.02, 80.19, 80.01, 78.47, 75.85, 75.07, 74.85, 74.21, 73.47, 73.31, 72.53, 69.33, 66.98, 62.97, 60.99, 55.16, 21.36, 20.70, 14.07; HR MALDI-TOF MS m/z calcd for $C_{55}H_{62}O_{15}$ $[M+Na]^+$ 985.3986, found 985.3898.

Methyl (3,6-Di-*O*-acetyl-4-*O*-benzyl-2-*O*-(*S*)-ethoxycarbonylbenzyl-*α*-D-glucopyranosyl)-(1→6)-2,3,4-tri-*O*-benzoyl-*α*-D-glucopyranoside (16*Sα*); $[\alpha]^{20}_D$ = -65.8° (*c* = 3.2, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87-8.01 (m, 6H, aromatic), 7.25-7.54 (m, 19H, aromatic), 6.19 (t, 1H, *J* = 10.0 Hz, H-3), 5.67 (t, 1H, *J* = 10.0 Hz, H-3'), 5.43 (t, 1H, *J* = 10.0 Hz, H-4), 5.29 (dd, 1H, *J* = 3.5, 10.0 Hz, H-2), 5.23 (d, 1H, *J* = 3.5 Hz, H-1), 5.08 (d, 1H, *J* = 3.0 Hz, H-1'), 5.05 (s, 1H, >C*H*Ph), 4.58 (d, 1H, *J* = 11.0 Hz, C*H*HPh), 4.53 (d, 1H, *J* = 11.0 Hz, CH*H*Ph), 4.42 (t, 1H, *J* = 9.5 Hz, H-5), 4.32 (d, 1H, *J* = 11.0 Hz, H-$6_{a'}$), 4.20-4.26 (m, 2H, H-$6_{b'}$, H-5'), 4.07-4.12 (m, 2H, COOC*H*$_2$CH$_3$), 3.92 (dd, 1H, *J* = 8.0, 10.5 Hz, H-6_a), 3.66 (d, 1H, *J* = 10.5 Hz, H-6_b), 3.57 (dd, 1H, *J* = 3.5, 10.5 Hz, H-2'), 3.52 (t, 1H, *J* = 9.5 Hz, H-4'), 3.50 (s, 3H, OCH_3), 2.10 (s, 3H, $COCH_3$), 1.86 (s, 3H, $COCH_3$), 1.15 (t, 3H, *J* = 7.0 Hz, $COOCH_2CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.82, 170.67, 169.59, 165.81, 165.48, 137.50, 136.17, 133.42, 133.29, 133.04, 129.96, 129.68, 129.29, 129.16, 128.92, 128.54, 128.48, 128.42, 128.39, 128.25, 128.01, 127.96, 126.86, 97.31, 96.61, 81.59, 78.32, 76.13, 73.82, 73.20, 72.21, 70.58, 69.84, 68.74, 68.59, 67.33, 62.91, 61.39, 55.64, 20.89, 14.01; HR MALDI-TOF MS m/z calcd for $C_{55}H_{56}O_{18}$ $[M+Na]^+$ 1027.3364, found 1027.3344.

Methyl (3,6-Di-*O*-acetyl-4-*O*-benzyl-2-*O*-(*S*)-ethoxycarbonylbenzyl-*β*-D-glucopyranosyl)-(1→6)-2,3,4-tri-*O*-benzoyl-*α*-D-glucopyranoside (16*Sβ*); $[\alpha]^{20}_D$ = +16.0° (*c* = 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84-7.98 (m, 6H, aromatic), 7.17-7.54 (m, 19H, aromatic), 6.17 (t, 1H, *J* = 10.0 Hz, H-3), 5.41 (t, 1H, *J* = 10.0 Hz, H-3'), 5.23-5.32 (m, 4H, H-4,

H-2, H-1, >C*H*Ph), 4.60 (d, 1H, *J* = 7.5 Hz, H-1'), 4.48 (d, 1H, *J* = 11.0 Hz, C*H*HPh), 4.38-4.43 (m, 2H, H-5, CH*H*Ph), 4.22 (dd, 1H, *J* = 2.5, 12.0 Hz, H-$6_{a'}$), 4.11-4.19 (m, 3H, H-$6_{b'}$, H-5', COOCH_2CH$_3$), 3.98 (dd, 1H, *J* = 2.5, 11.0 Hz, H-6_a), 3.82 (dd, 1H, *J* = 8, 11.0 Hz, H-6_b), 3.55-3.58 (m, 1H), 3.54 (s, 3H, OCH$_3$), 3.39 (t, 1H, *J* = 9.5 Hz, H-4'), 3.26 (dd, 1H, *J* = 8.0, 10.0 Hz, H-2'), 1.95 (s, 3H, COCH$_3$), 1.70 (s, 3H, COCH$_3$), 1.18 (t, 3H, *J* = 7.0 Hz, COOCH$_2$CH_3); ^{13}C NMR (75 MHz, CDCl$_3$) δ 170.62, 170.26, 169.48, 165.84, 165.79, 165.44, 137.18, 137.02, 133.53, 133.37, 133.10, 129.93, 129.88, 129.66, 129.24, 129.09, 128.91, 128.59, 128.52, 128.50, 128.43, 128.27, 128.07, 128.01, 127.83, 103.64, 96.93, 81.40, 78.61, 76.16, 74.68, 74.32, 72.60, 72.09, 70.30, 70.08, 69.77, 68.90, 62.99, 61.17, 55.89, 20.85, 20.67, 14.12; HR MALDI-TOF MS: m/z: calcd for $C_{55}H_{56}O_{18}$ $[M+Na]^+$: 1027.3364; found: 1027.3378.

Methyl (3,6-Di-*O*-acetyl-4-*O*-benzyl-2-*O*-(*R*)-ethoxycarbonylbenzyl-α-D-glucopyranosyl)-(1→6)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (16*Rα*); $[\alpha]^{20}_D$ = +144.3° (*c* = 0.7, CHCl$_3$); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.84-7.98 (m, 6H, aromatic), 7.09-7.54 (m, 19H, aromatic), 6.14 (t, 1H, *J* = 9.5 Hz, H-3), 5.68 (t, 1H, *J* = 9.5 Hz, H-3'), 5.34 (t, 1H, *J* = 10.0 Hz, H-4), 5.19 (s, 1H, H-1), 5.18 (dd, 1H, *J* = 3.5, 9.5 Hz, H-2), 4.96 (s, 1H, >C*H*Ph), 4.68 (d, 1H, *J* = 3.5 Hz, H-1'), 4.61 (d, 1H, *J* = 11.0 Hz, C*H*HPh), 4.54 (d, 1H, *J* = 11.0 Hz, CH*H*Ph), 4.24-4.28 (m, 2H, H-5, H-5'), 4.20 (dd, 1H, *J* = 4.5, 12.5 Hz, H-$6_{a'}$), 4.08-4.13 (m, 3H, H-$6_{b'}$, COOCH_2CH$_3$), 3.75 (dd, 1H, *J* = 8.5, 10.5 Hz, H-6_a), 3.61 (dd, 1H, *J* = 3.5, 9.5 Hz, H-2'), 3.55 (t, 1H, *J* = 10.0 Hz, H-4'), 3.49 (s, 3H, OCH$_3$), 3.33 (d, 1H, *J* = 10.5 Hz, H-6_b), 2.06 (s, 3H, COCH$_3$), 2.01 (s, 3H, COCH$_3$), 1.17 (t, 3H, *J* = 7.5 Hz, COOCH$_2$CH_3); ^{13}C NMR (75 MHz, CDCl$_3$) δ 170.63, 170.11, 169.89, 165.76, 165.36, 137.56, 136.77, 133.51, 133.31, 133.06, 129.94, 129.90, 129.66, 129.23, 129.12, 128.85, 128.58, 128.48, 128.41, 128.25, 128.01, 127.95, 127.03, 96.60, 96.48, 80.01, 77.90, 75.91, 73.88, 72.19, 72.14, 70.46, 69.72, 68.56, 68.52, 66.56,

62.82, 61.26, 55.62, 21.03, 20.86, 14.02; HR MALDI-TOF MS m/z calcd for $C_{55}H_{56}O_{18}$ $[M+Na]^+$ 1027.3364, found 1027.3405.

Methyl (3,6-Di-*O*-acetyl-4-*O*-benzyl-2-*O*-(*R*)-ethoxycarbonylbenzyl-*β*-D-glucopyranosyl)-(1→6)-2,3,4-tri-*O*-benzoyl-*α*-D-glucopyranoside (16*Rβ*); $[\alpha]^{20}_D$ = +164.4° (*c* = 1.6, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 7.84-7.99 (m, 6H, aromatic), 7.25-7.53 (m, 19H, aromatic), 6.17 (t, 1H, *J* = 9.5 Hz, H-3), 5.70 (s, 1H, >C*H*Ph), 5.36 (t, 2H, *J* = 9.5 Hz, H-3', H-4), 5.28 (s, 1H, H-1), 5.27 (dd, 1H, *J* = 4.0, 9.5 Hz, H-2), 4.66 (d, 1H, *J* = 10.5 Hz, C*H*HPh), 4.53 (d, 1H, *J* = 10.5 Hz, CH*H*Ph), 4.52 (d, 1H, *J* = 7.0 Hz, H-1'), 4.38 (t, 1H, *J* = 9.5 Hz, H-5), 4.13-4.21 (m, 3H, H-$6_{a'}$, COOC*H*$_2$CH$_3$), 4.06 (dd, 1H, *J* = 7.5, 10.5 Hz, H-$6_{b'}$), 4.00 (d, 1H, *J* = 10.0 Hz, H-6), 3.74 (dd, 1H, *J* = 9.0, 10.0 Hz, H-6_a), 3.55-3.61 (m, 2H, H-4', H-5'), 3.45 (s, 3H, OCH_3), 3.42 (t, 1H, *J* = 9.5 Hz, H-2'), 2.24 (s, 3H, $COCH_3$), 1.85 (s, 3H, $COCH_3$), 1.14 (t, 3H, *J* = 7.5 Hz, $COOCH_2CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) *δ* 170.97, 170.56, 170.44, 165.86, 165.74, 165.51, 137.37, 136.66, 133.58, 133.41, 133.13, 129.93, 129.84, 129.63, 129.16, 129.03, 128.72, 128.59, 128.53, 128.49, 128.44, 128.28, 128.06, 128.00, 127.14, 103.45, 96.85, 79.65, 78.21, 75.86, 74.94, 74.52, 72.78, 72.07, 70.27, 69.93, 68.88, 63.01, 60.88, 55.69, 21.31, 20.57, 14.08; HR MALDI-TOF MS m/z calcd for $C_{55}H_{56}O_{18}$ $[M+Na]^+$ 1027.3364, found 1027.3352.

3,6-Di-*O*-acetyl-4-*O*-benzyl-2-*O*-(*S*)-ethoxycarbonylbenzyl-*α*-D-glucopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-*α*-D-galactopyranose (18*Sα*). $[\alpha]^{20}_D$ = +169.4° (*c* = 1.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 7.23-7.40 (m, 10H, aromatic), 5.61 (t, 1H, *J* = 9.5 Hz, H-3'), 5.51 (d, 1H, *J* = 5.0 Hz, H-1), 5.09 (d, 1H, *J* = 3.5 Hz, H-1'), 5.08 (s, 1H, >C*H*Ph), 4.61 (dd, 1H, *J* = 2.5, 8.0 Hz, H-3), 4.54 (d, 1H, *J* = 11.5 Hz, C*H*HPh), 4.50 (d, 1H, *J* = 11.5 Hz, CH*H*Ph), 4.35 (dd, 1H, *J* = 2.0, 8.0 Hz, H-4), 4.30 (dd, 1H, *J* = 2.5, 5.0 Hz, H-2), 4.26-4.28 (m, 2H), 4.03-4.18 (m, 4H), 3.76-3.81 (m, 2H), 3.50 (t, 1H, *J* = 10.0 Hz, H-4'), 3.47 (dd, 1H, *J* = 3.5, 9.5 Hz,

H-2), 2.05 (s, 3H, $COCH_3$), 1.94 (s, 3H, $COCH_3$), 1.55 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 1.36 (s, 3H, CH_3), 1.32 (s, 3H, CH_3), 1.20 (t, 3H, J = 7.0 Hz, $COOCH_2CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.72, 170.42, 169.61, 137.49, 135.96, 128.79, 128.59, 128.48, 128.10, 127.96, 127.32, 109.25, 108.78, 97.41, 96.29, 80.45, 76.67, 75.96, 73.51, 73.24, 70.85, 70.69, 70.66, 68.17, 67.49, 66.44, 62.95, 61.31, 26.16, 26.13, 24.97, 24.65, 20.10, 20.90, 14.05; HR MALDI-TOF MS m/z calcd for $C_{39}H_{50}O_{15}$ $[M+Na]^+$ 781.3047, found 781.3033.

3,6-Di-*O*-acetyl-4-*O*-benzyl-2-*O*-(*S*)-ethoxycarbonylbenzyl-*β*-D-glucopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-*α*-D-galactopyranose (18*Sβ*). $[\alpha]^{20}_D$ = -98.7° (*c* = 0.6, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19-7.43 (m, 10H, aromatic), 5.55 (s, 1H, >C*H*Ph), 5.54 (d, 1H, J = 6.0 Hz, H-1), 5.34 (t, 1H, J = 9.5 Hz, H-3'), 4.61 (dd, 1H, J = 2.5, 7.5 Hz, H-3), 4.60 (d, 1H, J = 7.5 Hz, H-1'), 4.50 (d, 1H, J = 11.5 Hz, C*H*HPh), 4.42 (d, 1H, J = 11.5 Hz, CH*H*Ph), 4.33 (dd, 1H, J = 2.5, 5.0 Hz, H-2), 4.04-4.29 (m, 7H), 3.73 (dd, 1H, J = 9.0, 11.5 Hz), 3.54-3.57 (m, 1H, H-5), 3.42 (t, 1H, J = 9.5 Hz, H-4'), 3.23 (dd, 1H, J = 7.5, 9.5 Hz, H-2'), 2.03 (s, 3H, $COCH_3$), 1.86 (s, 3H, $COCH_3$), 1.60 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.34 (s, 6H, 2 × CH_3), 1.18 (t, 3H, J = 7.0 Hz, $COOCH_2CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.67, 170.57, 169.62, 137.26, 136.73, 128.58, 128.52, 128.50, 128.33, 128.05, 127.99, 109.50, 108.53, 104.06, 96.41, 80.19, 76.60, 76.01, 74.85, 74.37, 72.63, 71.30, 70.86, 70.35, 70.16, 67.00, 62.96, 60.98, 26.03, 26.00, 24.95, 24.52, 20.96, 20.88, 14.02; HR MALDI-TOF MS m/z calcd for $C_{39}H_{50}O_{15}$ $[M+Na]^+$ 781.3047, found 781.3028.

3,6-Di-*O*-acetyl-4-*O*-benzyl-2-*O*-(*R*)-ethoxycarbonylbenzyl-*α*-D-glucopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-*α*-D-galactopyranose (18*Rα*). $[\alpha]^{20}_D$ = +254.2° (*c* = 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28-7.53 (m, 10H), 5.66 (t, 1H, J = 9.5 Hz), 5.48 (d, 1H, J = 4.5 Hz), 5.07 (s, 1H), 4.91 (d, 1H, J = 4.0 Hz), 4.64 (d, 1H, J = 11.5 Hz), 4.57 (d, 1H, J =

11.5 Hz), 4.51 (d, 1H, *J* = 10.0 Hz), 3.96-4.34 (m, 8H), 3.57-3.73 (m, 4H), 2.12 (s, 3H), 2.07 (s, 3H), 1.56 (s, 3H), 1.44 (s, 3H), 1.33 (s, 3H), 1.27 (s, 3H), 1.23 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.71, 170.16, 170.06, 137.55, 136.51, 128.71, 128.67, 128.30, 127.10, 109.25, 108.80, 96.79, 96.26, 79.45, 77.22, 76.92, 75.76, 73.78, 72.87, 70.79, 70.62, 68.25, 66.93, 66.17, 62.89, 61.25, 26.15, 26.12, 24.93, 24.73, 21.18, 20.89, 14.10; HR MALDI-TOF MS m/z calcd for $C_{39}H_{50}O_{15}$ $[M+Na]^+$ 781.3047, found 781.3108.

3,6-Di-*O*-acetyl-4-*O*-benzyl-2-*O*-(*R*)-ethoxycarbonylbenzyl-*β*-D-glucopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-*α*-D-galactopyranose (18*Rβ*). $[\alpha]^{20}_D$ = +126.1° (*c* = 1.3, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49-7.51 (m, 2H), 7.26-7.35 (m, 8H), 5.66 (s, 1H), 5.53 (d, 1H, *J* = 4.5 Hz), 5.36 (t, 1H, *J* = 9.5 Hz), 4.68 (d, 1H, *J* = 11.5 Hz), 4.57 (dd, 1H, *J* = 3.5, 8.0 Hz), 4.55 (d, 1H, *J* = 11.5 Hz), 4.50 (d, 1H, *J* = 8.0 Hz), 4.29-4.32 (m, 2H), 4.24 (dd, 1H, *J* = 5.0, 12.0 Hz), 4.12-4.19 (m, 2H), 4.02-4.09 (m, 3H), 3.62-3.70 (m, 2H), 3.56-3.59 (m, 1H), 3.47 (dd, 1H, *J* = 8.0, 9.5 Hz), 2.26 (s, 3H), 2.07 (s, 3H), 1.54 (s, 3H), 1.43 (s, 3H), 1.37 (s, 3H), 1.34 (s, 3H), 1.19 (t, 3H, *J* = 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.28, 170.68, 170.50, 137.49, 136.96, 128.54, 128.30, 128.03, 127.36, 109.50, 108.65, 103.91, 96.25, 79.54, 77.94, 75.72, 75.11, 74.55, 72.87, 71.44, 70.76, 70.48, 69.98, 67.19, 62.91, 60.73, 26.13, 25.97, 25.12, 24.49, 21.35, 20.90, 14.14; HR MALDI-TOF MS m/z calcd for $C_{39}H_{50}O_{15}$ $[M+Na]^+$ 781.3047, found 781.3053.

Methyl (3,6-di-*O*-acetyl-4-*O*-benzyl-2-*O*-(*S*)-ethoxycarbonylbenzyl-α-D-glucopyranosyl)-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-*α*-D-glucopyranoside (20*Sα*). $[\alpha]^{20}_D$ = +101.4° (*c* = 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.64-7.57 (m, 20H), 5.59 (t, 1H, *J* = 9.5 Hz), 5.59 (s, 1H), 5.41 (d, 1H, *J* = 3.0 Hz), 4.87 (s, 1H), 4.71 (d, 1H, *J* = 3.5 Hz), 4.59 (s, 2H), 4.45 (d, 1H, *J* = 11.0 Hz), 4.38 (d, 1H, *J* = 11.0 Hz), 4.22-4.32 (m, 3H), 4.08-4.12 (m, 2H), 4.06

(d, 1H, *J* = 11.5 Hz), 3.82-3.86 (m, 2H), 3.66-3.74 (m, 3H), 3.40 (s, 3H), 3.35 (t, 1H, *J* = 9.5 Hz), 3.16 (dd, 1H, *J* = 4.0, 10.0 Hz), 2.06 (s, 3H), 1.98 (s, 3H), 1.22 (t, 3H, *J* = 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.60, 169.73, 169.64, 137.85, 137.39, 137.34, 134.93, 129.52, 128.72, 128.64, 128.54, 128.48, 128.40, 128.32, 128.04, 127.95, 127.84, 127.75, 127.14, 102.41, 98.34, 94.94, 82.60, 77.74, 77.53, 75.42, 73.72, 73.48, 73.01, 72.95, 72.78, 69.17, 67.78, 62.51, 61.81, 61.14, 55.33, 21.08, 20.81, 14.09; HR MALDI-TOF MS m/z calcd for $C_{48}H_{54}O_{15}$ $[M+Na]^+$ 893.3360, found: 893.3347.

Methyl (3,6-di-*O*-acetyl-4-*O*-benzyl-2-*O*-(*S*)-ethoxycarbonylbenzyl-*β*-D-glucopyranosyl)-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-*α*-D-glucopyranoside (20*Sβ*). $[\alpha]^{20}_D$ = -73.3˚ (*c* = 0.7, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14-7.52 (m, 20H), 5.54 (s, 1H), 5.35 (s, 1H), 5.24 (t, 1H, *J* = 9.5 Hz), 5.09 (d, 1H, *J* = 8.0 Hz), 4.88 (d, 1H, *J* = 12.0 Hz), 4.59 (d, 1H, *J* = 12.0 Hz), 4.55 (d, 1H, *J* = 4.0 Hz), 4.40 (d, 1H, *J* = 11.0 Hz), 4.37 (d, 1H, *J* = 11.0 Hz), 4.34 (t, 1H, *J* = 9.0 Hz), 4.23 (dd, 1H, *J* = 4.5, 10.0 Hz), 4.15-4.18 (m, 2H), 4.01-4.09 (m, 2H), 3.81 (dd, 1H, *J* = 4.5, 9.5 Hz), 3.71-3.75 (m, 2H), 3.57 (t, 1H, *J* = 9.5 Hz), 3.42 (t, 1H, *J* = 9.0 Hz), 3.34-3.37 (m, 2H), 3.32 (s, 3H), 1.93 (s, 3H), 1.66 (s, 3H), 1.18 (t, 3H, *J* = 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.65, 170.36, 169.56, 138.03, 137.39, 137.31, 137.02, 129.10, 128.67, 128.60, 128.57, 128.48, 128.45, 128.25, 128.15, 128.01, 127.93, 126.24, 101.94, 101.45, 98.40, 82.18, 80.64, 79.97, 79.17, 76.28, 75.44, 74.95, 74.16, 73.24, 72.17, 69.06, 62.96, 62.06, 61.08, 55.26, 20.88, 20.82, 14.07; HR MALDI-TOF MS m/z: calcd for C48H54O15 [M+Na]+ 893.3360, found 893.3328.

Methyl (3,6-di-*O*-acetyl-4-*O*-benzyl-2-*O*-(*R*)-ethoxycarbonylbenzyl-α-D-glucopyranosyl)-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-*α*-D-glucopyranoside (20*Rα*). $[\alpha]^{20}_D$ = +114.9˚ (*c* = 0.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.03-7.39 (m, 20H), 5.68 (t, 1H, *J* = 9.5

Hz), 5.59 (d, 1H, *J* = 3.5 Hz), 5.01 (s, 1H), 4.85 (s, 1H), 4.66 (d, 1H, *J* = 4.0 Hz), 4.63 (d, 1H, *J* = 11.5 Hz), 4.59 (d, 1H, *J* = 11.5 Hz), 4.58 (d, 1H, *J* = 11.0 Hz), 4.48 (d, 1H, *J* = 11.0 Hz), 4.38 (d, 1H, *J* = 10.5 Hz), 4.26 (t, 1H, *J* = 9.5 Hz), 4.08-4.14 (m, 2H), 4.00-4.05 (m, 2H), 3.96 (dd, 1H, *J* = 3.0, 12.5 Hz), 3.72-3.77 (m, 1H), 3.52-3.63 (m, 3H), 3.50 (dd, 1H, *J* = 3.5, 10.0 Hz), 3.45 (t, 1H, *J* = 10.0 Hz), 3.37 (s, 3H), 2.13 (s, 3H), 2.04 (s, 3H), 1.10 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.65, 170.37, 170.32, 137.97, 137.31, 137.11, 136.07, 129.18, 128.64, 128.53, 128.40, 128.35, 128.29, 128.21, 128.07, 127.96, 127.76, 126.29, 126.15, 126.11, 101.30, 98.29, 95.13, 82.46, 77.70, 77.57, 76.28, 75.31, 73.97, 73.11, 73.06, 72.97, 68.99, 68.05, 62.58, 61.64, 60.93, 55.29, 21.29, 20.88, 14.07; HR MALDI-TOF MS m/z calcd for $C_{48}H_{54}O_{15}$ $[M+Na]^+$ 893.3360, found 893.3384.

Methyl (3,6-di-*O*-acetyl-4-*O*-benzyl-2-*O*-(*R*)-ethoxycarbonylbenzyl-*β*-D-glucopyranosyl)-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-*α*-D-glucopyranoside (20*Rβ*). $[\alpha]^{20}_D$ = +168.5° (*c* = 1.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16-7.49 (m, 20H), 5.67 (s, 1H), 5.55 (s, 1H), 5.33 (t, 1H, *J* = 9.5 Hz), 4.95 (d, 1H, *J* = 8.5 Hz), 4.61 (d, 1H, *J* = 11.0 Hz), 4.51 (d, 1H, *J* = 11.0 Hz), 4.42 (d, 1H, *J* = 4.0 Hz), 4.06-4.25 (m, 7H), 3.98 (d, 1H, *J* = 11.0 Hz), 3.71-3.78 (m, 2H), 3.62 (d, 1H, *J* = 9.5 Hz), 3.58 (d, 1H, *J* = 9.5 Hz), 3.47 (dd, 1H, *J* = 8.0, 9.5 Hz), 3.37-3.43 (m, 2H), 3.27 (s, 3H), 2.22 (s, 3H), 1.93 (s, 3H), 1.17 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.03, 170.70, 170.54, 137.78, 137.51, 137.30, 137.01, 129.07, 128.49, 128.41, 128.38, 128.35, 128.22, 128.01, 127.99, 127.28, 126.13, 102.63, 101.25, 98.26, 80.85, 80.14, 79.62, 78.68, 77.20, 75.84, 74.95, 74.38, 73.20, 72.39, 68.93, 63.04, 61.99, 60.89, 55.21, 21.39, 20.81, 14.12; HR MALDI-TOF MS m/z calcd for $C_{48}H_{54}O_{15}$ $[M+Na]^+$ 893.3360, found 893.3356.

Methyl (3,6-Di-*O*-acetyl-4-*O*-benzyl-2-*O*-(*S*)-ethoxycarbonylbenzyl-*α*-D-glucopyranosyl)-(1→6)-2,3,4-tri-*O*-benzyl-*α*-D-glucopyranoside (22*Sα*); $[\alpha]^{20}_D$ = -112.6° (*c* =

2.8, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18-7.37 (m, 25H), 5.63 (t, 1H, J = 10.0 Hz), 5.32 (d, 1H, J = 3.0 Hz), 5.04 (s, 1H), 4.97 (d, 1H, J = 11.5 Hz), 4.87 (d, 1H, J = 11.0 Hz), 4.82 (d, 1H, J = 11.0 Hz), 4.76 (d, 1H, J = 12.5 Hz), 4.65 (d, 1H, J = 13.0 Hz), 4.63 (d, 1H, J = 13.0 Hz), 4.61 (d, 1H, J = 3.5 Hz), 4.54 (d, 1H, J = 9.5 Hz), 4.48 (d, 1H, J = 9.5 Hz), 4.26 (d, 1H, J = 12.0 Hz), 4.20 (dd, 1H, J = 4.5, 12.0 Hz), 3.96-4.07 (m, 4H), 3.72-3.83 (m, 4H), 3.65 (dd, 1H, J = 4.0, 9.5 Hz), 3.49 (t, 1H, J = 10.5 Hz), 3.47 (dd, 1H, J = 3.0, 10.0 Hz), 3.37 (s, 3H), 2.02 (s, 3H), 1.90 (s, 3H), 1.13 (t, 3H, J = 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.78, 170.62, 169.46,138.98, 138.52, 138.42, 137.42, 135.93, 128.61, 128.54, 128.49, 128.35, 128.34, 128.28, 128.10, 128.07, 128.00, 127.88, 127.71, 127.54, 127.46, 127.06, 98.01, 97.00, 82.16, 81.55, 80.18, 77.76, 76.17, 75.72, 75.04, 74.08, 73.07, 73.36, 70.82, 68.44, 65.59, 62.88, 61.30, 55.15, 20.96, 20.86, 14.03; HR MALDI-TOF MS m/z calcd for $C_{55}H_{62}O_{15}$ $[M+Na]^+$ 985.3986, found 985.3998.

Methyl (3,6-Di-*O*-acetyl-4-*O*-benzyl-2-*O*-(*S*)-ethoxycarbonylbenzyl-*β*-D-glucopyranosyl)-(1→6)-2,3,4-tri-*O*-benzyl-*α*-D-glucopyranoside (22*Sβ*); $[\alpha]^{20}_D$ = -198.9° (*c* = 1.3, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.17-7.37 (m, 25H), 5.27 (s, 1H), 5.26 (t, 1H, J = 9.5 Hz), 4.99 (d, 1H, J = 10.5 Hz), 4.89 (d, 1H, J = 11.0 Hz), 4.79-4.82 (m, 2H), 4.66 (d, 1H, J = 11.5 Hz), 4.59 (d, 1H, J = 3.3 Hz), 4.57 (d, 1H, J = 10.0 Hz), 4.47 (d, 1H, J = 11.5 Hz), 4.40-4.44 (m, 2H), 4.28 (d, 1H, J = 12.0 Hz), 4.13 (dd, 1H, J = 4.5, 12.0 Hz), 3.95-4.07 (m, 4H), 3.84-3.88 (m, 1H), 3.58 (dd, 1H, J = 6.0, 11.0 Hz), 3.48-3.53 (m, 2H), 3.41 (s, 3H), 3.35-3.42 (m, 2H), 3.28 (t, 1H, J = 8.5 Hz), 1.97 (s, 3H), 1.71 (s, 3H), 1.02 (t, 3H, J = 7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.58, 170.05, 169.48, 138.73, 138.17, 138.16, 137.24, 136.83, 128.67, 128.50, 128.47, 128.35, 128.16, 128.04, 127.96, 127.94, 127.89, 127.83, 127.61, 103.47, 98.03, 81.88, 81.23, 79.90, 78.31, 77.90, 76.12, 75.75, 75.01, 74.70, 74.34, 73.40, 72.59, 69.81, 69.28, 62.79,

61.07, 55.37, 20.91, 20.79, 13.96; HR MALDI-TOF MS m/z calcd for $C_{55}H_{62}O_{15}$ $[M+Na]^+$ 985.3986, found 985.3876.

Methyl (3,6-Di-*O*-acetyl-4-*O*-benzyl-2-*O*-(*R*)-ethoxycarbonylbenzyl-β-D-glucopyranosyl)-(1→6)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (22*R*β); $[\alpha]^{20}_D$ = +94.6° (*c* = 1.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.09-7.39 (m, 25H), 5.53 (s, 1H), 5.32 (t, 1H, *J* = 9.5 Hz), 4.96 (d, 1H, *J* = 11.0 Hz), 4.82 (d, 1H, *J* = 12.0 Hz), 4.76 (d, 1H, *J* = 11.0 Hz), 4.70 (d, 1H, *J* = 12.0 Hz), 4.68 (d, 1H, *J* = 11.5 Hz), 4.61 (d, 1H, *J* = 3.0 Hz), 4.55 (t, 2H, *J* = 11.0 Hz), 4.22-4.33 (m, 3H), 4.17 (dd, 1H, *J* = 4.5, 12.5 Hz), 4.12 (dd, 1H, *J* = 7.5, 11.0 Hz), 4.02-4.07 (m, 2H), 3.96 (t, 1H, *J* = 9.0 Hz), 3.76-3.80 (m, 1H), 3.63 (t, 1H, *J* = 9.5 Hz), 3.51 (dd, 1H, *J* = 3.5, 10.0 Hz), 3.39-3.48 (m, 3H), 3.31 (s, 3H), 3.29 (t, 1H, *J* = 9.5 Hz), 2.22 (s, 3H), 1.99 (s, 3H), 1.15 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.86, 170.63, 170.56, 138.78, 138.14, 138.12, 137.51, 136.59, 128.53, 128.49, 128.41, 128.34, 128.15, 128.05, 127.97, 127.70, 127.60, 127.0, 103.48, 97.99, 81.85, 79.89, 79.76, 78.17, 77.99, 75.73, 74.89, 74.76, 74.57, 73.33, 72.88, 69.70, 68.58, 62.75, 60.87, 55.29, 21.35, 20.81, 14.10; HR MALDI-TOF MS m/z calcd for $C_{55}H_{62}O_{15}$ 985.3986, found 985.3965.

Methyl α-D-Glucopyranosyl-(1→6)-α-D-glucopyranoside (23). Sodium methoxide (3.0 mg, 1.0 equiv) was added to a solution of methyl (3,6-di-*O*-acetyl-4-*O*-benzyl-2-*O*-(*S*)-ethoxycarbonylbenzyl-α-D-glucopyranosyl)-(1→6)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (**16*S*α,** 55 mg, 1.0 equiv) in methanol (5mL). The reaction mixture was stirred for 1 day, then quenched by Amberlite IRC-50 ion exchange resin (weakly acidic). After filtration, the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography on Iatrobeads (dichloromethane/methanol = 2/1) to afford methyl (4-*O*-benzyl-2-*O*-methoxycarbonylbenzyl-α-D-glucopyranosyl)-(1→6)-α-D-glucopyranoside (30 mg, 93%). A solution of methyl (4-*O*-

benzyl-2-*O*-methoxycarbonylbenzyl-α-D-glucopyranosyl)-(1→6)-α-D-glucopyranoside (30 mg, 0.0518 mmol) in THF (3 mL) was added to liquid ammonia (5 mL) at -78 °C. Sodium (~20 mg) was then added until a persistent blue color was obtained. Solid NH_4Cl (0.1 g) was then added, and the solvent were allowed to evaporate under air. The crude reaction mixture was purified by column chromatography on Iatrobeads (dichloromethane/methanol/H_2O = 15/5/1) to afford **23** (18 mg, 97%): R_f = 0.34 (dichloromethane/methanol/H_2O = 15/5/1); $[\alpha]^{20}_D$ = +26.9° (*c* = 1.0, CH_3OH); ^{1}H NMR (500 MHz, D_2O) δ 4.87 (d, 1H, *J* = 4.0 Hz), 4.73 (d, 1H, *J* = 3.5 Hz), 3.90 (dd, 1H, *J* = 4.5, 9.0 Hz), 3.76 (dd, 1H, *J* = 2.0, 12.5 Hz), 3.33-3.73 (m, 10H), 3.34 (s, 3H); ^{13}C NMR (75 MHz, D_2O) δ 99.56, 98.04, 73.56, 73.25, 72.02, 71.66, 71.34, 70.25, 69.70, 69.59, 65.67, 60.65, 55.38; HRMS (FAB) *m/z* calcd for $C_{13}H_{24}O_{11}$ (M+Na) 356.1319, found 356.1323.

1,6-Anhydro-4-*O*-benzyl-2-*O*-(*S*)-ethoxycarbonylbenzyl-*β*-D-galactopyranose (25*S*). BF_3-OEt_2 (218 μL, 1.7 mmol) was added dropwise to a mixture of 1,6:2,3-di-anhydro-4-*O*-benzyl-*β*-D-talopyranose (**24**, 2.0 g, 8.58 mmol), (*S*)-ethyl mandelate (4.6 g, 43 mmol) and activated molecular sieves (4Å, 2 g) in toluene (50 mL) at room temperature. After stirring for 1 h, the reaction mixture was quenched with an aqueous saturated solution of $NaHCO_3$ (50 mL) and then diluted with ethyl acetate (50 mL). The organic phase was dried ($MgSO_4$), filtered and the filtrate was concentrated *in vacuo*. The residue was purified by flash silica gel column chromatography (20% ethyl acetate in hexane) to afford **25*S*** (1.81 g, 51%): colorless syrup, R_f = 0.31 (ethyl acetate/hexane, 1/1); $[\alpha]^{20}_D$ = +52^o (*c* = 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21-7.41 (m, 10H, Ar), 5.60 (s, 1H, H-1), 5.03 (s, 1H, >CHPh), 4.61 (d, 1H, *J* = 11.5 Hz, C*H*HPh), 4.56 (d, 1H, *J* = 11.5Hz, CH*H*Ph), 4.39 (t, 1H, *J* = 4.5 Hz, H-5), 4.24 (d, 1H, *J* = 7.5Hz, H-6_a), 4.15 (q, 2H, *J* = 7.0 Hz, COOCH_2CH$_3$), 4.05 (dd, 1H, *J* = 1.5, 3.5 Hz, H-3), 3.81 (t, 1H, *J* = 4 Hz, H-4), 3.59 (s, 1H, H-2), 3.58 (d, 1H, *J* = 9.0 Hz, H-6_b), 2.79 (d, 1H, *J* = 2.0 Hz,

OH), 1.18 (t, 3H, J = 7.0 Hz, $COOCH_2CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.48, 137.15, 135.98, 128.54, 128.47, 128.40, 128.09, 127.65, 127.05, 127.00, 100.34, 80.14, 77.91, 71.99, 71.86, 71.69, 67.22, 63.73, 61.25, 13.87; HR MALDI-TOF MS m/z calcd for $C_{23}H_{26}O_7$ $[M+Na]^+$ 437.1577, found 437.1526.

1,6-Anhydro-4-*O*-benzyl-2-*O*-(*R*)-ethoxycarbonylbenzyl-β-D-galactopyranose (25*R*). Compound **25*R*** was synthesized from compound **24** and (*R*)-ethyl mandelate according to the procedure described for the synthesis of compound **25*S***: Colorless syrup, R_f = 0.49 (ethyl acetate/hexane, 1/1); $[\alpha]^{20}_D$ = -131° (c = 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.33-7.47 (m, 10H, Ar), 5.31 (s, 1H, H-1), 4.99 (s, 1H, >CHPh), 4.72 (d, 1H, J = 12.0 Hz, C*H*HPh), 4.65 (d, 1H, J = 12.0Hz, CH*H*Ph), 4.41 (t, 1H, J = 4.5 Hz, H-3), 4.24 (d, 1H, J = 7.0 Hz, H-6_a), 4.21-4.22 (m, 1H, H-5), 4.16 (q, 2H, J = 7.5 Hz, $COOCH_2CH_3$), 3.95 (t, 1H, J = 4.5 Hz, H-4), 3.57-3.60 (m, 2H, H-6_b, H-2), 2.79 (d, 1H, J = 2.0 Hz, OH), 2.68 (b, 1H, OH), 1.20 (t, 3H, J = 7.5 Hz, $COOCH_2CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.33, 137.36, 136.03, 128.95, 128.75, 128.70, 128.33, 127.86, 127.43, 100.23, 80.73, 77.80, 72.22, 72.17, 71.99, 67.72, 64.01, 61.44, 14.05; HR MALDI-TOF MS m/z calcd for $C_{23}H_{26}O_7$ $[M+Na]^+$ 437.1577, found 437.1524.

Acetyl 3,6-di-*O*-acetyl-4-*O*-benzyl-2-*O*-(*S*)-ethoxycarbonylbenzyl-α-D-galactopyranose (26*S*). Trimethylsilyl trifluoromethansulfonate (5 µL, 0.03 mmol) was added to a solution of compound **25*S*** (281 mg, 0.68 mmol) in acetic anhydride (10 mL) at 0 °C. After stirring the reaction mixture at 0 °C for 20 min, it was quenched with an aqueous saturated solution of $NaHCO_3$. The organic phase was washed with water (30 mL) and brine (30 mL) and dried ($MgSO_4$), filtered and the filtrate was concentrated *in vacuo*. The residue was purified by flash silica gel column chromatography (20% ethyl acetate in hexane) to afford **26*S*** (357 mg, 94%): colorless syrup, R_f = 0.57 (ethyl acetate/hexane, 1/1); $[\alpha]^{20}_D$ = -49° (c = 0.15, $CHCl_3$); ^1H

NMR (500 MHz, $CDCl_3$) δ 7.21-7.39 (m, 10H, Ar), 6.56 (d, 1H, J = 3.5 Hz, H-1), 5.21 (dd, 1H, J = 3.0, 10.5 Hz, H-3), 5.04 (s, 1H, >CHPh), 4.59 (d, 1H, J = 11.0 Hz, C*H*HPh), 4.48 (d, 1H, J = 11.0 Hz, CH*H*Ph), 4.17 (q, 2H, J = 7.5 Hz, $COOCH_2CH_3$), 4.10-4.16 (m, 3H, H-6_a, H-2, H-5), 4.02-4.05 (m, 2H, H-6_b, H-4), 2.15 (s, 3H, $COCH_3$), 2.00 (s, 3H, $COCH_3$), 1.91 (s, 3H, $COCH_3$), 1.20 (t, 3H, J = 7.5 Hz, $COOCH_2CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.39, 170.35, 170.28, 169.29, 137.32, 136.21, 128.76, 128.51, 128.47, 128.14, 128.10, 127.35, 90.44, 81.51, 75.28, 74.49, 72.66, 70.09, 62.23, 61.52, 21.02, 20.84, 20.78, 14.00; HR MALDI-TOF MS m/z calcd for $C_{29}H_{34}O_{11}$ $[M+Na]^+$ 581.1999, found 581.1913.

Acetyl 3,6-di-*O*-acetyl-4-*O*-benzyl-2-*O*-(*R*)-ethoxycarbonylbenzyl-α-D-galactopyranose (26*R*). Compound **26*R*** was synthesized according to the procedure described for the synthesis of compound **26*S***. R_f = 0.53 (ethyl acetate/hexane, 1/1); $[\alpha]^{20}_D$ = -70° (c = 1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31-7.37 (m, 10H, Ar), 6.23 (d, 1H, J = 4.0 Hz, H-1), 5.33 (dd, 1H, J = 2.5, 10.5 Hz, H-3), 5.03 (s, 1H, >CHPh), 4.74 (d, 1H, J = 11.0 Hz, CH*H*Ph), 4.55 (d, 1H, J = 11.5 Hz, C*H*HPh), 4.13-4.18 (m, 3H, H-6_a, H-2, H-4), 4.10 (q, 2H, J = 7.0 Hz, $COOCH_2CH_3$), 3.97-4.03 (m, 2H, H-6_b, H-5), 2.16 (s, 3H, $COCH_3$), 2.04 (s, 3H, $COCH_3$), 1.99 (s, 3H, $COCH_3$), 1.20 (t, 3H, J = 7.0 Hz, $COOCH_2CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.99, 170.91, 170.88, 169.48, 137.26, 136.20, 128.73, 128.56, 128.45, 128.14, 128.06, 126.95, 91.43, 80.11, 75.89, 74.92, 71.66, 71.12, 62.34, 60.21, 22.02, 21.84, 21.63, 14.15; HR MALDI-TOF MS m/z calcd for $C_{29}H_{34}O_{11}$ $[M+Na]^+$ 581.1999, found 581.1981.

3,6-Di-*O*-acetyl-4-*O*-benzyl-2-*O*-(*S*)-ethoxycarbonylbenzyl-α-D-galactopyranosyl trichloroacetimidate (28*S*). Hydrazinium acetate (80 mg, 0.87 mmol) was added to a solution of compound **26*S*** (440 mg, 0.79 mmol) in DMF (15 mL) at room temperature. After stirring the reaction mixture for 18 h, it was quenched with an aqueous saturated solution of $NaHCO_3$. The

organic phase was washed with an aqueous saturated solution of NH_4Cl (30 mL) and dried ($MgSO_4$), filtered and the filtrate was concentrated *in vacuo*. The residue was purified by flash silica gel column chromatography (20% ethyl acetate in hexane) to afford **27*S*** (391 mg, 96%). Trichloroacetonitrile (0.39 mL) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 45 μL) were added to a solution of **27*S*** (391 mg, 0.76 mmol) in dichloromethane (10 mL) at 0 °C. After stirring the reaction mixture at 0 °C for 1 h, it was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (20% ethyl acetate in hexane) to afford **21*S*** (452 mg, 90%): R_f = 0.69 (ethyl acetate/hexane, 1/1); $[\alpha]^{20}_D$ = +92° (*c* = 1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.67 (s, 1H, NH), 7.55-7.40 (m, 10H, Ar), 6.79 (d, 1H, *J* = 3.0 Hz, H-1), 5.28 (dd, 1H, *J* = 2.5, 10.5 Hz, H-3), 5.12 (s, 1H, >CHPh), 4.63 (d, 1H, *J* = 11.5 Hz, C*H*HPh), 4.50 (d, 1H, *J* = 11.5Hz, CH*H*Ph), 4.24-4.26 (m, 1H, H-5), 4.22 (dd, 1H, *J* = 3.0, 10.0 Hz, H-2), 4.12-4.17 (m, 1H, H-4), 4.14 (q, 2H, *J* = 7.0 Hz, $COOCH_2CH_3$), 4.11-4.12 (m, 1H, H-6_b), 4.07 (dd, 1H, *J* = 6.5, 11.0 Hz, H-6_a), 1.98 (s, 3H, $COCH_3$), 1.91 (s, 3H, $COCH_3$), 1.20 (t, 3H, *J* = 7.0 Hz, $COOCH_2CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.64, 170.34, 170.30, 161.15, 137.30, 136.23, 128.63, 128.55, 128.40, 128.19, 128.16, 127.07, 94.90, 81.95, 75.24, 74.38, 73.17, 73.10, 70.42, 62.34, 61.52, 20.86, 20.75, 14.04.

3,6-Di-*O*-acetyl-4-*O*-benzyl-2-*O*-(*R*)-ethoxycarbonylbenzyl-*α*-D-galactopyranosyl trichloroacetimidate (28*R*). Compound **28*R*** was synthesized according to the procedure described for the synthesis of compound **28*S*.** R_f = 0.69 (ethyl acetate/hexane, 1/1); $[\alpha]^{20}_D$ = +48° (*c* = 0.33, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.44 (s, 1H, NH), 7.28-7.40 (m, 10H, Ar), 6.41 (d, 1H, *J* = 3.5 Hz, H-1), 5.44 (dd, 1H, *J* = 2.5, 10 Hz, H-3), 5.08 (s, 1H, >CHPh), 4.75 (d, 1H, *J* = 11.5 Hz, C*H*HPh), 4.56 (d, 1H, *J* = 11.5 Hz, CH*H*Ph), 4.25 (dd, 1H, *J* = 4.0, 8.0 Hz, H-2), 4.22-4.24 (m, 1H, H-6_a), 4.14 (q, 2H, *J* = 7.0 Hz, $COOCH_2CH_3$), 4.10-4.11 (m, 1H, H-4), 4.09

(d, 1H, J = 2.0 Hz, H-6_b), 4.06 (dd, 1H, J = 6.0, 11.0 Hz, H-5), 2.15 (s, 3H, $COCH_3$), 1.96 (s, 3H, $COCH_3$), 1.19 (t, 3H, J = 7.5 Hz, $COOCH_2CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.46, 170.31, 169.96, 160.76, 137.38, 136.32, 128.67, 128.53, 128.46, 128.24, 128.15, 127.07, 94.24, 90.98, 80.82, 75.22, 74.44, 73.00, 71.59, 70.59, 62.32, 61.19, 21.09, 20.71, 14.06.

Methyl (3,6-di-*O*-acetyl-4-*O*-benzyl-2-*O*-(*S*)-ethoxycarbonylbenzyl-α-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (29*S*α). $[\alpha]^{20}_D$ = +191° (c = 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.17-7.34 (m, 25H, Ar), 5.93 (d, 1H, J = 3.5 Hz, H-3'), 5.19-5.22 (m, 1H, H-4'), 5.04 (s, 1H, >CHPh), 5.03 (d, 1H, J = 11.5 Hz, CH*H*Ph), 4.98 (d, 1H, J = 11.5 Hz, C*H*HPh), 4.68 (d, 1H, J = 11.5 Hz, C*H*HPh), 4.60 (t, 1H, J = 9.5 Hz, H-3), 4.57 (d, 1H, J = 11.5 Hz, CH*H*Ph), 4.54 (s, 1H, H-1'), 4.53 (d, 1H, J = 11.5 Hz, CH*H*Ph), 4.42 (d, 1H, J = 11.5 Hz, C*H*HPh), 4.10 (t, 1H, J = 9.5 Hz, H-4), 3.92-4.06 (m, 7H, H-2', H-1, H-6_b, H-6_a', H-6_b', $COOCH_2CH_3$), 3.87-3.89 (m, 1H, H-5'), 3.78 (dd, 1H, J = 4.5, 11.0 Hz, H-6_a), 3.65 (d, 1H, J = 9.5 Hz, H-5), 3.59 (dd, 1H, J = 3.0, 9.5 Hz, H-2), 3.37 (s, 3H, CH_3), 1.91 (s, 3H, $COCH_3$), 1.85 (s, 3H, $COCH_3$), 1.09 (t, 3H, J = 7.0 Hz, $COOCH_2CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.41, 170.17, 170.05, 139.26, 138.21, 138.01, 137.53, 136.21, 128.62, 128.42, 128.29, 128.19, 127.98, 127.90, 127.54, 127.46, 127.29, 127.07, 127.00, 97.61, 96.33, 81.56, 81.13, 80.36, 77.22, 75.03, 74.84, 73.95, 73.32, 73.27, 73.09, 72.54, 69.35, 68.22, 62.49, 61.24, 55.13, 20.93, 20.68, 14.02; HR MALDI-TOF MS m/z calcd for $C_{55}H_{62}O_{15}$ $[M+Na]^+$ 985.3986, found 985.3975.

Methyl (3,6-di-*O*-acetyl-4-*O*-benzyl-2-*O*-(*S*)-ethoxycarbonylbenzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (29*S*β). $[\alpha]^{20}_D$ = +253° (c = 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.15-7.37 (m, 25H, Ar), 5.06 (s, 1H, >CHPh), 4.95 (d, 1H, J = 10.5 Hz, C*H*HPh), 4.83 (d, 1H, J = 11.5 Hz, C*H*HPh), 4.73 (d, 1H, J = 10.5 Hz, CH*H*Ph), 4.71 (d, 1H, J = 12.5 Hz, C*H*HPh), 4.66 (dd, 1H, J = 4.5, 10.0 Hz, H-3'), 4.65 (d, 1H, J

= 11.5 Hz, CH*H*Ph), 4.60 (d, 1H, *J* = 4.0 Hz, H-1), 4.51 (d, 1H, *J* = 12.0 Hz, CH*H*Ph), 4.48 (d, 1H, *J* = 12.0 Hz, C*H*HPh), 4.39 (d, 1H, *J* = 12.0 Hz, C*H*HPh), 4.36 (d, 1H, *J* = 8.0 Hz, H-1'), 3.97-4.15 (m, 7H, H-4, H-6_a, H-6_b, H-6_a', H-6_b', COO*C*H_2CH_3), 3.81 (t, 1H, *J* = 9.0 Hz, H-3), 3.76-3.76 (m, 1H, H-4'), 3.66-3.69 (m, 2H, H-2', H-5'), 3.52 (dd, 1H, *J* = 4.0, 9.5 Hz, H-2), 3.38 (s, 3H, CH_3), 3.30 (t, 1H, *J* = 7.0 Hz, H-5), 1.97 (s, 3H, $COCH_3$), 1.64 (s, 3H, $COCH_3$), 1.19 (t, 3H, *J* = 6.5 Hz, $COOCH_2$*C*H_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.42, 170.26, 170.17, 139.06, 138.49, 138.04, 137.83, 136.99, 128.52, 128.48, 128.34, 128.19, 128.09, 127.99, 127.89, 127.82, 127.77, 127.48, 127.23, 101.46, 98.52, 82.80, 80.08, 78.89, 77.95, 75.49, 75.13, 74.58, 74.10, 73.66, 73.26, 71.53, 69.76, 68.17, 61.82, 60.97, 55.26, 20.79, 20.57, 14.15; HR MALDI-TOF MS m/z calcd for $C_{55}H_{62}O_{15}$ $[M+Na]^+$ 985.3986, found 985.3877.

Methyl (3,6-di-*O*-acetyl-4-*O*-benzyl-2-*O*-(*S*)-ethoxycarbonylbenzyl-α-D-galactopyranosyl)-(1$\rightarrow$6)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (30*S*α). $[\alpha]^{20}_D$ = +249^o (*c* = 1.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25-7.98 (m, 25H, Ar), 6.16 (t, 1H, *J* = 9.5 Hz, H-3), 5.48 (t, 1H, *J* = 9.5 Hz, H-4), 5.30 (dd, 1H, *J* = 3.0, 11.0 Hz, H-3'), 5.26 (dd, 1H, *J* = 3.5, 9.5 Hz, H-2), 5.23 (d, 1H, *J* = 3.5 Hz, H-1), 5.21 (d, 1H, *J* = 4.0 Hz, H-1'), 5.12 (s, 1H, >CHPh), 4.64 (d, 1H, *J* = 11.0 Hz, CH*H*Ph), 4.48 (d, 1H, *J* = 11.0 Hz, C*H*HPh), 4.37 (t, 1H, *J* = 8.5 Hz, H-5), 4.20 (t, 1H, *J* = 6.5 Hz, H-5'), 4.12-4.13 (m, 1H, H-2'), 4.09 (q, 2H, *J* = 7.0 Hz, COO*C*H_2CH_3), 4.05-4.08 (m, 1H, H-4'), 4.03-4.04 (m, 2H, H-6_a', H-6_b'), 3.93 (dd, 1H, *J* = 7.5, 11.0 Hz, H-6_a), 3.75 (d, 1H, *J* = 10.0 Hz, H-6_b), 3.44 (s, 3H, CH_3), 2.00 (s, 3H, $COCH_3$), 1.88 (s, 3H, $COCH_3$), 1.16 (t, 3H, *J* = 7.0 Hz, $COOCH_2$*C*H_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.63, 170.25, 170.13, 165.38, 164.64, 164.38, 129.94, 129.90, 129.67, 129.27, 129.15, 128.96, 128.50, 128.44, 128.40, 128.24, 128.20, 128.06, 126.96, 97.95, 96.63, 82.05, 75.35, 75.14, 74.85, 73.02,

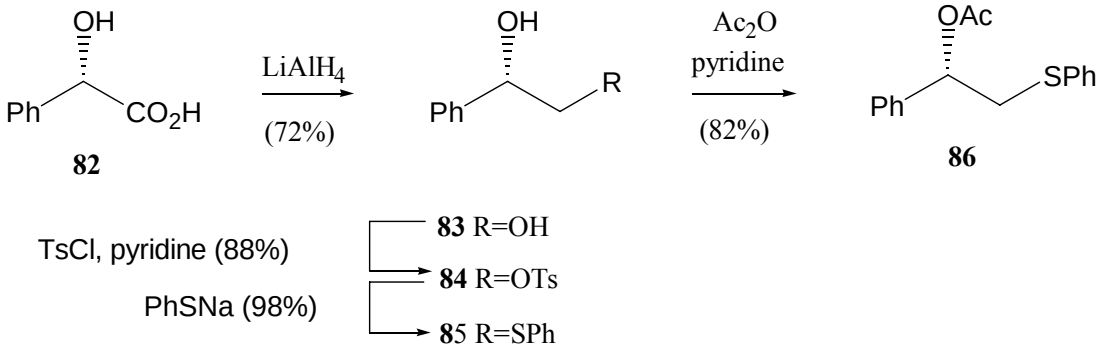
72.20, 70.62, 69.69, 68.71, 68.14, 66.96, 63.02, 61.39, 55.47, 20.87, 20.79, 14.03; HR MALDI-TOF MS m/z calcd for $C_{55}H_{56}O_{18}$ $[M+Na]^+$ 1027.3364, found 1027.3354.

Methyl (3,6-di-*O*-acetyl-4-*O*-benzyl-2-*O*-(*S*)-ethoxycarbonylbenzyl-β-D-galactopyranosyl)-(1→6)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (30*Sβ*). $[\alpha]^{20}_D = +155^o$ (*c* = 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.09-7.98 (m, 25H, Ar), 6.16 (t, 1H, *J* = 9.5 Hz, H-3), 5.37 (t, 1H, *J* = 9.5 Hz, H-4), 5.36 (s, 1H, >CHPh), 5.23 (dd, 1H, *J* = 3.5, 9.5 Hz, H-2), 5.22 (s, 1H, H-1), 4.92 (dd, 1H, *J* = 3.0, 10.0 Hz, H-3'), 4.57 (d, 1H, *J* = 7.5 Hz, H-1'), 4.48 (d, 1H, *J* = 12.0 Hz, CH*H*Ph), 4.40-4.43 (m, 1H, H-5), 4.39 (d, 1H, *J* = 12.0 Hz, C*H*HPh), 4.19 (q, 2H, *J* = 7.0 Hz, COO$CH_2$$CH_3$), 4.12 (dd, 1H, *J* = 7.0, 11.0 Hz, H-6_a'), 4.01 (dd, 1H, *J* = 2.0, 11.0 Hz, H-6_b), 3.95 (dd, 1H, *J* = 6.5, 11.0 Hz, H-6_b'), 3.82 (d, 1H, *J* = 2.0 Hz, H-4'), 3.78 (dd, 1H, H-6_a), 3.72 (dd, 1H, *J* = 7.5, 9.5 Hz, H-2'), 3.63 (t, 1H, *J* = 6.5 Hz, H-5'), 3.54 (s, 3H, CH_3), 1.89 (s, 3H, $COCH_3$), 1.75 (s, 3H, $COCH_3$), 1.20 (t, 3H, *J* = 7.0 Hz, $COOCH_2CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.51, 170.36, 170.23, 165.84, 165.75, 165.54, 137.45, 137.05, 133.50, 133.35, 133.07, 129.93, 129.86, 129.65, 129.25, 129.09, 128.82, 128.52, 128.47, 128.42, 128.31, 128.26, 128.09, 127.99, 127.86, 103.88, 96.77, 81.51, 74.06, 73.62, 72.18, 71.74, 70.33, 70.07, 69.53, 68.85, 62.15, 61.21, 55.82, 20.70, 20.60, 14.14; HR MALDI-TOF MS m/z calcd for $C_{55}H_{56}O_{18}$ $[M+Na]^+$ 1027.3364, found 1027.3382.

Methyl (3,6-di-*O*-acetyl-4-*O*-benzyl-2-*O*-(*R*)-ethoxycarbonylbenzyl-α-D-galactopyranosyl)-(1→6)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (30*Rα*). Selected ^1H NMR (300 MHz, $CDCl_3$) δ 4.73 (s, 1H, H-1'), 3.61 (s, 3H, CH_3), 2.04 (s, 3H, $COCH_3$), 1.99 (s, 3H, $COCH_3$), 1.19 (t, 3H, *J* = 7.2 Hz, $COOCH_2CH_3$).

Methyl (3,6-di-*O*-acetyl-4-*O*-benzyl-2-*O*-(*R*)-ethoxycarbonylbenzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (30*Rβ*). $[\alpha]^{20}_D = -53^o$ (*c* =

0.7, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.18-7.38 (m, 25H, aromatic), 5.05 (s, 1H, >CHPh), 4.93 (d, 1H, *J* = 11.0, C*H*HPh), 4.81 (dd, 1H, *J* = 3.3, 9.9 Hz, H-3'), 4.80 (d, 1H, *J* = 11.0 Hz, CH*H*Ph), 4.74 (d, 1H, *J* = 12.0 Hz, CH*H*Ph), 4.69 (d, 1H, *J* = 12.0 Hz, CH*H*Ph), 4.61 (d, 1H, *J* = 12.0 Hz, CH*H*Ph), 4.54 (d, 1H, *J* = 12.0 Hz, C*H*HPh), 4.53 (d, 1H, *J* = 12.0 Hz, C*H*HPh), 4.52 (d, 1H, *J* = 12.0 Hz, C*H*HPh), 4.50 (d, 1H, *J* = 3.0 Hz, H-1), 4.11 (d, 1H, *J* = 9.0 Hz, H-1'), 4.02-4.20 (m, 6H, H-6_a', H-6_b', H-5', C*H*HPh, COO*CH*$_2$CH$_3$), 3.88 (t, 1H, *J* = 9.0 Hz, H-4), 3.78 (d, 1H, *J* = 3.0 Hz, H-4'), 3.66-3.72 (m, 2H, H-2', H-3), 3.43 (dd, 1H, *J* = 3.0, 9.5 Hz, H-2), 3.31 (s, 3H, CH_3), 3.27-3.29 (m, 1H, H-6_a), 2.94-3.02 (m, 2H, H-5, H-6_b), 2.16 (s, 3H, $COCH_3$), 1.97 (s, 3H, $COCH_3$), 1.18 (t, 3H, *J* = 7.0 Hz, $COOCH_2$*CH*$_3$); HR MALDI-TOF MS m/z calcd for $C_{55}H_{62}O_{15}$ $[M+Na]^+$ 985.3986, found 985.3971.



(*S*)-Phenyl-1,2-ethanediol (83). To the solution of (*S*)-mandelic acid (**82**) (10.0 g, 65.7 mmol) in diethyl ether (50mL) was added slowly $LiAlH_4$ (5.0 g, 131 mmol). After the reaction mixture was refluxed for 2 h, ethyl acetate (20 mL) was added slowly and then poured into ice water (100 mL). The organic phase was separated and dried ($MgSO_4$), filtered and the filtrate was concentrated *in vacuo*. The residue was purified by recrystallization (hexane/ethyl acetate)

to afford **83** (6.54 g, 72%) as a white solid, R_f = 0.24 (ethyl acetate/hexane, 1/1); $[\alpha]^{20}_D$ = +60.5 (*c* 1.15, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37–7.26 (m, 5H, ArH), 4.82 (dd, 1H, *J* = 3.6, 8.1 Hz, C*H*OH), 3.76 (dd, 1H, *J* = 3.6, 11.4 Hz, C*H*HOH), 3.66 (dd, 1H, *J* = 8.1, 11.4 Hz, CH*H*OH), 2.42 (brs, 2H, OH). (Ref : Bradshaw, Jerald S. Jolley, Scott t.; Izatt, Reed M. *J. Org. Chem*. **1982**, *47*, 1229-1232.)

(*S*)-1-Phenyl-2-(tosyloxy)ethanol (84). To the solution of **83** (4.18 g, 30.3 mmol) in CH_2Cl_2 (60 mL) were sequentially added Bu_2SnO (151 mg, 0.6 mmol), TsCl (5.77 g, 30.3 mmol) and Et_3N (4.2 mL, 30.3 mmol). After stirring at room temperature for 3 h, the reaction mixture was diluted with CH_2Cl_2 (60 mL) and washed with brine (40 mL). The organic phase was dried ($MgSO_4$), filtered and the filtrate was concentrated *in vacuo*. The residue was purified by silica gel column chromatography (25% ethyl acetate in hexane) to afford **84** (7.81 g, 88%) as a colorless syrup, R_f = 0.69 (ethyl acetate/hexane, 1/1); $[\alpha]^{20}_D$ = +43.6 (*c* 1.12, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, 2H, *J* = 8.4 Hz, ArH), 7.37–7.26 (m, 7H, ArH), 5.01-4.96 (m, 1H, C*H*OH), 4.16 (dd, 1H, *J* = 3.3, 10.5 Hz, C*H*HOTs), 4.05 (dd, 1H, *J* = 8.4, 10.5, Hz,, CH*H*OTs), 2.53 (d, 1H, *J* = 3.3 Hz, CHO*H*), 2.45 (s, 3H, CH_3).

(Ref: Pandey, Rajesh Kumar; Fernandes, Rodney A.; Kumar, Pradeep. *Tetrahedron Lett*. **2002**, *43*, 4425-4426.)

(*S*)-1-Phenyl-2-(phenylthio)ethanol (85). To the solution of **84** (7.81 g, 26.7 mmol) in THF (40 mL) was added sodium benzenethiolate (90%, 5.11 g, 35.0 mmol). The reaction mixture was stirred at room temperature overnight, then concentrated *in vacuo*. The residue was dissolved with dichloromethane (50 mL) and washed with brine (50 mL). The organic phase was dried ($MgSO_4$), filtered and the filtrate was concentrated *in vacuo*. The residue was purified by silica gel column chromatography (25% ethyl acetate in hexane) to afford **85** (6.0 g, 98%) as a

colorless syrup, R_f = 0.30 (ethyl acetate/hexane, 1/4); $[\alpha]^{20}_D$ +21.0 (*c* 0.27, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34-7.12 (m, 10H, ArH), 4.73 (dd, 1H, *J* = 2.1, 5.7 Hz, C*H*OH), 3.33 (dd, 1H, *J* = 2.1, 8.4 Hz, C*H*HSPh), 3.10 (dd, 1H, *J* = 5.7, 8.4 Hz, CH*H*SPh), 2.81 (s, 1H, OH).

(Ref: Christoffers, Jens; Roessler, Ulrich. *Tetrahedron; Asymmetry*. **1999**, *10*, 1207-1215.)

(*S*)-(Phenylthiomethyl)benzyl acetate (86). To the solution of **85** (6.0 g, 26.0 mmol) in pyridine (30 mL) was added acetic anhydride (5.0 mL, 52.0 mmol). After stirring at 0 ^oC for 2 h, the reaction mixture was quenched with saturated sodium bicarbonate solution (50 mL) and then diluted with dichloromethane (50 mL). After separation, the organic phase was washed with saturated sodium bicarbonate solution (50 mL × 3) and brine (50 mL). The organic phase was dried ($MgSO_4$), filtered and the filtrate was concentrated *in vacuo*. The residue was purified by silica gel column chromatography (20% ethyl acetate in hexane) to afford **86** (5.82 g, 82%) as a colorless syrup, R_f = 0.47 (ethyl acetate/hexane, 1/4); $[\alpha]^{20}_D$ = +31.6 (*c* 1.52, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39-7.20 (m, ArH), 5.89 (dd, 1H, *J* = 5.4, 8.1 Hz), 3.41 (dd, 1H, *J* = 8.1, 14.1 Hz, *CH*HSPh), 3.23 (dd, 1H, *J* = 5.4, 14.1 Hz, *C*H*H*SPh) 2.02 (s, 3H, $COCH_3$).

(Ref: Bortolini, O.; Furia, F.; Licini, G.; Modena, G. *Phosphorus Sulfur*. **1988**, *37*, 171-174.)

1,6-Anhydro-4-*O*-benzyl-2-*O*-((*S*)-2-(hydroxymethyl)benzyl)-β-D-glucopyranose (31) To the solution of **9*S*** (1.2 g, 2.9 mmol) in THF (35 mL) was added slowly $LiAlH_4$ (0.16 g, 4.4 mmol). After the reaction mixture was refluxed for 4 h, ethyl acetate (20 mL) was added slowly and then poured into ice water (100 mL). The organic phase was separated and dried ($MgSO_4$), filtered and the filtrate was concentrated *in vacuo*. The residue was purified by flash column chromatography (hexane/ethyl acetate = 1/2) to afford **31** (915 mg, 85%) as a white solid, R_f = 0.24 (ethyl acetate/hexane, 2/1); $[\alpha]^{20}_D$ = +95˚ (*c* = 1.1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37-7.26 (m, 10H, aromatic), 5.58 (s, 1H, H-1), 4.68 (d, 1H, *J* = 12.0 Hz, C*H*HPh), 4.63-4.60

(m, 1H, H-3), 4.59 (d, 1H, J = 12.0 Hz, CH*H*Ph), 4.56-4.54 (m, 1H, C*H*Ph), 3.80-3.70 (m, 3H, H-4, H-6_a, H-6_b), 4.66-3.58 (m, 2H, H-5, H-2), 3.27-3.26 (m, 2H, CH_2) , 2.19 (bs, 1H, OH); HR MALDI-TOF MS (*m*/*z*) calcd for $C_{21}H_{24}O_6$ $[M + Na]^+$ 395.1573, found 395.1586.

1,6-Anhydro-4-*O*-benzyl-2-*O*-((*S*)-2-(tosyloxymethyl)benzyl)-*β*-D-glucopyranose (32) To the solution of **31** (300 mg, 0.81 mmol) in pyridine (10 mL) was added TsCl (170 mg, 0.89 mmol). After stirring at room temperature for 2 h, the solvent was evaporated *in vacuo*. The residue was purified by silica gel column chromatography (25% ethyl acetate in hexane) to afford **32** (391 g, 92%) as a colorless syrup, R_f = 0.57 (ethyl acetate/hexane, 1/1); $[\alpha]^{20}_D = +115^\circ$ (c = 0.7, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33-7.26 (m, 15H, aromatic), 5.44 (s, 1H, H-1), 4.75 (t, 1H, J = 8.0 Hz, C*H*Ph), 4.59 (d, 1H, J = 12.0 Hz, C*H*HPh), 4.51 (d, 1H, J = 12.0 Hz, CH*H*Ph), 4.53-4.49 (m, 1H, H-3), 4.13-4.11 (m, 2H, CH_2), 3.71-3.60 (m, 3H, H-4, H-6_a, H-6_b), 3.23-3.18 (m, 2H, H-5, H-2) , 1.96 (bs, 1H, OH); HR MALDI-TOF MS (*m*/*z*) calcd for $C_{28}H_{30}O_8S$ $[M + Na]^+$ 549.1661, found 549.1675.

1,6-Anhydro-4-*O*-benzyl-2-*O*-((*S*)-2-(phenylthiomethyl)benzyl)-*β*-D-glucopyranose (33) To the solution of **33** (120 mg, 0.16 mmol) in THF (5 mL) was added sodium benzenethiolate (90%, 37 mg, 0.17 mmol). The reaction mixture was stirred at room temperature overnight, then concentrated *in vacuo*. The residue was dissolved with dichloromethane (10 mL) and washed with brine (50 mL). The organic phase was dried ($MgSO_4$), filtered and the filtrate was concentrated *in vacuo*. The residue was purified by silica gel column chromatography (25% ethyl acetate in hexane) to afford **33** (114 mg, 95%) as a colorless syrup $[\alpha]^{20}_D = +68^\circ$ (c = 0.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38-7.28 (m, 15H, aromatic), 5.54 (s, 1H, H-1), 4.63 (d, 1H, J = 12.5 Hz, C*H*HPh), 4.58 (dd, 1H, J = 5.0, 9.0 Hz, C*H*Ph), 4.53 (d, 1H, J = 12.5 Hz, CH*H*Ph), 4.55-4.52 (m, 1H, H-3), 3.71-3.67 (m, 2H, H-6_a, H-6_b), 3.63-3.61 (m, 1H, H-4), 3.38

(dd, 1H, *J* = 9.0, 14.0 Hz, C*H*HSPh), 3.21-3.18 (m, 3H, CH*H*SPh, H-5, H-2), 1.98 (bs, 1H, OH); HR MALDI-TOF MS (*m*/*z*) calcd for $C_{28}H_{32}O_{10}S$ $[M + Na]^+$ 487.1657, found 487.1638.

Acetyl 3,4,6-Tri-*O*-acetyl-2-*O*-((S)-2-(phenylthiomethyl)benzyl)-α-D-glucopyranoside (41). Boron trifluoride etherate (381 μL, 3.0 mmol, 1.5 equiv) was added to the solution of acetyl 3, 4, 6-tri-*O*-acetyl-α-D-glucopyranoside (**38**) (697 mg, 2.0 mmol, 1 equiv), (*S*)-2-(phenylthiomethyl)benzyl acetate (**85**) (817 mg, 3.0 mmol, 1.5 equiv) and activated molecular sieves (4Å) in dichloromethane (10 mL) at 0 °C. After 30 min, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (10 mL) and then separated. The organic phase was dried ($MgSO_4$), filtered and the filtrate was concentrated *in vacuo*. The residue was purified by silica gel column chromatography (25% ethyl acetate in hexane) to afford **41** (796 mg, 71%): colorless syrup, R_f = 0.37 (ethyl acetate/hexane, 1/2); $[\alpha]^{20}_D$ = +124.6° (*c* = 0.6, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34-7.17 (m,10H, aromatic), 6.46 (d, 1H, *J* = 3.6 Hz, H-1), 5.39 (t, 1H, *J* = 9.6 Hz, H-3), 4.46 (t, 1H, *J* = 9.6 Hz, H-4), 4.46 (dd, 1H, *J* = 4.8, 8.1 Hz, H-7), 4.27-4.23 (m, 1H, H-6_a), 4.08-3.98 (m, 2H, H-6_b, H-5), 3.58 (dd, 1H, *J* = 3.6, 9.6 Hz, H-2), 3.22 (dd, 1H, *J* = 8.1, 13.8 Hz, H-8_a), 3.04 (dd, 1H, *J* = 4.8, 13.8 Hz, H-8_b), 2.18 (s, 3H, $COCH_3$), 2.04 (s, 3H, $COCH_3$), 1.98 (s, 3H, $COCH_3$), 1.82 (s, 3H, $COCH_3$); HR MALDI-TOF MS (*m*/*z*) calcd for $C_{28}H_{32}O_{10}S$ $[M + Na]^+$ 583.1614, found 583.1622.

3,4,6-Tri-*O*-acetyl-2-*O*-((S)-2-(phenylthiomethyl)benzyl)-α-D-glucopyranosyl trichloroacetimidate (43). Hydrazine acetate (261 mg, 2.84 mmol, 2.0 equiv) was added to the solution of **41** (796 mg, 1.42 mmol, 1 equiv) in DMF (5 mL) at room temperature. The reaction mixture was stirred overnight, then quenched with saturated aqueous $NaHCO_3$. The reaction mixture was extracted with ethyl acetate (20 mL). The organic phase was washed with saturated aqueous NH_4Cl (20 mL) and dried ($MgSO_4$), filtered and the filtrate was concentrated *in vacuo*.

The residue was purified by silica gel column chromatography (25% ethyl acetate in hexane) to afford 3,4,6-tri-*O*-acetyl-2-*O*-((S)-2-(phenylthiomethyl)benzyl)-α-D-glucopyranose (**42**) (612 mg, 83%). Trichloroacetonitrile (1.18 mL, 10 equiv) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 71 μL, 0.4 equiv) were added to the solution of **42** (612 mg, 1.18 mmol, 1 equiv) in dichloromethane (5 mL) at 0 °C. The reaction mixture was stirred at the same temperature for 1 h and then concentrated *in vacuo*. The residue was purified by silica gel column chromatography (20% ethyl acetate in hexane) to afford **43** (743 mg, 95%): R_f = 0.29 (ethyl acetate/hexane, 1/3); $[\alpha]^{20}_D$ = +50.0° (*c* = 0.2, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.87 (s, 1H, N*H*), 7.36-7.16 (m,10H, aromatic), 6.66 (d, 1H, *J* = 3.6 Hz, H-1), 5.44 (t, 1H, *J* = 9.6 Hz, H-3), 4.93 (t, 1H, *J* = 9.6 Hz, H-4), 4.53 (t, 1H, *J* = 6.3Hz, H-7), 4.26-4.16 (m, 2H, H-5, H-6_a), 4.06-4.03 (m, 1H, H-6_b), 3.67 (dd, 1H, *J* = 3.6, 9.6 Hz, H-2), 3.21 (dd, 1H, *J* = 7.5, 13.8 Hz, H-8_a), 3.06 (dd, 1H, *J* = 6.3, 13.8 Hz, H-8_b), 2.02 (s, 3H, $COCH_3$), 1.98 (s, 3H, $COCH_3$), 1.76 (s, 3H, $COCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.53, 169.90, 169.68, 160.86, 139.68, 136.17, 129.34, 129.02, 128.56, 126.99, 126.19, 93.02, 81.34, 75.31, 71.22, 69.77, 67.99, 61.51, 41.50, 20.65, 20.59 (2); HR MALDI-TOF MS (*m*/*z*) calcd for $C_{28}H_{30}Cl_3NO_9S$ $[M + Na]^+$ 684.0604, found 684.0602.

Acetyl 3,6-Di-*O*-acetyl-4-*O*-benzyl-2-*O*-((S)-2-(phenylthiomethyl)benzyl)-α-D-glucopyranoside (34). Boron trifluoride etherate (572 μL, 4.5 mmol, 1.5 equiv) was added to the solution of acetyl 3,6-di-*O*-acetyl-4-*O*-benzyl-α-D-glucopyranoside (**40**) (1.18 g, 3.0 mmol, 1 equiv), (*S*)-2-(phenylthiomethyl)-benzyl acetate (**85**) (1.23 g, 4.5 mmol, 1.5 equiv) and activated molecular sieves (4Å) in dichloromethane (10 mL) at 0 °C. After 10 min, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (10 mL) and then separated. The organic phase was dried ($MgSO_4$), filtered and the filtrate was concentrated *in vacuo*. The residue was purified by silica gel column chromatography (25% ethyl acetate in hexane) to afford **34** (1.35 g, 74%):

colorless syrup, R_f = 0.30 (ethyl acetate/hexane, 1/3); $[\alpha]^{20}_D$ = +8.8° (*c* = 1.7, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36-7.10 (m,15H, aromatic), 5.96-5.83 (m, 1H, OCH_2CHCH_2), 5.30-5.13 (m, 3H, H-3, OCH_2CHCH_2), 4.96 (t, 1H, *J* = 6.9 Hz, H-7), 4.43 (d, 1H, *J* = 8.4 Hz, H-1), 4.49-4.26 (m, 3H, H-6_a, $OCHHCHCH_2$, $CHHPh$), 4.17-4.10 (m, 2H, H-6_b, $OCHHCHCH_2$), 3.53-3.35 (m, 3H, H-4, H-5, H-8_a), 3.23 (dd, 1H, *J* = 8.4, 9.6 Hz, H-2), 3.08 (dd, 1H, *J* = 6.9, 13.5 Hz, H-8_b), 2.01 (s, 3H, $COCH_3$), 1.76 (s, 3H, $COCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.58, 169.75, 140.32, 137.26, 136.89, 133.71, 128.78, 128.49, 128.347, 128.29, 128.01, 127.89, 127.69, 125.69, 118.15, 102.66, 81.41, 77.19, 76.24, 75.09, 74.42, 72.49, 70.73, 62.80, 40.38, 21.09, 20.81; HR MALDI-TOF MS (*m*/*z*) calcd for $C_{34}H_{38}O_8S$ $[M + Na]^+$ 629.2185, found 629.2203.

3,6-Di-*O*-acetyl-4-*O*-benzyl-2-*O*-((S)-2-(phenylthiomethyl)benzyl)-α-D-glucopyranosyl trichloroacetimidate (36). Tetrakis(triphenylphosphine)palladium (2.56 g, 2.22 mmol, 1.0 equiv) was added to the solution of **34** (1.35 g, 2.22 mmol, 1 equiv) in acetic acid (15 mL) at room temperature. The reaction mixture was stirred overnight, then diluted with dichloromethane (20 mL) and quenched with saturated aqueous $NaHCO_3$. After separation the organic phase was dried ($MgSO_4$), filtered and the filtrate was concentrated *in vacuo*. The residue was purified by silica gel column chromatography (25% ethyl acetate in hexane) to afford 3,6-di-*O*-acetyl-4-*O*-benzyl-2-*O*-((S)-2-(phenylthiomethyl)benzyl)-α-D-glucopyranose (**35**) (1.13 g, 90%): R_f = 0.19 (ethyl acetate/hexane, 1/2). Trichloroacetonitrile (1.99 mL, 10 equiv) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (119 µL, 0.4 equiv) were added to the solution of **35** (1.13 g, 1.99 mmol, 1 equiv) in dichloromethane (10 mL) at 0 °C. The reaction mixture was stirred at the same temperature for 1 h and then concentrated. The residue was purified by silica gel column chromatography (20% ethyl acetate in hexane) to afford **36** (1.32 g, 93%): R_f = 0.45 (dichloromethane/acetone, 100/1); $[\alpha]^{20}_D$ = -0.03° (*c* = 6.0, $CHCl_3$); ^{1}H NMR

(300 MHz, $CDCl_3$) δ 8.61 (s, 1H, N*H*), 7.37-7.16 (m, 15H, aromatic), 6.62 (d, 1H, *J* = 3.6 Hz, H-1), 5.57 (t, 1H, *J* = 9.6 Hz, H-3), 4.52-4.42 (m, 1H, H-7), 4.50 (d, 1H, *J* = 10.5 Hz, C*H*HPh), 4.44 (d, 1H, *J* = 10.5 Hz, CH*H*Ph), 4.29-4.17 (m, 2H, H-6_a, H-6_b), 4.13-4.08 (m, 1H, H-5), 3.55 (dd, 1H, *J* = 3.6, 9.6 Hz, H-2), 3.49 (t, 1H, *J* = 9.6 Hz, H-4), 3.25 (dd, 1H, *J* = 6.9, 13.5 Hz, H-8_a), 3.05 (dd, 1H, *J* = 6.6, 13.5 Hz, H-8_b), 2.00 (s, 3H, $COCH_3$), 1.81 (s, 3H, $COCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.44, 169.49, 161.08, 139.80, 137.07, 136,21, 129.35, 128.97, 128.54, 128.53, 128.13, 127.22, 126.11, 93.07, 80.86, 75.51, 75.47, 74.54, 72.70, 70.96, 62.33, 41.27, 20.95, 20.77; HR MALDI-TOF MS (*m*/*z*) calcd for $C_{33}H_{34}Cl_3NO_8S$ $[M + Na]^+$ 732.0968, found 732.0957.

General Procedure for the Glycosylation Reaction Employing Glycosyl Donors 36 and 43. Protocol A. A mixture of donor **36** and **43** (0.04 mmol), glycosyl acceptor (0.06 mmol), and activated molecular sieves (4 Å) in DCM (5 mL) was stirred for 10 min under an atmosphere of argon at room temperature. After the mixture was cooled to -78 ^oC, trimethylsilyl trifluoromethanesulfonate (2.2 μL, 0.012 mmol) was added. The reaction mixture was allowed to warm slowly to 10 ^oC. After the donor was consumed, the reaction mixture was quenched with aqueous saturated $NaHCO_3$ (5 mL) and separated. The organic phase was dried ($MgSO_4$) and filtered, and the filtrate was concentrated in vacuo. The residue was purified by silica gel column chromatography (20% ethyl acetate in hexane).

Protocol B. A mixture of donor **36** and **43** (0.04 mmol) and activated molecular sieves (4 Å) in DCM (5 mL) was stirred for 10 min under an atmosphere of argon at room temperature. After the mixture was cooled to -78 ^oC, trimethylsilyl trifluoromethanesulfonate (7.2 μL, 0.04 mmol) was added, and the reaction mixture was allowed to warm to 0 ^oC over a period of 40 min. After cooling of the reaction mixture to -78 ^oC, glycosyl acceptor (0.06 mmol) and 2, 6-di-*tert*-

butyl-4-methylpyridine (16 mg, 0.08 mmol) were added. The reaction mixture was allowed to warm slowly to room temperature and kept overnight at room temperature. After quenching with aqueous saturated $NaHCO_3$ (5 mL), the organic phase was dried ($MgSO_4$) and filtered, and the filtrate was concentrated in vacuo. The residue was purified by silica gel column chromatography (20% ethyl acetate in hexane).

Methyl 3,4,6-Tri-*O*-acetyl-2-*O*-((*S*)-2-(phenylthiomethyl)benzyl)-α-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (45); $[\alpha]^{20}_D = +56.8^\circ$ (*c* = 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99-7.86 (m, 6H, aromatic), 7.53-7.08 (m, 19H, aromatic), 6.19 (t, 1H, *J* = 9.5 Hz, H-3), 5.45 (t, 1H, *J* = 10.0 Hz, H-3'), 5.41 (t, 1H, *J* = 10.0 Hz, H-4), 5.26 (dd, 1H, *J* = 4.0, 9.5 Hz, H-2), 5.23 (d, 1H, *J* = 4.0 Hz, H-1), 5.07 (d, 1H, *J* = 3.0 Hz, H-1'), 4.82 (t, 1H, *J* = 9.5 Hz, H-4'), 4.43-4.37 (m, 2H, H-5, H-7'), 4.24-4.16 (m, 2H, H-5', H-$6_{a'}$), 4.04-4.02 (m, 1H, H-6_a), 3.93-3.89 (m, 1H, H-$6_{b'}$), 3.79-3.77 (m, 1H, H-6_b), 3.54 (s, 3H, OCH_3), 3.48 (dd, 1H, *J* = 3.0, 10.0 Hz, H-2'), 3.24 (dd, 1H, *J* = 9.0, 14.0 Hz, H-$8_{a'}$), 3.06 (dd, 1H, *J* = 3.5, 14.0 Hz, H-$8_{b'}$), 2.06(s, 3H, $COCH_3$), 1.95 (s, 3H, $COCH_3$), 1.64 (s, 3H, $COCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.69, 170.02, 169.82, 165.87, 165.77, 165.56, 140.57, 136.40, 133.54, 133.366, 133.16, 133.09, 130.01, 129.96, 129.92, 129.67, 129.25, 129.09, 128.89, 128.80, 128.63, 128.58, 128.50, 128.43, 128.28, 126.54, 125.94, 96.68, 96.30, 82.20, 77.19, 72.26, 71.29, 70.47, 70.11, 68.71(2), 67.35, 67.10, 62.01, 55.61, 41.67, 20.76, 20.63, 20.56; HR MALDI-TOF MS (*m*/*z*) calcd for $C_{54}H_{54}O_{17}S$ $[M + Na]^+$ 1029.2979, found 1029.2910.

Methyl 3,6-Di-*O*-acetyl-4-*O*-benzyl-2-*O*-((*S*)-2-(phenylthiomethyl)benzyl)-α-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (46); $[\alpha]^{20}_D = -14.6^\circ$ (*c* = 0.3, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99-7.85 (m, 6H, aromatic), 7.52-7.09 (m, 24H, aromatic), 6.17 (t, 1H, *J* = 10.0 Hz, H-3), 5.54 (t, 1H, *J* = 9.0 Hz, H-3'), 5.42 (t, 1H, *J* = 10.0 Hz,

H-4), 5.26(dd, 1H, *J* = 4.0, 10.0 Hz, H-2), 5.19 (d, 1H, *J* = 4.0 Hz, H-1), 5.01 (d, 1H, *J* = 3.0 Hz, H-1'), 4.48 (d, 1H, *J* = 11.0 Hz, C*H*HPh), 4.43 (d, 1H, *J* = 11.0 Hz, CH*H*Ph), 4.38-4.36 (m, 2H, H-5, H-7'), 4.27-4.10 (m, 3H, H-5', H-$6_{a'}$,H-$6_{b'}$), 3.89 (t, 1H, *J* = 10.0 Hz, H-6_a), 3.75 (d, 1H, *J* = 10.0 Hz, H-6_b), 3.51 (s, 3H, OCH_3), 3.38-3.34 (m, 2H, H-2', H-4'), 3.26 (dd, 1H, *J* = 8.5, 14.0 Hz, H-$8_{a'}$), 3.03 (dd, 1H, *J* = 5.0, 14.0 Hz, H-$8_{b'}$), 2.04 (s, 3H, $COCH_3$), 1.70 (s, 3H, $COCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.66, 169.71, 165.81, 165.76, 165.57, 140.69, 137.53, 136.46, 133.46, 133.29, 133.04, 129.96, 129.93, 129.67, 129.28, 129.22, 129.14, 128.82, 128.59, 128.54, 128.46, 128.43, 128.39, 128.25, 128.08, 127.85, 127.06, 126.74, 125.85, 96.62, 96.19, 81.74, 77.22, 76.14, 73.81, 72.74, 72.23, 70.53, 69.93, 68.67, 68.34, 67.12, 62.87, 55.69, 41.43, 21.98, 20.88; HR MALDI-TOF MS (*m*/*z*) calcd for $C_{59}H_{58}O_{16}S$ $[M+Na]^+$ 1077.3342, found 1077.3396.

Methyl 3,4,6-Tri-*O*-acetyl-2-*O*-((*S*)-2-(phenylthiomethyl)benzyl)-α-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-α-D-manopyranoside (48); $[\alpha]^{20}_D$ = -11.0 ° (*c* = 0.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13-7.81 (m, 6H, aromatic), 7.64-7.08 (m, 19H, aromatic), 5.91(dd, 1H, *J* = 3.5, 10.0 Hz, H-3), 5.81 (t, 1H, *J* = 10.0 Hz, H-4), 5.69 (m, 1H, H-2), 5.45 (t, 1H, *J* = 9.5 Hz, H-3'), 5.06 (d, 1H, *J* = 3.50 Hz, H-1'), 4.93 (s, 1H, H-1), 4.82 (t, 1H, *J* = 9.5 Hz, H-4'), 4.41-4.37 (m, 2H, H-5, H-7'), 4.22-4.19 (m, 1H, H-5'), 4.13-4.10 (m, 1H, H-$6_{a'}$), 4.01-3.98 (m, 21H, H-6a, H-$6_{b'}$), 3.81-3.79 (m, 1H, H-6_b), 3.57 (s, 3H, OCH_3), 3.47 (dd, 1H, *J* = 3.0, 10.0 Hz, H-2'), 3.23 (dd, 1H, *J* = 8.5, 14.0 Hz, H-$8_{a'}$), 2.94 (dd, 1H, *J* = 4.5, 14.0 Hz, H-$8_{b'}$), 1.96 (s, 3H, $COCH_3$), 1.92 (s, 3H, $COCH_3$), 1.69 (s, 3H, $COCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.61, 169.94, 169.81, 165.78, 165.55, 165.40, 129.97, 129.83, 129.72, 129.37, 129.13, 128.96, 128.91, 128.70, 128.61, 128.51, 128.36, 98.51, 96.37, 81.83, 77.22, 71.32, 70.68, 70.01, 69.76, 68.66, 67.58, 67.43, 67.23, 61.98, 55.52, 41.34, 20.64 (3); HR MALDI-TOF MS (*m*/*z*) calcd for $C_{54}H_{54}O_{17}S$ $[M+Na]^+$ 1029.2979, found 1029.2934.

Methyl 3,6-Di-*O*-acetyl-4-*O*-benzyl-2-*O*-((*S*)-2-(phenylthiomethyl)benzyl)-α-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-α-D-mannopyranoside (49); $[\alpha]^{20}_{D}$ = -181.4° (*c* = 1.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12-7.81 (m, 6H, aromatic), 7.63-7.08 (m, 24H, aromatic), 5.90 (dd, 1H, *J* = 3.0, 10.0 Hz, H-3), 5.80 (t, 1H, *J* = 10.0 Hz, H-4), 5.67 (s, 1H, H-1), 5.57 (t, 1H, *J* = 10.0 Hz, H-3'), 5.04 (d, 1H, *J* = 3 Hz, H-1'), 4.90 (s, 1H, H-2), 4.96 (d, 1H, *J* = 11.0 Hz, C*H*HPh), 4.43 (d, 1H, *J* = 11.0 Hz, CH*H*Ph), 4.39-4.32 (m, 2H, H-5, H-7'), 4.23-4.21 (m, 1H, H-$6_{a'}$), 4.14-4.09 (m, 2H, H-5', H-$6_{b'}$), 3.99-3.95 (m, 1H, H-6_a), 3.78-3.76 (m, 1H, H-6_b), 3.54 (s, 3H, OCH_3), 3.39-3.34 (m, 2H, H-2', H-4'), 3.25 (dd, 1H, 2.06, *J* = 8.0, 14.0 Hz, H-$8_{a'}$), 2.92 (dd, 1H, *J* = 5.0, 14.0 Hz, H-$8_{b'}$), 1.92 (s, 3H, $COCH_3$), 1.74 (s, 3H, $COCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.59, 169.65, 165.76, 165.56, 165.41, 140.59, 137.59, 136.44, 133.48, 133.45, 133.08, 129.99, 129.87, 129.73, 129.40, 129.18, 128.93, 128.69, 128.58, 128.51, 128.47, 128.43, 128.32, 128.26, 127.88, 127.84, 126.81, 125.85, 98.47, 96.22, 81.40, 77.23, 76.06, 73.78, 72.82, 70.67, 70.07, 69.72, 68.32, 67.47, 62.87, 55.59, 41.14, 21.04, 20.74; HR MALDI-TOF MS (*m*/*z*) calcd for $C_{59}H_{58}O_{16}S$ $[M+Na]^+$ 1077.3342, found 1077.3396.

Methyl 3,4,6-Tri-*O*-acetyl-2-*O*-((*S*)-2-(phenylthiomethyl)benzyl)-α-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (50); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33-7.05 (m, 25H, aromatic), 5.36 (t, 1H, *J* = 9.5 Hz, H-3'), 5.19 (d, 1H, *J* = 3.5 Hz, H-1'), 4.97-4.90 (m, 2H, C*H*HPh), 4.84-4.79 (m, 2H, C*H*HPh, H-4'), 4.73-4.69 (m, 2H, C*H*HPh), 4.61-4.56 (m, 2H, C*H*HPh, H-1), 4.49 (dd, 1H, *J* = 5.0, 8.0 Hz, H-7'), 4.18-4.12 (m, 2H, H-4, H-$6_{a'}$), 4.06 (d, 1H, *J* = 11.0 Hz, H-$6_{b'}$), 4.01-3.95 (m, 3H, H-3, H-6_a, H-6_b), 3.60 (dd, 1H, *J* = 3.5, 9.5 Hz, H-2), 3.54-3.51 (m, 2H, H-5', H-5), 3.51 (dd, 1H, *J* = 3.5, 9.5 Hz, H-2'), 3.42 (s, 3H, OCH_3), 3.25 (dd, 1H, *J* = 8.0, 14.0 Hz, H-$8_{a'}$), 3.07 (dd, 1H, *J* = 5.0, 14.0 Hz, H-$8_{b'}$), 1.99 (s, 3H,

$COCH_3$), 1.94 (s, 3H, $COCH_3$), 1.65 (s, 3H, $COCH_3$); HR MALDI-TOF MS (*m*/*z*) calcd for $C_{54}H_{60}O_{14}S$ $[M+Na]^+$ 987.3601, found 987.3659.

Methyl 3,6-Di-*O*-acetyl-4-*O*-benzyl-2-*O*-((*S*)-2-(phenylthiomethyl)benzyl)-α-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (51); $[\alpha]^{20}_D$ = -221.7° (*c* = 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34-7.07 (m, 30H, aromatic), 5.51 (t, 1H, *J* = 9.5 Hz, H-3'), 5.14 (d, 1H, *J* = 3.0 Hz, H-1'), 4.96 (d, 1H, *J* = 12.0 Hz, C*H*HPh), 4.94 (d, 1H, *J* = 11.0 Hz, CH*H*Ph), 4.82 (d, 1H, *J* = 11.0 Hz, C*H*HPh), 4.69 (d, 1H, *J* = 12.0 Hz, CH*H*Ph), 4.67 (d, 1H, *J* = 12.0 Hz, C*H*HPh), 4.59 (d, 1H, *J* = 3.0 Hz, H-1), 4.58 (d, 1H, *J* = 12.0 Hz, CH*H*Ph), 4.47 (d, 1H, *J* = 11.0 Hz, C*H*HPh), 4.48-4.41 (m, 1H, H-7'), 4.40 (d, 1H, *J* = 11.0 Hz, CH*H*Ph), 4.20 (dd, 1H, *J* = 2.0, 12.0 Hz, H-$6_{a'}$), 4.13 (dd, 1H, *J* = 4.0, 12.0 Hz, H-$6_{b'}$), 3,99 (t, 1H, *J* = 9.5 Hz, H-3), 3.92-3.91 (m, 1H, H-5'), 3.85-3.83 (m, 1H, H-5), 3.80 (m, 2H, H-6_a, H-6_b), 3.64 (t, 1H, *J* = 9.5 Hz, H-4), 3.58 (dd, 1H, *J* = 3.0, 9.5 Hz, H-2), 3.40 (s, 3H, OCH_3), 3.38-3.34(m, 2H, H-2', H-4'), 3.31(dd, 1H, *J* = 7.0, 13.5 Hz, H-$8_{a'}$), 3.05(dd, 1H, *J* = 5.0, 13.5 Hz, H-$8_{b'}$), 1.99 (s, 3H, $COCH_3$), 1.72 (s, 3H, $COCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.61, 169.66, 140.41, 138.88, 138.40, 138.22, 137.50, 136.53, 128.94, 128.75, 128.49, 128.45, 128.40, 128.34, 128.27, 128.06, 127.92, 127.76, 127.62, 127.49, 126.87, 125.85, 97.88, 96.60, 82.27, 80.93, 80.24, 78.02, 77.23, 76.12, 75.69, 75.03, 74.03, 73.27, 73.05, 70.18, 68.32, 66.37, 62.80, 55.26, 41.49, 20.91, 20.84; HR MALDI-TOF MS (*m*/*z*) calcd for $C_{59}H_{64}O_{13}S$ $[M+Na]^+$ 1035.3965, found 1035.3988.

Methyl 3,4,6-Tri-*O*-acetyl-2-*O*-((*S*)-2-(phenylthiomethyl)benzyl)-α-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (52); $[\alpha]^{20}_D$ = +66.5° (*c* = 0.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38-6.97 (m, 25H, aromatic), 5.71 (d, 1H, *J* = 3.5 Hz, H-1'), 5.35 (t, 1H, *J* = 10.0 Hz, H-3'), 5.07 (d, 1H, *J* = 11.0 Hz, C*H*HPh), 4.96 (d, 1H, *J* = 11.0 Hz, C*H*HPh), 4.78 (t, 1H, *J* = 10.0 Hz, H-4'), 4.71 (d, 1H, *J* = 9.5 Hz, C*H*HPh), 4.63-4.54 (m, 3H, H-

1, CH*H*Ph), 4.35 (t, 1H, *J* = 7.0 Hz, H-7'), 4.17 (t, 1H, *J* = 9.5 Hz, H-3), 4.10-3.93 (m, 4H, H-4, H-5, H-6_a, H-5'), 3.85-3.82 (m, 1H, H-6_b), 3.76-3.74 (m, 1H, H-$6_{b'}$), 3.67-3.65 (m, 1H, H-6'), 3.60 (dd, 1H, *J* = 3.5, 9.5 Hz, H-2), 3.38 (s, 3H, OCH_3), 3.34 (dd, 1H, *J* = 3.5, 10.0 Hz, H-2'), 3.25 (dd, 1H, *J* = 7.0, 13.0 Hz, H-$8_{a'}$), 2.89 (dd, 1H, *J* = 7.0, 13.0 Hz, H-$8_{b'}$), 1.97 (s, 3H, $COCH_3$), 1.94 (s, 3H, $COCH_3$), 1.73 (s, 3H, $COCH_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.55, 170.04, 169.64, 140.08 139.31, 138.06, 137.97, 136.60, 128.87, 128.53, 128.54, 128.36, 128.28, 128.15, 127.92, 127.61, 127.36, 127.09, 126.87, 126.83, 125.68, 97.91, 94.97, 81.35, 81.28, 80.13, 77.22, 76.13, 74.23, 73.42, 73.29, 71.21, 69.66, 68.83, 68.69, 67.50, 61.92, 55.36, 40.83, 20.73, 20.65, 20.20; HR MALDI-TOF MS (*m*/*z*) calcd for $C_{54}H_{60}O_{14}S$ $[M+Na]^+$ 987.3601, found 987.3666.

Methyl 3,6-Di-*O*-acetyl-4-*O*-benzyl-2-*O*-((*S*)-2-phenylthiomethylbenzyl)-α-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (53); $[\alpha]^{20}_D$ = -103.65° (*c* =2, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39-6.98 (m, 30H, aromatic), 5.63 (d, 1H, *J* = 3.0 Hz, H-1'), 5.45 (t, 1H, *J* = 10.0 Hz, H-3'), 5.06 (d, 1H, *J* = 12.0 Hz, C*H*HPh), 4.97 (d, 1H, *J* = 12.0 Hz, CH*H*Ph), 4.72 (d, 1H, *J* = 12.0 Hz, C*H*HPh), 4.61 (d, 1H, *J* = 12.0 Hz, CH*H*Ph), 4.61(d, 1H, *J* = 3.0 Hz, H-1), 4.53 (d, 1H, *J* = 12.0 Hz, C*H*HPh), 4.50 (d, 1H, *J* = 12.0 Hz, CH*H*Ph), 4.47 (d, 1H, *J* = 12.0 Hz, C*H*HPh), 4.38 (d, 1H, *J* = 12.0 Hz, CH*H*Ph), 4.33 (t, 1H, *J* = 6.0 Hz, H-7'), 4.14 (t, 1H, *J* = 9.0 Hz, H-3), 4.08-3.89 (m, 5H, H-$6_{a'}$, H-$6_{b'}$, H-5', H-5, H-6_b), 3.71-3.69 (m, 1H, H-6_a), 3.63-3.61 (m, 1H, H-4), 3.58 (dd, 1H, *J* = 3.0, 9.0 Hz, H-2), 3.37 (s, 3H, OCH_3), 3.34-3.29 (m, 2H, H-4', H-$8_{b'}$), 3.22 (dd, 1H, *J* = 3.0, 10.0 Hz, H-2'), 2.87 (dd, 1H, *J* = 6.0, 14.0 Hz, H-$8_{a'}$), 1.96 (s, 3H, $COCH_3$), 1.81 (s, 3H, $COCH_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.51, 169.67, 140.08 139.45, 138.12, 138.02, 137.60, 136.70, 128.81, 128.47, 128.43, 128.33, 128.25, 128.21, 128.16, 127.92, 127.41, 127.141, 127.06, 126.95, 125.56, 97.91, 94.95, 81.55, 80.90, 80.01,

77.22, 76.80, 76.11 (2), 74.36, 74.23, 73.27 (2), 72.87, 69.66, 68.74, 62.82, 55.28, 40.53, 21.04, 20.86.; HR MALDI-TOF MS (*m*/*z*) calcd for $C_{59}H_{64}O_{13}S$ $[M+Na]^+$ 1035.3965, found 1035.3979.

Procedure for low-temperature NMR experiments. ^{1}H NMR spectrum of **36** (14 mg, 0.02 mmol) in CD_2Cl_2 (0.5 mL) was recorded; ^{1}H NMR (500 MHz, CD_2Cl_2) δ 8.67 (s, 1H, N*H*), 7.39-7.18 (m, 15H, aromatic), 6.58 (d, 1H, *J* = 3.0 Hz, H-1)**,** 5.48 (t, 1H, *J* = 10.0 Hz, H-3), 4.53 (t, 1H, *J* = 6.5 Hz, H-7), 4.49 (d, 1H, *J* = 10.5 Hz, C*H*HPh), 4.46 (d, 1H, *J* = 10.5 Hz, CH*H*Ph), 4.30-4.08 (m, 1H, H-6_a), 4.16-4.12 (m, 1H, H-6_b), 4.09-4.05 (m, 1H, H-5), 3.55 (dd, 1H, *J* = 3.0, 10.0 Hz, H-2), 3.51 (t, 1H, *J* = 10.0 Hz, H-4), 3.29 (dd, 1H, *J* = 7.0, 14.0 Hz, H-8_a), 3.08 (dd, 1H, *J* = 7.0, 14.0 Hz, H-8_b), 1.98 (s, 3H, $COCH_3$), 1.85 (s, 3H, $COCH_3$).

Trimethylsilyl trifluoromethanesulfonate (3.6 μL, 0.02 mmol) was added to the solution at -50 °C. The solution was allowed to warm slowly to 0 °C. The NMR spectra of **54** (^{1}H, ^{1}H TOCSY 1D, HSQC and HMBC) were recorded at -20 °C, **54**; ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.89-7.87 (m, 2H, aromatic), 7.76-7.74 (m, 1H, aromatic), 7.65-7.62 (m, 2H, aromatic), 7.41-7.16 (m, 10H, aromatic), 5.48 (t, 1H, *J* = 9.5 Hz, H-3), 5.35 (d, 1H, *J* = 11.0 Hz, H-7), 5.30 (d, 1H, *J* = 9.5 Hz, H-1)**,** 4.56 (d, 1H, *J* = 11.5 Hz, C*H*HPh), 4.50 (d, 1H, *J* = 11.5 Hz, CH*H*Ph), 4.32 (d, 1H, *J* = 11.0 Hz, H-8_{eq}), 4.16-4.08 (m, 3H, H-2, H-6_a, H-6_b), 3.81 (t, 1H, *J* = 9.5 Hz, H-4), 3.77 (m, 1H, H-5), 3.66 (t, 1H, *J* = 11.0 Hz, H-8_{ax}), 1.96 (s, 3H, $COCH_3$), 1.95 (s, 3H, $COCH_3$).

Methanol was added to the solution at the same temperature and ^{1}H NMR spectrum of the reaction mixture was recorded at 0 °C, **55**; ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.39-7.18 (m, 15H, aromatic), 5.47 (t, 1H, *J* = 9.0 Hz, H-3), 4.84 (d, 1H, *J* = 3.5 Hz, H-1), 4.44 (d, 1H, *J* = 11.5 Hz, C*H*HPh), 4.39 (d, 1H, *J* = 11.5 Hz, CH*H*Ph), 4.39 (t, 1H, *J* = 5.5 Hz, H-7), 4.27-4.11 (m, 2H, H-6_a, H-6_b), 3.81-3.77 (m, 1H, H-5), 3.40 (s, 3H, OCH_3), 3.36-3.26 (m, 3H, H-2, H-4, H-8_a), 3.10 (dd, 1H, *J* = 5.5, 14.0 Hz, H-8_b), 1.96 (s, 3H, $COCH_3$), 1.72 (s, 3H, $COCH_3$); ^{1}H NMR (300 MHz,

$CDCl_3$) δ 7.39-7.18 (m, 15H, aromatic), 5.49 (t, 1H, J = 9.6 Hz, H-3), 4.94 (d, 1H, J = 3.6 Hz, H-1), 4.49 (d, 1H, J = 11.1 Hz, C*H*HPh), 4.42 (d, 1H, J = 11.1 Hz, CH*H*Ph), 4.40 (t, 1H, J = 6.3 Hz, H-7), 4.25-4.22 (m, 2H, H-6_a, H-6_b), 3.92-3.86 (m, 1H, H-5), 3.44 (s, 3H, OCH_3), 3.41-3.30 (m, 3H, H-2, H-4, H-8_a), 3.10 (dd, 1H, J = 4.8, 13.8 Hz, H-8_b), 2.03 (s, 3H, $COCH_3$), 1.66 (s, 3H, $COCH_3$).

The ^{1}H NMR spectrum of **54** showed that the anomeric proton (H1) signal (δ 6.58, d, $J_{1,2}$ = 2.5 Hz, α-configuration) was shifted to upfield (δ 5.30, d, $J_{1,2}$ = 9.5 Hz, β-configuration). The change of anomeric configuration indicates that the α-imidate donor **36** was completely transformed to a new β-intermediate **54** after activation. H1, H7, $H8_{eq}$ and $H8_{ax}$ signals of **53** were assigned from ^{1}H TOCSY 1D data irradiated on H4 and H7. The anomeric carbon signal (C1, δ 88.0) of **54** was assigned from HSQC data. The HMBC spectrum of **54** showed the three-bond coupling between C1 (δ 88.0) and $H8_{eq}$ (δ 4.32) which confirmed the presence of C1-$H8_{eq}$ bond. So, the *trans*-decalin structure of the sulfonium ion **54** was proved directly from the low-temperature NMR experiments.

3,6-Di-*O*-acetyl-2,4-di-*O*-benzyl-α-D-glucopyranosyl trichloroacetimidate (56): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.60 (s, 1H, NH), 7.35-7.24 (m, 10H, aromatic), 6.47 (d, 1H, J = 3.5 Hz, H-1), 5.62 (t, 1H, J = 9.5 Hz, H-3), 4.68 (d, 1H, J = 12.0 Hz, C*H*HPh), 4.59 (d, 1H, J = 11.0 Hz, CH*H*Ph), 4.55 (d, 1H, J = 12.0 Hz, C*H*HPh), 4.53 (d, 1H, J = 11.0 Hz, CH*H*Ph), 4.31 (dd, 1H, J = 2.5, 12.5 Hz, H-6_a), 4.24 (dd, 1H, J = 4.5, 12.5 Hz, H-6_b), 4.14-4.09 (m, 1H, H-5), 3.66 (dd, 1H, J = 3.5, 9.5 Hz, H-2), 3.62 (t, 1H, J = 9.5 Hz, H-4), 2.03 (s, 3H, $COCH_3$), 1.99 (s, 3H, $COCH_3$).

Methyl 3,6-di-*O*-acetyl-2,4-di-*O*-benzyl- α/β-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (57) (mixture as α/β = 3/1): ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.55

(t, 1H, *J* = 9.5 Hz, H-3′-α), 5.22 (t, 1H, *J* = 9.0 Hz, H-3′-β), 4.96 (d, 1H, *J* = 3.0 Hz, H-1′-α), 4.38 (d, 1H, *J* = 8.5 Hz, H-1′-β), 3.36 (s, 3H, OCH_3-α), 3.34 (s, 3H, OCH_3-β), 2.01 (s, 3H, $COCH_3$-β), 2.00 (s, 3H, $COCH_3$- α), 1.97 (s, 3H, $COCH_3$-α), 1.86 (s, 3H, $COCH_3$-β).

3,6-Di-*O*-acetyl-4-*O*-benzyl-2-*O*-((1*R*)-phenyl-2-(phenylsulfanyl)-ethyl)-α-D-glucopyranosyl trichloroacetimidate (58). Compound 5**8** was synthesized according to the procedure described for the synthesis of compound **36**: colorless syrup; R_f = 0.43 (dichloromethane/acetone = 100/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.42 (s, 1H, NH), 7.26-7.36 (m, 15H, aromatic), 5.79 (d, 1H, *J* = 4.0 Hz, H-1), 5.68 (t, 1H, *J* = 10.0 Hz, H-3), 4.60 (d, 1H, *J* = 11.0 Hz, C*H*HPh), 4.53 (d, 1H, *J* = 11.0 Hz, CH*H*Ph), 4.50 (dd, 1H, *J* = 5.0, 8.0 Hz, H-7), 4.23-4.16 (m, 2H, H-6_a, H-6_b), 4.03-4.00 (m, 1H, H-5), 3.65 (dd, 1H, *J* = 4.0, 10.0 Hz, H-2), 3.60 (t, 1H, *J* = 10.0 Hz, H-4), 3.25 (dd, 1H, *J* = 8.0, 13.5 Hz, H-8_a), 3.05 (dd, 1H, *J* = 5.0, 13.5 Hz, H-8_b), 2.08 (s, 3H, $COCH_3$), 1.99 (s, 3H, $COCH_3$).

Methyl 3, 6-di-*O*-acetyl-4-*O*-benzyl-2-*O*-((1*R*)-phenyl-2-(phenylsulfanyl)ethyl)-α/β-D-glucopyranosyl-(1→6)-2, 3, 4-tri-*O*-benzyl-*α*-glucopyranoside (59) (mixture as α/β = 1/1): ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.59 (t, 1H, *J* = 10.0 Hz, H-3′-α), 5.28 (t, 1H, *J* = 9.0 Hz, H-3′-β), 4.24 (d, 1H, *J* = 6.5 Hz, H-1′-β), 4.23 (d, 1H, *J* = 3.5 Hz, H-1′-α), 2.04 (s, 3H, $COCH_3$-α), 2.00 (s, 3H, $COCH_3$-β), 1.98 (s, 3H, $COCH_3$-β), 1.95 (s, 3H, $COCH_3$-α).

2-hydroxy-3-cyclohexen-1-yl phenyl sulfide (62) Scheme 2.14: Phenyl disulfide (3.3 g, 15 mmol) was added to the solution of lead tetraacetate (6.65 g, 15 mmol) in DCM (20 mL) at -40^{o}C, trifluoroacetic acid (11.56 mL, 0.15 mol) was added to the reaction mixture followed by the addition of cyclohexadiene (0.84 g. 0.01 mol). The reaction mixture was stirred at -40 ^{o}C for 1h and quenched with saturated aqueous $NaHCO_3$ solution (20 mL). The organic phase was washed with brine and dried over $MgSO_4$, filtered and the filtrate was concentrated *in vacuo*. The

residue was purified by flash silica gel column chromatography (Hexane/EtOAc = 7/1) to afford **62** (678mg, 32%): colorless syrup, R_f = 0.63 (hexane/ethyl acetate = 1/1); Scheme 2.15: Benzenethio (2.6 mL, 25 mmol) was added slowly to the solution of N-chlorosuccinimide (3.34 g, 25 mmol) in DCM (60 mL) at room temperature. The reaction mixture was stirred for 30mins. Cyclohexadiene (2.6 mL, 27 mmol) was added to the above solution. The reaction mixture was stirred for 6h before quenched by saturated aqueous $NaHCO_3$ (30 mL) and washed with brine (30 mL). The organic phase was washed with brine and dried over $MgSO_4$, filtered and the filtrate was concentrated *in vacuo*. The residue was purified by flash silica gel column chromatography (Hexane/EtOAc = 9/1) to afford **62** (3.3 g, 60%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49-7.24 (m, 5H, aromatic), 5.81-5.70 (m, 2H, CHOHC*H*CH, CHOHCHC*H*), 4.13-4.10 (m, 1H, CHOH), 3.16-3.09 (m, 1H, CHSPh), 2.36 (s, 1H, OH), 2.13-2.06 (m, 3H, CH_2, C*H*H), 1.77-1.66 (m, 1H, CH*H*); HR MALDI-TOF MS m/z calcd for $C_{12}H_{14}OS$ $[M+Na]^+$ 229.0847, found 229.0854.

(1*R*, 2*S*)-2-hydroxy-3-cyclohexen-1-yl phenyl sulfide (63) Isopropenyl Acetate (3.16 mL, 29.12 mmol) was added to the solution of 2-hydroxy-3-cyclohexen-1-yl phenyl sulfide **(62)** (3.0g, 14.56 mmol) in isopropyl ether (50 mL). Amano lipase PS C-I (7.2 g) was added to the above solution and stirred overnight at room temperature. The enzyme was filtered and the filtrate was evaporated under *vacuo.* The residue was purified by flash silica gel column chromatography (Hexane/EtOAc = 10/1) to afford **63** (1.5g, 50%): colorless syrup, R_f = 0.63 (hexane/ethyl acetate = 1/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49-7.24 (m, 5H, aromatic), 5.81-5.70 (m, 2H, CHOHC*H*CH, CHOHCHC*H*), 4.13-4.10 (m, 1H, CHOH), 3.16-3.09 (m, 1H, CHSPh), 2.36 (s, 1H, OH), 2.13-2.06 (m, 3H, CH_2, C*H*H), 1.77-1.66 (m, 1H, CH*H*); HR MALDI-TOF MS m/z calcd for $C_{12}H_{14}OS$ $[M+Na]^+$ 229.0847, found 229.0854.

Acetyl 3,4,6-tri-*O*-acetyl-((1*S*,6*R*)-(phenylsulfanyl)-cyclohexene-2-yl)-α-D-galactopyranose (68). Compound **67** (3.21g, 9.22 mmol) was added to a solution of **65** (380 mg, 1.84 mmol) in THF (25 mL) at RT. After the solution was cooled to -20 ^{o}C, TfOH (276 mg, 0.16mL) was added. The reaction mixture was allowed to warm up slowly to RT. After stirring at RT for 1h, the reaction mixture was quenched with aqueous saturated $NaHCO_3$ (10 mL) and washed with brine (10 mL). The organic phase was dried ($MgSO_4$) and filtered, the filtrate was concentrated in vacuo. The residue was purified by flash silica gel column chromatography (Hexane/EtOAc = 2/1) to afford **68** (450 mg, 44%): colorless syrup; R_f = 0.54 (Hexane/EtOAc = 1/1); $[\alpha]^{20}_{D}$ = +32 ° (*c* = 0.7, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47-7.22 (m, 10H, aromatic), 6.47 (d, 1H, *J* = 3.9 Hz, H-1), 6.39 (d, 1H, *J* = 3.6 Hz, H-1'), 5.93 (dd, 1H, *J* = 3.9, 10.2 Hz, C*H*CHCO), 5.88-5.85 (m, 1H, CHC*H'*CO), 5.76-5.71 (m, 1H, CHC*H*CO), 5.65-5.61 (m, 1H, CHC*H*'CO), 5.48-5.46 (m, 2H, H-4, H-4'), 5.25 (dd, 1H, *J* = 3.3, 10.5 Hz, H-3), 5.15 (dd, 1H, *J* = 3.3, 10.5 Hz, H-3'), 4.32-4.25 (m, 2H, H-5, H-5'), 4.12-3.90 (m, 4H, H-6_a, H-6_b, H-$6_{a'}$, H-$6_{b'}$), 3.81-3.80 (m, 2H, C*H*OCHSPh, C*H'*OCHSPh), 3.30-3.25 (m, 2H, CHOC*H*SPh, CHOC*H'*SPh), 2.14 (s, 6H, $2COCH_3$), 2.08 (s, 3H, $COCH_3$'), 2.03 (s, 6H, $2COCH_3$'), 2.02 (s, 3H, $COCH_3$), 2.19 (s, 3H, $COCH_3$), 1.98 (s, 3H, $COCH_3$), 1.78-1.59 (m, 8H, $2CH_2$, $2CH_2$'); HR MALDI-TOF MS (*m*/*z*) calcd for $C_{26}H_{32}O_{10}S$ $[M + Na]^+$ 559.1716, found 559.1765.

3,4,6-tri-*O*-acetyl-((1*S*,6*R*)-(phenylsulfanyl)-cyclohexene-2-yl)-α-D-galactopyranosyl trichloroacetimidate (70) Hydrazinium acetate (131 mg, 1.42 mmol) was added to a solution of compound **68** (635 mg, 0.46 mmol) in DMF (10 mL) at room temperature. After stirring the reaction mixture for 4 h, it was quenched with an aqueous saturated solution of $NaHCO_3$. The organic phase was washed with an aqueous saturated solution of NH_4Cl (10 mL) and dried ($MgSO_4$), filtered and the filtrate was concentrated *in vacuo*. The residue was purified by flash

silica gel column chromatography (ethyl acetate/hexane = 1/3) to afford **69**. Trichloroacetonitrile (0.67 mL) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 45 μL) were added to a solution of **69** (331 mg, 0.67 mmol) in dichloromethane (10 mL) at 0 °C. After stirring the reaction mixture at 0 °C for 30 mins, it was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (30% ethyl acetate in hexane) to afford **70** (394 mg, 92%): ***α***, R_f = 0.58 (DCM/ethyl acetate/hexane, 2/1/2); $[\alpha]^{20}_D = +85^o$ (c = 1.3, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.63 (s, 1H, -NH), 7.44-7.32 (m, 5H, aromatic), 6.57 (d, 1H, J = 3.5 Hz, H-1), 5.90 (dd, J = 4.0, 10.5 Hz, 1H, -C*H*CHCO), 5.74-5.72 (m, 1H, -CHC*H*CO), 5.53 (d, 1H, J = 2.5 Hz, H-4), 5.24 (dd, 1H, J = 3.5, 10.5 Hz, H-3), 4.40 (t, 1H, J = 6.5 Hz, H-5), 4.13 (dd, 1H, J = 6.5, 11.0 Hz, H-6_a), 4.02 (dd, 1H, J = 7.0, 11.5 Hz, H-6_b), 4.02 (dd, 1H, J = 3.5, 10.5 Hz, H-2), 3.99-3.98 (m, 1H, CO*H*CHSPh), 3.80-3.79 (m, 1H, COHC*H*SPh), 2.16 (s, 3H, $COCH_3$), 2.11-2.08 (m, 2H, CH_2), 2.01 (s, 3H, $COCH_3$), 1.99 (s, 3H, $COCH_3$), 1.71-1.65 (m, 2H, CH_2) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.46, 170.22, 169.97, 161.58, 135.93, 131.48, 131.40, 130.42, 129.87, 126.98, 95.21, 74.21, 71.56, 69.54, 68.95, 67.98, 61.85, 44.21, 26.84, 25.74, 20.95, 20.72, 20.70; ***α'*** R_f = 0.54 (DCM/ethyl acetate/hexane, 2/1/2); $[\alpha]^{20}_D = +73^o$ (c = 1.1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.64 (s, 1H, -NH), 7.40-7.22 (m, 5H, aromatic), 6.54 (d, 1H, J = 3.6 Hz, H-1), 5.89 (dd, J = 3.3, 10.5 Hz, 1H, -C*H*CHCO), 5.84-5.81 (m, 1H, -CHC*H*CO), 5.54 (d, 1H, J = 2.4 Hz, H-4), 5.28 (dd, 1H, J = 3.3, 10.5 Hz, H-3), 4.41 (t, 1H, J = 6.3 Hz, H-5), 4.17-4.02 (m, 4H, H-6_a, H-6_b, H-2, CO*H*CHSPh), 3.76-3.74 (m, 1H, COHC*H*SPh), 2.17 (s, 3H, $COCH_3$), 2.16-2.06 (m, 2H, CH_2), 2.04 (s, 3H, $COCH_3$), 2.02 (s, 3H, $COCH_3$), 1.89-1.88 (m, 2H, CH_2) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.37, 170.03, 169.95, 161.36, 135.50, 131.36, 130.38, 129.81, 128.99, 126.94, 94.96, 74.01, 71.46, 69.21, 68.93, 67.95, 61.41, 43.59, 26.37, 25.84, 20.82, 20.70, 20.66; ***β***, R_f = 0.48 (DCM/ethyl acetate/hexane, 2/1/2); $[\alpha]^{20}_D = +78^o$ (c = 0.9, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$)

δ 8.74 (s, 1H, -NH), 7.41-7.16 (m, 5H, aromatic), 5.89 (dd, *J* = 3.6, 10.2 Hz, 1H, -C*H*CHCO), 5.82-5.81 (m, 1H, -CHC*H*CO), 5.78 (d, 1H, *J* = 8.1 Hz, H-1), 5.42 (d, 1H, *J* = 3.3 Hz, H-4), 4.98 (dd, 1H, *J* = 3.3, 9.9 Hz, H-3), 4.16-4.14 (m, 3H, H-6_a, H-6_b, CO*H*CHSPh), 4.02 (t, 1H, *J* = 6.3 Hz, H-5), 3.86-3.80 (m, 2H, H-2, COHC*H*SPh), 2.16 (s, 3H, $COCH_3$), 2.06-2.03 (m, 2H, CH_2), 2.02 (s, 3H, $COCH_3$), 1.99 (s, 3H, $COCH_3$), 1.72-1.65 (m, 2H, CH_2).

General Procedure for the Glycosylation Employing 3,4,6-tri-*O*-acetyl-((1*S*,6*R*)-(phenylsulfanyl)-cyclohexene-2-yl)-α-D-galactopyranosyl trichloroacetimidate (70) A mixture of donor (20 mg, 0.03 mmol, 1 equiv), acceptor (0.036 mmol, 1.2 equiv) and activated molecular sieves (4Å) in DCM (10 mL) was stirred for 1 h under an atmosphere of argon at RT, then cooled to -78 ^oC. After addition of trimethylsilyl trifluoromethanesulfonate (2.2 µL, 0.012 mmol, 0.4 equiv), the reaction mixture was stirred at -78 ^oC for 1 h and allowed to warm over 1 h to 0 ^oC. The reaction mixture was quenched with aqueous saturated $NaHCO_3$ (10 mL) and separated. The organic phase was dried ($MgSO_4$), filtered and the filtrate was concentrated *in vacuo*. The residue was purified by silica gel column chromatography (DCM/n-hexane/ethyl acetate = 2/2/1).

Methyl 3,4,6-tri-*O*-acetyl-((1*S*,6*R*)-(phenylsulfanyl)-cyclohexene-2-yl)-α-D-galactopyranosyl-(1→6)-2, 3, 4-tri-*O*-benzoyl-α-mannopyranoside (71) ^1H NMR (300 MHz, $CDCl_3$) δ 8.08-7.11 (m, 20H, aromatic), 5.84 (dd, 1H, *J* = 3.0, 9.5 Hz, H-3), 5.77-5.74 (m, 1H, C*H*'CHCO), 5.72 (t, 1H, *J* = 10.0 Hz, H-4), 5.66 (dd, 1H, *J* = 1.5, 3.0 Hz, H-2), 5.59 (dd, 1H, *J* = 2.0, 9.5 Hz, CHC*H*'CO), 5.43 (d, 1H, *J* = 2.5 Hz, H-4'), 5.31 (dd, 1H, *J* = 3.5, 10.5 Hz, H-3'), 5.02 (d, 1H, *J* = 3.5 Hz, H-1'), 4.91 (s, 1H, H-1), 4.42 (t, 1H, *J* = 6.5 Hz, H-5'), 4.33 (t, 1H, *J* = 8.0 Hz, H-5), 4.09 (dd, 1H, *J* = 6.0, 11.5 Hz, H-6_a'), 3.96-3.89 (m, 4H, C*H*'OCHSPh, H-2', H-6_a, H-6_b'), 3.64-3.62 (m, 1H, H-6_b), 3.52 (s, 3H, OCH_3), 3.26-3.23 (m, 1H, CHOC*H*'SPh), 2.13 (s,

3H, $COCH_3$'), 2.06-1.98 (m, 2H, CH_2'), 2.01 (s, 3H, $COCH_3$), 1.85 (s, 3H, $COCH_3$), 1.64-1.55 (m, 2H, CH_2'); HR MALDI-TOF MS (*m*/*z*) calcd for $C_{52}H_{54}O_{17}S$ $[M + Na]^+$ 1005.3082, found 1005.3075.

Methyl 3,4,6-tri-*O*-acetyl-((1*S*,6*R*)-(phenylsulfanyl)-cyclohexene-2-yl)-α-D-galactopyranosyl-(1→6)-2, 3, 4-tri-*O*-benzoyl-α-glucopyranoside (72) ^1H NMR (300 MHz, $CDCl_3$) δ 8.03-7.21 (m, 20H, aromatic), 6.14 (t, 1H, J = 9.3 Hz, H-3), 5.91-5.69 (m, 1H, C*H*'CHCO, CHC*H*'CO), 5.54-5.44 (m, 2H, H-2, H-4), 5.30-5.31 (m, 1H, H-4'), 5.27 (s, 1H, H-1'), 5.21 (s, 1H, H-1), 4.96 (dd, 1H, J = 3.5, 10.5 Hz, H-3'), 4.36-4.30 (m, 2H, H-5, H-5'), 4.15-3.70 (m, 7H, H-6_a', C*H*'OCHSPh, H-2', H-6_a, H-6_b', H-6_b, CHOC*H*'SPh), 3.47 (s, 3H, OCH_3), 2.13 (s, 3H, $COCH_3$'), 2.04-1.97 (m, 2H, CH_2'), 2.04 (s, 3H, $COCH_3$), 1.99 (s, 3H, $COCH_3$), 1.70-1.59 (m, 2H, CH_2'); HR MALDI-TOF MS (*m*/*z*) calcd for $C_{52}H_{54}O_{17}S$ $[M + Na]^+$ 1005.3082, found 1005.3090.

Methyl 3,4,6-tri-*O*-acetyl-((1*S*,6*R*)-(phenylsulfanyl)-cyclohexene-2-yl)-α-D-galactopyranosyl-(1→6)-2, 3, 4-tri-*O*-benzyl-α-glucopyranoside (73) ^1H NMR (300 MHz, $CDCl_3$) δ 7.19-7.08 (m, 20H, aromatic), 5.81-5.78 (m, 1H, C*H*'CHCO), 5.39-5.38 (m, 1H, CHC*H*'CO), 5.25-5.23 (m, 1H, -H-4'), 5.16 (dd, 1H, J = 3.3, 10.8 Hz, H-3'), 5.08 (d, 1H, J = 3.6 Hz, H-1'), 4.97 (d, 1H, J = 10.8 Hz, C*H*HPh), 4.89 (d, 1H, J = 10.8 Hz, CH*H*Ph), 4.81 (d, 1H, J = 10.8 Hz, C*H*HPh), 4.76 (d, 1H, J = 10.8 Hz, CH*H*Ph), 4.65 (d, 1H, J = 10.8 Hz, C*H*HPh), 4.61 (d, 1H, J = 10.8 Hz, CH*H*Ph), 4.55 (d, 1H, J = 3.6 Hz, H-1), 4.16-3.94 (m, 6H, H-6_a', H-2', H-4, H-5, H-5', H-6_b'), 3.82-3.76 (m, 3H, H-2, H-6_a, H-6_b,), 3.64-3.61 (m, 1H, C*H*'OCHSPh), 3.48-3.43 (m, 1H, CHOC*H*'SPh), 3.36 (s, 3H, OCH_3), 2.12 (s, 3H, $COCH_3$'), 2.04-1.98 (m, 2H, CH_2'), 1.98 (s, 3H, $COCH_3$), 1.96 (s, 3H, $COCH_3$), 1.70-1.55 (m, 2H, CH_2'); HR MALDI-TOF MS (*m*/*z*) calcd for $C_{52}H_{60}O_{14}S$ $[M + Na]^+$ 963.3704, found 963.3721.

Methyl 3,4,6-tri-*O*-acetyl-((1*S*,6*R*)-(phenylsulfanyl)-cyclohexene-2-yl)-α-D-galactopyranosyl-(1→6)-2, 3, 4-tri-*O*-acetyl-β-galactopyranoside (74) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41-7.18 (m, 5H, aromatic), 5.96 (dd, 1H, J = 3.6, 9.9 Hz, C*H*'CHCO), 5.88-5.84 (m, 1H, CHC*H*'CO), 5.44-5.43 (m, 1H, H-4), 5.41 (d, 1H, J = 3.0 Hz), 5.22-5.18 (d, 1H, C*H*'OCHSPh), 5.17 (dd, 1H, J = 3.6, 7.8 Hz, H-3'), 5.03 (dd, 1H, J = 3.3, 10.5 Hz, H-3), 4.87 (d, 1H, J = 3.6 Hz, H-1'), 4.39 (d, 1H, J = 8.1 Hz, H-1), 4.25 (t, 1H, J = 6.3 Hz, H-5'), 4.06-4.02 (m, 4H, H-5, CHOC*H*'SPh, H-6_a, H-6_b), 3.93-3.91 (m, 2H, H-6_a', H-6_b'), 3.84-3.77 (m, 2H, H-2, H-2'), 3.51 (s, 3H, OCH_3), 2.14 (s, 3H, $COCH_3$'), 2.13 (s, 3H, $COCH_3$), 2.07-2.06 (m, 2H, CH_2'), 2.06 (s, 3H, $COCH_3$'), 2.04 (s, 3H, $COCH_3$), 1.97 (s, 3H, $COCH_3$'), 1.96 (s, 3H, $COCH_3$), 1.78-1.61 (m, 2H, CH_2'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.39, 170.31, 170.08, 169.94, 169.77, 169.58, 131.80, 131.23, 129.25, 128.98, 127.08, 102.06, 97.95, 72.50, 71.99, 71.02, 68.99, 68.50, 67.99, 66.71, 66.54, 61.69, 57.12, 25.52, 24.75, 20.83, 20.74, 20.69, 20.57; HR MALDI-TOF MS (*m*/*z*) calcd for $C_{37}H_{48}O_{17}S$ $[M + Na]^+$ 819.2612, found 819.2620.

3,4,6-tri-*O*-acetyl-((1*S*,6*R*)-(phenylsulfanyl)-cyclohexene-2-yl)-α-D-galactopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (75) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42-7.25 (m, 5H, aromatic), 5.91 (dd, 1H, J = 4.0, 10.5 Hz, C*H*CHCO), 5.87 (dd, 1H, J = 3.0, 10.0 Hz, CHC*H*CO), 5.50 (d, 1H, J = 5.0 Hz, H-1), 5.45 (d, 1H, J = 3.0 Hz, H-4'), 5.19 (dd, 1H, J = 3.5, 11.0 Hz, H-3'), 5.03 (d, 1H, J = 3.0 Hz, H-1'), 4.61 (dd, 1H, J = 1.5, 8.0 Hz, H-3), 4.31-4.23 (m, 3H, H-2, H-4, H-6_a), 4.12-4.08 (m, 2H, H-5, H-6_b), 4.01 (t, 1H, J = 6.5 Hz, H-5'), 3.94-3.92 (m, 1H, C*H*'OCHSPh), 3.82 (dd, 1H, J = 4.0, 11.0 Hz, CHOC*H*'SPh), 3.78-3.72 (m, 3H, H-2', H-6_a', H-6_b'), 2.13 (s, 3H, $COCH_3$), 2.05-2.03 (m, 2H, CH_2), 2.04 (s, 3H, $COCH_3$), 1.96 (s, 3H, $COCH_3$), 1.73-1.64 (m, 2H, CH_2), 1.54 (s, 3H, CH_3), 1.44 (s, 3H, CH_3), 1.32 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.73, 170.36, 170.03, 132.13, 131.05, 129.97, 129.20, 127.37,

109.42, 108.93, 98.21, 96.53, 72.85, 72.31, 70.98, 70.87, 70.80, 69.28, 68.86, 67.25, 66.58, 66.21, 62.01, 43.92, 26.34, 26.28, 25.87, 25.14, 24.91, 20.97; HR MALDI-TOF MS (*m*/*z*) calcd for $C_{36}H_{48}O_{14}S$ $[M + Na]^+$ 759.2765, found 759.2761.

Acetyl 3,4,6-tri-*O*-acetyl-((1*S*,2*R*)-(phenylsulfanyl)-cyclohexanyl)-α-D-galactopyranose (76). Pd/C (10%, 1.55g) was added to a solution of Compound **68** in Ethanol in the atmosphere of H_2 (1 atm), the reaction mixture was stirred at RT overnight and then filtered, the filtrate was concentrated under vacuo. The residue was purified by flash silica gel column chromatography (Hexane/EtOAc/ DCM = 4/1/6) to afford **76** (100 mg, 40%): colorless syrup; R_f = 0.57 (Hexane/EtOAc = 1/1); $[\alpha]^{20}_D$ = +32 ° (*c* = 0.7, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42-7.18 (m, 5H, aromatic), 6.41 (d, 1H, *J* = 3.5 Hz, H-1), 5.47 (d, 1H, *J* = 2.5 Hz, H-4), 5.25 (dd, 1H, *J* = 3.5, 10.5 Hz, H-3), 4.25 (t, 1H, *J* = 6.0 Hz, H-5), 4.14-4.03 (m, 2H, H-6_a, H-6_b), 3.81 (dd, 1H, *J* = 3.5, 11.0 Hz, H-2), 3.35-3.32 (m, 1H, C*H*OCHSPh), 3.08-3.03 (m, 1H, C*H*SPhCHO), 2.15 (s, 3H, $COCH_3$), 2.08-2.04 (m, 2H, CH_2), 2.02 (s, 6H, $2COCH_3$), 1.98 (s, 3H, $COCH_3$), 1.69-1.61 (m, 3H, CH_2), 1.44-1.22 (m, 3H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.24, 169.90, 169.88, 169.11, 135.52, 131.79, 128.61, 126.39, 90.04, 80.96, 71.83, 70.54, 67.76, 61.25, 51.12, 31.17, 30.29, 24.22, 22.98, 20.91, 20.83, 20.70, 20.66, 20.63; HR MALDI-TOF MS (*m*/*z*) calcd for $C_{26}H_{34}O_{10}S$ $[M + Na]^+$ 561.1825, found 561.1865.

3,4,6-Tri-*O*-acetyl-((1*S*,2*R*)-(phenylsulfanyl)-cyclohexanyl)-α-D-galactopyranosyl trichloroacetimidate (78). Hydrazinium acetate (64 mg, 0.69 mmol) was added to a solution of compound **76** (248 mg, 0.46 mmol) in DMF (10 mL) at room temperature. After stirring the reaction mixture for 12 h, it was quenched with an aqueous saturated solution of $NaHCO_3$. The organic phase was washed with an aqueous saturated solution of NH_4Cl (30 mL) and dried ($MgSO_4$), filtered and the filtrate was concentrated *in vacuo*. The residue was purified by flash

silica gel column chromatography (ethyl acetate/hexane = 1/3) to afford **77**. Trichloroacetonitrile (0.19 mL) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 45 μL) were added to a solution of **77** (89 mg, 0.18 mmol) in dichloromethane (10 mL) at 0 °C. After stirring the reaction mixture at 0 °C for 2 h, it was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (20% ethyl acetate in hexane) to afford **78** (122 mg, 90%): R_f = 0.60 (α), 0.46 (β) (DCM/ethyl acetate/hexane, 2/1/2); $[\alpha]^{20}_D = +92^o$ (c = 1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) **78*α*** δ 8.58 (s, 1H, -NH), 7.40-7.20 (m, 5H, aromatic), 6.58 (d, 1H, J = 3.3 Hz, H-1), 5.52 (d, 1H, J = 2.4 Hz, H-4), 5.30 (dd, 1H, J = 3.3, 10.2 Hz, H-3), 4.40 (t, 1H, J = 6.9 Hz, H-5), 4.16-3.98 (m, 3H, H-6_a, H-6_b, H-2), 3.51-3.45 (m, 1H, -C*H*OCHSPh), 3.20-3.14 (m, 1H, -CHOC*H*SPh), 2.15 (s, 3H, $COCH_3$), 2.01 (s, 3H, $COCH_3$), 2.00 (s, 3H, $COCH_3$), 1.61-1.23 (m, 8H, $4CH_2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.33, 170. 06, 169. 92, 160. 99, 135.34, 131.35, 128.91, 126.65, 94.58, 91.12, 79.84, 72.71, 69.59, 68.82, 67.89, 61.40, 53.44, 50.37, 31.59, 29.57, 29.03, 23.15, 22.07, 20.77, 20.68, 20.65, 14.21, 14.13. **78*β*** 8.73 (s, 1H, -NH), 7.36-7.16 (m, 5H, aromatic), 5.82 (d, 1H, J = 7.5 Hz, H-1), 5.40-5.39 (m, 1H, H-4), 4.97 (dd, 1H, J = 3.5, 9.5 Hz, H-3), 4.15-4.01 (m, 2H, H-6_a, H-6_b), 4.00 (t, 1H, J = 2.5 Hz, H-5), 3.83 (dd, 1H, J = 7.5, 9.5 Hz, H-2), 3.79-3.76(m, 1H, -C*H*OCHSPh), 3.27-3.23 (m, 1H, -CHOC*H*SPh), 2.15 (s, 3H, $COCH_3$), 2.02 (s, 6H, $2COCH_3$), 1.66-1.30 (m, 8H, $4CH_2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.36, 170.18, 169.85, 160.69, 136.01, 131.08, 128.73, 126.36, 97.95, 80.21, 73.10, 72.02, 71.12, 66.94, 60.96, 50.18, 29.70, 29.35, 23.34, 23.34, 20.71, 20.70, 20.66.

Procedure for low-temperature NMR experiments. ^{1}H NMR spectrum of **78** (14 mg, 0.02 mmol) in CD_2Cl_2 (0.5 mL) was recorded; ^{1}H NMR (500 MHz, CD_2Cl_2) δ 8.58 (s, 1H, -NH), 7.40-7.20 (m, 5H, aromatic), 6.58 (d, 1H, J = 3.3 Hz, H-1), 5.52 (d, 1H, J = 2.4 Hz, H-4), 5.30 (dd, 1H, J = 3.3, 10.2 Hz, H-3), 4.40 (t, 1H, J = 6.9 Hz, H-5), 4.16-3.98 (m, 3H, H-6_a, H-6_b, H-2),

3.51-3.45 (m, 1H, -C*H*OCHSPh), 3.20-3.14 (m, 1H, -CHOC*H*SPh), 2.15 (s, 3H, $COCH_3$), 2.01 (s, 3H, $COCH_3$), 2.00 (s, 3H, $COCH_3$), 1.61-1.23 (m, 8H, $4CH_2$).

Trimethylsilyl trifluoromethanesulfonate (3.6 μL, 0.02 mmol) was added to the solution at -20 °C. The solution was allowed to warm slowly to RT. The NMR spectra of **79** (^{1}H, COSY and NOESY) were recorded at RT, **79**; ^{1}H NMR (500 MHz, CD_2Cl_2) δ 8.21-7.25 (m, 5H, aromatic), 6.07 (d, 1H, J = 9.0 Hz, H-1), 5.53 (d, 1H, J = 2.5 Hz, H-4), 5.38 (dd, 1H, J = 3.5, 10.5 Hz, H-3)**,** 4.47 (t, 1H, J = 11.0 Hz, H-5), 4.31-4.26 (m, 2H, H-8, H-6_a), 4.08 (dd, 1H, J = 3.5, 9.0 Hz, H-2), 3.98-3.91 (m, 2H, H-7, H-6_b), 2.18 (s, 3H, $COCH_3$), 2.04(s, 3H, $COCH_3$), 1.87 (s, 3H, $COCH_3$),1.83-1.43 (m, 8H, $4CH_2$).

Upon activation, the aromatic and anomeric proton of **78** (δ 6.58, d, $J_{1,2}$ = 3.3 Hz) shifted upfield (6.07, d, $J_{1,2}$ = 9.0 Hz) and the large vicinal coupling constant of anomeric proton established an equatorial orientation of the anomeric substituent. The coupling constants of the other saccharide protons showed no conformational distortion of the saccharide ring had occurred. The NOESY spectrum, which allows the determination of space relationship of protons, showed a correlation between H-1 and H-8, proving the tricyclic system **79** had been formed.

General Procedure for the Glycosylation Reaction Employing Glycosyl Donors 78 A mixture of donor **78** (0.04 mmol) and activated molecular sieves (4 Å) in DCM (5 mL) was stirred for 1h under an atmosphere of argon at room temperature. After the mixture was cooled to -78 °C, trimethylsilyl trifluoromethanesulfonate (7.2 μL, 0.04 mmol) was added, and the reaction mixture was allowed to warm to RT over a period of 2h. After cooling of the reaction mixture to -78 °C, glycosyl acceptor (0.06 mmol) was added. The reaction mixture was allowed to warm slowly to room temperature and kept overnight at room temperature. After quenching with aqueous saturated $NaHCO_3$ (5 mL), the organic phase was dried ($MgSO_4$) and filtered, and the

filtrate was concentrated in vacuo. The residue was purified by silica gel column chromatography (20% ethyl acetate in hexane).

3,4,6-Tri-*O*-acetyl-((1*S*,2*R*)-(phenylsulfanyl)-cyclohexanyl)-α-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (80) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40-7.05 (m, 20H, aromatic), 5.38 (d, 1H, J = 2.1 Hz, H-4'), 5.20 (dd, 1H, J = 3.6, 10.5 Hz, H-3'), 5.09 (d, 1H, J = 3.3 Hz, H-1'), 4.96 (d, 1H, J = 11.1 Hz, C*H*HPh), 4.88 (d, 1H, J = 11.1 Hz, CH*H*Ph), 4.79 (d, 1H, J = 11.1 Hz, C*H*HPh), 4.69 (d, 1H, J = 11.1 Hz, CH*H*Ph), 4.60 (d, 1H, J = 11.1 Hz, C*H*HPh), 4.58 (d, 1H, J = 11.1 Hz, CH*H*Ph), 4.55 (d, 1H, J = 3.6 Hz, H-1), 4.19 (t, 1H, J = 6.6 Hz, H-5'), 4.10-4.04 (m, 2H, H-$6_{a'}$, H-$6_{b'}$), 3.97-3.92 (m, 2H, H-3, H-6_a), 3.84 (dd, 1H, J = 3.3, 10.5 Hz, H-2'), 3.79-3.72 (m, 2H, H-5, H-6_b), 3.51-3.45 (m, 2H, H-2, H-4), 3.37 (s, 3H, -OCH_3), 3.37-3.31 (m, 1H, -C*H*OCHSPh), 3.20-3.13 (m, 1H, -CHOC*H*SPh), 2.12 (s, 3H, $COCH_3$), 1.98 (s, 3H, $COCH_3$), 1.95 (s, 3H, $COCH_3$), 1.60 (s, 2H, $2CH_2$), 1.41-1.22 (m, 2H, $2CH_2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.36, 170.21, 169.92, 138.76, 138.37, 138.15, 135.40, 131.37, 128.80, 128.39, 128.33, 127.96, 127.92, 127.81, 127.59, 127.53, 126.53, 97.78, 97.64, 82.16, 81.37, 80.14, 78.17, 77.20, 75.68, 74.87, 74.49, 73.14, 69.89, 69.85, 68.72, 66.78, 66.27, 61.99, 55.11, 51.35, 30.96, 24.08, 23.08, 20.77, 20.71, 20.68; HR MALDI-TOF MS (*m*/*z*) calcd for $C_{52}H_{62}O_{14}S$ $[M + Na]^+$ 965.3860, found 965.3879.

3,4,6-Tri-*O*-acetyl-{(1*S*)-(2*R*)-(phenylsulfanyl)-cyclohexanyl}-α-D-galactopyranosyl-(1→6)-2,3,4-tri-O-benzoyl-α-D-manoyranoside (81) ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09-7.06 (m, 20H, aromatic), 5.82 (dd, 1H, J = 3.3, 9.9 Hz, H-3), 5.70 (t, 1H, 1H, J = 10.2 Hz, H-4), 5.66-5.65 (m, 1H, H-2), 5.43 (d, 1H, J = 3.0 Hz, H-4'), 5.32-5.27 (m, 1H, H-3'), 5.00 (d, 1H, J = 3.0 Hz, H-1'), 4.91 (s, 1H, H-1), 4.41 (t, 1H, J = 6.6 Hz, H-5'), 4.24 (t, 1H, J = 8.7 Hz, H-5), 4.13-4.06 (m, 2H, H-$6_{a'}$, H-$6_{b'}$), 3.97-3.84 (m, 2H, H-2', H-6_a), 3.61-3.58 (m, 1H, H-6_b), 3.56 (s, 3H, -

OCH_3), 3.28-3.21 (m, 1H, C*H*OCHSPh), 3.07-2.99 (m, 1H, CHOC*H*SPh), 2.13 (s, 3H, $COCH_3$), 2.01 (s, 3H, $COCH_3$), 1.84 (s, 3H, $COCH_3$), 1.37-1.10 (m, 8H, $4CH_2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.63, 170.45, 170.04, 165.94, 165.75, 165.57, 136.03, 133.65, 133.66, 133.31, 131.23, 130.10, 129.96, 129.88, 129.61, 129.33, 129.14, 128.94, 128.82, 128.65, 128.47, 126.62, 98.63, 97.69, 82.67, 77.44, 74.98, 70.89, 70.23, 69.79, 69.71, 69.13, 67.64, 67.47, 66.64, 62.39, 55.67, 52.34, 32.20, 31.89, 29.92, 24.97, 23.75, 21.04, 20.96, 20.76; HR MALDI-TOF MS (*m*/*z*) calcd for $C_{52}H_{56}O_{17}S$ $[M + Na]^+$ 1007.3238, found 1007.3235.

CHAPTER 4

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