Study of silyl protecting groups in anomerisation reactions. Total synthesis of a glycolipid from *Plakortis simplex* and its mimetics.

by

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Declaration

This thesis has not been submitted before, in whole or in part, to this or any other university for any degree, and is, except stated otherwise, the original work of the author.

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Amélie Roux

Acknowledgments

First of all, I'd like to thank my supervisor Prof. Paul Murphy for hosting me in his group for four years. It has been an incredible adventure which I wouldn't have achieved without your help throughout it.

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Abstract

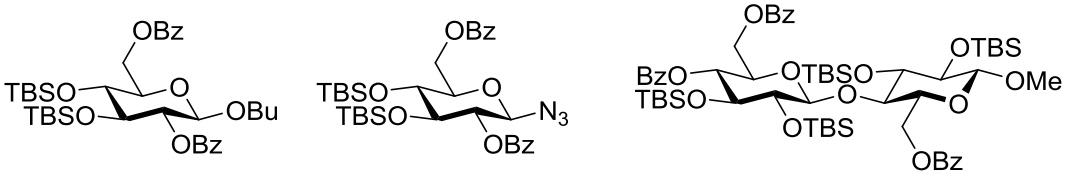
This thesis deals with anomerisation, which is, in other words, epimerisation at the anomeric centre, usually interpreted as being from the equatorial to the axial anomer. An objective was to enhance the knowledge of this reaction, in particular to gain knowledge about the behaviour of silylated pyranosides towards Lewis acids that promote anomerisation. Gaining a greater understanding of how silyl protection influences reactivity could lead to wider applications of the reaction more generally.

The thesis begins with a short introduction to carbohydrate chemistry. This includes a description of two reactions that take place at the anomeric centre, glycosylation and anomerisation.

The second chapter focuses on the synthesis of various silylated butyl β-*O*-D-glucopyranosides. These carbohydrates are then anomerised using a Lewis acid, with the rate of each reactant being determined using NMR spectroscopy. From this NMR study, it is demonstrated that the reactivity depends on structure and how it influences Lewis acid coordination, as well as the inductive effects of the protecting groups and finally on the conformation adopted by the saccharide. The presence of multiple silyl protecting groups, with a focus on TBS and TIPS groups, as well as their precise location is shown to influence conformation and reactivity. Two di-TBS protected glucopyranosides display significant rate enhancements in the presence of $SnCl_4$ which encouraged further exploitation of these protecting group patterns.

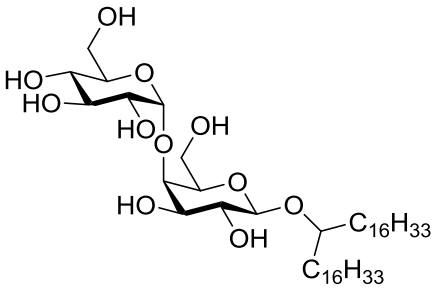
Based on the reactivity enhancements identified in Chapter 2, a protecting group strategy was thus designed for a disaccharide derived from cellobiose, with a view to investigating its anomerisation (Chapter 3). Synthesis of two silylated cellobiose derivatives is achieved and their behaviour to $SnCl_4$ and $TiCl_4$ investigated. In this latter case the disaccharides were shown to have different conformational preferences to the monosaccharidic butyl glycosides, which may account for different behaviour of these disaccharides to the monosaccharide, where successful anomerisation reactions were not attained. Nevertheless, some interesting products were observed and characterised, including those from a silylated glycosyl azide, which support the endocyclic cleavage mechanism for anomerisation.

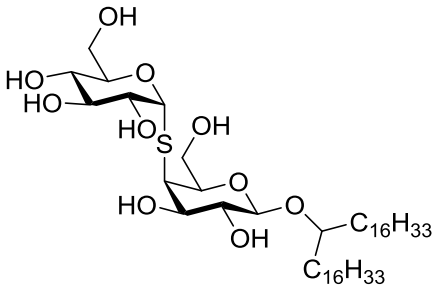
Examples of reactants synthesized for anomerisation tests are shown below.



The fourth and fifth chapter is about simplexide synthesis and includes applications of anomerisation. Simplexides are an important class of glycolipids. It was found recently that they induced expression and release of cytokines and chemokines from human monocytes. It was furtherly proposed that this is CD1d dependent, which could suggest that their mode of action is relatable to the mode of action of α-GalCer to human monocytes, a very important glycolipid. In these two chapters, the synthesis of a natural simplexide and five of its mimetics is achieved. These reaction steps include anomerisation reaction, *S*-glycosylation, *O*-glycosylation using the trichloroacetimidate donors, and the Birch reduction for benzyl group cleavage. Their biological activities are described, with some interesting results, which encourage further synthesis of simplexides and their mimetics, including those based on *S*-glycosides and simpler lipids.

Examples of compounds synthesized in this thesis are shown below.





Symbols and Abbreviations

α-GalCer	α-galactosylceramide
Ac	acetyl
AcOH	acetic acid
aq.	aqueous
Ar	aromatic
β-GluCer	β-glucosylceramide
Bn	benzyl
BnBr	benzyl bromide
BRM	Biological Response Modifier
Bu	butyl
Bz	benzoyl
BzCl	benzoyl chloride
°C	degrees Celcius
calcd	calculated
CAN	Ceric Ammonium Nitrate
cat.	catalytic
CSA	Camphor Sulfonic Acid
δ	chemical shift in ppm
d	doublet
DBU	diazabicycloundecene
dd	doublet of doublet
ddd	doublet of doublet of doublet
DEIPS	diethylisopropylsilyl
DMAP	4-Dimethylaminopyridine

DMF	*N*,*N*-dimethylformamide
DMPS	dimethylphenylsilyl
DMSO	dimethyl sulfoxide
eq	equivalent
ES-HRMS	High-Resolution Mass Spectrometry - Electrospray Ionization
Et_2O	diethylether
Et_2NH	diethylamine
Et_3N	triethylamine
EtOAc	ethyl acetate
EtOH	ethanol
g	gram
h	hour(s)
*i*Pr	isopropyl
IR	Infrared
J	coupling constant (NMR), in Hz
k_f	rate of forward anomerisation reaction
k_r	rate of reverse anomerisation reaction
KSAc	potassium thioacetate
LR	Lawesson's Reagent
m	multiplet
mg	milligram
MHz	Mega Hertz
mL	milliliter
MS	molecular sieves
MsCl	methanesulfonyl chloride

NBS	N-bromosuccinimide
NBu_4Br	tetra-n-butylammonium bromide
NIS	N-iodosuccinimide
NKTs	Natural Killer T cells
NMR	Nuclear Magnetic Resonance
PBMC	Peripheral Blood Mononuclear Cells
PMP	*p*-methoxyphenyl
PPh_3	triphenylphosphine
PPTS	pyridinium *p*-toluenesulfonate
p-TsOH	*p*-toluenesulfonic acid
q	quadruplet
RRV	Relative Rate Values
rx	reflux
s	singlet
satd.	saturated
SN_1	Nucleophile Substitution 1
SN_2	Nucleophile Substitution 2
t	triplet
TBAF	tetra-N-butylammonium fluoride
TBDPS	tert-butyldiphenylsilyl
TBS	tert-butyldimethylsilyl
TBSOTf	tert-Butyldimethylsilyl trifluoromethanesulfonate
TCR	T Cell Receptor
td	triplet of doublet
TES	triethylsilyl

Tf	trifluoromethanesulfonate
Tf_2O	trifluoromethanesulfonic anhydride
TFA	trifluoroacetic acid
THF	tetrahydrofuran
$TIPDSiCl_2$	1,3-Dichloro-1,1,3,3-tetraisopropyl-1,3-disiloxane
TIPS	triisopropylsilyl
TIPSOTf	triisopropylsilyl trifluoromethanesulfonate
TMS	trimethylsilyl
$TMSN_3$	trimethylsilyl azide
TMSOTf	trimethylsilyl trifluoromethanesulfonate
Tol	tolluyl
TPS	triphenylsilyl
TsCl	4-toluenesulfonyl chloride
µg	microgram
µL	microliter

Chapter 1 General introduction on carbohydrates

1.1. What are carbohydrates

Carbohydrates are an important class of compounds in Chemistry, Biology and Medicine[1]. Their general formula is often $C_m(H_2O)_n$, with *m* and *n* being equal or greater than three. Two examples of carbohydrates are shown in Figure 1.

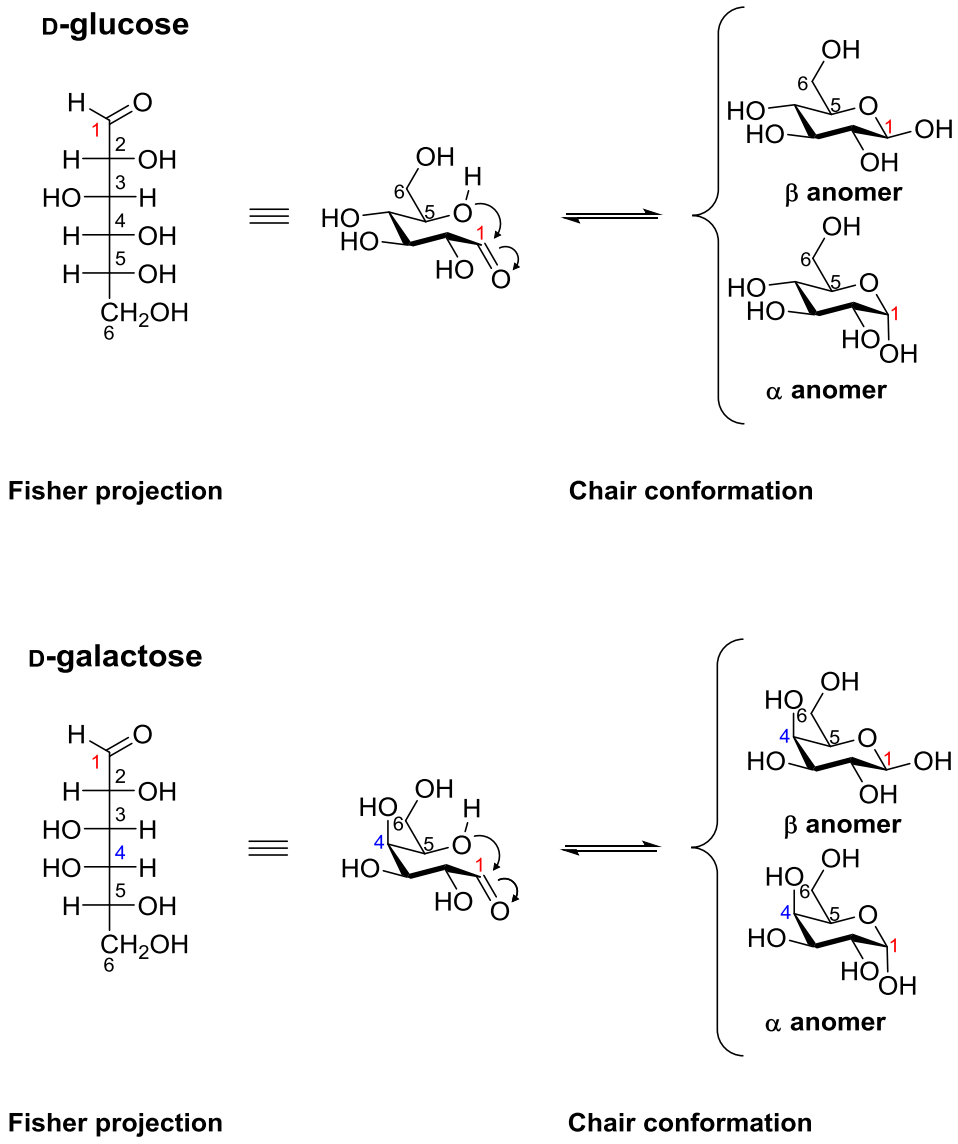


Figure 1 Fisher and chair structure of D-glucose and D-galactose.

Carbohydrates can exist in two different forms. In their open form, there is an aldehyde at carbon numbered 1 (C-1). This is the aldohexose form, and is often represented by its Fisher projection. However, usually carbohydrates exist in a cyclic structure, as a result of cyclisation from nucleophilic attack by the oxygen atom in position 5 with the aldehyde carbonyl leading to a hemi-acetal after proton transfer. For an aldohexose like D-glucose this gives the

glucopyranose, which usually prefers the chair conformation shown in Figure 1. When comparing galactose and glucose, it is important to notice that their difference lies in the configuration at position C-4: in the chair structure, glucose has the C-4 hydroxyl group in an equatorial conformation, whereas for galactose it is axial. Converting glucose to galactose is possible with the help of an enzyme called UDP-galactose-4-epimerase[2]. In other words, and more generally, each substituent in positions 2 to 5 are fixed in their configurations unless epimerisation can be brought about. Therefore, depending on the configuration and nature of the substituents, there exists a variety of different carbohydrates. In Figure 2, some different hexoses present in Nature are shown.

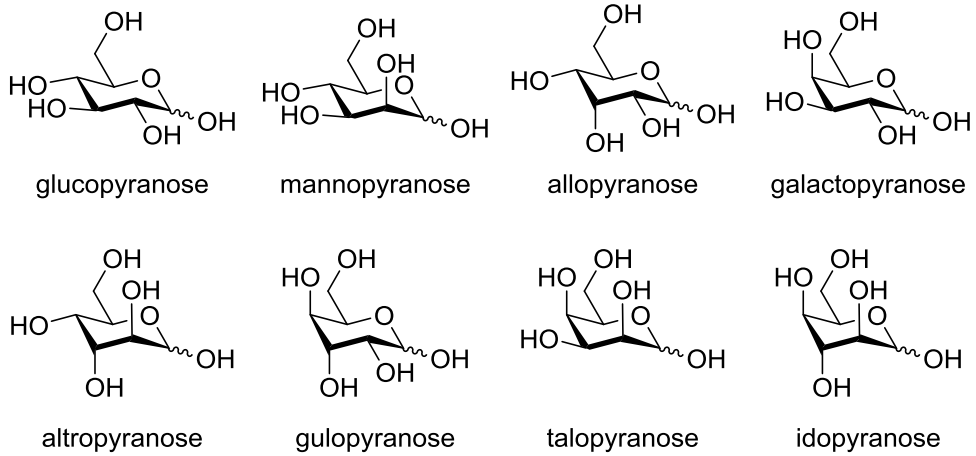


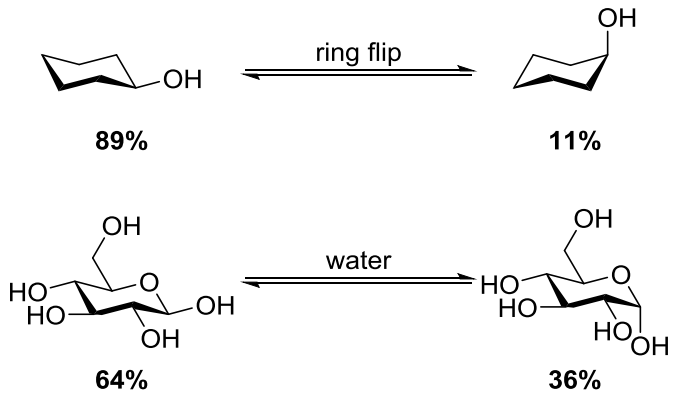
Figure 2 Different hexoses in Nature.

Those monosaccharides have different names as indicated in Figure 2[3]. They also have properties in Nature, and different reactivities in a synthetic laboratory.

The only position that can swap freely from axial to equatorial, and from equatorial to axial is at C-1 (the anomeric carbon). This process is called mutarotation, and the resulting two diastereoisomers are called anomers. The preference for one anomer to the other is based on properties of the specific carbohydrate that influence anomeric orientation.

1.2. Anomeric effect

In a cyclohexane, the substituents prefer to adopt an equatorial position (Scheme 1). However, when swapping a ring-carbon to a more electronegative atom (like oxygen), the preference to adopt an axial orientation can be increased if the substituent is also electron withdrawing. If this preference is greater than in cyclohexane then this is the definition of the anomeric effect[4].



Scheme 1 The anomeric effect increases the preference for an axial substituent.

This effect was first discovered by Edward[5] in 1955 and named by Lemieux[6] in 1958. With an attempt to explain this effect, Edward mentioned the repulsive dipolar interaction between the C(5)-O bond and the C(1)-X bond (X being the polar substituent in position C-1) as shown in Figure 3. Indeed, the dipole moment induced by the two lone pairs of the ring oxygen is pointing in the same direction as the dipole moment of the equatorial bond in the anomeric position; in contrast, the dipoles partially cancel each other out more when the hydroxyl group is axial. A molecule will generally have an increased preference for structures where the overall dipole moment is reduced, which explains why there is an increase in α-anomer.

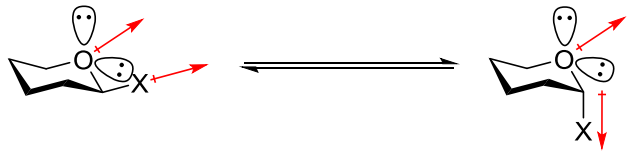


Figure 3 Axial substituent stabilized with dipole cancellation.

However, the β-anomer can still be favoured, as the role of solvents also has to be considered. It was indeed noticed that non polar solvents increased the amount of axial anomers, whereas polar solvents, and therefore solvents with a high dielectric constant, favoured the equatorial anomer[7-8]. This was explained by the fact that equatorial substituents have more hydrogen bonding with the polar solvent, and therefore favour the equatorial anomer.

Since this discovery, many research groups attempted to have a full knowledge of how and why the anomeric effect existed. Apart from the dipole moment, hyperconjugation between one of the two 2π- type lone pair on the oxygen and the antibonding σ* of the C(1)-X unit were also envisaged[9-10] (Figure 4). When the substituent is axial, there is an overlap of the two orbitals, which is stabilizing the molecule. However, when the substituent is equatorial, this overlap is non-existent, therefore making the carbohydrate less stabilized. This was confirmed

by the decreased bond length between O and C-1, and the increased bond length between C-1 and X[11].

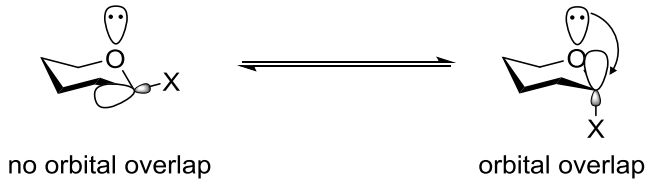


Figure 4 Axial substituent stabilized by hyperconjugation.

Both explanations only rely on the substituent on the anomeric position and the ring-oxygen of a carbohydrate.

Coulombic interaction was also hypothesized as an explanation for this important effect (Figure 5)[6, 12]. With X being electron-withdrawing, its partial charge is negative. The oxygen being electronegative, the adjacent carbons (C-1 and C-5) are partially positive. X and C-5 being close in the molecule and of different partial charge, they are attracted to each other. This attraction is made possible only when X is axial, the equatorial alternative distancing the two actors of this interaction.

Figure 5 Axial substituent stabilized by Coulombic interaction.

From this observation, Nishio's group focused on a non-classical hydrogen bonding between X and axial hydrogens distanced by 3 bonds, especially on C-5[13-16]. As shown in Figure 6, hydrogen bonding between H-5 and X is only possible when the substituent is axial. This hypothesis was confirmed by Wiberg et. al[17] in their attempt to rationalise the anomeric effect. Introducing more electron-withdrawing substituents in position C-3 and C-5 of cyclohexane molecules led the electronegative C-1 substituent to be more axial favoured. This discovery was in agreement with recent studies from within the research group at NUI Galway showing that electron-withdrawing substituents increased the ratio of axial anomer over the equatorial anomer[18].

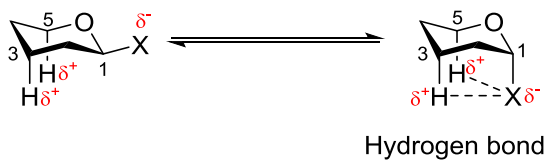
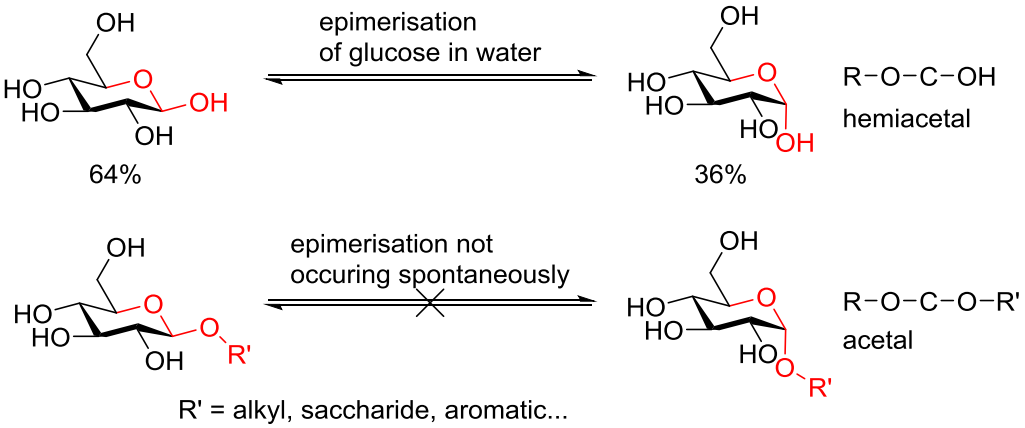


Figure 6 Axial substituent stabilized by hydrogen bonding.

To summarize, there exists an epimerisation at the anomeric position between the two anomers (axial and equatorial) through a ring opening. There is an increase in axial anomer preference in carbohydrates compared to cyclohexane. The conversion of the equatorial anomer to the axial anomer is often called anomerisation.

This is often referred to as mutarotation and it can happen spontaneously when the substituent on the anomerisation is a hydroxyl group (i.e. for a hemiacetal functional group). However, when the substituent is an alkoxy group (i.e. there is an acetal group), it does not occur spontaneously (Scheme 2) and would need a catalyst or promoter.



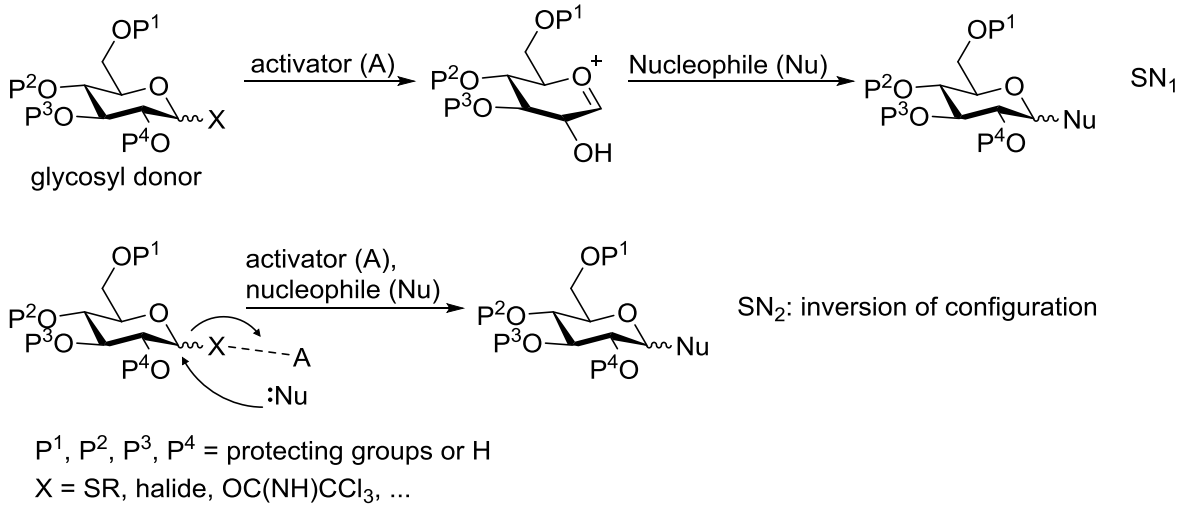
Scheme 2 Epimerisation of carbohydrates.

Because the biological and chemical properties of the anomers are not equivalent, there is a great interest in stereoselective synthesis of them, particularly glycosides (acetals). Two important reactions still being studied by researchers to improve the stereoselective synthesis of carbohydrates are more commonly glycosylation and much less commonly anomerisation.

1.3. Important reactions in carbohydrate chemistry

1.3.1. Glycosylation

Glycosylation is a very important reaction in carbohydrate chemistry[19]. It can be carried out between a glycosyl donor and an acceptor. The glycosyl donor has a leaving group at the anomeric carbon atom that can be activated by a promoter to enable reaction with a nucleophile (Scheme 3).

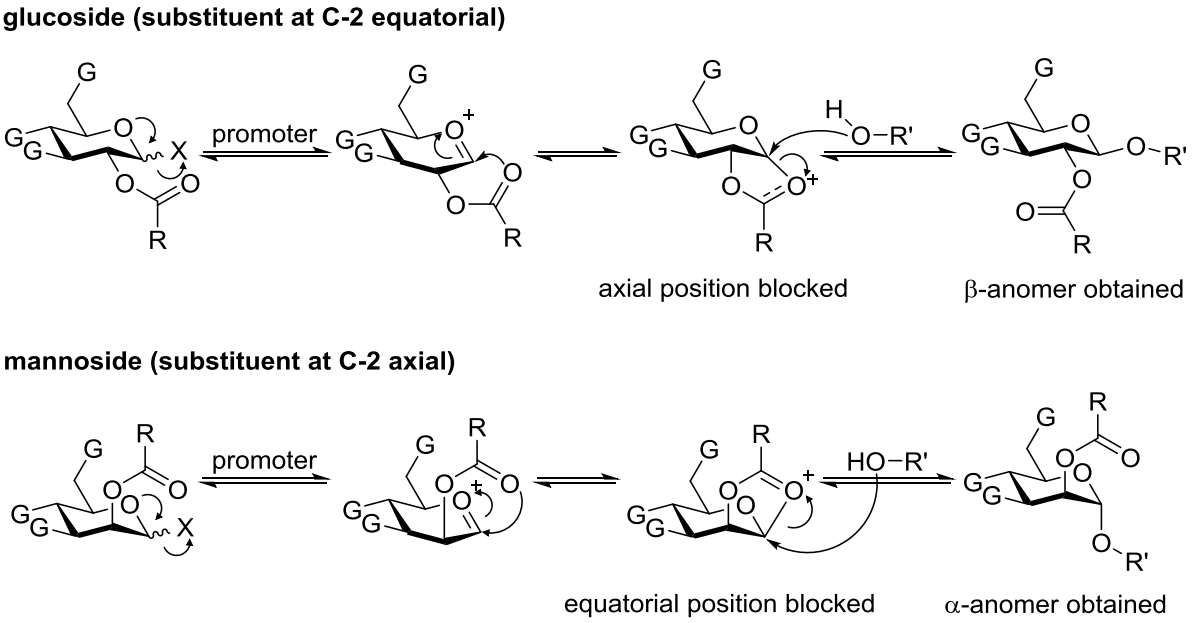


Scheme 3 General scheme for the glycosylation reaction.

The nucleophile can be either a simple alcohol, or an alcohol group in a carbohydrate acceptor. In the latter case a disaccharide is obtained. Successive glycosylations have been shown to lead to polysaccharides. Many articles have reported synthesis of different polysaccharides through glycosylation[20-21].

A recurring problem encountered when performing a glycosylation can be low stereoselectivity leading to a mixture of epimers, which can in some cases be difficult to separate. Glycosylation can in principle happen through an SN_1 or an SN_2 mechanistic pathways[22]. In the latter case inversion of configuration would be stereospecific and depend on the stereochemical configuration of the donor. However, often SN_1 processes may be operating and the configuration of the leaving group on the SN_1 has no impact on the configuration of the final compound. In this latter case, many factors can influence the outcome, such as solvent or structural features of the donor[23-25].

Neighbouring group participation can influence the outcome of glycosylation reactions[26]. The departure of the leaving group in the anomeric position leads to carbocation formation which can be stabilised through resonance with the adjacent oxygen to give an oxacarbenium ion. This charge can be stabilized by interaction with the adjacent carbonyl group at C-2 as shown in Scheme 4. Depending on the configuration of the substituent in C-2 (equatorial or axial), then one face is blocked from attack by the incoming nucleophile. This renders the glycosylation stereoselective as shown in Scheme 4.



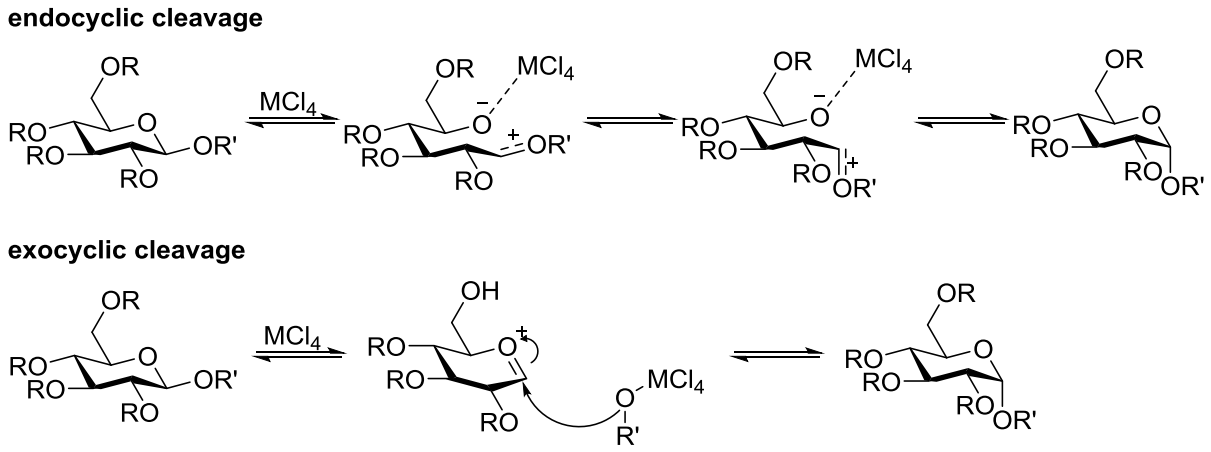
Scheme 4 Neighbouring participating group induce stereoselective glycosylation.

Other published articles have shown different ways to obtain a stereoselective glycosylation, by using different solvents[27], chiral auxiliaries[28], α or β-selective catalysts[29]. Another contribution would be through the development of anomerisation reactions, which is the main topic of this thesis work. This has been of interest to some carbohydrate research groups.

1.3.2. Anomerisation

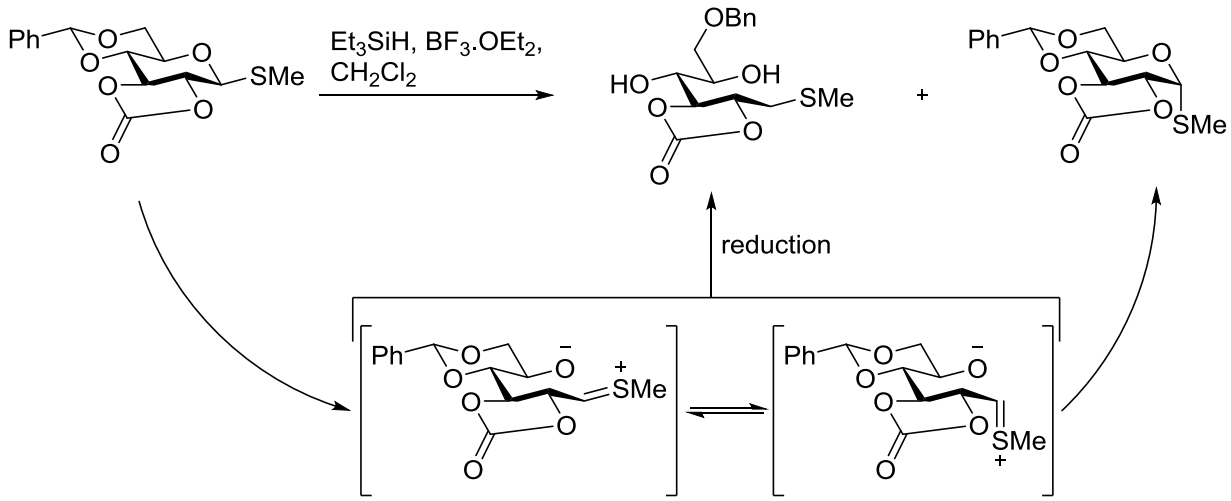
Anomerisation is the epimerisation of carbohydrates at the specific anomeric position and is often associated with formation of the thermodynamically more stable anomer, which can be the axial anomer. Normally, in this reaction, the two anomers are in equilibrium. In 1930, Pacsu[30] discovered that the use of the Lewis acid $TiCl_4$ could convert simple β-anomers to the α-anomer. Since then, a summary of progress in this reaction was reviewed by Murphy[31].
Lindberg[32] and Lemieux[33] showed two possible mechanisms (Scheme 5). Lindberg suggested that anomerisation of glycosides could go through an endocyclic pathway. The heterocycle opens at the bond between the ring oxygen and the anomeric carbon. The anomeric substituent is now able to rotate freely to adopt the most favourable configuration, and the stereoselectivity then relies on factors stabilising the axial anomer. The other pathway suggested by Lemieux involves an exocyclic cleavage. This mechanism is similar to the one that can happen during a glycosylation. The Lewis acid used activates the substituent on the anomeric position, which cleaves it from the carbohydrate. In anomerisation, the cleaved group reforms a bond with the

anomeric carbon. Again, the factors which determine the stereoselectivity are those which influence the relative stability of the two anomers.



Scheme 5 Endocyclic and exocyclic cleavage pathways.

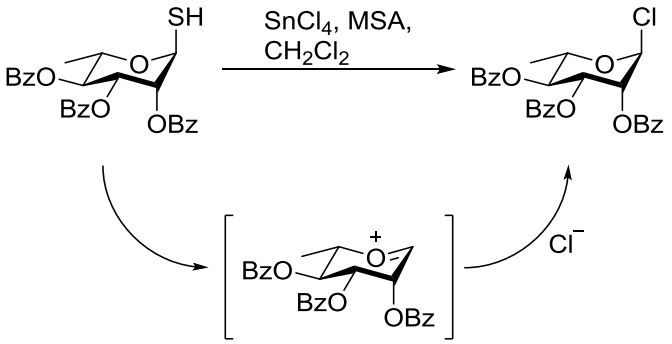
Since then, many research group tried to understand and determine which mechanism was preferred. Manabe et al.[34] discovered that they were getting a ring-opened product as well as the anomerisation product when treating cyclic carbonate derivatives of a thioglycoside donor. This experiment suggests that the thioglyoside anomerises via an endocyclic cleavage pathway to the axial anomer (Scheme 6).



Scheme 6 Ring-opened product suggesting an endocyclic pathway[34].

Furthermore, anomerisation on peracetylated and perbenzoylated carbohydrates was performed in Murphy's group[35]. Trapping of the intermediate associated with endocyclic cleavage was achieved in some cases.

However, many other articles report to obtain the chloride side product, which may suggest the exocyclic cleavage of the anomeric substituent as shown in Scheme 7[35-38]. Therefore, both pathways may be competing.



Scheme 7 Product suggesting an exocyclic pathway[36].

Despite publications in this area, anomerisation still has limited scope. Until now, anomerisation has been more successful with uronic acids, such as glucuronic and galacturonic acid where it is significantly faster than for related glycopyranosides[39-40]. It has also been applied successfully in cyclic carbonate or carbamate protected glycosides[41-42]. Other studies found that factors like the solvent or the protecting group used have an impact on the reaction[18, 35, 43-44]. Likewise, the nature of the anomeric substituent has an influence. *O*-Glycoside anomerisation is common, but the reaction has also been carried out for thioglycosides[35] (from equatorial to axial mostly) and for thiols (from equatorial to axial, but also from axial to equatorial)[36]. Anomerisation of *C*-glycosyl compounds[45], going from the axial anomer to the equatorial one is common, as stereoelectronic effects become less important in stabilising the axial anomer and steric reactions then favour the *C*-glycosyl substituent being equatorial. Equatorial to axial anomerisation of *Se*-glycosides[46] or even N_3-glucuronic acid[39] were also successfully achieved.

Unfortunately, disaccharide anomerisation has not been well developed to date and this is the reason why its study is still of current interest[36, 47-49]. This thesis work is in the first instance concerned with a study of the effect of silicon based protecting groups on the rate of Lewis acid anomerisation. This is studied with a view to developing protecting group strategies that would later be investigated in disaccharide anomerisation. An introduction to silicon protecting groups and their influence on carbohydrate reactivity is firstly reviewed in the next chapter and this is followed by a systematic study of the influence of TBS and TIPS derivatives on the anomerisation of a glucopyranoside.

1.4. References

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Chapter 2 Synthesis and anomerisation of silylated carbohydrates

2.1. Pyranose conformation

As pyranose conformation became relevant during the course of this study on anomerisation of silylated glucopyranosides, a short review of relevant conformational analysis is included first of all. Hence, six-membered rings molecules, such as cyclohexane, can adopt different conformations. Usually, the chair conformation is the most preferred, as it is the most stable[1]. However, many other conformations can be observed, and their representations is shown in Figure 7.

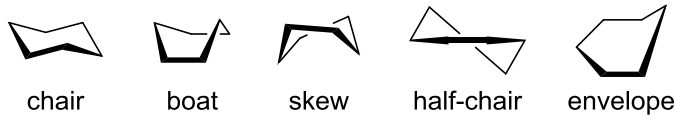
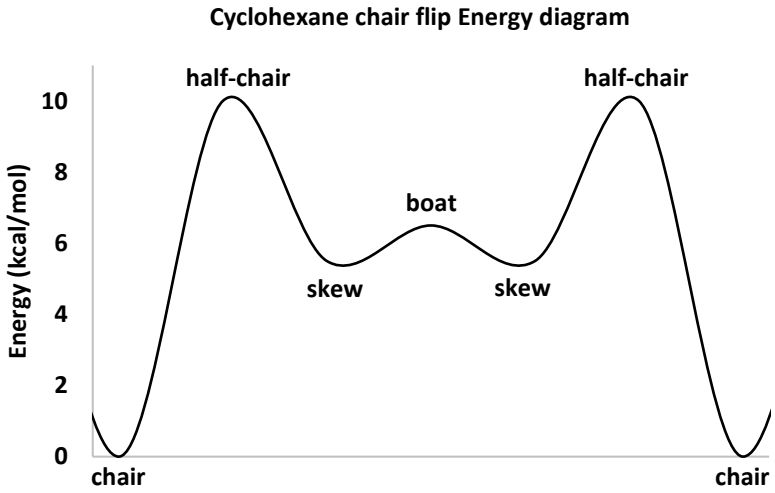


Figure 7 Different conformation that a cyclohexane can adopt.

The energy of each conformation is displayed in the diagram bellow.



Similarly, a glucopyranoside can adopt the same conformations[2]. However, because of the presence of the ring oxygen, and the fact that the molecule is asymmetric, there is two different type of chair (Figure 8), 6 boats, 6 skew, 12 half-chairs, and 12 envelopes[3].

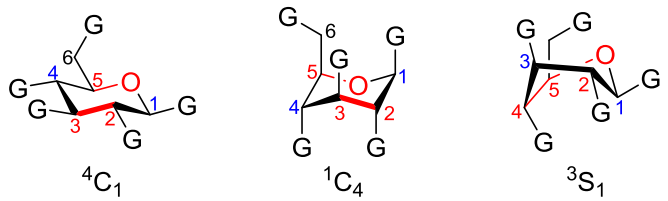


Figure 8 Three different conformation of glucose with their nomenclature (plane is shown in red, and the atoms above and below the plane are shown in blue).

Therefore, a nomenclature was used containing a letter and one or two numbers. The letter corresponds to the type of conformation (C for chair, B for boat, S for skew, H for half-chair, and E for envelope). The superscript numbers correspond to the atom(s) above plane, and the subscript numbers correspond to the atom(s) below a plane defined by the other 4 atoms.
Similarly to cyclohexane, the usual conformation of glucopyranosides is a chair, and more specifically in glucopyranoside, the $^4C_1$ conformer is highly preferred, usually, in order to have all the substituents equatorial, except at C-1, which can prefer to be axial. However, it is possible that the ring could adopt a different conformation, or that there could be an equilibrium between two conformers, depending on the nature of the ring substituents or protecting groups.

2.2. Protecting groups in glycosylation

In carbohydrate synthesis, many factors can influence whether a transformation can be successful. Different factors influence reactivity. There have been studies on the influence of such factors on glycosylation and work is still continuing in this area[4-6]. Fraser-Reid and co-workers studied how protecting groups influenced reactivity of a donor in glycosylation[7]. They introduced the 'arming' or 'disarming' terminology to indicate how protecting groups enabled glycosylation reactions to be faster or slower (Figure 9). The general conclusion out of this study is that ether substituents (e.g. OBn), which are less electron withdrawing compared to *O*-acyl substituents, are therefore considered 'arming', facilitating a faster reaction than the *O*-acyl counterpart; the *O*-acyl group is considered 'disarming'.

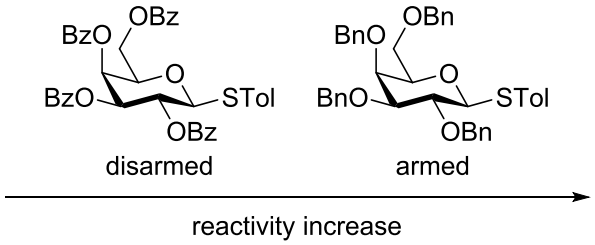


Figure 9 Increased reactivity when a carbohydrate is armed.

Consequently, Wong's research group tried to classify glycosyl donors depending on their reactivity[8]. To investigate their reactivity, Wong and co-workers set up experiments where two different glycosyl donors competed in the same pot for glycosylation carried out in the presence of an activator and acceptor. From these experiments they determined relative reactivity values (RRVs) for a variety of glycosyl donors (Figure 10). These were all compared to a baseline donor which is a thioglycoside of mannose which is given an RRV = 1.0.

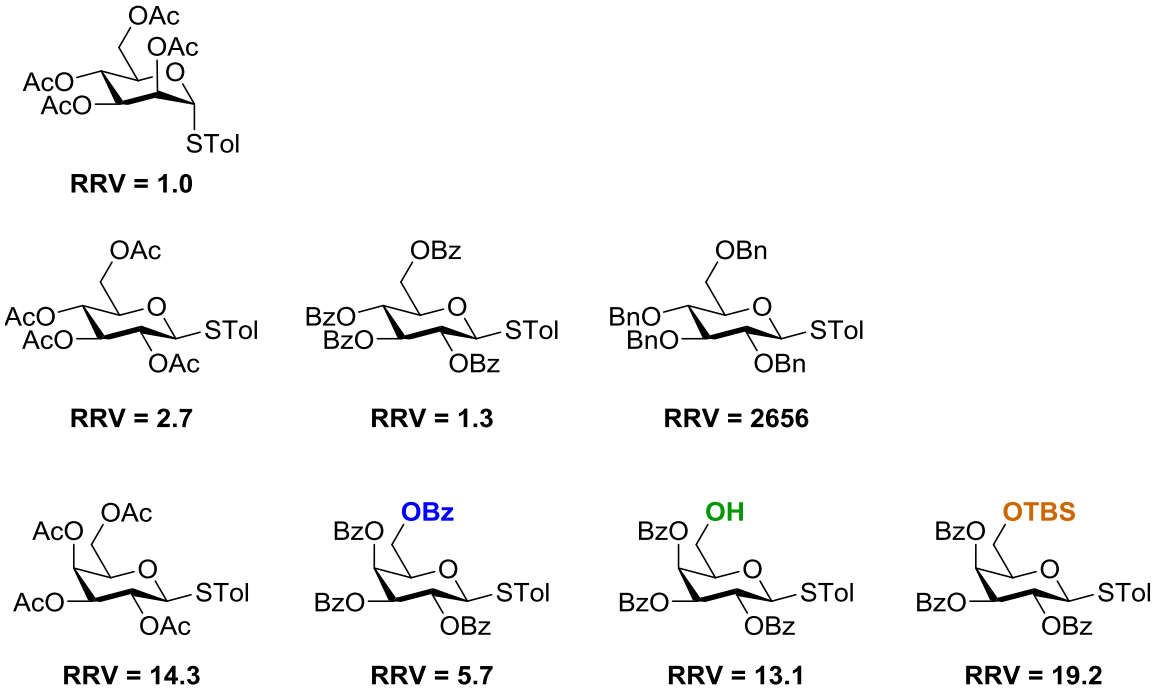


Figure 10 Relative reactivity values of selected glycosyl donors.

Through this approach, Wong's group analysed factors that influenced the RRVs[9]. They showed that as well as protecting group, the nature of the sugar used influenced reactivity of the glycosylation. Generally, the reactivity order was fucose > galactose > mannose > glucose > sialic acid. In the same manner, the solvent used or the type of leaving group have a significant effect. Most importantly, though, it was discovered that not only the 'arming' or 'disarming' effect of protecting groups were important, but their location and bulkiness also influenced the reactivity of glycosyl donors. This study allowed development of programmable one pot oligosaccharide synthesis which led to successful one pot syntheses of different oligosaccharides based on the donor RRV data[8, 10-11].

A class of protecting groups to consider when studying the effect of bulkiness, the electron withdrawing properties and the location on glycoside reactivity is the silylated class.

2.2.1. Silylated protecting groups

Silyl protecting groups can be classified as ether-like groups. Therefore, when used to protect carbohydrates, they are less electron withdrawing than acyl groups and thus are 'arming', making glycosylation faster. The most commonly used silyl groups are illustrated in Figure 11.

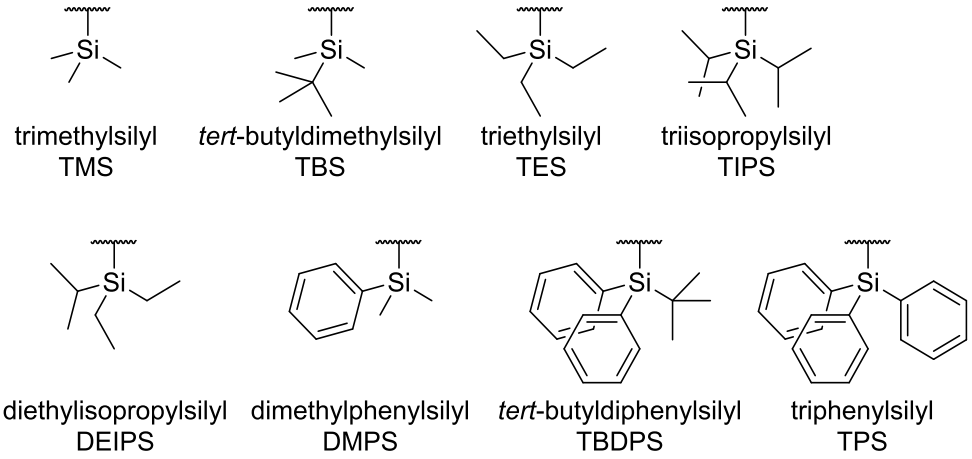


Figure 11 Most common silyl protecting groups.

The groups surrounding the silicon atom can be of various sizes and shapes. The bigger they are, the more hindering they are. Some studies from two different groups discovered that using bulky silylated groups on carbohydrates can make glycosylation faster[12-15]. The Bols group called them 'super armed' protecting groups, as they could make the reaction much faster than 'armed' protecting groups (Figure 12).

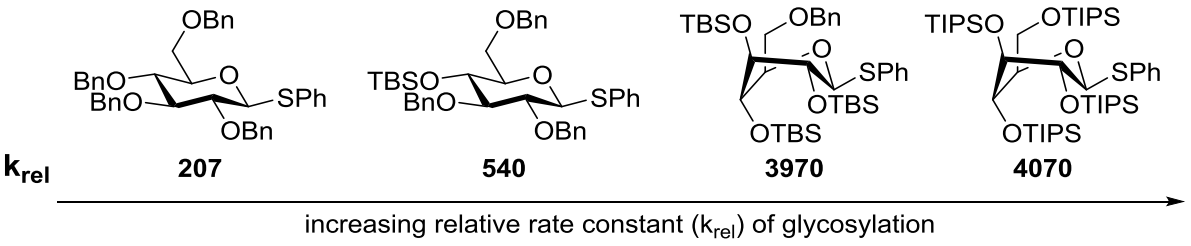


Figure 12 Super armed carbohydrates increase notably the relative rate constant of glycosylation.

Both groups explained the increase of rate of glycosylation with the fact that the presence of the sterically bulky groups could change the $^4C_1$ conformation to a twisted boat (i.e. skew) conformation so that substituents adopt a pseudo-axial conformation, to reduce steric interactions between each other. The $^1C_4$ configuration is the configuration aimed, as all substituents would be completely axial (Figure 13). Axial substituents being less electron withdrawing than equatorial substituents[16], they have been shown to increase the reactivity of

glycosyl donors, therefore it can be concluded that hindering protecting groups increase the rate of glycosylation through inducing conformational change.

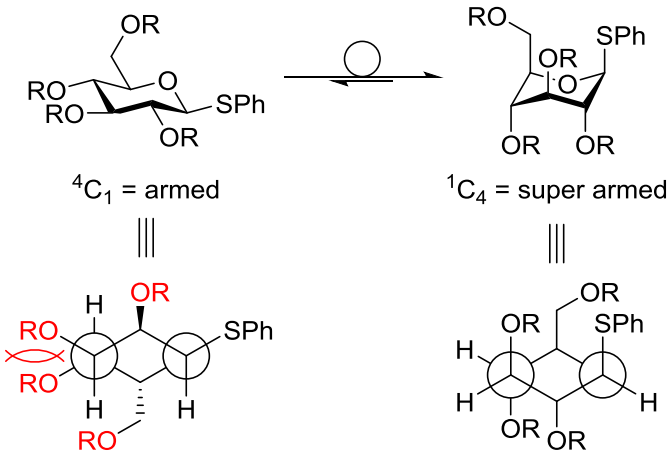


Figure 13 Ring flip into a $^1C_4$ conformation favoured with bulky groups. R = bulky groups.

Wong's group also carried out a study on TBS and TIPS protecting groups, and how they influenced the reactivity of glycosylation[17]. They synthesized various silyl protected donors. They compared the RRV with other usual protecting groups (e.g. acetyl, benzoyl, benzyl groups), or even hydroxyl groups that are not protected, and discovered that the silyl groups increased reactivity in all cases and were generally much faster. They also concluded that the number of silyl protecting groups and their position on the saccharide have an undeniable importance (Figure 14, Figure 15 and Figure 16).

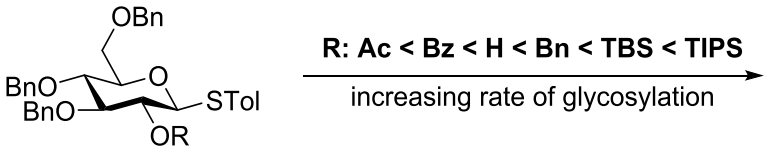


Figure 14 TBS and TIPS substituents at C-2 make the glycosylation faster.

It was also noticed that when one benzyl group on a donor was swapped for either TIPS or TBS, that the TIPS group made the glycosylation faster than the TBS. However, if two benzyl groups were swapped with two TBS or two TIPS groups, that this trend was reversed and that the di-*O*-TBS derivatives had a faster rate compared to the di-*O*-TIPS derivative (Figure 15 and Figure 16).

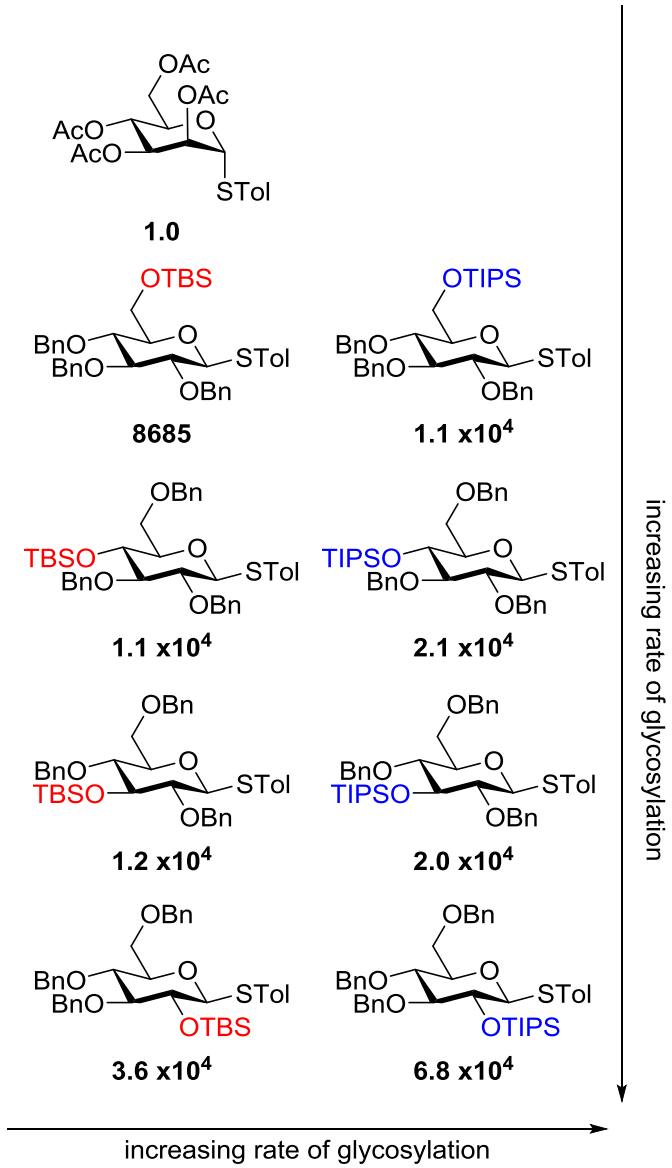


Figure 15 Relative rate values (relative to the mannose tetraacetate donor) for mono-silylated carbohydrates (drawn as shown in the paper).

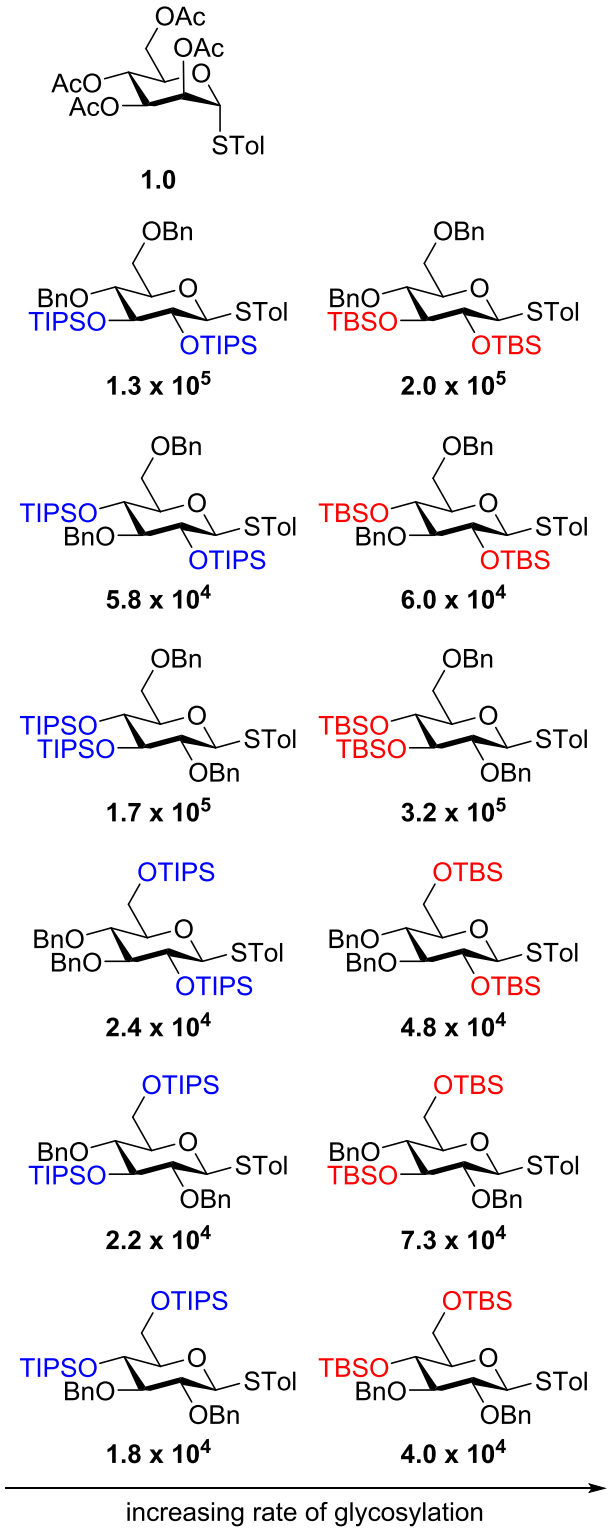


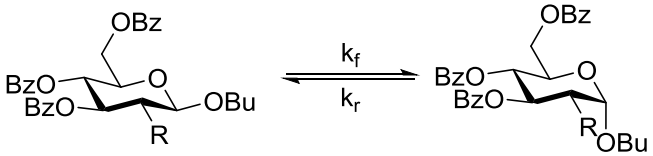
Figure 16 Relative rate values (relative to the mannose tetraacetate donor) for di-silylated carbohydrates (drawn as shown in the paper).

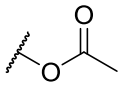
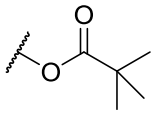
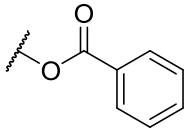
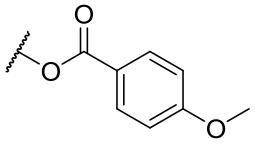
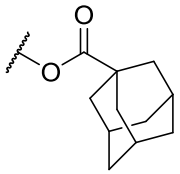
As mentioned earlier, the anomerisation reaction can be performed through an endocyclic or an exocyclic cleavage. The latter mechanism can give a carbocation intermediate and therefore it was considered interesting to investigate if silylated protecting groups increase the rate of anomerisation promoted by Lewis acids as is the case for glycosylation.

2.2.2. Aim of the project

Previously in Murphy's group, rate of anomerisations of various *O*-butyl saccharides were determined[18-20] (Table 1).

Table 1 Previous results on the ($k_f + k_r$) of reactants differing by the acyl groups.



R	$10^6 (k_f + k_r)$ (s^{-1})
	3.7
	9.9
	15.7
	23
	32

Reaction conditions: ($SnCl_4$ (0.5 equiv.), 30 °C).

The focus was mostly on ester protecting groups, modifying the nature of the acyl group. Subsequently, the combination of protecting groups that occasioned the best rate of anomerisation were applied for the anomerisation of useful reactants where the anomerisation was not successful yet[21]. To illustrate this, some relative rates for reactants towards

anomerisation, as determined by Wayne Pilgrim (left) are shown in Figure 17. Reactants which were anomerised by Wayne Pilgrim and Mark Farrell[18-19, 21-23] (right) are also shown in Figure 17.

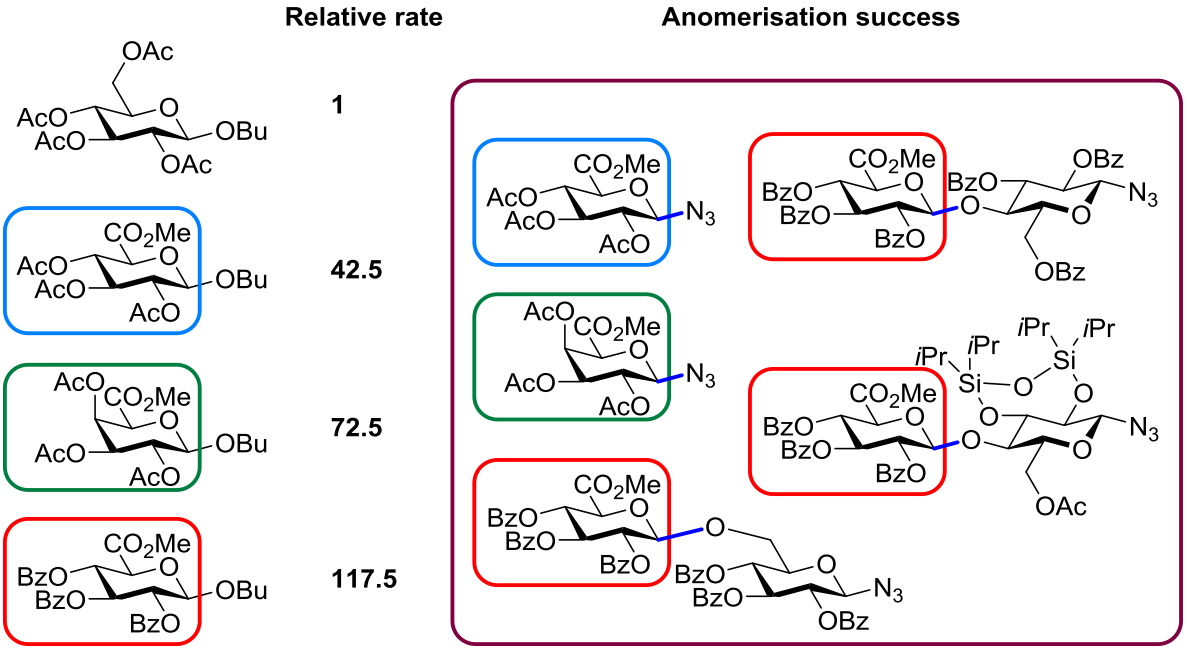


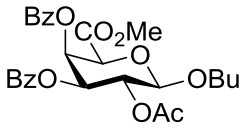
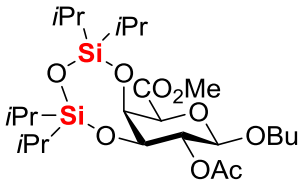
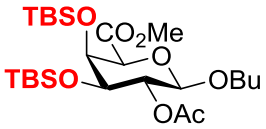
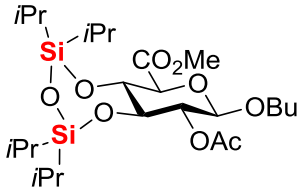
Figure 17 Wayne Pilgrim's high rates of anomerisation of three uronic acids (left) allowed the anomerisation of disaccharides and glycosyl azides using the same substituents on positions 2-6 (right).

Generally, azide or saccharide residues have lower reactivity than simple *O*-glycosides such as when *O*-butyl groups are present. Therefore, having knowledge of reactivity was important in developing synthetic applications of this reaction. Here the presence of carbonyl group at the C-5 gives rise to rate increases. Indeed, it can be seen from the information in Figure 17 that the azides on the disaccharides did not anomerise with addition of the Lewis added, but that the *O*-glycosidic linkage did and this is explained as being due to the reactivity increase brought about by the presence of the C-5 carbonyl. Also important here is the presence of benzoyl protecting groups as use of acetyl groups was unsuccessful for the anomerisation of disaccharides. These experiments give an insight into the reactivity problem in Lewis acid promoted anomerisation, and trying to make the reaction successful for reactants which lack the C-5 carbonyl group is still a challenge.

Some previous studies were done by Louise Kerins in the Galway research group to determine the rate of anomerisation of reactants containing silylated protecting groups (Table 2), however

the thesis work was not particularly focused on them[20], and the early results obtained were not successful in terms of achieving reactivity increases.

Table 2 Previous results for the rate of anomerisation of silylated compounds determined by Louise Kerins at NUI Galway.

Substrate	10^6 (k_f + k_r) (s^{-1})
	268
	22
	82
	5

Consequently, the project was focused firstly on studying the rate of anomerisation of *O*-butyl glycosides where TBS or TIPS protecting groups are present (Figure 18). It was proposed to generate a series of silylated derivatives and to determine their behaviour and rates of anomerisation and to compare these with the tetra-*O*-benzoylated derivative as the baseline compound. The ultimate idea behind this study was to identify whether a silylated protecting strategy would eventually be useful in enabling anomerisation of glycopyranosyl azides or disaccharides such as those derived from cellobiose or lactose.

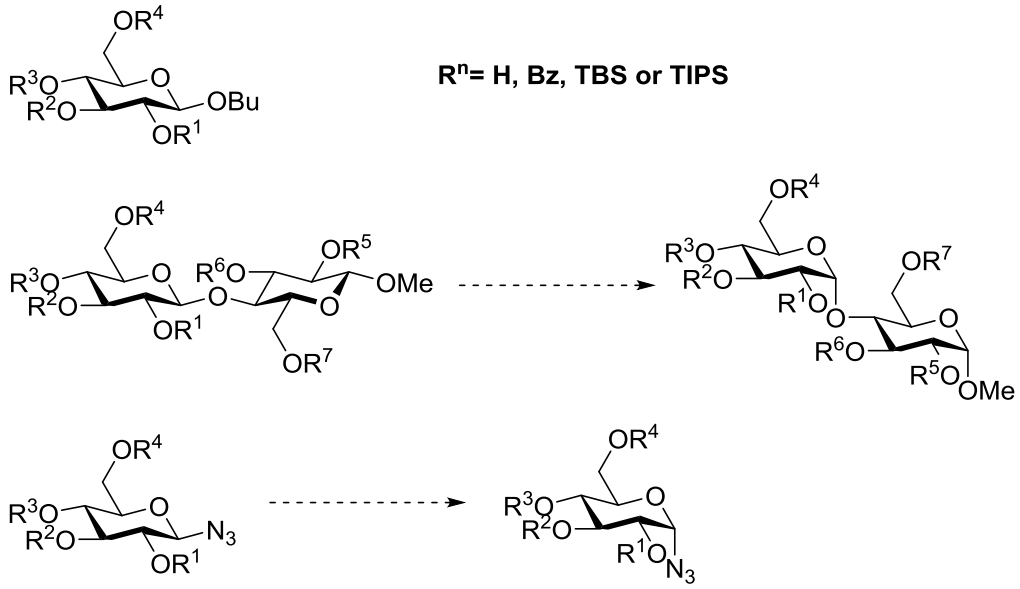
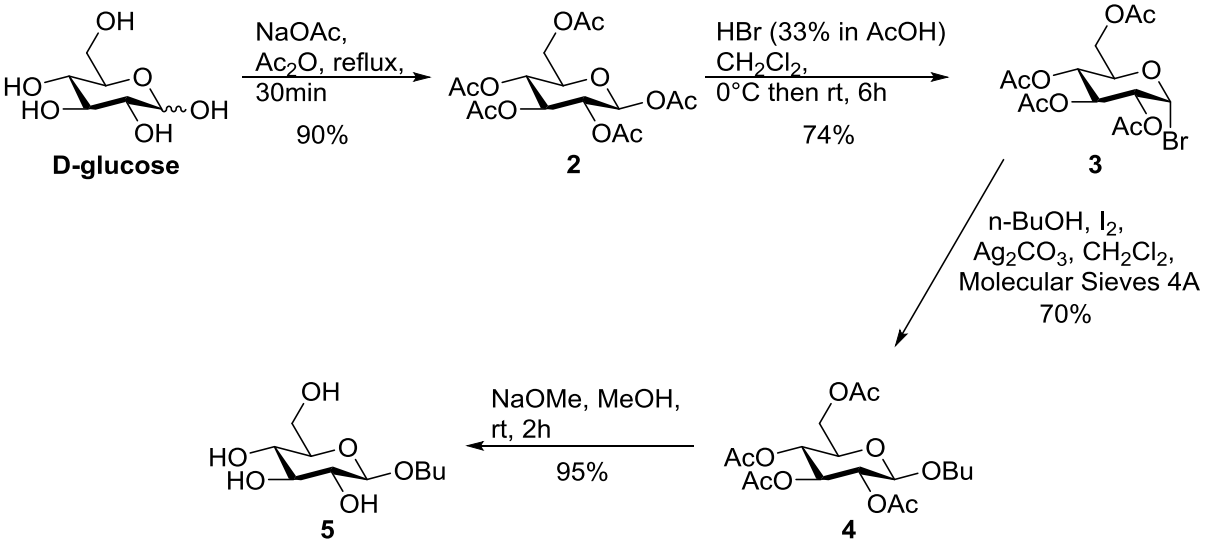


Figure 18 Objective of the thesis work: to investigate if a protecting group strategy can be developed to enable anomerisation of disaccharides or glycosyl azides which do not have a C-6 carbonyl group.

2.3. Synthesis of silylated monosaccharides

2.3.1. Building block

In this study all reactants were synthesized from butyl β-D-glucopyranoside **5**. This compound was prepared from D-glucopyranose as previously described[18, 23] (Scheme 8). This commercially available compound was fully acetylated using the classical conditions[24] to give **2**. This pentaacetate was then converted to the glycosyl bromide **3**[25]. With the bromide in hand, it allowed the glycosylation of n-butanol to be carried out using conditions described by Deffieux et al.[26]. Finally, deprotection gave the desired product **5** in an overall yield of 44% over 4 steps.

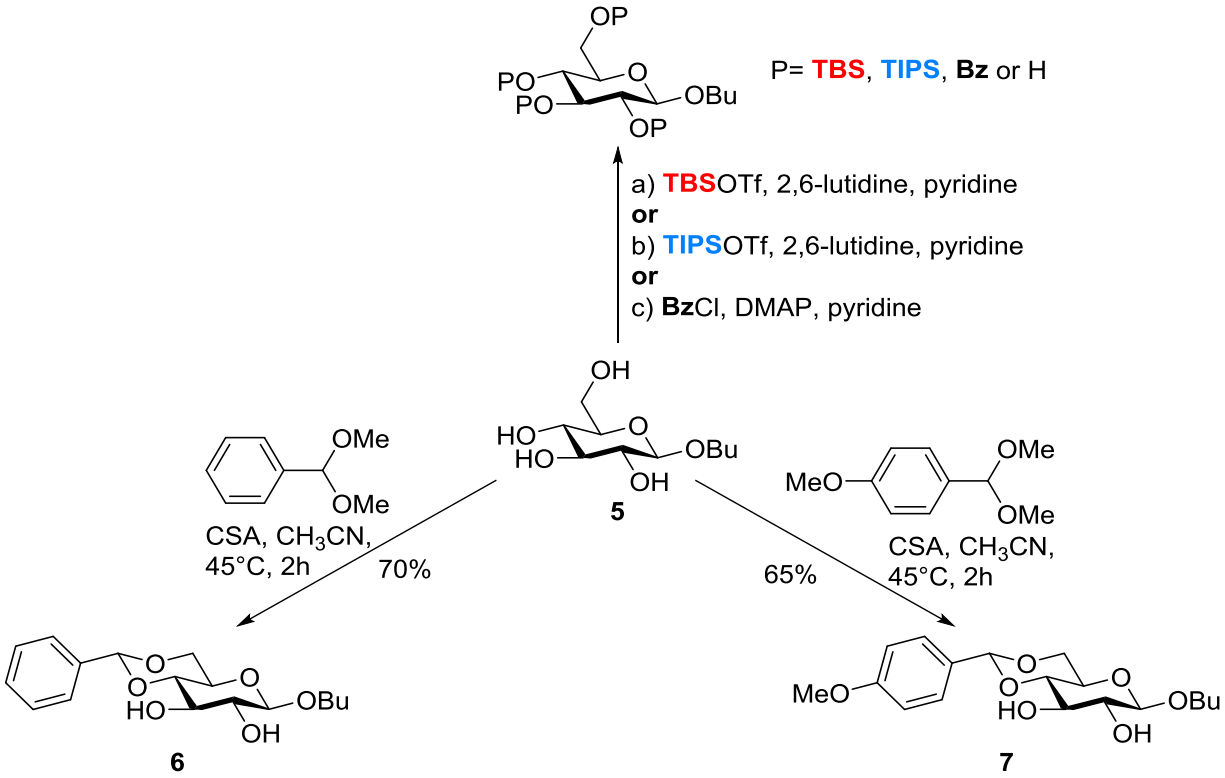


Scheme 8 Synthesis of *O*-butyl-β-D-glucopyranoside.

The synthesis of this compound was scaled up (with over 10 g of **5** prepared) to facilitate the synthesis of all the silylated glycosides required for the anomerisation study.

2.3.2. Approaches for the synthesis of target compounds

Three different routes were used for the synthesis of the silylated compounds and these are summarised in Scheme 9.



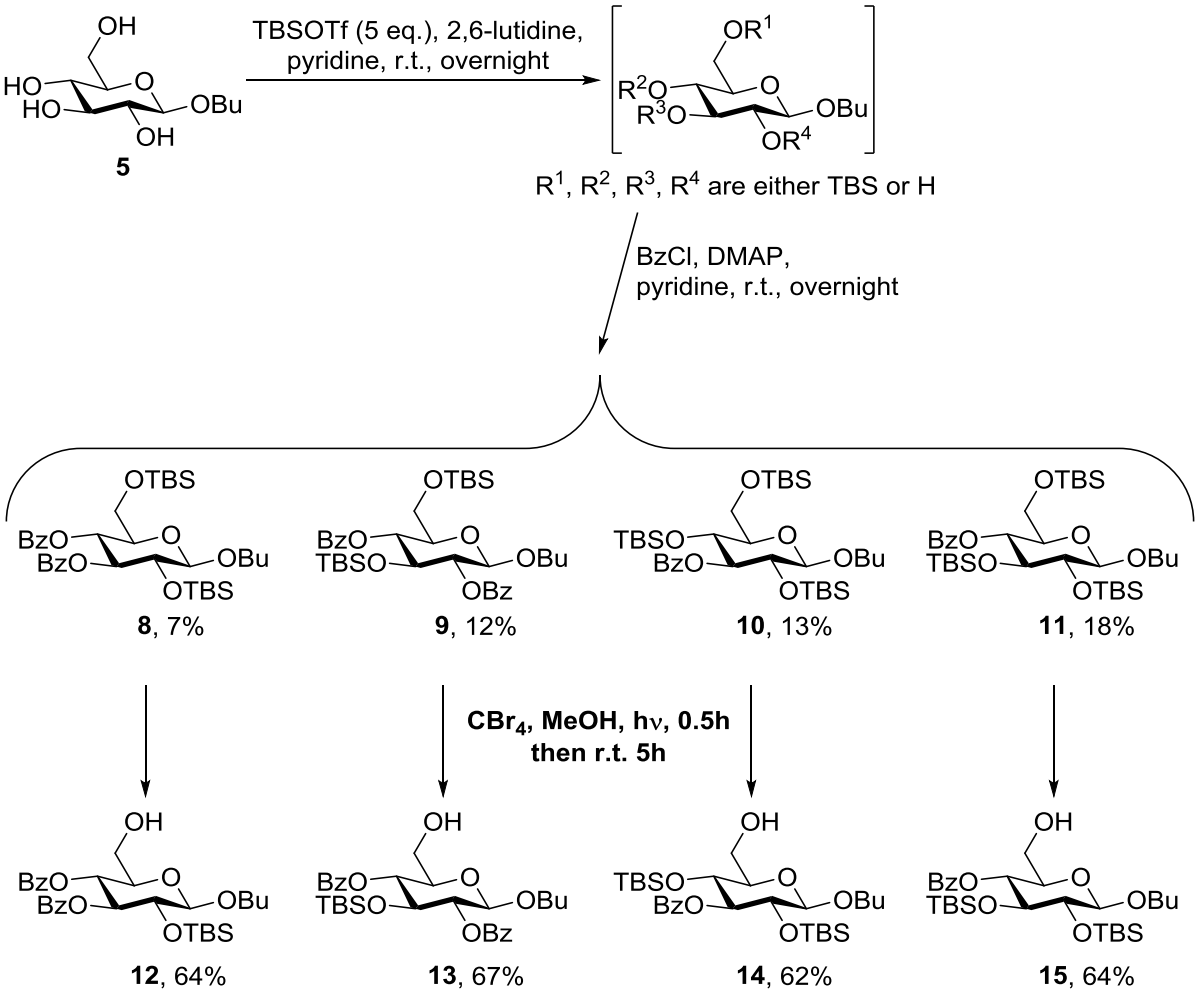
Scheme 9 Three routes used for the synthesis of the desired reactants.

The first option was to protect the carbohydrate with either TBS, TIPS or Bz protecting groups. The second and third option involved the use of benzylidene or *p*-methoxybenzylidene protecting groups that regioselectively protect the oxygen atoms at C-4 and C-6 and to follow this with silylation reactions.

2.3.2.1. Direct protection with TBS

Firstly, the direct protection of the free carbohydrate with TBS was achieved. Around 4 equivalents of *tert*-butyldimethylsilyl trifluoromethanesulfonate (TBSOTf) were used in the presence of a base, 2,6-lutidine. As expected, the primary alcohol (i.e. the 6-OH group) was first to react. It was found there was no particular reactivity order for reactions of the secondary alcohols present in the saccharide, and a mixture of carbohydrates protected differently were obtained (Scheme 10). The components in the mixture were difficult to separate using column chromatography at this stage. However, benzoylation of the free hydroxyl groups in the mixture

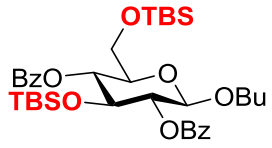
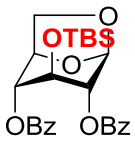
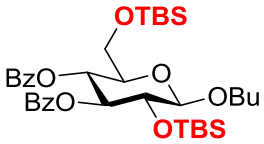
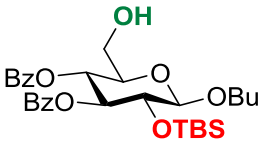
of compounds did give substances **8-11**, shown in Scheme 10, which could be separated by chromatography.



Scheme 10 Four reactants synthesized 12-15 through previously separated compounds 8-11.

Preliminary investigation of the behaviour of these silylated compounds **8-11** towards the anomerisation conditions using $SnCl_4$ or $TiCl_4$ led only to cleavage of the silyl protecting group from the oxygen atom at C-6 (Table 3), and for **9**, the 1,6-anhydro compound **13-anhydro** was obtained.

Table 3 Primary TBS group deprotected.

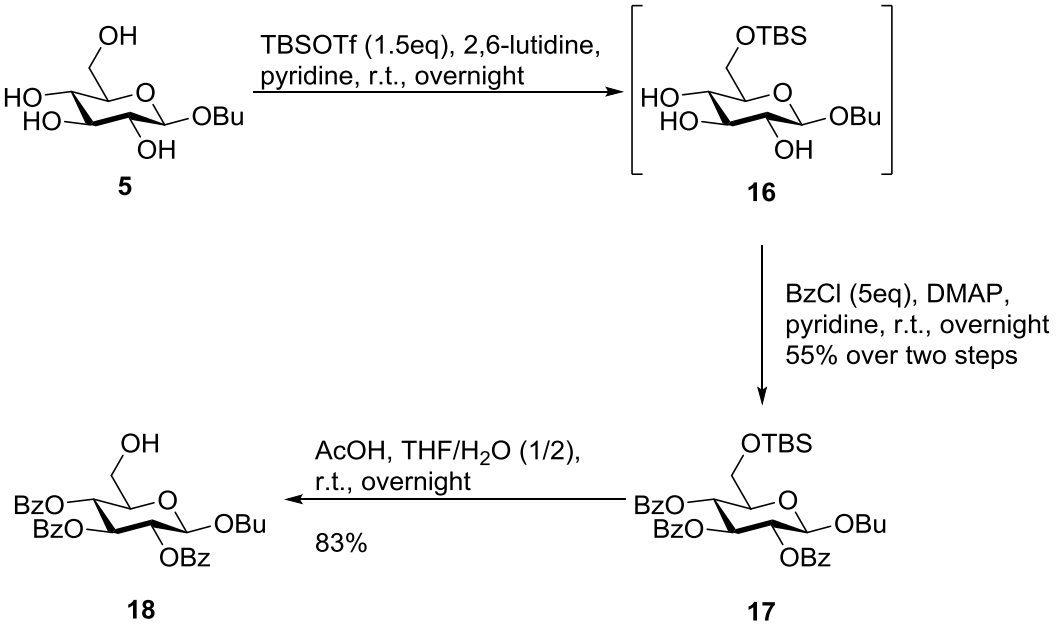
Reactants	Products
 **9**	 **13-anydro**
 **8**	 **12**

Reaction conditions: $TiCl_4$ (2.5 eq) or $SnCl_4$ (0.5 eq), CH_2Cl_2, r.t., overnight.

In Wong's glycosylation study, it was found that having a silyl ether protecting group at C-6 did not increase significantly the rate of glycosylation. Therefore, it was decided to have exclusively either a benzoyl group or an unprotected hydroxyl at position C-6, as it could be interesting to investigate anomerisation in the presence of a free alcohol also.

Chen's[27] method to selectively deprotect primary tert-butyldimethylsilyl ethers from **8-11** was thus next performed. This method involves use of a catalytic amount of carbon tetrabromide (CBr_4) in methanol, which, under irradiation, renders the pH of the solution mildly acidic, and consequently deprotects selectively the primary alcohol, not removing the TBS groups located at oxygen atoms O-2 to O-4 present in the glucopyranoside. Four new primary alcohol derivatives **12-15** were obtained, which were ready for investigation of their anomerisation.

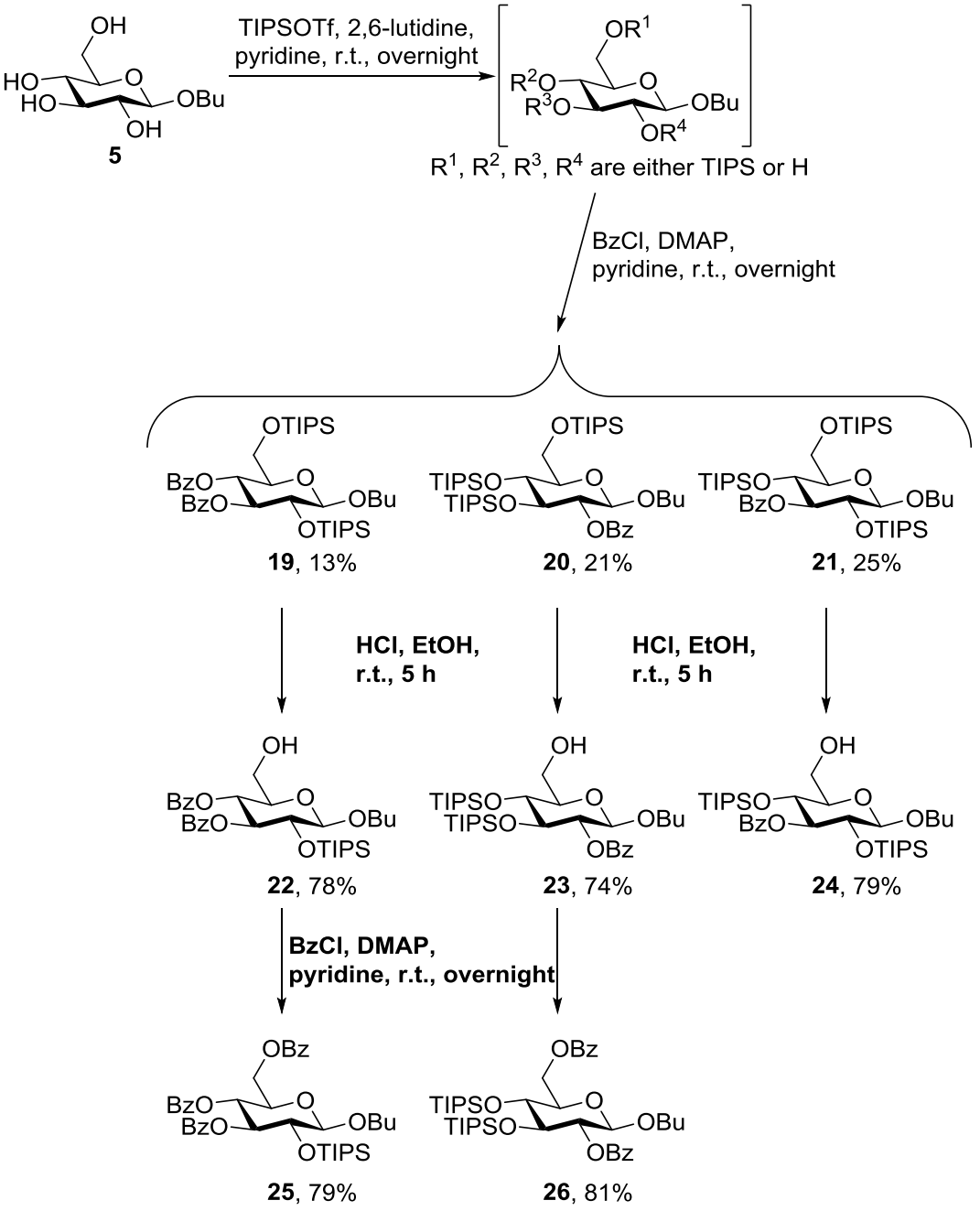
Compound **18** was synthesized in a similar way using a lower amount of TBSOTf, as shown in Scheme 11. In the preparation of **18** the removal of the TBS group was performed using acetic acid in THF and water (ratio 1:2, respectively), as described by Shioe et al[28].



Scheme 11 Synthesis of a default reactant 18 with a free hydroxyl group at position C-6.

2.3.2.2. Direct protection with TIPS

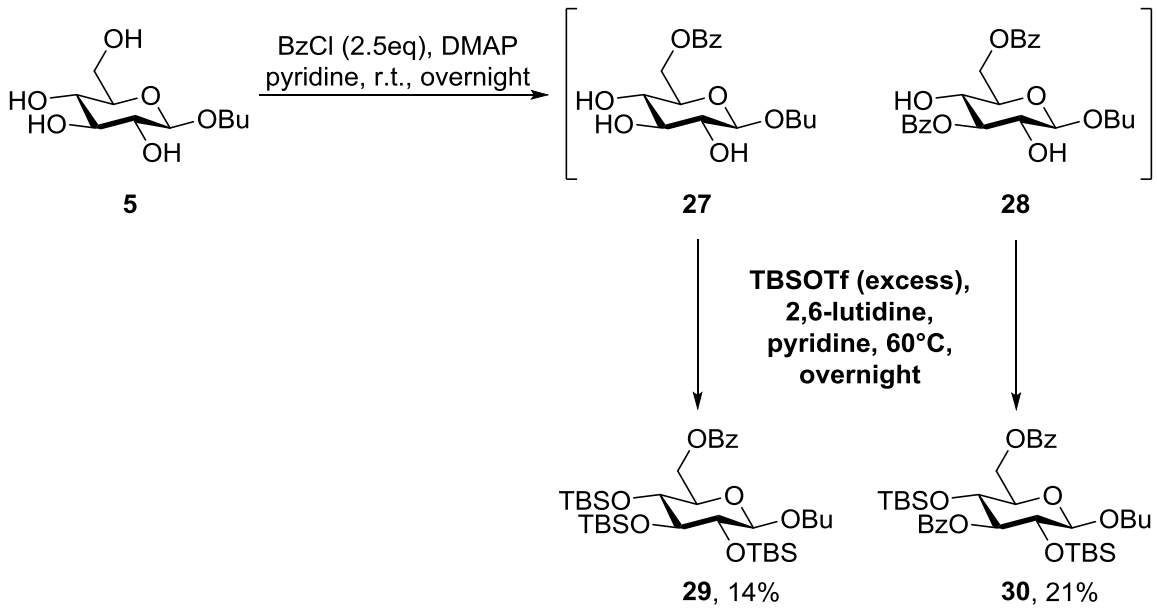
The reaction of **5** with TIPSOTf in the presence of 2,6-lutidine was next explored. Triisopropylsilyl ether protecting groups are considered to be more sterically hindering than TBS[29]. This increased bulkiness is consistent with heating being required to get three of the glucoside's OH groups to react (Scheme 12). After the silylation reaction, benzoylation was again carried out and this gave three separable compounds **19-21**. The primary TIPS was next deprotected using Shiina's[30] conditions, with hydrochloric acid in ethanol to give **22-24**. Benzoylation of **22** and **23** gave **25** and **26** respectively. The synthesis of these compounds enabled direct comparison with TBS derivatives **12-15** (vide supra).



Scheme 12 Synthesis of 24, 25 and 26 through direct protection with TIPSOTf.

2.3.2.3. Regioselective benzoylation

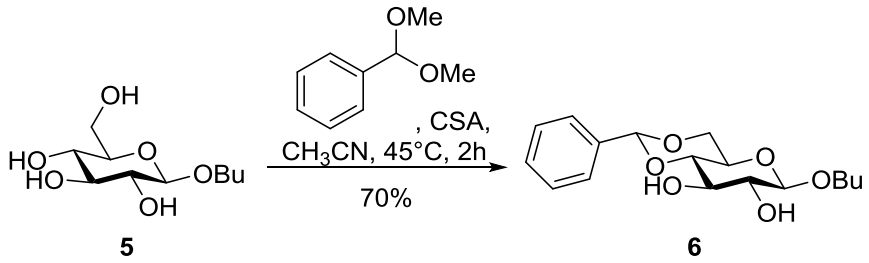
Similarly to silylation, regioselective benzoylation reactions were next investigated and direct benzoylation of **5** could be used to prepare regioselective compounds **27** and **28** using conditions as described by Jiang et al.[31] for regioselective pivalylations on a β-thioglycoside. Reaction of these two substances with TBSOTf in the presence of 2,6-lutidine gave **29** and **30**, which were ready for testing in the anomerisation reaction.



Scheme 13 Synthesis of two reactants through first benzoylation then silylation.

2.3.2.4. Use of benzaldehyde dimethyl acetal

Benzylidene groups are known to protect selectively the fourth and sixth position[32-34] (Scheme 14). Hereby, benzaldehyde dimethyl acetal can be used in the presence of an acid catalyst.



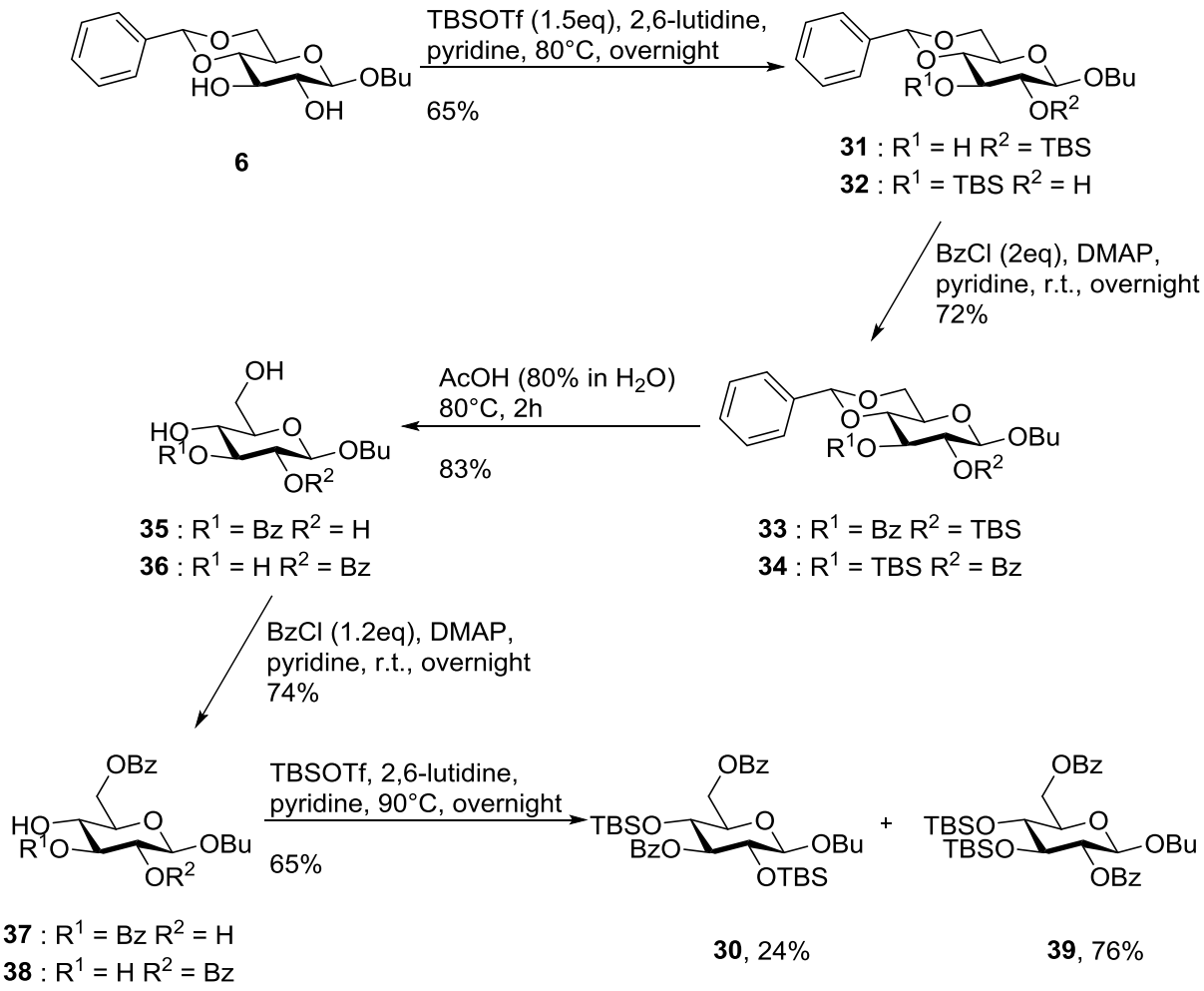
Scheme 14 Selective protection at C-4 and C-6 with benzaldehyde dimethyl acetal.

The reaction of **5** with benzaldehyde dimethyl acetal was performed using Nifantiev's[35] conditions, and product **6** was obtained in good yield (70%).

However, removal of the benzylidene can require the use of highly acidic conditions, which may not be compatible with silicon protecting groups as they can be hydrolysed, as experienced by Seeberger et al.[36] and also in this thesis work as summarised in Scheme 15.

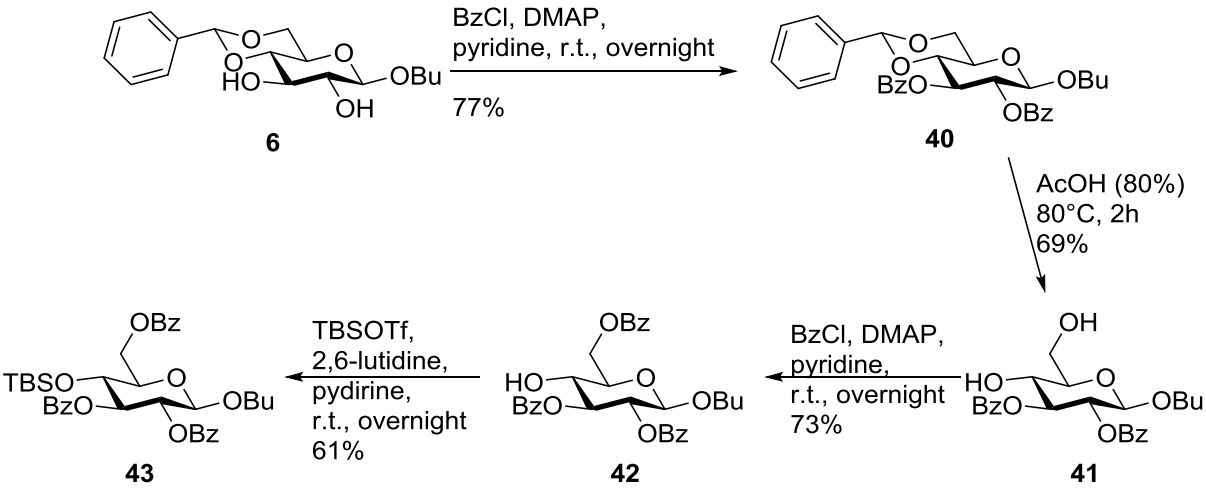
Hence, reaction of **6** with one equivalent of TBSOTf in the presence of 2,6-lutidine gave the monosilylated compounds **31** and **32**. Subsequent benzoylation gave compounds **33** and **34** respectively. The materials were then subjected to 80% AcOH at 80°C, which led to removal of the TBS group, as well as the benzylidene group. Next, the protection of the primary alcohol with a benzoyl group, followed by the protection of the two remaining hydroxyl groups with

TBS gave previously synthesized compound **30** and newly synthesized **39** ready for anomerisation.



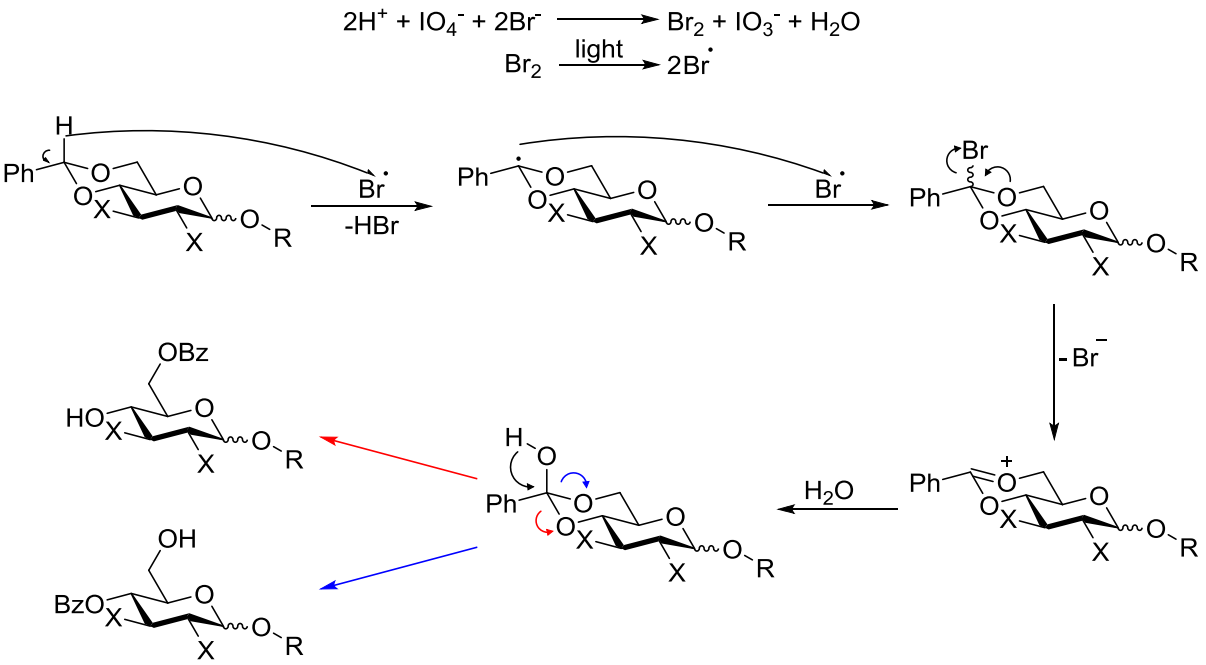
Scheme 15 Synthesis of compounds 30 and 39.

Next, benzoylation of **6** gave **40**, followed by removal of the benzylidene group to give **41**. This was converted to **42** and subsequent silylation gave TBS derivative **43** in an overall yield of 24% over 4 steps (Scheme 16).



Scheme 16 Synthesis of compound 43 through selective protection from benzylidene 6.

Another alternative to prevent the requirement to use 80% AcOH, is to instead oxidatively partially cleave the benzylidene group, using periodic acid, tetrabutylammonium bromide and wet alumina, as summarised in Scheme 17[37], to give a benzoyl protected saccharide.

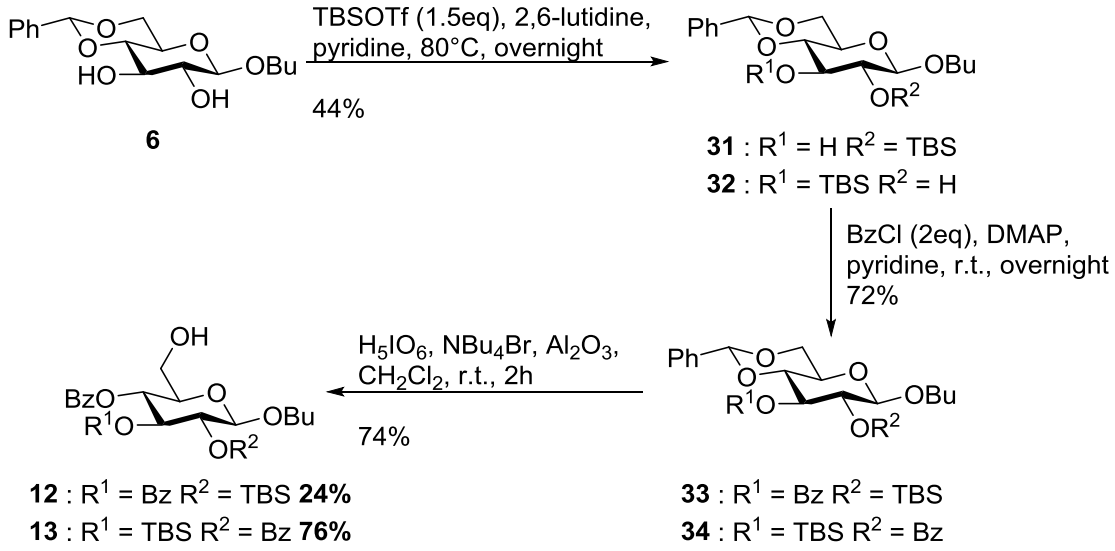


Scheme 17 Possible mechanism for partial oxidative cleavage of a benzylidene group (X= OBn, OAc, OTBS, OTIPS…).

The role of the alumina is to control the acidity of the solution. Thereby, it prevents the hydrolysis of the benzylidene itself, but also avoids the deprotection of silyl protecting groups which are located at O-2 and O-3. Use of this approach enabled preparation of compounds **12**,

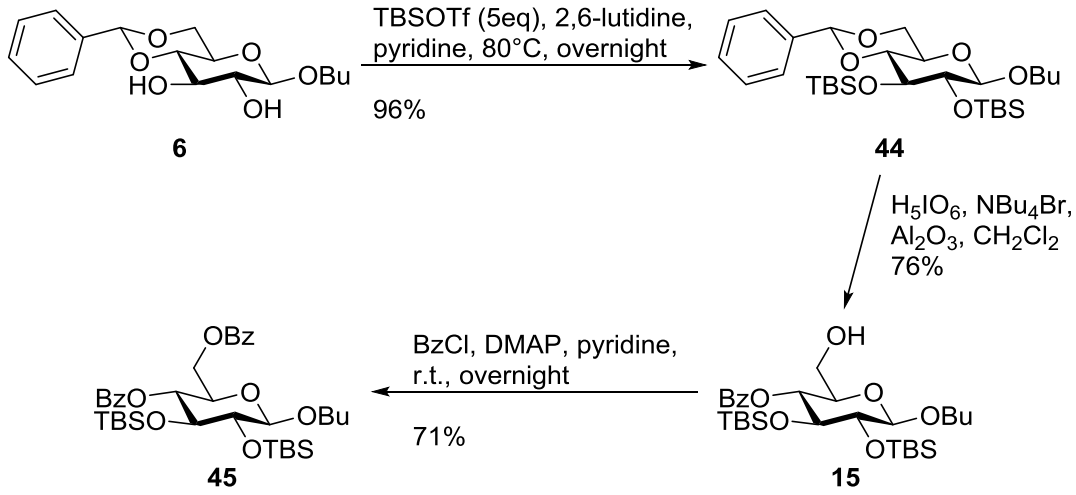
13 and **15** to be improved, rendering a more selective synthesis route, which also had a better overall yield.

Hence, the reaction of one equivalent of TBSOTf with compound **6** gave **31** and **32**, which were then benzoylated to give **33** and **34** respectively (Scheme 18). Oxidative partial cleavage of the benzylidene from **33** and **34** gave **12** and **13**. Aside from the improvement in yield, the chromatographic purifications were also less problematic.



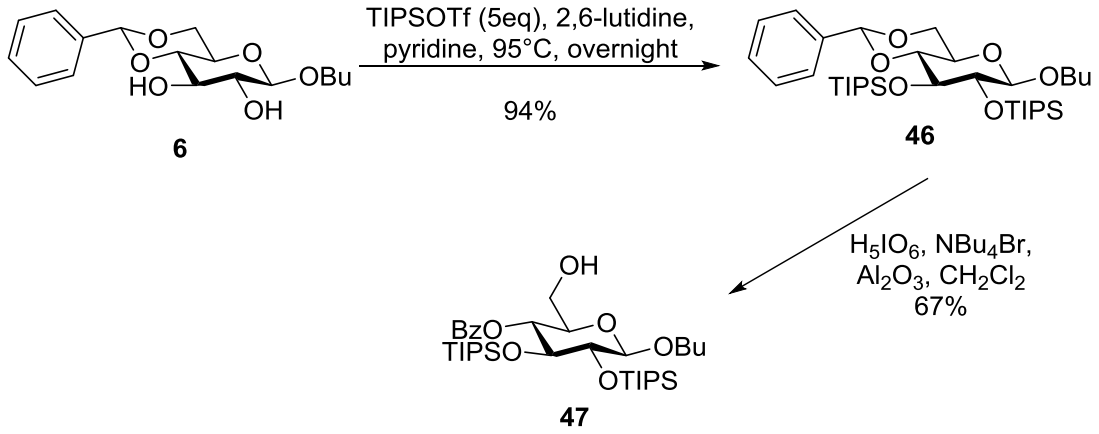
Scheme 18 Improved synthesis of 12 and 13 via benzylidene 6.

Adding an excess of TBSOTf to **6** gave disilylated product **44** which, after partial oxidative cleavage, gave exclusively reactant **15** in an overall yield of 73% over two steps (Scheme 19); this was significantly higher than its earlier synthesis (Scheme 10). Subsequent benzoylation gave fully protected **45**.



Scheme 19 Improved synthesis of 15, and synthesis of 45.

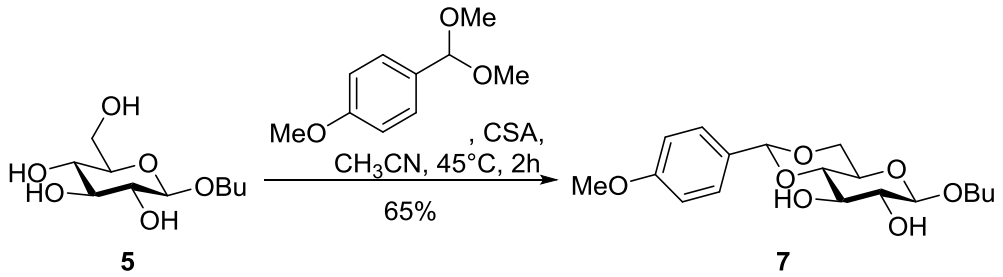
Similarly, by reacting **6** with an excess of TIPSOTf, and subsequent heating of the reaction, compound **46** was obtained, which underwent oxidation to give di-*O*-TIPS derivative **47**, ready for anomerisation.



Scheme 20 Synthesis of compound 47, inspired by the improved synthesis of 15.

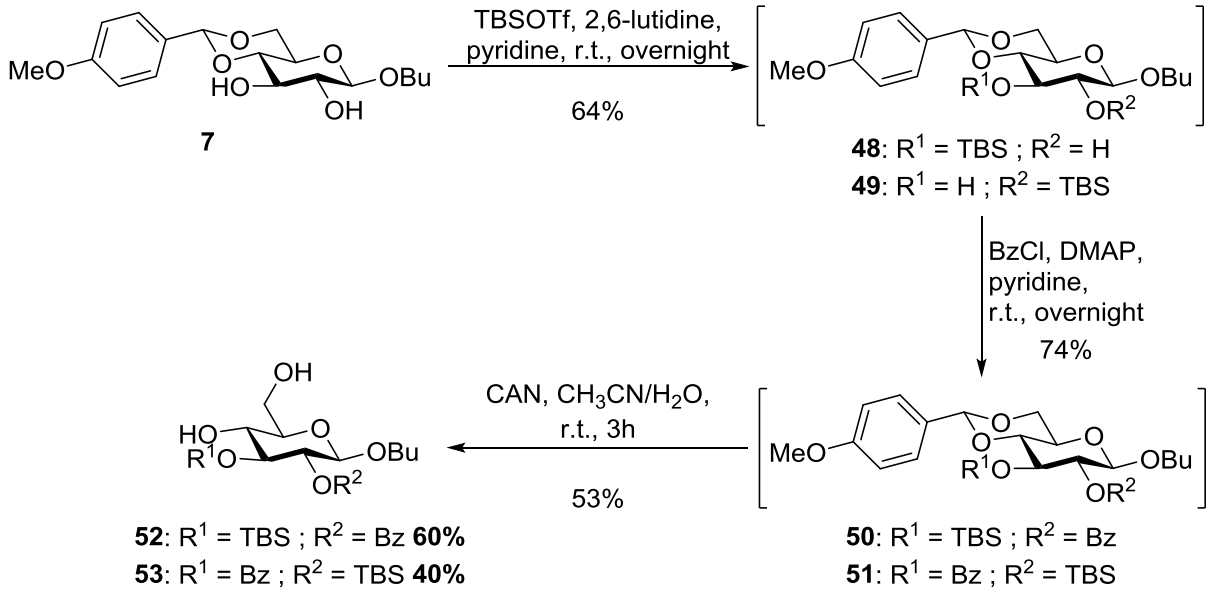
2.3.2.5. Using *p*-methoxybenzaldehyde dimethyl acetal

The use of *p*-methoxybenzaldehyde dimethyl acetal (Scheme 21) was next explored, given that it can be removed by different reagents such as ceric ammonium nitrate.



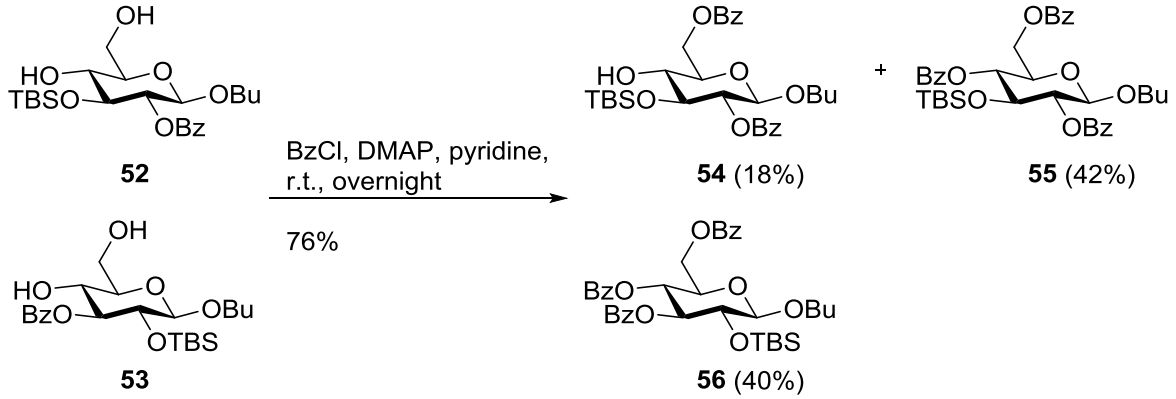
Scheme 21 Selective protection of positions C-4 and C-6 with *p*-methoxybenzylidene.

These conditions are compatible with silyl groups, as the solution is very slightly acidic.
With compound **7** in hand, one equivalent of TBSOTf was added in the presence of 2,6-lutidine to give **48** and **49** and this was followed by benzoylation to give **50** and **51** (Scheme 22). The *p*-methoxybenzylidene was then deprotected, which gave diols **52** and **53** in an overall yield of 25% over 3 steps (ratio **52**:**53** = 1.5:1).



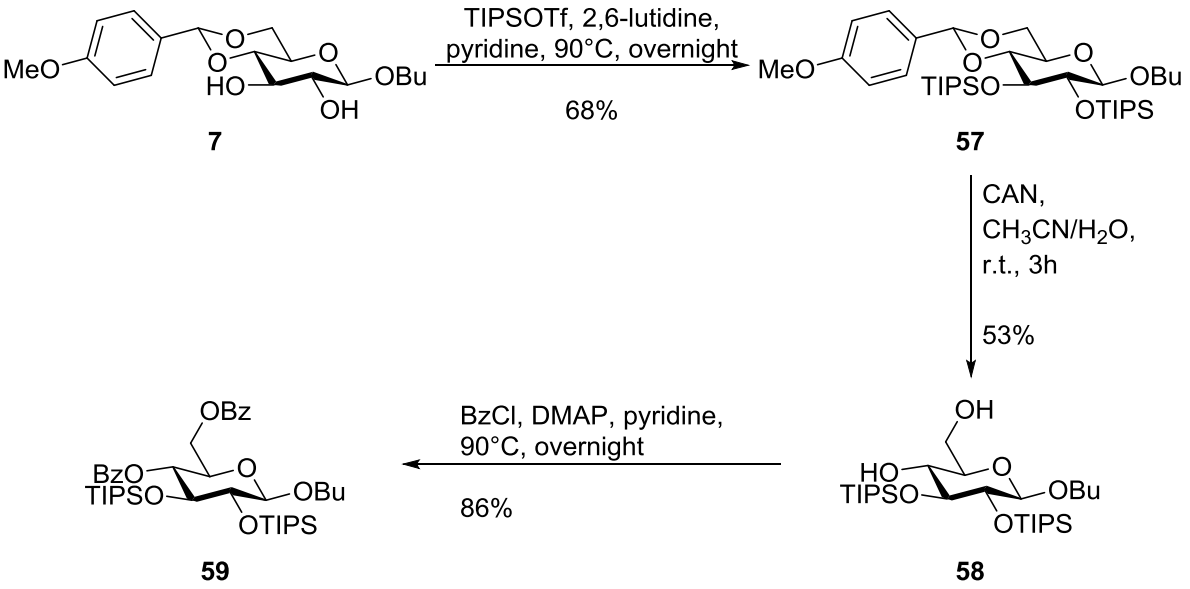
Scheme 22 Synthesis of 52 and 53.

Benzoylation of **52** and **53** was next explored. However, even after leaving the solution to react overnight, the benzoylation did not go to completion for compound **52**, and both **54** and **55** were obtained. This can be explained by the steric hindrance caused by the silyl group at position 3 reducing the nucleophilicity of O-4, which therefore makes it slower to react. Benzoylation of **53** did go to completion, and gave exclusively **56**.



Scheme 23 Synthesis of three reactants ready for the anomerisation tests.

A similar scheme was used for the synthesis of **59** (Scheme 24). Two equivalents of TIPSOTf were added to **7** to give **57**. Again, due to lower reactivity of the TIPSOTf compared to TBSOTF, due to steric hindrance, the reaction had to be heated up overnight to make sure the two positions were protected. Then, deprotection of the *p*-methoxybenzylidene group, and reprotection of positions 4 and 6 with benzoyl groups gave **59** in good yields.



Scheme 24 Synthesis of 59.

2.3.3. Conclusions on synthesis of silylated compounds

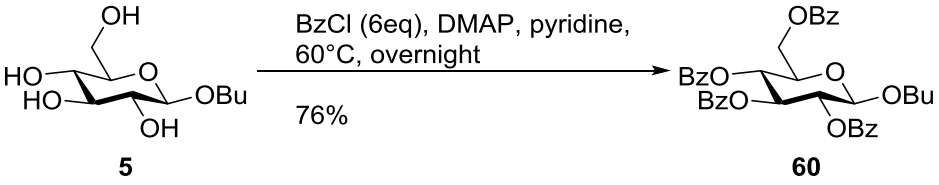
In total, five different routes were used to obtain silylated derivatives, with each of them having advantages and drawbacks. It was convenient to use protection of compound **5** via direct silylation or benzoylation, with different products obtained in one pot. However, the purification was then rendered more difficult. Many times, chromatographic separations had to be done a second, or even a third time to give pure compounds for the anomerisation study. Furthermore, selectivity towards some protected compounds were low, due to hydroxyl group reactivity differences.

The use of *p*-methoxybenzylidene worked well, but the yields of reactions in this sequence were lower than other sequences investigated.

The most reliable route was via the benzylidene group. The only drawback noticed using this method is that position 4 was always benzoylated as the partial cleavage conditions used always gave the 4-*O*-benzoyl derivative.

Nonetheless, with these different routes used, it was possible to obtain 18 different reactants, ready for the anomerisation study and these are summarised in Figure 19.

Compound **60** was synthesized as well, to be able to compare the rate of anomerisation of various silylated compounds with this known compound (Scheme 25), which has been studied previously.



5 **60**

Scheme 25 Synthesis of known compound 60.

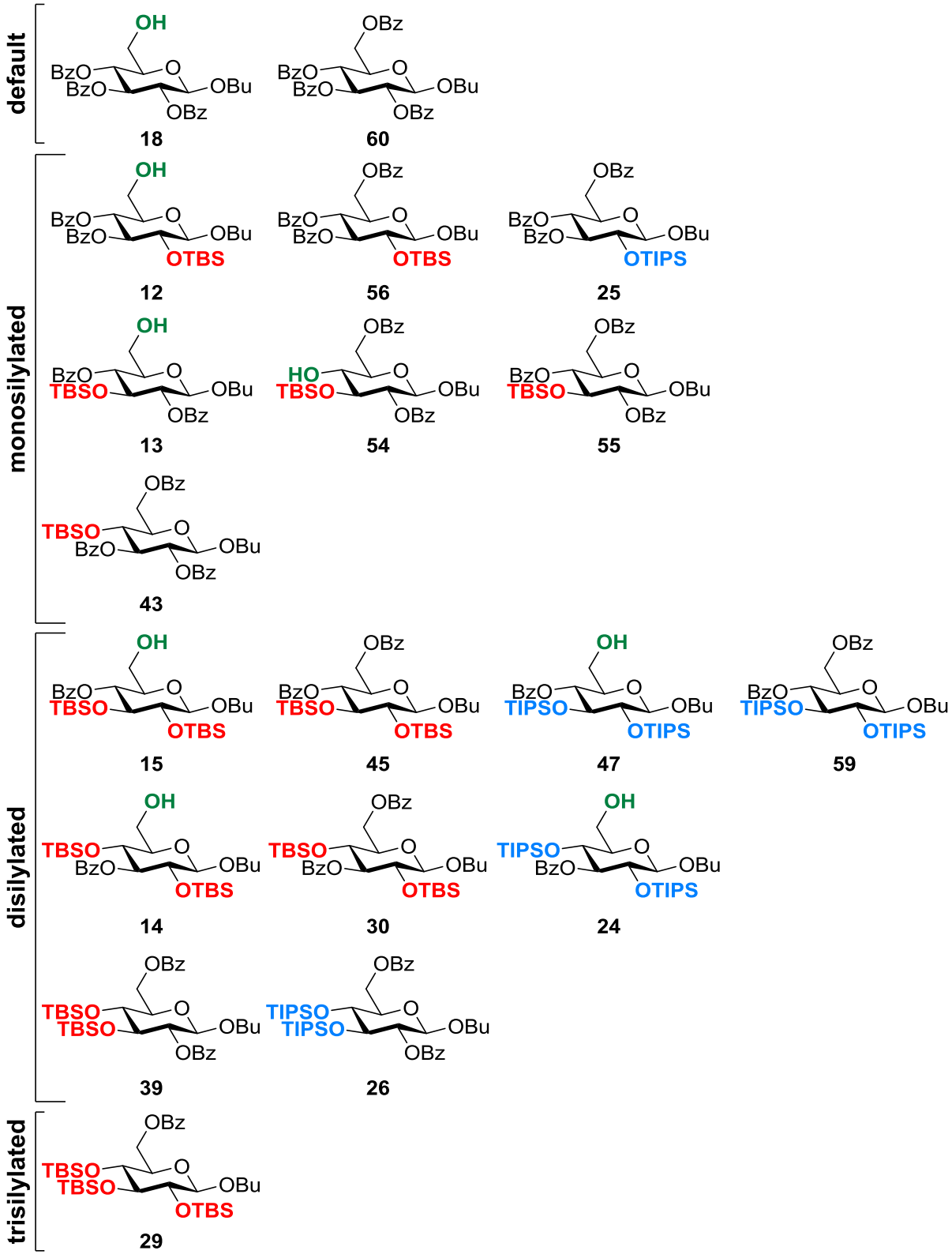


Figure 19 Structures and compound numbers for 18 reactants synthesized for anomerisation study.

2.4. Study of Lewis acid promoted anomerisation of silylated glucopyranosides

2.4.1. Method used for kinetic measurements

The anomerisation reactions and kinetic measurements were performed as described by Pilgrim et al.[18]. Every reactant was subjected to the same conditions (solvent, promoter, concentration). The reactant was freeze dried overnight. The NMR tube was also dried in an oven at 170 °C for 15 minutes. $CDCl_3$ was distilled under P_2O_5 and molecular sieves 4Å for at least 2 h before being transferred in a conical flask containing molecular sieves 4Å which had been pre-dried over a Bunsen burner. The solution of $SnCl_4$ (0.15 mol/L) was prepared 20 minutes before putting it to the NMR tube in a Bunsen burner dried round bottom flask.

The reactant (0.03 mmol) was dissolved in $CDCl_3$ (0.4 μL) and transferred into an NMR tube. $SnCl_4$ (0.1 mL, 0.15 mol/L) was then added to the tube. It was subsequently shaken, and ^1H NMR spectra were collected every 5, 10 or 30 minutes for at least 12 h. For the reactions studied, the appearance of the α-anomer generally was observed with the concomitant disappearance of the β-anomer; this is depicted as shown in Figure 20, which provides a series of NMR spectra obtained during the reaction.

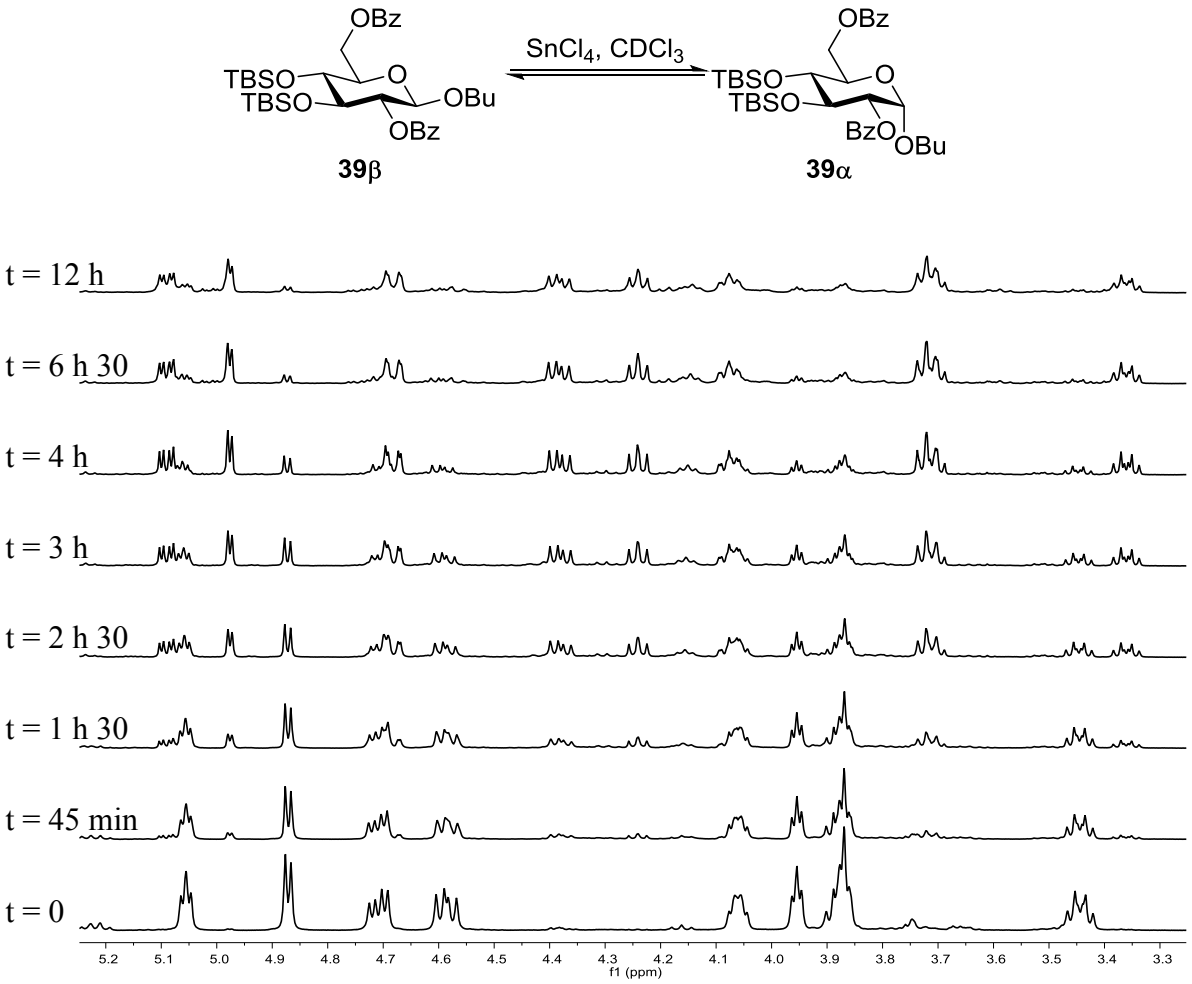
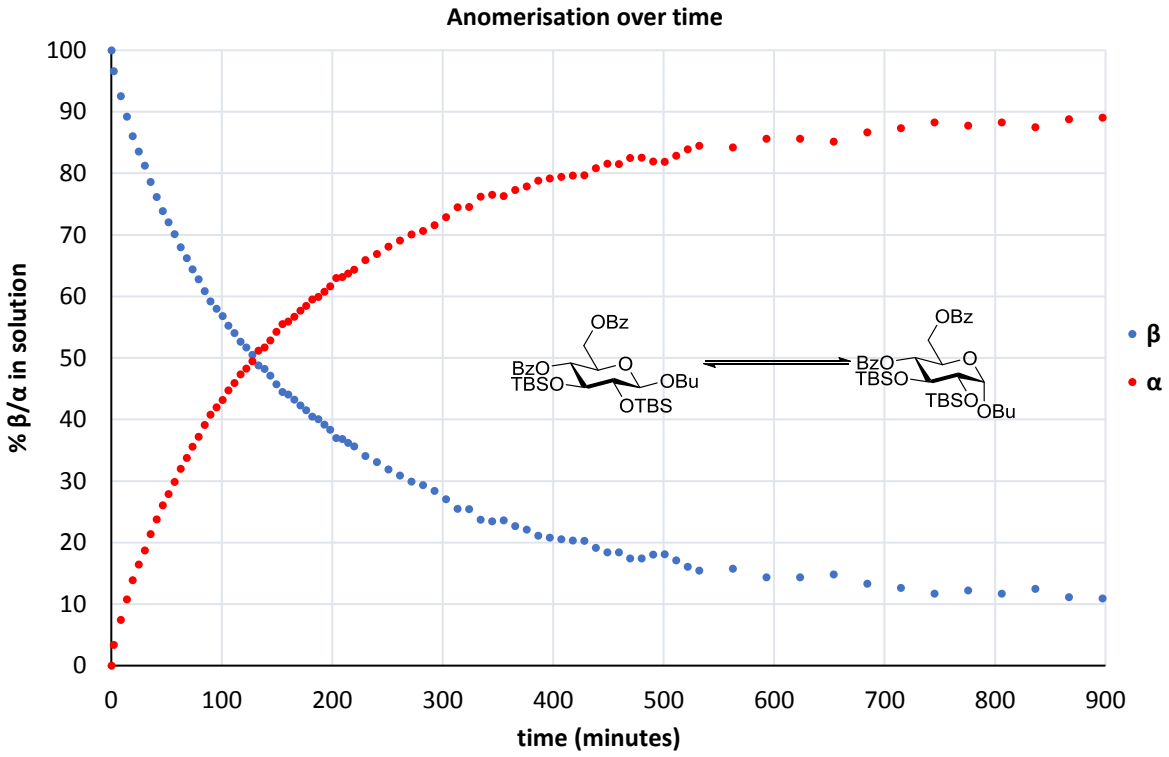


Figure 20 Appearance of the α-anomer and disappearance of the β-anomer shown by ^{1}H NMR spectra (500 MHz) obtained during the $SnCl_4$ promoted anomerisation of 39β.

The reaction was then left in the NMR tube until equilibrium was attained and the ratio α:β could be obtained. (Graph 1).



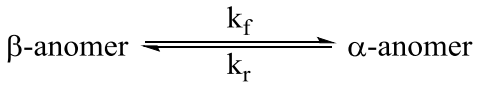
Graph 1 Graph showing the appearance of the α-anomer and the disappearance of the β-anomer with time.

The sum of the integration values for both β and α anomers remained approximately constant throughout the experiment, which meant that there was no side reaction happening that could alter the rate determination.

By the integration of the signals in the ^{1}H-NMR spectra, it was possible to calculate the concentration of both anomers as a function of time. Furthermore, the ratio, and therefore the concentration, at the equilibrium was determined. Assuming that each reaction followed the kinetics of first order reversible reactions[38-39], these data were fitted with the equation:

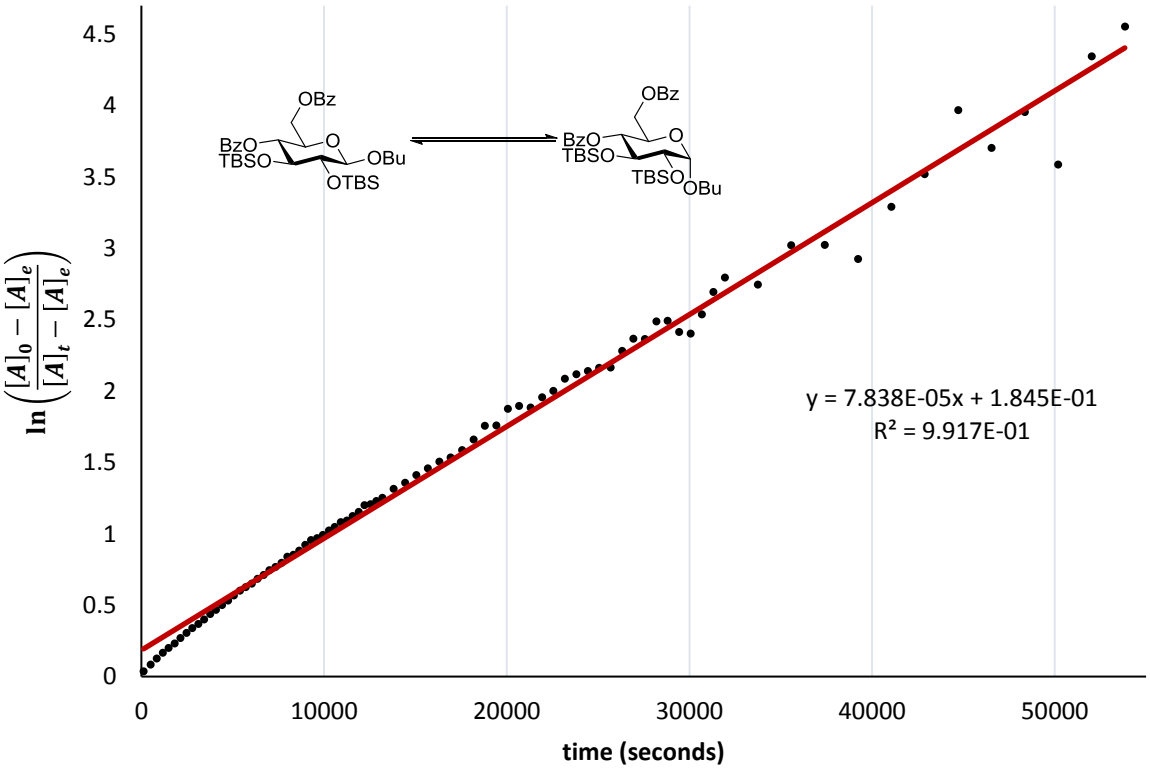
$$\ln\left(\frac{[A]_0 - [A]_e}{[A]_t - [A]_e}\right) = (k_f + k_r)t$$

Where $[A]_0$ is the initial concentration of the β-anomer, $[A]_e$ is at the equilibrium, $[A]_t$ is the concentration at time t and $k_f + k_r$ is the sum of the rate constants for the forward and reverse reactions (Scheme 26). The line plots obtained as exemplified in Graph 2 enabled determination of $k_f + k_r$ which is the slope of the line.



Scheme 26 Representation of k_f and k_r, rate constants of the anomerisation.

All reactants gave lines with R^2 values between 0.95 and 0.99 using this approach and this gave the various $k_f + k_r$ values. In the example in Graph 2, the $k_f + k_r$ value is 7.84×10^{-5} s^{-1}.

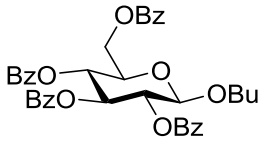
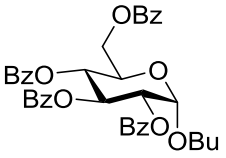
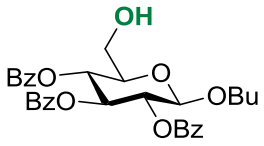
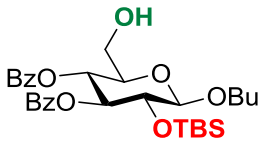
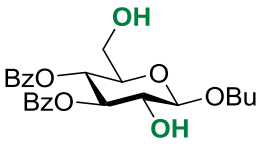
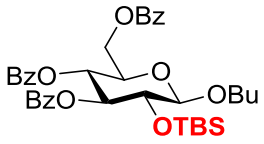
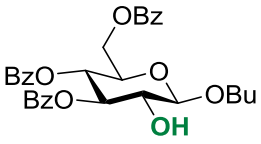
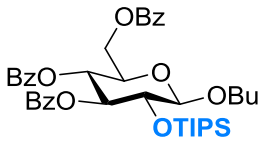
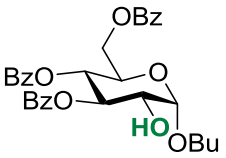


Graph 2 ($k_f + k_r$) determination for $SnCl_4$ catalysed anomerisation of 45 in $CDCl_3$.

2.4.2. Results and discussion

The rates of anomerisation were determined for each reactants synthesized, and the results are summarized in Table 4, Table 5, Table 6 and Table 7.

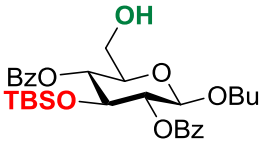
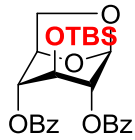
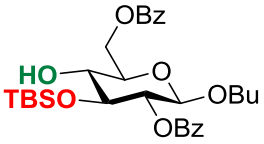
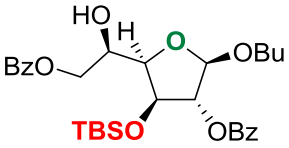
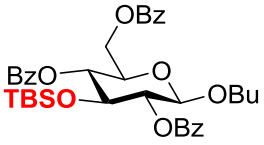
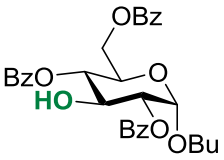
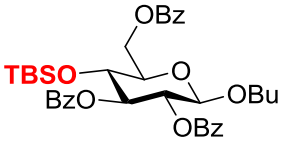
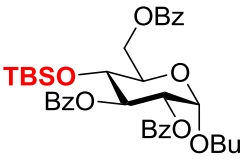
Table 4 Rates of anomerisation of reactants synthesized[a].

Substrate	Product	$10^6(k_f + k_r)$ (s^{-1}) ($10^6\ k_f$) (s^{-1})	Relative ($k_f + k_r$)	α:β
 **60β**	 **60α**	**0.968 (0.96)**	**1**	**99:1**
 **18β**	**-**	**-**	**-**	**0:1[b]**
 **12β**	 **61β**	**n.d.**	**n.d.**	**0:1**
 **56β**	 **62β**	**n.d.**	**n.d.**	**0:1**
 **25β**	 **62α**	**0.51 (0.51)**	**0.53**	**99:1**

[a]Reactions were carried out at 25°C with the reactants (0.06 mol/L) and $SnCl_4$ (0.03 mol/L). [b]Starting material was recovered.

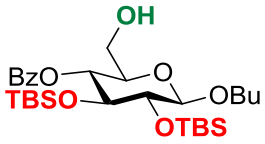
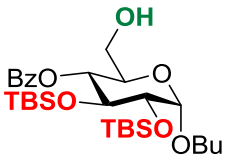
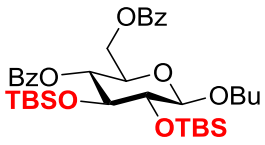
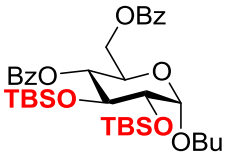
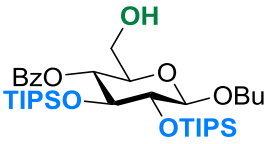
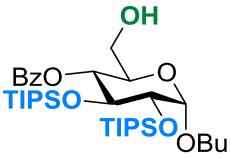
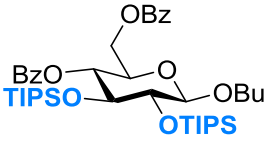
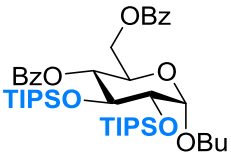
A first observation from Table 4, is that the rate of anomerisation of **60β** is less than that measured by previous PhD students in the group (~15 x 10^{-6} s^{-1}). However, this difference may be explained by the higher concentration that was previously used (0.08 mol/L compared to 0.06 mol/L for this research thesis). Additionally, in Wayne Pilgrim's study,[22] the temperature in the NMR was 30 °C compared to 25 °C in this research thesis. Mark Farrell[19] also used 1 equivalent of $SnCl_4$, compared to the 0.5 equivalent used in this research thesis.

Table 5 Rates of anomerisation of reactants synthesized[a].

Substrate	Product	$10^6(k_f + k_r)$ (s^{-1}) ($10^6\ k_f$) (s^{-1})	Relative ($k_f + k_r$)	α:β
 **13β**	 **13-anhydro**	**n.d.**	**n.d.**	**-**
 **54β**	 **54-furanose**	**n.d.**	**n.d.**	**-**
 **55β**	 **63α**	**31.9 (28.7)**	**32.9**	**90:10**
 **43β**	 **43α**	**8.88 (7.1)**	**9.17**	**80:20**

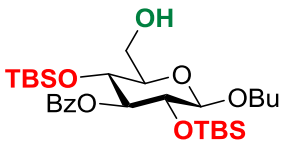
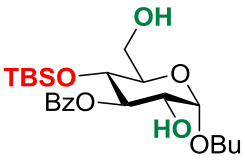
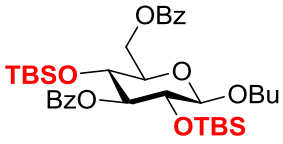
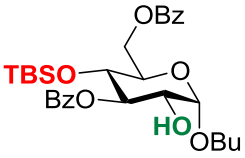
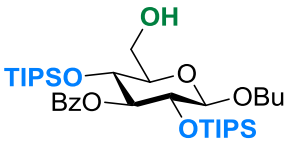
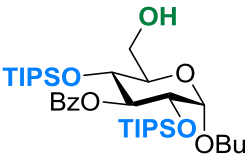
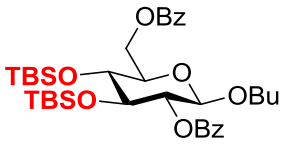
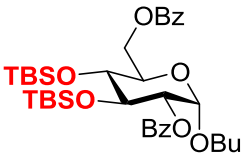
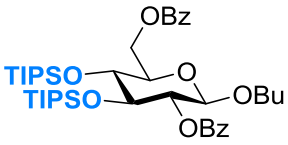
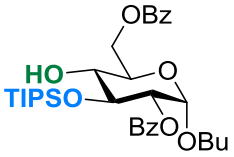
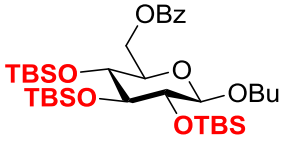
[a]Reactions were carried out at 25°C with the reactants (0.06 mol/L) and $SnCl_4$ (0.03 mol/L).

Table 6 Rates of anomerisation of reactants synthesized[a].

Substrate	Product	$10^6(k_f + k_r)$ (s^{-1}) ($10^6\ k_f$) (s^{-1})	Relative ($k_f + k_r$)	α:β
 **15β**	 **15α**	**10.0 (9.5)**	**10.3**	**95:5**
 **45β**	 **45α**	**78.4 (70.6)**	**81.0**	**90:10**
 **47β**	 **47α**	**7.65 (7.58)**	**7.9**	**99:1**
 **59β**	 **59α**	**38.8 (31)**	**40.0**	**80:20**

[a]Reactions were carried out at 25°C with the reactants (0.06 mol/L) and $SnCl_4$ (0.03 mol/L).

Table 7 Rates of anomerisation of reactants synthesized[a].

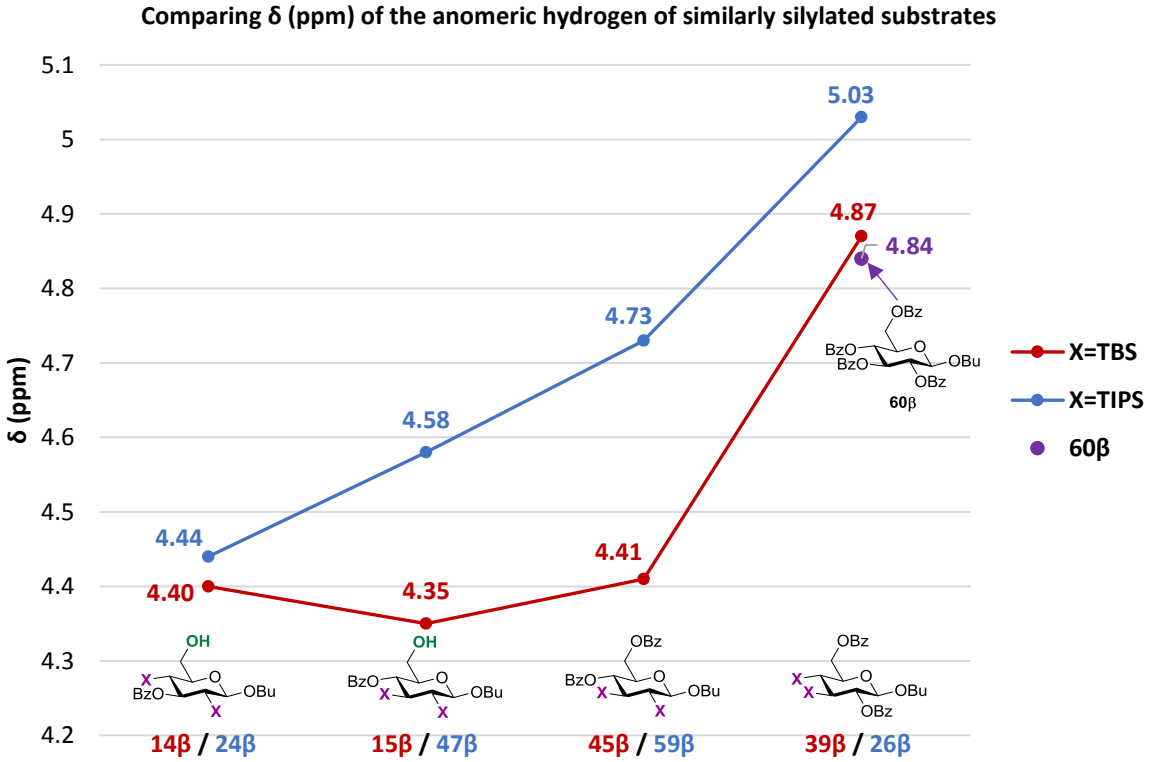
Substrate	Product	$10^6(k_f + k_r)$ (s^{-1}) ($10^6\ k_f$) (s^{-1})	Relative ($k_f + k_r$)	α:β
 **14β**	 **64α**	**12.2 (11.6)**	**12.6**	**95:5**
 **30β**	 **65α**	**14.1 (12.7)**	**14.6**	**90:10**
 **24β**	 **24α**	**13.2 (10.5)**	**13.6**	**80:20**
 **39β**	 **39α**	**160 (132)**	**165**	**83:17**
 **26β**	 **66α**	**67.5 (57.3)**	**69.73**	**85:15**
 **29β**	-	-	-	**0:1[b]**

[a]Reactions were carried out at 25°C with the reactants (0.06 mol/L) and $SnCl_4$ (0.03 mol/L).

[b]Starting material was recovered.

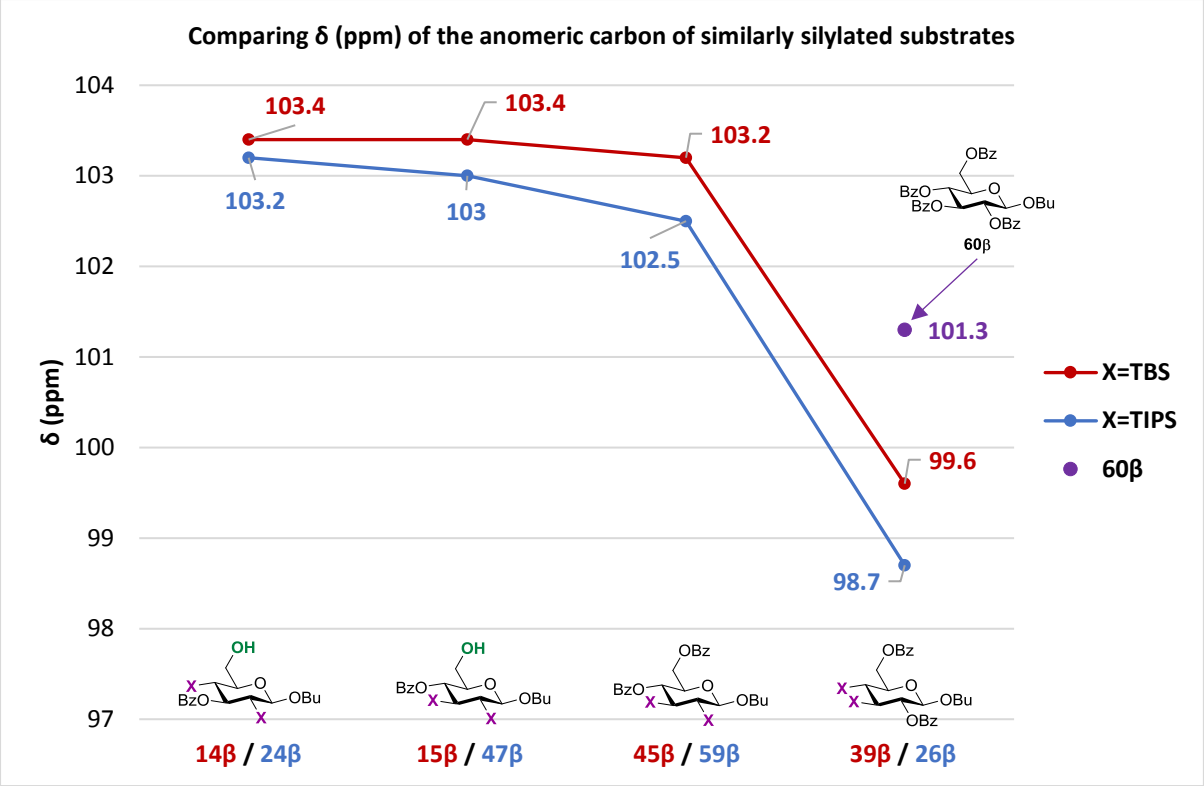
Many comments can be made about these results.

Firstly, an attempt to correlate the chemical shifts of H-1 and coupling constant between H-1 and H-2 with the different rates obtained from reactants only differing by the type of silyl group protecting them was made. The data were placed in three different graphs, regrouping the different chemical shifts (δ) of the anomeric hydrogen (Graph 3), the chemical shifts (δ) of the anomeric carbon (Graph 4), the coupling constants between H-1 and H-2 (Graph 5), and the different rates observed (Graph 6).



Graph 3 Comparing the chemical shift of the anomeric hydrogen of similarly protected reactants.

It is noticeable that, when comparing two carbohydrates only differing by the type of silyl group protecting them (**14β** with **24β**, **15β** with **47β**, **45β** with **59β** and **39β** with **26β**), even though they are similar, the chemical shifts are changed. Indeed, presence of TIPS groups makes the chemical shifts more downfield than TBS groups. Additionally, the chemical shifts of **39β** and **26β** are more downfield than the fully benzoylated compound **60β**. Usually, in D-pyranose in $^4C_1$ conformation, the axial anomer is shifted downfield compared to the equatorial anomer[40-41]. We next compared the chemical shifts of the anomeric carbon (Graph 4).



Graph 4 Comparing the chemical shifts of the anomeric carbons of similarly protected reactants.

Similarly, the TIPS substituents make the chemical shift of the anomeric carbon more upfield than when TBS substituents are present in the carbohydrate. Again, usually, in D-pyranose in $^4C_1$ conformation, the axial anomer is shifted upfield compared to the equatorial anomer. It could then be suggested that the $^4C_1$ chair configuration is substantially less populated or not populated due to the bulkiness of the protecting groups. The anomeric substituent adopts then an axial-like or pseudo-axial position and this has the effect of shifting the chemical shifts downfield. This hypothesis is supported by an analysis of the coupling constants observed between the hydrogens in positions 1 and 2 (Graph 5). Coupling constants are based on the dihedral angle between two hydrogens[42-43]. The closer to 90° the angle between the two protons is, the lower the coupling constant is. For example, when both substituents are equatorial, the two hydrogens are therefore axial, being separated by a dihedral angle of 180°. In contrast, when the two substituents are axial, the hydrogen are consequently equatorial, making the angle between each other of 60° (Figure 21).

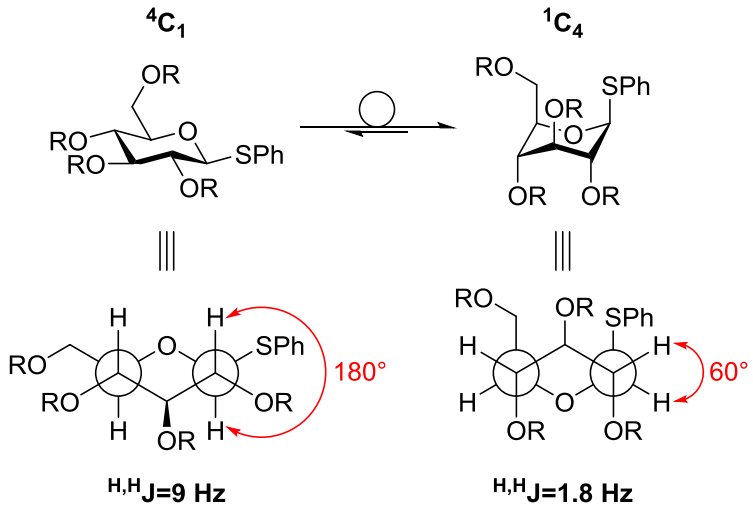
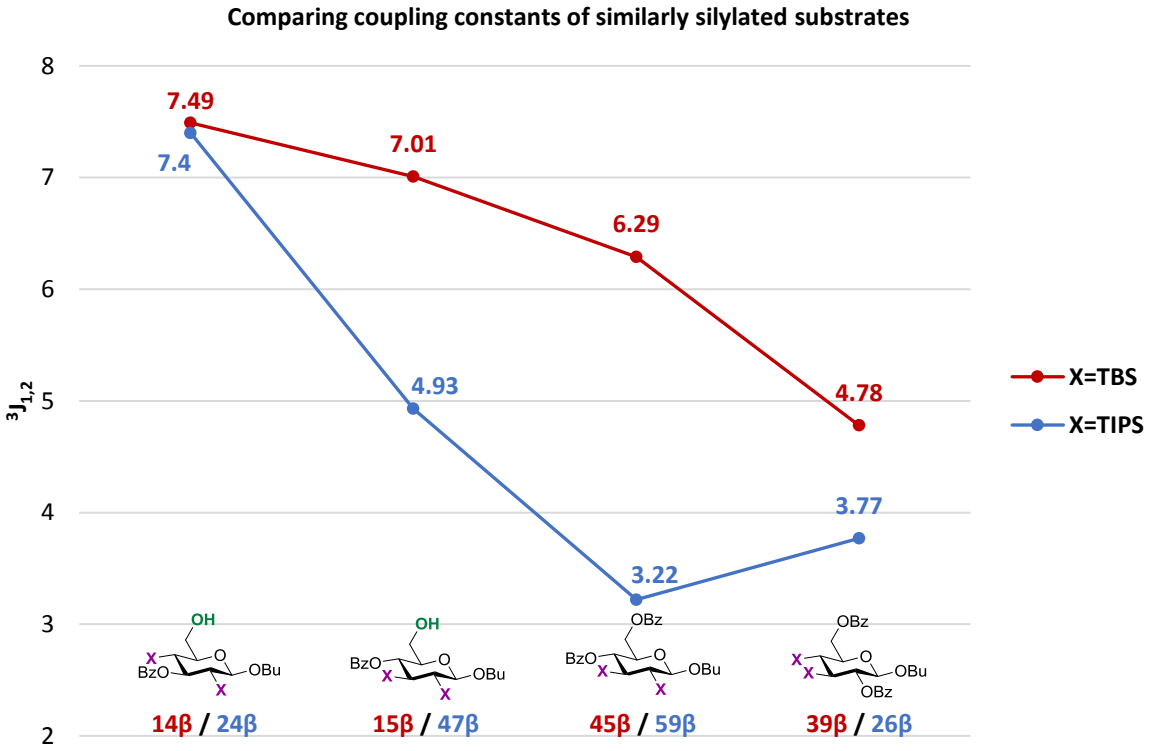
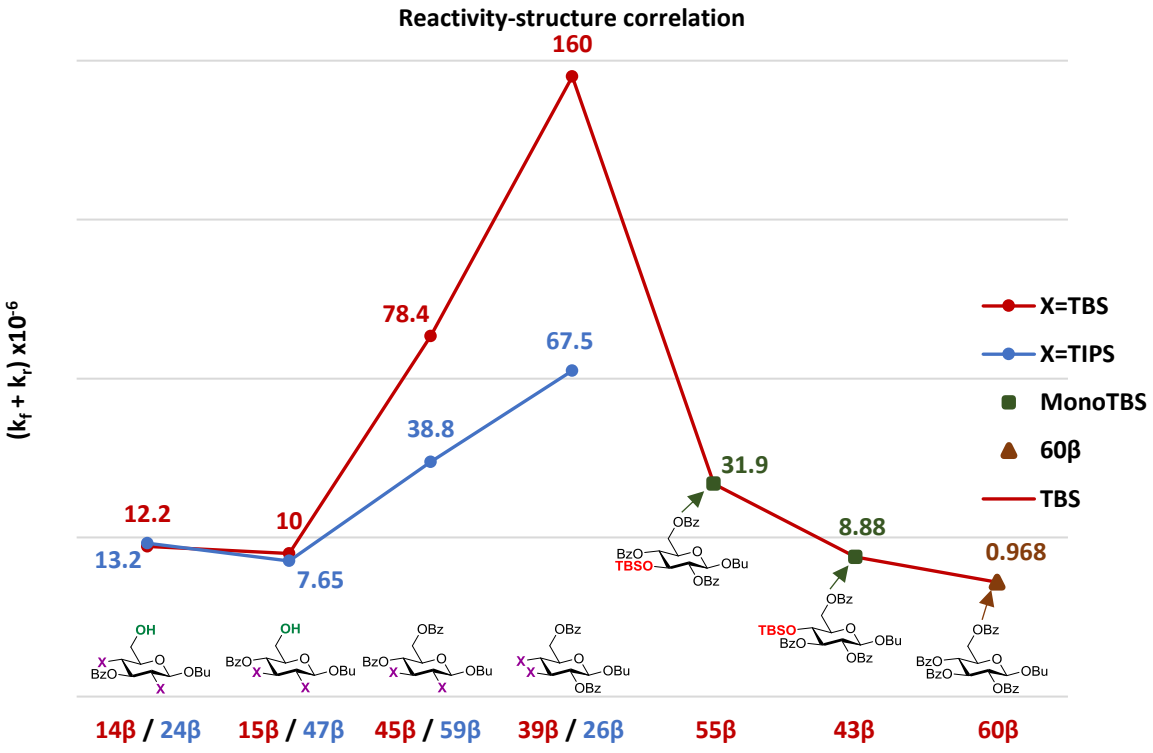


Figure 21 Dihedral angle and coupling constants between H^1 and H^2, with a $^4C_1$ and $^1C_4$ configuration in a thioglycoside.



Graph 5 Comparing the coupling constant between H^1 and H^2 of similarly protected reactants.

On Graph 5, it can be observed that the coupling constant is smaller with TIPS than with TBS protecting groups, which confirms the fact that bulkier protecting groups induce the carbohydrate to adopt a conformation other than $^4C_1$, with substituents axial or pseudoaxial rather than equatorial.



Graph 6 Reactivity-structure correlation.

Next, the rate of anomerisation of different reactants were compared in a graph. What can be observed from Graph 6, is that there is a correlation between the reactivity and the structure of the carbohydrate.

First of all, it was interesting to compare the rate of anomerisation between **15β** and **45β**, as their difference lies in the presence or not of a Bz in position C-6. **45β** being more reactive than **15β**, it was supposed that a coordination of $SnCl_4$ with the free hydroxyl group could happen (this hypothesis will be discussed later in the paragraph).

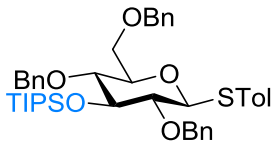
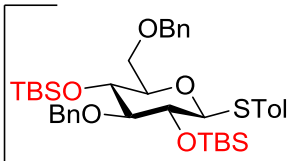
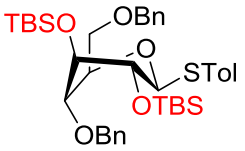
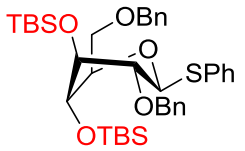
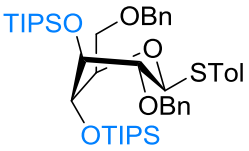
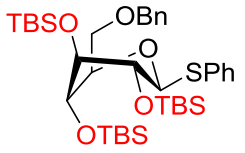
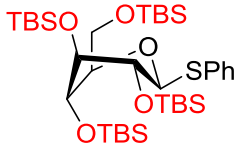
Additionally, disilylated carbohydrates **45β** and **39β** were compared, as the latter contains a benzoyle group in position C-2 compared to a TBS group for **45β**. . It is noticed that **39β** reacts faster than **45β**, which means that a resonance contribution from the Bz could be important for the positively charged intermediate induced by the anomerisation promoter to be stabilised. This discovery was in accordance with a recently published paper within Murphy group, that sustain the importance of having a Bz group in position C-2 for the obtaining of an improved rate of anomerisation compared to when acetate is present[23].

However, the importance of having two silyl group in the carbohydrate was stressed when comparing disilylated **45β** and **39β**, having a higher rate of anomerisation than monosilylated **55β** and **43β**.

This difference of rate was explained by the reduced in population of $^4C_1$ conformation of **45β** and **39β**, making the substituents to adopt an axial-like or pseudo-axial position. However, this said, TIPS groups, which render the carbohydrates less in a $^4C_1$ conformation than TBS groups, for example, make the anomerisation slower. These results are in agreement with Wong's group, who found that two TBS on the same carbohydrate make the glycosylation faster than their TIPS counterpart[17].

Going deeper, the coupling constants of target compounds and their α-anomer (Table 9) were compared with those of compounds previously synthesized (Table 8) by Bols[13], Yamada[44-45] and more recently Wong's[17] groups. This would enable us to determine the type of conformation adopted by the different compounds.

Table 8 Coupling constant and conformation of previously synthesized compounds[13, 17].

		$^3J_{H,H}$ (Hz)						
		$H_{1,2}$	$H_{2,3}$	$H_{3,4}$	$H_{4,5}$	$H_{5,6a}$	$H_{5,6b}$	Conformation
monosilylated	 **A**	9.4	8.1	8.1	9.3	4.5	2.2	$^4C_1$
disilylated	 **B**	9.2	8.2	8.2	9.1	7.1	2.1	$^4C_1$
	 **C**	6.2	3.1	4.6	n.d.	5.6	n.d.	$^3S_1$
	 **D**	8.3	3.2	4.7	3.9	5.9	9.7	$^3S_1$
	 **E**	8.6	<2	3.3	<2	6.9	6.9	$^3S_1$
trisilylated	 **F**	7.6	1.2	1.2	2.1	6.6	6.6	$^3S_1$
tetrasilylated	 **G**	7.6	<2	2.8	1.4	n.d.	n.d.	$^3S_1$

From the data obtained, it can be observed that monosilylated (**A**) and 2,4-disilylated (**B**) compounds kept the $^4C_1$ (chair) conformation unchanged.
On the other hand, it can be noticed that for compounds **C-G**, the coupling constant between H-1 and H-2 is quite large compared to the very low coupling constants observed elsewhere in the carbohydrate. This difference of coupling constants means that the conformation adopted by the carbohydrates is neither $^4C_1$ or $^1C_4$, as the values would be roughly similar throughout the saccharide. Bols and Yamada groups both concluded that the conformation adopted by the carbohydrate was rather a twisted-boat (also known as a skew) conformation, that would confirm the odd coupling constant observed. A crystal structure determined by Demchenko's group[46] of a 2,3-di-*O*-silylated saccharide confirmed the skew conformation, and additionally explained the coupling constants observed.

We could compare those preliminary results to the coupling constant values of the reactants synthesized in this thesis work, presented in Table 9.

Table 9 Coupling constant (J (Hz)) observed in ^{1}H NMR spectra of target compounds and their α anomers.

X	Specificity (position)			^{3}J values (Hz)						^{1}C$_4$ / ^{4}C$_1$
	TBS	TIPS	OH	$H_{1,2}$	$H_{2,3}$	$H_{3,4}$	$H_{4,5}$	$H_{5,6a}$	$H_{5,6b}$	
18β	-	-	1 (6)	7.9	9.7	9.7	n.d.	n.d.	n.d.	^{4}C$_1$
60β	-	-	-	7.8	9.7	9.7	9.7	3.3	5.3	^{4}C$_1$
60α	-	-	-	3.7	9.8	9.8	9.7	n.d.	n.d.	^{4}C$_1$
12β	1 (2)	-	1 (6)	7.5	9.4	9.4	9.7	n.d.	n.d.	^{4}C$_1$
56β	1 (2)	-	-	7.6	9.4	9.4	9.8	3.4	5.8	^{4}C$_1$
25β	-	1 (2)	-	n.d.	9.3	9.3	9.7	3.4	n.d.	^{4}C$_1$
13β	1 (3)	-	1 (6)	8.1	n.d.	n.d.	9	9	9	^{4}C$_1$
54β	1 (3)	-	1 (4)	8	9.3	n.d.	n.d.	2	4.2	^{4}C$_1$
55β	1 (3)	-	-	8.4	8.4	9.3	9.3	3.4	5.5	^{4}C$_1$
43β	1 (4)	-	-	7.9	9.9	8.9	9.1	2.2	4.9	^{4}C$_1$
43α	1 (4)	-	-	3.8	10	8.5	n.d.	2.1	4.5	^{4}C$_1$
15β	2 (2,3)	-	1 (6)	7	n.d.	8.1	8.1	n.d.	n.d.	**^{4}C$_1$ (86%) + ^{1}C$_4$**
15α	2 (2,3)	-	1 (6)	3.4	8.8	8.8	10	3	3	**^{4}C$_1$ (mainly)**
45β	2 (2,3)	-	-	6.4	6.4	7.6	7.6	4.3	6.5	**^{4}C$_1$ (76%) + ^{1}C$_4$**
45α	2 (2,3)	-	-	3.4	8.9	9.6	9.6	2.8	6.5	**^{4}C$_1$ (mainly)**
47β	-	2 (2,3)	1 (6)	4.9	4.2	5.8	7.2	n.d.	n.d.	**^{4}C$_1$ (51%) + ^{1}C$_4$**
47α	-	2 (2,3)	1 (6)	3.2	8.2	8.2	n.d.	n.d.	n.d.	**^{4}C$_1$ (mainly)**
59β	-	2 (2,3)	-	3.2	3.2	4.6	4.6	n.d.	n.d.	**^{4}C$_1$ + ^{1}C$_4$ (78%)**
59α	-	2 (2,3)	-	3.1	7.6	6.8	9.3	n.d.	n.d.	**^{4}C$_1$ (mainly)**
14β	2 (2,4)	-	1 (6)	7.5	9.2	9.2	n.d.	n.d.	n.d.	^{4}C$_1$
30β	2 (2,4)	-	-	n.d.	9	9	9.2	2.3	6	^{4}C$_1$
24β	-	2 (2,4)	1 (6)	7.4	9	9	9	n.d.	n.d.	^{4}C$_1$
24α	-	2 (2,4)	1 (6)	3.5	9.3	9.1	9.1	n.d.	n.d.	^{4}C$_1$
39β	2 (3,4)	-	-	4.8	4.7	4.5	n.d.	4.8	7.1	**^{4}C$_1$+ ^{1}C$_4$ (51%)**
39α	2 (3,4)	-	-	3.7	8.9	7.3	9.5	2.5	7	**^{4}C$_1$ (mainly)**
26β	-	2 (3,4)	-	3.7	<2	2.7	<2	7.4	7.4	**^{4}C$_1$+ ^{1}C$_4$ (69%)**
29β	3 (2,3,4)	-	-	6.1	<2	3.2	1.1	n.d.	n.d.	**^{3}S$_1$**
62α	-	-	1 (2)	3.9	9.8	9.9	9.8	2.8	5.6	^{4}C$_1$
63α	-	-	1 (3)	3.8	9.9	n.d.	10	2.1	5.2	^{4}C$_1$
64α	1 (4)	-	2 (2,6)	4	9.9	9.5	9.3	2.2	4.1	^{4}C$_1$
65α	1 (4)	-	1 (2)	3.9	n.d.	n.d.	n.d.	n.d.	n.d.	^{4}C$_1$
66α	-	1 (3)	1 (4)	3.8	9.6	8.5	10	2.2	4.6	^{4}C$_1$
13-anhydro				1.9	<1	<1	<1	1.5	5.8	**^{1}C$_4$**
60β				7.8	9.7	9.7	9.7	3.3	5.3	^{4}C$_1$

Conformations in red are majorly adopted.

Comparably, monosilylated as well as 2,4-disilylated reactants did not modify the chair conformation of the carbohydrate.

On the other hand, compounds shaded in green (**15β**, **26β**, **39β**, **45β**, **47β** and **59β**) had their coupling constants equally lowered throughout the carbohydrate. It is therefore not the skew like conformation observed by Bols and Yamada, as $J_{1,2}$ would be higher than the rest of the coupling constants. It could be suggested that the conformation adopted by the carbohydrates is an equilibrium between $^4C_1$ and $^1C_4$. Indeed, Todaro's group[47] demonstrated that silyl groups could induce an equilibrium between the two chair conformations. The resulting room temperature ^{1}H NMR (25 °C) would give a mean of both coupling constants.

Based on the $J_{1,2}$ values of **60β** (which has a $^4C_1$ conformation) and **13-anhydro** (which is forced into a $^1C_4$ conformation), an approximative percentage of each conformation was determined using this equation[48]:

$$J_{1,2}(\mathbf{60\beta}) * \boldsymbol{x} + J_{1,2}(\mathbf{13\text{-}anhydro}) * (100 - \boldsymbol{x}) = J_{1,2}(\boldsymbol{X})$$

Where $\boldsymbol{x}$ is the percentage of $^4C_1$ conformation of compound **X**, $J_{1,2}$(**60β**) and $J_{1,2}$(**13-anhydro**) are the coupling constants of **60β** and **13-anhydro** respectively, and $J_{1,2}(\boldsymbol{X})$ is the coupling constant of compound ***X***. The values are reported on Table 9. From those approximative values, it can be seen that a hydroxyl in position C-6 decreases the ratio of $^1C_4$ conformation of the molecule. It can also be noticed that TIPS groups induce a higher proportion of $^1C_4$ than TBS, which is in accordance with what was previously noticed.

Interestingly, the alpha anomers (shaded in yellow) had their equilibrium consisting in mostly a $^4C_1$ conformation. The approximative percentage of both conformation could not be calculated. This could be explained by the fact that the anomeric effect induces the anomeric substituent to be axial, and therefore forces the rest of the chair to have a $^4C_1$ conformation (entries **45α**, **47α**, **59α** and **39α**).

Finally, the compound shaded in orange (**29β**) had a high $J_{1,2}$ value, and the other coupling constants were low. It could be then suggested that the conformation adopted by this reactant is a skew (or twisted boat), as it was determined by previous group[17].

It is interesting to notice here that the anomerisation was not successful when the silyl protected carbohydrate adopted the skew conformation, whereas it was successful when there was a $^4C_1/^1C_4$ equilibrium. It could be hypothesized that the conformation adopted by a carbohydrate could enhance its reactivity towards anomerisation, however there are many other factors to be aware of.

For example, it was noticed that having a free hydroxyl group at C-6 did not lead to a rate increase. Indeed, when comparing reactants with hydroxyl groups at C-6 with their benzoylated counterpart (i.e. comparing **60β** with **18β**, **12β** with **56β**, **13β** with **55β** etc), it was noticed that either the anomerisation did not occur, or was considerably slower than the reactant with a benzoyl group at C-6.

It was therefore considered relevant to compare the ^{1}H NMR spectrum of a reactant before and just after adding $SnCl_4$ as the Lewis acid. The results were paired with reactants only differing by the presence or not of a substituent in position 6 (Figure 22, Figure 23, and Figure 24).

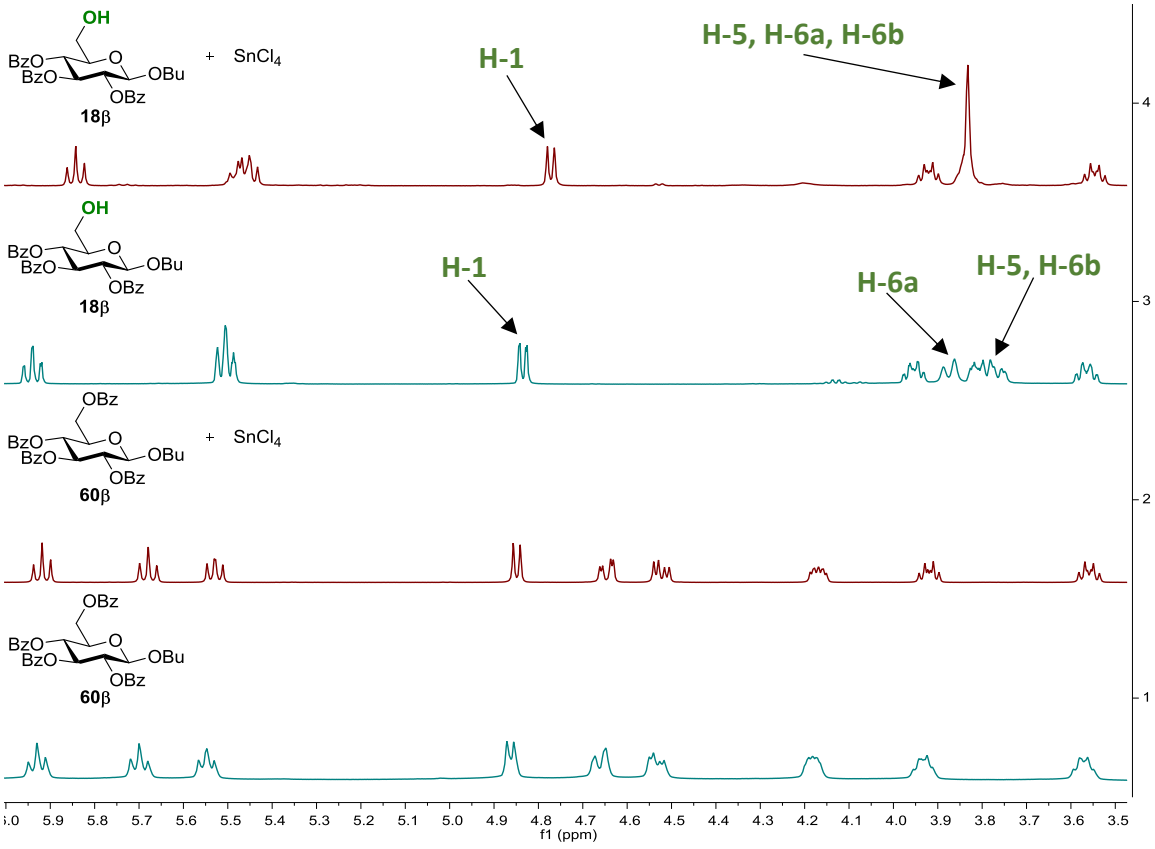


Figure 22 Comparison of ^{1}H NMR (500 MHz) before and just after adding $SnCl_4$ between 18β and 60β.

We can see that the addition of the Lewis acid does not significantly affect the ^{1}H NMR of the fully protected reactant **60β**, the sharpening of signals being probably due to how well the instrument was shimmed. However, for **18β** the signal for H-1 is shifted upfield by 0.07 ppm, and H-5 (shifted downfield by 0.08 ppm), H-6a (shifted upfield by 0.03 ppm) and H-6b (shifted downfield by 0.03 ppm) are now overlapping and the H-6 protons appear to become a broad singlet.

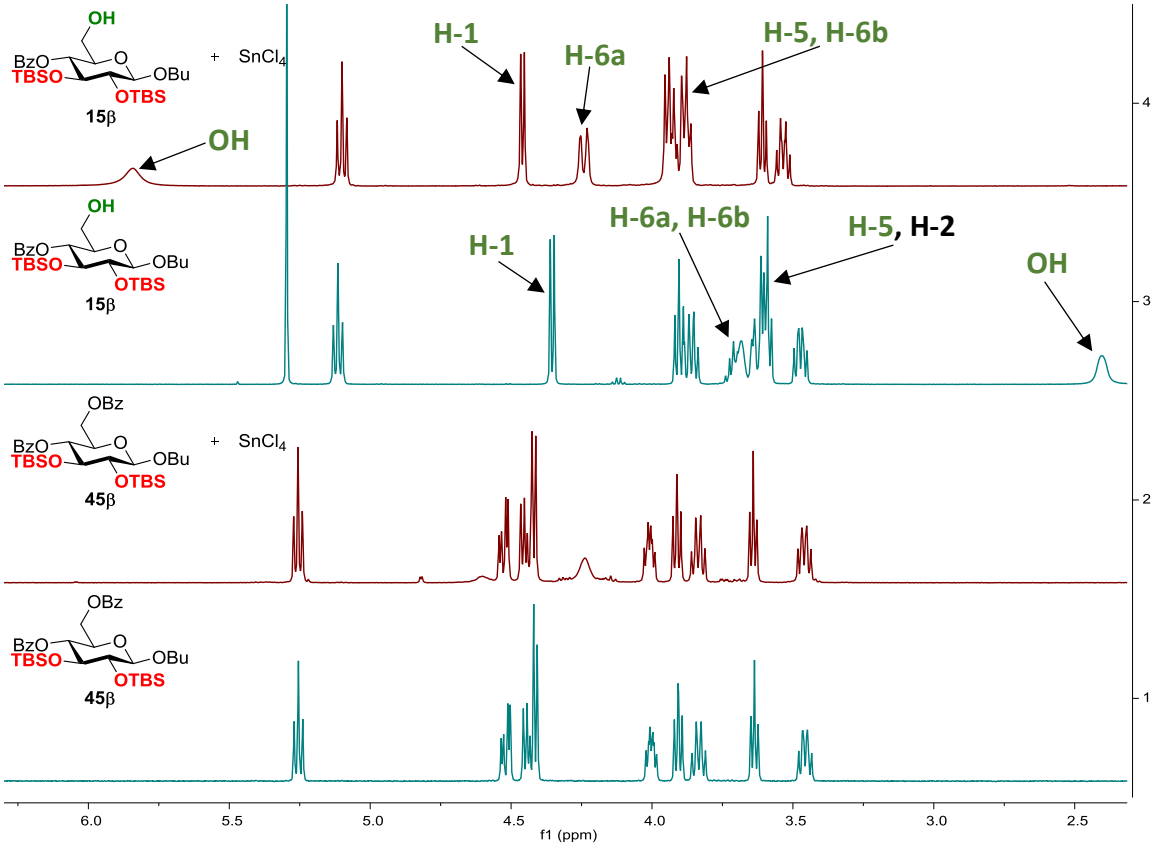


Figure 23 Comparison of ^{1}H NMR (500 MHz) before and just after adding $SnCl_4$ between 15β and 45β.

Similarly to **60β**, the ^{1}H NMR spectrum of compound **45β** did not show major changes by the addition of $SnCl_4$. On the other hand, for compound **15β**, one of the H-6 protons was considerably shifted downfield by 0.56 ppm. H-1 was also shifted downfield by 0.11 ppm, H-5 by 0.34 ppm and the other H-6 proton by 0.26 ppm. The hydrogen from the hydroxyl was also hugely shifted downfield (from 2.40 ppm to 5.84 ppm) and broadened. This probably indicates strongly that the $SnCl_4$ is coordinating to the hydroxyl group.

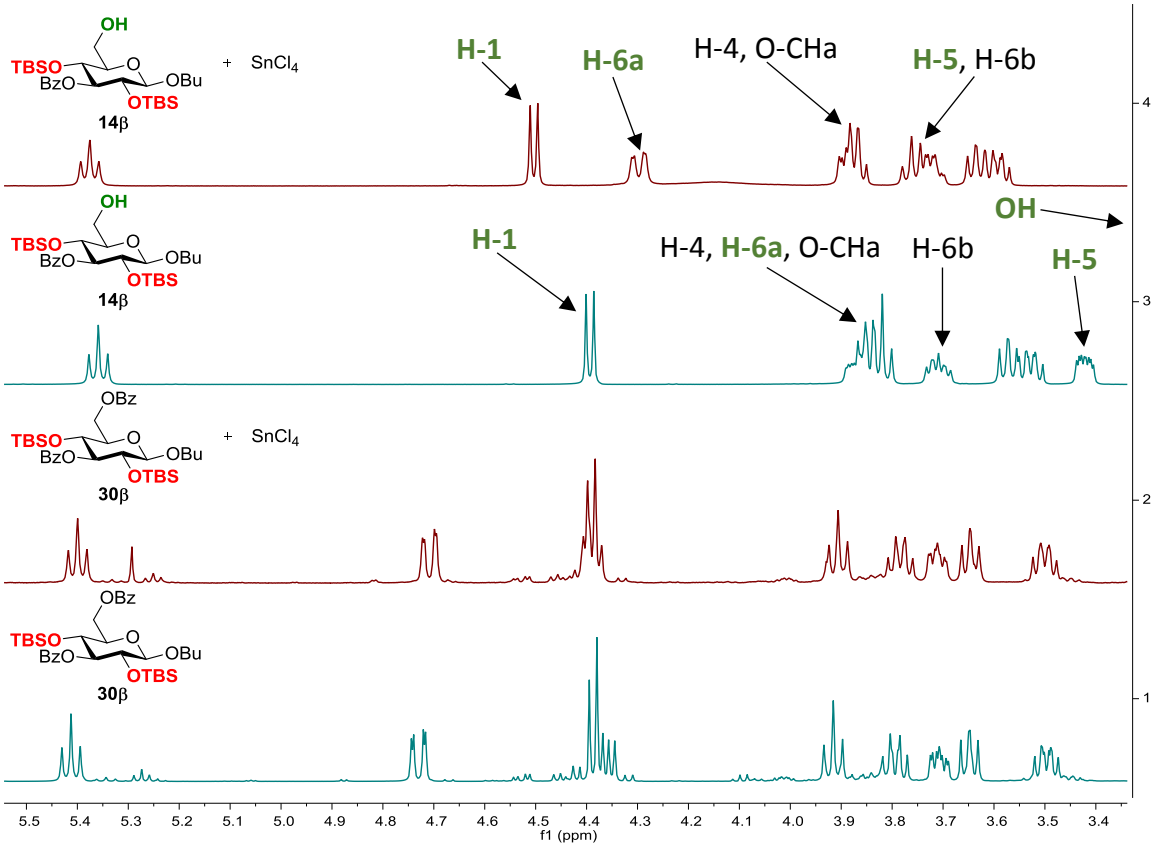


Figure 24 Comparison of ^{1}H NMR (500 MHz) before and just after adding $SnCl_4$ between 14β and 30β.

The last example chosen showed the same pattern as the last two. The ^{1}H NMR of fully protected **30β** was unchanged with the addition of the Lewis acid, when, once again, for **14β**, H-1 was shifted downfield by 0.11 ppm, H-5 by 0.32 ppm and H-6a by 0.42 ppm. Moreover, the hydrogen from the hydroxyl has disappeared. Similarly to compound **15β** in Figure 23, it is likely that $SnCl_4$ is coordinating to the hydroxyl group.

When explaining faster rates of anomerisation of uronic acids, compared to glucopyranoside it was suggested that coordination of the carbonyl oxygen to $SnCl_4$ was facilitating this reaction. However, in this work there is evidence from NMR for coordination of a hydroxyl group to the $SnCl_4$ but this does not lead to faster anomerisation compared to when there is a benzoate at C-6. Perhaps in the latter case coordination is occurring, but not chelation to the pyranose oxygen atom or the anomeric oxygen atom, that would be needed to promote endocyclic cleavage.

Another observation from the rate of anomerisation obtained is that the position of the silyl group had a huge importance on the rate of anomerisation (Figure 25). Putting a silyl group in position 3 made the reaction faster than in position 4. And putting the TBS group at C-2 stopped the reaction from happening. The latter was surprising given that the TBS group would be less electron withdrawing than a Bz group, which would therefore stabilize the positive charge induced by the anomerisation promoter.

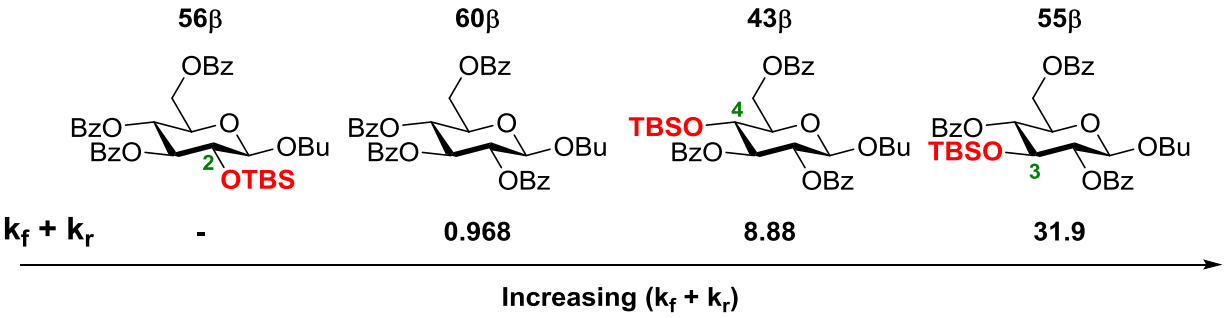
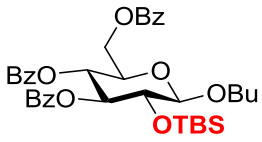
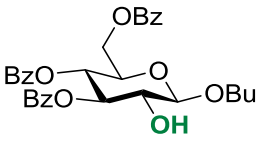
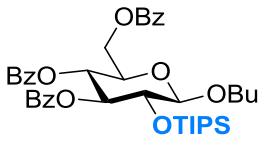
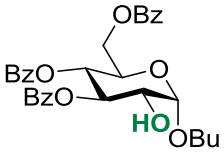


Figure 25 Increasing rate of anomerisation depending on the position protected with silylated group.

To try to explain this unpredicted result, it is interesting to notice the difference between compounds **25β** and **56β**, gathered in Table 10.

Table 10 Comparison between 56 and 25.

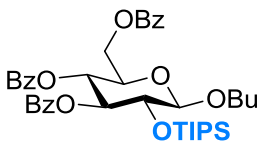
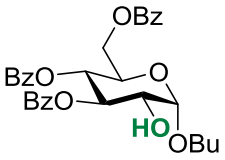
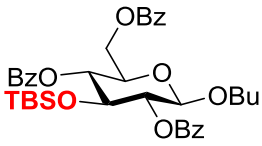
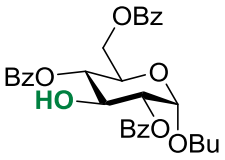
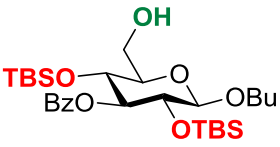
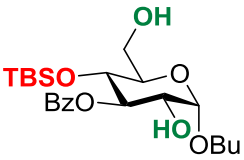
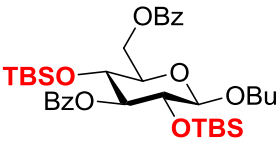
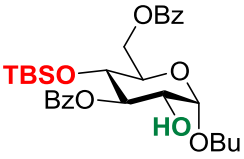
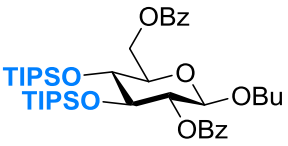
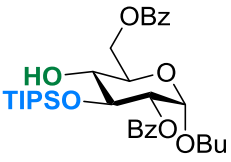
Substrate	Product	$10^6(k_f + k_r)$ (s^{-1}) (10^6 k_f) (s^{-1})	Relative ($k_f + k_r$)	α:β
 **56β**	 **62β**	n.d.	n.d.	0:1
 **25β**	 **62α**	0.51 (0.51)	0.53	99:1

It can be noticed that the reaction is successful with a TIPS in position 2 instead of a TBS, although very slow. For both cases, the silyl group was deprotected. Hypothetically, TBS gets cleaved faster than the anomerisation reaction, and the free hydroxyl on position C-2 coordinates to the $SnCl_4$, which prevents the anomerisation from occurring. When in presence

of a TIPS, the anomerisation happens first, which subsequently induce the cleavage of the TIPS. Unfortunately, this hypothesis could not be verified with the kinetics experiments, as there was no particular evidence of a change of chemical shifts or appearance of the hydroxyl proton, as the $SnCl_4$ might coordinate to it. The anomerisation of **25β** being slower than the fully benzoylated **60β** confirmed once again the importance of having a Bz in position C-2, for the resonance contribution to stabilise the positively charged intermediate.

For some reactants, silyl groups were (regioselectively) deprotected during the anomerisation reaction as shown in Table 11.

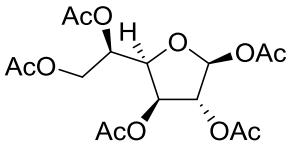
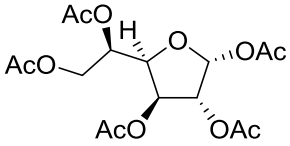
Table 11 Reactants that underwent a deprotection as well as the anomerisation.

Substrate	Product	$10^6(k_f + k_r)$ (s^{-1}) ($10^6\ k_f$) (s^{-1})	Relative ($k_f + k_r$)	α:β
 **25β**	 **62α**	**0.51 (0.51)**	**0.53**	**99:1**
 **55β**	 **63α**	**31.9 (28.7)**	**32.9**	**90:10**
 **14β**	 **64α**	**12.2 (11.6)**	**12.6**	**95:5**
 **30β**	 **65α**	**14.1 (12.7)**	**14.6**	**90:10**
 **26β**	 **66α**	**67.5 (57.3)**	**69.73**	**85:15**

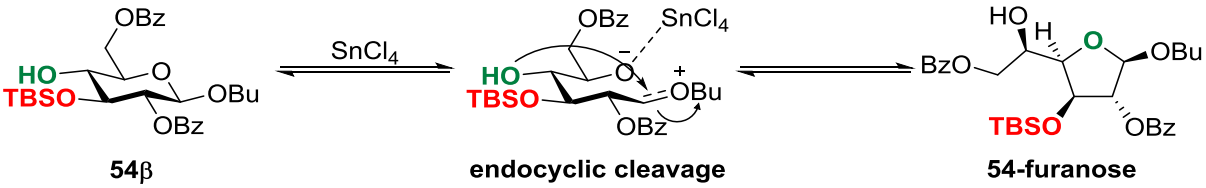
To try to explain why this deprotection is regioselective, it is interesting to remember the fact that the deprotection reaction under acidic conditions could involve generation of positive charge on the oxygen bonded to the silicon atom. The more stabilized this charge is, the more favoured the deprotection is. Generating an axial substituent at C-1, which is less electron withdrawing than an equatorial one at C-1, leads to a more electron releasing oxygen atom at C-2, which means that the deprotection of silyl group in that same position is favoured. Similarly, the TBS on C-3 in **55β** was cleaved. However, it was surprising to have the TIPS on C-4 deprotected in **26β** and not the TIPS on C-3.
It would be interesting to know the way the metal is coordinating to the reactant, which could also explain the deprotection of some silyl ether groups.

Finally, the result observed for **54β** was interesting. A furanose was obtained, and its anomeric configuration was determined by comparing the coupling constant observed with the NMR data in the literature[49-50] as reported in Table 12. The very low coupling constants for $J_{1,2}$ and $J_{2,3}$ suggested that the furanose obtained was in a β configuration. However, this is only a supposition, as the difference in substituent could also modify the coupling constants.

Table 12 Comparison of coupling constants to determine the configuration of the anomeric carbon of the synthesized furanose 54-furanose.

		$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6a}$	$J_{5,6b}$	$J_{6a,6b}$
	**Ferrières et al.**	**<1**	**<1**	**4.8**	**9.1**	**2.5**	**5.0**	**12.4**
	Stevens	**0.46**	**0.89**	**4.82**	**9.38**	**2.49**	**5.12**	**12.34**
β-D-glucofuranose pentaacetate								
	**Ferrières et al.**	**4.6**	**3.0**	**4.8**	**8.5**	**2.6**	**5.6**	**12.3**
	Stevens	**4.58**	**2.93**	**5.00**	**8.51**	**2.68**	**5.72**	**12.26**
α-D-glucofuranose pentaacetate								
54-furanose		**<1**	**<1**	**4.9**	**n.d.**	**n.d.**	**n.d.**	**n.d.**

Obtaining the furanose proved that the mechanism pathway used was through an endocyclic cleavage, as shown in Scheme 27.

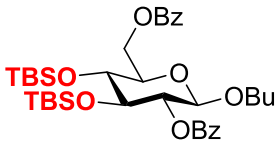
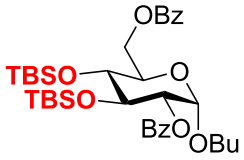
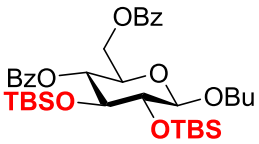
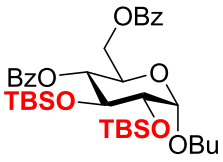


Scheme 27 Product 54-furanose suggests an endocyclic cleavage pathway.

From this study, two reactants stood out to have a very high rate of anomerisation. They are represented in Table 13.

These are the reactants that inspired the synthesis of disaccharides and monosaccharide with an azide on the anomeric position to try the so far unsuccessful anomerisation.

Table 13 Two reactants with the highest rate of anomerisation of those studied.

Substrate	Product	$10^6(k_f+k_r)$ (s^{-1}) (10^6 k_f) (s^{-1})	Relative Rate	α:β
 39β	 39α	160 (132)	165	83:17
 45β	 45α	78.4 (70.6)	81.0	90:10

2.5. Conclusion

In this Chapter, the synthesis of many *O*-butyl glucopyranosides protected differently with silylated groups (TBS or TIPS) and benzoyles groups was achieved. In total, 19 different carbohydrates were synthesized and characterized. Their rate of anomerisation was then determined through NMR spectroscopy, collecting spectra every 5, 10 or 30 minutes for at least 12 h.

Many observations could be made from the results obtained, and they are summarized in this conclusion.

Previous groups already synthesized glucopyranosides with at least two silyl groups protecting the substituents in positions 2-6[12-15]. Their observation demonstrated that when two silyl groups were protecting neighbour hydroxyls in the carbohydrates, the conformation was changed from a chair to a skew[46]. This conformation allowed the substituents to be in a pseudo axial configuration, which has the particularity to be less electron withdrawing than the equatorial configuration. In their cases, this change of conformation allowed faster rate of glycosylation.
When comparing Bols and Yamada groups coupling constants observed with the ones obtained during the course of the thesis, it was noticed that the conformation obtained was different than a skew. Instead, the carbohydrates are supposedly in an equilibrium between the $^4C_1$ and $^1C_4$ chair conformations.
The obtained equilibrium between the two chairs increased the rate of anomerisation compared to carbohydrates that had their conformation unchanged ($^4C_1$). On the other hand, the one carbohydrate that adopted a skew conformation (**29β**) had an unsuccessful anomerisation.
Additionally to the change of conformation, it was noticed that when a carbohydrate had a free hydroxyl in position C-6, the Lewis acid ($SnCl_4$) would coordinate to it and prevent it from coordinating to the ring oxygen and the anomeric oxygen. The anomerisation reaction was then slowed down or even stopped.
It was also observed that, although TIPS groups are more stable under acidic conditions, carbohydrates containing TBS groups made the anomerisation faster. This result concurred with what Wong observed during the glycosylation tests of disilylated carbohydrates[17].

From those observation, it could be possible to predict how a yet unsynthesized compound would behave towards anomerisation. For example, fully protected carbohydrates should be favoured to prevent unwanted Lewis acid coordination. Also, saccharides that have their conformation changed to a mixture of $^4C_1$ and $^1C_4$ should increase the rate of anomerisation. Finally, having the position C-2 containing a benzene ring should contribute to a resonance effect which could be important for the anomerisation to react faster.
Ideally, these observations are applicable for any other type of saccharides (galactosides, mannosides, …).

Two disilylated carbohydrates (**39β** and **45β**) had very high rates of anomerisation. The next Chapter will see the synthesis of a glucopyranoside azide and two disaccharides protected similarly for further anomerisation tests.

2.6. References

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Chapter 3 Anomerisation on azides and disaccharides

3.1. Objective of the research

An objective of this research was to use the reactivity data obtained as described in Chapter 2 to design a protecting group strategy to enable anomerisation of a more complex disaccharide and a glycosyl azide (Figure 26). As shown earlier, both a 2,3- and 3,4-di-*O*-TBS protected glucopyranosides were found considerably more reactive towards $SnCl_4$ promoted anomerisation than reactants where there were only benzoyl groups at these positions. In addition, Wayne Pilgrim[1] also showed that butyl 2,3,4,6-tetra-*O*-methyl-D-glucopyranoside had ~20 fold increase in reactivity compared to the fully benzoylated analogue. Thus, four target modules **67β-70β** were prepared as part of this work and their behaviour to $SnCl_4$ was investigated.

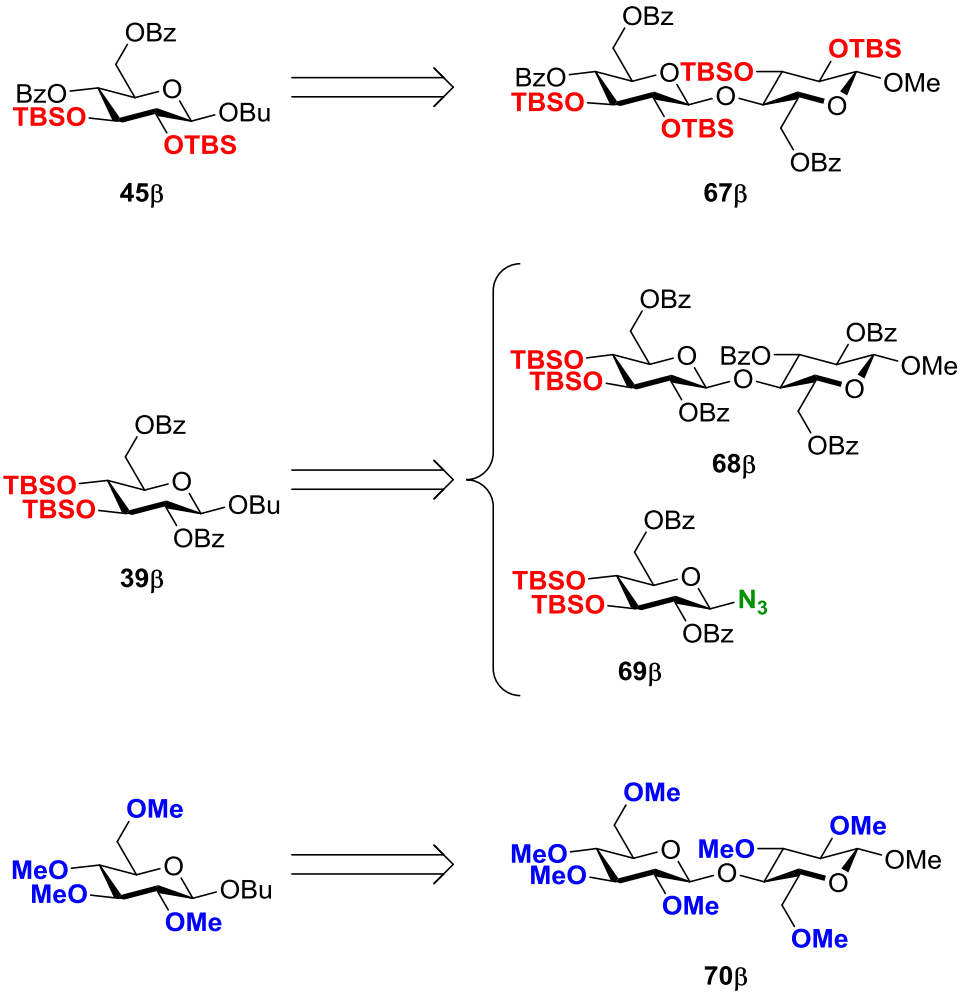


Figure 26 Objective of synthesis of disaccharides and azide glucopyranosides for anomerisation tests.

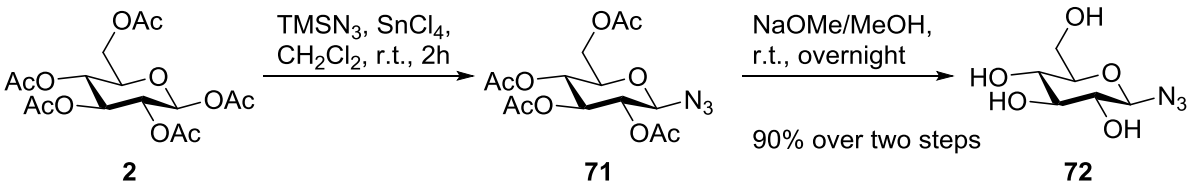
The synthesis started from cellobiose for the disaccharide, and the previously synthesized pentaacetylglucose **2** for the glycosyl azide.

3.1. Results and discussion

3.1.1. Synthesis

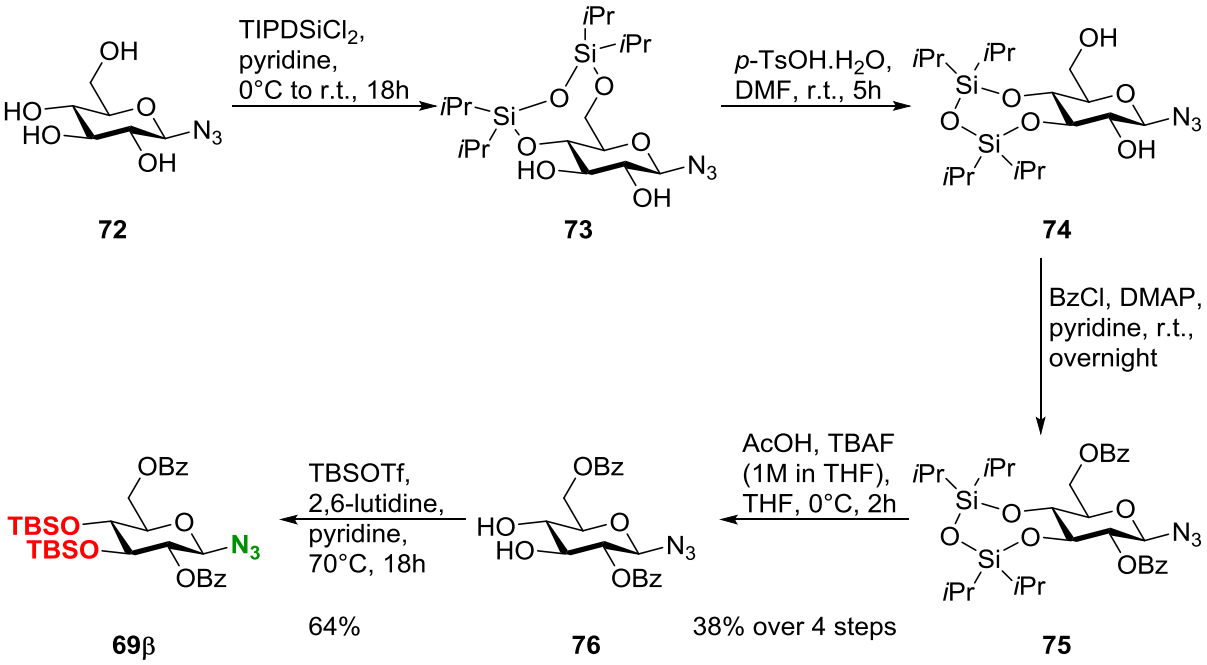
3.1.1.1. Azide glucopyranoside

Firstly, the azide was introduced on the anomeric position, using conditions used by Kéri's group[2] (Scheme 28). Tin(IV) chloride activated the acetyl group at the anomeric position to promote the glycosylation of the azide to obtain **71**. The remaining four acetals were deprotected using sodium methoxide in methanol which led to the glycopyranosyl azide **72** in very good overall yield.



Scheme 28 Obtainment of 72, starting material for the synthesis of compound 69.

The synthesis of **69β** commenced from this precursor. The synthesis of **39β** described earlier had too many steps and was not regioselective, so it was decided to investigate another route (Scheme 29). As described by van Boom et al.[3], treatment of 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane ($TIPDSCl_2$) with pyridine at low temperature gave compound **73** protected in position C-4 and C-6. Without any purification, the protecting group was then rearranged under acidic conditions to give **74**, where the disilyloxy group was located at C-3 and C-4. After benzoylation at C-2 and C-6 followed by removal of silyl protection, purification led to isolation of **76** with an overall yield of 38% over 4 steps from **72**. Finally, protection of positions C-3 and C-4 with TBS groups gave **69β** with a yield of 64% (24% over 5 steps).

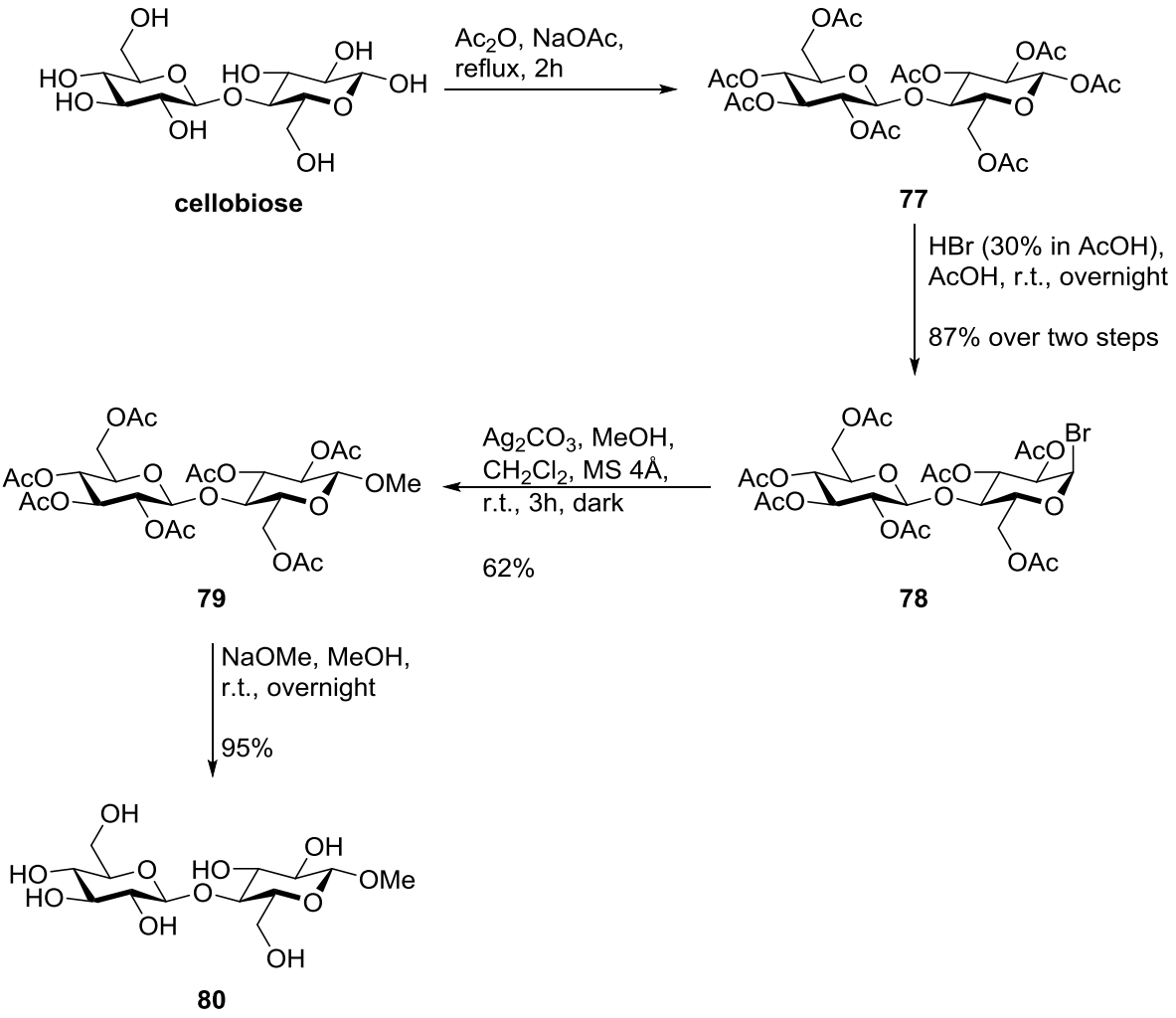


Scheme 29 Synthesis of one target substrate, 69β.

Once **69β** was obtained, the focus was then turned to the synthesis of the disaccharides.

3.1.1.2. *O*-Methyl-β-cellobioside

Three different disaccharides were prepared and all of them contained the methoxy group at the anomeric position (i.e. are methyl cellobiosides). In order to introduce this substituent, cellobiose was first fully acetylated to allow preparation of the glycosyl bromide (Scheme 30). Compound **78** was therefore obtained in a yield of 87% over two steps. Glycosylation of methanol followed by deprotection of the acetyl groups gave desired reactant **80** with an overall yield of 51% over 4 steps. This reaction sequence was first described by Fairweather et al[4].



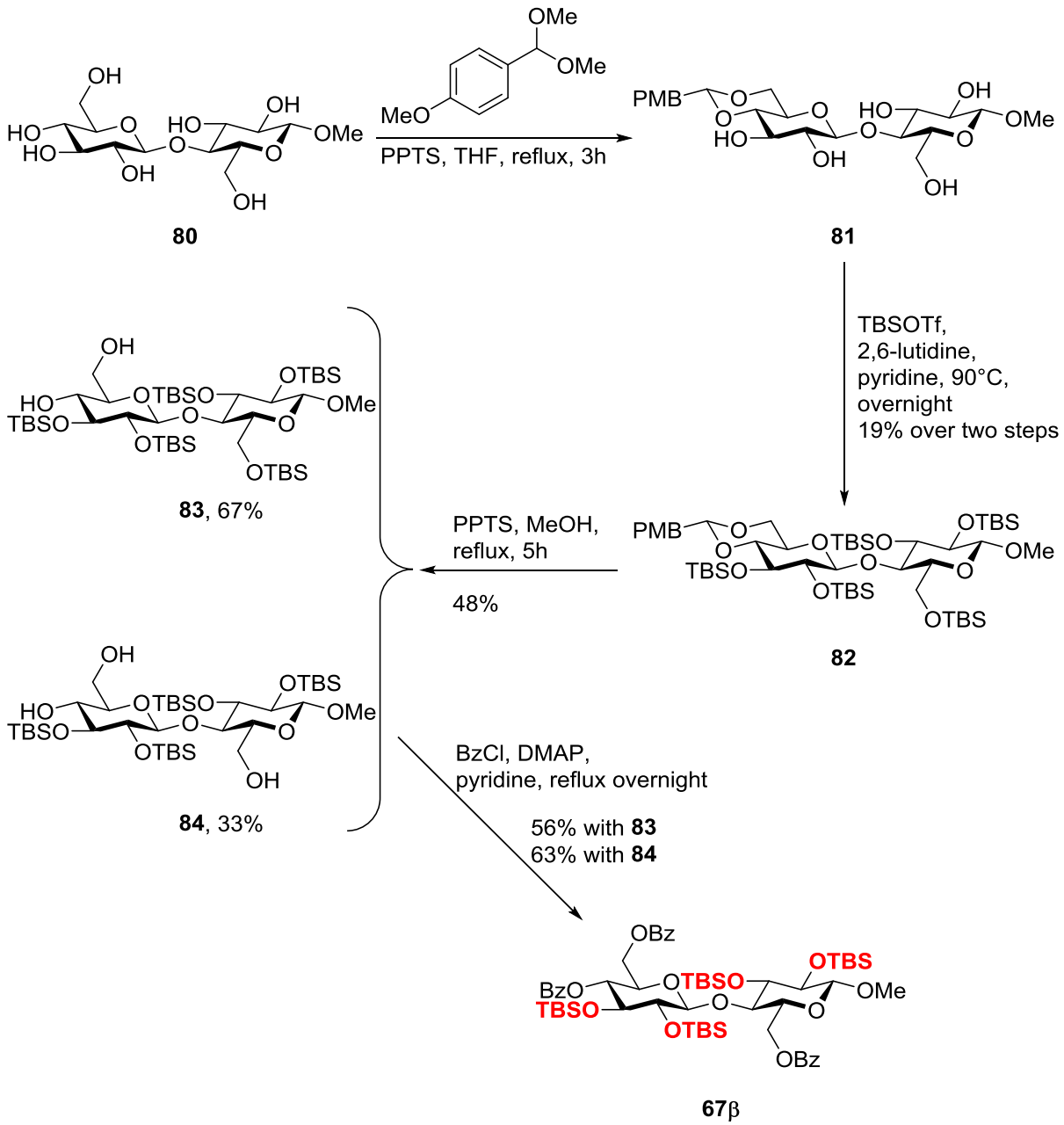
Scheme 30 Synthesis of *O*-methyl-β-cellobioside, starting material of the two targeted substrates.

The preparation of **80** was carried out on 20 g scale.

3.1.1.2.1. Silylated disaccharides

From *O*-methyl-β-cellobioside **80**, the synthesis of **67β** was started (Scheme 31). Positions C-4 and C-6 were protected with *p*-methoxybenzylidene to give **81**. The five remaining positions were then protected with TBS groups, which gave **82** with a yield of 19% over two steps. The low yield was due to the high temperature necessary to introduce five TBS groups onto the disaccharide. Purification also gave issues as the product had to be separated from other TBS derivatives. The use of pyridinium *p*-toluenesulfonate in methanol gave **83** with free OH groups at C-4 and C-6 as well as **84**, which arose from competitive removal of the TBS group at the C-6 position, which is more reactive as it is derived from a primary alcohol. Additionally, the heating used for the protecting group removal increased the likelihood of this side reaction. After reacting independently **83** and **84** with benzoyl chloride in pyridine under reflux, only

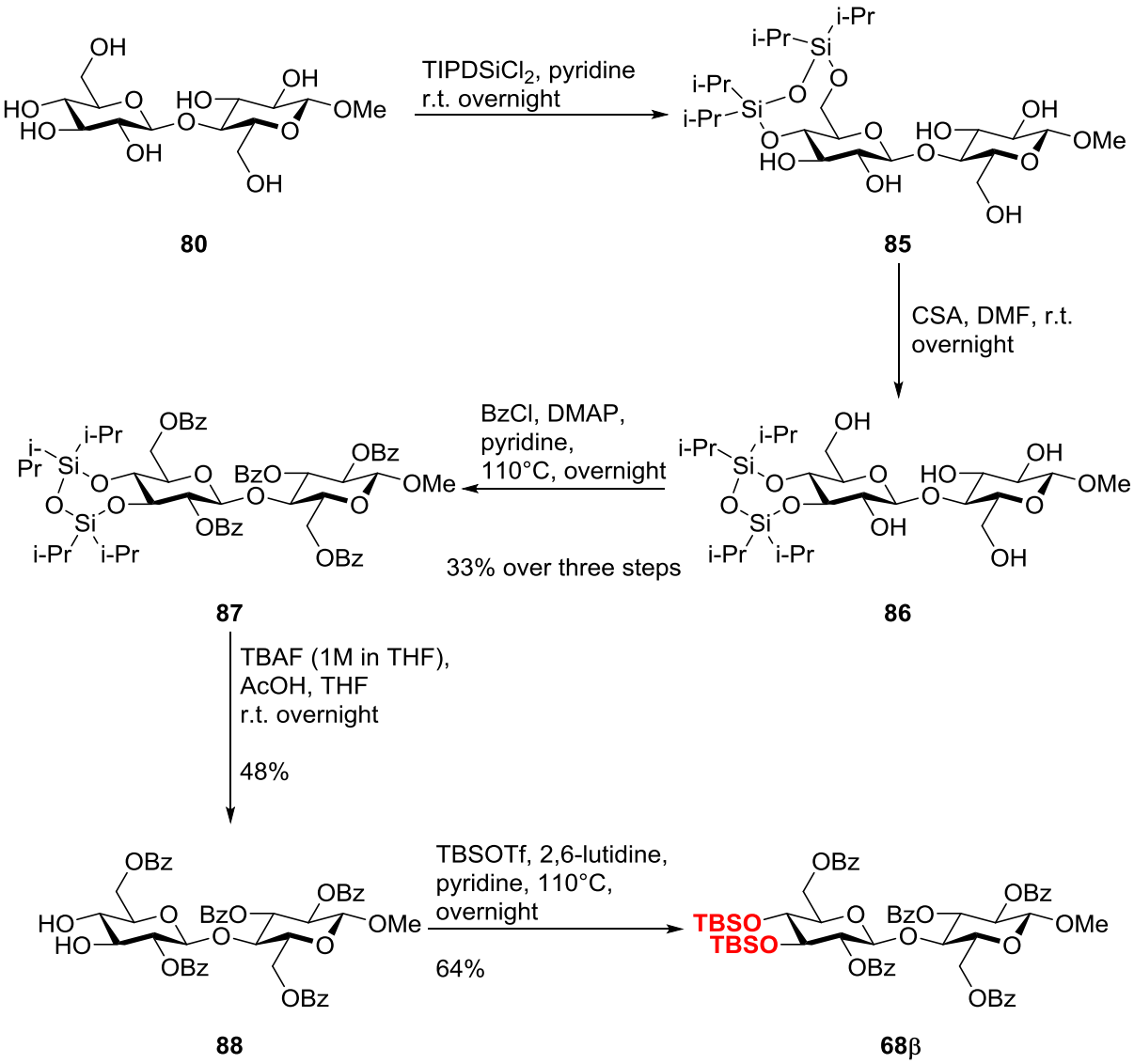
compound **67β** was obtained where the primary TBS ether had been converted to a benzoate ester.



Scheme 31 synthesis of 67β from starting material 80.

Subsequently, synthesis of **68β** was initiated (Scheme 32). The route used was similar to that used for preparing glycosyl azide **69β**. Positions C-3 and C-4 were protected with tetraisopropyldisiloxane through rearrangement of **85** under acidic conditions to give **86**. Without any further purification, the remaining positions were protected with benzoyl groups, which gave **87** with an overall yield of 33% over three steps. The benzoyl groups were stable to the acidic conditions used for the deprotection of the tetraisopropyldisiloxanyl group (TBAF

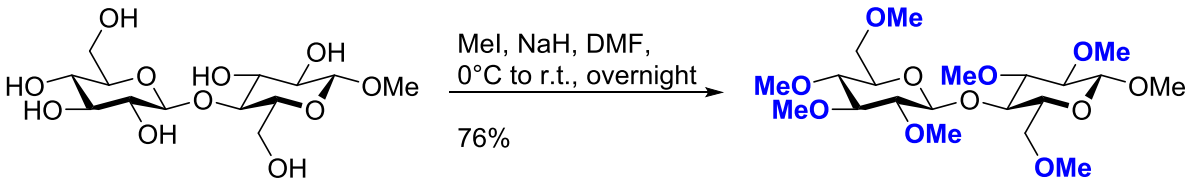
and acetic acid in THF) which gave **88** with a low yield of 48%. The free hydroxyl groups in **88** were then protected with TBS to give **68β** with an overall yield of 10% over 5 steps.



Scheme 32 Synthesis of substrate 68β from starting material 80.

3.1.1.2.2. Disaccharide fully protected with methoxy

Synthesis of **70β** was achieved in one step from **80**, using an excess of methyl iodide with sodium hydride in DMF. The desired compound was obtained in a yield of 76%.



80 **70β**

Scheme 33 Synthesis of substrate 70β from starting material 80.

3.1.2. NMR data

Similarly to what was achieved for the NMR data of the monosaccharides, Table 14 is showing the coupling constant values of the three reactants synthesized for anomerisation study, along with the coupling constants values of **39β** and **45β**, for comparison purposes.

Table 14 Coupling constant of reactants synthesized for anomerisations purposes.

X		TBS (position)	^3J values (Hz)						$^1C_4$ / $^4C_1$
			$H_{1,2}$	$H_{2,3}$	$H_{3,4}$	$H_{4,5}$	$H_{5,6a}$	$H_{5,6b}$	
39β		**2 (3, 4)**	4.8	4.7	4.5	n.d.	4.8	7.1	**$^4C_1$ (49%) + $^1C_4$**
69β		**2 (3, 4)**	6.6	3.9	4.1	4.7	4.9	6.8	**$^3S_1$**
68β	**1**	**-**	7.8	9.4	9.4	9.5	2	4.1	**$^4C_1$**
	2	**2 (3', 4')**	7	3.5	5	3.7	6.2	7	**$^3S_1$**
45β		**2 (2,3)**	6.4	6.4	7.6	7.6	4.3	6.5	**$^4C_1$ (76%) + $^1C_4$**
67β	**1**	**2 (2, 3)**	6.3	6.3	7.9	7.9	3	3.6	**$^4C_1$ (74%) + $^1C_4$**
	2	**2 (2', 3')**	6.7	2.6	4.9	3.5	3.4	6	**$^3S_1$**

It is noticeable that, although the conformation of **39β** is interpreted as being an equilibrium between $^4C_1$ and $^1C_4$, the J values for **69β** and **68β** indicate that different ring conformations are preferred for these compared to **39β**. Indeed, high $J_{1,2}$ values combined with low other coupling constants suggests that the conformation is now a skew (twisted boat). Therefore, the reactivity towards anomerisation and endocyclic cleavage could have been modified due to this

conformational difference. Thus, the size of substituent at the anomeric carbon influences the conformational preference in the carbohydrate.

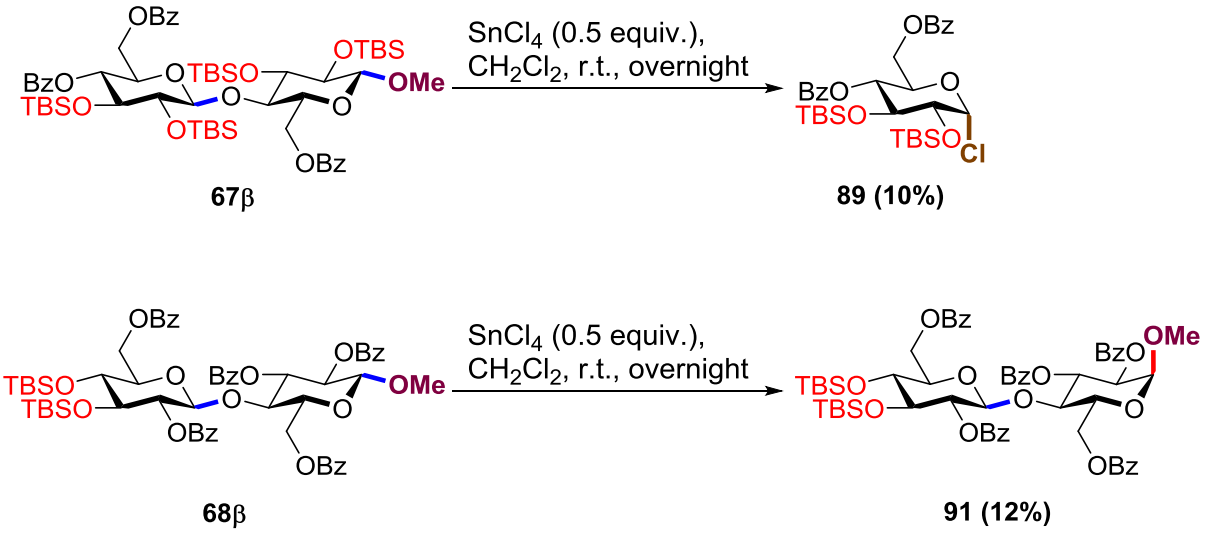
For **67β**, the two monosaccharide were protected each with two TBS at C-2 and C-3. For the monosaccharide connected to the methoxy, the conformation is similar to **45β**, which is an equilibrium between $^4C_1$ and $^1C_4$. However, the monosaccharide where the anomerisation would be interesting has a high $J_{1,2}$ value, and low other coupling constants, which suggests again that the conformation could be a skew (twisted boat) and again is influenced by the larger substituent at the anomeric carbon.

From the coupling constant data, it can be concluded that the nature of the anomeric substituent influences the conformation the saccharides will adopt.

It was then investigated if the change in conformational preference has an impact on the behaviour of the saccharides towards Lewis acids and this is described below.

3.1.3. Behaviour towards $SnCl_4$

Once the reactants were synthesized, they were subjected to Lewis acids. The first reaction was performed by subjecting **67β** using 0.5 equivalent of $SnCl_4$, at room temperature and overnight (Scheme 34). The anomerisation was unsuccessful, and cleavage of the disaccharide happened instead to give **89** with a low yield of 10%, some recovered reactant (5%) and other intractable products. Due to the difficulty to separate the mixture obtained, only **89** was isolated and characterized.

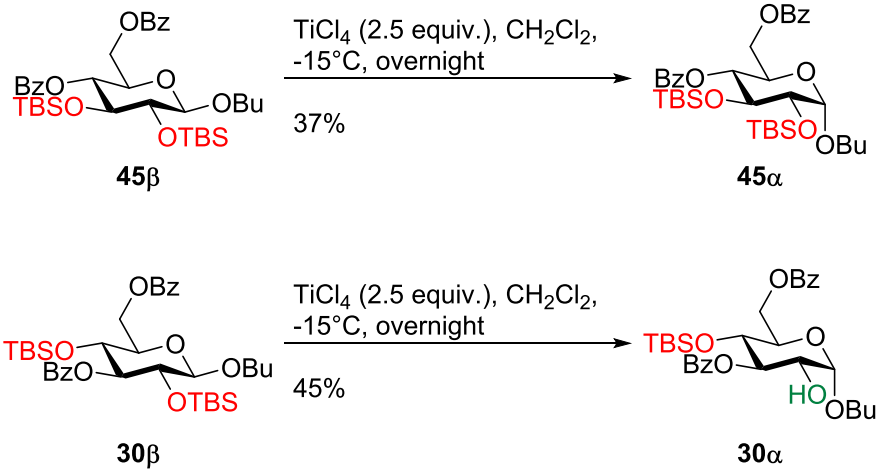


Scheme 34 Reaction tests with $SnCl_4$ (0.5 equiv.) at room temperature overnight.

The same conditions were tried on reactant **68β** and the anomerisation occurred on the anomeric carbon containing the methoxy substituent (methyl glycoside) giving **91** in 12% yield, but no reaction took place at the disaccharide linkage. The reactant was recovered with a yield of 28%. Because of the unsuccessful reaction using $SnCl_4$, it was decided to try reactions with $TiCl_4$.

3.1.4. Behaviour towards $TiCl_4$

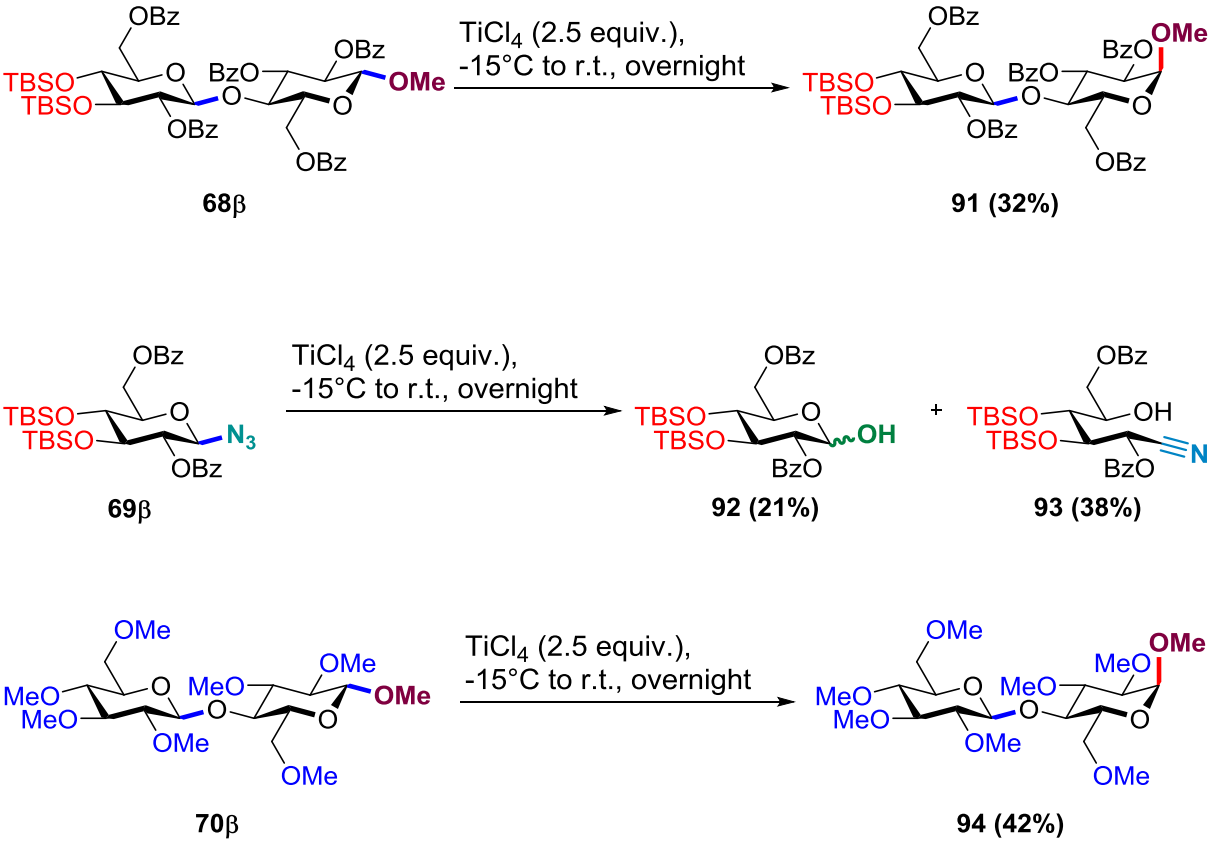
Some preliminary reactions on monosaccharides were tested out to have a better understanding on the behaviour of di-*O*-TBS protected carbohydrates (Scheme 35). From previous results from the group[5], it was decided to lower the reaction temperature to -15 °C.



Scheme 35 Preliminary anomerisation reactions using $TiCl_4$.

Although the yields were low (37-45%), it was due to the reactant being decomposed rather than not reacting or reacting slowly at lower temperature. That the anomerisation product had been observed encouraged efforts to investigate the anomerisation reaction on the desired compounds.

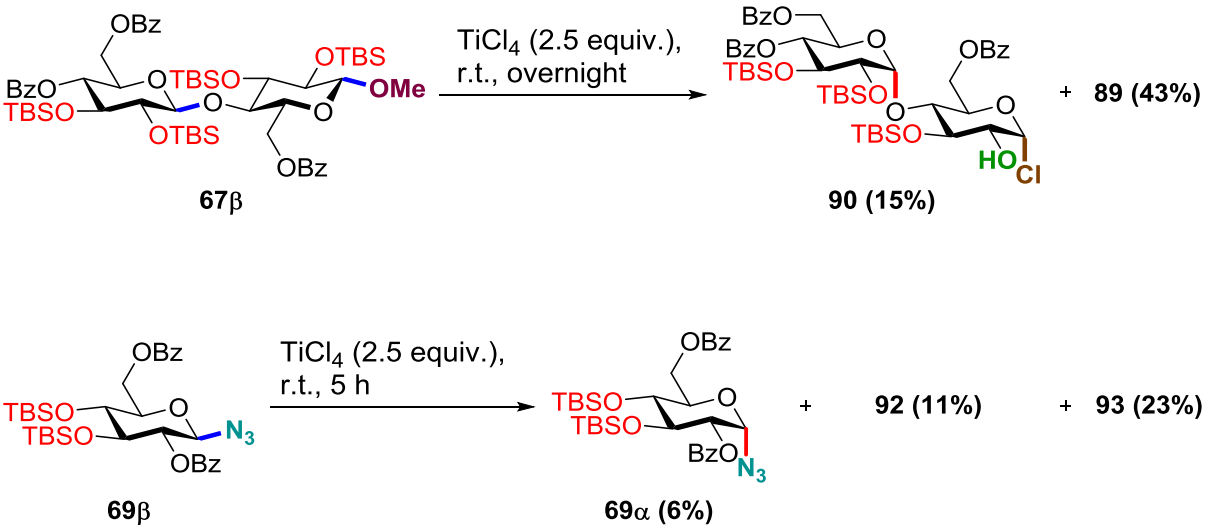
Reactants **68β**, **69β** and **70β** were subjected to 2.5 equivalents of $TiCl_4$ at -15 °C. This mixture was allowed to attain room temperature and the results are summarised in Scheme 36. Similar behaviour was observed for **68β** as when $SnCl_4$ was used, although a higher yield was obtained for **91** (32% instead of 12%). The reactant was also recovered (11%), and other side products were obtained but these could not be characterised due to the difficulty of separating them. For reactant **70β**, anomerisation was successful at the anomeric carbon containing the methoxy substituent (i.e. the methyl glycoside), but no reaction took place at the disaccharide linkage. No reactant was recovered, however it was suspected that there was some cleavage into two monosaccharides, although the purification did not give materials that could be characterized. The products obtained from the reaction of azide **69β** were the hemi-acetal **92** and nitrile **93**.



Scheme 36 Behaviour towards $TiCl_4$ (2.5 equiv.) from -15 °C to room temperature overnight.

These results suggested that while the methyl glycoside reacted, as would have been expected, the di-*O*-TBS protecting group strategy was not able to increase the reactivity sufficiently to get anomerisation or even efficient cleavage of the disaccharide linkage.

Another reaction was carried out with **67β**, using 2.5 equivalent of $TiCl_4$, which was stirred at room temperature for ~ 16 h (Scheme 37). After purification, two products were identified. One was the same monosaccharide **89** obtained previously but on this occasion, it was isolated in improved yield (43%). The second product obtained, on the other hand, was the anomerised disaccharide **90** where glycosyl chloride formation had also occurred as did regioselective removal of the TBS group at C-2. The anomerisation reaction was re-tried using **69β** using 2.5 equivalent of $TiCl_4$ at room temperature. This time the reaction time was diminished to just 5 h. After purification, three different products were obtained. Two of them were the same as obtained previously, **92** and **93** when the reaction was left overnight. The third compound obtained was the anomerisation product **69α**. The isolation of the nitrile **93** is consistent with endocyclic cleavage.



Scheme 37 Successful anomerisations albeit in very low yields.

3.2. General conclusion on the anomerisation reaction

Rates of anomerisation were determined on *O*-butyl glycopyranosyl substrates (Chapter 2) containing silyl protecting groups. Two disilylated glucopyranosides stood out in having a >70 fold increase in reactivity to $SnCl_4$ compared to the fully benzoylated substrate. From these results, a disaccharide and glucopyranosyl azide were protected similarly, and their behaviour to Lewis acids investigated. Whereas anomerisation of the butyl glycosides were relatively successful, the reactions were less productive for the disaccharides. Although, the use of $TiCl_4$

at room temperature overnight resulted in the anomerisation of the anomeric carbon linking the two monosaccharides, albeit in low yield. The anomerisation of the glycosyl azide proceeded also in low yield but did also yield a nitrile product, providing evidence for the endocyclic cleavage pathway in the case of the glycosyl azide. The relative success in these studied may be due to the effect of the aglycon on pyranose ring conformation, as it appears the silylated pyranose adopts a different conformational preference when comparing the butyl glycoside and the disaccharide. Thus, more studies would be required to identify strategies to increase yields of anomerisation reactions from disaccharides derived from cellobiose using Lewis acids.

3.3. References

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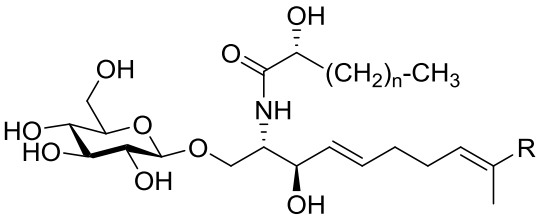
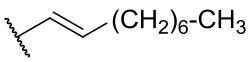
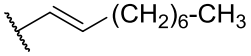
Chapter 4 Synthesis of a simplexide mimetic with an S-disaccharide

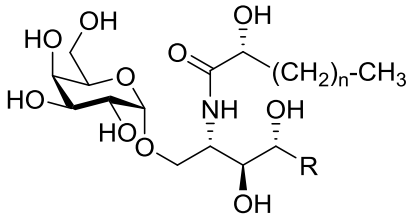
4.1. Introduction to simplexides

The wide diversity of the marine environment is an incredible source of interesting natural products with specific bioactivities[1]. In particular, marine sponges have been of a huge interest for pharmaceutical discoveries[2-5]. The sponges have a relatively unprotected body, are sessile but yet they are still surviving in all the danger that the sea abounds. Therefore, their defence mechanism lies in the production and presence of secondary metabolites[6]. Among them, glycolipids (i.e. monosaccharides or polysaccharides with a lipid on the glycosidic linkage) are of great interest for pharmaceutical discoveries[7-10].

For instance, a number of agelasphins were extracted and isolated from the marine sponge Agelas Mauritanus[11] (Figure 27).



	n	R
Agelasphin-**10**	21	
Agelasphin-**12**	22	



	n	R
Agelasphin-**7a**	21	$-(CH_2)_{11}-CH_3$
Agelasphin-**7b-1**	20	$-(CH_2)_{10}-CH(CH_3)-C_2H_5$ **and/or** $-(CH_2)_{11}-CH(CH_3)_2$
Agelasphin-**7b-2**	21	$-(CH_2)_9-CH(CH_3)-C_2H_5$ **and/or** $-(CH_2)_{10}-CH(CH_3)_2$
Agelasphin-**9a**	21	$-(CH_2)_{12}-CH_3$
Agelasphin-**9b**	21	$-(CH_2)_{11}-CH(CH_3)_2$
Agelasphin-**11**	21	$-(CH_2)_{11}-CH(CH_3)-C_2H_5$
Agelasphin-**13**	22	$-(CH_2)_{11}-CH(CH_3)-C_2H_5$

Figure 27 Agelasphins isolated from Agelas Mauritanus.

These molecules are part of the glycosphingolipids class of glycolipids, as they contain a sphingolipid metabolite. In this case, the sphingosine is linked with a fatty acid, and this lipid combination is called a ceramide.

Two of the Agelasphins characterized had a glucose β-linked with a ceramide (β-GluCer) (Agelasphins **10** and **12**). The others have a galactose α-linked with a ceramide (α-GalCer) (Agelasphins **7a**, **7b**, **9a**, **9b**, **11** and **13**). It was found that the α-GalCer type showed better antitumor activities than β-GluCer. A study by Motoki et al refined the research by postulating that these molecules were activating the immune system[12], classifying them in the Biological Response Modifier (BRM)[13] type of antitumor agent (as opposed to the chemotherapeutic agent type). Because of these positive results, the total synthesis of many mimetics of natural compounds was achieved (Figure 28), which were brilliantly combined in a review by Tashiro et al[14], and their biological activity reported to be promising.

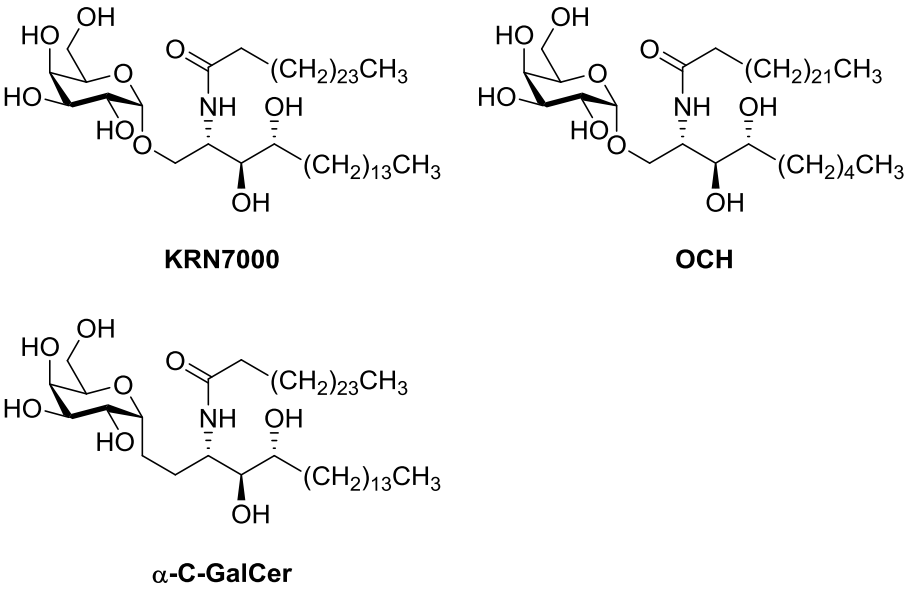


Figure 28 Selected mimetics of Agelasphins that were synthesized[12, 15-16].

A simple way to describe how such glycolipids can activate Natural Killer T cells (NKTs) is shown in Figure 29[17].

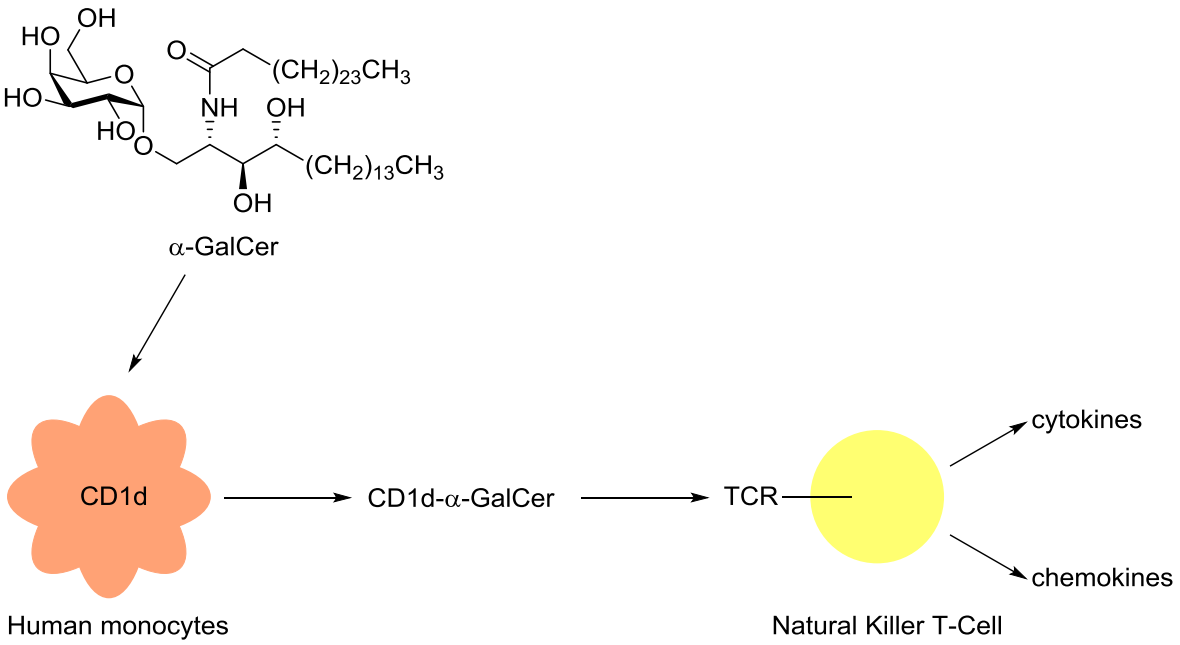


Figure 29 α-GalCer's mode of activation of NKT cells.

The molecules enter the monocytes and then bind to CD1d, an antigen-presenting molecule. CD1d presents the molecule to the T Cell Receptor (TCR), which recognize it at very high affinity. It then activates the NKTs, which subsequently release chemokines and cytokines. The latter have an important role influencing immune responses and pathogenic processes[18-19].

The α-S-GalCer version of agelasphins was also envisaged[20-22], as sulfur atoms have the same valence electron number as oxygen atoms. Sulfur linked glycolipids are also more stable under enzymatic reactions and chemical degradation[23-24] (Figure 30).

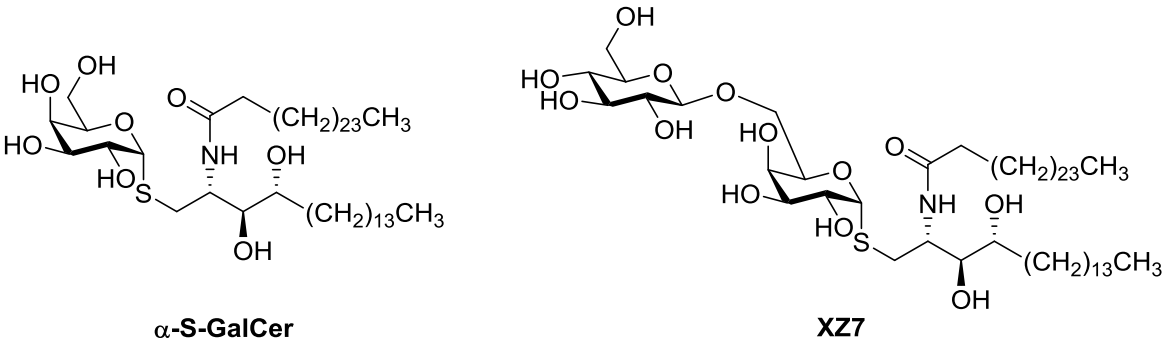


Figure 30 Thioglycoside analogue of KRN7000 synthesized.

Their biological activity was then studied, and it was shown that even though **α-S-GalCer** did not stimulate iNKT cells, Zhu's compound **XZ7** did stimulate cytokine production[25], although less potently than the non sulfured **α-GalCer**.

Recently, another class of glycolipids was isolated from the sponge *Plakortis simplex*[1]. This class was called simplexide and differs from other glycolipids by the absence of functional groups on the lipid chain. The natural simplexide is a mixture of 5 glycolipids differing by the alkyl chain's length and the presence or not of ramifications (Figure 31).

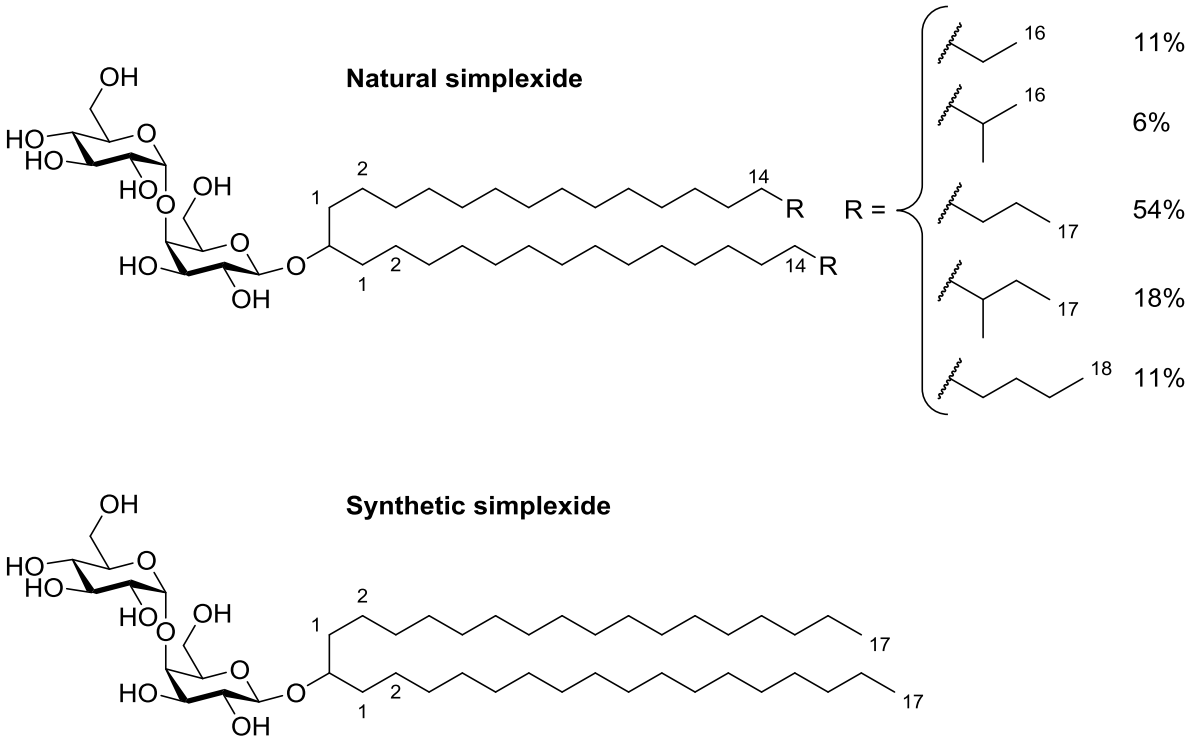


Figure 31 Structure of natural simplexides and their respective percentage in the sponge.

Biological studies on this new class of glycolipids found that it induced expression and release of cytokines and chemokines from human monocytes[26]. Further investigation indicated that this production is CD1d dependent. It could therefore be hypothesized that simplexides activate the release of cytokines the same way α-GalCer are. Loffredo's group also compared this promising bioactivity with a synthetic simplexide shown in Figure 31, and found similar results, although the solubility in DMSO was lowered, and the quantity of each cytokines studied released was slightly decreased.

4.2. Objective of the project

The research described in this chapter was focused on synthesizing one analogue of simplexide, and compare its bioactivity with the natural and previously synthesized one. The mimetic would contain one less carbon atom in both ends of the lipid chains, and would possess a sulfur atom instead of an oxygen in the glycosidic link between the two monosaccharide, as shown

in Figure 32. This, way it was hoped that the increased stability of the molecule for enzymatic cleavage will increase the amount of cytokines released by the NKT cells.

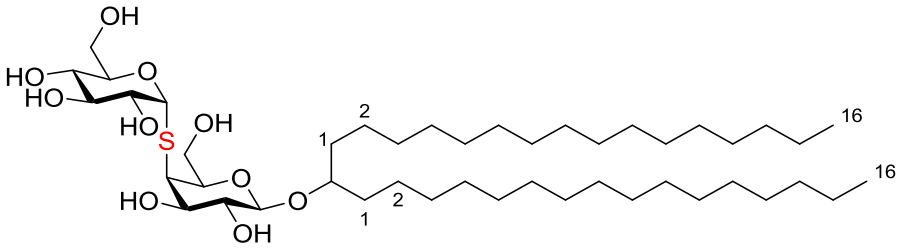
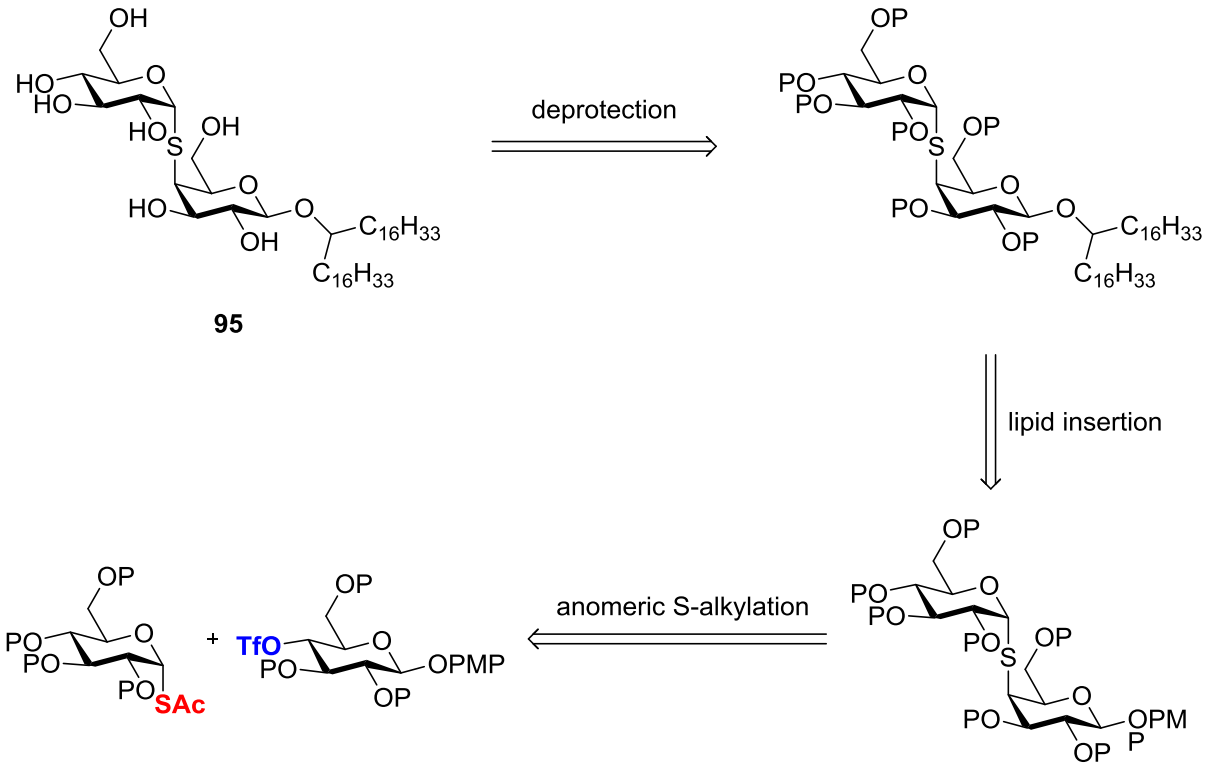


Figure 32 Target analogue to synthesize.

4.3. Design of the target compound

4.3.1. Retrosynthesis approach

The plan for the synthesis of the target compound is to start with an S-glycoside bond formation between two monosaccharide derivatives, a glycosyl thiol and a triflate (Scheme 38). Once the disaccharide is synthesized, this would be followed by glycosylation of an alcohol with a lipid chain. Subsequent deprotection would give the desired compound.



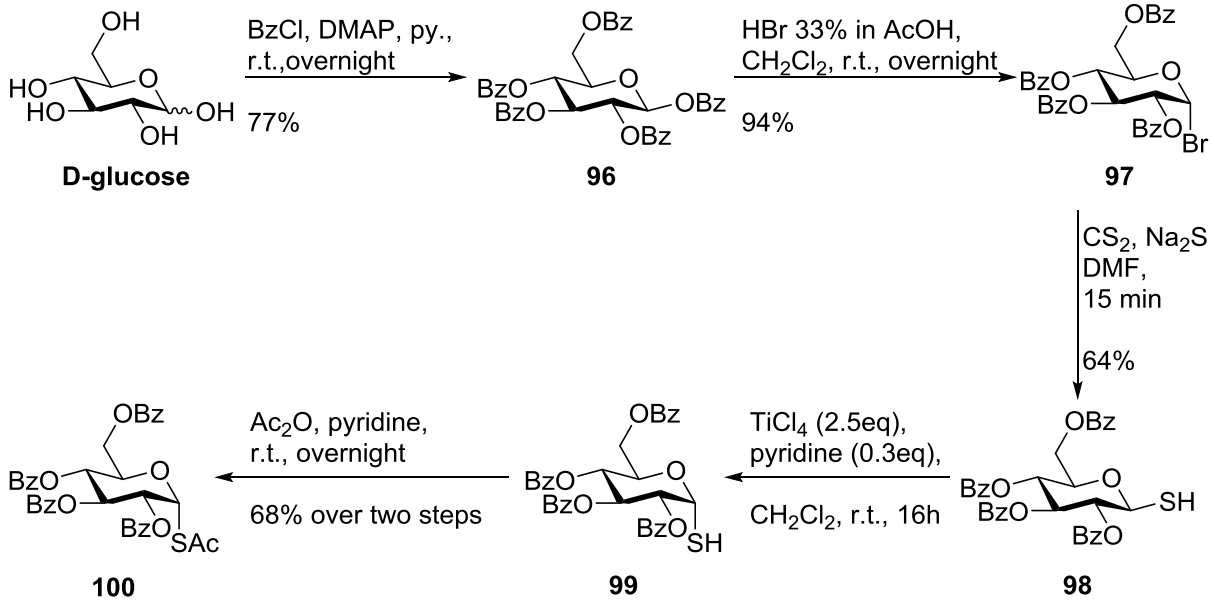
Scheme 38 Retrosynthesis for the target compound (P = protecting groups).

The synthesis of the thio-glucoside precursor would involve an anomerisation reaction, to obtain the required α-anomer. The S-glycoside bond synthesis was proposed to involve an SN_2 between the thioacetate (red) and the triflate (blue), leading to a change of configuration on C-4.

4.3.2. Synthesis

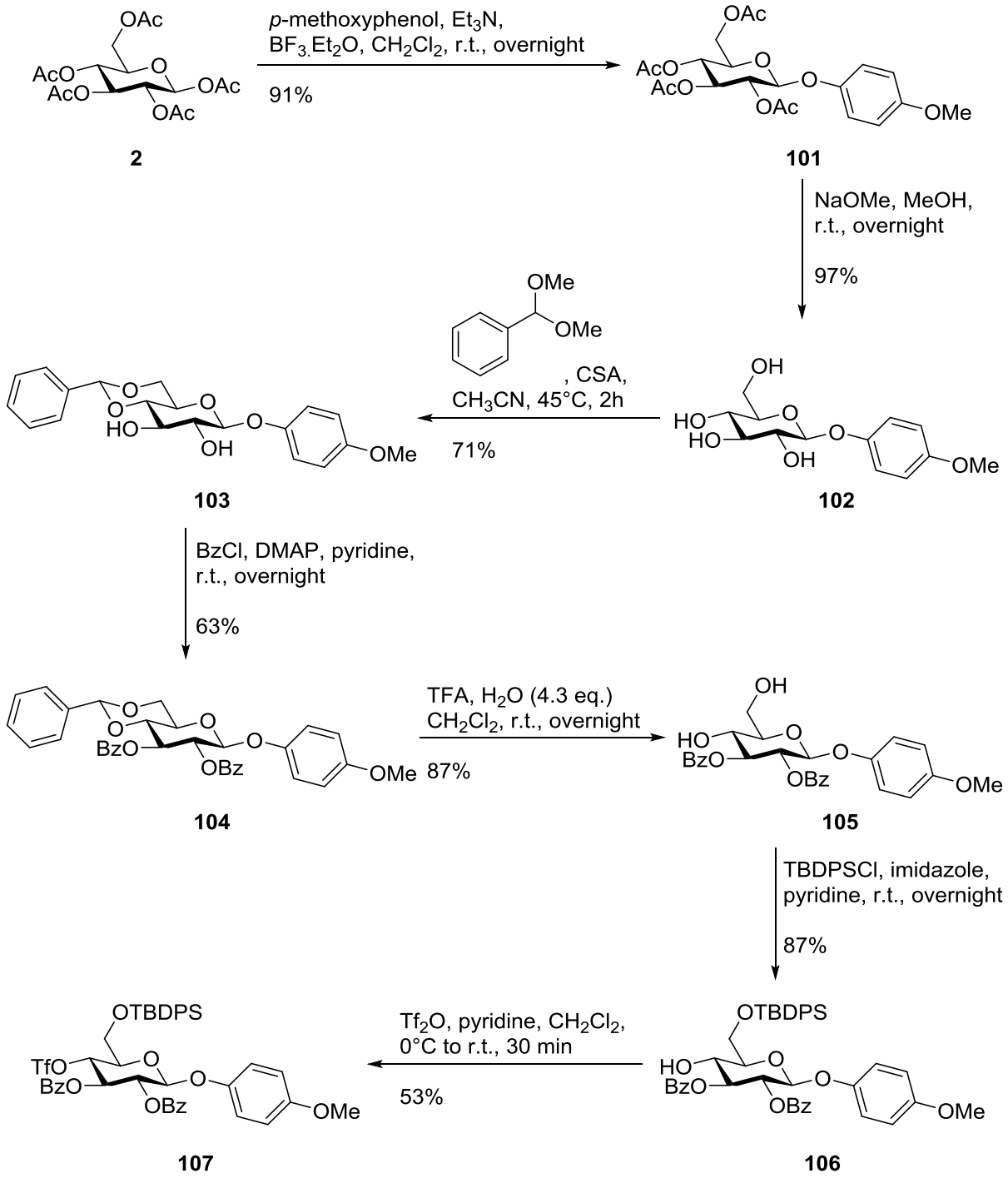
4.3.2.1. Monosaccharides

The synthesis of the thioglycoside started from the fully benzoylation of D-glucose to give β-D-glucose pentabenzoate **96** (Scheme 39). The glucosyl bromide was next formed to allow the formation of the glucosyl thiol using Jana's method[27], which gave **98** in a moderate yield ($J_{1,2}$ = 9.6 Hz). This method uses carbon disulphide and sodium sulphide nonahydrate in dimethylformamide and is one less step compared to the usual method involving an SN_2 of glycosyl halides or acetate with thiourea or thioacetate, followed by hydrolysis or de-acetylation[28]. The anomerisation was then performed using Murphy group's optimized conditions[29], with $TiCl_4$ in the presence of 0.3 equivalent of pyridine to give **99** ($J_{1,2}$ = 5.6 Hz). As Shane O'Sullivan had problems trying to get isolated and clean α-product[30], it was decided to acetylate[31] the thiol to enable the necessary purification and give clean compound **100** in an overall yield of 31% over 5 steps. The preparation of this reactant was scaled up to give 10 g to enable the numerous reactions to be carried out.



Scheme 39 Synthesis of 100.

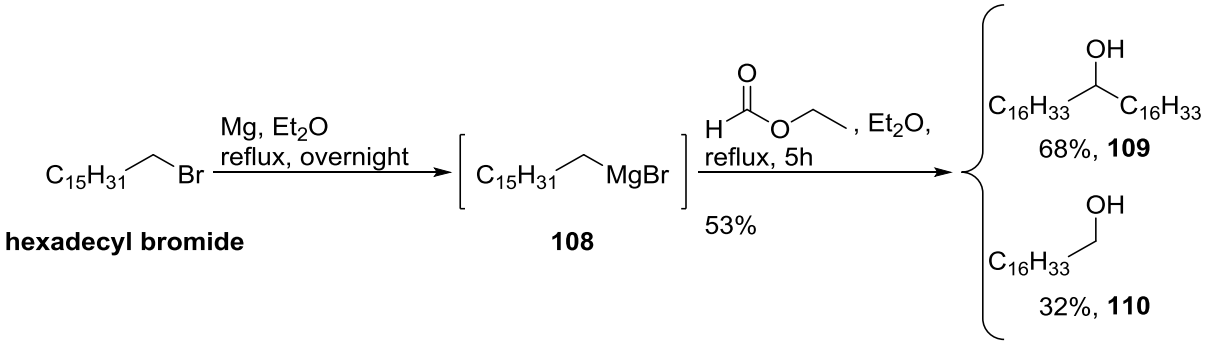
Next, the synthesis of the triflate **107** was achieved (Scheme 40), starting from glucose pentaacetate **2**. The anomeric position was protected as the *p*-methoxyphenyl glycoside, and the rest of the acetyl groups were deprotected to give **102**. This compound was then protected selectively on C-4 and C-6 with benzylidene to give **103**, which allowed the selective protection of C-2 and C-3 with benzoyl groups. Subsequent deprotection of the benzylidene gave **105**, whose primary alcohol was protected with a bulky silyl group, TBDPS, which gave **106** with a yield of 30% over 6 steps. This preparative sequence was scaled up to 10 g, to allow the successive reactions to give the target compound. The triflate **107** was synthesized just before the glycoside forming reaction, as it was found to be not stable for any prolonged period.



Scheme 40 Synthesis of the glycosyl acceptor 107.

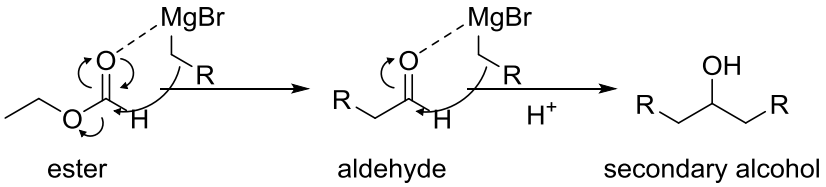
4.3.2.2. Lipid synthesis

The lipid was synthesized using a Grignard reaction (Scheme 41). Hexadecyl bromide was added to a suspension of magnesium in diethyl ether, and the mixture was stirred at reflux overnight to form hexadecyl magnesium bromide **108**. In the same pot, ethyl formate was added at room temperature, and the mixture was stirred at reflux for 5 h. After working up the reaction and separation, it was discovered that two compounds were obtained - the desired compound **109**, and the side product **110**, which is a primary alcohol.



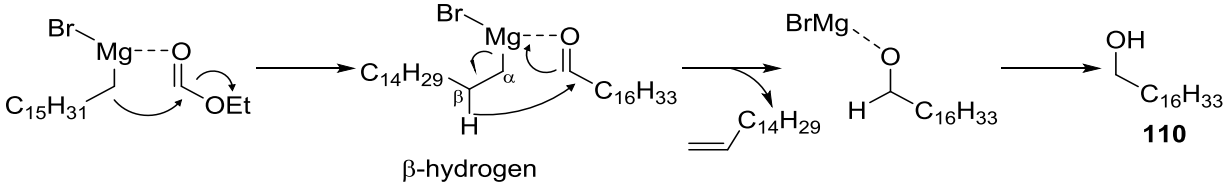
Scheme 41 Lipid synthesis.

The formation of **109** comes from the addition of two of the alkyl magnesium bromide reagents with the formate ester. The first addition forms an aldehyde, which then reacts a second time to form the secondary alcohol (Scheme 42).



Scheme 42 Mechanism of the Grignard reaction with the formate ester.

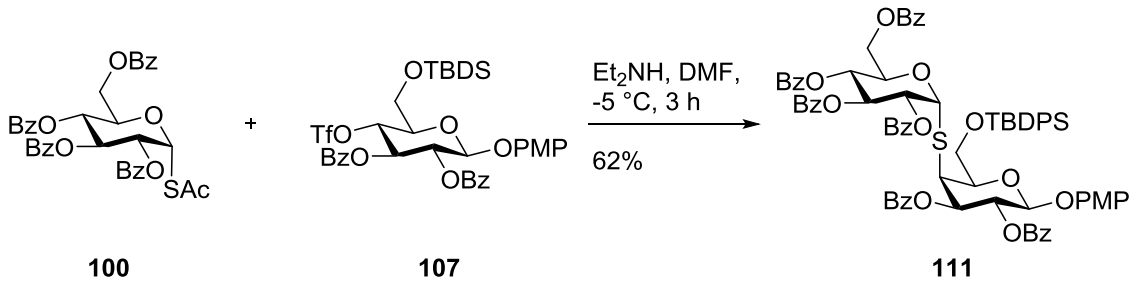
The side reaction that produces the primary alcohol is due to the fact that the alkyl magnesium bromide contains a β-hydrogen (Scheme 6). There is therefore a hydride transfer, and a double bond formation, reducing the aldehyde into a primary alcohol, as shown in Scheme 43[32].



Scheme 43 Side reaction that explains 110.

4.3.2.3. Glycosylation

Once the two monosaccharide precursors were synthesized, the glycosylation between them could be envisaged (Scheme 44). This is not a classical glycosylation, as usually the anomeric position contains the leaving group that would be substituted by the alcohol acceptor. In this case, a sulfur atom is needed on the anomeric position, which induce inversion of the roles. The conditions used were the same used by Feng et al.[33], that use it to invert the configuration of glucose derivatives to galactose derivatives.

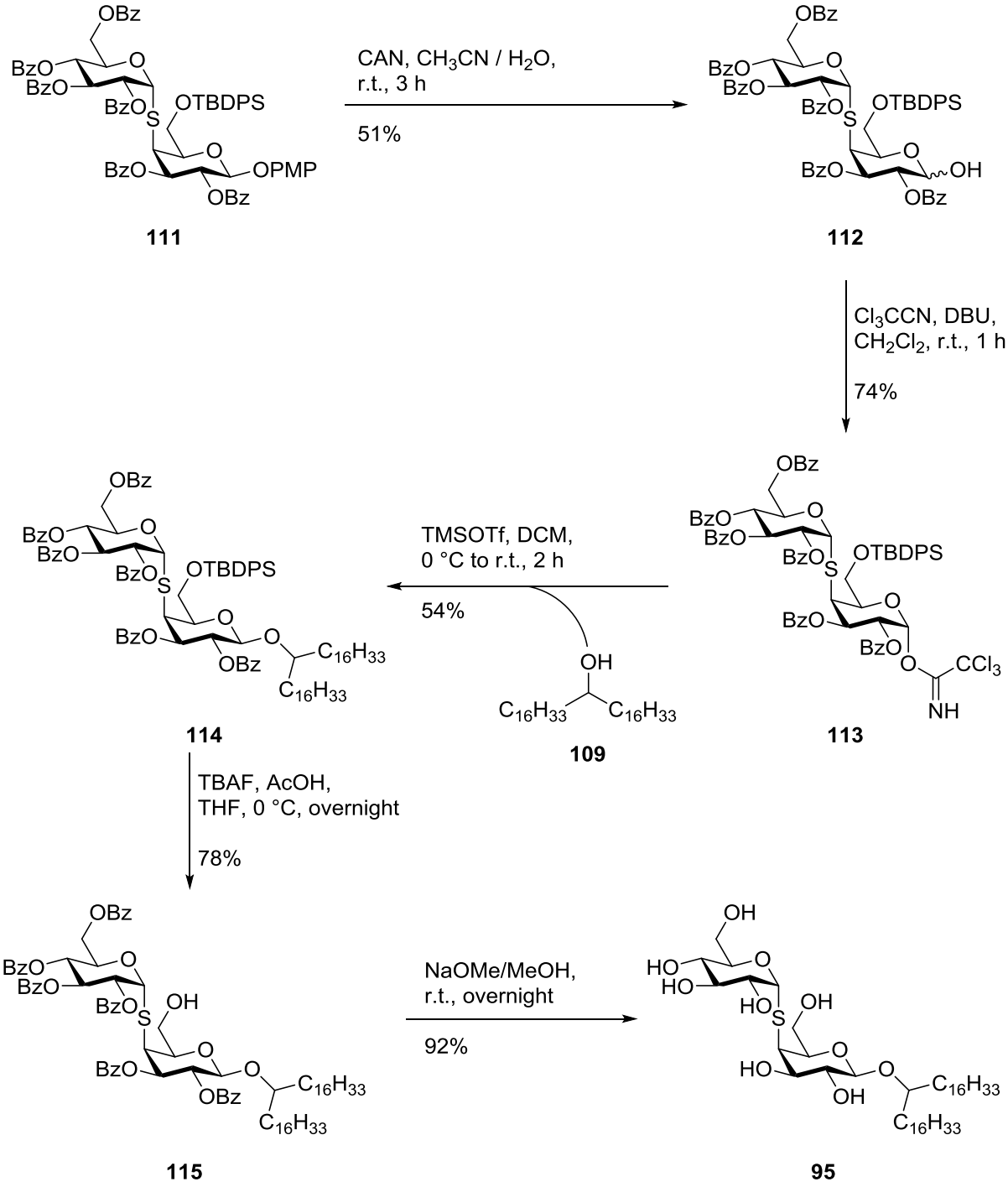


100 **107** **111**

Scheme 44 Glycosylation reaction.

The same inversion was observed in this case, and the desired compound **111** was obtained in moderate yields.

The *p*-methoxyphenyl glycoside was then hydrolysed in the presence of CAN and water, to allow the formation of the trichloroacetimidate to give **113** (Scheme 45). This allowed the glycosylation of the lipid alcohol **109** with **113** to give **114** in 54% yield. Successive removal of the silyl group and the benzoyl groups gave the target compound **95** in 72 % yield over two steps.

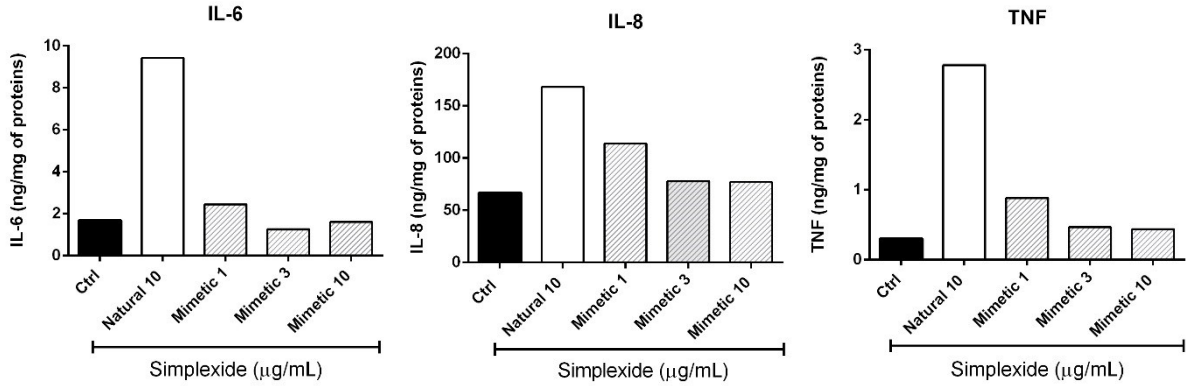


Scheme 45 Lipid glycosylation and deprotection.

4.4. Biological results

This compound was sent to collaborating laboratory at the University of Naples Federico II in Italy. It was tested there for its ability to release three cytokines, IL-6, IL-8 and TNF. It was compared with the natural simplexide ability to release the same cytokines.

For biological tests, peripheral blood mononuclear cells (PBMC) were incubated for 6 hours with target compound **95** at different concentrations (1, 3 and 10 μg/L). After that time, the amount of three different cytokines (IL-6, IL-8 and TNF) released was measured. The results are shown in three graphs (Graph 7).



Graph 7 Release of cytokines by the natural simplexide and its mimetic 95.

From the results shown above, it was found that, in the dose response study, increasing the quantity of mimetics did not increase the amount of cytokines released by the cells. Therefore, it can be concluded that the mimetics did not have biological activities, at least not the one that it was expected to have.

4.5. Conclusion

In this chapter the synthesis of a mimetic of simplexide, containing a sulfur atom on the glycosidic linkage located in between the two monosaccharides, was achieved. Unfortunately, biological evaluation was not satisfactory, as increasing the concentration of compound incubated did not increase the amount of cytokines released.

This research project was consequently expanded in the synthesis of many more mimetics in order to look for biologically active synthetic compounds.

4.6. References

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Chapter 5 Synthesis of mimetics of simplexides based on changing the lipid moiety

5.1. Objective of the project

For this research described in this chapter, it was decided to prepare a number of different analogues of simplexide as summarised in Figure 33. It was proposed to compare having a sulfur atom instead of an oxygen at the linkage between the galactose (Gal) residue and the lipid and to vary the stereochemistry at this position. In addition, it was proposed to simplify the structure of the lipid also.

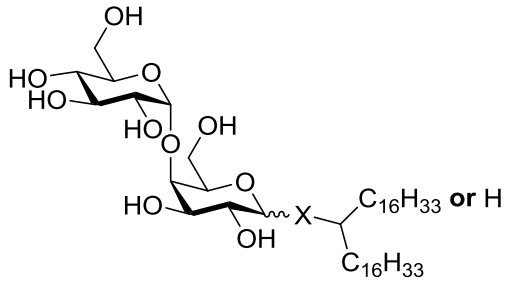


Figure 33 Target simplexide mimetics for synthesis where X = O or S.

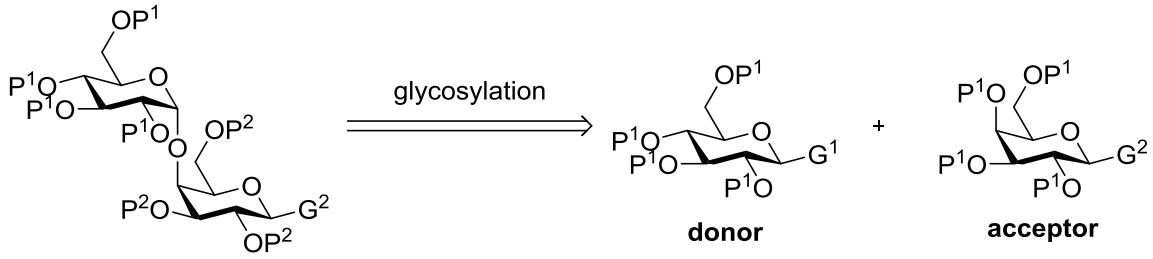
It was proposed to also synthesize one of the natural simplexides, not prepared in pure form previously.

5.2. Synthesis

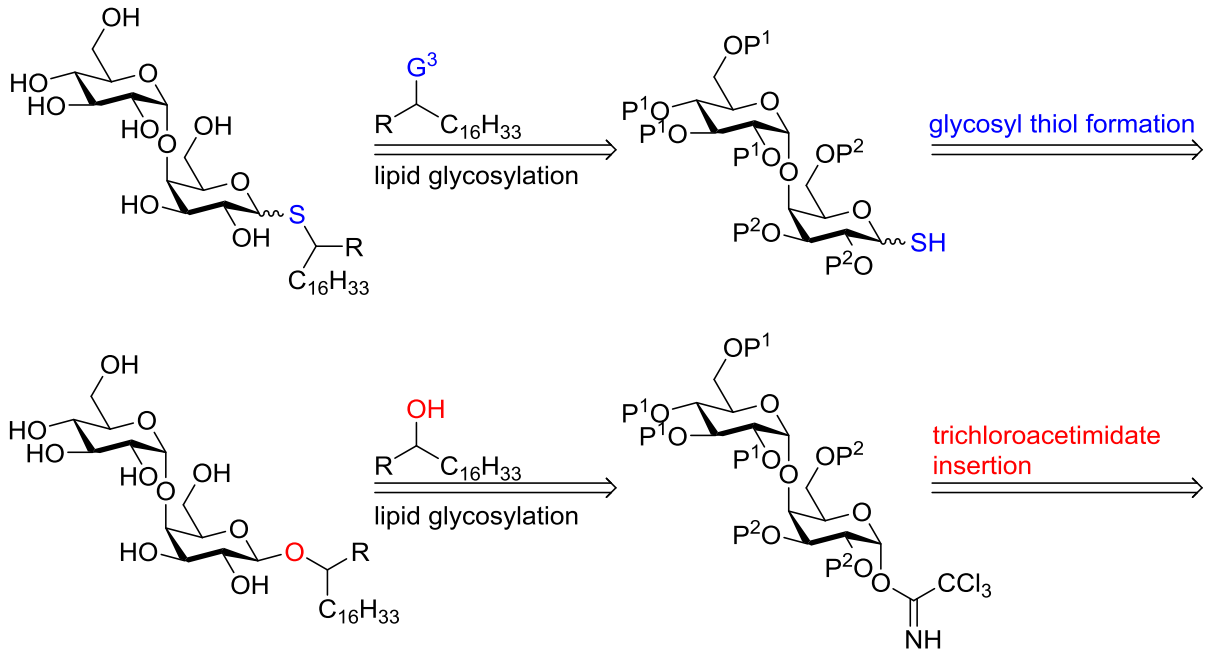
5.2.1. Retrosynthetic approach

The target compounds were envisaged to be synthesized from the same two monosaccharides (Scheme 46). The glucosyl donor would incorporate protecting groups that facilitate α-*O*-glycosylation.

From then, the lipid glycosylation would be performed (Scheme 47). This was envisaged to be formed via the trichloroacetimidate for the *O*-glycosides. For the synthesis of the S-glycosides it was envisaged to incorporate a thiol on the anomeric position as indicated in Chapter 4. From this, the nucleophile substitution was envisaged to incorporate the lipid chain, and thus obtain mimetics of simplexide containing a sulfur atom between the galactose residue and the lipid.



Scheme 46 Retrosynthesis for the α-*O*-glycosylation of two monosaccharides. P^1 and P^2 are protecting groups, G^1 allows the glycosylation between the two monosaccharides, G^2 is easily deprotected.



Scheme 47 Retrosynthetic approach for the synthesis of *O*- and *S*- simplexides analogues. G^3 allows the nucleophile substitution with the glycosyl thiol. R = H or $C_{16}H_{33}$.

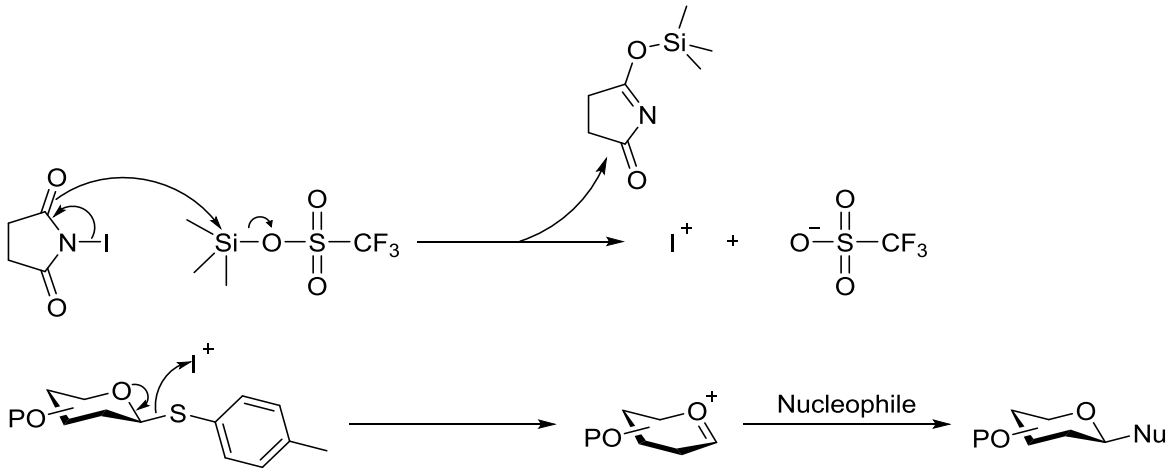
5.2.2. Synthesis

5.2.2.1. Monosaccharide synthesis

5.2.2.1.1. Difficulties encountered

Following the same pathway as to synthesize the first analogue, the anomeric positions of the two monosaccharide precursors were initially protected as their *p*-methoxyphenyl glycosides. However, hydrolysis of this glycoside was later found to give a very low yield, which was not considered suitable when multiple reaction needed to be performed subsequently.

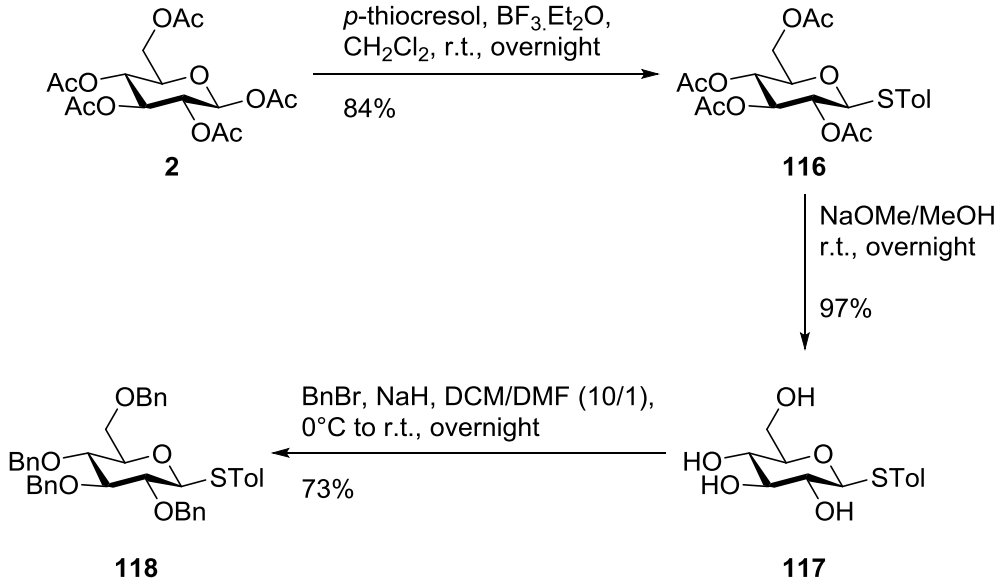
The solution to this problem was found by using the *p*-thiocresol group, where direct glycosylation can be made possible using N-iodosuccinimide and TMSOTf as activators as shown in Scheme 48.



Scheme 48 Activation of *p*-thiocresol through NIS and TMSOTf.

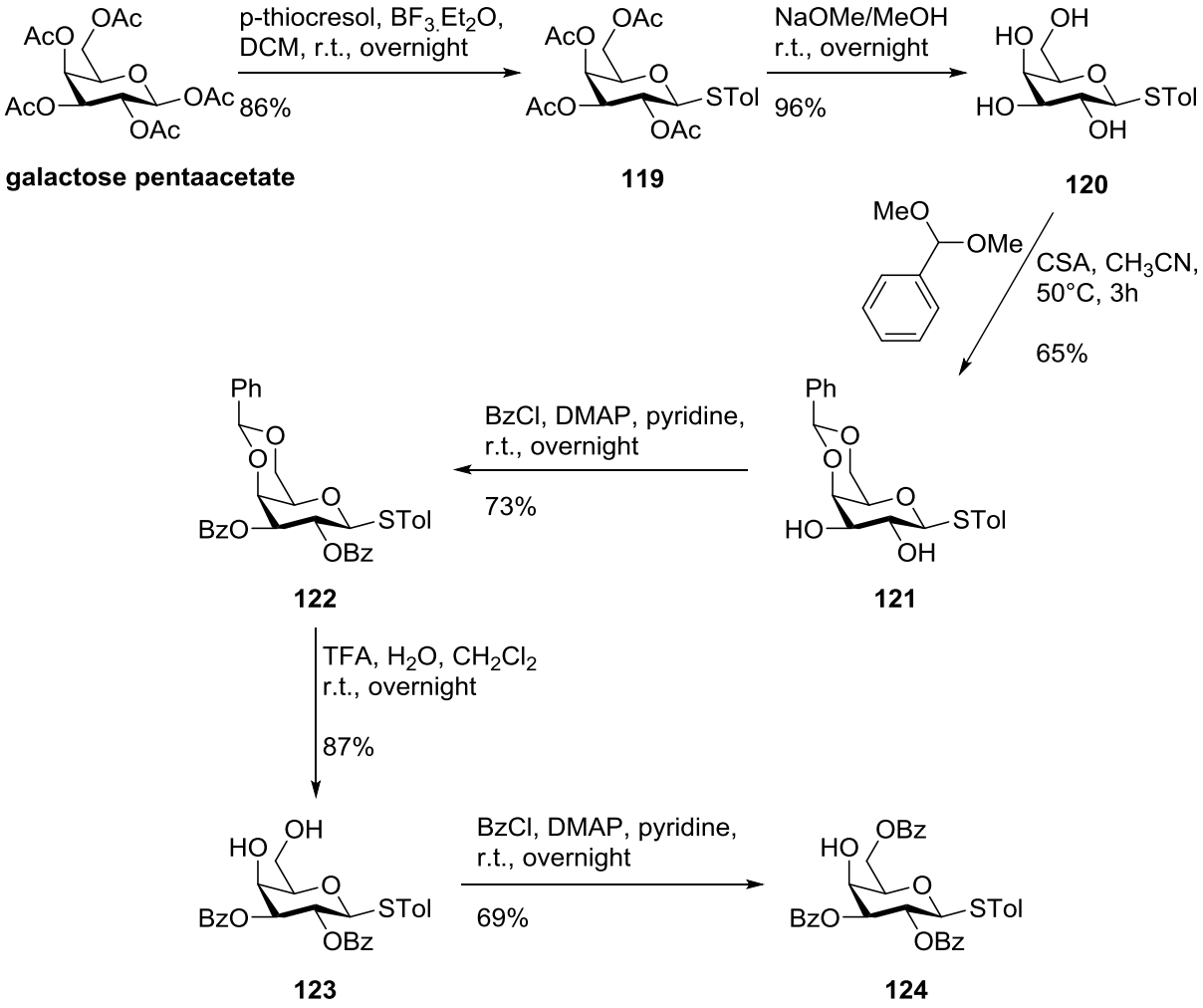
5.2.2.1.2. Synthesis

The synthesis of the glucosyl donor started from glucose pentaacetate **2** (Scheme 49). This compound was glycosylated with *p*-thiocresol and the acetates were subsequently deprotected to give **117**. The free hydroxyls were then deprotected with benzyl groups to give **118** in 59% yield over 3 steps. These groups were chosen as protecting groups because of their "arming" capacities. Furthermore, they are not a participating group, which means that the α-glycosylation will not be blocked.



Scheme 49 Synthesis of the glycosyl donor 118.

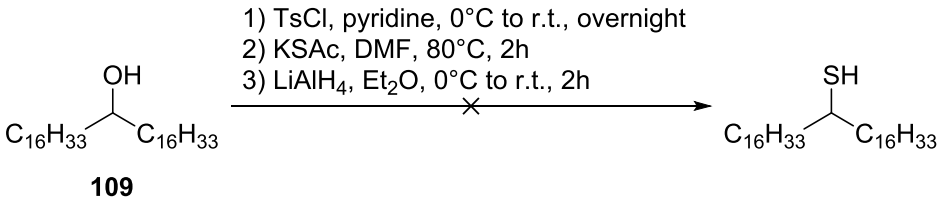
Next, synthesis of the galactosyl acceptor started from commercially available galactose pentaacetate (Scheme 50). This compound was glycosylated with *p*-thiocresol using the same procedure as for the glucosyl donor to give **119** in 86% yield. The acetates were then deprotected, and **120** was protected selectively on C-4 and C-6 using benzylidene to give **121** in 62% over two steps. The remaining free hydroxyl groups were benzoylated, and the benzylidene was then removed to give **123** in 63% over two steps. Mono benzoylation gave **124** in 69% yield, leaving a free hydroxyl group on C-4 giving an acceptor to be later used in *O*-glycosylation.



Scheme 50 Synthesis of the galactosyl acceptor 124.

5.2.2.2. Iodation of lipids

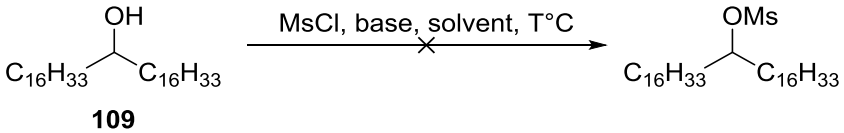
In order to prepare an *S*-glycosidic linkage at the anomeric linkage between the disaccharide and the lipid, it was first decided to prepare a lipid containing a thiol group instead of an alcohol. Blank's procedure was envisaged[1], involving three reaction steps (Scheme 51). Firstly, the alcohol would be tosylated providing a good leaving group. Next, the thiol, in the guise of a thioacetate would be reacted with the leaving group. Finally, removal of the acetate from the sulfur atom would give the wanted thiol. Unfortunately, this reaction sequence was not successful. Additionally, these three reactions were performed sequentially, therefore it was not possible to know where it had failed. For these reasons, it was decided to proceed with an alternative route.



109

Scheme 51 Unsuccessful conversion of alcohol to thiol.

The next pathway envisaged was to use a glycosyl thiol. In this way, the lipid only needs a good leaving group to allow a substitution reaction with the glycosyl thiol. The first leaving group that was investigated was *O*-mesylate (Scheme 52). In order to introduce this group to the alcohol, four different reactions were tried, with different base, solvents and temperature. Unfortunately, the starting material was recovered each time, with no any other product being formed, therefore it was decided to use another leaving group instead.



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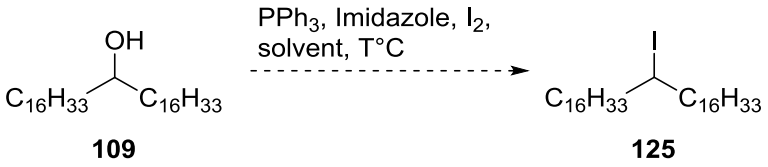
Base	Solvent	T°C	Yield
DMAP, Et_3N	CH_2Cl_2	0°C	0%
DMAP, pyridine	CH_2Cl_2	0°C	0%
Et_3N	CH_2Cl_2	0°C	0%
Et_3N	THF	r.t.	0%

Scheme 52 Unsuccessful mesylation of lipid.

The next leaving group envisaged was iodine. Halogenation using triphenylphosphine and imidazole was used.

Different solvents and temperature were tried out to get this reaction to work (Scheme 53).



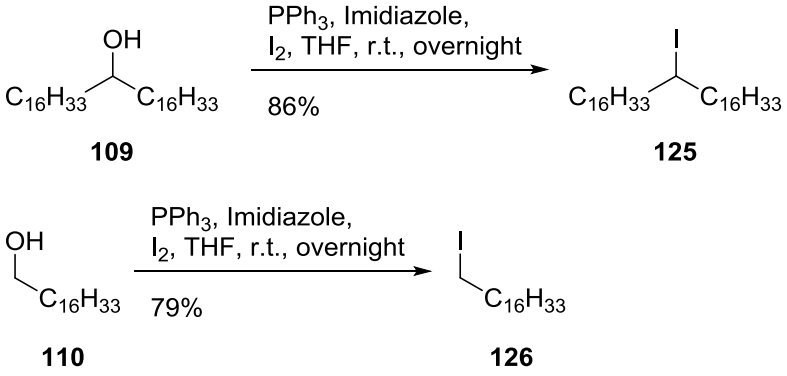
109 **125**

Solvent	Temperature	Yield
Et_2O	0°C	0%
CH_2Cl_2	0°C	0%
THF	r.t. to 45°C	86%

Scheme 53 Attempts for iodination of lipid.

It was found that the use of THF at 45 °C overnight gave the desired compound **125** in 86 % yields. The heating was used as it increased solubility of the lipid alcohol, which was hardly soluble in solvents at room temperature.

The same reaction was successfully performed with the primary alcohol, and a yield of 79% was obtained (Scheme 54).



109 **125**

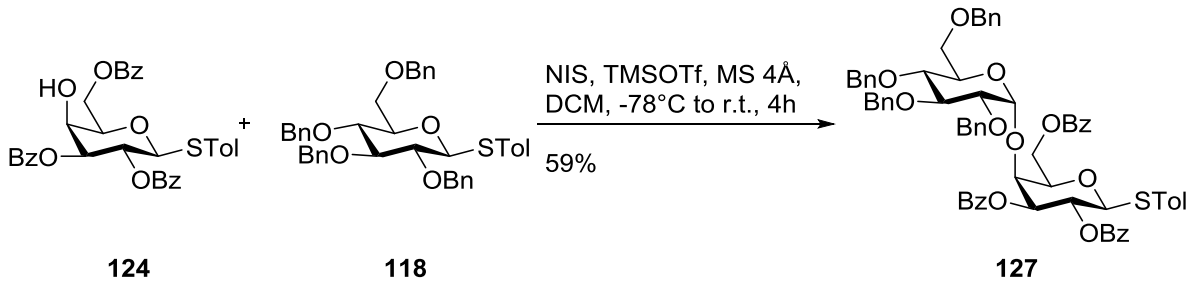
110 **126**

Scheme 54 Iodination of lipids.

Next the glycosylation was initiated.

5.2.2.3. Glycosylation between the monosaccharides

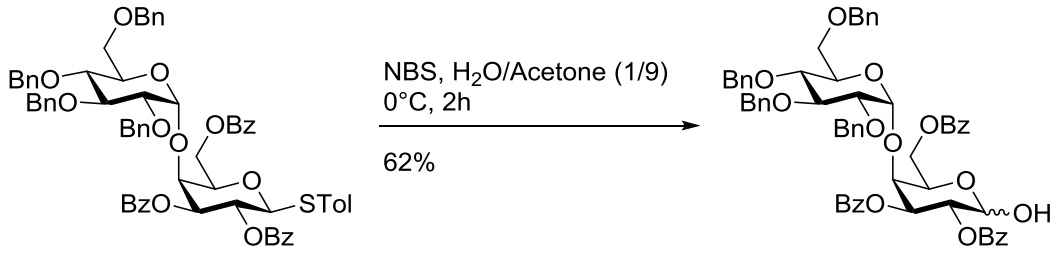
Glycosylation between **118** and **124** was achieved using the now classical procedure described by Cai et al.[2] (Scheme 55). As expected, the "arming" (benzyl group) and "disarming" (benzoyl groups) effect of the protecting groups used led to only one glycosylation taking place between the more reactive acceptor and the nucleophile – compound **124** did not get activated under the conditions. Additionally, the axially oriented product **127** was isolated in a moderate yield of 59%.



124 **118** **127**

Scheme 55 Glycosylation reaction.

Next the deprotection of the *p*-thiocresol was achieved using classical conditions as described by Fan et al.[3] to give **128** in 62% yield (Scheme 56).



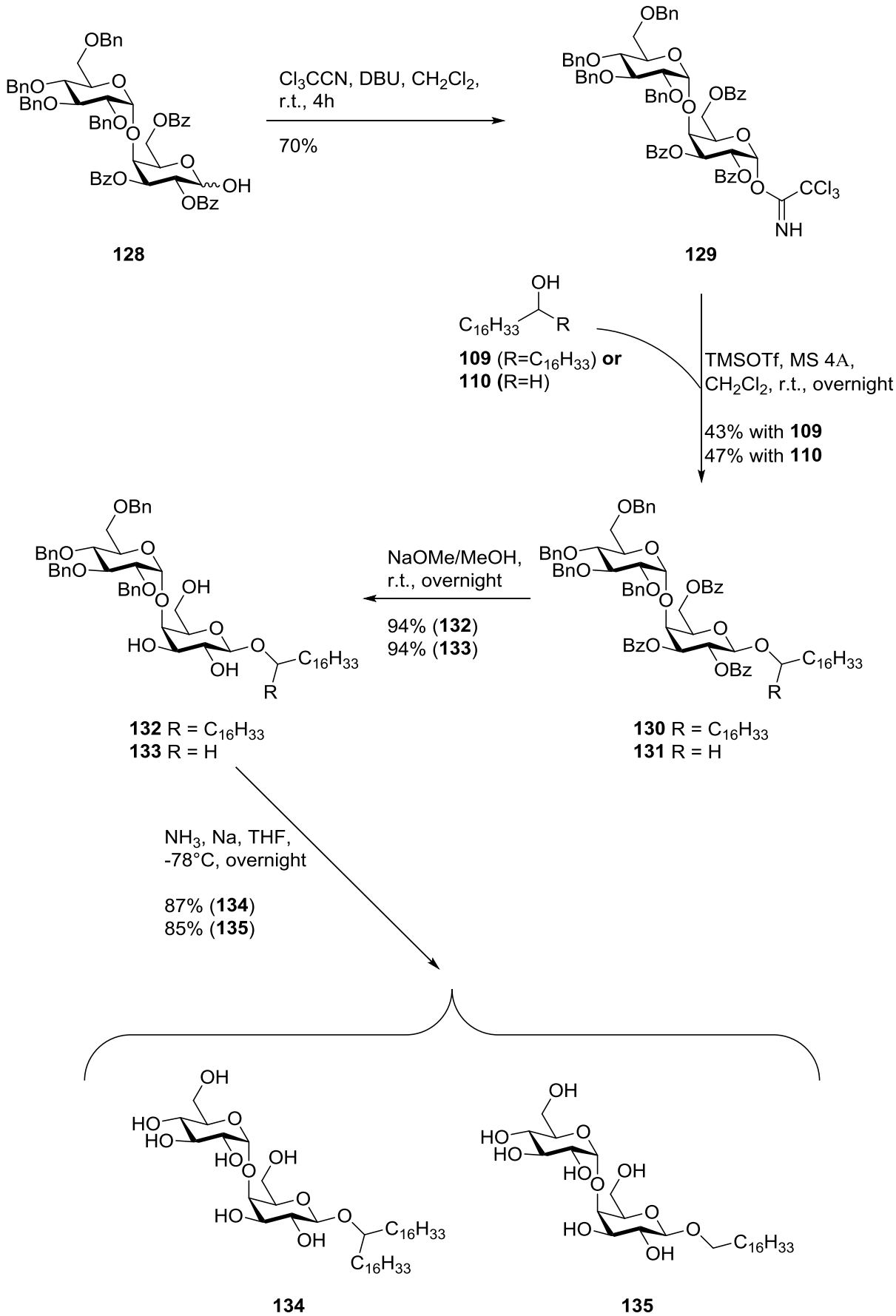
127 **128**

Scheme 56 Deprotection of thioglycoside.

5.2.2.4. Glycosylation of lipid

5.2.2.4.1. *O*-glycosylation

The next focus was on introducing the lipids at the anomeric position. The first reaction tried was centred on the classical glycosylation, with an oxygen nucleophile (Scheme 57). The direct glycosylation with the *p*-thiocresol was unsuccessful, therefore leaving group trichloroacetimidate was introduced to the anomeric position of **128** to give **129** in 70% yield. The glycosylation was then performed using two different lipids, **109** and **110**, which gave **130** (43%) and **131** (47%) respectively. Benzoyl groups and subsequently the benzyl protecting groups were then removed to give natural compound **134** and mimetic **135**.

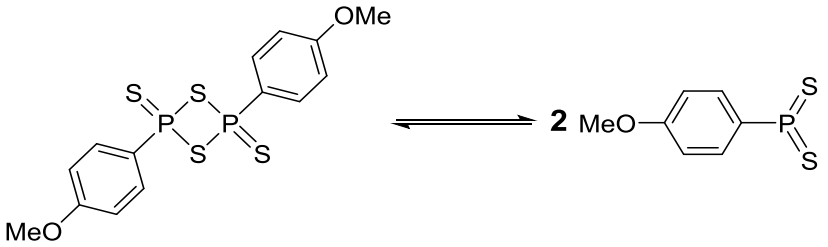


Scheme 57 Glycosylation and deprotection to obtain 134 and 135.

The natural compound **134** is different from the natural compound synthesized by Loffredo's[4] group by the length of the lipid chains. It would therefore be interesting to compare them to see if there is a difference in their biological activity.

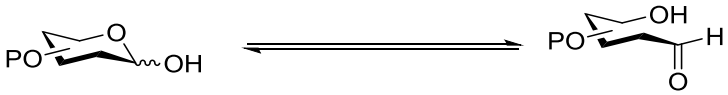
5.2.2.4.2. *S*-glycosylation

The next focus was on S-glycoside formation. The first reaction to achieve was to manage the substitution of a hemi-acetal into a glycosyl thiol. Bernardes et al.[5] described a way to accomplish this task in one step using Lawesson's reagent (Scheme 58).



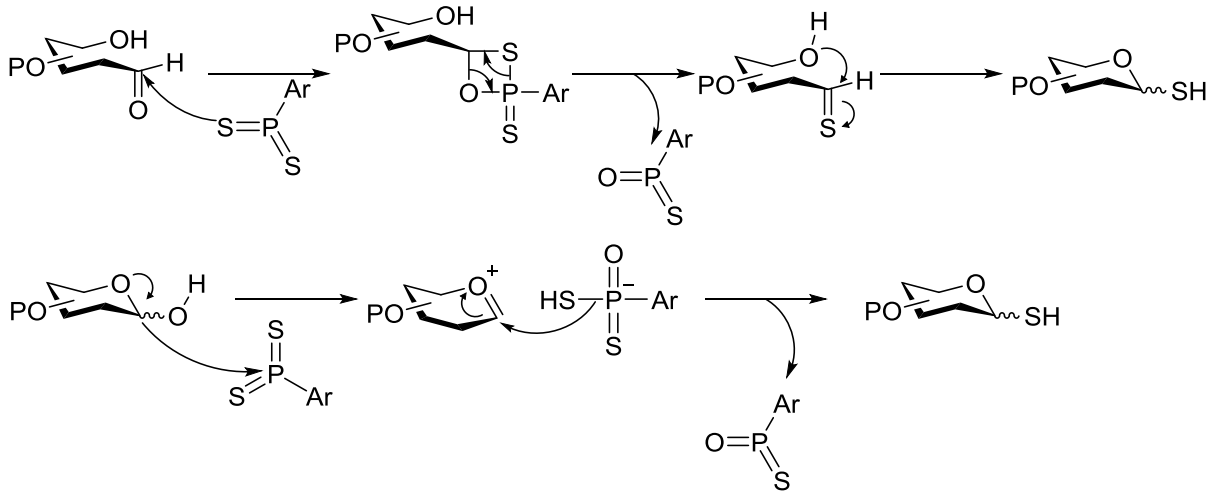
Scheme 58 Dissociation of the Lawesson's reagent.

This reagent dissociates easily into the reactive intermediate[6-7]. The Lawesson's reagent, by the presence of phosphorus, is an oxophilic electrophile additionally to being a sulfur source. There are two possible mechanisms for the formation of a thioglucoside using the Lawesson's reagent. One of the mechanisms is based on the fact that a free hydroxyl on the anomeric position is in equilibrium with its aldehyde form (Scheme 59).



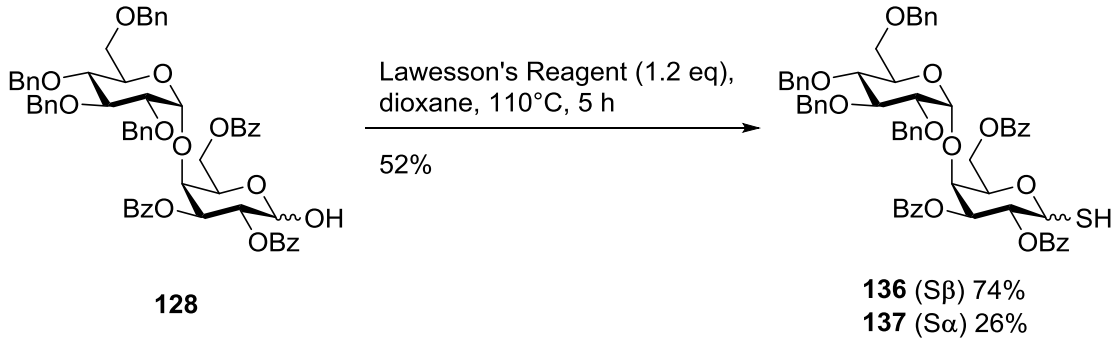
Scheme 59 The two forms of a hemi-acetal.

The aldehyde could undergo a 2+2 cycloaddition and after rearrangement, a thioaldehyde was obtained, which gives the desired products after ring formation (Scheme 60). Alternatively, the formation of the thiol could be as a result of exocyclic cleavage, with the oxygen binding to the phosphorus. Sulfur being nucleophilic attacks the positively charged anomeric position.



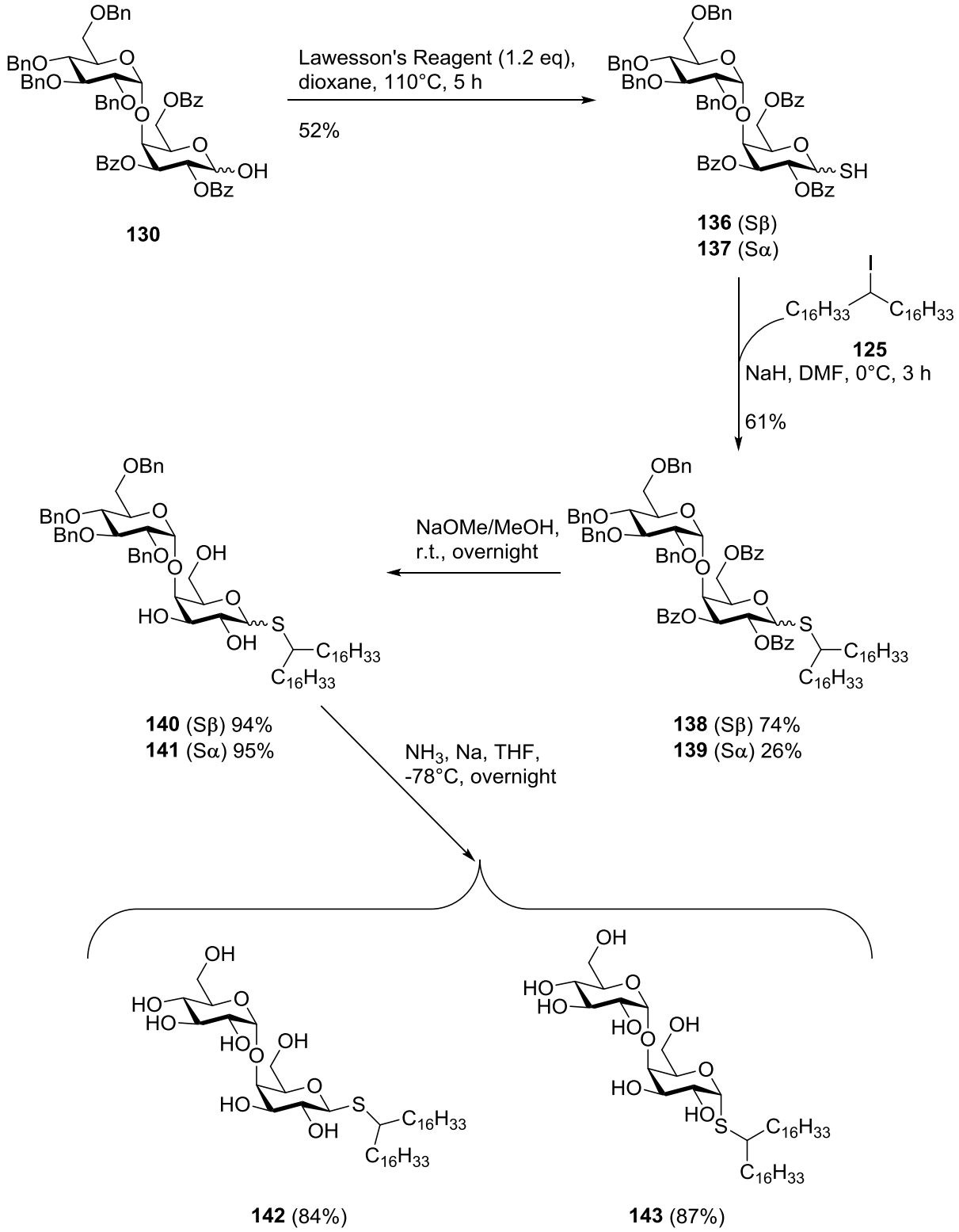
Scheme 60 Possible mechanisms for the formation of glycosyl thiol through the open chain, or an oxacarbenium ion[6-7].

From Bernardes' study, it was discovered that 1.2 equivalent of Lawesson's reagent worked best for most of the carbohydrates. Therefore, it was decided to use the same number of equivalent for the disaccharide **128**. Heating up the reaction at 110 °C for 5 h gave the desired α (**137**) and β (**136**) products with a ratio of α:β 1:3 (Scheme 61).



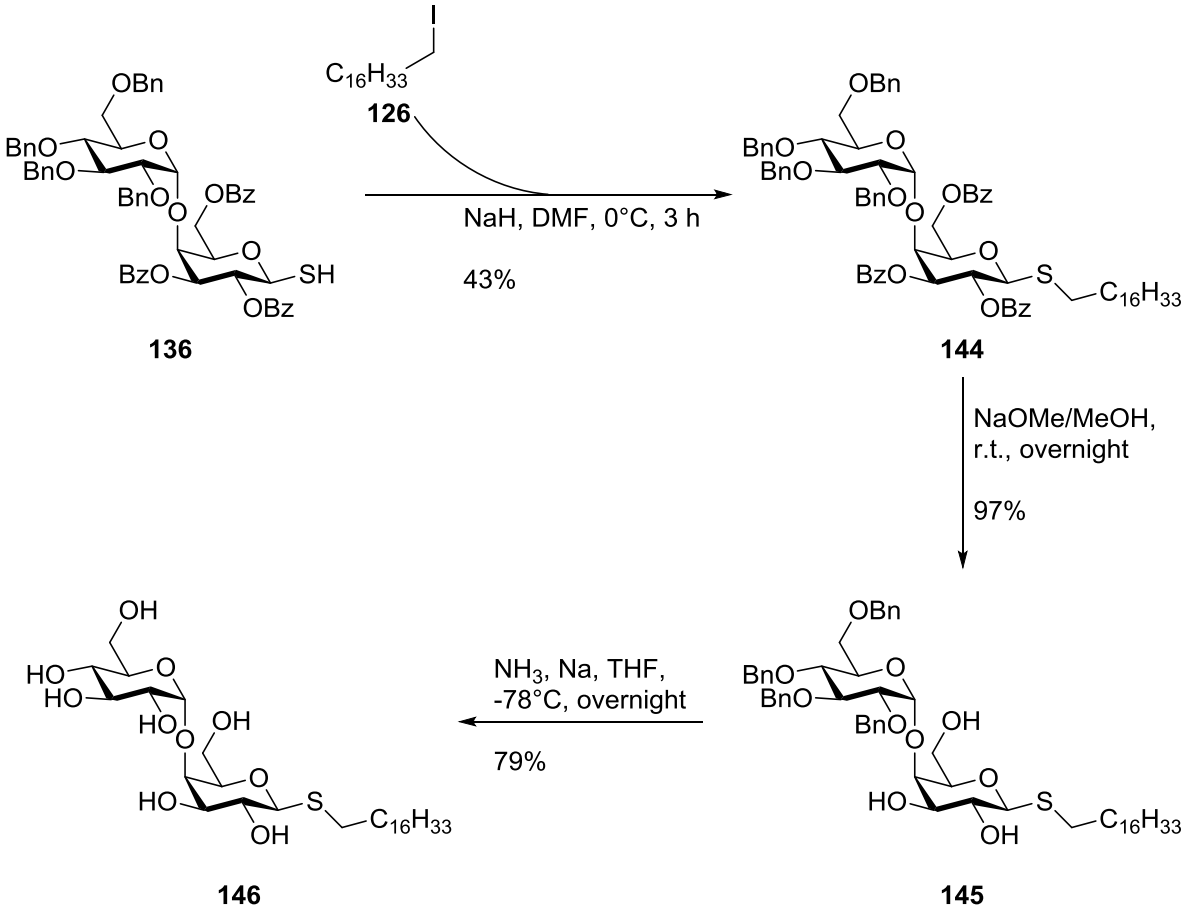
Scheme 61 Insertion of a thiol on the anomeric position[5].

These compounds were then subjected to substitution reaction with **125** to give **138** (from **136**) and **139** (from **137**) (Scheme 62). The benzoyl groups were then removed to give **140** and **141**. The Birch reduction conditions were used in order to remove the benzyl groups, which gave mimetics **142** and **143**.



Scheme 62 Synthesis of 142 and 143.

The same procedure was used with the primary iodinated lipid **126** reacting it with the equatorial thiol **136** to give **144** (Scheme 63). Then, deprotection gave mimetic **146** in an overall yield of 33% over three steps.



Scheme 63 Synthesis of 146.

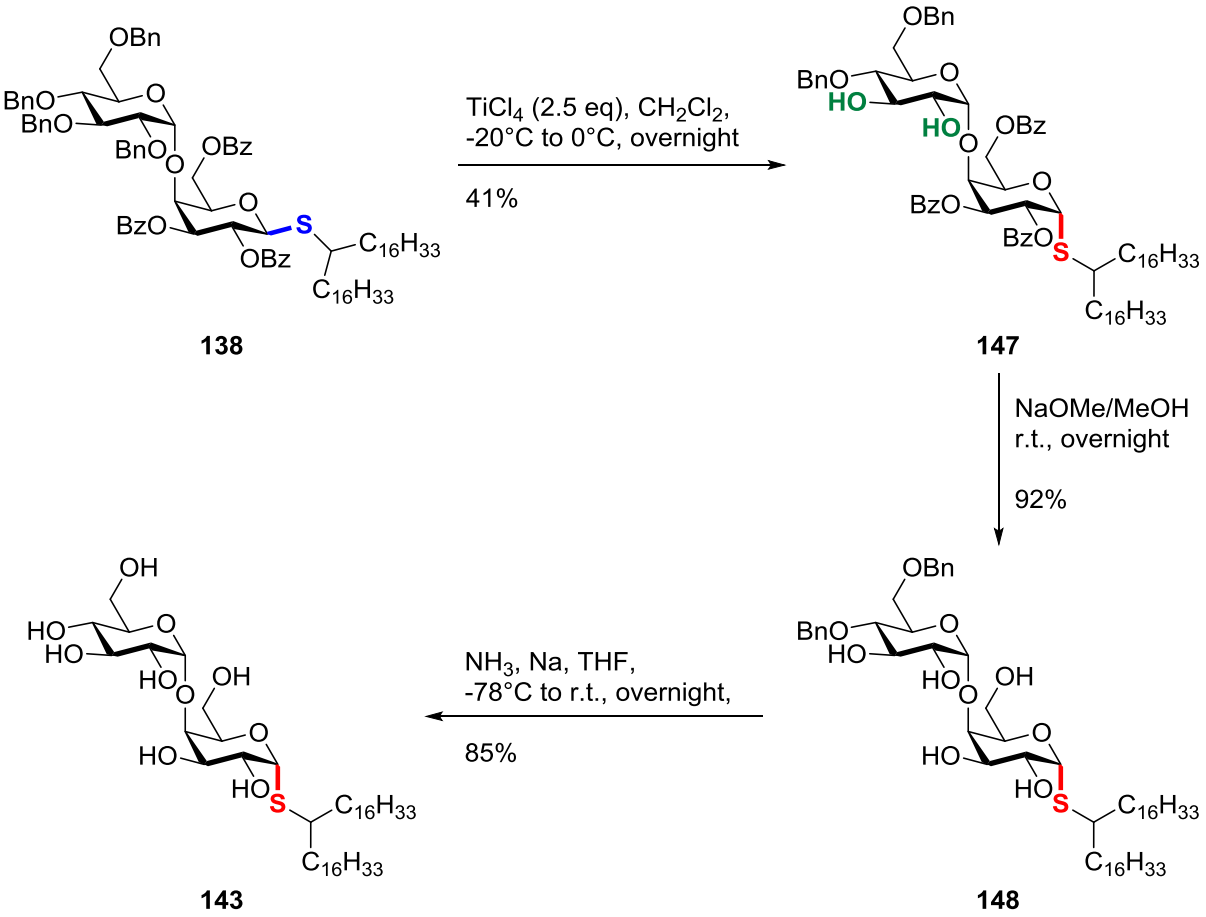
5.2.2.5. Anomerisation in synthesis of a simplexide mimetic

The anomerisation reaction was tested on **138** to further demonstrate that this reaction can be applied to generate simplexide mimetic (Scheme 64).

The conditions used were the same used by Mark Farrell in his research thesis[8-9].

The anomerisation was found to be successful, with, remarkably, two benzyls being also cleaved simultaneously, on C-2 and C-3 of the galactose residue to give **147** with a yield of 41%. Some other fractions were collected, with one suspected to be the resulting anomerisation without any further deprotection. However, the full characterization of this fraction was not performed due to the very low quantity (<10%) obtained. The starting material also decomposed. For the main product obtained, **147**, the selective deprotection was surprising, as the benzyl ether derived from a primary alcohol (C-6) is usually removed before an ether derived from a secondary alcohol.

The protecting groups were then removed to give the mimetic formerly synthesized **143**.



Scheme 64 Anomerisation of 138, followed by deprotection of protecting groups to give 143.

5.3. Library of compounds synthesized

A natural simplexide and 5 of its mimetics were synthesized (Figure 34). These mimetics differ from the natural simplexide by the lipid chain, the presence or not of sulfur in one of the anomeric positions, and the configuration of the anomeric linkage between the disaccharide and the lipid.

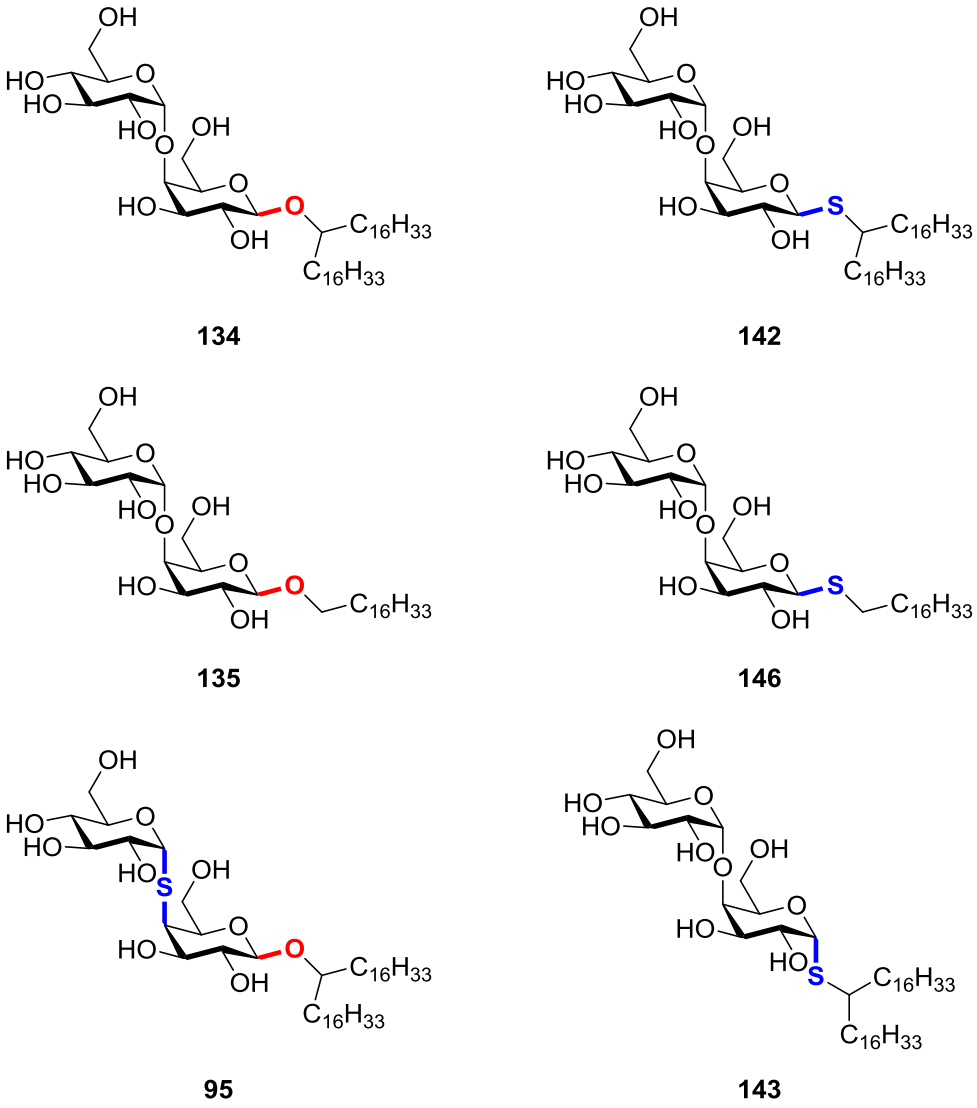


Figure 34 Library of compounds synthesized.

5.4. Biological results

The mimetics which were synthesised, as well as the natural product **134** (**149a**), were evaluated by Stefania Loffredo, at the University of Naples Federico II in Italy, as mentioned in Chapter 4. There, they were tested for their ability to release three cytokines, IL-6, IL-8 and TNF and they were compared with the naturally isolated simplexide's ability to release the same cytokines. They were also compared to one of the components of this isolated fraction **149c**, which had been synthesised previously[4] (Figure 35).

For the biological tests, peripheral blood mononuclear cells (PBMC) were incubated for 6 hours with target compounds at different concentrations (3, 10 and 30 μg/L). After that time, the amount of three different cytokines released was measured. The results are displayed in 3 different figures (Figure 36, Figure 37 and Figure 38). The positive controls are the natural simplexide **149** (mixture of 5 simplexides **149a-e**) and the synthetic simplexide **149c** synthesized by Loffredo et al (Figure 35).

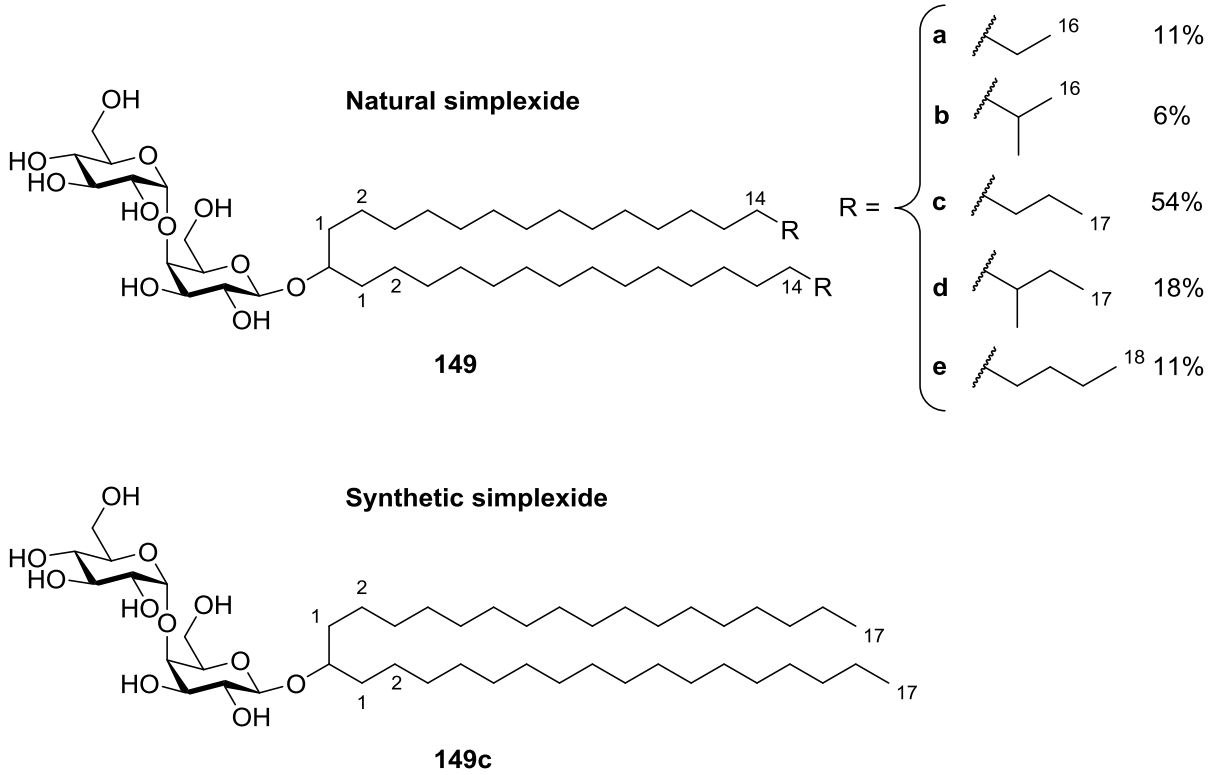


Figure 35 Positive control for biological tests.

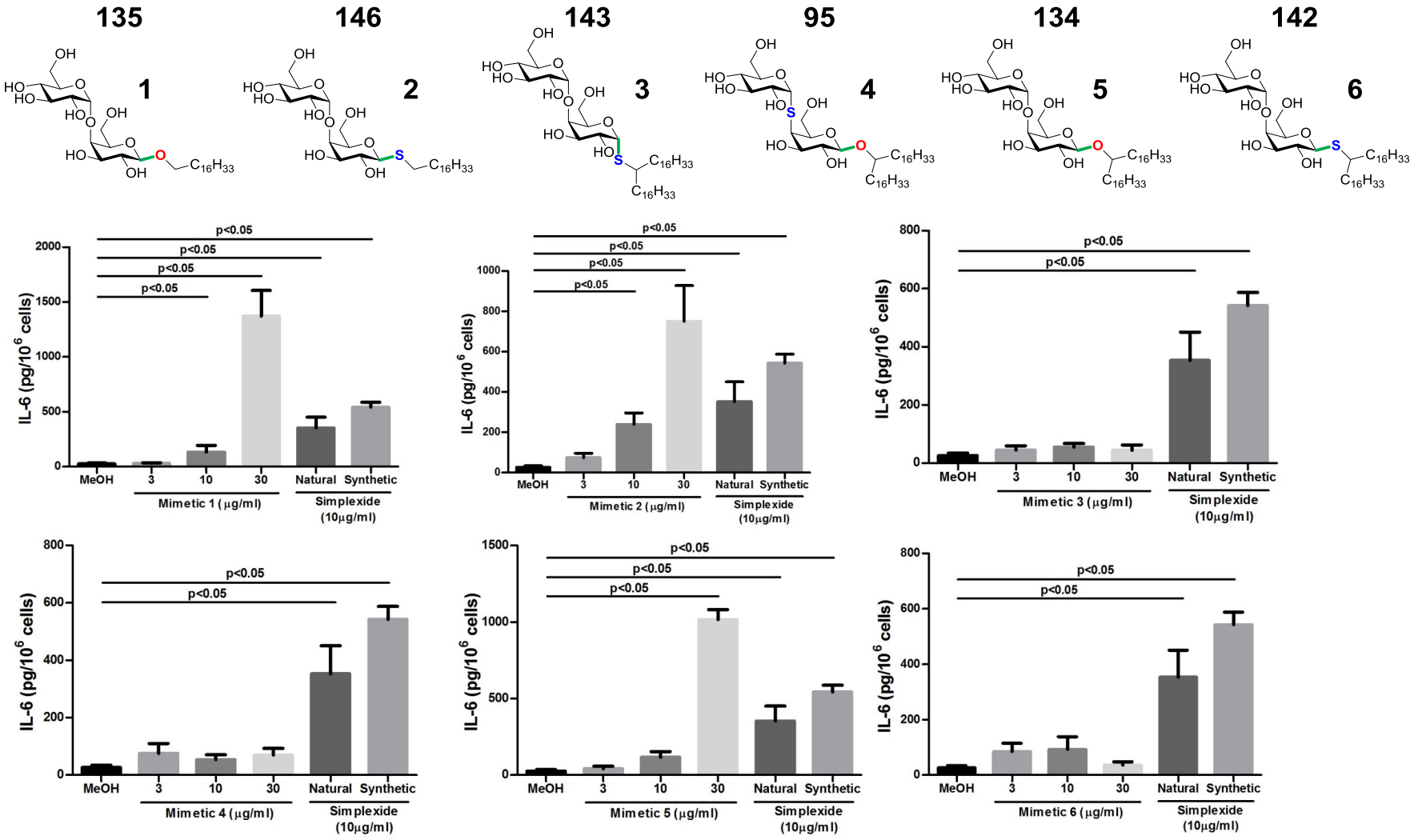


Figure 36 Effect of Mimetic 1-4 and 6 and synthetic simplexide 5 (149a) on IL-6 production from PBMC. Positive control: That which is labelled as Natural (149, mixture of 149a-e) and synthetic simplexide refers to 149c.

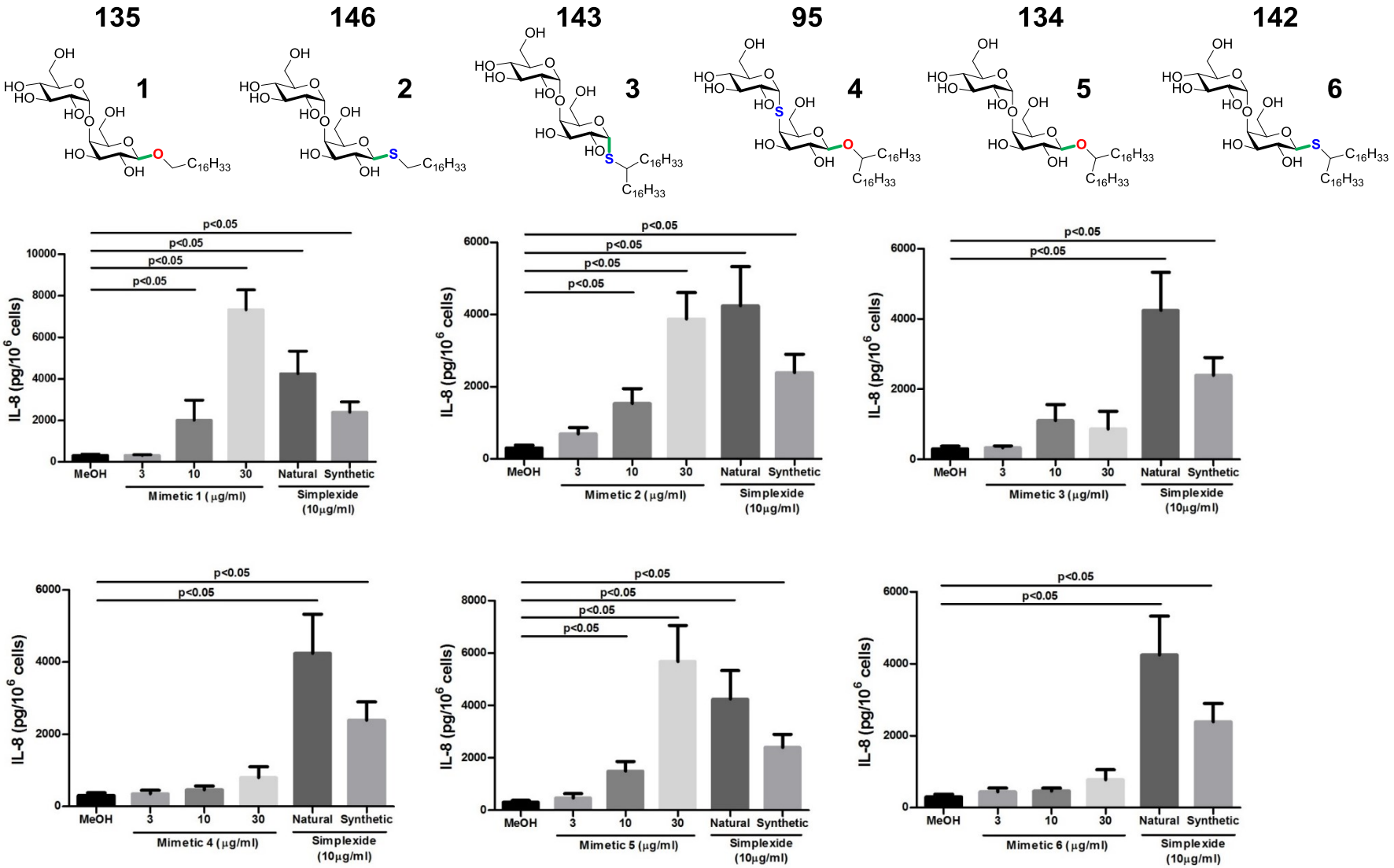


Figure 37 Effect of Mimetic 1-4 and 6 and synthetic simplexide 5 (149a) on IL-8 production from PBMC. Positive control: That which is labelled as Natural (149, mixture of 149a-e) and synthetic simplexide refers to 149c.

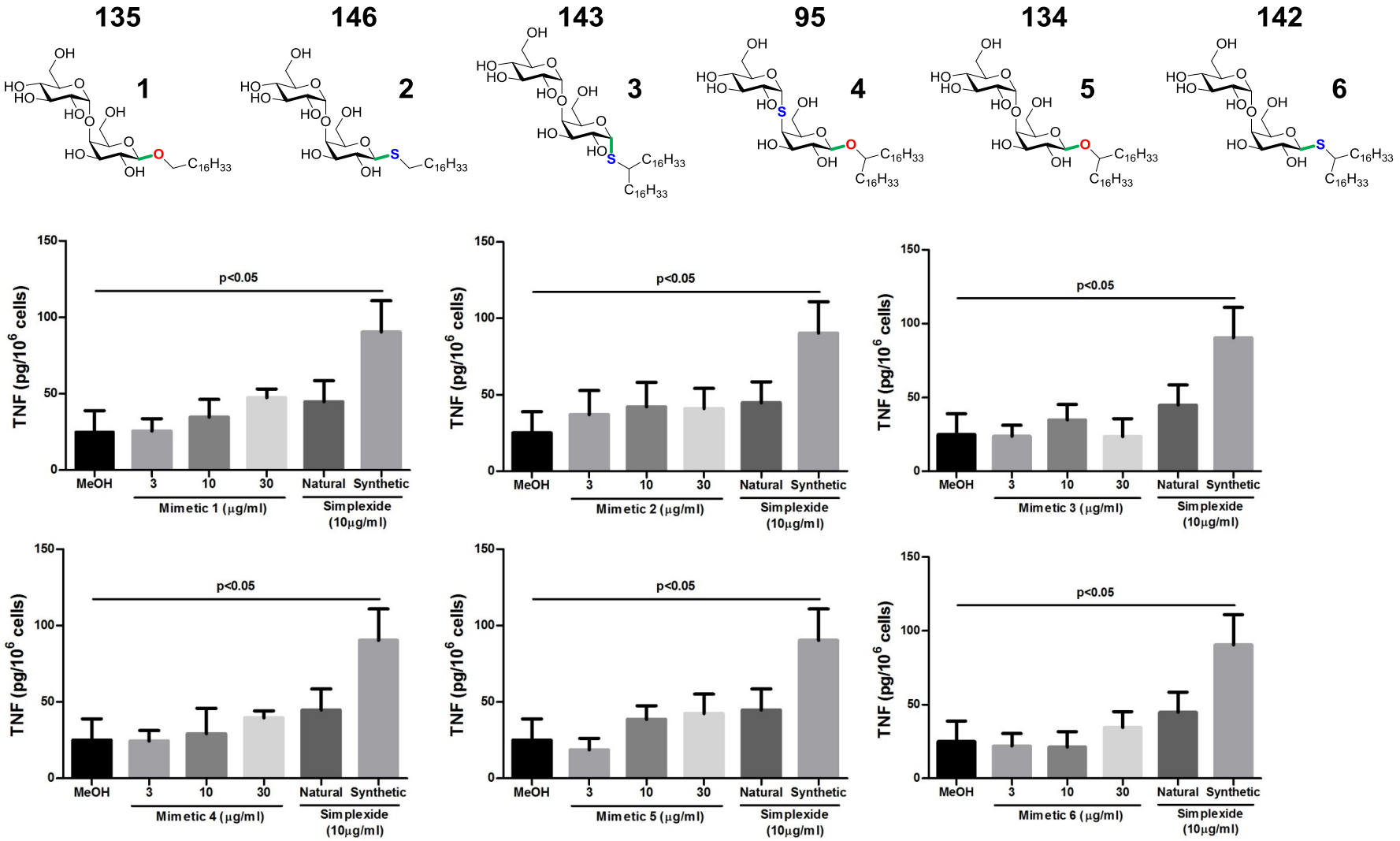
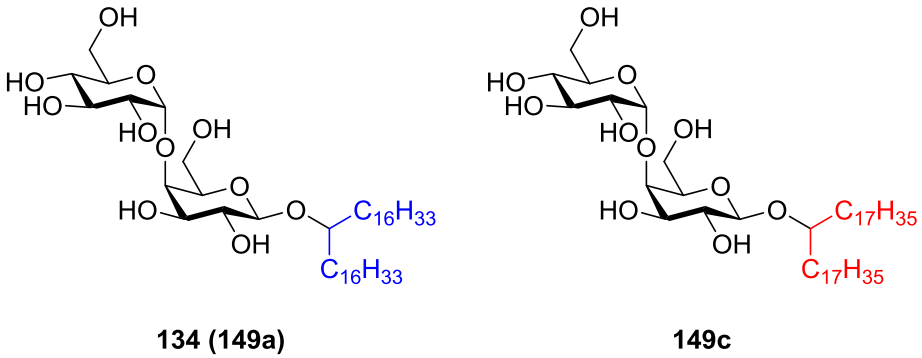


Figure 38 Effect of Mimetic 1-4 and 6 and synthetic simplexide 5 (149a) on TNF production from PBMC. Positive control: That which is labelled as Natural (149, mixture of 149a-e) and synthetic simplexide refers to 149c.

From the results obtained, it can be concluded that compounds **95** (mimetic **4** on the figures), **142** (mimetic **6** on the figures) and **143** (mimetic **3** on the figures) were not active, not releasing any significant amount of cytokines.

On the other hand, natural simplexide **134** (**149a** in the natural isolate, mimetic **5** in the figures), and mimetics **135** (mimetic **1** on the figures) and **146** (mimetic **2** on the figures) release cytokines IL-6 and IL-8, but have no or only slight activities on the release of TNF, whereas the natural and synthetic simplexides **149** and **149c** showed some capability to release same. Compounds **135** and **146** have particularly interesting behaviour, as their lipid chain is truncated significantly compared to **134** (**149a**), and they only differ by having either the oxygen or sulfur linking the disaccharide to the lipid.

It was interesting to notice that synthetic simplexide **134** (**149a**) is less active than simplexide **149c** (Figure 39), differing in the number of carbons in the lipid chain.



134 (149a) **149c**

Figure 39 The difference between this research group's and Loffredo et al.'s synthetic natural simplexide lies on the length of the lipid chain.

It is therefore demonstrated here that differing components in the mixture (**149a-e**) have different activity. An interesting study to follow up would be to synthesize individually all the molecules present in the natural simplexide and study them separately.

Additionally, Loffredo suggested that simplexides could have the same mode of action of KRN7000 in the human monocytes. It could therefore be interesting to compare the individually synthesized simplexides with KRN7000 in this regard also. With these results in hand, it might help direct the research towards the synthesis of a simple and efficient simplexide analogue.

5.5. Conclusion

In this research study (Chapter 4 and Chapter 5), one of the components of the natural simplexide was synthesised as well as five new mimetics (Figure 40).

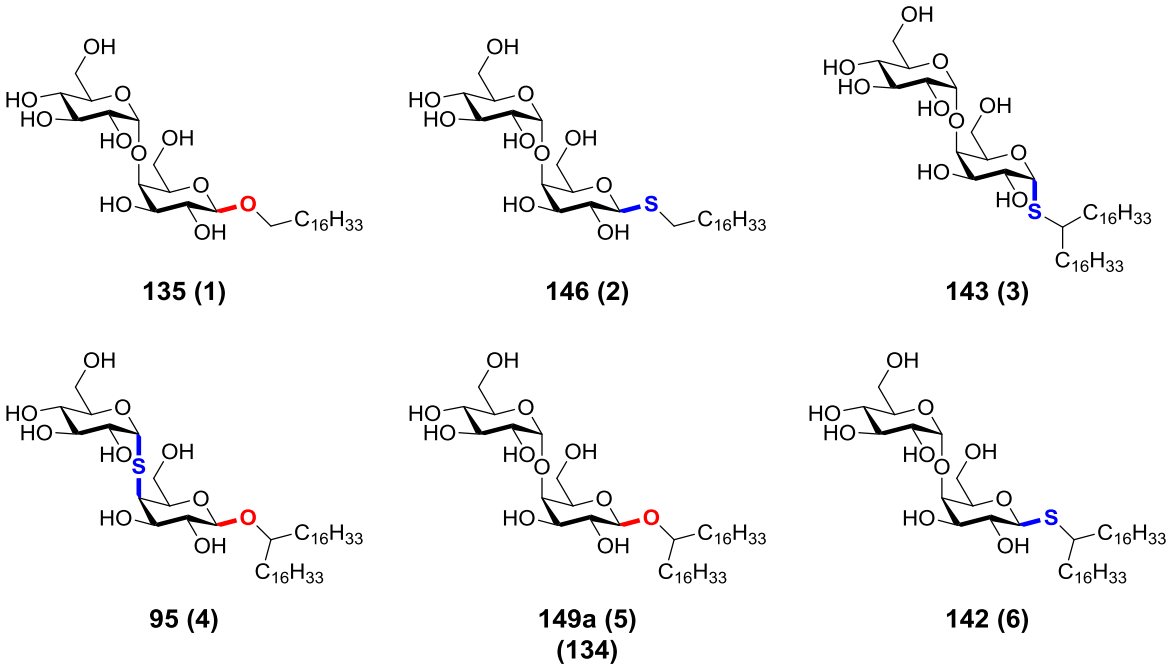


Figure 40 Summary of compounds synthesized for this research study.

The total synthesis of **95** involved use of a glycosyl thiol which had been prepared by Lewis acid promoted anomerisation reaction, a method developed at NUI Galway recently[10-11]. This was used to give the S-disaccharide, and the incorporation of the lipid chain was via a glycosylation from a trichloroacetimidate donor.

The rest of the targets synthesized featured an *O*-disaccharide building block which were converted to glycosyl thiols for the synthesis of S-linked mimetics **142**, **143** and **146** through a nucleophile substitution with a lipid iodide. The natural simplexide **149a** (**134**) and its mimetic **135** were obtained from the *O*-disaccharide building block using classical trichloroacetimidate method.

From the biological results, summarized in Figure 41, it could be suggested that the molecules containing a sulfur did not have a particularly high activity towards the release of cytokines.

It was also noticed that the length and type of lipid has an undeniable influence on the biological activity of the molecules. The study indicates that synthesis of other natural simplexides could help clarify the contribution of the properties of each component to those displayed by the natural isolate. Also, the results indicate that other non-natural analogues will be interesting to synthesize and evaluate.

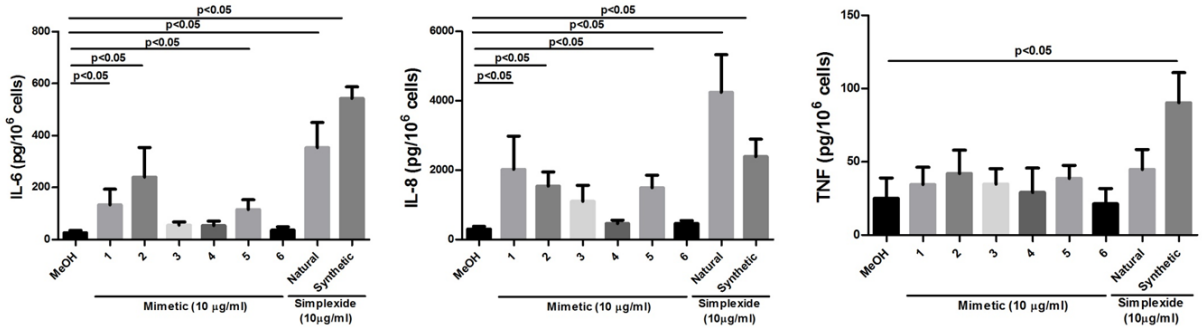


Figure 41 Summary of the effect of Mimetic 1-4 and 6 and synthetic simplexide 5 (149a) on cytokine production from PBMC compared to the same concentration of natural (149a-e) and synthetic simplexide (149c).

In this research thesis, it was also shown that the anomerisation reaction can be productive for various silyl protected reactants. The high rate of anomerisation observed on monosaccharide compounds allowed the anomerisation of disaccharides and glucopyranosyl azide which was formerly unsuccessful.

There are still much studies that could be conduced on this anomerisation reaction, and the aim would be to try to improve it so that the yield is increased, and there are no side products obtained. Ultimately, it would be interesting to have the anomerisation reaction successful for every type of saccharides, especially disaccharides.

5.6. References

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Chapter 6 Experimental Part

I. General experimental conditions

NMR spectra were recorded with a 500 MHz or 600 MHz Varian spectrometer. Chemical shifts are referenced to the internal solvent signal. All NMR assignments were assigned with the aid of COSY, HSQC and HMBC experiments. Coupling constants *J* are reported in Hertz (Hz). Compounds that are known in the literature already have been cited herein. Unless otherwise stated analytical data e.g.^{1}H NMR and/or ^{13}C NMR, obtained during this thesis work has been found to be in agreement with previously published data.

The IR spectra were recorded as thin films using a PerkinElmer Spectrum 100 FT-IR Spectrometer with an ATR attachment.

High resolution mass spectra were recorded using a Waters LCT Premier XE (ESI-TOF instrument).

Silica gel (pore size 60 Å, particle size 40-60 μm 230-400 mesh particle size) was purchased from Sigma-Aldrich. Dichloromethane, THF and DMF reaction solvents were obtained from a Pure Solv™ Solvent Purification System.

Acetone and anhydrous pyridine were obtained from Sigma-Aldrich. 1M $TiCl_4$ in CH_2Cl_2 was purchased from Sigma Aldrich.

II. General procedures

A. Deacetylation / debenzoylation

This reaction was carried out as previously described[1].

The reactant was dissolved in methanol (10 mL per mmol). Solid sodium prewashed with petroleum ether (0.2 equiv.) was then added to the solution. The mixture was stirred at room temperature overnight. It was then acidified to pH = 6 with Amberlite (IR-120, strongly acidic, hydrogen form), filtered, and the solvent was removed under reduced pressure to give the product.

B. Benzoylation

The reactant was dissolved in pyridine (10 mL per 1 mmol) and the solution was cooled down to 0 °C. DMAP (0.05 equiv.) and BzCl (1.2 equiv. per OH) were then added, and the solution was stirred at room temperature overnight. The mixture was then diluted with EtOAc. The organic phase was washed with HCl until the aqueous phase was acidic, then water and brine. It was then dried over Na_2SO_4, filtered, and the solvent was removed under reduced pressure to give the product after chromatography.

C. Silylation

The reactant was dissolved in pyridine (10 mL per 1 mmol) and the solution was cooled down to 0°C. 2,6-lutidine (3.5 equiv.) and TIPSOTf (1.5 equiv. per OH group) **or** TBSOTf (1.2 equiv. per OH) were then added, and the solution was stirred at room temperature overnight. The mixture was then diluted with EtOAc. The organic phase was washed with HCl (until the aqueous phase was acidic), water and brine. It was then dried over Na_2SO_4, filtered, and the solvent was removed under reduced pressure to give the product after chromatography.

D. Removal of primary TBS groups

This reaction was carried out using reagents and conditions reported previously[2].
The reactant was dissolved in MeOH (10 mL per 1 mmol). CBr_4 (0.05 equiv.) was added, and the solution was irradiated at 245 nm for 2 h, followed by stirring at room temperature for another 2 h. After completion of the reaction, the solvent was removed under reduced pressure to give the product after chromatography.

E. Removal of primary TIPS groups

This reaction was carried out using reagents and conditions reported previously[3].
The reactant was dissolved in EtOH (50 mL for 14 mmol), and conc. HCl (1 mL for 14 mmol) was added. The mixture was stirred at room temperature for 5 h. The solvent was then evaporated, and the crude mixture was dissolved in EtOAc. The organic phase was then washed with water until pH became neutral. It was then dried over Na_2SO_4, filtered and the solvent removed under reduced pressure to give the product after chromatography.

F. Oxidation of benzylidene groups

This reaction was carried out using reagents and conditions reported previously[4].
Wet alumina was prepared by adding 10 mL of water to 50 g of neutral alumina. The mixture was stirred until a homogeneous powder was obtained.
The reactant was dissolved in CH_2Cl_2 (10 mL per 1 mmol). Wet alumina (2.2 g/1 mmol), NBu_4Br (0.5 equiv.) and periodic acid (H_5IO_6) (3 equiv.) were successively added, and the combination was stirred vigorously at room temperature for 3 h. The solvent was then removed under reduced pressure to give the product after chromatography.

G. Oxidative cleavage of *p*-methoxybenzylidene

This reaction was carried out using reagents and conditions reported previously[5].
The reactant was dissolved in a mixture of CH_3CN-H_2O (4:1, 25 mL for 2 mmol). Ceric ammonium nitrate (2.5 equiv.) was then added and the solution was stirred at room temperature for 3 h. The mixture was diluted with EtOAc and washed with water. The aqueous phase was extracted with EtOAc and the combined organic phases were washed with $NaHCO_3$. The solvent was then removed under reduced pressure to give the product after chromatography.

H. Protection with 1,3-dichloro-1,1,3,3-tetraisopropyl-1,3-disiloxane

This reaction was carried out using reagents and conditions reported previously[6].
The reactant was dissolved in pyridine (10 mL per 3.5 mmol) and the solution was cooled down at 0 °C. Then, 1,3-dichloro-1,1,3,3-tetraisopropyl-1,3-disiloxane (1.2 equiv.) was added and the mixture was stirred at room temperature overnight. Methanol was then added to quench the reaction. The product was extracted with EtOAc, and the organic phase was washed with HCl 1mol/L until the pH was acidic. It was then washed with water, brine, dried over Na_2SO_4, filtered and evaporated under reduced pressure to give the crude product used without any further purification.

I. Rearrangement of 1,3-dichloro-1,1,3,3-tetraisopropyl-1,3-disiloxanyl protecting groups

This reaction was carried out using reagents and conditions reported previously[6].
The reactant was dissolved in DMF (10 mL per 1.8 mmol). *p*-TsOH.H_2O (0.2 equiv.) was then added, and the reaction was stirred at room temperature for 5 h. It was then diluted with EtOAc, and the organic phase was washed with water, a saturated aqueous solution $NaHCO_3$, brine, dried over Na_2SO_4, filtered, and the solvent removed under reduced pressure to give the crude product used without any further purification.

J. Removal of 1,3-dichloro-1,1,3,3-tetraisopropyl-1,3-disiloxane

This reaction was carried out using reagents and conditions reported previously[7].
The reactant was dissolved in THF (10 mL per 0.75 mmol) and the solution was cooled down at 0 °C. Acetic acid (3 equiv.) and TBAF (1 mol/L in THF, 2 equiv.) were then added, and the mixture was stirred at same temperature for 2h. Hydrochloric acid was then added to the reaction, and the aqueous mixture was extracted with EtOAc. The organic phase was washed with water and brine, dried over Na_2SO_4, and the solvent evaporated under reduced pressure to give the product after chromatography.

K. Anomerisation reactions

This reaction was carried out using reagents and conditions reported previously[1].
The reactant was dissolved in CH_2Cl_2 (10 mL per 1 mmol). To this solution, either $SnCl_4$ (0.5 eq, 1 mol/L in CH_2Cl_2) **or** $TiCl_4$ (2.5 eq, 1 mol/L in CH_2Cl_2) was added, and the solution was stirred at room temperature. The mixture was then diluted in EtOAc and washed with a saturated solution of NH_4Cl. The aqueous phase was extracted with EtOAc and the combined organic phases were washed with a saturated solution of $NaHCO_3$, brine, it was then dried, filtered and evaporated under reduced pressure to give the product after chromatography.

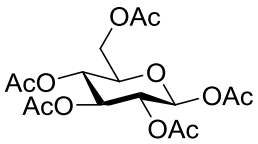
L. Determination of the kinetics of anomerisation by NMR

This reaction was carried out using reagents and conditions reported previously[1].
The reactant was freeze dried overnight. The NMR tube was dried in an oven at 170 °C for 15 minutes. $CDCl_3$ was distilled under P_2O_5 and molecular sieves 4Å for 2h before being transferred in a conical flask which had been pre-dried over a bunsen burner containing molecular sieves 4Å. The solution of $SnCl_4$ (0.15 mol/L) was prepared 20 minutes before putting it to the NMR tube in a Bunsen burner dried round bottom flask.
The reactant (0.03 mmol) was dissolved in $CDCl_3$ (0.4 μL) and transferred into a NMR tube. $SnCl_4$ (0.1 mL, 0.15 mol/L) was then added to the tube. It was subsequently shaken, and ^1H NMR spectra were collected every 5, 10 or 30 minutes for at least 12 h. When the reaction attained an equilibrium, which may have been over a number of days, it was then diluted with EtOAc, and washed with a saturated solution of NH_4Cl. The aqueous phase was extracted with EtOAc, and the combined organic phases were washed with a saturated solution of $NaHCO_3$, brine, it was then dried, filtered and evaporated under reduced pressure to give the product after chromatography.

M. *O*-Debenzylation

This reaction was carried out using reagents and conditions reported previously[8].
The reactant was dissolved in THF and solid sodium prewashed with petroleum ether (20 equiv.) was added. The round bottom flask was cooled to -78 °C and a needle bubbled gaseous NH_3 into the mixture. The reaction was stirred vigorously overnight (room temperature was then reached), and the mixture was quenched with water and extracted with EtOAc three times. The organic phase was dried over Na_2SO_4, filtered and the solvent removed under reduced pressure to give the product after chromatography.

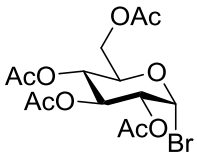
III. Experimental data



β-D-Glucose pentaacetate (2)

This compound was prepared as previously described[9].

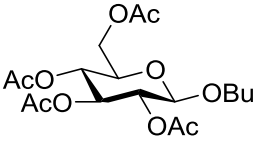
Sodium acetate (2.3 g, 27 mmol) was diluted in acetic anhydride (52 mL, 0.5 mol). This solution was warmed until a gentle reflux was obtained. D-Glucose (10 g, 55 mmol) was then added over a period of 5 min. This solution was stirred at reflux for 30 min. After cooling down at room temperature, the solution was quenched with ice water under sonication. The solid that was obtained was filtered and washed with water until disappearance of the odour of acetic acid had occurred. Without any further purification, the desired compound **2** (19.5 g, 65%) was obtained as a white solid. The NMR spectral data was in accordance with the previous report[9].



2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl bromide (3)

This compound was prepared as previously described[10].

Compound **2** (19.5g, 50 mmol) was dissolved in CH_2Cl_2 (40 mL). The solution was cooled down at 0°C, and HBr (33% in AcOH, 80 mL) was added carefully. The mixture was let to stir at room temperature overnight. The resulting solution was diluted in CH_2Cl_2. The organic phase was washed with water, a saturated solution of $NaHCO_3$ (four times), water, and brine. It was then dried over Na_2SO_4, and the solvent was removed under reduced pressure. No further purification gave the wanted compound **3** (15.2 g, 74%) as a white solid. The NMR spectral data was in accordance with the previous report[10].

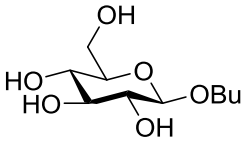


Butyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (4)

This compound was prepared as previously described[11].

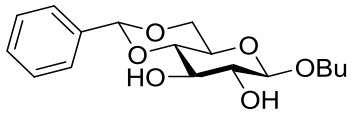
A solution of Ag_2CO_3 (31 g, 0.1 mol), iodine (1 crystal), butanol (17 mL, 0.2 mol), molecular sieves 4 Å in CH_2Cl_2 (100 mL) was prepared and stirred for 15 min. Another solution was

prepared, containing **3** (15.2 g, 37 mmol), molecular sieves 4Å and CH_2Cl_2 (100 mL) and was stirred for 15 min. The latter solution was then added to the first solution. The final mixture was shielded from light and stirred at room temperature for 4 h. The resulting mixture was diluted with EtOAc, filtered through celite, and the solvents were removed under reduced pressure. Column chromatography gave the desired compound **4** (10.5 g, 70%) as a white solid. The NMR spectral data was in accordance with the previous report[1].



Butyl β-D-glucopyranoside (5)

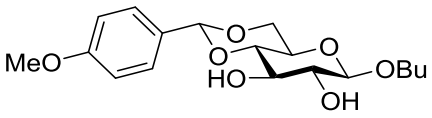
Compound **4** (10.5 g, 26 mmol) was reacted as described in the general procedure II.A to give **5** (5.85 g, 95%) as a white solid. The NMR spectral data was in accordance with the previous report[12].



Butyl 4,6-*O*-benzylidene-β-D-glucopyranoside (6)

This compound was prepared as previously described[13].

Compound **5** (2 g, 9 mmol) was dissolved in CH_3CN (15 mL). Benzaldehyde dimethyl acetal (4 mL, 3 equiv.) and camphor sulfonic acid (0.1 g, 0.05 equiv.) were added and the mixture was stirred at 45 °C for 3h. It was then neutralised with Et_3N and the solvent was evaporated, and the crude product was purified by flash chromatography (CH_2Cl_2-MeOH, 8:2) to give **6** (2.02 g, 70%) as a white solid. The NMR spectral data was in accordance with the previous report[14].



Butyl 4,6-*O*-(4-methoxybenzylidene)-β-D-glucopyranoside (7)

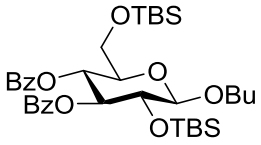
This compound was prepared as previously described[15].

Compound **5** (500 mg, 2.1 mmol) was dissolved in CH_3CN (4 mL). To this was added benzaldehyde dimethyl acetal (1 mL, 3 equiv.), and camphor-10-sulfonic acid (β) (25 mg, 0.05 equiv.), and the mixture was stirred at 45°C for 3 h. To quench the solution, trimethylamine was added, and the solution was stirred for another hour. The solvent was evaporated, and the

crude product purified through column chromatography (CH_2Cl_2-MeOH, 9:1) to give **7** (448 mg, 65%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (overlapping signals, 2H, aromatic H), 6.86 (overlapping signals, 2H, aromatic H), 5.42 (s, 1H, C*H*-Ar), 4.30 (d, *J* = 7.7 Hz, 1H, H-1), 4.26 (dd, *J* = 10.4, 5.0 Hz, 1H, H-6a), 3.83 (dt, *J* = 9.6, 6.9 Hz, 1H, butyl C*H*(H)O), 3.76 (s, 3H, O-C*H*$_3$), 3.71 (overlapping signals, 2H, H-3, H-6b), 3.52 (dt, *J* = 9.6, 6.9 Hz, 1H, butyl C*H*(H)O), 3.44 (overlapping signals, 2H, H-2, H-4), 3.33 (td, *J* = 9.7, 5.0 Hz, 1H, H-5), 1.60 (m, 2H, OCH_2CH_2), 1.35 (m, 2H, $OCH_2CH_2CH_2$), 0.91 (t, *J* = 7.4 Hz, 3H, $OCH_2CH_2CH_2CH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.2 (C), 129.6 (CH), 127.7 (CH), 113.6 (C), 103.1 (C-1), 101.7 (*C*H-Ar), 80.5 (C-4), 74.4 (C-2), 73.0 (C-3), 70.2 (OCH_2), 68.6 (C-6), 66.3 (C-5), 55.3 (O-CH_3), 31.6 (OCH_2CH_2), 19.1 ($OCH_2CH_2CH_2$), 13.8 ($OCH_2CH_2CH_2CH_3$).

- **Preparation of 8, 9, 10 and 11:**

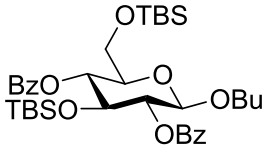
Compound **5** (1.5 g, 6.3 mmol) was reacted as described in the general procedure II.C using an excess of TBSOTf (7.3 mL, 5 equiv.) at 50 °C overnight. After workup, the mixture obtained was reacted as described in the general procedure II.B, using an excess of BzCl. Chromatography (cyclohexane-EtOAc, 20:0 to 15:5) gave **8** (0.3 g, 7% over two steps) as a white solid, **9** (0.5 g, 12% over two steps) as a white solid, **10** (0.6 g, 13% over two steps) as a white solid, and **11** (0.8 g, 18% over two steps) as a white solid.



Butyl 3,4-di-*O*-benzoyl-2,6-di-*O*-(tert-butyldimethylsilyl)-β-D-glucopyranoside (8)

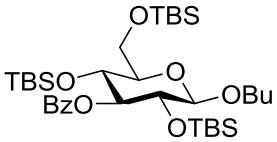
8: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (overlapping signals, 4H, aromatic H), 7.45 (overlapping signals, 2H, aromatic H), 7.32 (overlapping signals, 4H, aromatic H), 5.62 (t, *J* = 9.5 Hz, 1H, H-3), 5.31 (t, *J* = 9.5 Hz, 1H, H-4), 4.47 (d, *J* = 7.5 Hz, 1H, H-1), 3.94 (dt, *J* = 9.3, 7.1 Hz, 1H, butyl C*H*(H)), 3.76 (overlapping signals, 4H, H-2, H-5, H-6a, H-6b), 3.59 (ddd, *J* = 9.4, 7.3, 6.0 Hz, 1H, butyl C*H*(H)O), 1.65 (m, 2H, OCH_2CH_2), 1.43 (m, 2H, $OCH_2CH_2CH_2$), 0.95 (m, 3H, $OCH_2CH_2CH_2CH_3$), 0.87 (s, 9H, $SiC(CH_3)_3$), 0.75 (s, 9H, $SiC(CH_3)_3$), 0.08 (s, 3H, $SiCH_3$), 0.03 (s, 3H, $SiCH_3$), 0.02 (s, 3H, $SiCH_3$), -0.11 (s, 3H, $SiCH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.8 (C=O), 165.4 (C=O), 133.1 (C), 132.8 (C), 129.9 (CH), 129.7 (CH), 129.7 (CH), 129.3 (CH), 128.3 (CH), 128.2 (CH), 103.4 (C-1), 76.0 (C-3), 75.0 (C-5), 73.5 (C-2), 70.1 (C-4), 69.9 (OCH_2), 63.1 (C-6), 31.7 (OCH_2CH_2), 25.8 (CH_3, TBS), 25.5 (CH_3, TBS), 19.2 ($OCH_2CH_2CH_2$), 18.3 (C, TBS), 17.9 (C, TBS), 13.9 ($OCH_2CH_2CH_2CH_3$), -4.2 (CH_3, TBS), -

4.9 (CH_3, TBS), -5.3 (CH_3, TBS), -5.4 (CH_3, TBS). IR (film) cm^{-1}: 2926, 1716, 1451, 1275, 1026, 777, 705. ESI-HRMS calcd for $C_{36}H_{56}O_8Si_2Na$ 695.3406, found *m/z* 695.3398 $[M+Na]^+$.



Butyl 2,4-di-*O*-benzoyl-3,6-di-*O*-(tert-butyldimethylsilyl)-β-D-glucopyranoside (9)

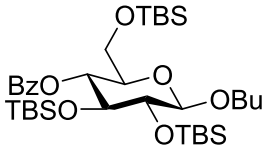
9: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (overlapping signals, aromatic H), 7.58 (overlapping signals, 2H, aromatic H), 7.46 (overlapping signals, 4H, aromatic H), 5.23 (overlapping signals, 2H, H-2, H-4), 4.58 (d, *J* = 8.0, 1H, H-1), 4.16 (m, 1H, H-3), 3.87 (ddd, *J* = 9.2, 6.9, 5.5 Hz, 1H, butyl C*H*(H)O), 3.76 (overlapping signals, 2H, H-6a, H-6b), 3.68 (m, 1H, H-5), 3.47 (dt, *J* = 9.2, 6.7 Hz, 1H, butyl C*H*(H)O), 1.45 (m, 2H, OCH_2CH_2), 1.17 (m, 2H, $OCH_2CH_2CH_2$), 0.84 (s, 9H, $SiC(CH_3)_3$), 0.71 (td, *J* = 7.4, 1.4 Hz, 3H, $OCH_2CH_2CH_2CH_3$), 0.63 (s, 9H, $SiC(CH_3)_3$), 0.01 (s, 3H, $SiCH_3$), -0.01 (s, 3H, $SiCH_3$), -0.19 (s, 3H, $SiCH_3$), -0.22 (s, 3H, $SiCH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.2 (C, C=O x2, overlapping signals), 133.2 (C), 132.9 (C), 129.8 (CH), 129.7 (CH), 128.4 (CH), 128.3 (CH), 101.0 (C-1), 75.4 (C-5), 74.7 (C-2), 73.5 (C-3), 72.8 (C-4) 69.3 (OCH_2), 63.5 (C-6), 31.4 (OCH_2CH_2), 25.8 (CH_3, TBS), 25.4 (CH_3, TBS), 18.9 (overlapping signals, $OCH_2CH_2CH_2$, and C, TBS), 13.5 ($OCH_2CH_2CH_2CH_3$), -4.4 (CH_3, TBS), -4.6 (CH_3, TBS), -5.3 (CH_3, TBS), -5.4 (CH_3, TBS). IR (film) cm^{-1}: 2928, 1731, 1722, 1451, 1252, 1057, 834, 776.



Butyl 3-*O*-benzoyl-2,4,6-tri-*O*-(tert-butyldimethylsilyl)-β-D-glucopyranoside (10)

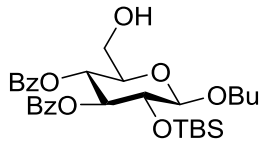
10: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (overlapping signals, 2H, aromatic H), 7.55 (m, 1H, aromatic H), 7.43 (overlapping signals, 2H, aromatic H), 5.34 (t, *J* = 9.2 Hz, 1H, H-3), 4.33 (d, *J* = 7.5 Hz, 1H, H-1), 3.87 (overlapping signals, 2H, H-6a, butyl C*H*(H)O), 3.78 (overlapping signals, 2H, H-4, H-6b), 3.52 (overlapping signals, 2H, H-2, butyl C*H*(H)O), 3.32 (ddd, *J* = 9.4, 4.7, 2.0 Hz, 1H, H-5), 1.63 (m, 2H, OCH_2CH_2), 1.37 (m, 2H, $OCH_2CH_2CH_2$), 0.91 (overlapping signals, 12H, $OCH_2CH_2CH_2CH_3$, $SiC(CH_3)_3$), 0.74 (s, 9H, $SiC(CH_3)_3$), 0.69 (s, 9H, $SiC(CH_3)_3$), 0.06 (overlapping signals, 12H, $SiCH_3$), -0.18 (s, 3H, $SiCH_3$), -0.20 (s, 3H, $SiCH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.4 (C=O), 132.7 (C), 130.8 (CH), 130.0 (CH), 128.1 (CH), 103.0 (C-1), 78.8 (C-3), 76.8 (C-5), 73.9 (C-2), 69.3 (O-CH_2), 69.0 (C-4), 62.1 (C-6),

31.7 (OCH_2CH_2), 25.9 (CH_3, TBS), 25.7 (CH_3, TBS), 25.6 (CH_3, TBS), 19.3 ($OCH_2CH_2CH_2$), 18.4 (C, TBS), 17.8 (C, TBS), 13.9 ($OCH_2CH_2CH_2CH_3$), -4.0 (CH_3, TBS), -4.3 (CH_3, TBS), -4.6 (CH_3, TBS), -4.9 (CH_3, TBS), -5.0 (CH_3, TBS), -5.4 (CH_3, TBS). IR (film) cm^{-1}: 2952, 1729, 1461, 1366, 1217, 1093, 829, 776, 711.



Butyl 4-*O*-benzoyl-2,3,6-tri-*O*-(tert-butyldimethylsilyl)-β-D-glucopyranoside (11)

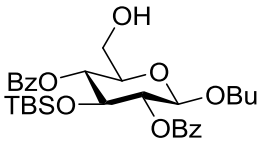
11: ^1H NMR (500 MHz, $CDCl_3$) δ 8.02 (overlapping signals, 2H, aromatic H), 7.56 (m, 1H, aromatic H), 7.43 (overlapping signals, 2H, aromatic H), 5.08 (t, *J* = 7.7 Hz, 1H, H-4), 4.34 (d, *J* = 6.8 Hz, 1H, H-1), 3.87 (overlapping signals, 2H, H-3, butyl C*H*(H)O), 3.73 (overlapping signals, 2H, H-6a, H-6b), 3.65 (td, *J* = 7.0, 4.2 Hz, 1H, H-5), 3.56 (t, *J* = 6.7 Hz, 1H, H-2), 3.46 (ddd, *J* = 9.2, 7.6, 6.0 Hz, 1H, butyl C*H*(H)O), 1.64 (m, 2H, OCH_2CH_2), 1.38 (m, 2H, $OCH_2CH_2CH_2$), 0.92 (t, *J* = 7.4 Hz, 3H, $OCH_2CH_2CH_2CH_3$), 0.87 (s, 9H, $SiC(CH_3)_3$), 0.83 (s, 9H, $SiC(CH_3)_3$), 0.78 (s, 9H, $SiC(CH_3)_3$), 0.13 (s, 3H, $SiCH_3$), 0.08 (s, 3H, $SiCH_3$), 0.07 (s, 3H, $SiCH_3$), -0.02 (s, 3H, $SiCH_3$), -0.04 (s, 3H, $SiCH_3$), -0.07 (s, 3H, $SiCH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.5 (C=O), 133.0 (C), 130.2 (CH), 129.9 (CH), 128.2 (CH), 103.2 (C-1), 75.9 (C-5), 75.8 (C-2), 75.3 (C-3), 72.4 (C-4), 69.3 (OCH_2), 63.8 (C-6), 31.7 (OCH_2CH_2), 26.2 (CH_3, TBS), 25.9 (CH_3, TBS), 25.8 (CH_3, TBS), 19.3 ($OCH_2CH_2CH_2$), 18.3 (C, TBS), 18.2 (C, TBS), 17.9 (C, TBS), 13.9 ($OCH_2CH_2CH_2CH_3$), -3.0 (CH_3, TBS), -3.2 (CH_3, TBS), -3.6 (CH_3, TBS), -3.9 (CH_3, TBS), -5.4 (CH_3, TBS), -5.5 (CH_3, TBS). IR (film) cm^{-1}: 3659, 2958, 2931, 2890, 2858, 1733, 1473, 1250, 1151, 1113, 1086, 1068, 1046, 831, 773, 707, 681, 670. ESI-HRMS calcd for $C_{35}H_{66}O_7Si_3Na$ 705.4014, found *m/z* 705.4037 $[M+Na]^+$.



Butyl 3,4-di-*O*-benzoyl-2-*O*-(tert-butyldimethylsilyl)-β-D-glucopyranoside (12β)

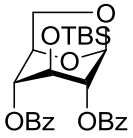
Compound **8** (0.3 g, 0.44 mmol) was reacted as described in the general procedure II.D. Chromatography (cyclohexane-EtOAc 7:3) gave **12β** (157 mg, 64%) as a white solid. ^1H NMR (500 MHz, $CDCl_3$) δ 7.93 (overlapping signals, 4H, aromatic H), 7.50 (overlapping signals, 2H, aromatic H), 7.35 (overlapping signals, 4H, aromatic H), 5.69 (t, *J* = 9.4 Hz, 1H, H-3), 5.32 (t, *J* = 9.7 Hz, 1H, H-4), 4.49 (d, *J* = 7.5 Hz, 1H, H-1), 3.93 (dt, *J* = 9.3, 7.2 Hz, 1H, butyl

C*H*(H)O), 3.80 (overlapping signals, 2H, H-2, H-6a), 3.68 (overlapping signals, 2H, H-5, H-6b), 3.57 (ddd, *J* = 9.3, 7.4, 6.1 Hz, 1H, butyl C*H*(H)O), 1.66 (m, 2H, OCH_2CH_2), 1.41 (m, 2H, $OCH_2CH_2CH_2$), 0.95 (t, *J* = 7.4 Hz, 3H, $OCH_2CH_2CH_2CH_3$), 0.74 (s, 9H, $SiC(CH_3)_3$), 0.08 (s, 3H, $SiCH_3$), -0.11 (s, 3H, $SiCH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.3 (C=O), 165.8 (C=O), 133.5 (C), 133.0 (C), 129.9 (CH), 129.7 (CH), 128.7 (CH), 128.4 (CH), 128.2 (CH), 103.6 (C-1), 75.4 (C-3), 74.1 (C-5), 73.3 (C-2), 70.1 (O-CH_2), 69.8 (C-4), 61.5 (C-6), 31.7 (OCH_2CH_2), 25.5 (CH_3, TBS), 19.2 ($OCH_2CH_2CH_2$), 17.9 (C, TBS), 13.9 ($OCH_2CH_2CH_2CH_3$), -4.2 (CH_3, TBS), -4.9 (CH_3, TBS). IR (film) cm^{-1}: 3510, 2981, 2888, 1726, 1603, 1473, 1452, 1382, 1274, 1251, 1091, 1069, 1026, 854, 837, 779, 686. ESI-HRMS calcd for $C_{30}H_{42}O_8SiNa$ 581.2547, found *m/z* 581.2518 $[M+Na]^+$.



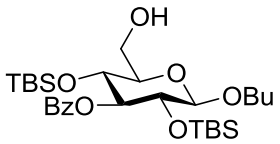
Butyl 2,4-di-*O*-benzoyl-3-*O*-(tert-butyldimethylsilyl)-β-D-glucopyranoside (13β)

Compound **9** (0.5 g, 0.8 mmol) was reacted as described in the general procedure II.D. Chromatography (cyclohexane-EtOAc 7:3) gave **13β** (284 mg, 67%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (overlapping signals, 4H, aromatic H), 7.58 (overlapping signals, 2H, aromatic H), 7.45 (overlapping signals, 4H, aromatic H), 5.27 (overlapping signals, 2H, H-2, H-4), 4.62 (d, *J* = 8.1 Hz, 1H, H-1), 4.23 (t, *J* = 9.0 Hz, 1H, H-5), 3.87 (dt, *J* = 9.7, 6.2 Hz, 1H, butyl C*H*(H)O), 3.74 (d, *J* = 12.3 Hz, 1H, H-6a), 3.65 (overlapping signals, 2H, H-3, H-6b), 3.47 (dt, *J* = 9.7, 6.8 Hz, 1H, butyl C*H*(H)O), 2.42 (s, 1H, OH), 1.45 (m, 2H, OCH_2CH_2), 1.16 (m, 2H, $OCH_2CH_2CH_2$), 0.69 (t, *J* = 7.4 Hz, 3H, $OCH_2CH_2CH_2CH_3$), 0.62 (s, 9H, $SiC(CH_3)_3$), -0.19 (s, 6H, $SiCH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.9 (C=O), 165.0 (C=O), 133.5 (C), 133.0 (C), 130.2 (CH), 129.8 (CH), 129.7 (CH), 129.3 (CH), 128.5 (CH), 128.3 (CH), 101.3, (C-1) 74.6 (C-2), 74.5 (C-3), 73.3 (C-5), 72.2 (C-4), 69.6 (OCH_2), 61.8 (C-6), 31.4 (OCH_2CH_2), 25.4 (CH_3, TBS), 18.8 ($OCH_2CH_2CH_2$), 17.7 (C, TBS), 13.5 ($OCH_2CH_2CH_2CH_3$), -4.4 (CH_3, TBS), -4.6 (CH_3, TBS). IR (film) cm^{-1}: 3659, 2891, 2889, 1723, 1382, 1253, 1148, 1087, 1069, 1027, 955, 835, 779, 710.



1,6-Anhydro-2,4-di-O-benzoyl-3-O-(tert-butyldimethylsilyl)-β-D-glucopyranose (13-anydro)

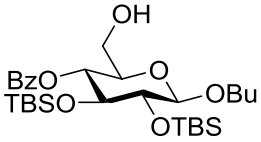
Compound **13β** (17 mg, 0.03 mmol) was reacted as described in the general procedure II.L. Chromatography (cyclohexane:EtOAc 5:1) gave **13-anhydro** (11 mg, 72%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (overlapping signals, 4H, aromatic H), 7.57 (overlapping signals, 2H, aromatic H), 7.38 (overlapping signals, 4H, aromatic H), 5.62 (d, *J* = 1.9 Hz, 1H, H-1), 4.89 (m, 1H, H-4), 4.84 (s, 1H, H-2), 4.78 (m, 1H, H-5), 4.41 (dq, *J* = 7.2, 1.1 Hz, 1H, H-6a), 3.99 (m, 1H, H-3), 3.86 (ddd, *J* = 7.3, 5.8, 1.9 Hz, 1H, H-6b), 0.93 (s, 9H, $SiC(CH_3)_3$), 0.19 (s, 3H, $SiCH_3$), 0.15 (s, 3H, $SiCH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.7, 165.5 (each C=O), 133.5 (C), 133.5 (C), 130.1 (CH), 130.1 (CH), 129.8 (CH), 129.7 (CH), 128.5 (CH), 100.0 (C-1), 74.0 (C-5), 73.3 (C-4), 71.8 (C-2), 69.9 (C-3), 65.4 (C-6), 29.8 (CH_3, TBS), 25.8 (CH_3, TBS), 18.0 (C, TBS), -4.9 (CH_3, TBS), -5.1 (CH_3, TBS). ESI-HRMS calcd for $C_{26}H_{32}O_7SiNa$ 507,1815 found *m/z* 507.1817 $[M+Na]^+$.



Butyl 3-*O*-benzoyl-2,4-di-*O*-(tert-butyldimethylsilyl)-β-D-glucopyranoside (14β)

Compound **10** (0.6 g, 0.83 mmol) was reacted as described in the general procedure II.D. Chromatography (cyclohexane-EtOAc 4:1) gave **14β** (291 mg, 62%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (overlapping signals, 2H, aromatic H), 7.52 (m, 1H, aromatic H), 7.40 (overlapping signals, 2H, aromatic H), 5.35 (t, *J* = 9.2 Hz, 1H, H-3), 4.39 (d, *J* = 7.5 Hz, 1H, H-1), 3.84 (overlapping signals, 3H, H-4, H-6a, butyl C*H*(H)O), 3.70 (ddd, *J* = 11.8, 5.0, 2.6 Hz, 1H, H-6b), 3.57 (dd, *J* = 9.8, 7.6 Hz, 1H, H-2), 3.51 (ddd, *J* = 9.5, 6.2, 2.4 Hz, 1H, butyl C*H*(H)O), 3.41 (ddd, *J* = 9.9, 5.1, 2.6 Hz, 1H, H-5), 2.05 (m, 1H, OH), 1.61 (m, 2H, OCH_2CH_2), 1.37 (m, 2H, $OCH_2CH_2CH_2$), 0.91 (td, *J* = 6.1, 4.8, 2.5 Hz, 3H, $OCH_2CH_2CH_2CH_3$), 0.70 (overlapping signals, 18H, $SiC(CH_3)_3$ x 2), 0.03 (overlapping signals, 6H, $SiCH_3$ x2), -0.22 (overlapping signals, 6H, $SiCH_3$ x 2). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.3 (C=O), 132.8 (C), 130.6 (CH), 130.0 (CH), 128.1 (CH), 103.4 (C-1), 78.4 (C-3), 76.2 (C-5), 73.6 (C-2), 70.0 (O-CH_2), 69.0 (C-4), 61.6 (C-6), 31.7 (OCH_2CH_2), 25.6 (CH_3, TBS), 25.5 (CH_3, TBS), 19.2 ($OCH_2CH_2CH_2$), 17.7 (C, TBS), 13.8 ($OCH_2CH_2CH_2CH_3$), -4.0 (CH_3, TBS), -4.2 (CH_3, TBS), -4.6 (CH_3, TBS), -4.8 (CH_3, TBS). IR (film) cm^{-1}: 3514, 2956,

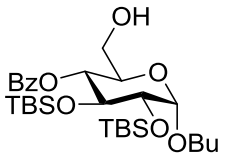
1731, 1452, 1264, 1080, 1069, 1026, 834, 777, 706, 674. ESI-HRMS calcd for $C_{29}H_{52}O_7Si_2Na$ 591.3149, found *m/z* 591.3121 $[M+Na]^+$.



Butyl 4-*O*-benzoyl-2,3-di-*O*-(tert-butyldimethylsilyl)-β-D-glucopyranoside (15β)

Compound **11** (0.8 g, 1.1 mmol) was reacted as described in the general procedure II.D. Chromatography (cyclohexane-EtOAc 4:1) gave **15β** (416 mg, 64%) as a white solid.

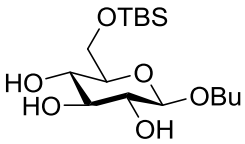
This compound was also synthesized from **44** (2.6 g, 4.7 mmol), subjecting it to general procedure II.F. Chromatography (cyclohexane-EtOAc, 4:1) gave **15β** (2 g, 76%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (overlapping signals, 2H, aromatic H), 7.59 (m, 1H, aromatic H), 7.45 (overlapping signals, 2H, aromatic H), 5.11 (t, *J* = 8.1 Hz, 1H, H-4), 4.35 (d, *J* = 7.0 Hz, 1H, H-1), 3.91 (m, 1H, H-3), 3.86 (dt, *J* = 8.8, 7.4 Hz, 1H, butyl C*H*(H)O), 3.67 (overlapping signals, 2H, H-6a, H-6b), 3.60 (overlapping signals, 2H, H-2, H-5), 3.47 (ddd, *J* = 9.0, 7.7, 5.9 Hz, 1H, butyl C*H*(H)O), 2.40 (m, 1H, OH), 1.64 (m, 2H, OCH_2CH_2), 1.38 (m, 2H, $OCH_2CH_2CH_2$), 0.93 (t, *J* = 7.6 Hz, 3H, $OCH_2CH_2CH_2CH_3$), 0.90 (s, 9H, $SiC(CH_3)_3$), 0.76 (s, 9H, $SiC(CH_3)_3$), 0.14 (s, 3H, $SiCH_3$), 0.10 (s, 3H, $SiCH_3$), 0.07 (s, 3H, $SiCH_3$), -0.06 (s, 3H, $SiCH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.2 (C=O), 133.4 (C), 129.9 (overlapping signals, CH x2), 128.4 (CH), 103.4 (C-1), 75.7 (C-2), 75.4 (C-3), 74.9 (C-5), 72.3 (C-4), 69.6 (OCH_2), 62.3 (C-6), 31.6 (OCH_2CH_2), 26.2 (CH_3, TBS), 25.8 (CH_3, TBS), 19.3 ($OCH_2CH_2CH_2$), 18.3 (C, TBS), 17.9 (C, TBS), 13.9 ($OCH_2CH_2CH_2CH_3$), -2.9 (CH_3, TBS), -3.0 (CH_3, TBS), -3.6 (CH_3, TBS), -3.9 (CH_3, TBS). IR (film) cm^{-1}: 3520, 2931, 1732, 1473, 1269, 1251, 1089, 1026, 837, 774, 707. ESI-HRMS calcd for $C_{29}H_{52}O_7Si_2Na$ 591.3149, found *m/z* 591.3151 $[M+Na]^+$.



Butyl 4-*O*-benzoyl-2,3-di-*O*-(tert-butyldimethylsilyl)-α-D-glucopyranoside (15α)

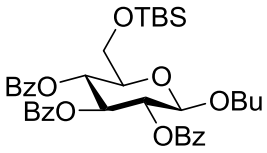
Compound **15β** (17 mg, 0.03 mmol) was reacted as described in the general procedure II.L. Chromatography (cyclohexane-EtOAc 4:1) gave **15α.** ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (overlapping signals, 2H, aromatic H), 7.59 (m, 1H, aromatic H), 7.45 (overlapping signals, 2H, aromatic H), 5.09 (m, 1H, H-4), 4.82 (d, *J* = 3.4 Hz, 1H, H-1), 4.17 (t, *J* = 8.8 Hz, 1H, H-3), 3.75 (dt, *J* = 10.2, 3.0 Hz, 1H, H-5), 3.69 (overlapping signals, 2H, H-2, butyl C*H*(H)O),

3.63 (dd, *J* = 13.0, 3.8 Hz, 1H, H-6a), 3.53 (dd, *J* = 13.0, 3.8 Hz, 1H, H-6b), 3.42 (dt, *J* = 9.8, 6.8 Hz, 1H, butyl C*H*(H)O), 2.54 (s, 1H, OH), 1.64 (m, 2H, OCH_2CH_2), 1.41 (m, 2H, $OCH_2CH_2CH_2$), 0.94 (overlapping signals, 12H, $SiC(CH_3)_3$, $OCH_2CH_2CH_2CH_3$), 0.71 (s, 9H, $SiC(CH_3)_3$), 0.11 (s, 3H, $SiCH_3$), 0.10 (s, 3H, $SiCH_3$), 0.06 (s, 3H, $SiCH_3$), -0.09 (s, 3H, $SiCH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.0 (C=O), 133.6 (C), 130.1 (CH), 129.7 (CH), 128.5 (CH), 99.5 (C-1), 74.4 (C-2), 72.6 (C-4), 72.0 (C-3), 69.9 (C-5), 68.4 (OCH_2), 61.5 (C-6), 31.8(OCH_2CH_2), 26.3 (CH_3, TBS), 25.9 (CH_3, TBS), 19.6 ($OCH_2CH_2CH_2$), 18.4 (C, TBS), 18.0 (C, TBS), 14.1 ($OCH_2CH_2CH_2CH_3$), -2.8 (CH_3, TBS), -3.4 (CH_3, TBS), -4.1 (CH_3, TBS), -4.2 (CH_3, TBS). IR (film) cm^{-1}: 3493, 2956, 1728, 1452, 1361, 1251, 1156, 1105, 1069, 1026, 990, 930, 861, 835, 774, 709, 680, 668. ESI-HRMS calcd for $C_{29}H_{52}O_7Si_2Na$ 591.3149, found *m/z* 591.3156 $[M+Na]^+$.



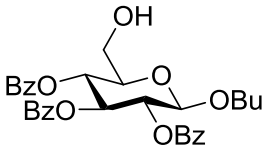
Butyl 6-*O*-(tert-butyldimethylsilyl)-β-D-glucopyranoside (16)

Compound **5** (241 mg, 1 mmol) was reacted as described in the general procedure II.C using TBSOTf (0.28 mL, 1.2 equiv.) at room temperature overnight. Chromatography (cyclohexane-EtOAc, 3:2) gave **16** (233 mg, 65%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.23 (d, *J* = 7.8 Hz, 1H, H-1), 3.89 (dd, *J* = 11.1, 3.3 Hz, 1H, H-6a), 3.82 (dt, *J* = 9.5, 7.0 Hz, 1H, butyl C*H*(H)O), 3.76 (dd, *J* = 11.1, 5.8 Hz, 1H, H-6b), 3.49 (overlapping signals, 2H, H-4, butyl C*H*(H)O), 3.36 (t, *J* = 9.2 Hz, 1H, H-3), 3.29 (overlapping signals, 2H, H-5, H-2), 1.58 (m, 2H, OCH_2CH_2), 1.34 (m, 2H, $OCH_2CH_2CH_2$), 0.88 (overlapping signals, 12H, $OCH_2CH_2CH_2CH_3$, $SiC(CH_3)_3$), 0.06 (overlapping signals, 6H, $SiCH_3$ x2). ^{13}C NMR (126 MHz, $CDCl_3$) δ 102.3 (C-1), 76.3 (C-2, C-3, C-4 (overlapping signals)), 73.2 (C-5), 69.6 (OCH_2), 63.7 (C-6), 31.6 (OCH_2CH_2), 25.9 (CH_3, TBS), 19.1 ($OCH_2CH_2CH_2$), 18.3 (C, TBS), 13.8 ($OCH_2CH_2CH_2CH_3$), -5.3 (CH_3, TBS), -5.3 (CH_3, TBS).



Butyl 2,3,4-tri-*O*-benzoyl-6-*O*-(tert-butyldimethylsilyl)-β-D-glucopyranoside (17)

Compound **16** (233 mg, 0.67 mmol) was reacted as described in the general procedure II.B using an excess of BzCl. Chromatography (cyclohexane-EtOAc, 4:1) gave **17** (375 mg, 85%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (overlapping signals, 2H, aromatic H), 7.94 (overlapping signals, 2H, aromatic H), 7.83 (overlapping signals, 2H, aromatic H), 7.62 (overlapping signals, 3H, aromatic H), 7.49 (overlapping signals, 2H, aromatic H), 7.40 (overlapping signals, 2H, aromatic H), 7.28 (d, *J* = 7.7 Hz, 2H, aromatic H), 5.85 (t, *J* = 9.7 Hz, 1H, H-3), 5.47 (overlapping signals, 2H, H-2, H-4), 4.78 (d, *J* = 7.8 Hz, 1H, H-1), 3.93 (dt, *J* = 9.6, 6.4 Hz, 1H, butyl C*H*(H)O), 3.84 (overlapping signals, 3H, H-5, H6a, H6b), 3.55 (dt, *J* = 9.7, 6.7 Hz, 1H, butyl C*H*(H)O), 1.51 (m, 2H, OCH_2CH_2), 1.25 (m, 2H, $OCH_2CH_2CH_2$), 0.87 (s, 9H, $SiC(CH_3)_3$), 0.77 (t, *J* = 7.4 Hz, 3H, $OCH_2CH_2CH_2CH_3$), 0.05 (overlapping signals, 6H, $SiCH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.9 (C=O), 165.2 (C=O), 165.1 (C=O), 133.8 (C), 133.2 (C), 133.1 (C), 133.0 (CH), 130.2 (CH), 129.8 (CH), 129.7 (CH), 129.7 (CH), 129.5 (CH), 129.3 (CH), 129.2 (CH), 129.0 (CH), 128.5 (CH), 128.3 (CH), 128.3 (CH), 128.2 (CH), 101.0 (C-1), 75.3 (C-5), 73.3 (C-3), 72.1 (C-2), 69.8 (C-4), 69.6 (OCH_2), 62.9 (C-6), 31.4 (OCH_2CH_2), 25.8 (CH_3, TBS), 18.9 ($OCH_2CH_2CH_2$), 18.3 (C, TBS), 13.6 ($OCH_2CH_2CH_2CH_3$), 1.0 (CH_3, TBS), -5.4 (CH_3, TBS). IR (film) cm^{-1}: 2981, 2889, 1731, 1688, 1382, 1251, 1152, 1070, 953, 706.



Butyl 2,3,4-tri-*O*-benzoyl-6-*O*-(tert-butyldimethylsilyl)-β-D-glucopyranoside (18β)

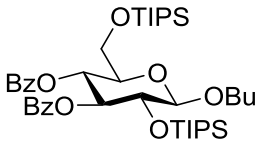
Compound **18β**, a new compound, was prepared by deprotection of the primary TBS of **17** using reagents and conditions reported previously[16].

Thus, **17** (375 mg, 0.57 mmol) was diluted in THF (1 mL), H_2O (2 mL), and AcOH (6 mL). The mixture was stirred at room temperature overnight. The solution was extracted with Et_2O three times. The organic phase was then washed with a saturated aqueous solution of $NaHCO_3$, water and brine. It was then dried over Na_2SO_4, filtered and removed under reduced pressure. Chromatography (cyclohexane-EtOAc, 7:3) gave **18β** (257 mg, 83%) as a white solid. ^{1}H NMR

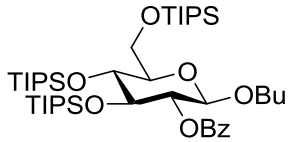
(500 MHz, $CDCl_3$) δ 7.96 (overlapping signals, 4H, aromatic H), 7.85 (overlapping signals, 2H, aromatic H), 7.53 (overlapping signals, 2H, aromatic H), 7.40 (overlapping signals, 5H, aromatic H), 7.29 (overlapping signals, 2H, aromatic H), 5.94 (t, *J* = 9.7 Hz, 1H, H-3), 5.50 (overlapping signals, 2H, H-2, H-4), 4.84 (d, *J* = 7.9 Hz, 1H, H-1), 3.95 (dt, *J* = 9.8, 6.3 Hz, 1H, butyl C*H*(H)O), 3.87 (d, *J* = 12.5 Hz, 1H, H-6a), 3.79 (overlapping signals, 2H, H-5, H-6b), 3.56 (dt, *J* = 8.4, 6.7 Hz, 1H, butyl C*H*(H)O), 1.53 (m, 2H, OCH_2CH_2), 1.26 (m, 2H, $OCH_2CH_2CH_2$), 0.77 (td, *J* = 7.4, 1.7 Hz, 3H, $OCH_2CH_2CH_2CH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.0 (C=O), 165.9 (C=O), 165.1 (C=O), 133.6 (C), 133.2 (C), 133.1 (C), 129.9 (CH), 129.7 (CH), 129.7 (CH), 129.4 (CH), 128.9 (CH), 128.6 (CH), 128.5 (CH), 128.3 (CH), 128.3 (CH), 101.3 (C-1), 74.6 (C-5), 72.8 (C-3), 71.9 (C-4), 70.0 (OCH_2), 69.6 (C-2), 61.4 (C-6), 31.4 (OCH_2CH_2), 18.9 ($OCH_2CH_2CH_2$), 13.6 ($OCH_2CH_2CH_2CH_3$). IR (film) cm^{-1}: 3659, 2980, 2884, 1730, 1602, 1451, 1379, 1251, 1176, 1148, 1087, 1068, 1026, 837, 778, 685. ESI-HRMS calcd for $C_{31}H_{32}O_9Na$ 571.1944, found *m/z* 571.1918 $[M+Na]^+$.

- **Preparation 19, 20 and 21:**

Compound **5** (1.5 g, 6.35 mmol) was reacted as described in the general procedure II.C using an excess of TIPSOTf (8.5 mL, 5 equiv.) at 50 °C overnight. After workup, the mixture was reacted as described in the general procedure II.B, using an excess of BzCl. Chromatography (cyclohexane-EtOAc, 20:0 to 15:5) gave **19** (625 mg, 13% over two steps) as a colourless oil, **20** (1.07 g, 21% over two steps) as a colourless oil, and **21** (1.28 g, 25% over two steps) as a colourless oil.



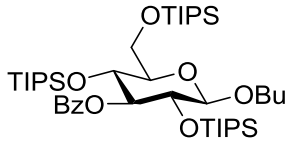
Butyl 3,4-di-*O*-benzoyl-2,6-di-*O*-triisopropylsilyl-β-D-glucopyranoside (19)



Butyl 2-*O*-benzoyl-3,4,6-tri-*O*-triisopropylsilyl-β-D-glucopyranoside (20)

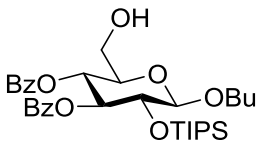
20: ^1H NMR (500 MHz, $CDCl_3$) δ 8.06 (overlapping signals, 2H, aromatic H), 7.55 (m, 1H, aromatic H), 7.41 (overlapping signals, 2H, aromatic H), 5.17 (d, *J* = 5.3 Hz, 1H, H-2), 5.03 (d, *J* = 5.3 Hz, 1H, H-1), 4.20 (overlapping signals, 2H, H-3, H-4), 4.13 (dd, *J* = 9.6, 8.2 Hz, 1H, H-6a), 4.06 (dd, *J* = 8.3, 5.3 Hz, 1H, H-5), 3.92 (dd, *J* = 9.6, 5.2 Hz, 1H, H-6b), 3.87 (dt, *J*

= 9.6, 6.5 Hz, 1H, butyl C*H*(H)O), 3.44 (dt, *J* = 9.8, 6.7 Hz, 1H, butyl C*H*(H)O), 1.50 (m, 2H, OCH_2CH_2), 1.29 (m, 2H, $OCH_2CH_2CH_2$), 1.21 – 1.05 (overlapping signals, 63H, $Si(CH(CH_3)_2)_3$ x 3), 0.79 (t, *J* = 7.4 Hz, 3H, $OCH_2CH_2CH_2CH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.3 (C=O), 132.8 (C), 130.3 (CH), 129.8 (CH), 129.6 (CH), 128.0 (CH), 98.7 (C-1), 82.1 (C-5), 75.0 (C-2), 74.3 (C-3), 70.0 (C-4), 68.9 (OCH_2), 64.8 (C-6), 31.5 (OCH_2CH_2), 19.1 ($OCH_2CH_2CH_2$), 18.1 (CH_3, TIPS), 18.1 (CH_3, TIPS), 18.0 (CH_3, TIPS), 18.0 (CH_3, TIPS), 17.9 (CH_3, TIPS), 17.9 (CH_3, TIPS), 13.7 (CH, TIPS), 13.6 ($OCH_2CH_2CH_2CH_3$), 13.1 (CH, TIPS). IR (film) cm^{-1}: 2943, 1737, 1462, 1366, 1217, 1067, 882, 680.



Butyl 3-*O*-benzoyl-2,4,6-tri-*O*-triisopropylsilyl-β-D-glucopyranoside (21)

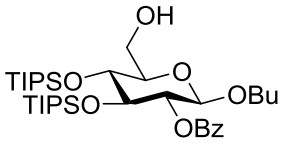
21: ^1H NMR (500 MHz, $CDCl_3$) δ 8.05 (overlapping signals, 2H, aromatic H), 7.54 (m, 1H, aromatic H), 7.42 (overlapping signals, 2H, aromatic H), 5.37 (t, *J* = 8.7 Hz, 1H, H-3), 4.41 (d, *J* = 7.5 Hz, 1H, H-1), 4.05 (dd, *J* = 10.7, 2.4 Hz, 1H, H-6a), 3.98 (t, *J* = 8.8 Hz, 1H, H-4), 3.89 (overlapping signals, 2H, H-6b, butyl C*H*(H)O), 3.76 (dd, *J* = 8.8, 7.4 Hz, 1H, H-2), 3.47 (overlapping signals, 2H, H-5, butyl C*H*(H)O), 1.59 (m, 2H, OCH_2CH_2), 1.36 (m, 2H, $OCH_2CH_2CH_2$), 1.08 (overlapping signals, 21H, $Si(CH(CH_3)_2)_3$), 0.94 (overlapping signals, 45H, $Si(CH(CH_3)_2)_3$ x2, $OCH_2CH_2CH_2CH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.1 (C=O), 132.7 (C), 130.6 (CH), 129.6 (CH), 128.0 (CH), 102.8 (C-1), 79.4 (C-3), 78.0 (C-5), 74.4 (C-2), 70.4 (C-4), 69.2 (OCH_2), 63.3 (C-6), 31.7 (OCH_2CH_2), 19.3 ($OCH_2CH_2CH_2$), 18.1 (CH_3, TIPS), 18.1 (CH_3, TIPS), 18.0 (CH_3, TIPS), 18.0 (CH_3, TIPS), 17.9 (CH_3, TIPS), 17.9 (CH_3, TIPS), 13.9 ($OCH_2CH_2CH_2CH_3$), 13.6 (CH, TIPS), 13.1 (CH, TIPS), 12.0 (CH, TIPS). IR (film) cm^{-1}: 2943, 1737, 1463, 1366, 1217, 1091, 882, 679.



Butyl 3,4-di-*O*-benzoyl-2-*O*-triisopropylsilyl-β-D-glucopyranoside (22)

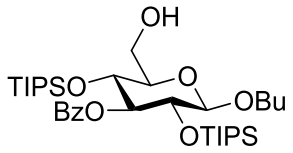
Compound **19** (625 mg, 1.21 mmol) was reacted as described in the general procedure II.E. Chromatography (cyclohexane-EtOAc, 17:3) gave **22** (567 mg, 78%) as a colourless oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.91 (overlapping signals, 4H, Ar-H), 7.45 (overlapping signals, 2H, Ar-H), 7.32 (overlapping signals, 4H, Ar-H), 5.69 (t, *J* = 9.4 Hz, 1H, H-3), 5.30 (t, *J* = 9.7 Hz, 1H, H-4), 4.49 (d, *J* = 7.5 Hz, 1H, H-1), 4.00 (dd, *J* = 9.1, 7.4 Hz, 1H, H-2), 3.92 (m, 1H,

butyl C*H*(H)O), 3.80 (m, 1H, H-6a), 3.68 (overlapping signals, 2H, H-5, H-6b), 3.54 (m, 1H, butyl C*H*(H)O), 1.63 (m, 2H, OCH_2CH_2), 1.40 (m, 2H, $OCH_2CH_2CH_2$), 0.95 (overlapping signals, 24H, $OCH_2CH_2CH_2CH_3$, $Si(CH(CH_3)_2)_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.4 (C=O), 165.8 (C=O), 133.5 (C), 133.0 (C), 130.1 (CH), 129.9 (CH), 129.7 (CH), 129.5 (CH), 128.7 (CH), 128.4 (CH), 128.3 (CH), 128.1 (CH), 103.7 (C-1), 75.9 (C-3), 74.0 (C-5), 73.7 (C-2), 70.1 (C-4), 69.8 (OCH_2), 61.4 (C-6), 31.6 (OCH_2CH_2), 26.9 (CH_3, TIPS), 19.2 ($OCH_2CH_2CH_2$), 18.0 (CH_3, TIPS), 17.9 (CH_3, TIPS), 13.9 ($OCH_2CH_2CH_2CH_3$), 12.8 (CH, TIPS). ESI-HRMS calcd for $C_{33}H_{48}O_8SiNa$ 623.3016, found *m/z* 623.3033 $[M+Na]^+$.



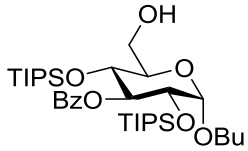
Butyl 2-*O*-benzoyl-3,4-di-*O*-triisopropylsilyl-β-D-glucopyranoside (23)

Compound **20** (1.07 g, 1.33 mmol) was reacted as described in the general procedure II.E. Chromatography (cyclohexane-EtOAc, 18:2) gave **23** (643 mg, 74%) as a colourless oil. ^1H NMR (500 MHz, $CDCl_3$) δ 8.04 (overlapping signals, 2H, Ar-H), 7.55 (m, 1H, Ar-H), 7.41 (overlapping signals, 2H, Ar-H), 5.20 (d, *J* = 5.9 Hz, 1H, H-2), 5.03 (d, *J* = 5.9 Hz, 1H, H-1), 4.17 (d, *J* = 2.9 Hz, 1H, H-3), 4.11 (dd, *J* = 7.5, 3.9 Hz, 1H, H-5), 3.99 (overlapping signals, 2H, H-4, H-6a), 3.85 (dt, *J* = 9.5, 6.6 Hz, 1H, butyl C*H*(H)O), 3.79 (dd, *J* = 11.2, 4.1 Hz, 1H, H-6b), 3.48 (dt, *J* = 9.6, 6.7 Hz, 1H, butyl C*H*(H)O), 1.51 (m, *J* = 6.9 Hz, 2H, OCH_2CH_2), 1.27 (m, 2H, $OCH_2CH_2CH_2$), 1.08 (overlapping signals, 42H, $Si(CH(CH_3)_2)_3$ x2), 0.78 (t, *J* = 7.4 Hz, 3H, $OCH_2CH_2CH_2CH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.2 (C=O), 133.6, 130.2, 128.5 (all aromatic carbons), 99.6 (C-1), 82.6 (C-5), 75.2 (C-2), 74.4 (C-3), 70.8 (C-4), 69.2 (OCH_2), 64.0 (C-6), 31.5 (OCH_2CH_2), 19.0 ($OCH_2CH_2CH_2$), 18.3 (CH_3, TIPS), 18.3 (CH_3, TIPS), 18.1 (CH_3, TIPS), 18.1 (CH_3, TIPS), 18.1 (CH_3, TIPS), 18.0 (CH_3, TIPS), 17.9 (CH_3, TIPS), 17.9 (CH_3, TIPS), 17.8 (CH_3, TIPS), 17.7 (CH_3, TIPS), 17.6 (CH_3, TIPS), 13.7 ($OCH_2CH_2CH_2CH_3$), 13.2 (CH, TIPS), 13.0 (CH, TIPS), 12.6 (CH, TIPS), 12.3 (CH, TIPS), 12.2 (CH, TIPS), 12.1 (CH, TIPS). ESI-HRMS calcd for $C_{35}H_{64}O_7Si_2Na$ 675.4088, found *m/z* 675.4078 $[M+Na]^+$.



Butyl 3-*O*-benzoyl-2,4-di-*O*-triisopropylsilyl-β-D-glucopyranoside (24β)

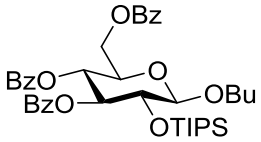
Compound **21** (1.28 g, 1.6 mmol) was reacted as described in the general procedure II.E. Chromatography (cyclohexane-EtOAc, 9:1) gave **24β** (816 mg, 79%) as a colourless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (overlapping signals, 2H, aromatic H), 7.54 (m, 1H, aromatic H), 7.41 (overlapping signals, 2H, aromatic H), 5.36 (t, *J* = 9.0 Hz, 1H, H-3), 4.45 (d, *J* = 7.4 Hz, 1H, H-1), 4.01 (t, *J* = 9.0 Hz, 1H, H-4), 3.91 (d, *J* = 11.7 Hz, 1H, H-6a), 3.85 (dt, *J* = 9.1, 7.3 Hz, 1H, butyl C*H*(H)O), 3.77 (overlapping signals, 2H, H-2, H-6b), 3.50 (overlapping signals, 2H, H-5, butyl C*H*(H)O), 2.00 (d, *J* = 7.2 Hz, 1H, OH), 1.61 (m, 2H, OCH_2CH_2), 1.39 (m, 2H, $OCH_2CH_2CH_2$), 0.91 (overlapping signals, 45H, $OCH_2CH_2CH_2CH_3$, $Si(CH(CH_3)_2)_3$ x2). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.1 (C=O), 132.8 (C), 130.5 (CH), 129.6 (CH), 128.0 (CH), 103.2 (C-1), 78.9 (C-3), 76.5 (C-5), 74.3 (C-2), 70.1 (C-4), 69.6 (O-CH2), 62.1 (C-6), 31.7 (OCH_2CH_2), 19.2 ($OCH_2CH_2CH_2$), 18.1 (CH_3, TIPS), 18.0 (CH_3, TIPS), 13.8 ($OCH_2CH_2CH_2CH_3$), 13.5 (CH, TIPS), 13.2 (CH, TIPS). IR (film) cm^{-1}: 3510, 2919, 1866, 1724, 1603, 1452, 1265, 1115, 1068, 1026, 883, 813, 708, 680. ESI-HRMS calcd for $C_{35}H_{64}O_7Si_2Na$ 675.4112, found *m/z* 675.4115 $[M+Na]^+$.



Butyl 3-*O*-benzoyl-2,4-di-*O*-triisopropylsilyl-α-D-glucopyranoside (24α)

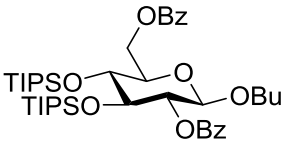
Compound **24β** (19.6 mg, 0.03 mmol) was reacted as described in the general procedure II.L. Chromatography (cyclohexane:EtOAc, 9:1) gave **24α**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (overlapping signals, 2H, aromatic H), 7.53 (m, 1H, aromatic H), 7.41 (overlapping signals, 2H, aromatic H), 5.64 (t, *J* = 9.3 Hz, 1H, H-3), 4.83 (d, *J* = 3.5 Hz, 1H, H-1), 4.01 (t, *J* = 9.1 Hz, 1H, H-4), 3.90 (dd, *J* = 9.8, 3.5 Hz, 1H, H-2), 3.86 (m, 1H, H-6a), 3.79 (ddd, *J* = 12.1, 7.0, 4.9 Hz, 1H, H-6b), 3.72 (overlapping signals, 2H, H-5, butyl C*H*(H)O), 3.38 (dt, *J* = 9.2, 6.7 Hz, 1H, butyl C*H*(H)O), 1.89 (t, *J* = 6.4 Hz, 1H, OH), 1.65 (m, 2H, OCH_2CH_2), 1.43 (m, 2H, $OCH_2CH_2CH_2$), 0.95 (overlapping signals, 45H, $OCH_2CH_2CH_2CH_3$, $Si(CH(CH_3)_2)_3$ x2). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.3 (C=O), 132.8 (C), 129.8 (CH), 128.1 (CH), 99.1 (C-1), 76.6 (C-3), 72.8 (C-2), 72.4 (C-5), 70.3 (C-4), 68.1 (OCH_2), 62.1 (C-6), 31.8 (OCH_2CH_2), 19.6 ($OCH_2CH_2CH_2$), 18.3 (CH_3, TIPS), 18.2 (CH_3, TIPS), 18.2 (CH_3, TIPS), 18.1 (CH_3, TIPS),

18.1 (CH_3, TIPS), 18.0 (CH_3, TIPS), 18.0 (CH_3, TIPS), 17.8 (CH_3, TIPS), 14.1 (CH, TIPS), 13.7 ($OCH_2CH_2CH_2CH_3$), 13.3 (CH, TIPS), 12.9 (CH, TIPS), 12.4 (CH, TIPS). IR (film) cm^{-1}: 3510, 2944, 2867, 1734, 1464, 1266, 1092, 1068, 1040, 1026, 1015, 882, 781, 707, 680. ESI-HRMS calcd for $C_{35}H_{64}O_7Si_2Na$ 675.4088, found *m/z* 675.4063 $[M+Na]^+$.



Butyl 3,4,6-tri-*O*-benzoyl-2-*O*-triisopropylsilyl-β-D-glucopyranoside (25β)

Compound **22** (567 mg, 0.94 mmol) was reacted as described in the general procedure II.B. Chromatography (cyclohexane-EtOAc, 19:1) gave **25β** (523 mg, 79%) as a white solid. ^1H NMR (500 MHz, $CDCl_3$) δ 7.99 (overlapping signals, 2H, aromatic H), 7.93 (overlapping signals, 2H, aromatic H), 7.89 (overlapping signals, 2H, aromatic H), 7.51 (m, 1H, aromatic H), 7.46 (overlapping signals, 2H, aromatic H), 7.34 (overlapping signals, 6H, aromatic H), 5.69 (t, *J* = 9.3 Hz, 1H, H-3), 5.47 (t, *J* = 9.7 Hz, 1H, H-4), 4.58 (dd, *J* = 12.0, 3.4 Hz, 1H, H-6a), 4.50 (overlapping signals, 2H, H-1, H-6b), 4.05 (overlapping signals, 2H, H-2, H-5), 3.89 (q, *J* = 7.9 Hz, 1H, butyl C*H*(H)O), 3.56 (m, 1H, butyl C*H*(H)O), 1.65 (m, 2H, OCH_2CH_2), 1.38 (m, 2H, $OCH_2CH_2CH_2$), 0.98 (overlapping signals, 21H, $Si(CH(CH_3)_2)_3$), 0.91 (t, *J* = 7.5 Hz, 3H, $OCH_2CH_2CH_2CH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.1 (C=O), 165.8 (C=O), 165.5 (C=O), 133.2 (C), 133.0 (C), 132.9 (C), 129.8 (CH), 129.8 (CH), 129.7 (CH), 129.7 (CH), 129.6 (CH), 129.0 (CH), 128.3 (CH), 128.3 (CH), 128.1 (CH), 103.7 (C-1), 76.1 (C-3), 73.8 (C-2), 71.7 (C-5), 70.6 (C-4), 69.9 (OCH_2), 63.8 (C-6), 31.6 (OCH_2CH_2), 19.1 ($OCH_2CH_2CH_2$), 18.0 (CH_3, TIPS), 18.0 (CH_3, TIPS), 13.8 ($OCH_2CH_2CH_2CH_3$), 12.8 (CH, TIPS). IR (film) cm^{-1}: 3659, 2971, 2867, 1723, 1452, 1265, 1176, 1092, 1068, 1026, 998, 883, 811, 706, 684. ESI-HRMS calcd for $C_{40}H_{52}O_9SiNa$ 727.3278, found *m/z* 727.3301 $[M+Na]^+$.



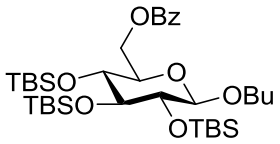
Butyl 2,6-di-*O*-benzoyl-3,4-di-*O*-triisopropylsilyl-β-D-glucopyranoside (26β)

Compound **23** (643 mg, 0.98 mmol) was reacted as described in the general procedure II.B. Chromatography (cyclohexane-EtOAc, 39:1) gave **26β** (601 mg, 81%) as a white solid. ^1H NMR (500 MHz, $CDCl_3$) δ 8.06 (overlapping signals, 4H, aromatic H), 7.68 (overlapping signals, 2H, aromatic H), 7.43 (overlapping signals, 4H, aromatic H), 5.18 (d, *J* = 3.7 Hz, 1H, H-2), 5.04 (d, *J* = 3.8 Hz, 1H, H-1), 4.80 (dd, *J* = 11.2, 7.4 Hz, 1H, H-6a), 4.70 (dd, *J* = 11.1,

7.1 Hz, 1H, H-6b), 4.34 (t, *J* = 7.2 Hz, 1H, H-5), 4.24 (d, *J* = 2.7 Hz, 1H, H-3), 4.16 (m, 1H, H-4), 3.94 (dt, *J* = 12.4, 6.6 Hz, 1H, butyl C*H*(H)O), 3.45 (m, 1H, butyl C*H*(H)O), 1.54 (m, 2H, OCH_2CH_2), 1.24 (m, 2H, $OCH_2CH_2CH_2$), 1.10 (overlapping signals, 21H, $Si(CH(CH_3)_2)_3$), 1.02 (overlapping signals, 21H, $Si(CH(CH_3)_2)_3$), 0.81 (td, *J* = 7.4, 1.3 Hz, 3H, $OCH_2CH_2CH_2CH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.3 (C=O), 165.4 (C=O), 133.0 (C), 132.9 (C), 129.9 (CH), 129.6 (CH), 128.3 (CH), 128.1 (CH), 98.7 (C-1), 77.5 (C-5), 73.3 (C-2), 72.2 (C-3), 69.6 (C-4), 69.1 (OCH_2), 65.8 (C-6), 31.5 (OCH_2CH_2), 19.1 ($OCH_2CH_2CH_2$), 18.1 (CH_3, TIPS), 18.0 (CH_3, TIPS), 13.8 ($OCH_2CH_2CH_2CH_3$), 12.3 (CH, TIPS), 12.3 (CH, TIPS). IR (film) cm^{-1}: 2945, 1722, 1452, 1263, 1211, 1095, 920, 766, 708, 681. ESI-HRMS calcd for $C_{42}H_{68}O_8Si_2Na$ 779.4350, found *m/z* 779.4349 $[M+Na]^+$.

- **Preparation of 29β and 30β:**

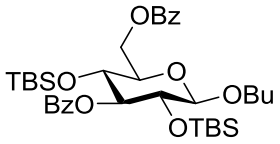
Compound **5** (1 g, 4.23 mmol) was reacted as described in the general procedure II.B with BzCl (1.2 mL, 2.5 equiv.). A mixture of **27** and **28** was obtained, which was then reacted as described in the general procedure II.C using an excess of TBSOTf (3.7 mL, 5 equiv.). Chromatography (cyclohexane-EtOAc, 1:0 to 4:1) gave **29β** (404 mg, 14%) as a white solid, and **30β** (598 mg, 21%) as a white solid.



Butyl 6-*O*-benzoyl-2,3,4-tri-*O*-(tert-butyldimethylsilyl)-β-D-glucopyranoside (29β)

29β: ^1H NMR (500 MHz, $CDCl_3$) δ 8.06 (overlapping signals, 2H, aromatic H), 7.56 (m, 1H, aromatic H), 7.43 (overlapping signals, 2H, aromatic H), 4.75 (d, *J* = 6.1 Hz, 1H, H-1), 4.52 (overlapping signals, 2H, H6a, H6b), 4.14 (t, *J* = 7.0 Hz, 1H, H-5), 3.90 (overlapping signals, 2H, H-3, butyl C*H*(H)O), 3.83 (m, 1H, H-4), 3.66 (d, *J* = 6.2 Hz, 1H, H-2), 3.41 (dt, *J* = 9.3, 7.1 Hz, 1H, butyl C*H*(H)O), 1.63 (m, 2H, OCH_2CH_2), 1.37 (m, 2H, $OCH_2CH_2CH_2$), 0.90 (overlapping signals, 30H, $OCH_2CH_2CH_2CH_3$, $SiC(CH_3)_3$ x3), 0.13 (s, 3H, $SiCH_3$), 0.12 (s, 3H, $SiCH_3$), 0.11 (s, 3H, $SiCH_3$), 0.07 (overlapping signals, 6H, $SiCH_3$), 0.05 (s, 3H, $SiCH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.3 (C=O), 133.0 (C), 130.3 (CH), 129.8 (CH), 128.4 (CH), 101.9 (C-1), 78.9 (C-5), 78.6 (C-4), 77.2 (C-2), 71.0 (C-3), 69.5 (OCH_2), 65.9 (C-6), 31.9(OCH_2CH_2), 26.1 (CH_3, TBS), 26.0 (CH_3, TBS), 25.9 (CH_3, TBS), 19.4 ($OCH_2CH_2CH_2$), 18.2 (C, TBS), 18.0 (C, TBS), 14.1 ($OCH_2CH_2CH_2CH_3$), -4.1 (CH_3, TBS), -4.3 (CH_3, TBS), -

4.4 (CH_3, TBS), -4.5 (CH_3, TBS), -4.8 (CH_3, TBS), -4.9 (CH_3, TBS). IR (film) cm^{-1}: 2956, 2930, 1728, 1472, 1463, 1269, 1252, 1094, 1069, 1027, 833, 774, 709, 668. ESI-HRMS calcd for $C_{35}H_{66}O_7Si_3Na$ 705.4014, found *m/z* 705.3987 $[M+Na]^+$.



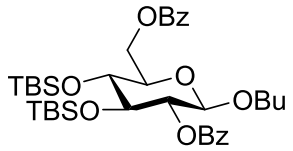
Butyl 3,6-di-*O*-benzoyl-2,4-di-*O*-(tert-butyldimethylsilyl)-β-D-glucopyranoside (30β)

30β: ^1H NMR (500 MHz, $CDCl_3$) δ 8.08 (overlapping signals, 4H, aromatic H), 7.54 (overlapping signals, 2H, aromatic H), 7.42 (overlapping signals, 5H, aromatic H), 5.42 (t, *J* = 9.0 Hz, 1H, H-3), 4.74 (dd, *J* = 11.7, 2.3 Hz, 1H, H-6a), 4.38 (overlapping signals, 2H, H-1, H-6b), 3.92 (t, *J* = 9.2 Hz, 1H, H-4), 3.80 (dt, *J* = 9.4, 7.3 Hz, 1H, butyl C*H*(H)O), 3.71 (ddd, *J* = 9.0, 6.0, 2.3 Hz, 1H, H-5), 3.65 (m, 1H, H-2), 3.50 (ddd, *J* = 9.5, 7.6, 6.0 Hz, 1H butyl C*H*(H)O), 1.59 (m, 2H, OCH_2CH_2), 1.31 (m, 2H, $OCH_2CH_2CH_2$), 0.85 (t, *J* = 7.4 Hz, 3H $OCH_2CH_2CH_2CH_3$), 0.75 (s, 9H, $SiC(CH_3)_3$), 0.70 (s, 9H, $SiC(CH_3)_3$), 0.04 (s, 3H, $SiCH_3$), 0.02 (s, 3H, $SiCH_3$), -0.17 (s, 3H, $SiCH_3$), -0.20 (s, 3H, $SiCH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.3 (C=O), 165.4 (C=O), 133.1 (C), 133.0 (CH), 132.9 (CH), 130.6 (CH), 130.2 (CH), 130.1 (CH), 130.0 (CH), 129.7 (CH), 128.4 (CH), 128.4 (CH), 128.3 (CH), 103.4 (C-1), 78.6 (C-3), 74.3 (C-5), 73.8 (C-2), 70.1 (C-4), 69.8 (OCH_2), 63.8 (C-6), 31.6 (OCH_2CH_2), 25.9 (CH_3, TBS), 25.6 (CH_3, TBS), 19.2 ($OCH_2CH_2CH_2$), 17.9 (C, TBS), 17.9 (C, TBS), 13.8 ($OCH_2CH_2CH_2CH_3$), -3.9 (CH_3, TBS), -4.0 (CH_3, TBS), -4.5 (CH_3, TBS), -4.7 (CH_3, TBS). IR (film) cm^{-1}: 2955, 2930, 2858, 1727, 1603, 1472, 1463, 1452, 1263, 1089, 1069, 834, 777, 708. ESI-HRMS calcd for $C_{36}H_{56}O_8Si_2Na$ 695.3411, found *m/z* 695.3428 $[M+Na]^+$.

- **Preparation of 30β and 39β:**

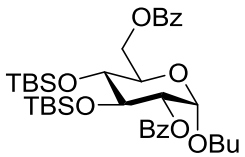
Compound **6** (2.5 g, 7.7 mmol) was reacted as described in the general procedure II.C using TBSOTf (0.65 mL, 1 equiv.). Chromatography (cyclohexane-EtOAc, 9:1) gave a mixture of **31** and **32** (2.2 g, 65%), which was then reacted as described in the general procedure II.B using BzCl (0.8 mL, 2 equiv.). Chromatography (cyclohexane-EtOAc, 16:4) gave a mixture of **33** and **34** (1.96 g, 72%) which was reacted as previously described[17]. Compounds **33** and **34** (1.96 g, 3.6 mmol) was diluted in AcOH (80%) (20 mL) and stirred at 80 °C for 2 h. The mixture was then diluted in EtOAc, and washed with water, a saturated solution of $NaHCO_3$, and brine. The organic phase was then dried with Na_2SO_4, filtered and the solvent evaporated under

reduced pressure. Chromatography (cyclohexane-EtOAc, 1:1) gave **35** and **36** (1.02 g, 83%), which was then reacted as described in the general procedure II.B using BzCl (0.4 mL, 2 equiv.). Chromatography (cyclohexane-EtOAc, 17:3) gave a mixture of **37** and **38** (986 mg, 74%), which was then reacted as described in the general procedure II.C using an excess of TBSOTf. Chromatography (cyclohexane-EtOAc, 19:1 to 4:1) gave **30β** (233 mg, 16%) as a white solid, and **39β** (738 mg, 49%) as a white solid.



Butyl 2,6-di-*O*-benzoyl-3,4-di-*O*-(tert-butyldimethylsilyl)-β-D-glucopyranoside (39β)

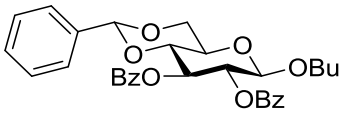
39β: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (overlapping signals, 4H, aromatic H), 7.56 (overlapping signals, 2H, aromatic H), 7.44 (overlapping signals, 4H, aromatic H), 5.05 (d, *J* = 4.7 Hz, 1H, H-2), 4.87 (d, *J* = 4.8 Hz, 1H, H-1), 4.71 (dd, *J* = 11.5, 4.8 Hz, 1H, H-6a), 4.57 (dd, *J* = 11.5, 7.1 Hz, 1H, H-6b), 4.06 (m, 1H, H-5), 3.95 (d, *J* = 4.5 Hz, 1H, H-3), 3.88 (overlapping signals, 2H, H-4, butyl C*H*(H)O), 3.44 (m, 1H, butyl C*H*(H)O), 1.48 (m, 2H, OCH_2CH_2), 1.25 (m, 2H, $OCH_2CH_2CH_2$), 0.87 (overlapping signals, 18H, $SiC(CH_3)_3$ x2), 0.77 (tt, *J* = 8.4, 3.8 Hz, 3H, $OCH_2CH_2CH_2CH_3$), 0.15 (s, 3H , $SiCH_3$), 0.11 (s, 3H , $SiCH_3$), 0.08 (s, 3H , $SiCH_3$), 0.04 (s, 3H , $SiCH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.2 (C=O), 165.4 (C=O), 133.0 (C), 132.9 (C), 130.1 (CH), 130.1 (CH), 129.9 (CH), 129.6 (CH), 128.3 (CH), 128.2, 99.6 (C-1), 76.6 (C-5), 74.2 (C-2), 73.3 (C-3), 70.6 (C-4), 69.2 (OCH_2), 65.2 (C-6), 31.5 (OCH_2CH_2), 25.9 (CH_3, TBS), 25.8 (CH_3, TBS), 19.0 ($OCH_2CH_2CH_2$), 18.0 (C, TBS), 18.0 (C, TBS), 13.7 ($OCH_2CH_2CH_2CH_3$), -3.9 (CH_3, TBS), -4.1 (CH_3, TBS), -4.3 (CH_3, TBS), -4.6 (CH_3, TBS). ESI-HRMS calcd for $C_{36}H_{56}O_8Si_2Na$ 695.3411, found *m/z* 695.3379 $[M+Na]^+$.



Butyl 2,6-di-*O*-benzoyl-3,4-di-*O*-(tert-butyldimethylsilyl)-α-D-glucopyranoside (39α)

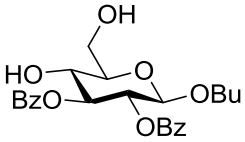
Compound **39β** (20.2 mg, 0.03 mmol) was reacted as described in the general procedure II.L. Chromatography (cyclohexane-EtOAc, 19:1 to 4:1) gave **39α**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (overlapping signals, 4H, aromatic H), 7.56 (overlapping signals, 2H, aromatic H), 7.44 (overlapping signals, 3H, aromatic H), 5.09 (dd, *J* = 8.9, 3.7 Hz, 1H, H-2), 4.97 (d, *J* = 3.7 Hz,

1H, H-1), 4.69 (m, 1H, H-6a), 4.37 (dd, *J* = 11.5, 6.9 Hz, 1H, H-6b), 4.24 (dd, *J* = 8.8, 7.3 Hz, 1H, H-3), 4.07 (ddd, *J* = 9.5, 7.0, 2.5 Hz, 1H, H-5), 3.71 (overlapping signals, 2H, H-4, butyl C*H*(H)O), 3.36 (dt, *J* = 9.8, 6.7 Hz, 1H, butyl C*H*(H)O), 1.52 (m, 2H, $OCH_2C\mathit{H_2}$), 1.31 (m, 2H, $OCH_2CH_2C\mathit{H_2}$), 0.92 (s, 9H, $SiC(C\mathit{H_3})_3$), 0.82 (t, *J* = 7.4 Hz, 3H, $OCH_2CH_2CH_2C\mathit{H_3}$), 0.76 (s, 9H, $SiC(C\mathit{H_3})_3$), 0.15 (s, 3H, $SiC\mathit{H_3}$), 0.13 (s, 3H, $SiC\mathit{H_3}$), 0.09 (s, 3H, $SiC\mathit{H_3}$), 0.07 (s, 3H, $SiC\mathit{H_3}$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.5 (C=O x2 (overlapping signals), 133.2 (C), 133.1 (C), 130.5 (CH), 130.2 (CH), 130.0 (CH), 129.8 (CH), 128.5 (CH), 128.4 (CH), 95.8 (C-1), 73.7 (C-2), 73.0 (C-4), 72.8 (C-3), 71.2 (C-5), 68.0 (OCH_2), 64.4 (C-6), 31.6 (OCH_2CH_2), 26.3 (CH_3, TBS), 26.1 (CH_3, TBS), 26.0 (CH_3, TBS), 26.0 (CH_3, TBS), 19.4 ($OCH_2CH_2CH_2$), 18.3 (C, TBS), 13.9 ($OCH_2CH_2CH_2CH_3$), -2.2 (TBS CH_3,), -2.3 (CH_3, TBS), -3.4 (CH_3, TBS), -3.8 (CH_3, TBS). IR (film) cm^{-1}: 2959, 1722, 1452, 1266, 1096, 1068, 1054, 835, 774, 709, 678. ESI-HRMS calcd for $C_{36}H_{56}O_8Si_2Na$ 695.3411, found *m/z* 695.3423 $[M+Na]^+$.



Butyl 4,6-*O*-benzylidene-2,3-di-*O*-benzoyl-β-D-glucopyranoside (40)

Compound **6** (1.10 g, 3.4 mmol) was reacted as described in the general procedure II.B. Chromatography gave **40** (1.39 g 77%) as a white solid. The NMR spectral data was in accordance with the previous report[14].

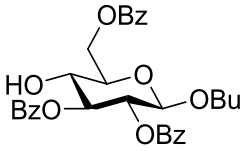


Butyl 2,3-di-*O*-benzoyl-β-D-glucopyranoside (41)

This compound was prepared as previously described[17].

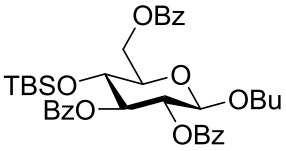
Compound **40** (1.39 g, 2.6 mmol) was diluted in AcOH (80%) (20 mL) and stirred at 80 °C for 2 h. The mixture was then diluted in EtOAc, and washed with water, a saturated solution of $NaHCO_3$, and brine. The organic phase was then dried with Na_2SO_4, filtered and the solvent evaportated under reduced pressure. Chromatography (cyclohexane-EtOAc, 5:3) gave **41** (800 mg, 69%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (overlapping signals, 4H, aromatic H), 7.51 (overlapping signals, 2H, aromatic H), 7.37 (overlapping signals, 4H, aromatic H), 5.41 (overlapping signals, 2H, H-2, H-3), 4.72 (m, 1H, H-1), 4.01 (dd, *J* = 11.9, 3.4 Hz, 1H, H-6a), 3.97 (m, 1H, H-4), 3.90 (overlapping signals, 2H, H-6b, butyl C*H*(H)O),

3.59 (ddd, *J* = 9.6, 4.7, 3.4 Hz, 1H, H-5), 3.52 (dt, *J* = 9.7, 6.7 Hz, 1H, butyl C*H*(H)O), 1.48 (m, 2H, $OCH_2C\mathit{H_2}$), 1.22 (m, 2H, $OCH_2CH_2C\mathit{H_2}$), 0.74 (t, *J* = 7.4 Hz, 3H, $OCH_2CH_2CH_2C\mathit{H_3}$).



Butyl 2,3,6-tri-*O*-benzoyl-β-D-glucopyranoside (42)

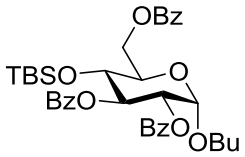
Compound **41** (800 mg, 1.8 mmol) was reacted as described in the general procedure II.B using BzCl (0.3 mL, 1.5 equiv.). Chromatography (cyclohexane-EtOAc, 3:1) gave **42** (720 mg, 73%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (overlapping signals, 2H, aromatic H), 7.95 (overlapping signals, 4H, aromatic H), 7.52 (m, 1H, aromatic H), 7.40 (overlapping signals, 4H, aromatic H), 7.28 (overlapping signals, 4H, aromatic H), 5.63 (t, *J* = 9.5 Hz, 1H, H-3), 5.44 (dd, *J* = 9.8, 7.9 Hz, 1H, H-2), 4.80 (d, *J* = 7.9, 1H, H-1), 4.71 (overlapping signals, 2H, H-6a, H-6b), 4.00 (m, 1H, H-4), 3.89 (overlapping signals, 2H, H-5, butyl C*H*(H)O), 3.52 (dt, *J* = 10.0, 6.7 Hz, 1H, butyl C*H*(H)O), 1.47 (m, 2H, $OCH_2C\mathit{H_2}$), 1.18 (m, 2H, $OCH_2CH_2C\mathit{H_2}$), 0.69 (t, *J* = 7.4 Hz, 3H, $OCH_2CH_2CH_2C\mathit{H_3}$).



Butyl 2,3,6-tri-*O*-benzoyl-4-(tert-butyldimethylsilyl)-β-D-glucopyranoside (43β)

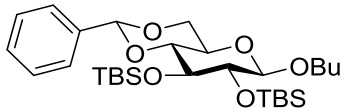
Compound **42** (720 mg, 1.3 mmol) was reacted as described in the general procedure II.C using TBSOTf (0.75 mL, 2.5 equiv.). Chromatography (cyclohexane-EtOAc, 8:1) gave **43β** (531 mg, 61%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (overlapping signals, 2H, aromatic H), 7.94 (overlapping signals, 2H, aromatic H), 7.90 (overlapping signals, 2H, aromatic H), 7.56 (m, 1H, aromatic H), 7.45 (overlapping signals, 4H, aromatic H), 7.31 (overlapping signals, 4H, aromatic H), 5.66 (dd, *J* = 9.9, 8.9 Hz, 1H, H-3), 5.37 (dd, *J* = 9.9, 7.9 Hz, 1H, H-2), 4.79 (dd, *J* = 11.9, 2.2 Hz, 1H, H-6a), 4.76 (d, *J* = 7.9 Hz, 1H, H-1), 4.44 (dd, *J* = 11.9, 4.9 Hz, 1H, H-6b), 4.17 (t, *J* = 9.1 Hz, 1H, H-4), 3.84 (overlapping signals, 2H, H-5, butyl C*H*(H)O), 3.49 (dt, *J* = 9.8, 6.7 Hz, 1H, butyl C*H*(H)O), 1.45 (m, 2H, $OCH_2C\mathit{H_2}$), 1.18 (m, 2H, $OCH_2CH_2C\mathit{H_2}$), 0.77 (s, 9H, $SiC(C\mathit{H_3})_3$), 0.69 (t, *J* = 7.4 Hz, 3H, $OCH_2CH_2CH_2C\mathit{H_3}$), 0.02 (s, 3H, $SiC\mathit{H_3}$), -0.17 (s, 3H, $SiC\mathit{H_3}$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.2 (C=O), 165.9 (C=O), 165.3 (C=O), 133.1 (C), 133.1 (C), 132.9 (C), 129.9 (CH), 129.7 (CH), 129.7 (CH), 129.7 (CH), 129.6 (CH), 129.5 (CH), 128.4 (CH), 128.3 (CH), 128.2 (CH), 101.1 (C-1), 75.8 (C-3),

74.6 (C-5), 72.4 (C-2), 69.7 (C-4), 69.7 (O*C*H$_2$), 63.3 (C-6), 31.4 (OCH$_2$*C*H$_2$), 25.7 (CH$_3$, TBS), 25.6 (CH$_3$, TBS), 18.8 (OCH$_2$CH$_2$*C*H$_2$), 17.8 (C, TBS), 13.5 (OCH$_2$CH$_2$CH$_2$*C*H$_3$), -4.2 (CH$_3$, TBS), -4.8 (CH$_3$, TBS). IR (film) cm^{-1}: 2958, 2859, 1724, 1602, 1585, 1452, 1264, 1093, 1068, 1026, 836, 777, 706, 686. ESI-HRMS calcd for $C_{37}H_{46}O_9SiNa$ 685.2809, found *m/z* 685.2807 $[M+Na]^+$.



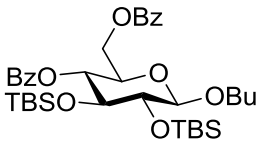
Butyl 2,3,6-tri-*O*-benzoyl-4-(tert-butyldimethylsilyl)-α-D-glucopyranoside (43α)

Compound **43β** (19.9 mg, 0.03 mmol) was reacted as described in the general procedure II.L. Chromatography (cyclohexane:EtOAc, 8:1) gave **43α** (5 mg, 25%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.10 (overlapping signals, 2H, aromatic H), 7.97 (overlapping signals, 2H, aromatic H), 7.93 (overlapping signals, 2H, aromatic H), 7.60 (m, 1H, aromatic H), 7.49 (overlapping signals, 2H, aromatic H), 7.35 (overlapping signals, 6H, aromatic H), 5.92 (dd, *J* = 10.2, 8.5 Hz, 1H, H-3), 5.21 (d, *J* = 3.8 Hz, 1H, H-1), 5.13 (dd, *J* = 10.2, 3.8 Hz, 1H, H-2), 4.71 (dd, *J* = 11.9, 2.1 Hz, 1H, H-6a), 4.46 (dd, *J* = 11.9, 4.5 Hz, 1H, H-6b), 4.13 (overlapping signals, 2H, H-4, H-5), 3.73 (m, 1H, butyl C*H*(H)O), 3.42 (m, 1H, butyl C*H*(H)O), 1.55 (m, 2H, OCH$_2$C*H$_2$*), 1.31 (m, 2H, OCH$_2$CH$_2$C*H$_2$*), 0.81 (t, *J* = 7.4 Hz, 3H, OCH$_2$CH$_2$CH$_2$C*H$_3$*), 0.78 (d, *J* = 2.0 Hz, 9H, SiC(C*H$_3$*)$_3$), 0.03 (s, 3H, SiC*H$_3$*), -0.16 (s, 3H, SiCH$_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.3, 166.0, 165.7 (each C=O), 133.6 (C), 133.3 (C), 133.2 (C), 133.1 (CH), 133.1 (CH), 133.0 (CH), 130.0 (CH), 130.0 (CH), 129.9 (CH), 129.8 (CH), 129.7 (CH), 129.7 (CH), 129.6 (CH), 129.1 (CH), 128.5 (CH), 128.4 (CH), 128.4 (CH), 128.3 (CH), 128.3 (CH), 95.8 (C-1), 73.4 (C-3), 72.4 (C-2), 70.0 (C-4), 69.7 (C-5), 68.4 (O-*C*H$_2$), 63.4 (C-6), 31.3 (OCH$_2$*C*H$_2$), 25.6 (CH$_3$, TBS), 19.1 (overlapping peaks, OCH$_2$CH$_2$*C*H$_2$ and C, TBS), 13.6 (OCH$_2$CH$_2$CH$_2$*C*H$_3$), -4.1 (CH$_3$, TBS), -4.8 (CH$_3$, TBS). IR (film) cm^{-1}: 2958, 2931, 1722, 1603, 1452, 1264, 1093, 1069, 1027, 836, 778, 707, 687. ESI-HRMS calcd for $C_{37}H_{46}O_9SiNa$ 685.2809, found *m/z* 685.2786 $[M+Na]^+$.



Butyl 4,6-*O*-benzylidene-2,3-di-*O*-(tert-butyldimethylsilyl)-β-D-glucopyranoside (44)

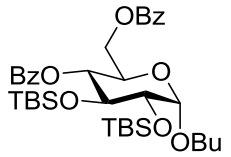
Compound **6** (1.6 g, 4.9 mmol) was reacted as described in the general procedure II.C using TBSOTf (4.5 mL, 4 equiv.). Chromatography gave **44** (2.6 g, 96%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (overlapping signals, 2H, aromatic H), 7.35 (overlapping signals, 3H, aromatic H), 5.41 (s, 1H, Ar-C*H*), 4.30 (overlapping signals, 2H, H-1, H-6a), 3.83 (m, 1H, butyl C*H*(H)O), 3.73 (overlapping signals, 2H, H-3, H-6b), 3.49 (overlapping signals, 2H, H-2, butyl C*H*(H)O), 3.40 (overlapping signals, 2H, H-4, H-5), 1.63 (m, 2H, OCH_2CH_2), 1.37 (m, 2H, $OCH_2CH_2CH_2$), 0.92 (overlapping signals, 12H, $OCH_2CH_2CH_2CH_3$, $SiC(CH_3)_3$), 0.79 (s, 9H, $SiC(CH_3)_3$), 0.13 (s, 3H, $SiCH_3$), 0.11 (s, 3H, $SiCH_3$), 0.01 (s, 3H, $SiCH_3$), -0.03 (s, 3H, $SiCH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.2 (C), 129.1 (CH), 128.1 (CH), 126.5 (CH), 103.9 (C-1), 102.4 (*C*HPh), 81.8 (C-4) 76.4 (C-2), 75.7 (C-3), 69.9 (OCH_2), 69.0 (C-6), 65.9 (C-5), 31.6 (OCH_2CH_2), 26.2 (CH_3, TBS), 26.2 (CH_3, TBS), 19.2 ($OCH_2CH_2CH_2$), 18.4 (C, TBS), 18.2 (C, TBS), 13.9 ($OCH_2CH_2CH_2CH_3$), -2.9 (CH_3, TBS), -3.1 (CH_3, TBS), -3.7 (CH_3, TBS), -3.7 (CH_3, TBS).



Butyl 4,6-di-*O*-benzoyl-2,3-di-*O*-(tert-butyldimethylsilyl)-β-D-glucopyranoside (45β)

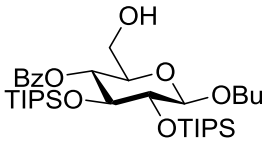
Compound **15β** (1 g, 1.8 mmol) was reacted as described in the general procedure II.B. Chromatography gave **45β** (841 mg, 71%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (overlapping signals, 4H, aromatic H), 7.53 (overlapping signals, 2H, aromatic H), 7.39 (overlapping signals, 4H, aromatic H), 5.25 (t, J = 7.6 Hz, 1H, H-4), 4.52 (dd, J = 11.7, 4.3 Hz, 1H, H-6a), 4.43 (overlapping signals, 2H, H-1, H-6b), 4.00 (ddd, J = 7.7, 6.5, 4.3 Hz, 1H, H-5), 3.91 (dd, J = 7.5, 6.4 Hz, 1H, H-3), 3.83 (m, 1H, butyl C*H*(H)O), 3.64 (t, J = 6.4 Hz, 1H, H-2), 3.46 (ddd, J = 9.2, 7.6, 6.2 Hz, 1H, butyl C*H*(H)O), 1.63 (m, 2H, OCH_2CH_2), 1.33 (m, 2H, $OCH_2CH_2CH_2$), 0.88 (overlapping signals, 12H, $OCH_2CH_2CH_2CH_3$, $SiC(CH_3)_3$), 0.79 (s, 9H, $SiC(CH_3)_3$), 0.14 (s, 3H, $SiCH_3$), 0.08 (overlapping signals, 6H, $SiCH_3$ x2), -0.05 (s, 3H, $SiCH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.2 (C=O), 165.5 (C=O), 133.2 (C), 132.9 (C), 130.6 (CH), 129.9 (CH), 129.9 (CH), 129.8 (CH), 129.6 (CH), 128.9 (CH), 128.3 (CH), 128.2 (CH),

103.2 (C-1), 75.4 (C-2), 74.9 (C-3), 72.5 (C-5), 72.1 (C-4), 69.5 (O*C*H_2), 64.5 (C-6), 31.6 (OCH$_2$*C*H$_2$), 26.2 (CH_3, TBS), 25.8 (CH_3, TBS), 19.2 (OCH$_2$CH$_2$*C*H$_2$), 18.2 (C, TBS), 17.9 (C, TBS), 13.8 (OCH$_2$CH$_2$CH$_2$*C*H$_3$), -3.1 (CH_3, TBS), -3.3 (CH_3, TBS), -3.7 (CH_3, TBS), -4.0 (CH_3, TBS). IR (film) cm^{-1}: 2958, 2932, 1789, 1710, 1603, 1452, 1280, 1041, 835, 783, 692. ESI-HRMS calcd for $C_{36}H_{56}O_8Si_2Na$ 695.3411, found *m/z* 695.3411 $[M+Na]^+$.



Butyl 4,6-di-*O*-benzoyl-2,3-di-*O*-(tert-butyldimethylsilyl)-α-D-glucopyranoside (45α)

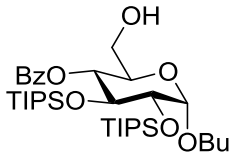
Compound **45β** (20.2 mg, 0.03 mmol) was reacted as described in the general procedure II.L. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (overlapping signals, 2H, aromatic H), 7.99 (overlapping signals, 2H, aromatic H), 7.53 (overlapping signals, 2H, aromatic H), 7.40 (overlapping signals, 4H, aromatic H), 5.24 (t, *J* = 9.6 Hz, 1H, H-4), 4.81 (d, *J* = 3.4 Hz, 1H, H-1), 4.44 (dd, *J* = 12.0, 2.8 Hz, 1H, H-6a), 4.30 (dd, *J* = 12.1, 6.5 Hz, 1H, H-6b), 4.16 (overlapping signals, 2H, H-3, H-5), 3.74 (dd, *J* = 8.9, 3.2 Hz, 1H, H-2), 3.69 (m, 1H, butyl C*H*(H)O), 3.42 (dt, *J* = 10.0, 6.9 Hz, 1H, butyl C*H*(H)O), 1.64 (m, 2H, OCH$_2$C*H$_2$*), 1.36 (m, 2H, OCH$_2$CH$_2$C*H$_2$*), 0.92 (overlapping signals, 12H, OCH$_2$CH$_2$CH$_2$*C*H$_3$, SiC(C*H$_3$*)$_3$), 0.73 (s, 9H, SiC(C*H$_3$*)$_3$), 0.11 (overlapping signals, 6H, SiC*H$_3$* x2), 0.06 (s, 3H, SiC*H$_3$*), -0.13 (s, 3H, SiC*H$_3$*). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.4, 165.6 (each C=O), 133.3 (C), 133.0 (C), 130.1 (CH), 130.0 (CH), 130.0 (CH), 129.8 (CH), 128.5 (CH), 128.4 (CH), 99.3 (C-1), 74.3 (C-2), 72.6 (C-4), 72.3 (C-3), 68.4 (O*C*H$_2$), 68.1 (C-5), 64.0 (C-6), 31.8 (OCH$_2$*C*H$_2$), 26.3 (CH_3, TBS), 25.9 (CH_3, TBS), 19.6 (OCH$_2$CH$_2$*C*H$_2$), 18.5 (C, TBS), 17.9 (C, TBS), 14.0 (OCH$_2$CH$_2$CH$_2$*C*H$_3$), -2.9 (CH_3, TBS), -3.3 (CH_3, TBS), -4.2 (CH_3, TBS). IR (film) cm^{-1}: 2956, 1720, 1453, 1251, 1144, 1107, 1068, 1028, 855, 835, 774, 707, 687. ESI-HRMS calcd for $C_{36}H_{56}O_8Si_2Na$ 695.3411, found *m/z* 695.3403 $[M+Na]^+$.



Butyl 4-*O*-benzoyl-2,3-di-*O*-triisopropylsilyl-β-D-glucopyranoside (47β)

Compound **6** (1.42 g, 4.0 mmol) was reacted as described in the general procedure II.C using an excess of TIPSOTf at 70°C overnight. Chromatography (cyclohexane-EtOAc, 9:1) gave **46** (2.5 g, 94%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (overlapping signals, 2H, aromatic H), 7.35 (overlapping signals, 3H, aromatic H), 5.41 (s, 1H, C*H*Ph), 4.44 (d, *J* = 6.3 Hz, 1H, H-1), 4.31 (dd, *J* = 10.4, 4.9 Hz, 1H, H-6a), 3.91 (dd, *J* = 8.4, 6.2 Hz, 1H, H-3), 3.82 (dt, *J* = 9.1, 7.2 Hz, 1H, butyl C*H*(H)O), 3.74 (t, *J* = 6.3 Hz, 1H, H-2), 3.71 (t, *J* = 9.8 Hz, 1H, H-6b), 3.64 (dd, *J* = 9.6, 8.4 Hz, 1H, H-4), 3.54 (td, *J* = 9.8, 4.9 Hz, 1H, H-5), 3.44 (ddd, *J* = 9.1, 7.4, 5.7 Hz, 1H, butyl C*H*(H)O), 1.60 (m, 2H, OCH_2CH_2), 1.39 (m, 2H, $OCH_2CH_2CH_2$), 1.15 (overlapping signals, 21H, $Si(CH(CH_3)_2)_3$), 1.01 (overlapping signals, 21H, $Si(CH(CH_3)_2)_3$), 0.93 (t, *J* = 7.4 Hz, 3H, $OCH_2CH_2CH_2CH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.3 (C), 129.1 (CH), 128.1 (CH), 126.4 (CH), 103.3 (C-1), 102.2 (*C*HPh), 81.9 (C-4), 77.3 (C-2), 76.6 (C-3), 69.3 (C-6), 68.9 (OCH_2), 65.0 (C-5), 31.7 (OCH_2CH_2), 19.3 ($OCH_2CH_2CH_2$), 18.3 (CH_3, TIPS), 18.3 (CH_3, TIPS), 18.2 (CH_3, TIPS), 18.2 (CH_3, TIPS), 13.8 ($OCH_2CH_2CH_2CH_3$), 13.4 (CH, TIPS), 13.4 (CH, TIPS).

Compound **46** (2.5 g, 3.8 mmol) was reacted as described in the general procedure II.F. Chromatography (cyclohexane:EtOAc 9:1) gave **47β** (1.6 g, 67%) as a colourless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (overlapping signals, 2H, aromatic H), 7.53 (m, 1H, aromatic H), 7.38 (overlapping signals, 2H, aromatic H), 5.16 (dd, *J* = 7.2, 5.7 Hz, 1H, H-4), 4.58 (d, *J* = 4.9 Hz, 1H, H-1), 4.15 (dd, *J* = 5.9, 4.2 Hz, 1H, H-3), 3.94 (m, 1H, butyl C*H*(H)O), 3.86 (dd, *J* = 4.9 Hz, 4.2 Hz, 1H, H-2), 3.73 (overlapping signals, 3H, H-5, H-6a, H-6b), 3.41 (dt, *J* = 9.2, 6.3 Hz, 1H, butyl C*H*(H)O), 1.57 (m, 2H, OCH_2CH_2), 1.38 (m, 2H, $OCH_2CH_2CH_2$), 1.08 (overlapping signals, 42H, $Si(CH(CH_3)_2)_3$ x2), 0.89 (td, *J* = 7.4, 2.0 Hz, 3H, $OCH_2CH_2CH_2CH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.3 (C=O), 133.3 (C), 129.7 (CH), 128.2 (CH), 103.0 (C-1), 76.0 (C-2), 75.5 (C-3), 74.8 (C-5), 72.9 (C-4), 68.6 (OCH_2), 62.6 (C-6), 31.7 (OCH_2CH_2), 19.2 ($OCH_2CH_2CH_2$), 18.7 (CH_3, TIPS), 18.2 (CH_3, TIPS), 18.1 (CH_3, TIPS), 18.0 (CH_3, TIPS), 13.8 ($OCH_2CH_2CH_2CH_3$), 13.2 (CH, TIPS), 13.1 (CH, TIPS), 12.7 (CH, TIPS), 12.5 (CH, TIPS). IR (film) cm^{-1}: 3445, 2944, 2867, 1723, 1603, 1464, 1267, 1111, 1067, 882, 792, 679, 710. ESI-HRMS calcd for $C_{35}H_{64}O_7Si_2Na$ 675.4088, found *m/z* 675.4066 $[M+Na]^+$.

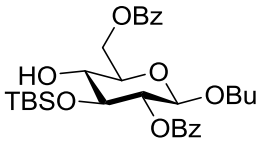


Butyl 4-*O*-benzoyl-2,3-di-*O*-triisopropylsilyl-α-D-glucopyranoside (47α)

Compound **47β** (19.6 mg, 0.03 mmol) was reacted as described in the general procedure II.L. Chromatography (cyclohexane:EtOAc 9:1) gave **47α**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (overlapping signals, 2H, aromatic H), 7.57 (m, 1H, aromatic H), 7.43 (overlapping signals, 2H, aromatic H), 5.04 (m, 1H, H-4), 4.89 (d, J = 3.2 Hz, 1H, H-1), 4.43 (t, J = 8.2 Hz, 1H, H-3), 3.89 (dd, J = 8.2, 3.2 Hz, 1H, H-2), 3.77 (m, 1H, H-5), 3.69 (d, J = 3.8 Hz, 1H, butyl C*H*(H)O), 3.63 (m, 1H, H-6a), 3.57 (m, 1H, H-6b), 3.38 (m, 1H, butyl C*H*(H)O), 1.60 (m, 2H, OCH_2CH_2), 1.41 (m, 2H, $OCH_2CH_2CH_2$), 1.08 (overlapping signals, 42H, $Si(CH(CH_3)_2)_3$ x2), 0.92 (t, *J* = 7.5 Hz, 3H, $OCH_2CH_2CH_2CH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.5 (C=O), 133.5 (C), 129.9 (CH), 128.4 (CH), 98.9 (C-1), 74.8 (C-2), 73.2 (C-4), 72.7 (C-3), 70.3 (C-5), 67.5 (OCH2), 61.6 (C-6), 31.9 (OCH_2CH_2), 19.4 ($OCH_2CH_2CH_2$), 18.4 (CH_3, TIPS), 18.3 (CH_3, TIPS), 18.3 (CH_3, TIPS), 18.3 (CH_3, TIPS), 18.3 (CH_3, TIPS), 18.2 (CH_3, TIPS), 18.2 (CH_3, TIPS), 14.0 ($OCH_2CH_2CH_2CH_3$), 13.4 (CH, TIPS), 13.2 (CH, TIPS). IR (film) cm^{-1}: 3507, 2944, 2867, 1724, 1452, 1267, 1109, 1068, 1042, 1027, 1015, 882, 710, 679. ESI-HRMS calcd for $C_{35}H_{64}O_7Si_2Na$ 675.4088, found *m/z* 675.4070 $[M+Na]^+$.

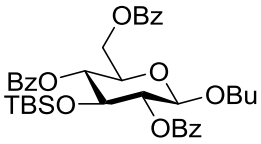
- **Preparation of 54β, 55β and 56β:**

Compound **7** (1 g, 2.8 mmol) was reacted as described in the general procedure II.C using TBSOTf (0.65 mL, 1 equiv.). Chromatography (cyclohexane-EtOAc, 15:5) gave a mixture of **48** and **49** (846 mg, 64%), which was then reacted as described in the general procedure II.B using BzCl (0.4 mL, 2 equiv.). Chromatography (cyclohexane-EtOAc, 17:3) gave a mixture of **50** and **51** (763 mg, 74%), which was then reacted as described in the general procedure II.G. Chromatography (cyclohexane-EtOAc, 13:7) gave a mixture of **52** and **53** (320 mg, 53%). (Ratio **52**:**53** 3:2), which was then reacted as described in the general procedure II.B using an excess of benzoyle. Chromatography (cyclohexane-EtOAc, 19:1 to 6:1) gave **54β** (54 mg, 14%) as a white solid, **55β** (150 mg, 32%) as a white solid, and **56β** (142 mg, 30%) as a white solid.



Butyl 2,6-di-*O*-benzoyl-3-*O*-(tert-butyldimethylsilyl)-β-D-glucopyranoside (54β)

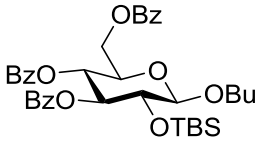
54β: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (overlapping signals, 4H, aromatic H), 7.58 (overlapping signals, 2H, aromatic H), 7.46 (overlapping signals, 4H, aromatic H), 5.15 (dd, *J* = 9.3, 8.0 Hz, 1H, H-2), 4.74 (dd, *J* = 12.0, 4.2 Hz, 1H, H-6a), 4.62 (dd, *J* = 12.0, 2.0 Hz, 1H, H-6b), 4.54 (d, *J* = 8.0 Hz, 1H, H-1), 3.85 (overlapping signals, 2H, H-3, butyl C*H*(H)O), 3.64 (overlapping signals, 2H, H-4, H-5), 3.45 (dt, *J* = 9.8, 6.8 Hz, 1H, butyl C*H*(H)O), 1.42 (m, 2H, OCH_2CH_2), 1.14 (m, 2H, $OCH_2CH_2CH_2$), 0.77 (s, 9H, $SiC(CH_3)_3$), 0.67 (m, 3H, $OCH_2CH_2CH_2CH_3$), 0.11 (s, 3H, $SiCH_3$), -0.07 (s, 3H, $SiCH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.2 (C=O), 165.2 (C=O), 133.3 (C), 132.9 (CH), 130.2 (CH), 130.2 (CH), 129.9 (CH), 129.7 (CH), 129.7 (CH), 128.5 (CH), 128.4 (CH), 128.3 (CH), 101.5 (C-1), 75.8 (C-3), 74.1 (C-2), 73.9 (C-5), 71.2 (C-4), 69.6 (OCH_2), 63.8 (C-6), 31.4 (OCH_2CH_2), 25.7 (CH_3, TBS), 18.8 ($OCH_2CH_2CH_2$), 18.0 (C, TBS), 13.5 ($OCH_2CH_2CH_2CH_3$), -4.2 (CH_3, TBS), -4.7 (CH_3, TBS). IR (film) cm^{-1}: 3661, 3495, 2981, 2888, 1720, 1603, 1585, 1452, 1381, 1266, 1127, 1084, 1069, 1026, 836, 779, 707, 685, 668. ESI-HRMS calcd for $C_{30}H_{42}O_8SiNa$ 581.2547, found *m/z* 581.2544 $[M+Na]^+$.



Butyl 2,4,6-tri-*O*-benzoyl-3-*O*-(tert-butyldimethylsilyl)-β-D-glucopyranoside (55β)

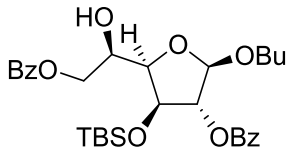
55β: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (overlapping signals, 6H, aromatic H), 7.56 (overlapping signals, 3H, aromatic H), 7.37 (overlapping signals, 6H, aromatic H), 5.53 (t, *J* = 9.3 Hz, 1H, H-4), 5.38 (t, *J* = 8.4 Hz, 1H, H-2), 4.70 (d, *J* = 7.8 Hz, 1H, H-1), 4.62 (dd, *J* = 12.0, 3.4 Hz, 1H, H-6a), 4.48 (dd, *J* = 12.1, 5.5 Hz, 1H, H-6b), 4.28 (t, *J* = 8.9 Hz, 1H, H-3), 4.04 (dt, *J* = 9.4, 4.5 Hz, 1H, H-5), 3.89 (dq, *J* = 12.5, 6.8, 6.1 Hz, 1H, butyl C*H*(H)O), 3.50 (dt, *J* = 9.7, 6.7 Hz, 1H, butyl C*H*(H)O), 1.44 (m, 2H, OCH_2CH_2), 1.17 (m, 2H, $OCH_2CH_2CH_2$), 0.80 (m, 3H, $OCH_2CH_2CH_2CH_3$), 0.68 (s, 9H, $SiC(CH_3)_3$), 0.14 (s, 3H, $SiCH_3$), -0.15 (s, 3H, $SiCH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.4 (C=O), 165.3 (C=O), 165.2 (C=O), 133.4 (C), 133.1 (C), 133.0 (C), 130.2 (CH), 129.9 (CH), 129.8 (CH), 129.7 (CH), 129.7 (CH), 129.7 (CH), 129.6 (CH), 129.4 (CH), 128.4 (CH), 128.3 (CH), 101.3 (C-1), 74.6 (C-2), 73.3 (C-3), 72.4 (C-4), 72.0 (C-5), 69.7 (OCH_2), 63.8 (C-6), 31.4 (OCH_2CH_2), 25.7 (CH_3, TBS), 25.6 (CH_3,

TBS), 25.6 (CH_3, TBS), 25.4 (CH_3, TBS), 18.9 ($OCH_2CH_2\mathit{C}H_2$), 17.7 (C, TBS), 13.5 ($OCH_2CH_2CH_2\mathit{C}H_3$), -3.7 ($CH_3$, TBS), -4.4 ($CH_3$, TBS). IR (film) cm^{-1}: 2955, 1723, 1684, 1602, 1584, 1453, 1255, 1111, 1094, 1069, 1027, 1046, 836, 779, 706, 667. ESI-HRMS calcd for $C_{37}H_{46}O_9SiNa$ 685.2809, found *m/z* 685.2797 $[M+Na]^+$.



Butyl 3,4,6-tri-*O*-benzoyl-2-*O*-(tert-butyldimethylsilyl)-β-D-glucopyranoside (56β)

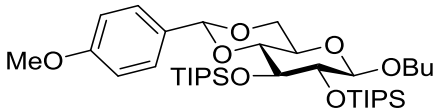
56β: ^1H NMR (500 MHz, $CDCl_3$) δ 7.99 (overlapping signals, 2H, aromatic H), 7.93 (overlapping signals, 2H, aromatic H), 7.86 (overlapping signals, 2H, aromatic H), 7.52 (m, 1H, aromatic H), 7.45 (overlapping signals, 2H, aromatic H), 7.34 (overlapping signals, 6H, aromatic H), 5.67 (t, *J* = 9.4 Hz, 1H, H-3), 5.49 (t, *J* = 9.8 Hz, 1H, H-4), 4.57 (dd, *J* = 12.0, 3.4 Hz, 1H, H-6a), 4.51 (d, *J* = 7.6 Hz, 1H, H-1), 4.48 (dd, *J* = 12.0, 5.8 Hz, 1H, H-6b), 4.04 (ddd, *J* = 9.6, 5.8, 3.4 Hz, 1H, H-5), 3.89 (dt, *J* = 9.4, 7.2 Hz, 1H, butyl C*H*(H)O), 3.83 (dd, *J* = 9.2, 7.5 Hz, 1H, H-2), 3.58 (ddd, *J* = 9.4, 7.4, 6.2 Hz, 1H, butyl C*H*(H)O), 1.63 (m, 2H, $OCH_2C\mathit{H}_2$), 1.38 (m, 2H, $OCH_2CH_2C\mathit{H}_2$), 0.91 (t, *J* = 7.4 Hz, 3H, $OCH_2CH_2CH_2\mathit{C}H_3$), 0.75 (s, 9H, $SiC(C\mathit{H}_3)_3$), 0.08 (s, 3H, $SiC\mathit{H}_3$), -0.10 (s, 3H, $SiC\mathit{H}_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.1 (C=O), 165.8 (C=O), 165.4 (C=O), 133.2 (C), 133.0 (C), 132.9 (C), 129.8 (CH), 129.7 (CH), 129.7 (CH), 129.7 (CH), 129.0 (CH), 128.3 (CH), 128.3 (CH), 128.2 (CH), 103.6 (C-1), 75.6 (C-3), 73.3 (C-2), 71.8 (C-5), 70.2 (C-4), 70.1 ($O\mathit{C}H_2$), 63.6 (C-6), 31.6 ($OCH_2\mathit{C}H_2$), 25.5 (CH_3, TBS), 19.1 ($OCH_2CH_2\mathit{C}H_2$), 17.9 (C, TBS), 13.8 ($OCH_2CH_2CH_2\mathit{C}H_3$), -4.2 ($CH_3$, TBS), -4.9 ($CH_3$, TBS). IR (film) cm^{-1}: 3660, 2981, 2888, 1723, 1602, 1585, 1452, 1264, 1176, 1092, 1068, 1026, 837, 779, 706, 686. ESI-HRMS calcd for $C_{37}H_{46}O_9SiNa$ 685.2809, found *m/z* 685.2819 $[M+Na]^+$.



Butyl 2,6-di-*O*-benzoyl-3-*O*-(tert-butyldimethylsilyl)-α-D-Glucofuranoside (54-furanose)

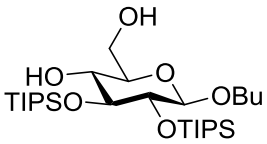
Compound **54β** (16.8 mg, 0.03 mmol) was reacted as described in the general procedure II.L. Chromatography (cyclohexane:EtOAc 7:1) gave **54-furanose**. ^1H NMR (500 MHz, $CDCl_3$) δ 8.09 (overlapping signals, 2H, aromatic H), 8.02 (overlapping signals, 2H, aromatic H), 7.58

(overlapping signals, 2H, aromatic H), 7.46 (overlapping signals, 4H, aromatic H), 5.38 (s, 1H, H-2), 5.24 (overlapping signals, 2H, H-4, H-5), 5.19 (s, 1H, H-1), 4.77 (d, *J* = 4.9 Hz, 1H, H-3), 4.24 (overlapping signals, 2H, H-6a, H-6b), 3.77 (q, *J* = 7.3 Hz, 1H, butyl C*H*(H)O), 3.40 (q, *J* = 7.5 Hz, 1H, butyl C*H*(H)O), 1.59 (m, 2H, OCH_2CH_2), 1.33 (m, 2H, $OCH_2CH_2CH_2$), 0.90 (overlapping signals, 12H, $OCH_2CH_2CH_2CH_3$, $SiC(CH_3)_3$), 0.07 (s, 3H, $SiCH_3$), 0.00 (s, 3H, $SiCH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.0 (C=O), 165.3 (C=O), 133.6 (C), 133.5 (C), 130.0 (CH), 129.9 (CH), 129.9 (CH), 129.9 (CH), 129.6 (CH), 129.4 (CH), 128.6 (CH), 128.6 (CH), 128.5 (CH), 108.1 (C-1), 85.7 (C-3), 82.6 (C-2), 81.9 (C-4), 74.0 (C-5), 68.9 (C-6), 68.5 (OCH_2), 31.5 (OCH_2CH_2), 29.9 (CH_3, TBS), 25.8 (CH_3, TBS), 19.4 (overlapping peaks, $OCH_2CH_2CH_2$ and C, TBS), 14.0 ($OCH_2CH_2CH_2CH_3$), 1.2 (CH_3, TBS), 0.2 (CH_3, TBS). IR (film) cm^{-1}: 3301, 2958, 1721, 1603, 1452, 1262, 1108, 1070, 1040, 1026, 709. ESI-HRMS calcd for $C_{30}H_{42}O_8SiNa$ 581.2547, found *m/z* 581.2527 $[M+Na]^+$.



Butyl 4,6-*O*-(4-methoxybenzylidene)-2,3-di-*O*-triisopropylsilyl-β-D-glucopyranoside (57)

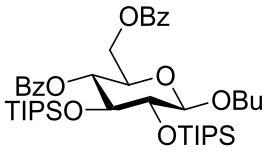
Compound **7** (1.42 g, 4.0 mmol) was reacted as described in the general procedure II.C using an excess of TIPSOTf at 90°C overnight. Chromatography (cyclohexane-EtOAc, 9:1) gave **57** (1.81g, 68%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (m, 2H, aromatic H), 6.85 (d, J = 8.6 Hz, 2H, aromatic H), 5.35 (s, 1H, C*H*-Ar), 4.41 (d, J = 6.3 Hz, 1H, H-1), 4.27 (dd, J = 10.4, 4.9 Hz, 1H, H-6a), 3.88 (dd, J = 8.4, 6.3 Hz, 1H, H-3), 3.79 (overlapping signals, 3H, butyl C*H*(H)O, O-CH_3), 3.71 (t, J = 6.4 Hz, 1H, H-2), 3.67 (t, J = 10.5 Hz, 1H, H-5), 3.59 (t, J = 9.0 Hz, 1H, H-4), 3.50 (td, J = 9.8, 4.9 Hz, 1H, H-6b), 3.42 (ddd, J = 9.2, 7.4, 5.7 Hz, 1H, butyl C*H*(H)O), 1.57 (m, 2H, OCH_2CH_2), 1.37 (m, 2H, $OCH_2CH_2CH_2$), 1.04 (overlapping signals, 42H, $Si(CH(CH_3)_2)_3$ x2), 0.91 (t, J = 7.3 Hz, 3H, $OCH_2CH_2CH_2CH_3$).



Butyl 2,3-di-*O*-triisopropylsilyl-β-D-glucopyranoside (58)

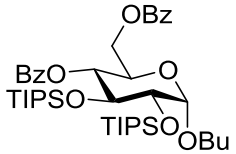
Compound **57** (1.81 g, 2.7 mmol) was reacted as described in the general procedure II.G. Chromatography (cyclohexane-EtOAc, 17:3) gave **58** (0.95 g, 64%) as a colourless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.58 (d, *J* = 3.5 Hz, 1H, H-1), 3.98 (dd, *J* = 11.5, 6.5 Hz, 1H, H-6a), 3.92 (t, *J* = 4.9 Hz, 1H, H-3), 3.83 (overlapping signals, 3H, H-3, H-2, H-6b, butyl

C*H*(H)O), 3.72 (td, *J* = 6.0, 4.2 Hz, 1H, H-5), 3.66 (m, 1H, H-4), 3.41 (dt, *J* = 9.3, 6.6 Hz, 1H, butyl C*H*(H)O), 3.04 (d, *J* = 8.4 Hz, 1H, OH), 1.56 (m, 2H, $OCH_2C\mathit{H_2}$), 1.37 (m, 2H, $OCH_2CH_2C\mathit{H_2}$), 1.09 (overlapping signals, 42H, $Si(C\mathit{H}(C\mathit{H_3})_2)_3$ x2), 0.90 (t, *J* = 7.4 Hz, 3H, $OCH_2CH_2CH_2C\mathit{H_3}$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 102.6 (C-1), 77.3 (C-5), 74.5 (C-3), 74.1 (C-2), 70.7 (C-4), 69.2 (O-*C*H_2), 63.8 (C-6), 31.9 (O-$CH_2C\mathit{H_2}$), 19.4 (O-$CH_2CH_2C\mathit{H_2}$), 18.3 (CH_3, TIPS), 18.3 (CH_3, TIPS), 14.0 (O-$CH_2CH_2CH_2C\mathit{H_3}$, 13.1 (CH, TIPS), 13.0 (CH, TIPS).



Butyl 4,6-di-*O*-benzoyl-2,3-di-*O*-triisopropylsilyl-β-D-glucopyranoside (59β)

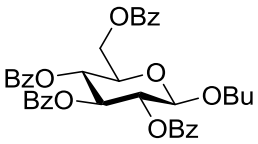
Compound **58** (0.95 g, 1.7 mmol) was reacted as described in the general procedure II.B. Chromatography (cyclohexane-EtOAc, 19:1) gave **59β** (1.13 g, 86%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (overlapping signals, 4H, aromatic H), 7.53 (overlapping signals, 2H, aromatic H), 7.39 (overlapping signals, 4H, aromatic H), 5.30 (t, *J* = 4.6 Hz, 1H, H-4), 4.73 (d, *J* = 3.2 Hz, 1H, H-1), 4.65 (overlapping signals, 2H, H-6a, H6b), 4.34 (overlapping signals, 2H, H-3, H-5), 3.94 (t, *J* = 3.3 Hz, 1H, H-2), 3.90 (m, 1H, butyl C*H*(H)O), 3.39 (dt, *J* = 9.3, 6.7 Hz, 1H, butyl C*H*(H)O), 1.56 (m, 2H, $OCH_2C\mathit{H_2}$), 1.29 (m, 2H, $OCH_2CH_2C\mathit{H_2}$), 1.06 (overlapping signals, 42H, $Si(C\mathit{H}(C\mathit{H_3})_2)_3$ x2), 0.87 (td, *J* = 7.1, 4.6 Hz, 3H, $OCH_2CH_2CH_2C\mathit{H_3}$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.2 (C=O), 165.6 (C=O), 133.0 (C), 132.8 (C), 130.0 (CH), 129.9 (CH), 129.9 (CH), 129.6 (CH), 128.2 (CH), 128.1 (CH), 102.5 (C-1), 73.9 (C-2), 72.9 (C-3), 72.3 (C-5), 71.5 (C-4), 68.8 (O*C*H_2), 65.3 (C-6), 31.6 ($OCH_2C\mathit{H_2}$), 19.2 ($OCH_2CH_2C\mathit{H_2}$), 18.1 (CH_3, TIPS), 18.1 (CH_3, TIPS), 18.1 (CH_3, TIPS), 13.8 ($OCH_2CH_2CH_2C\mathit{H_3}$), 12.8 (CH, TIPS), 12.7 (CH, TIPS). IR (film) cm^{-1}: 2971, 1737, 1451, 1366, 1217, 1109, 1067, 882, 709, 680.



Butyl 4,6-di-*O*-benzoyl-2,3-di-*O*-triisopropylsilyl-α-D-glucopyranoside (59α)

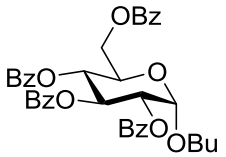
Compound **59β** (22.7 mg, 0.03 mmol) was reacted as described in the general procedure II.L. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (overlapping signals, 2H, aromatic H), 7.98 (overlapping signals, 2H, aromatic H), 7.55 (m, 1H, aromatic H), 7.51 (m, 1H, aromatic H), 7.41 (overlapping signals, 2H, aromatic H), 7.36 (overlapping signals, 2H, aromatic H), 5.16 (dd, *J* = 9.3, 6.8 Hz, 1H, H-4), 4.91 (d, *J* = 3.1 Hz, 1H, H-1), 4.41 (overlapping signals, 3H, H-3, H-

6a, H-6b), 4.26 (m, 1H, H-5), 3.97 (dd, *J* = 7.6, 3.2 Hz, 1H, H-2), 3.73 (dt, *J* = 9.2, 7.1 Hz, 1H, butyl C*H*(H)O), 3.39 (dt, *J* = 9.2, 6.5 Hz, 1H, butyl C*H*(H)O), 1.59 (m, 2H, $OCH_2C\mathit{H_2}$), 1.35 (m, 2H, $OCH_2CH_2C\mathit{H_2}$), 1.09 (overlapping signals, 21H, $Si(C\mathit{H}(C\mathit{H_3})_2)_3$), 1.00 (overlapping signals, 21H, $Si(C\mathit{H}(C\mathit{H_3})_2)_3$), 0.90 (t, *J* = 7.4 Hz, 3H, $OCH_2CH_2CH_2C\mathit{H_3}$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.2 (C=O), 165.8 (C=O), 133.2 (C), 132.9 (C), 130.0 (CH), 129.9 (CH), 129.8 (CH), 129.6 (CH), 128.2 (CH), 128.2 (CH), 128.2 (CH), 128.1 (CH), 98.1 (C-1), 74.0 (C-2), 73.2 (C-4), 72.8 (C-3), 69.0 (C-5), 67.7 ($OC\mathit{H_2}$), 64.3 (C-6), 31.7 ($OCH_2C\mathit{H_2}$), 19.4 ($OCH_2CH_2C\mathit{H_2}$), 18.3 (CH_3, TIPS), 18.2 (CH_3, TIPS), 18.2 (CH_3, TIPS), 18.1 (CH_3, TIPS), 18.1 (CH_3, TIPS), 13.9 ($OCH_2CH_2CH_2C\mathit{H_3}$), 13.5 (CH, TIPS), 13.5 (CH, TIPS), 12.8 (CH, TIPS), 12.7 (CH, TIPS). IR (film) cm^{-1}: 2944, 1726, 1464, 1452, 1263, 1157, 1106, 1068, 1027, 883, 804, 708, 680. ESI-HRMS calcd for $C_{42}H_{68}O_8Si_2Na$ 779.4350, found *m/z* 779.4316 $[M+Na]^+$.



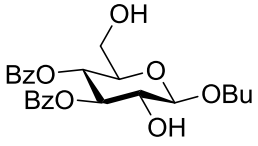
Butyl 2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranoside (60β)

Compound **5** (1 g, 4.2 mmol) was reacted as described in the general procedure II.B using an excess of BzCl (3 mL, 6 equiv.) and stirred at 60 °C. Chromatography (2.11 g, 76%) as a white solid. The NMR spectral data was in accordance with the previous report[1].



Butyl 2,3,4,6-tetra-*O*-benzoyl-α-D-glucopyranoside (60α)

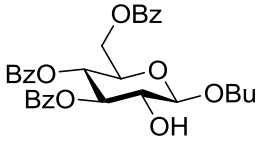
Compound **60β** (21.5 mg, 0.03 mmol) was reacted as described in the general procedure II.L. The NMR spectral data was in accordance with the previous report[1].



Butyl 3,4-di-*O*-benzoyl-β-D-glucopyranoside (61β)

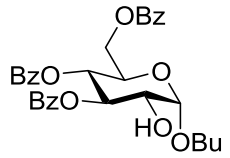
Compound **12β** (17 mg, 0.03 mmol) was reacted as described in the general procedure II.L. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (overlapping signals, 4H, Ar-H), 7.51 (overlapping signals, 2H, Ar-H), 7.37 (overlapping signals, 4H, Ar-H), 5.65 (t, *J* = 9.6 Hz, 1H, H-3), 5.40 (t, *J* = 9.6

Hz, 1H, H-4), 4.54 (d, *J* = 7.8 Hz, 1H, H-1), 3.98 (dt, *J* = 9.6, 6.7 Hz, 1H, butyl C*H*(H)O), 3.80 (overlapping signals, 2H, H-2, H-6a), 3.70 (overlapping signals, 2H, H-5, H-6b), 3.62 (dt, *J* = 9.6, 6.8 Hz, 1H, butyl C*H*(H)O), 2.59 (d, *J* = 2.7 Hz, 1H, C2-O*H*), 2.55 (m, 1H, C6-O*H*), 1.65 (overlapping signals, 2H, $OCH_2C\mathit{H_2}$), 1.41 (overlapping signals, 2H, $OCH_2CH_2C\mathit{H_2}$), 0.94 (t, *J* = 7.4 Hz, 3H, $OCH_2CH_2CH_2C\mathit{H_3}$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.5 (C=O), 166.4 (C=O), 133.8 (C), 133.4 (C), 130.0 (CH), 130.0 (CH), 129.4 (CH), 128.8 (CH), 128.6 (CH), 128.5 (CH), 103.1 (C-1), 74.8 (C-3), 74.6 (C-5), 72.9 (C-2), 70.4 (O-$C\mathit{H_2}$), 69.5 (C-4), 61.5 (C-6), 31.7 ($OCH_2C\mathit{H_2}$), 19.3 ($OCH_2CH_2C\mathit{H_2}$), 14.0 ($OCH_2CH_2CH_2C\mathit{H_3}$). IR (film) cm^{-1}: 3514, 3458, 2959, 1725, 1712, 1603, 1451, 1263, 1130, 1112, 1066, 1026, 1012, 981, 709, 686. ESI-HRMS calcd for $C_{24}H_{28}O_8Na$ 467.1682 found *m/z* 467.1672 $[M+Na]^+$.



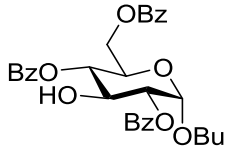
Butyl 3,4,6-tri-*O*-benzoyl-β-D-glucopyranoside (62β)

Compound **56β** (19.9 mg, 0.03 mmol) was reacted as described in the general procedure II.L. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (overlapping signals, 4H, aromatic H), 7.90 (overlapping signals, 2H, aromatic H), 7.50 (overlapping signals, 3H, aromatic H), 7.35 (overlapping signals, 6H, aromatic H), 5.62 (m, 1H, H-3), 5.59 (s, 1H, H-4), 4.59 (m, 1H, H-6a), 4.57 (d, *J* = 8.1 Hz, 1H, H-1), 4.47 (dd, *J* = 12.1, 5.6 Hz, 1H, H-6b), 4.06 (ddd, *J* = 9.3, 5.3, 3.4 Hz, 1H, H-5), 3.94 (dt, *J* = 9.9, 6.8 Hz, 1H, butyl C*H*(H)O), 3.81 (t, *J* = 8.4 Hz, 1H, H-2), 3.63 (dt, *J* = 9.8, 6.9 Hz, 1H, butyl C*H*(H)O), 2.62 (d, *J* = 2.8 Hz, 1H, OH), 1.63 (m, 2H, $OCH_2C\mathit{H_2}$), 1.39 (m, 2H, $OCH_2CH_2C\mathit{H_2}$), 0.91 (td, *J* = 7.4, 1.4 Hz, 3H, $OCH_2CH_2CH_2C\mathit{H_3}$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.6, 166.3, 165.5 (each C=O), 133.5 (C), 133.4 (C), 133.2 (C), 130.0 (CH), 129.9 (CH), 129.8 (CH), 129.8 (CH), 129.3 (CH), 129.0 (CH), 128.5 (CH), 128.5 (CH), 128.4 (CH), 103.1 (C-1), 75.2 (C-3), 72.9 (C-2), 72.2 (C-5), 70.4 ($OC\mathit{H_2}$), 69.8 (C-4), 63.6 (C-6), 31.7 ($OCH_2C\mathit{H_2}$), 19.2 ($OCH_2CH_2C\mathit{H_2}$), 13.9 ($OCH_2CH_2CH_2C\mathit{H_3}$). IR (film) cm^{-1}: 3457, 2957, 1720, 1602, 1454, 1264, 1110, 1094, 1068, 1025, 705, 686. ESI-HRMS calcd for $C_{31}H_{32}O_9Na$ 571.1944, found *m/z* 571.1957 $[M+Na]^+$.



Butyl 3,4,6-tri-*O*-benzoyl-α-D-glucopyranoside (62α)

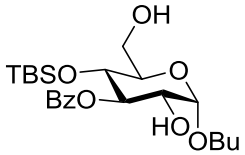
Compound **25β** (21.5 mg, 0.03 mmol) was reacted as described in the general procedure II.L. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (overlapping signals, 2H, aromatic H), 7.97 (overlapping signals, 2H, aromatic H), 7.93 (overlapping signals, 2H, aromatic H), 7.54 (m, 1H, aromatic H), 7.49 (overlapping signals, 2H, aromatic H), 7.41 (overlapping signals, 2H, aromatic H), 7.36 (overlapping signals, 4H, aromatic H), 5.71 (t, *J* = 9.8 Hz, 1H, H-4), 5.55 (t, *J* = 9.9 Hz, 1H, H-3), 5.02 (d, *J* = 3.9 Hz, 1H, H-1), 4.57 (dd, *J* = 12.1, 2.8 Hz, 1H, H-6a), 4.44 (dd, *J* = 12.1, 5.6 Hz, 1H, H-6b), 4.34 (ddd, *J* = 10.0, 5.5, 2.8 Hz, 1H, H-5), 3.91 (dd, *J* = 9.8, 3.9 Hz, 1H, H-2), 3.84 (dt, *J* = 9.7, 6.8 Hz, 1H, butyl C*H*(H)O), 3.57 (dt, *J* = 9.7, 6.6 Hz, 1H, butyl C*H*(H)O), 2.28 (d, *J* = 11.4 Hz, 1H, OH), 1.69 (m, 2H, OCH_2CH_2), 1.43 (m, 2H, $OCH_2CH_2CH_2$), 0.96 (t, *J* = 7.4 Hz, 3H, $OCH_2CH_2CH_2CH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.0, 166.3, 165.5 (each C=O carbons), 133.5 (C), 133.3 (C), 133.2 (C), 130.0 (CH), 129.8 (CH), 129.5 (CH), 129.1 (CH), 128.5 (CH), 128.5 (CH), 128.5 (CH), 98.5 (C-1), 74.2 (C-4), 71.6 (C-2), 69.2 (C-3), 68.9 (OCH_2), 68.2 (C-5), 63.3 (C-6), 31.7 (OCH_2CH_2), 19.5 ($OCH_2CH_2CH_2$), 14.0 ($OCH_2CH_2CH_2CH_3$). IR (film) cm^{-1}: 3467, 2959, 1717, 1451, 1265, 1128, 1095, 1069, 1028, 974, 704, 685. ESI-HRMS calcd for $C_{31}H_{32}O_9Na$ 571.1944, found *m/z* 571.1939 $[M+Na]^+$.



Butyl 2,4,6-tri-*O*-benzoyl-α-D-glucopyranoside (63α)

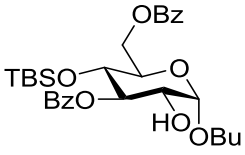
Compound **55β** (19.9 mg, 0.03 mmol) was reacted as described in the general procedure II.L. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (overlapping signals, 6H, aromatic H), 7.57 (overlapping signals, 3H, aromatic H), 7.44 (overlapping signals, 6H, aromatic H), 5.37 (m, 1H, H-4), 5.21 (d, *J* = 3.8, 1H, H-1), 5.11 (dd, *J* = 9.9, 3.7, 1H, H-2), 4.61 (dt, *J* = 12.0, 2.1 Hz, 1H, H-6a), 4.44 (overlapping signals, 2H, H-3, H-6b), 4.34 (ddd, *J* = 10.1, 5.2, 2.4 Hz, 1H, H-5), 3.76 (ddd, *J* = 10.1, 7.3, 5.7 Hz, 1H, butyl C*H*(H)O), 3.47 (m, 1H, butyl C*H*(H)O), 2.58 (d, *J* = 5.1 Hz, 1H, OH), 1.59 (m, 2H, OCH_2CH_2), 1.34 (m, 2H, $OCH_2CH_2CH_2$), 0.85 (td, *J* = 7.4, 1.5 Hz, 3H, $OCH_2CH_2CH_2CH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.4, 166.4, 166.4 (each C=O), 133.7 (C), 133.5 (C), 133.2 (C), 130.1 (CH), 130.0 (CH), 129.9 (CH), 129.7 (CH), 129.3 (CH), 128.6

(CH), 128.6 (CH), 128.5 (CH), 96.2 (C-1), 74.3 (C-2), 72.4 (C-4), 70.7 (C-3), 68.6 (OCH_2), 67.7 (C-5), 63.4 (C-6), 31.5 (OCH_2CH_2), 19.4 ($OCH_2CH_2CH_2$), 13.8 ($OCH_2CH_2CH_2CH_3$). IR (film) cm^{-1}: 3484, 2958, 1721, 1602, 1452, 1263, 1107, 1095, 1069, 1040, 1026, 836, 707. ESI-HRMS calcd for $C_{31}H_{32}O_9Na$ 571.1944, found *m/z* 571.1948 $[M+Na]^+$.



Butyl 3-*O*-benzoyl-4-*O*-(tert-butyldimethylsilyl)-α-D-glucopyranoside (64α)

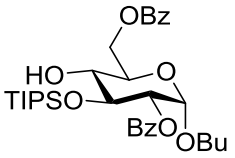
Compound **14β** (17.1 mg, 0.03 mmol) was reacted as described in the general procedure II.L. ^1H NMR (500 MHz, $CDCl_3$) δ 8.07 (overlapping signals, 2H, aromatic H), 7.56 (m, 1H, aromatic H), 7.45 (overlapping signals, 2H, aromatic H), 5.43 (t, *J* = 9.5 Hz, 1H, H-3), 4.89 (d, *J* = 4.0 Hz, 1H, H-1), 3.89 (t, *J* = 9.3 Hz, 1H, H-4), 3.83 (m, 1H, H-6a), 3.78 (overlapping signals, 2H, H-6b, butyl C*H*(H)O), 3.72 (ddd, *J* = 8.9, 4.1, 2.2 Hz, 1H, H-5), 3.64 (ddd, *J* = 11.7, 9.9, 4.6 Hz, 1H, H-2), 3.47 (dtd, *J* = 8.7, 6.6, 1.7 Hz, 1H, butyl C*H*(H)O), 2.03 (d, *J* = 12.0 Hz, 1H, OH), 1.64 (m, 2H, OCH_2CH_2), 1.41 (m, 2H, $OCH_2CH_2CH_2$), 0.96 (td, *J* = 7.3, 1.7 Hz, 3H, $OCH_2CH_2CH_2CH_3$), 0.76 (s, 9H, $SiC(CH_3)_3$), 0.09 (s, 3H, $SiCH_3$), -0.12 (s, 3H, $SiCH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.0 (C=O), 133.2 (C), 130.0 (CH), 128.5 (CH), 98.5 (C-1), 77.0 (C-3), 72.4 (C-5), 72.0 (C-2), 68.7 (C-4), 68.5 (OCH_2), 61.6 (C-6), 31.7 (OCH_2CH_2), 29.9 (CH_3, TBS), 25.8 (CH_3, TBS), 25.7 (CH_3, TBS), 19.5 ($OCH_2CH_2CH_2$), 18.1 (C, TBS), 14.0 ($OCH_2CH_2CH_2CH_3$), -4.0 (CH_3, TBS), -4.6 (CH_3, TBS). IR (film) cm^{-1}: 3445, 2929, 1725, 1452, 1271, 1148, 1084, 1056, 1027, 909, 836, 778, 708, 688. ESI-HRMS calcd for $C_{23}H_{38}O_7SiNa$ 477.2285, found *m/z* 477.2269 $[M+Na]^+$.



Butyl 3,6-di-*O*-benzoyl-2,4-di-*O*-(tert-butyldimethylsilyl)-α-D-glucopyranoside (65α)

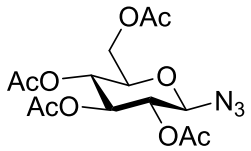
Compound **30β** (20.2 mg, 0.03 mmol) was reacted as described in the general procedure II.L. ^1H NMR (500 MHz, $CDCl_3$) δ 8.09 (overlapping signals, 4H, aromatic H), 7.58 (overlapping signals, 2H, aromatic H), 7.46 (overlapping signals, 4H, aromatic H), 5.47 (m, 1H, H-3), 4.91 (d, *J* = 3.9 Hz, 1H, H-1), 4.72 (m, 1H, H-6a), 4.41 (m, 1H, H-6b), 4.02 (m, 1H, H-5), 3.98 (m, 1H, H-4), 3.78 (dt, *J* = 9.5, 6.9 Hz, 1H, butyl C*H*(H)O), 3.70 (m, 1H, H-2), 3.49 (dt, *J* = 9.6, 6.7 Hz, 1H, butyl C*H*(H)O), 2.06 (d, *J* = 11.9 Hz, 1H, OH), 1.66 (m, 2H, OCH_2CH_2), 1.40 (m,

2H, $OCH_2CH_2CH_2$), 0.94 (t, *J* = 7.4 Hz, 3H, $OCH_2CH_2CH_2CH_3$), 0.77 (s, 9H, $SiC(CH_3)_3$), 0.04 (s, 3H, $SiCH_3$), -0.12 (s, 3H, $SiCH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.0 (C=O), 166.4 (C=O), 133.3 (C), 133.2 (C), 130.3 (CH), 130.1 (CH), 129.7 (CH), 128.6 (CH), 98.3 (C-1), 77.0 (C-3), 71.9 (C-2), 70.5 (C-5), 69.4 (C-4), 68.6 (OCH_2), 63.7 (C-6), 31.6 (OCH_2CH_2), 25.7 (CH_3, TBS), 19.2 ($OCH_2CH_2CH_2$), 18.1 (C, TBS), 13.9 ($OCH_2CH_2CH_2CH_3$), -4.0 (CH_3, TBS), -4.6 (CH_3, TBS). IR (film) cm^{-1}: 3477, 2957, 1721, 1452, 1265, 1094, 1068, 1047, 1026, 836, 777, 707, 670, 687. ESI-HRMS calcd for $C_{30}H_{42}O_8SiNa$ 581.2547, found *m/z* 581.2547 $[M+Na]^+$.



Butyl 2,6-di-*O*-benzoyl-3-*O*-triisopropylsilyl-α-D-glucopyranoside (66α)

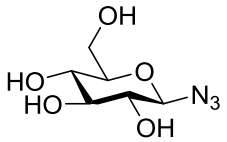
Compound **26β** (22.7 mg, 0.03 mmol) was reacted as described in the general procedure II.L. ^1H NMR (600 MHz, $CDCl_3$) δ 8.09 (overlapping signals, 2H, aromatic H), 8.04 (overlapping signals, 2H, aromatic H), 7.58 (overlapping signals, 2H, aromatic H), 7.46 (overlapping signals, 4H, aromatic H), 5.07 (d, *J* = 3.8 Hz, 1H, H-1), 4.97 (dd, *J* = 9.6, 3.8 Hz, 1H, H-2), 4.76 (dd, *J* = 12.1, 4.6 Hz, 1H, H-6a), 4.54 (dd, *J* = 12.0, 2.2 Hz, 1H, H-6b), 4.36 (dd, *J* = 9.7, 8.5 Hz, 1H, H-3), 4.00 (ddd, *J* = 10.1, 4.6, 2.2 Hz, 1H, H-5), 3.70 (m, 1H, butyl C*H*(H)O), 3.56 (ddd, *J* = 10.0, 8.4, 3.4 Hz, 1H, H-4), 3.37 (dt, *J* = 9.9, 6.5 Hz, 1H, butyl C*H*(H)O), 2.77 (d, *J* = 3.5 Hz, 1H, OH), 1.56 (m, 2H, OCH_2CH_2), 1.32 (m, 2H $OCH_2CH_2CH_2$), 0.98 (overlapping signals, 21H, $Si(CH(CH_3)_2)_3$), 0.82 (t, *J* = 7.4 Hz, 3H $OCH_2CH_2CH_2CH_3$). ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.3, 166.3 (each C=O), 133.4 (C), 133.3 (C), 130.0 (CH), 129.8 (CH), 128.6 (CH), 128.4 (CH), 96.4 (C-1), 74.4 (C-2), 73.0 (C-3), 71.9 (C-4), 69.8 (C-5), 68.1 (OCH_2), 64.0 (C-6), 31.6 (OCH_2CH_2), 29.9 (CH_3, TIPS), 19.4 ($OCH_2CH_2CH_2$), 18.2 (CH_3, TIPS), 18.2 (CH_3, TIPS), 13.9 ($OCH_2CH_2CH_2CH_3$), 12.9 (CH, TIPS). IR (film) cm^{-1}: 3627, 2961, 1724, 1452, 1261, 1015, 795, 711, 663. ESI-HRMS calcd for $C_{33}H_{48}O_8SiNa$ 623.3016 found *m/z* 623.3010 $[M+Na]^+$.



2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl azide (71)

This compound was prepared as previously described[18].

Compound **2** (5.5 g, 14 mmol) was dissolved in CH_2Cl_2 (110 mL). Trimethylsilyl azide (2 mL, 1.1 equiv.) and $SnCl_4$ (1.4 mL 0.9 equiv.) were then added, and the mixture was stirred at room temperature for 2 h. The mixture was then washed with a saturated aqueous solution $NaHCO_3$ before being extracted with EtOAc. It was then washed with water and brine, dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure to obtain **71** (5.0 g, 95%) as a white solid. The NMR spectral data was in accordance with the previous report[18].

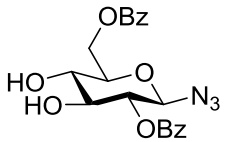


β-D-Glucopyranosyl azide (72)

Compound **71** (5.0 g, 13.4 mmol) was reacted as described in the general procedure II.A to give **72** (2.6 g, 95%) as a white solid. The NMR spectral data was in accordance with the previous report[6].

- **Preparation of 76**

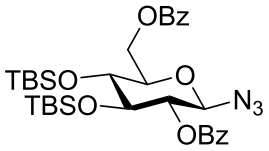
Compound **72** (1 g, 4.87 mmol) was reacted as described in the general procedure II.H to give **73**, which was then reacted as described in the general procedure II.I. to give **74**, which was sequentially reacted as described in the general procedure II.B with an excess of benzoyle to give **75**, which was finally reacted with the general procedure II.J. Chromatography (cyclohexane-EtOAc, 5:2) gave **76** (765 mg, 38% over four steps) as a white solid.



2,6-Di-*O*-benzoyl-β-D-glucopyranosyl azide (76)

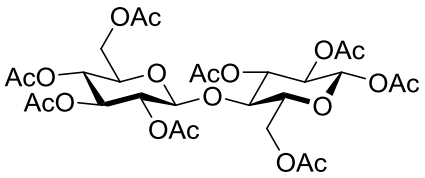
76: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (overlapping signals, 4H, aromatic H), 7.59 (overlapping signals, 2H, aromatic H), 7.46 (overlapping signals, 5H, aromatic H), 5.01 (dd, *J* = 9.5, 8.7 Hz, 1H, H-2), 4.78 (overlapping signals, 2H, H-1, H-6a), 4.60 (dd, *J* = 12.3, 2.2 Hz,

1H, H-6b), 3.85 (t, *J* = 9.2 Hz, 1H, H-3), 3.73 (ddd, *J* = 9.3, 5.0, 2.5 Hz, 1H, H-5), 3.63 (m, 1H, H-4). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.4 (C=O), 166.1 (C=O), 133.6 (C), 133.5 (C), 130.0 (CH), 129.9 (CH), 129.3 (CH), 129.0 (CH), 128.5 (CH) (all C-Ar), 88.2 (C-1), 76.3 (C-5), 75.0 (C-3), 73.6 (C-2), 70.1 (C-4), 63.2 (C-6).



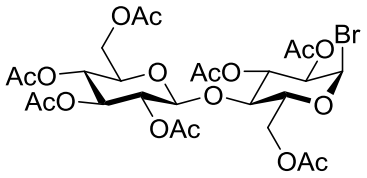
2,6-Di-*O*-benzoyl-3,4-di-*O*-(tert-butyldimethylsilyl)-β-D-glucopyranosyl azide (69β)

Compound **76** (765 mg, 1.85 mmol) was reacted as described in the general procedure II.C using TBSOTf (1.1 mL, 2.5 equiv.) at 60 °C. Chromatography (cyclohexane-EtOAc, 9:1) gave **69** (760 mg, 64%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (overlapping signals, 4H, aromatic H), 7.55 (overlapping signals, 2H, aromatic H), 7.43 (overlapping signals, 4H, aromatic H), 5.11 (d, *J* = 6.6 Hz, 1H, H-1), 5.08 (dd, *J* = 6.6, 3.9 Hz, 1H, H-2), 4.71 (dd, *J* = 11.5, 4.9 Hz, 1H, H-6a), 4.55 (dd, *J* = 11.5, 6.8 Hz, 1H, H-6b), 4.15 (dt, *J* = 6.8, 4.7 Hz, 1H, H-5), 3.99 (t, *J* = 4.3 Hz, 1H, H-3), 3.92 (t, *J* = 4.6 Hz, 1H, H-4), 0.89 (s, 9H, $SiC(CH_3)_3$), 0.89 (s, 9H, $SiC(CH_3)_3$), 0.16 (s, 3H, $SiCH_3$), 0.13 (s, 3H, $SiCH_3$), 0.11 (s, 3H, $SiCH_3$), 0.08 (s, 3H, $SiCH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.2 (C=O), 165.2 (C=O), 133.4 (C), 133.1 (C), 129.9 (CH), 129.9 (CH), 129.7 (CH), 129.5 (CH), 128.4 (CH), 86.9 (C-1), 78.2 (C-5), 74.2 (C-3), 74.1 (C-2), 70.8 (C-4), 64.5 (C-6), 25.8 (CH_3, TBS), 25.8 (CH_3, TBS), 18.0 (C, TBS), 18.0 (C, TBS), -3.8 (CH_3, TBS), -4.1 (CH_3, TBS), -4.3 (CH_3, TBS), -4.6 (CH_3, TBS). ESI-HRMS calcd for $C_{32}H_{51}N_4O_7Si_2$ 659.3296 found *m/z* 659.3288 $[M+NH_4]^+$.



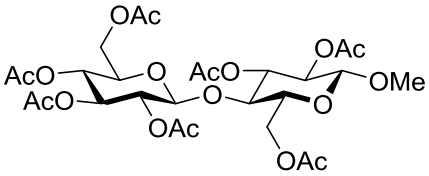
β-Cellobiose octaacetate (77)

Cellobiose (20 g, 58 mmol) was put into suspension in acetic anhydride (180 mL). Then, NaOAc (10 g) and the mixture was stirred under reflux until it became clear. After cooling, the solution was poured into ice-cold water. The precipitate was filtered and dissolved in CH_2Cl_2, and the organic phase was washed with water until pH neutral, dried over Na_2SO_4, filtered and the solvent evaporated under reduced pressure to give **77** (37.2 g, 94%) as a white solid. The NMR spectral data was in accordance with the previous report[19].



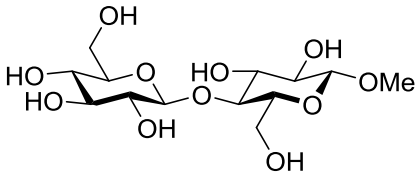
4-*O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-2,3,6-tri-*O*-acetyl-α-D-glucopyranosyl bromide (78)

Compound **77** (37.2 g, 55 mmol) was dissolved in AcOH (150 mL). HBr (30% in AcOH, 10 mL) was added, and the solution was stirred at room temperature overnight. The mixture was diluted with CH_2Cl_2, and the organic phase was washed with water, a saturated aqueous solution $NaHCO_3$, water and brine, dried over Na_2SO_4, filtered, and the solvent removed under reduced pressure to give **78** (35.6 g, 93%) as a white solid. The NMR spectral data was in accordance with the previous report[20].



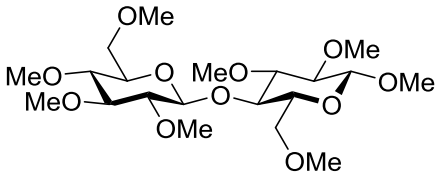
Methyl 4-*O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-2,3,6-tri-*O*-acetyl-β-D-glucopyranoside (79)

Ag_2CO_3 (7.05 g, 0.5 equiv.) and molecular sieves (3Å, 10 g) were put into CH_2Cl_2 (100 mL) and MeOH (100 mL), and the resulting suspension was shielded from light and stirred at room temperature for 15 min. A solution of **78** (35.6 g, 51 mmol) in CH_2Cl_2 (20 mL) was added to the suspension, and the resulting mixture was stirred at room temperature for 3 h. It was then filtered through a plug of silica, washed with EtOAc, and the filtrate was evaporated under reduced pressure to give **79** (20.5 g, 62%) as a white solid. The NMR spectral data was in accordance with the previous report[21].



Methyl 4-*O*-(β-D-glucopyranosyl)-β-D-glucopyranoside (80)

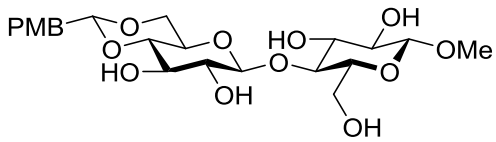
Compound **79** (20.5 g, 32 mmol) was reacted as described in the general procedure II.A to give **80** (10.6 g, 95%) as a white solid. The NMR spectral data was in accordance with the previous report[22].



Methyl 2,3,6-tri-*O*-methyl-4-*O*-(2,3,4,6-tetra-*O*-methyl-β-D-glucopyranosyl)-β-D-glucopyranoside (70β)

Compound **70β**, a new compound, was prepared by protection of **80** using reagents and conditions reported previously[23].

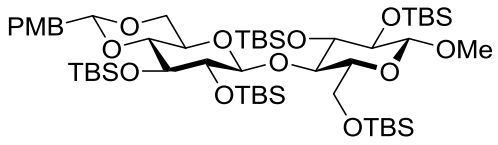
Compound **80** (1 g, 2.8 mmol) was dissolved in DMF (25 mL), and the solution was cooled down to 0 °C. NaH (1.6 g, 14 equiv.) was then added in portions and left to stir until no more gas evolved. MeI (3.5 mL, 20 equiv.) was finally added dropwise and the mixture was stirred at 0 °C overnight. Methanol was added to quench the reaction, and the solution was poured into water. It was then extracted with EtOAc, and the organic phase was dried over Na_2SO_4, filtered and evaporated under reduced pressure. Chromatography (cyclohexane-EtOAc, 1:1) gave **70** (972 mg, 76%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.24 (d, *J* = 7.9 Hz, 1H, H-1'), 4.09 (d, *J* = 7.7 Hz, 1H, H-1), 3.64 (overlapping signals, 2H, H-6a, H-6b), 3.56 (overlapping signals, 5H, H-4, H-6'a, H-6'b, OC*H*$_3$), 3.51 (s, 3H, OC*H*$_3$), 3.49 (s, 3H, OC*H*$_3$), 3.48 (s, 3H, OC*H*$_3$), 3.46 (s, 3H, OC*H*$_3$), 3.45 (s, 3H, OC*H*$_3$), 3.33 (s, 3H, OC*H*$_3$), 3.32 (s, 3H, OC*H*$_3$), 3.29 (m, 1H, H-5), 3.18 (t, *J* = 8.9 Hz, 1H, H-3), 3.13 (overlapping signals, 2H, H-4', H-5'), 3.06 (t, *J* = 8.5 Hz, 1H, H-3'), 2.95 (m, 1H, H-2), 2.86 (m, 1H, H-2'). ^{13}C NMR (126 MHz, $CDCl_3$) δ 104.1 (C-1'), 103.1 (C-1), 86.9 (C-3'), 84.5 (C-3), 84.0 (C-2'), 83.0 (C-2), 79.2 (C-4'), 77.7 (C-4), 74.6 (C-5, C-5' (overlapping signals)), 71.1 (C-6'), 70.5 (C-6), 60.6, 60.5, 60.3, 60.2, 60.1, 59.2, 59.0, 56.8 (all *C*H$_3$). ESI-HRMS calcd for $C_{20}H_{38}O_{11}Na$ 477.2312 found *m/z* 477.2320 $[M+Na]^+$.



Methyl 4-*O*-(4,6-*O*-(4-methoxybenzylidene)-β-D-glucopyranosyl)-β-D-glucopyranoside (81)

Compound **80** (4.4 g, 12 mmol) was dissolved in THF (50 mL), and pyridinium *p*-toluenesulfonate (0.5 g, 0.15 equiv.) followed by *p*-methoxybenzylidene dimethyl acetal (6.3 mL, 3 equiv.) were added. The mixture was stirred under reflux for 3 h. After cooling down, the solution was quenched with $NaHCO_3$, and the product was extracted with EtOAc. The organic phase was washed with water and brine, dried over Na_2SO_4, and the solvent evaporated

under reduced pressure to give **81** as a crude product, which was put to the next step without any further purification.



Methyl 4-*O*-(4,6-*O*-(4-methoxybenzylidene)-2,3-di-*O*-(tert-butyldimethylsilyl)-β-D-glucopyranosyl)-2,3,6-tri-*O*-(tert-butyldimethylsilyl)-β-D-glucopyranoside (82)

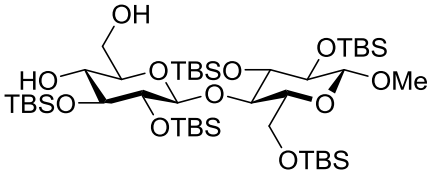
Compound **81** was reacted as described in the general procedure II.C using an excess of TBSOTf at 90 °C overnight. Chromatography (cyclohexane-EtOAc, 8:2) gave **82** (2.45 g, 19% over two steps) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (overlapping signals, 2H, aromatic H), 6.87 (overlapping signals, 2H, aromatic H), 5.32 (s, 1H, Ph-C*H*), 4.54 (d, *J* = 7.5 Hz, 1H, H-1'), 4.24 (dd, *J* = 10.5, 4.6 Hz, 1H, H-6'a), 4.20 (d, *J* = 6.7 Hz, 1H, H-1), 3.95 (dd, *J* = 10.9, 3.6 Hz, 1H, H-6a), 3.81 (s, 3H, Ph-OC*H*$_3$), 3.78 (overlapping signals, 2H, H-4, H-6b), 3.71 (t, *J* = 8.2 Hz, 1H, H-3'), 3.65 (overlapping signals, 2H, H-3, H-6'b), 3.49 (dt, *J* = 6.7, 4.2 Hz, 1H, H-5), 3.45 (dd, *J* = 6.8, 5.9 Hz, 1H, H-2), 3.40 (s, 4H, H-2', OC*H*$_3$), 3.32 (overlapping signals, 2H, H-4', H-5'), 0.93 (s, 9H, SiC(C*H*$_3$)$_3$), 0.90 (overlapping signals, 27H, SiC(C*H*$_3$)$_3$ x3), 0.77 (s, 9H, SiC(C*H*$_3$)$_3$), 0.13 (s, 3H, SiC*H*$_3$), 0.11 (s, 3H, SiC*H*$_3$), 0.10 (s, 3H, SiC*H*$_3$), 0.09 (s, 3H, SiC*H*$_3$), 0.08 (overlapping signals, 12H, SiC*H*$_3$ x4), -0.01 (s, 3H, SiC*H*$_3$), -0.04 (s, 3H, SiC*H*$_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.1 (Ph-*C*-OMe), 129.8 (C), 127.9 (CH), 113.4 (CH), 103.9 (C-1), 102.6 (C-1'), 102.4 (Ph-CH), 82.0 (C-4'), 76.6 (C-2), 76.6 (C-5), 76.5 (C-3), 76.3 (C-3'), 76.2 (C-2'), 75.8 (C-4), 69.0 (C-6'), 66.1 (C-5'), 62.2 (C-6), 56.0 (O*C*H$_3$), 55.2 (Ph-O*C*H$_3$), 26.5 (CH$_3$, TBS), 26.4 (CH$_3$, TBS), 26.4 (CH$_3$, TBS), 26.3 (CH$_3$, TBS), 25.9 (CH$_3$, TBS), 18.6 (C, TBS), 18.5 (C, TBS), 18.3 (C, TBS), 18.0 (C, TBS), 18.0 (C, TBS), -2.2 (CH$_3$, TBS), -2.5 (CH$_3$, TBS), -3.1 (CH$_3$, TBS), -3.1 (CH$_3$, TBS), -3.4 (CH$_3$, TBS), -3.5 (CH$_3$, TBS), -3.7 (CH$_3$, TBS), -3.8 (CH$_3$, TBS), -5.0 (CH$_3$, TBS), -5.4 (CH$_3$, TBS).

- **Preparation of 83 and 84**

Compounds **83** and **84**, a new compound, was prepared by deprotection of the benzilidene of **82** using reagents and conditions reported previously[24].

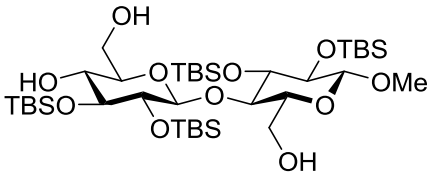
Compound **82** (2.45 g, 2.3 mmol) was dissolved in MeOH. Then, pyridinium *p*-toluenesulfonate was added and the mixture was heated under reflux for 1 h. After cooling down, Et_3N was added to quench the reaction, and the solvent was evaporated under reduced

pressure. Chromatography (cyclohexane-EtOAc, 10:0 to 6:4) gave **83** (695 mg, 32%) and **84** (305 mg, 16%) as white solids.



Methyl 4-*O*-(2,3-di-*O*-(tert-butyldimethylsilyl)-β-D-glucopyranosyl)-2,3,6-tri-*O*-(tert-butyldimethylsilyl)-β-D-glucopyranoside (83)

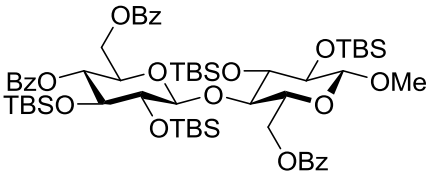
83: ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.51 (d, *J* = 7.3 Hz, 1H, H-1'), 4.25 (d, *J* = 6.5 Hz, 1H, H-1), 3.93 (dd, *J* = 10.9, 3.7 Hz, 1H, H-6'a), 3.79 (overlapping signals, 4H, H-6a, H-6b, H-4, H-6'b), 3.70 (dd, *J* = 6.6, 5.2 Hz, 1H, H-3), 3.51 (overlapping signals, 3H, H-5', H-3', H-2), 3.44 (td, *J* = 8.7, 4.4 Hz, 1H, H-4'), 3.40 (s, 3H, O-C*H*$_3$), 3.34 (m, 1H, H-2'), 3.30 (m, 1H, H-5), 2.23 (d, *J* = 4.5 Hz, 1H, OH), 0.93 (s, 9H, SiC(C*H*$_3$)$_3$), 0.91 (overlapping signals, 27H, SiC(C*H*$_3$)$_3$ x3), 0.89 (s, 9H, SiC(C*H*$_3$)$_3$), 0.14 (s, 3H, SiC*H*$_3$), 0.13 (overlapping signals, 6H, SiC*H*$_3$ x2), 0.11 (s, 3H, SiC*H*$_3$), 0.10 (s, 3H, SiC*H*$_3$), 0.09 (s, 3H, SiC*H*$_3$), 0.08 (overlapping signals, 9H, SiC*H*$_3$ x 3), 0.07 (s, 3H, SiC*H*$_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 103.6 (C-1), 102.2 (C-1'), 78.8 (C-3'), 78.0, (C-3) 76.7 (C-5'), 76.0 (C-4), 75.2 (C-5), 74.8 (C-2'), 72.1 (C-4'), 62.9 (C-6), 62.4 (C-6'), 55.9 (O*C*H$_3$), 26.5, 26.5 , 26.3, 26.2, 26.0, 18.6, 18.4, 18.4, 18.1, 18.0, -2.3, -2.6, -3.2, -3.3, -3.4, -3.5, -3.6, -4.0, -5.0, -5.4 (all TBS carbons).



Methyl 4-*O*-(2,3-di-*O*-(tert-butyldimethylsilyl)-β-D-glucopyranosyl)-2,3-di-*O*-(tert-butyldimethylsilyl)-β-D-glucopyranoside (84)

84: ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.54 (d, *J* = 5.5 Hz, 1H, H-1'), 4.10 (d, *J* = 7.5 Hz, 1H, H-1), 3.84 (overlapping signals, 4H, H-6a, H-6b, H-6'a, H-6'b), 3.60 (overlapping signals, 3H, H-4', H-3', H-4), 3.51 (overlapping signals, 3H, H-5', H-3, H-2'), 3.46 (s, 3H, OC*H*$_3$), 3.30 (dd, *J* = 8.8, 7.5 Hz, 1H, H-2), 3.26 (m, 1H, H-5), 2.50 (d, *J* = 5.1 Hz, 1H, OH), 0.91 (s, 9H, SiC(C*H*$_3$)$_3$), 0.90 (s, 9H, SiC(C*H*$_3$)$_3$), 0.89 (s, 9H, SiC(C*H*$_3$)$_3$), 0.89 (s, 9H, SiC(C*H*$_3$)$_3$), 0.12 (overlapping signals, 6H, SiC*H*$_3$ x2), 0.11 (s, 3H, SiC*H*$_3$), 0.10 (s, 3H, SiC*H*$_3$), 0.08 (overlapping signals, 6H, SiC*H*$_3$ x2), 0.07 (overlapping signals, 6H, SiC*H*$_3$ x2). ^{13}C NMR (126 MHz, $CDCl_3$) δ 104.1 (C-1), 102.2 (C-1'), 77.3 (C-4), 77.2 (C-3'), 75.8 (C-3), 75.8 (C-5'), 75.3 (C-2), 75.0 (C-5), 74.6 (C-2'), 71.3 (C-4'), 62.6 (C-6'), 61.7 (C-6), 56.7 (O*C*H$_3$), 26.3 (CH$_3$,

TBS), 26.1 (CH_3, TBS), 25.9 (CH_3, TBS), 25.8 (CH_3, TBS), 18.3 (C, TBS), 18.3 (C, TBS), 18.0 (C, TBS), -3.1 (CH_3, TBS), -3.5 (CH_3, TBS), -3.8 (CH_3, TBS), -4.0 (CH_3, TBS), -4.5 (CH_3, TBS), -4.7 (CH_3, TBS), -5.0 (CH_3, TBS), -5.3 (CH_3, TBS).



Methyl 6-*O*-benzoyl-4-*O*-(4,6-di-*O*-benzoyl-2,3-di-*O*-(tert-butyldimethylsilyl)-β-D-glucopyranosyl)-2,3-di-*O*-(tert-butyldimethylsilyl)-β-D-glucopyranoside (67β)

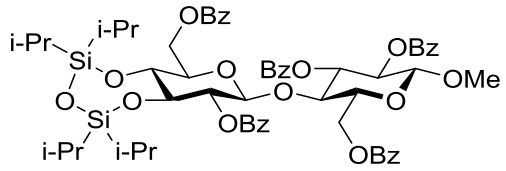
Compound **83** (695 mg, 0.71 mmol) was reacted as described in the general procedure II.B using an excess of BzCl (0.5 mL, 6 equiv.) stirred under reflux and overnight. Chromatography (cyclohexane-EtOAc, 8:2) gave **67** (450 mg, 56%) as a white solid.

This compound was also synthesized from **84** (305 mg, 16%), which was reacted as described in the general procedure II.B using BzCl (0.3 mL, 6 equiv.) stirred under reflux and overnight. Chromatography (cyclohexane-EtOAc, 8:2) gave **67** (266 mg, 63%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (overlapping signals, 2H, aromatic H), 7.94 (overlapping signals, 2H, aromatic H), 7.86 (overlapping signals, 2H, aromatic H), 7.54 (overlapping signals, 2H, aromatic H), 7.43 (overlapping signals, 3H, aromatic H), 7.39 (overlapping signals, 2H, aromatic H), 7.26 (overlapping signals, 2H, aromatic H), 5.12 (dd, *J* = 4.8, 3.5 Hz, 1H, H-4'), 4.86 (dd, *J* = 11.9, 3.0 Hz, 1H, H-6a), 4.76 (d, *J* = 6.7 Hz, 1H, H-1'), 4.52 (overlapping signals, 2H, H-6b, H-6'a), 4.45 (dd, *J* = 11.2, 6.0 Hz, 1H, H-6'b), 4.31 (d, *J* = 6.3 Hz, 1H, H-1), 4.11 (t, *J* = 7.9 Hz, 1H, H-4), 4.00 (td, *J* = 6.5, 3.4 Hz, 1H, H-5'), 3.95 (dd, *J* = 4.9, 2.7 Hz, 1H, H-3'), 3.85 (dt, *J* = 7.9, 3.6 Hz, 1H, H-5), 3.80 (dd, *J* = 6.8, 2.6 Hz, 1H, H-2'), 3.73 (dd, *J* = 7.5, 6.3 Hz, 1H, H-3), 3.60 (t, *J* = 6.3 Hz, 1H, H-2), 3.41 (s, 3H, OC*H*$_3$), 0.93 (s, 9H, SiC(C*H*$_3$)$_3$), 0.90 (s, 9H, SiC(C*H*$_3$)$_3$), 0.89 (s, 9H, SiC(C*H*$_3$)$_3$), 0.79 (s, 9H, SiC(C*H*$_3$)$_3$), 0.19 (s, 3H, SiC*H*$_3$), 0.15 (s, 3H, SiC*H*$_3$), 0.14 (overlapping signals, 6H, SiC*H*$_3$ x2), 0.12 (overlapping signals, 6H, SiC*H*$_3$ x2), 0.12 (s, 3H, SiC*H*$_3$), 0.08 (s, 3H, SiC*H*$_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.1 (C=O), 165.9 (C=O), 165.3 (C=O), 133.2 (C), 133.1 (C), 133.0 (C), 130.6 (CH), 130.0 (CH), 129.8 (CH), 129.8 (CH), 129.7 (CH), 129.6 (CH), 129.4 (CH), 129.3 (CH), 128.9 (CH), 128.3 (CH), 104.0 (C-1), 101.8 (C-1'), 76.5 (C-3), 76.1 (C-2), 76.0 (C-2'), 75.6 (C-5'), 75.1 (C-3'), 75.0 (C-4), 73.3 (C-5), 71.3 (C-4'), 64.8 (C-6'), 63.6 (C-6), 56.2 (O-*C*H_3), 26.3 (CH_3, TBS), 26.3 (CH_3, TBS), 25.9 (CH_3, TBS), 25.8 (CH_3, TBS), 18.4 (CH, TBS), 18.0 (CH, TBS), 17.9 (CH, TBS), 17.8 (CH, TBS), -2.6 (CH_3, TBS), -2.8 (CH_3, TBS), -3.5 (CH_3, TBS), -3.7 (CH_3, TBS), -3.8 (CH_3, TBS), -3.9 (CH_3, TBS), -4.1 (CH_3, TBS), -4.2 (CH_3, TBS). IR (film) cm^{-1}:

2954, 1725, 1472, 1462, 1452, 1268, 1249, 1093, 1052, 1026, 1006, 873, 835, 776, 705, 684, 675.

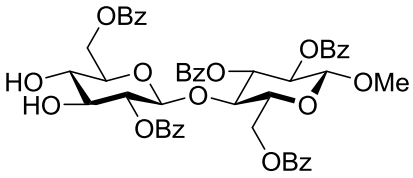
- **Preparation of 87**

Compound **80** (1 g, 4.87 mmol) was sequentially reacted as described in the general procedures II.H, II.I., and finally II.B with an excess of benzoyle. Chromatography (cyclohexane-EtOAc, 8:2) gave **87** (1.76 g, 33% over three steps) as a white solid.



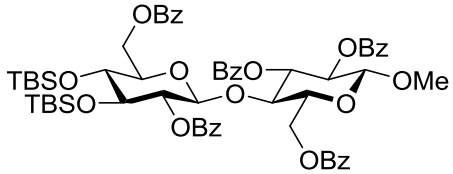
Methyl 2,3,6-tri-*O*-benzoyl-4-*O*-(2,6-di-*O*-benzoyl-3,4-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-β-D-glucopyranosyl)-β-D-glucopyranoside (87)

87: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (overlapping signals, 2H, aromatic H), 8.02 (overlapping signals, 4H, aromatic H), 7.91 (overlapping signals, 4H, aromatic H), 7.59 (overlapping signals, 3H, aromatic H), 7.53 (overlapping signals, 2H, aromatic H), 7.31 (overlapping signals, 6H, aromatic H), 7.08 (overlapping signals, 2H, aromatic H), 5.78 (t, *J* = 9.4 Hz, 1H, H-3), 5.42 (dd, *J* = 9.7, 7.8 Hz, 1H, H-2), 5.27 (dd, *J* = 9.3, 8.1 Hz, 1H, H-2'), 4.70 (d, *J* = 8.1 Hz, 1H, H-1'), 4.60 (overlapping signals, 3H, H-1, H-6a, H-6b), 4.28 (dd, *J* = 11.7, 2.0 Hz, 1H, H-6'a), 4.20 (t, *J* = 9.5 Hz, 1H, H-4), 3.84 (ddd, *J* = 9.9, 4.5, 2.3 Hz, 1H, H-5), 3.78 (dd, *J* = 9.3, 8.3 Hz, 1H, H-3'), 3.71 (dd, *J* = 11.7, 5.8 Hz, 1H, H-6'b), 3.65 (dd, *J* = 9.4, 8.3 Hz, 1H, H-4'), 3.42 (s, 3H, O-C*H*$_3$), 3.37 (ddd, *J* = 9.5, 6.1, 2.2 Hz, 1H, H-5'), 0.88 (overlapping signals, 28H, $Si(CH(CH_3)_2)_2)_2$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.1, 165.9, 165.5, 165.3, 164.7 (each C=O), 133.3 (C), 133.2 (C), 133.1 (C), 133.1 (C), 133.0 (C), 129.9 (CH), 129.8 (CH), 129.7 (CH), 129.6 (CH), 129.6 (CH), 129.5 (CH), 129.4 (CH), 129.3 (CH), 129.2 (CH), 128.5 (CH), 128.5 (CH), 128.4 (CH), 128.3 (CH), 128.0 (CH), 101.8 (C-1), 100.8 (C-1'), 77.7 (C-3'), 76.3 (C-4), 74.3 (C-5'), 73.5 (C-2'), 73.2 (C-5), 73.0 (C-4'), 72.7 (C-3), 72.0 (C-2), 63.1 (C-6'), 62.8 (C-6), 57.0 (O-*C*H_3), 17.2 (CH_3, TIPDS), 17.2 (CH_3, TIPDS), 17.1 (CH_3, TIPDS), 17.1 (CH_3, TIPDS), 17.1 (CH_3, TIPDS), 17.0 (CH_3, TIPDS), 17.0 (CH_3, TIPDS), 12.6 (CH, TIPDS), 12.6 (CH, TIPDS), 12.1 (CH, TIPDS), 12.0 (CH, TIPDS).



Methyl 2,3,6-tri-*O*-benzoyl-4-*O*-(2,6-di-*O*-benzoyl-β-D-glucopyranosyl)-β-D-glucopyranoside (88)

Compound **87** (1.76 g, 1.6 mmol) was reacted as described in the general procedure II.J. Chromatography (cyclohexane-EtOAc, 5:2) gave **88** (662 mg, 48%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (overlapping signals, 2H, aromatic H), 7.94 (overlapping signals, 4H, aromatic H), 7.88 (overlapping signals, 4H, aromatic H), 7.54 (overlapping signals, 2H, aromatic H), 7.45 (overlapping signals, 3H, aromatic H), 7.31 (overlapping signals, 8H, aromatic H), 7.10 (overlapping signals, 2H, aromatic H), 5.72 (t, J = 9.4 Hz, 1H, H-3), 5.37 (dd, J = 9.7, 7.8 Hz, 1H, H-2), 5.05 (dd, J = 9.6, 7.9 Hz, 1H, H-2'), 4.68 (d, J = 7.9 Hz, 1H, H-1'), 4.56 (overlapping signals, 3H, H-1, H-6a, H-6b), 4.16 (overlapping signals, 2H, H-4, H-6'a), 3.81 (overlapping signals, 2H, H-5, H-6'b), 3.65 (dd, J = 9.6, 8.3 Hz, 1H, H-3'), 3.40 (s, 3H, O-C*H*$_3$), 3.35 (overlapping signals, 2H, H-4', H-5'). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.5, 166.0, 165.9, 165.5, 165.3 (each C=O), 133.3 (C), 133.3 (C), 133.1 (C), 133.1 (C), 129.8 (CH), 129.8 (CH), 129.7 (CH), 129.5 (CH), 129.5 (CH), 129.4 (CH), 129.2 (CH), 128.9 (CH), 128.5 (CH), 128.5 (CH), 128.3 (CH), 128.1 (CH), 101.7 (C-1), 100.7 (C-1'), 76.2 (C-4), 75.2 (C-3'), 74.3 (C-2'), 74.1 (C-5'), 73.1 (C-5), 72.9 (C-3), 72.0 (C-2), 70.4 (C-4'), 63.2 (C-6'), 62.7 (C-6), 57.0 (O-*C*H$_3$).



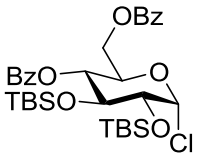
Methyl 2,3,6-tri-*O*-benzoyl-4-*O*-(2,6-di-*O*-benzoyl-3,4-di-*O*-(tert-butyldimethylsilyl)-β-D-glucopyranosyl)-β-D-glucopyranoside (68β)

Compound **88** (662 mg, 0.75 mmol) was reacted as described in the general procedure II.C using TBSOTf (0.5 mL, 3 equiv.) at 60 °C. Chromatography (cyclohexane-EtOAc, 9:1) gave **68β** (534 mg, 64%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (overlapping signals, 2H, aromatic H), 8.01 (overlapping signals, 6H, aromatic H), 7.94 (overlapping signals, 2H, aromatic H), 7.58 (m, 1H, aromatic H), 7.49 (overlapping signals, 4H, aromatic H), 7.36 (overlapping signals, 8H, aromatic H), 7.25 (overlapping signals, 2H, aromatic H), 5.76 (t, J = 9.4 Hz, 1H, H-3), 5.42 (dd, J = 9.8, 7.8 Hz, 1H, H-2), 5.01 (overlapping signals, 2H, H-1', H-2'), 4.70 (dd, J = 12.0, 2.0 Hz, 1H, H-6a), 4.58 (d, J = 7.8 Hz, 1H, H-1), 4.43 (dd, J = 12.1, 4.1

Hz, 1H, H-6b), 4.32 (dd, J = 11.1, 6.2 Hz, 1H, H-6'a), 4.25 (t, J = 9.5 Hz, 1H, H-4), 3.81 (ddd, J = 9.9, 4.1, 2.1 Hz, 1H, H-5), 3.78 (dd, J = 5.0, 3.5 Hz, 1H, H-3'), 3.69 (td, J = 6.5, 3.7 Hz, 1H, H-5'), 3.61 (t, J = 4.4 Hz, 1H, H-4'), 3.51 (dd, J = 11.1, 7.0 Hz, 1H, H-6'b), 3.42 (s, 3H, O-CH_3), 0.77 (s, 9H, SiC(CH_3)$_3$), 0.75 (s, 9H, SiC(CH_3)$_3$), 0.06 (s, 3H, SiCH_3), 0.01 (s, 3H, SiCH_3), -0.09 (s, 3H, SiCH_3), -0.16 (s, 3H, SiCH_3). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.8, 165.7, 165.4, 165.3, 165.0 (each C=O), 133.2 (C), 133.2 (C), 133.1 (C), 133.1 (C), 132.9 (C), 129.9 (CH), 129.9 (CH), 129.8 (CH), 129.8 (CH), 129.8 (CH), 129.7 (CH), 129.6 (CH), 129.5 (CH), 129.4 (CH), 128.5 (CH), 128.4 (CH), 128.4 (CH), 128.3 (CH), 128.2 (CH), 101.9 (C-1), 100.1 (C-1'), 78.2 (C-5'), 76.2 (C-2'), 75.6 (C-4), 75.0 (C-3'), 73.1 (C-5), 73.0 (C-3), 71.9 (C-2), 70.8 (C-4'), 64.4 (C-6'), 62.4 (C-6), 57.0 (O-*C*H$_3$), 25.8 (CH_3, TBS), 17.8 (C, TBS), 17.8 (C, TBS), -4.0 (CH_3, TBS), -4.1 (CH_3, TBS), -4.5 (CH_3, TBS), -4.7 (CH_3, TBS) (all TBS carbons).

- **Anomerisation of 67β**

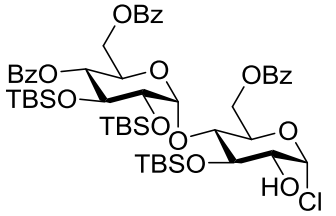
Compound **67β** (95 mg, 0.085 mmol) was reacted as described in the general procedure II.K using $TiCl_4$ (1 mol/L, 0.2 mL, 2.5 equiv.). Chromatography (cyclohexane-EtOAc, 1:0 to 8:1) gave **89** (23 mg, 43%) as a white solid and **90** (13 mg, 15%) as a white solid.



4,6-Di-*O*-benzoyl-2,3-di-*O*-(tert-butyldimethylsilyl)-α-D-glucopyranosyl chloride (89)

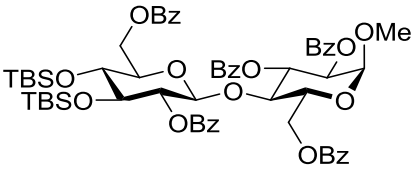
89: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (overlapping signals, 4H, aromatic H), 7.56 (overlapping signals, 2H, aromatic H), 7.42 (overlapping signals, 5H, aromatic H), 6.04 (d, *J* = 3.5 Hz, 1H, H-1), 5.37 (dd, *J* = 10.5, 8.9 Hz, 1H, H-4), 4.51 (overlapping signals, 2H, H-5, H-6a), 4.31 (m, 1H, H-6b), 4.23 (t, *J* = 8.8 Hz, 1H, H-3), 3.91 (dd, *J* = 8.7, 3.7 Hz, 1H, H-2), 0.95 (overlapping signals, 18H, SiC(CH_3)$_3$ x3), 0.75 (d, *J* = 1.1 Hz, 9H, SiC(CH_3)$_3$), 0.15 (s, 3H, SiCH_3), 0.15 (s, 3H, SiCH_3), 0.07 (s, 3H, SiCH_3), -0.10 (s, 3H, SiCH_3). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.3 (C=O), 165.3 (C=O), 133.5 (C), 133.2 (C), 130.1 (CH), 129.9 (CH), 129.8 (CH), 129.7 (CH), 128.6 (CH), 128.5 (CH), 104.5 (C-1), 74.3 (C-2), 72.0 (C-3), 71.2 (C-5), 71.2 (C-4), 63.0 (C-6), 26.3 (CH_3, TBS), 18.4 (C, TBS), 18.1 (C, TBS), 18.1 (C, TBS), 17.9 (C, TBS), -2.9 (CH_3, TBS), -3.3 (CH_3, TBS), -4.1 (CH_3, TBS), -4.3 (CH_3, TBS). IR (film) cm^{-1}: 2954, 2930, 2858, 1726, 1603, 1473, 1463, 1452, 1252, 1158, 1093, 1069, 1027, 1001, 836,

775, 707, 672. ESI-HRMS calcd for $C_{32}H_{51}NO_7Si_2Cl$ 652.2893 found *m/z* 652.2875 $[M+NH_4]^+$.



2-*O*-Benzoyl-4-*O*-(4,6-di-*O*-benzoyl-2,3-di-*O*-(tert-butyldimethylsilyl)-α-D-glucopyranosyl)-α-D-glucopyranosyl chloride (90)

90: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (overlapping signals, 4H, aromatic H), 7.97 (overlapping signals, 2H, aromatic H), 7.53 (overlapping signals, 3H, aromatic H), 7.39 (overlapping signals, 6H, aromatic H), 5.90 (d, *J* = 4.1 Hz, 1H, H-1), 5.32 (dd, *J* = 7.1, 4.9 Hz, 1H, H-4'), 4.80 (d, *J* = 4.4 Hz, 1H, H-1'), 4.61 (overlapping signals, 2H, H-6a, H-6b), 4.56 (dd, *J* = 12.0, 3.8 Hz, 1H, H-6'a), 4.47 (dd, *J* = 11.5, 7.0 Hz, 1H, H-6'b), 4.33 (m, 1H, H-5), 4.25 (td, *J* = 5.6, 3.3 Hz, 1H, H-5'), 3.95 (overlapping signals, 2H, H-3, H-3'), 3.87 (d, *J* = 1.8 Hz, 1H, OH), 3.79 (dd, *J* = 4.1, 3.1 Hz, 1H, H-2'), 3.73 (dd, *J* = 9.1, 4.0 Hz, 1H, H-2), 3.68 (dd, *J* = 9.4, 8.3 Hz, 1H, H-4), 0.86 (overlapping signals, 18H, $SiC(CH_3)_3$ x2), 0.81 (s, 9H, $SiC(CH_3)_3$), 0.11 (s, 3H, $SiCH_3$), 0.06 (overlapping signals, 6H, $SiCH_3$ x2), 0.04 (s, 3H, $SiCH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.5 (C=O), 166.2 (C=O), 165.4 (C=O), 133.5 (C), 133.4 (C), 133.2 (C), 130.0 (CH), 129.9 (CH), 129.8 (CH), 129.8 (CH), 129.8 (CH), 129.6 (CH), 128.6 (CH), 128.6 (CH), 128.5 (CH), 103.1 (C-1'), 95.1 (C-1), 78.7 (C-4), 75.3 (C-2'), 74.7 (C-3'), 73.3 (C-2), 72.8 (C-5'), 72.0 (C-3), 71.9 (C-4'), 70.9 (C-5), 64.3 (C-6'), 62.6 (C-6), 26.0 (CH_3, TBS), 25.9 (CH_3, TBS), 25.8 (CH_3, TBS), 18.2 (C, TBS), 18.0 (C, TBS), 18.0 (C, TBS), -3.9 (CH_3, TBS), -4.0 (CH_3, TBS), -4.1 (CH_3, TBS), -4.1 (CH_3, TBS). IR (film) cm^{-1}: 3511, 2955, 2929, 2857, 1723, 1603, 1472, 1259, 1095, 1069, 1027, 1006, 835, 777, 708, 686, 674. ESI-HRMS calcd for $C_{51}H_{79}NO_{13}Si_3Cl$ 1032.4548 found *m/z* 1032.4548 $[M+NH_4]^+$.

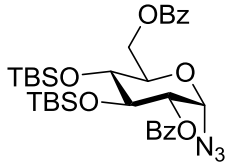


Methyl 2,3,6-tri-*O*-benzoyl-4-*O*-(2,6-di-*O*-benzoyl-3,4-di-*O*-(tert-butyldimethylsilyl)-β-D-glucopyranosyl)-α-D-glucopyranoside (91)

Compound **68β** (166 mg, 0.15 mmol) was reacted as described in the general procedure II.K using $TiCl_4$ (1 mol/L, 0.4 mL, 2.5 equiv.) and stirring at -15 °C to room temperature overnight. Chromatography (cyclohexane-EtOAc, 9:1) gave **91** (53 mg, 32%) as white solid and other products not characterized. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (overlapping signals, 8H, aromatic H), 7.96 (overlapping signals, 2H, aromatic H), 7.56 (overlapping signals, 2H, aromatic H), 7.47 (overlapping signals, 4H, aromatic H), 7.40 (overlapping signals, 3H, aromatic H), 7.34 (overlapping signals, 4H, aromatic H), 7.27 (overlapping signals, 2H, aromatic H), 6.03 (dd, J = 10.3, 9.1 Hz, 1H, H-3), 5.18 (dd, J = 10.2, 3.6 Hz, 1H, H-2), 5.09 (d, J = 3.6 Hz, 1H, H-1), 5.05 (d, J = 6.9 Hz, 1H, H-1'), 4.99 (dd, J = 6.9, 2.9 Hz, 1H, H-2'), 4.67 (dd, J = 12.1, 2.0 Hz, 1H, H-6a), 4.44 (dd, J = 12.1, 4.0 Hz, 1H, H-6b), 4.29 (dd, J = 10.9, 6.5 Hz, 1H, H-6'a), 4.18 (t, J = 9.6 Hz, 1H, H-4), 4.10 (m, 1H, H-5), 3.78 (dd, J = 4.6, 2.9 Hz, 1H, H-3'), 3.74 (dd, J = 6.5, 2.9 Hz, 1H, H-4'), 3.66 (overlapping signals, 2H, H-5', H-6'b), 3.35 (s, 3H, O-C*H*$_3$), 0.77 (s, 9H, $SiC(CH_3)_3$), 0.74 (s, 9H, $SiC(CH_3)_3$), 0.07 (s, 3H, Si-CH_3), 0.00 (s, 3H, Si-CH_3), -0.11 (s, 3H, Si-CH_3), -0.17 (s, 3H, Si-CH_3). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.0 (C=O), 165.8 (C=O), 165.8 (C=O), 165.4 (C=O), 165.0 (C=O), 133.2 (C), 133.1 (C), 133.1 (C), 132.8 (C), 130.1 (CH), 130.0 (CH), 129.9 (CH), 129.8 (CH), 129.8 (CH), 129.7 (CH), 129.6 (CH), 129.5 (CH), 129.4 (CH), 129.1 (CH), 128.4 (CH), 128.4 (CH), 128.3 (CH), 128.1 (CH), 100.1 (C-1'), 96.9 (C-1), 78.5 (C-4'), 76.5 (C-2'), 75.8 (C-4), 75.0 (C-3'), 72.1 (C-2), 70.5 (C-5'), 70.4 (C-3), 68.5 (C-5), 64.6 (C-6'), 62.4 (C-6), 55.4 (O-*C*H_3), 25.7 (CH_3, TBS), 25.7 (CH_3, TBS), 17.8 (C, TBS), 17.8 (C, TBS), -4.2 (CH_3, TBS), -4.4 (CH_3, TBS), -4.6 (CH_3, TBS), -4.8 (CH_3, TBS).

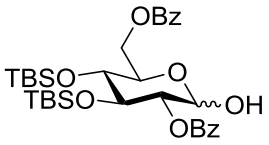
- **Reaction of 69β with $TiCl_4$**

Compound **69β** (234 mg, 0.36 mmol) was reacted as described in the general procedure II.K using $TiCl_4$ (1 mol/L, 0.9 mL, 2.5 equiv.), and stirred for 5 h. Chromatography (cyclohexane-EtOAc, 1:0 to 8:1) gave **69α** (15 mg, 6%) as a white solid, **93** (52 mg, 23%) as a white solid and **92** (25 mg, 11%) as a white solid.



2,6-Di-*O*-benzoyl-3,4-di-*O*-(tert-butyldimethylsilyl)-α-D-glucopyranosyl azide (69α)

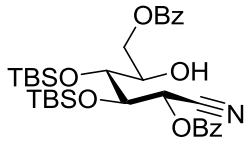
69α: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (overlapping signals, 3H, aromatic H), 7.57 (overlapping signals, 2H, aromatic H), 7.45 (overlapping signals, 5H, aromatic H), 5.47 (d, *J* = 2.6 Hz, 1H, H-1), 5.07 (m, 1H, H-2), 4.66 (m, 1H, H-6a), 4.54 (dt, *J* = 11.9, 2.7 Hz, 1H, H-6b), 4.33 (ddt, *J* = 8.2, 5.6, 2.4 Hz, 1H, H-5), 4.18 (m, 1H, H-3), 3.73 (m, 1H, H-4), 0.86 (s, 9H $SiC(CH_3)_3$), 0.80 (s, 9H $SiC(CH_3)_3$), 0.18 (s, 3H, $SiCH_3$), 0.14 (s, 3H, $SiCH_3$), 0.08 (s, 3H, $SiCH_3$), 0.03 (s, 3H, $SiCH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.5 (C=O), 166.0 (C=O), 133.5 (C), 133.3 (C), 130.3 (CH), 130.1 (CH), 130.0 (CH), 129.9 (CH), 129.9 (CH), 129.7 (CH), 128.5 (CH), 83.4 (C-1), 76.2 (C-5), 71.5 (C-2), 71.3 (C-3), 70.9 (C-4), 63.1 (C-6), 29.9 (CH_3, TBS), 25.9 (CH_3, TBS), 18.1 (C, TBS), -3.5 (CH_3, TBS), -3.7 (CH_3, TBS), -4.1 (CH_3, TBS), -4.4 (CH_3, TBS). IR (film) cm^{-1}: 3356, 2954, 2929, 2857, 2115, 1723, 1603, 1472, 1463, 1452, 1251, 1091, 1068, 1027, 833, 776, 709, 687. ESI-HRMS calcd for $C_{32}H_{51}N_4O_7Si_2$ 659.3296 found *m/z* 659.3288 $[M+NH_4]^+$.



2,6-Di-*O*-benzoyl-3,4-di-*O*-(tert-butyldimethylsilyl)-β-D-glucopyranose (92)

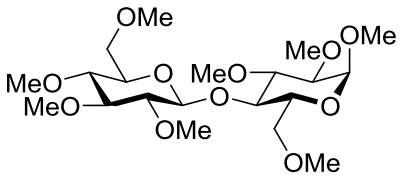
92: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (overlapping signals, 13H, aromatic H), 7.57 (overlapping signals, 7H, aromatic H), 7.44 (overlapping signals, 14H, aromatic H), 5.46 (dt, J = 8.6, 2.8 Hz, 3H, H-1α), 5.18 (m, 1H, H-1β), 5.04 (overlapping signals, 3H, H-2α, H-2β), 4.68 (ddd, J = 11.8, 4.9, 2.2 Hz, 1H, H-6βa), 4.59 (m, 5H, H-6αa, H-6αb), 4.50 (m, 1H, H-6βb), 4.36 (dd, J = 6.8, 4.3 Hz, 2H, H-5α), 4.24 (dt, J = 6.0, 3.1 Hz, 2H, H-3α), 4.09 (overlapping signals, 2H, H-3β, H-5β), 3.91 (dt, J = 6.3, 3.1 Hz, 1H, H-4β), 3.81 (dt, J = 6.2, 3.0 Hz, 3H, H-4α), 3.60 (dd, J = 8.6, 2.5 Hz, 3H, Ohα, OHβ), 0.88 (s, 9H, $SiC(CH_3)_3$), 0.81 (s, 9H, $SiC(CH_3)_3$), 0.18 (s, 3H, $SiCH_3$), 0.14 (s, 3H, $SiCH_3$), 0.08 (s, 3H, $SiCH_3$), 0.05 (s, 3H, $SiCH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.5 (C=O), 166.0 (C=O), 133.4 (C), 133.2 (C), 130.1 (CH), 130.1 (CH), 129.8 (CH), 128.5 (CH), 94.7 (C-1β), 88.9 (C-1α), 76.1 (C-5β), 75.2 (C-2β), 74.7 (C-5α), 73.7 (C-3β), 72.7 (C-2α), 71.7 (C-3α), 71.1 (C-4β), 70.9 (C-4α), 65.2 (C-6β), 63.8 (C-6α), 29.8 (CH_3, TBS), 27.1 (CH_3, TBS), 25.9 (CH_3, TBS), 25.9 (CH_3, TBS), 18.1 (C, TBS), -3.8 (CH_3,

TBS), -4.0 (CH_3, TBS), -4.2 (CH_3, TBS), -4.5 (CH_3, TBS). IR (film) cm^{-1}: 3447, 2955, 2930, 2896, 2858, 1720, 1603, 1473, 1463, 1452, 1268, 1095, 1069, 1027, 994, 834, 775, 708, 687. ESI-HRMS calcd for $C_{32}H_{52}NO_8Si_2$ 634.3232 found *m/z* 634.3218 $[M+NH_4]^+$.



2,6-Di-*O*-benzoyl-3,4-di-*O*-(tert-butyldimethylsilyl)-D-gluconic acid nitrile (93)

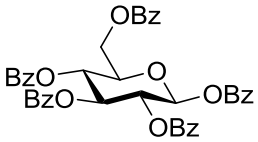
93: ^1H NMR (500 MHz, $CDCl_3$) δ 8.13 (overlapping signals, 2H, aromatic H), 8.00 (overlapping signals, 2H, aromatic H), 7.58 (overlapping signals, 2H, aromatic H), 7.49 (overlapping signals, 3H, aromatic H), 7.42 (overlapping signals, 2H, aromatic H), 5.95 (d, *J* = 3.9 Hz, 1H, H-2), 4.55 (dt, *J* = 11.9, 2.1 Hz, 1H, H-6a), 4.35 (t, *J* = 4.0 Hz, 1H, H-3), 4.30 (dd, *J* = 11.9, 4.6 Hz, 1H, H-6b), 4.13 (dd, *J* = 7.9, 4.1 Hz, 1H, H-4), 4.06 (ddd, *J* = 8.4, 4.3, 2.1 Hz, 1H, H-5), 3.65 (s, 1H, OH), 0.94 (overlapping signals, 18H, $SiC(CH_3)_3$ x2), 0.27 (s, 3H, $SiCH_3$), 0.22 (s, 3H, $SiCH_3$), 0.19 (s, 3H, $SiCH_3$), 0.12 (s, 3H, $SiCH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.7 (C=O), 164.8 (C=O), 134.3 (C), 133.2 (C), 130.2 (CH), 129.7 (CH), 128.9 (CH), 128.5 (CH), 116.3 (Cq, CN), 75.6 (C-3), 72.4 (C-5), 70.8 (C-4), 65.5 (C-6), 61.2 (C-2), 27.0 (CH_3, TBS), 25.7 (CH_3, TBS), 18.1 (C, TBS), -4.1 (CH_3, TBS), -4.4 (CH_3, TBS), -4.8 (CH_3, TBS). IR (film) cm^{-1}: 3498, 2954, 2931, 2894, 2859, 2161, 1724, 1602, 1472, 1363, 1316, 1253, 1090, 1068, 1027, 1027, 1006, 834, 778, 708, 687. ESI-HRMS calcd for $C_{32}H_{51}N_2O_7Si_2$ 631.3235 found *m/z* 631.3235 $[M+NH_4]^+$.



Methyl 2,3,6-tri-*O*-methyl-4-*O*-(2,3,4,6-tetra-*O*-methyl-β-D-glucopyranosyl)-α-D-glucopyranoside (94)

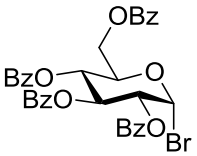
Compound **70β** (160 mg, 0.35 mmol) was reacted as described in the general procedure II.K using $TiCl_4$ (1 mol/L, 0.9 mL, 2.5 equiv.), and stirred overnight. Chromatography (cyclohexane-EtOAc 1:1) gave **94** (68 mg, 42%) as a white solid. ^1H NMR (500 MHz, $CDCl_3$) δ 4.75 (d, *J* = 3.6 Hz, 1H, H-1), 4.21 (d, *J* = 7.9 Hz, 1H, H-1'), 3.69 (m, 1H, H-6a), 3.59 (overlapping signals, 2H, H-4, H-5), 3.54 (overlapping signals, 6H, H-6b, H-6'a, H-6'b, OCH_3), 3.50 (s, 3H, OCH_3), 3.49 (s, 3H, OCH_3), 3.45 (overlapping signals, 4H, H-3, OCH_3), 3.43 (s, 3H, OCH_3), 3.34 (s, 3H, OCH_3), 3.33 (s, 3H, OCH_3), 3.32 (s, 3H, OCH_3), 3.15

(overlapping signals, 2H, H-2, H-5'), 3.12 (t, *J* = 8.9 Hz, 1H, H-4'), 3.06 (t, *J* = 8.6 Hz, 1H, H-3'), 2.86 (dd, *J* = 9.0, 7.9 Hz, 1H, H-2'). ^{13}C NMR (126 MHz, $CDCl_3$) δ 103.2 (C-1), 97.4 (C-1'), 86.9 (C-3'), 84.0 (C-2'), 81.4 (C-3), 81.1 (C-2), 79.3 (C-4'), 77.9c (C-4), 74.7 (C-5), 71.1 (C-6'), 70.2 (C-6), 69.7 (C-5), 60.6 (OCH_3), 60.5 (OCH_3), 60.5 (OCH_3), 60.2 (OCH_3), 59.3 (OCH_3), 58.9 (OCH_3), 55.1 (OCH_3). ESI-HRMS calcd for $C_{20}H_{38}O_{11}Na$ 477.2312 found *m/z* 477.2308 $[M+Na]^+$.



1,2,3,4,6-Penta-*O*-benzoyl-β-D-glucopyranose (96)

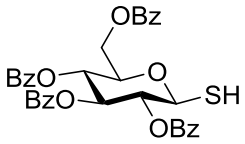
D-Glucose (10 g, 55 mmol) was reacted as described in the general procedure II.A using an excess of BzCl (39 mL, 6 equiv.) at room temperature overnight. Chromatography (cyclohexane:EtOAc 1:1) gave **96** (30 g, 77%) as a white solid. The NMR spectral data was in accordance with the previous report[25].



2,3,4,6-Tetra-*O*-benzoyl-β-D-glucopyranosyl bromide (97)

This compound was prepared as previously described[26].

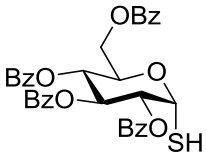
Glucose pentabenzoate **96** (30 g, 43 mmol) was dissolved in CH_2Cl_2 (100 mL) and the solution was cooled to 0 °C. HBr (33% in AcOH, 30 mL) was then added, and the mixture was stirred at room temperature overnight. The resulting solution was diluted in CH_2Cl_2. The organic phase was washed with water, a saturated solution of $NaHCO_3$ (four times), water, and brine. It was then dried over Na_2SO_4, and the solvent was removed under reduced pressure. No further purification gave the wanted compound **97** (26.5 g, 94%) as a white solid. The NMR spectral data was in accordance with the previous report[27].



2,3,4,6-Tetra-*O*-benzoyl-thio-β-D-glucopyranoside (98)

This compound was prepared as previously described[28].

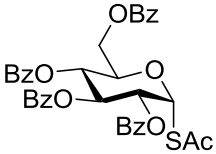
Sodium sulfide (19 g, 80 mmol) was dissolved in DMF (200 mL) and carbon disulfide (3.6 mL, 60 mmol) was added dropwise at room temperature. The solution became red. After addition of **97** (26.5 g, 40.2 mmol), the yellow mixture was stirred at room temperature for 1h. The reaction was diluted with water and then extracted with EtOAc. The organic phase was washed with water and brine, dried with Na_2SO_4, filtered and the solvent was removed under reduced pressure. Chromatography (cyclohexane-EtOAc, 7:3) gave **98** (15.7 g, 64%) as a white solid. The NMR spectral data was in accordance with the previous report[28].



2,3,4,6-Tetra-*O*-benzoyl-thio-α-D-glucopyranoside (99)

This compound was synthesized using O'Sullivan's method[29].

Compound **98** (5 g, 8.2 mmol) was dissolved in CH_2Cl_2 (75 mL). To this solution, pyridine (330 µL, 0.5 equiv.) and $TiCl_4$ (1 mol/L, 24.5 mL, 3 equiv.) were added and the resulting mixture was stirred at room temperature for 16 h. It was then diluted with EtOAc, and the organic phase was washed with a saturated solution of NH_4Cl, $NaHCO_3$ and brine, dried over Na_2SO_4, and the solvent was removed under reduced pressure. The crude product was brought to the next step without any further purification. The NMR spectral data was in accordance with the previous report[29].

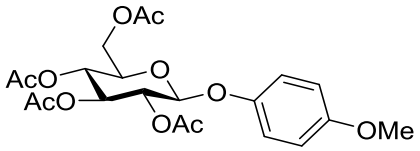


2,3,4,6-Tetra-*O*-benzoyl-1-*S*-acetyl-1-thio-α-D-glucopyranoside (100)

Compound **100**, a new compound, was prepared by acetylation of **99** using reagents and conditions reported previously[30].

Crude **99** (5 g, 8.2 mmol) was diluted in pyridine (50 mL) and acetic anhydride (7.7 mL, 10 equiv.), and the solution was stirred at room temperature overnight. The mixture was then

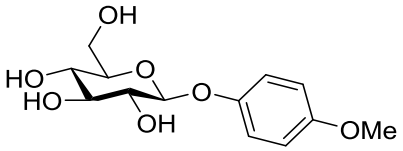
cooled to 0 °C and methanol was added. The solution was diluted with EtOAc, and the organic phase was washed with water, HCl 1 mol/L (until the pH of the aqueous phase was acidic), water and brine. It was then dried over Na_2SO_4, filtered and the solvent evaporated under reduced pressure. Chromatography (cyclohexane-EtOAc, 7:2) gave **100** (3.63 g, 68%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (overlapping signals, 2H, aromatic H), 7.93 (overlapping signals, 4H, aromatic H), 7.87 (overlapping signals, 2H, aromatic H), 7.52 (overlapping signals, 4H, aromatic H), 7.39 (overlapping signals, 6H, aromatic H), 7.30 (overlapping signals, 2H, aromatic H), 6.55 (d, *J* = 5.5 Hz, 1H, H-1), 5.87 (t, *J* = 9.8 Hz, 1H, H-3), 5.71 (overlapping signals, 2H, H-2, H-4), 4.59 (dd, *J* = 11.9, 2.6 Hz, 1H, H-6a), 4.47 (overlapping signals, 2H, H-5, H-6b), 2.37 (s, 3H, CH_3). ^{13}C NMR (126 MHz, $CDCl_3$) δ 191.2 (S-C=O), 166.1 (C=O), 165.7 (C=O), 165.1 (C=O), 165.0 (C=O), 133.6 (C), 133.5 (C), 133.3 (C), 133.1 (C), 129.9 (CH), 129.8 (CH), 129.8 (CH), 129.8 (CH), 129.7 (CH), 129.7 (CH), 129.6 (CH), 128.8 (CH), 128.7 (CH), 128.6 (CH), 128.5 (CH), 128.4 (CH), 128.4 (CH), 128.3 (CH), 128.3 (CH), 80.8 (C-1), 71.7 (C-5), 71.6 (C-3), 70.1 (C-4), 68.9 (C-2), 62.7 (C-6), 31.5 (CH_3). IR (film) cm^{-1}: 2982, 1722, 1601, 1451, 1263, 1178, 1090, 1069, 1026, 707, 687.



***p*-Methoxyphenyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (101)**

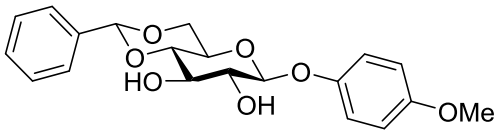
This compound was prepared as previously described[31].

Glucose pentaacetate **2** (30 g, 77 mmol) was diluted in CH_2Cl_2 (200 mL). *p*-methoxyphenol (14 g, 1.4 equiv.), triethylamine (5.6 mL, 0.52 equiv.) and $BF_3.Et_2O$ (23 mL, 2.5 equiv.) were then added, and the solution was stirred at room temperature overnight. The resulting mixture was then diluted with CH_2Cl_2, and the organic phase was washed with water, a saturated solution of $NaHCO_3$ and brine, dried over Na_2SO_4, and the solvent removed under reduced pressure. Chromatography (cyclohexane-EtOAc, 3:1) gave **101** (31.8 g, 91%) as a white solid. The NMR spectral data was in accordance with the previous report[31].



***p*-Methoxyphenyl β-D-glucopyranoside (102)**

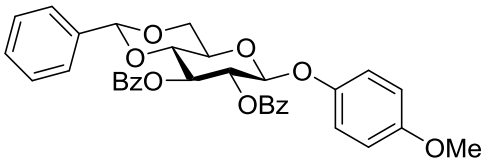
Compound **101** (31.8 g, 70 mmol) was reacted as described in the general procedure II.A to give **102** (19.7 g, 91%) as a white solid. The NMR spectral data was in accordance with the previous report[32].



***p*-Methoxyphenyl 4,6-*O*-benzylidene-β-D-glucopyranoside (103)**

This compound was prepared as previously described[33].

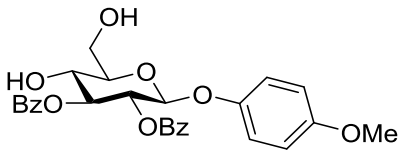
Compound **102** (19.7 g, 69 mmol) was dissolved in CH_3CN (110 mL). Benzaldehyde dimethyl acetal (15.5 mL, 1.5 equiv.) and camphor sulfonic acid (3.2 g, 20%) were added and the mixture was stirred at 45 °C for 3 h. It was then neutralised with Et_3N and the solvent was evaporated, and the crude product was purified by flash chromatography (CH_2Cl_2-MeOH, 8:2) to give **103** (18.3 g, 71%) as a white solid. The NMR spectral data was in accordance with the previous report[34].



***p*-Methoxyphenyl 4,6-*O*-benzylidene-2,3-di-*O*-benzoyl-β-D-glucopyranoside (104)**

Compound **103** (18.3 g, 1.8 mmol) was reacted as described in the general procedure II.B using an excess of BzCl (17 mL, 3 equiv.). Chromatography (cyclohexane-EtOAc, 3:1) gave **104** (17.9 g, 63%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (ddd, *J* = 8.5, 5.1, 1.3 Hz, 4H, aromatic H), 7.50 (overlapping signals, 3H, aromatic H), 7.40 (overlapping signals, 6H, aromatic H), 7.32 (overlapping signals, 2H, aromatic H), 6.92 (overlapping signals, 2H, aromatic H), 6.78 (overlapping signals, 2H, aromatic H), 5.84 (t, *J* = 9.5 Hz, 1H, H-3), 5.71 (dd, *J* = 9.3, 7.8 Hz, 1H, H-2), 5.58 (s, 1H, C*H*-Ar), 5.25 (d, *J* = 7.7 Hz, 1H, H-1), 4.47 (dd, *J* = 10.5, 4.9 Hz, 1H, H-6a), 4.04 (t, *J* = 9.5 Hz, 1H, H-4), 3.94 (t, *J* = 10.3 Hz, 1H, H-6b), 3.79 (td, *J* = 9.7, 4.9 Hz, 1H, H-5), 3.75 (s, 3H, Ar-OC*H*$_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.6 (C=O), 165.2 (C=O), 155.8 (C), 151.0 (C), 133.6 (C), 133.3 (C), 133.1 (C), 130.2 (CH), 129.8

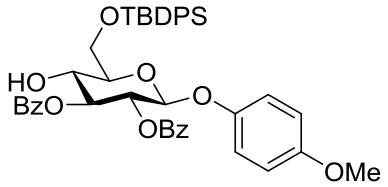
(CH), 129.8 (CH), 129.3 (CH), 129.1 (CH), 128.5 (CH), 128.4 (CH), 128.3 (CH) , 128.2 (CH), 126.1 (CH), 119.0 (CH), 114.6 (CH), 101.6 (*C*H-Ar), 101.4 (C-1), 78.6 (C-4), 72.4 (C-2), 72.0 (C-3), 68.6 (C-6), 66.8 (C-5), 55.6 (Ar-O*C*H$_3$). IR (film) cm^{-1}: 2973, 1737, 1724, 1602, 1508, 1453, 1267, 1253, 1219, 1094, 1071, 833, 758, 709, 700, 686.



_p_-Methoxyphenyl 2,3-di-_O_-benzoyl-β-D-glucopyranoside (105)

This compound was prepared as previously described[35].

Compound **104** (17.9 g, 31 mmol) was dissolved in CH_2Cl_2 (100 mL) and trifluoroacetic acid (17 mL, 7.4 equiv.) and water (2.4 mL, 4.3 equiv.) were subsequently added. The solution was stirred at room temperature for 3 h. It was then diluted with CH_2Cl_2, washed with a saturated solution of $NaHCO_3$, water and brine, dried over Na_2SO_4, filtered and the solvent removed under reduced pressure. Chromatography (cyclohexane-EtOAc, 2:1) gave **105** (13.2 g, 87%) as a white solid. The NMR spectral data was in accordance with the previous report[36].

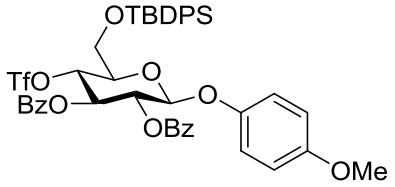


_p_-Methoxyphenyl 2,3-di-_O_-benzoyl-6-_O_-tert-butyldiphenylsilyl-β-D-glucopyranoside (106)

This compound was prepared as previously described[37].

Compound **105** (13.2 g, 27 mmol) was dissolved in DMF (100 mL) and the solution was cooled to 0 °C. Imidazole (5.4 g, 3 equiv.) and TBDPSCl (10 mL, 1.5 equiv.) were then added to the solution, and the mixture was stirred at 0 °C for 3 h. It was then diluted with CH_2Cl_2, washed with HCl (5%), a saturated solution of $NaHCO_3$ and water, dried over Na_2SO_4, filtered and the solvent removed under reduced pressure. Chromatography (cyclohexane-EtOAc, 4:1) gave **106** (17.0 g, 87%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (overlapping signals, 4H, aromatic H), 7.71 (overlapping signals, 4H, aromatic H), 7.52 (overlapping signals, 2H, aromatic H), 7.40 (overlapping signals, 10H, aromatic H (TBDPS)), 6.94 (overlapping signals, 2H, aromatic H (PMP)), 6.72 (overlapping signals, 2H, aromatic H (PMP)), 5.65 (dd, J = 9.8, 7.9 Hz, 1H, H-2), 5.49 (t, J = 9.5 Hz, 1H, H-3), 5.14 (d, J = 7.9 Hz, 1H, H-1), 4.06 (overlapping signals, 2H, H-4, H-6a), 4.01 (dd, J = 11.0, 5.3 Hz, 1H, H-6b), 3.73 (overlapping signals, 4H,

H-5, OC*H*$_3$), 3.20 (s, 1H, OH), 1.08 (s, 9H, Si-C(C*H*$_3$)$_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.4 (C=O), 165.3 (C=O), 155.5 (C), 151.3 (C), 136.3 (C), 135.7 (C), 135.6 (C), 133.5 (C), 133.2 (C), 132.7 (C), 130.0 (CH), 129.8 (CH), 129.7 (CH), 128.4 (CH), 128.4 (CH), 127.8 (CH), 126.4 (CH), 126.3 (CH), 118.8 (CH), 114.5 (CH), 110.0 (CH), 100.7 (C-1), 77.2 (C-2), 76.1 (C-5), 71.4 (C-3), 70.7 (C-4), 64.0 (C-6), 55.6 (O-CH_3), 26.8 (TBDPS), 19.2 (TBDPS). IR (film) cm^{-1}: 2982, 1722, 1601, 1451, 1263, 1178, 1090, 1069, 1026, 707, 687.



***p*-Methoxyphenyl 2,3-di-*O*-benzoyl-6-*O*-tert-butyldiphenylsilyl-4-*O*-trifluoromethansulfonyl-β-D-glucopyranoside (107)**

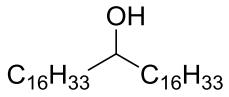
This compound was prepared as previously described[38].

Compound **106** (5 g, 6.8 mmol) was dissolved in CH_2Cl_2 (43 mL) and the solution was cooled to 0 °C. Pyridine (1.7 mL, 3 equiv.) and triflic anhydride (1.6 mL 1.4 equiv.) were then added, and the mixture was stirred at room temperature for 1 h. It was then diluted with CH_2Cl_2, washed with HCl 1 mol/L, water and brine, dried over Na_2SO_4, filtered and the solvent removed under reduced pressure. Chromatography (cyclohexane-EtOAc, 8:1) gave **107** (3.1 g, 53%).

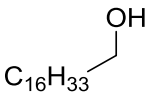
- **Preparation of 109 and 110**

These compounds was prepared as previously described[39].

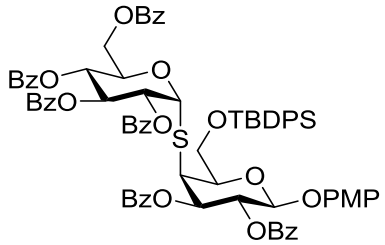
Magnesium turnings (1.2 g, 49 mmol) was put in suspension to dry Et_2O (50 mL), and a crystal of iodine was added to the mixture. The solution was warmed to reflux, and hexadecyl bromide (15 mL, 49 mmol) was added dropwise. The solution went from dark red to colourless. After stirring at reflux overnight, hexadecylmagnesium bromide **108** was obtained, and the solution was cooled to room temperature. Ethyl formate (2 mL, 0.5 equiv.) was then added dropwise, and the mixture was stirred to reflux for 5 h. The solution was cooled to 0 °C and water was added, followed by HCl 1 mol/L, and the aqueous phase was extracted with Et_2O. The combined organic phases were washed with water, a saturated solution of $NaHCO_3$ and brine, dried over Na_2SO_4, and removed under reduced pressure. Chromatography (cyclohexane-EtOAc, 19:1) gave **109** (8.5 g, 36%) and **110** (2.1 g, 17%) as two white solids. The NMR spectral data for both substances was in accordance with the previous report[40-41].



Tritriacontane-17-ol (109)



1-Heptadecanol (110)

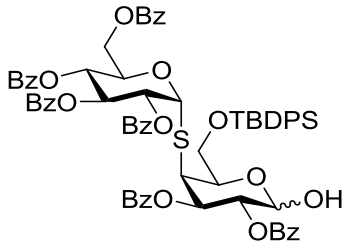


***p*-Methoxyphenyl 2,3-di-*O*-benzoyl-4-*S*-(2,3,4,6-tetra-*O*-benzoyl-α-D-glucopyranosyl)-4-thio-6- tert-butyldiphenylsilyl-β-D-galactopyranoside (111)**

Compound **111**, a new compound, was prepared by glycosylation between **100** and **107** using reagents and conditions reported previously[42].

Compound **100** (1 g, 1.5 mmol) and **107** (5.28 g, 4 equiv.) were dissolved in DMF (66 mL) and the solution was cooled to 0 °C. Diethylamine (3.2 mL, 20 equiv.) were then added and the mixture was stirred at 0 °C for 5 h. It was then washed with water and extracted with EtOAc. The organic phase was dried over Na_2SO_4, filtered and the solvent removed under reduced pressure. Chromatography (cyclohexane-EtOAc, 5:1) gave **111** (1.26 g, 62%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (overlapping signals, 2H, aromatic H), 8.00 (overlapping signals, 6H, aromatic H), 7.89 (overlapping signals, 2H, aromatic H), 7.80 (overlapping signals, 2H, aromatic H), 7.69 (overlapping signals, 5H, aromatic H), 7.44 (overlapping signals, 3H, aromatic H), 7.41 (overlapping signals, 11H, aromatic H), 7.21 (overlapping signals, 5H, aromatic H), 6.81 (overlapping signals, 2H, aromatic H), 6.67 (overlapping signals, 2H, aromatic H), 6.31 (d, *J* = 5.6 Hz, 1H, H-1'), 6.11 (t, *J* = 9.9 Hz, 1H, H-3'), 5.71 (overlapping signals, 2H, H-2, H-4'), 5.60 (dd, *J* = 10.5, 4.7 Hz, 1H, H-3), 5.53 (dd, *J* = 10.3, 5.9 Hz, 1H, H-2'), 4.95 (d, *J* = 7.8 Hz, 1H, H-1), 4.60 (dt, *J* = 10.1, 2.9 Hz, 1H, H-5'), 4.11 (m, 1H, H-4), 4.05 (dd, *J* = 10.7, 7.8 Hz, 1H, H-6a), 3.98 (dd, *J* = 12.6, 2.7 Hz, 1H, H-6'a), 3.88 (dd, *J* = 10.7, 5.7 Hz, 1H, H-6b), 3.76 (t, *J* = 6.9 Hz, 1H, H-5), 3.69 (s, 3H, OCH_3), 3.57 (dd, *J* = 12.7, 3.0 Hz, 1H, H-6'b), 1.07 (s, 9H, Si-C(CH_3)$_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.8 (C=O), 165.6 (C=O), 165.5 (C=O), 165.3 (C=O), 165.2 (C=O), 164.8 (C=O), 155.4 (C), 151.1 (C), 135.6 (C), 135.6 (C), 135.6 (C), 133.7 (C), 133.6 (C), 133.3 (C), 133.2 (C), 133.2 (C), 133.1 (C), 133.0 (CH), 132.7 (CH), 130.1 (CH), 130.0 (CH), 129.9 (CH), 129.9 (CH), 129.9 (CH), 129.7 (CH), 129.7

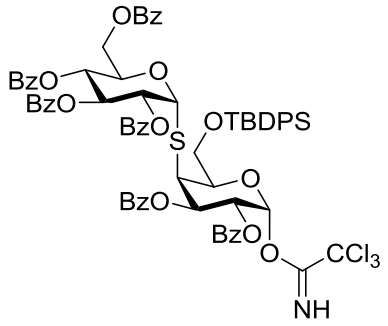
(CH), 129.3 (CH), 129.1 (CH), 128.8 (CH), 128.8 (CH), 128.7 (CH), 128.6 (CH), 128.6 (CH), 128.4 (CH), 128.3 (CH), 128.3 (CH), 128.3 (CH), 128.3 (CH), 127.9 (CH), 127.8 (CH), 118.4 (CH), 114.4 (CH), 101.1 (C-1), 82.3 (C-1'), 74.6 (C-5), 72.7 (C-3), 71.5 (C-2'), 70.8 (C-3'), 70.6 (C-2), 68.7 (C-4'), 68.0 (C-5'), 62.6 (C-6), 61.7 (C-6'), 55.6 (O-CH3), 46.3 (C-4), 26.8 (TBDPS), 19.0 (TBDPS). IR (film) cm^{-1}: 2935, 2858, 1725, 1602, 1507, 1451, 1259, 1178, 1090, 1067, 1026, 825, 801, 743, 703, 687. ESI-HRMS calcd for $C_{77}H_{70}O_{17}SSiNa$ 1349.4001, found *m/z*. 1349.4005 $[M+Na]^+$.



2,3-Di-*O*-benzoyl-4-*S*-(2,3,4,6-tetra-*O*-benzoyl-α-D-glucopyranosyl)-4-thio-6-tert-butyldiphenylsilyl-β-D-galactopyranose (112)

Compound **112**, a new compound, was prepared by deprotection of the *p*-methoxymethanol on **111** using reagents and conditions reported previously [43].

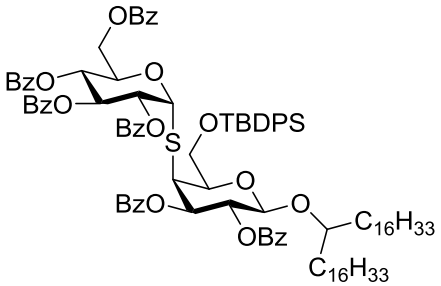
Compound **111** (1.26 g, 0.95 mmol) was dissolved in a mixture of H_2O-CH_3CN (3:17, 20 mL) and ammonium cerium nitrate (2.6 g, 5 equiv.) was added. The mixture was stirred at room temperature for 1 h. The solution was diluted in EtOAc, washed with water, a saturated solution of $NaHCO_3$, dried over Na_2SO_4, filtered and the solvent removed under reduced pressure. Chromatography (cyclohexane-EtOAc, 4:1) gave **112** (0.59 g, 51%) as a white solid. IR (film) cm^{-1}: 3463, 3069, 2933, 2857, 1724, 1655, 1602, 1451, 1315, 1259, 1178, 1089, 1068, 1026, 1001, 824, 704, 686. ESI-HRMS calcd for $C_{70}H_{64}O_{16}SSiNa$ 1243.3582, found *m/z*. 1243.3538 $[M+Na]^+$.



2,3-Di-*O*-benzoyl-4-*S*-(2,3,4,6-tetra-*O*-benzoyl-α-D-glucopyranosyl)-4-thio-6-tert-butyldiphenylsilyl-β-D-galactopyranosyl trichloroacetimidate (113)

Compound **113**, a new compound, was prepared by insertion of the trichloroacetimidate on **112** using reagents and conditions reported previously[44].

Compound **112** (0.59 g, 0.48 mmol) was dissolved in CH_2Cl_2 (15 mL). Cl_3CCN (1 mL, 20 equiv.) and DBU (0.1 mL, 1.2 equiv.) were then added to the solution, which was furtherly stirred at room temperature for 1 h. The solvent was then removed under reduced pressure. Chromatography (cyclohexane-EtOAc, 6:1) gave **113** (0.49 g, 74%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.47 (s, 1H, NH), 8.18 (overlapping signals, 2H, aromatic H), 8.07 (overlapping signals, 2H, aromatic H), 8.02 (overlapping signals, 3H, aromatic H), 8.98 (overlapping signals, 3H, aromatic H), 7.91 (overlapping signals, 2H, aromatic H), 7.79 (overlapping signals, 3H, aromatic H), 7.66 (overlapping signals, 5H, aromatic H), 7.41 (overlapping signals, 31H, aromatic H), 6.63 (d, *J* = 3.8 Hz, 1H, H-1), 6.58 (d, *J* = 5.7 Hz, 1H, H-1'), 6.17 (t, *J* = 9.9 Hz, 1H, H-3'), 6.10 (dd, *J* = 10.9, 4.5 Hz, 1H, H-3), 5.70 (overlapping signals, 2H, H-2, H-4'), 5.60 (m, 1H, H-2'), 4.65 (dt, *J* = 10.1, 3.0 Hz, 1H, H-5'), 4.39 (overlapping signals, 2H, H-4, H-5), 4.04 (m, 1H, H-6'a), 4.00 (m, 1H, H-6a), 3.78 (dd, *J* = 10.6, 5.3 Hz, 1H, H-6b), 3.64 (dd, *J* = 12.6, 3.4 Hz, 1H, H-6'b), 1.04 (s, 9H, Si-C(C*H*$_3$)$_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.8 (C=O), 165.6 (C=O), 165.4 (C=O), 165.4 (C=O), 165.3 (C=O), 164.8 (C=O), 160.5 (*C*=NH), 135.7 (C), 135.6 (C), 133.6 (C), 133.5 (C), 133.4 (C), 133.2 (C), 133.0 (C), 132.9 (CH), 132.6 (CH), 130.0 (CH), 130.0 (CH), 129.9 (CH), 129.8 (CH), 129.8 (CH), 129.7 (CH), 129.7 (CH), 129.1 (CH), 129.0 (CH), 128.9 (CH), 128.8 (CH), 128.7 (CH), 128.7 (CH), 128.6 (CH), 128.4 (CH), 128.3 (CH), 128.3 (CH), 128.3 (CH), 127.9 (CH), 127.8 (CH), 127.7 (CH), 93.5 (C-1), 90.7 (C*C*l$_3$), 81.5 (C-1'), 71.8 (C-5), 71.5 (C-2'), 70.8 (C-3'), 69.4 (C-3), 69.0 (C-2), 68.8 (C-4'), 68.0 (C-5'), 62.0 (C-6), 61.7 (C-6'), 45.9 (C-4), 26.7 (TBDPS), 19.1 (TBDPS). IR (film) cm^{-1}: 2931, 1726, 1452, 1264, 1106, 1093, 1070, 796, 735, 707. ESI-HRMS calcd for $C_{72}H_{64}Cl_3NO_{16}SSiNa$ 1386.2678, found *m/z* 1386.2642 $[M+Na]^+$.

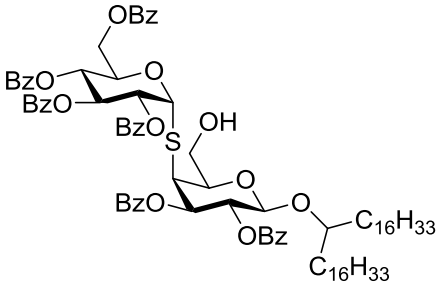


17-Tritriacontyl 2,3-di-*O*-benzoyl-4-*S*-(2,3,4,6-tetra-*O*-benzoyl-α-D-glucopyranosyl)-4-thio-6-tert-butyldiphenylsilyl-β-D-galactopyranoside (114)

Compound **114**, a new compound, was prepared by glycosylation between **113** and **109** using reagents and conditions reported previously[45].

Compound **113** (490 mg, 0.36 mmol) and **109** (345 mg, 2 equiv.) were dissolved in CH_2Cl_2 (18 mL) in a round bottom flask containing molecular sieves 4Å. A 0.1 mol/L solution of TMSOTf in CH_2Cl_2 (0.720 mL, 0.2 equiv.) was then added, and the mixture was stirred at room temperature for 3h. the reaction was quenched with triethylamine, filtered, and the solvent removed under reduced pressure. Chromatography (cyclohexane-EtOAc, 8:1) gave **114** (326 mg, 54%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (overlapping signals, 2H aromatic H), 8.02 (overlapping signals, 2H aromatic H), 7.95 (overlapping signals, 4H aromatic H), 7.85 (overlapping signals, 2H aromatic H), 7.77 (overlapping signals, 2H aromatic H), 7.66 (overlapping signals, 2H aromatic H), 7.60 (overlapping signals, 2H aromatic H), 7.53 (overlapping signals, 3H aromatic H), 7.37 (overlapping signals, 16H aromatic H), 7.25 (overlapping signals, 6H aromatic H), 6.25 (d, *J* = 5.7 Hz, 1H, H-1'), 6.04 (t, *J* = 9.9 Hz, 1H, H-3'), 5.62 (t, *J* = 9.8 Hz, 1H, H-4'), 5.47 (overlapping signals, 3H, H-2', H-2, H-3), 4.56 (dt, *J* = 10.1, 2.9 Hz, 1H, H-5'), 4.44 (d, *J* = 7.4 Hz, 1H, H-1), 4.02 (dd, *J* = 4.5, 1.3 Hz, 1H, H-4), 3.94 (dd, *J* = 10.6, 8.4 Hz, 1H, H-6a), 3.89 (dd, *J* = 12.6, 2.8 Hz, 1H, H-6'a), 3.72 (dd, *J* = 10.6, 5.4 Hz, 1H, H-6b), 3.58 (dd, *J* = 8.1, 6.0 Hz, 1H, H-5), 3.50 (dd, *J* = 12.6, 3.0 Hz, 1H, H-6'b), 3.40 (m, 1H, C*H*-($C_{16}H_{33}$)$_2$), 1.60 (s, 4H, lipid), 1.47 – 1.04 (overlapping signals, 54H, lipid), 1.00 (s, 9H, Si-C(C*H*$_3$)$_3$), 0.89 (m, 6H, lipid). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.8 (C=O), 165.6 (C=O), 165.4 (C=O), 165.3 (C=O), 165.0 (C=O), 164.8 (C=O), 135.6 (C), 135.5 (C), 133.5 (C), 133.4 (C), 133.3 (C), 133.2 (C), 133.0 (C), 133.0 (C), 132.9 (CH), 132.8 (CH), 130.1 (CH), 129.9 (CH), 129.9 (CH), 129.8 (CH), 129.7 (CH), 129.7 (CH), 129.7 (CH), 129.6 (CH), 129.1 (CH), 129.0 (CH), 128.9 (CH), 128.7 (CH), 128.6 (CH), 128.5 (CH), 128.2 (CH), 128.2 (CH), 128.2 (CH), 127.8 (CH), 127.7 (CH), 101.2 (C-1), 82.1 (C-1'), 81.2 (*C*H-($C_{16}H_{33}$)$_2$), 73.9 (C-5), 73.0 (C-3), 71.3 (C-2'), 71.2 (C-2), 70.8 (C-3'), 68.7 (C-4'), 67.8 (C-5'), 62.4 (C-6), 61.7 (C-6'), 46.5 (C-4), 34.6, 33.9, 31.9, 29.8, 29.7, 29.7, 29.6, 29.6, 29.6, 29.6, 29.5, 29.4,

29.4 (all lipid carbons), 26.7 (CH_3, TBDPS), 25.0 (lipid), 24.8 (lipid), 22.7 (lipid), 19.0 (C, TBDPS), 14.1 (lipid). IR (film) cm^{-1}: 3057, 2964, 1697, 1597, 1573, 1528, 1395, 1293, 1260, 1234, 1088, 992, 875, 794, 742, 695. ESI-HRMS calcd for $C_{103}H_{130}O_{16}SSiNa$ 1705.8747, found *m/z* 1705.8724 $[M+Na]^+$.

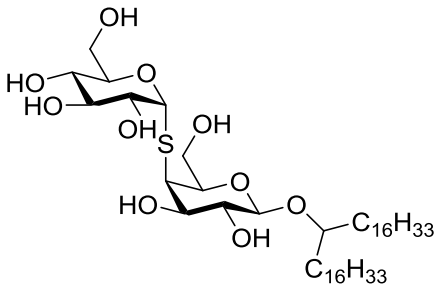


17-Tritriacontyl 2,3-di-*O*-benzoyl-4-*S*-(2,3,4,6-tetra-*O*-benzoyl-α-D-glucopyranosyl)-4-thio-β-D-galactopyranoside (115)

Compound **115**, a new compound, was prepared by deprotection of TBDPS on **114** using reagents and conditions reported previously[37].

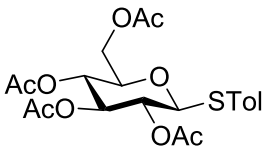
Compound **114** (326 mg, 0.19 mmol) was dissolved in THF (5 mL) and acetic acid (0.05 mL) and the solution was cooled to 0 °C. TBAF (1 mol/L in THF, 0.4 mL, 2 equiv.) was then added and the mixture was stirred at room temperature overnight. The solution was diluted in CH_2Cl_2 and the organic phase was washed with water, a saturated solution of $NaHCO_3$, water and brine, dried over Na_2SO_4, filtered, and the solvent was removed under reduced pressure. Chromatography (cyclohexane-EtOAc, 7:1) gave **115** (218 mg, 78%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (overlapping signals, 4H, aromatic H), 7.96 m, 3H, aromatic H), 7.88 (overlapping signals, 2H, aromatic H), 7.82 (overlapping signals, 2H, aromatic H), 7.52 (overlapping signals, 3H, aromatic H), 7.39 (overlapping signals, 7H, aromatic H), 7.28 (overlapping signals, 5H, aromatic H), 6.01 (overlapping signals, 2H, H-1, H-3), 5.63 (t, *J* = 10.0 Hz, 1H, H-4), 5.50 (overlapping signals, 2H, H-2', H-3'), 5.32 (dd, *J* = 10.5, 6.0 Hz, 1H, H-2), 4.64 (d, *J* = 6.3 Hz, 1H, H-1'), 4.52 (d, *J* = 10.2 Hz, 1H, H-5), 3.90 (overlapping signals, 2H, H-4', H-5'), 3.71 (overlapping signals, 3H, H-6a, H-6'a, H-6'b), 3.48 (overlapping signals, 2H, H-6b, O-C*H*), 1.58 (overlapping signals, 4H, lipid), 1.25 (overlapping signals, 56H, lipid), 0.88 (t, *J* = 6.6 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.7, 165.4, 165.1, 164.9, 164.9, 164.8 (each C=O), 133.7 (C), 133.6 (C), 133.3 (C), 133.1 (C), 132.9 (C), 130.1 (CH), 130.1 (CH), 129.9 (CH), 129.8 (CH), 129.8 (CH), 129.7 (CH), 129.7 (CH), 129.1 (CH), 128.6 (CH), 128.6 (CH), 128.3 (CH), 127.6 (CH), 101.6 (C-1'), 84.2 (C-1), 81.8 (O-*C*H), 74.2 (C-4'), 73.2 (C-3'), 72.2 (C-2), 71.1 (C-2), 70.5 (C-3), 68.4 (C-5), 61.6 (C-6'), 61.6 (C-6), 48.9 (C-5'), 31.9,

29.7, 29.6, 29.4, 22.7, 14.1 (all lipid carbons). IR (film) cm^{-1}: 3366, 2954, 2915, 2850, 1747, 1627, 1470, 1372, 1226, 1091, 1053, 815, 717, 670.



17-Tritriacontyl 4-*S*-(α-D-glucopyranosyl)-4-thio-β-D-galactopyranoside (95)

Compound **115** (218 mg, 0.8 mmol) was reacted as described in the general procedure II.A to give **95** (114 mg, 92%) as a white solid. ^{1}H NMR (500 MHz, CD_3OD) δ 5.33 (d, J = 5.4 Hz, 1H, H-1'), 4.23 (d, J = 7.5 Hz, 1H, H-1), 4.14 (ddd, J = 10.0, 6.0, 2.4 Hz, 1H, H-5'), 3.95 (dd, J = 10.6, 7.8 Hz, 1H, H-6a), 3.84 (dd, J = 11.8, 2.4 Hz, 1H, H-6'a), 3.74 (overlapping signals, 2H, H-3, H-6b), 3.68 (overlapping signals, 3H, H-5, H-2', H-6'b), 3.61 (m, 1H, C*H*-$(C_{16}H_{33})_2$), 3.55 (dd, J = 9.8, 8.8 Hz, 1H, H-3'), 3.38 (dd, J = 4.6, 1.4 Hz, 1H, H-4), 3.26 (overlapping signals, 2H, H-2, H-4'), 1.49 (overlapping signals, 4H, lipid), 1.26 (overlapping signals, 56H, lipid), 0.88 (t, J = 6.9 Hz, 6H, lipid). ^{13}C NMR (126 MHz, CD_3OD) δ 102.9 (C-1), 87.3 (C-1'), 79.3 (*C*H-$(C_{16}H_{33})_2$), 74.2 (C-3'), 74.2 (C-5), 73.3 (C-3), 73.1 (C-5'), 72.8 (C-2), 72.1 (C-2'), 70.4 (C-4'), 61.3 (C-6'), 61.0 (C-6), 51.7 (C-4), 34.4, 33.7, 31.7, 29.6 , 29.4, 29.4, 29.3, 29.1, 24.8, 24.7, 22.4, 13.3 (all lipid carbons). IR (film) cm^{-1}: 3351, 2981, 2915, 2850, 1737.5, 1471, 1462, 1381, 1251, 1152, 1070, 955, 828, 717. ESI-HRMS calcd for $C_{45}H_{88}O_{10}SCl$ 855.5787, found *m/z* 855.5795 $[M+Cl]^-$.

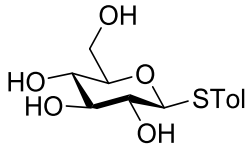


4-Methylphenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (116)

This compound was prepared as previously described[47].

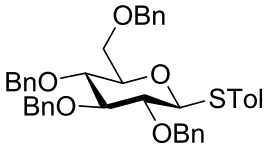
Glucose pentaacetate **2** (15 g, 38 mmol) and *p*-thiocresol (7.16 g, 1.5 equiv.) were dissolved in CH_2Cl_2 (100 mL). $BF_3.Et_2O$ (6.16 mL, 1.3 equiv.) was then added, and the solution was stirred at room temperature overnight. The mixture was diluted with CH_2Cl_2 and the organic phase was washed with a saturated solution of $NaHCO_3$, HCl 1 mol/L and brine, dried over Na_2SO_4, filtered, and the solvent removed under reduced pressure. Chromatography (cyclohexane-

EtOAc, 1:1) gave **116** (14.67 g, 84%). The NMR spectral data was in accordance with the previous report[48].



4-Methylphenyl 1-thio-β-D-glucopyranoside (117)

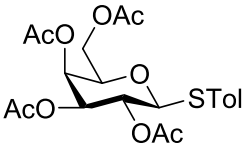
Compound **116** (14.67 g, 32 mmol) was reacted as described in the general procedure II.A to give **117** (8.92 g, 97%) as a white solid. The NMR spectral data was in accordance with the previous report[48].



4-Methylphenyl 2,3,4,6-tetra-*O*-benzyl-1-thio-β-D-glucopyranoside (118)

This compound was prepared as previously described[49].

Compound **117** (8.92 g, 31 mmol) and benzyl bromide (22 mL, 6 equiv.) were dissolved into CH_2Cl_2 (200 mL) and DMF (20 mL) and the solution was cooled to 0 °C. NaH (60% dispersion in mineral oil, 6.2 g, 5eq) was then carefully added, and the mixture was stirred at room temperature overnight. Methanol was then added to quench the reaction, and the organic phase was washed with brine, dried over Na_2SO_4, filtered, and the solvent removed under reduced pressure. Chromatography (cyclohexane-EtOAc, 15:1) gave **118** (14.71 g, 73%) as a white solid. The NMR spectral data was in accordance with the previous report[47].

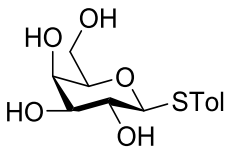


4-Methylphenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranoside (119)

This compound was prepared as previously described[47].

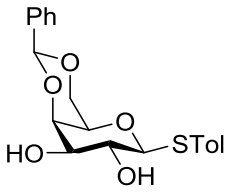
Glucose pentaacetate **2** (15 g, 38 mmol) and *p*-thiocresol (7.2 g, 1.5 equiv.) were dissolved in CH_2Cl_2 (100 mL). $BF_3.Et_2O$ (6.2 mL, 1.3 equiv.) was then added, and the solution was stirred at room temperature overnight. The mixture was diluted with CH_2Cl_2 and the organic phase was washed with a saturated solution of $NaHCO_3$, HCl 1 mol/L and brine, dried over Na_2SO_4, filtered, and the solvent removed under reduced pressure. Chromatography (cyclohexane-

EtOAc, 1:1) gave **119** (15.02 g, 86%). The NMR spectral data was in accordance with the previous report[50].



4-Methylphenyl 1-thio-β-D-galactopyranoside (120)

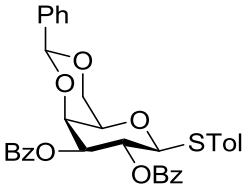
Compound **119** (15.02 g, 32 mmol) was reacted as described in the general procedure II.A to give **120** (9.12 g, 96%) as a white solid. The NMR spectral data was in accordance with the previous report[51].



4-Methylphenyl 4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside (121)

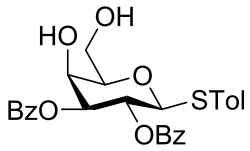
This compound was prepared as previously described[33].

Compound **120** (9.12 g, 32 mmol) was dissolved in CH_3CN (100 mL). Benzaldehyde dimethyl acetal (10 mL, 2.2 equiv.) and camphor sulfonic acid (0.3 g, 5%) were added and the mixture was stirred at 45 °C for 3 h. It was then neutralised with Et_3N and the solvent was evaporated, and the crude product was purified by flash chromatography (CH_2Cl_2-MeOH, 8:2) to give **121** (7.75 g, 65%) as a white solid. The NMR spectral data was in accordance with the previous report[52].



4-Methylphenyl 4,6-*O*-benzylidene-2,3-di-*O*-benzoyl-1-thio-β-D-galactopyranoside (122)

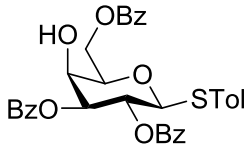
Compound **121** (7.75 g, 21 mmol) was reacted as described in the general procedure II.B using BzCl (10 mL, 4 equiv.). Chromatography (cyclohexane-EtOAc, 1:1) gave **122** (8.8 g, 73%) as a white solid. The NMR spectral data was in accordance with the previous report[53].



4-Methylphenyl 2,3-di-*O*-benzoyl-1-thio-β-D-galactopyranoside (123)

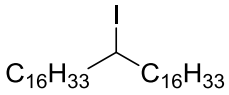
This compound was prepared as previously described[35].

Compound **122** (8.8 g, 15 mmol) was dissolved in CH_2Cl_2 (100 mL) and trifluoroacetic acid (8.6 mL, 7.4 equiv.) and water (1.2 mL, 4.3 equiv.) were subsequently added. The solution was stirred at room temperature for 3 h. It was then diluted with CH_2Cl_2, washed with a saturated solution of $NaHCO_3$, water and brine, dried over Na_2SO_4, filtered and the solvent removed under reduced pressure. Chromatography (cyclohexane-EtOAc, 2:1) gave **123** (6.50 g, 87%) as a white solid. The NMR spectral data was in accordance with the previous report[54].



4-Methylphenyl 2,3,6-tri-*O*-benzoyl-1-thio-β-D-galactopyranoside (124)

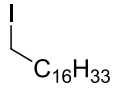
Compound **123** (6.50 g, 13 mmol) was reacted as described in the general procedure II.B using BzCl (1.5 mL, 1 equiv.). Chromatography (cyclohexane-EtOAc, 3:1) gave **124** (5.43 g, 69%) as a white solid. The NMR spectral data was in accordance with the previous report[53].



17-Iodo-tritriacontane (125)

Compound **125**, a new compound, was prepared by iodation of **109** using reagents and conditions reported previously[46].

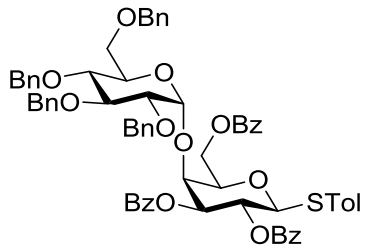
Compound **109** (2 g, 4.2 mmol) was dissolved in THF (50 mL). To this suspension were added imidazole (850 mg, 3 equiv.), triphenylphosphine (3.3 g, 3 equiv.) and iodine (3.2 g, 3 equiv.), and the resulting mixture was stirred at 45 °C overnight. Methanol was then added to the solution, and the solvent was removed under reduced pressure. Chromatography (100 % of cyclohexane) gave **125** (2.11 g, 86%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.12 (tt, J = 8.8, 4.6 Hz, 1H, I-C*H*), 1.85 (overlapping signals, 2H), 1.68 (overlapping signals, 2H), 1.51 (overlapping signals, 2H), 1.26 (overlapping signals, 54H), 0.88 (t, J = 6.8 Hz, 6H).



1-Iodo-heptadecane (126)

This compound was prepared as previously described[46].

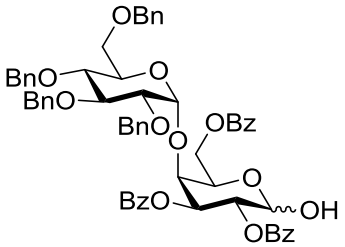
Compound **110** (1 g, 3.9 mmol) was dissolved in THF (50 mL). To this suspension were added imidazole (0.8 g, 3 equiv.), triphenylphosphine (3 g, 3 equiv.) and iodine (3 g, 3 equiv.), and the resulting mixture was stirred at 45 °C overnight. Methanol was then added to the solution, and the solvent was removed under reduced pressure. Chromatography (100 % of cyclohexane) gave **126** (1.13 g, 79%) as a white solid. The NMR spectral data was in accordance with the previous report[55].



4-Methylphenyl 4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-2,3,6-tri-*O*-benzoyl-1-thio-β-D-galactopyranoside (127)

Compound **127**, a new compound, was prepared by glycosylation between **125** and **119**, using reagents and conditions reported previously[48].

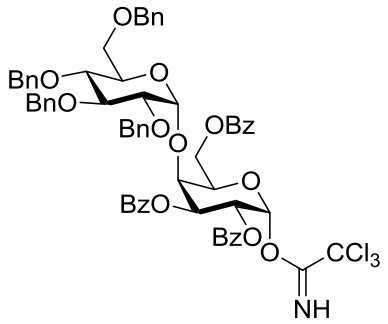
Compound **125** (4.5 g, 7.5 mmol) and **119** (14.6 g, 22 mmol) were dissolved in CH_2Cl_2 (100 mL) in a round bottom flask containing molecular sieves 4Å. This solution was stirred at room temperature for 15 minutes before being cooled to -78 °C. N-iodosuccinimide (1.7 g, 1.25 equiv.) TMSOTf (340 µL, 0.25 equiv.) were then added and the temperature was let to go to room temperature and stirred for 4 h. It was then diluted with CH_2Cl_2 and the organic phase was washed with a saturated solution of $NaHCO_3$, water and brine, dried over Na_2SO_4, filtered and the solvent removed under reduced pressure. Chromatography (cyclohexane-EtOAc, 4:1) gave **127** (4.97 g, 59%). ESI-HRMS calcd for $C_{68}H_{64}O_{13}SNa$ 1143.3965, found *m/z*. 1143.4008 $[M+Na]^+$.



4-*O*-(2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyl)-2,3,6-tri-*O*-benzoyl-1-thio-β-D-galactopyranose (128)

Compound **128**, a new compound, was prepared by removing the anomeric thiotolyl group on **127** using reagents and conditions reported previously[56].

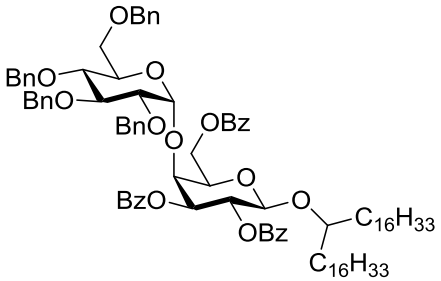
Compound **127** (3.20 g, 2.8 mmol) was dissolved in acetone-H_2O (9:1, 12 mL). *N*-Bromosuccinimide (1.5 g, 3 equiv.) was then added and the solution was stirred at room temperature for 4 h. The mixture was then diluted with EtOAc, and the organic phase was washed with a saturated solution of $NaHCO_3$, water and brine, dried over Na_2SO_4, filtered and the solvent removed under reduced pressure. Chromatography (cyclohexane-EtOAc, 3:1) gave **128** (1.80 g, 62%) as a yellow oil.



4-*O*-(2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyl)-2,3,6-tri-*O*-benzoyl-1-thio-β-D-galactopyranosyl trichloroacetimidate (129)

Compound **129**, a new compound, was prepared by insertion of trichloroacetimidate on **128** using reagents and conditions reported previously[44].

Compound **128** (1 g, 0.98 mmol) was dissolved in CH_2Cl_2 (30 mL). Cl_3CCN (2 mL, 20 equiv.) and DBU (0.2 mL, 1.2 equiv.) were then added to the solution, which was furtherly stirred at room temperature for 1 h. The solvent was then removed under reduced pressure. Chromatography (cyclohexane-EtOAc, 5:1) gave **129** (0.80 g, 70%) as a white solid.

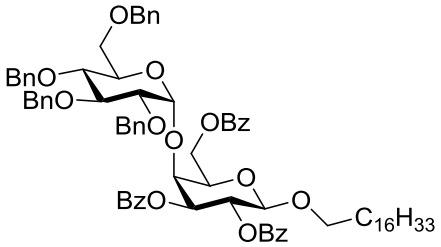


17-Tritriacontyl 4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-2,3,6-tri-*O*-benzoyl-1-thio-β-D-galactopyranoside (130)

Compound **130**, a new compound, was prepared by glycosylation between **129** using reagents and conditions reported previously[45].

Compound **129** (400 mg, 0.34 mmol) and **109** (664 mg, 4 equiv.) were dissolved with CH_2Cl_2 (17 mL) in a round bottom flask containing molecular sieves 4Å, and the solution was cooled to 0 °C. TMSOTf (0.1 mol/L in CH_2Cl_2, 0.9 mL, 0.25 equiv.) was then added, and the mixture was stirred at room temperature for 3 h. Triethylamine was added to quench the reaction. After filtration, the solvent was removed under reduced pressure. Chromatography (cyclohexane-EtOAc, 9:1) gave **130** (219 mg, 43%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (overlapping signals, 2H, aromatic H), 7.94 (overlapping signals, 4H, aromatic H), 7.57 (overlapping signals, 2H, aromatic H), 7.45 (overlapping signals, 6H, aromatic H), 7.34 (overlapping signals, 4H, aromatic H), 7.27 (overlapping signals, 12H, aromatic H), 7.15 (overlapping signals, 5H, aromatic H), 5.69 (t, *J* = 9.3 Hz, 1H, H-2), 5.25 (d, *J* = 10.6 Hz, 1H, H-3), 5.00 (d, *J* = 11.0 Hz, 1H, Bn-C*H*), 4.92 (overlapping signals, 2H, H-1, Bn-C*H*), 4.79 (overlapping signals, 2H, Bn-C*H* x2), 4.71 (overlapping signals, 4H, H-1', H-6a, H-6b, Bn-C*H*), 4.41 (overlapping signals, 2H, H-4, Bn-C*H*), 4.34 (d, *J* = 12.0 Hz, 1H, Bn-C*H*), 4.17 (t, *J* = 9.6 Hz, 1H, H-3'), 4.09 (t, *J* = 11.7 Hz, 1H, H-5'), 4.03 (overlapping signals, 2H, H-5, Bn-C*H*), 3.71 (t, *J* = 9.6 Hz, 1H, H-4'), 3.55 (overlapping signals, 3H, H-2', O-C*H*), 3.34 (d, *J* = 11.0 Hz, 1H, H-6'a), 2.94 (d, *J* = 10.9 Hz, 1H, H-6'b), 1.66 (overlapping signals, 4H, lipid), 1.23 (overlapping signals, 56H, lipid), 0.88 (t, *J* = 7.0 Hz, 6H, lipid). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.4, 166.2, 165.3 (each C=O), 139.0 (C), 138.7 (C), 138.2 (C), 138.0 (C), 133.4 (C), 133.3 (C), 133.1 (C), 130.1 (CH), 130.0 (CH), 129.9 (CH), 129.8 (CH), 129.8 (CH), 129.5 (CH), 129.0 (CH), 128.6 (CH), 128.6 (CH), 128.5 (CH), 128.4 (CH), 128.4 (CH), 128.4 (CH), 128.4 (CH), 128.3 (CH), 128.3 (CH), 128.1 (CH), 128.0 (CH), 127.8 (CH), 127.8 (CH), 127.7 (CH), 127.6 (CH), 127.6 (CH), 127.6 (CH), 127.5 (CH), 127.5 (CH), 101.8 (C-1), 100.6 (C-1'), 82.4 (*C*H-O), 81.8 (C-3'), 79.9 (C-2'), 77.7 (C-4'), 76.2 (C-4), 75.7 (Bn-*C*H_2), 74.9 (Bn-*C*H_2), 74.3 (C-3), 73.9 (Bn-*C*H_2), 73.4 (Bn-*C*H_2), 72.8 (C-5), 71.5 (C-5'), 70.2 (C-2), 67.9 (C-

6'), 63.0 (C-6), 35.1, 34.3, 32.1, 30.0, 29.9, 29.9, 29.8, 29.8, 29.5, 29.5, 25.5, 25.2, 22.8, 14.3 (all lipid carbons). IR (film) cm^{-1}: 2923, 2852, 1725, 1651, 1601, 1452, 1271, 1095, 1070, 1028, 709. ESI-HRMS calcd for $C_{94}H_{128}O_{14}N$ 1494.9335, found *m/z*. 1494.9321 $[M+NH_4]^+$.

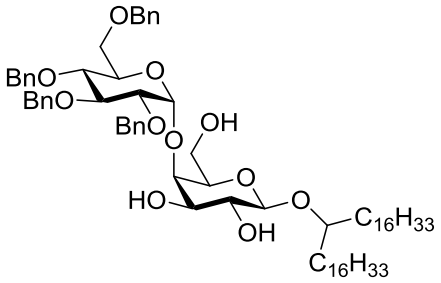


1-Heptadecanyl 4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-2,3,6-tri-*O*-benzoyl-β-D-galactopyranoside (131)

Compound **131**, a new compound, was prepared by glycosylation between **129** and **110** using reagents and conditions reported previously [45].

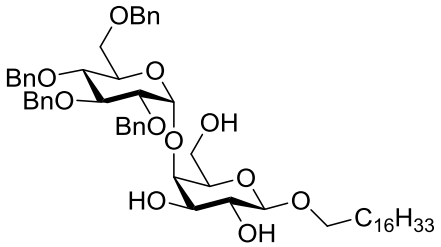
Compound **129** (400 mg, 0.34 mmol) and **110** (0.35 g, 4 equiv.) were dissolved with CH_2Cl_2 (17 mL) in a round bottom flask containing molecular sieves 4Å, and the solution was cooled to 0 °C. TMSOTf (0.1 mol/L in CH_2Cl_2, 0.9 mL, 0.25 equiv.) was then added, and the mixture was stirred at room temperature for 3 h. Triethylamine was added to quench the reaction. After filtration, the solvent was removed under reduced pressure. Chromatography (cyclohexane-EtOAc, 9:1) gave **131** (203 mg, 47%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (overlapping signals, 2H, aromatic H), 7.95 (overlapping signals, 4H, aromatic H), 7.57 (m, 1H, aromatic H), 7.45 (overlapping signals, 5H, aromatic H), 7.35 (overlapping signals, 4H, aromatic H), 7.27 (overlapping signals, 13H, aromatic H), 7.15 (overlapping signals, 6H, aromatic H), 5.70 (dd, *J* = 10.6, 7.7 Hz, 1H, H-2), 5.28 (dd, *J* = 10.6, 3.1 Hz, 1H, H-3), 5.00 (d, *J* = 10.9 Hz, 1H, Bn-C*H*), 4.93 (overlapping signals, 2H, H-1, Bn-C*H*), 4.79 (overlapping signals, 4H, H-6a, H-6b, Bn-C*H* x2), 4.69 (overlapping signals, 2H, H-1', Bn-C*H*), 4.42 (overlapping signals, 2H, H-4, Bn-C*H*), 4.35 (d, *J* = 12.1 Hz, 1H, Bn-C*H*), 4.16 (t, *J* = 9.5 Hz, 1H, H-3'), 4.10 (m, 1H, H-5'), 4.05 (overlapping signals, 2H, H-5, Bn-C*H*), 3.94 (dt, *J* = 9.9, 6.2 Hz, 1H, butyl C*H*(H)O), 3.72 (t, *J* = 9.6 Hz, 1H, H-4'), 3.55 (m, 1H, H-2'), 3.51 (m, 1H, butyl C*H*(H)O), 3.34 (dd, *J* = 11.0, 2.1 Hz, 1H, H-6'a), 2.93 (dd, *J* = 11.0, 2.0 Hz, 1H, H-6'b), 1.53 (m, 2H, lipid), 1.34 (m, 28H, lipid), 0.88 (m, 3H, lipid). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.2, 166.1, 165.3 (each C=O), 138.9 (C), 138.6 (C), 138.0 (C), 137.9 (C), 133.3 (C), 133.2 (C), 133.0 (C), 130.2 (CH), 130.0 (CH), 129.8 (CH), 129.7 (CH), 129.7 (CH), 129.6 (CH), 129.3 (CH), 128.7 (CH), 128.5 (CH), 128.4 (CH), 128.3 (CH), 128.3 (CH), 128.2 (CH), 128.2 (CH), 128.0 (CH), 127.9 (CH), 127.9 (CH), 127.7 (CH), 127.6 (CH), 127.5 (CH), 127.4 (CH), 127.4 (CH), 101.6 (C-1), 100.6 (C-1'), 81.7 (C-3'), 79.7 (C-2'), 77.6 (C-4'), 75.9 (C-4), 75.6

(Bn-*C*H$_2$), 74.7 (Bn-*C*H$_2$), 73.9 (C-3), 73.9 (Bn-*C*H$_2$), 73.3 (Bn-*C*H$_2$), 72.7 (C-5), 71.4 (C-5'), 70.2(*C*H$_2$-O), 69.9 (C-2), 67.7 (C-6'), 62.5 (C-6), 32.8, 31.9, 29.7, 29.7, 29.7, 29.6, 29.6, 29.6, 29.6, 29.5, 29.5, 29.4, 29.4, 29.3, 26.9, 25.8, 25.8, 22.7, 14.1 (all lipid). IR (film) cm^{-1}: ESI-HRMS calcd for $C_{78}H_{96}O_{14}N$ 1270.6831, found *m/z*. 1270.6843 $[M+NH_4]^+$.



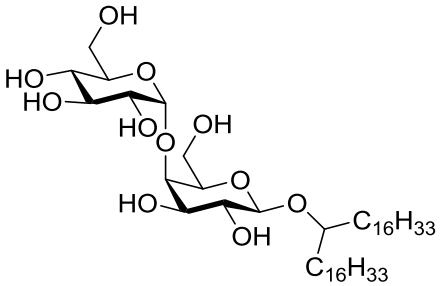
17-Tritriacontyl 4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-β-D-galactopyranoside (132)

Compound **130** (219 mg, 0.15 mmol) was reacted as described in the general procedure II.A to give **132** (163 mg, 94%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (overlapping signals, 18H, aromatic H), 7.18 (overlapping signals, 2H, aromatic H), 4.92 (s, 2H, Bn-C*H* x2), 4.84 (overlapping signals, 2H, Bn-C*H* x2), 4.75 (d, *J* = 3.5 Hz, 1H, H-1'), 4.64 (d, *J* = 12.0 Hz, 1H, Bn-C*H*), 4.56 (d, *J* = 12.0 Hz, 1H, Bn-C*H*), 4.51 (d, *J* = 11.0 Hz, 1H, Bn-C*H*), 4.44 (d, *J* = 11.9 Hz, 1H, Bn-C*H*), 4.20 (d, *J* = 7.2 Hz, 1H, H-1), 4.10 (dd, *J* = 10.4, 5.2 Hz, 1H, H-5'), 4.05 (t, *J* = 9.4 Hz, 1H, H-3'), 3.95 (s, 1H, H-4), 3.80 (dt, *J* = 10.6, 7.4 Hz, 1H, H-6a), 3.70 (overlapping signals, 2H, H-5, H-6b), 3.57 (overlapping signals, 5H, H-2', H-4', H-6'a, H-6'b, O-C*H*), 3.47 (td, *J* = 10.9, 2.9 Hz, 1H, H-3), 3.40 (m, 1H, H-2), 2.18 (s, 1H, OH), 1.55 (overlapping signals, 4H, lipid), 1.26 (overlapping signals, 56H, lipid), 0.89 (t, *J* = 6.8 Hz, 6H, lipid). ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.3 (C), 137.8 (C), 137.6 (C), 136.9 (C), 128.9 (CH), 128.7 (CH), 128.7 (CH), 128.6 (CH), 128.6 (CH), 128.6 (CH), 128.3 (CH), 128.3 (CH), 128.2 (CH), 128.2 (CH), 128.1 (CH), 128.0 (CH), 128.0 (CH), 128.0 (CH), 102.8 (C-1), 100.7 (C-1'), 81.8 (C-3'), 80.9 (C-4), 80.7 (*C*H-O), 79.1 (C-4'), 78.3 (C-2'), 75.9 (Bn-*C*H$_2$), 75.4 (Bn-*C*H$_2$), 74.9 (Bn-*C*H$_2$), 74.1 (C-3), 73.7 (Bn-*C*H$_2$), 73.6 (C-5), 72.7 (C-2), 71.8 (C-5'), 68.6 (C-6'), 60.4 (C-6), 34.9, 34.2, 32.1, 30.0, 29.9, 29.9, 29.8, 29.8, 29.8, 29.8, 29.5, 25.3, 22.8, 14.3 (all lipid carbons). IR (film) cm^{-1}: 3385, 2923, 2853, 1647, 1600, 1496, 1454, 1412, 1360, 1152, 1122, 1032, 1004, 831, 774, 734, 695, 668. ESI-HRMS calcd for $C_{73}H_{112}O_{11}Na$ 1187.8102, found *m/z*. 1187.8090 $[M+Na]^+$.



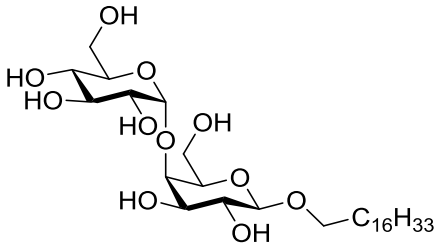
1-Heptadecanyl 4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-β-D-galactopyranoside (133)

Compound **131** (219 mg, 0.15 mmol) was reacted as described in the general procedure II.A to give **133** (143 mg, 94%) as a white solid.



17-Tritriacontyl 4-*O*-(α-D-glucopyranosyl)-β-D-galactopyranoside (134)

Compound **132** (15 mg, 0.013 mmol) was reacted as described in the general procedure II.M. Chromatography (CH_2Cl_2-MeOH, 9:1) gave **134** (9 mg, 87%) as a white solid. ^{1}H NMR (600 MHz, Pyridine-d_5) δ 5.81 (d, J = 3.8 Hz, 1H, H-1'), 4.93 (ddd, J = 10.1, 5.7, 2.5 Hz, 1H, H-5'), 4.86 (d, J = 7.5 Hz, 1H, H-1), 4.75 (d, J = 3.3 Hz, 1H, H-4), 4.70 (t, J = 9.6 Hz, 1H, H-6a), 4.58 (t, J = 9.3 Hz, 1H, H-3'), 4.48 (dd, J = 11.5, 2.5 Hz, 1H, H-6'a), 4.38 (dd, J = 9.9, 7.6 Hz, 1H, H-2), 4.33 (overlapping signals, 2H, H-6b, H-6'b), 4.20 (overlapping signals, 3H, H-3, H-2', H-4'), 4.16 (m, 1H, H-5), 3.98 (m, 1H, O-C*H*), 1.76 (overlapping signals, 4H, lipid), 1.52 (overlapping signals, 2H, lipid), 1.29 (overlapping signals, 54H), 0.88 (t, J = 6.9 Hz, 6H, lipid). ^{13}C NMR (151 MHz, Pyridine-d_5) δ 105.1 (C-1), 103.1 (C-1'), 80.4 (*C*H-O), 80.1 (C-4), 76.0 (C-5), 75.6 (C-3), 75.4 (C-3'), 75.2 (C-5'), 74.6 (C-2'), 73.4 (C-2), 72.5 (C-4'), 62.9 (C-6'), 60.9 (C-6), 35.9, 35.0, 32.5, 30.7, 30.5, 30.4, 30.4, 30.4, 30.3, 30.3, 30.0, 26.1, 25.8, 23.3, 14.7 (all lipid carbons). IR (film) cm^{-1}: 3400, 2955, 2915, 2850, 1470, 1111, 1042, 1024, 992, 793, 718, 660, 668. ESI-HRMS calcd for $C_{45}H_{88}O_{11}Cl$ 839.6015, found *m/z*. 839.6030 $[M+Cl]^-$.



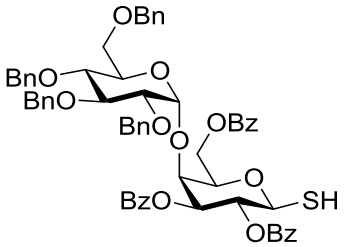
1-Heptadecanyl 4-*O*-(α-D-glucopyranosyl)-β-D-galactopyranoside (135)

Compound **133** (15 mg, 0.016 mmol) was reacted as described in the general procedure II.M. Chromatography (CH_2Cl_2-MeOH, 9:1) gave **135** (8 mg, 85%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.98 (d, *J* = 3.8 Hz, 1H, H-1'), 4.28 (d, *J* = 7.4 Hz, 1H, H-1), 4.03 (overlapping signals, 2H, H-4, H-4'), 3.86 (overlapping signals, 3H, H-6a, H6'a, O-C*H*-lipid), 3.76 (dd, *J* = 11.1, 5.7 Hz, 1H, H-6b), 3.70 (overlapping signals, 2H, H-3', H-6'b), 3.64 (m, 1H, H-5), 3.56 (overlapping signals, 2H, H-3, O-C*H*-lipid), 3.50 (dd, *J* = 10.1, 7.4 Hz, 1H, H-2), 3.46 (dd, *J* = 9.8, 3.7 Hz, 1H, H-2'), 3.30 (dd, *J* = 10.0, 9.0 Hz, 1H, H-5'), 1.64 (overlapping signals, 2H, lipid), 1.27 (s, 28H, lipid), 0.90 (m, 3H, lipid). ^{13}C NMR (126 MHz, $CDCl_3$) δ 104.2 (C-1), 101.5 (C-1'), 78.9 (C-4), 74.8 (C-5), 74.1 (C-3), 74.0 (C-3'), 73.5 (C-4'), 73.1 (C-2'), 72.1 (C-2), 71.2 (C-5'), 71.0 (O-*C*H_2-lipid), 62.2 (C-6'), 60.1 (C-6), 32.4, 30.2, 30.1, 29.9, 26.4, 23.2, 14.3 (all lipid carbons). IR (film) cm^{-1}: 3358, 2915, 2850, 1653, 1471, 1376, 1262, 1099, 1047, 1020, 794, 717. ESI-HRMS calcd for $C_{29}H_{56}O_{11}Cl$ 615.3511, found *m/z*. 615.3499 $[M+Cl]^-$. ESI-HRMS calcd for $C_{29}H_{56}O_{11}Na$ 603.3720, found *m/z*. 603.3743 $[M+Na]^+$.

- **Preparation of 136 and 137**

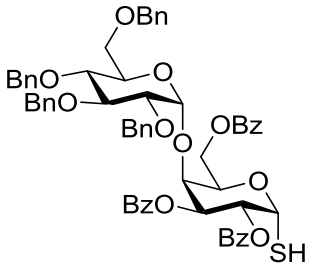
Compounds **136** and **137**, new compounds, were prepared by formation of glycosyl thiol of **128** using reagents and conditions reported previously [57].

Compound **128** (700 mg, 0.69 mmol) was dissolved in dioxane (17 mL). Lawesson's reagent (0.4 g, 1.5 equiv.) was then added, and the mixture was stirred at 100 °C overnight. The solvent was then removed under reduced pressure. Chromatography (cyclohexane-EtOAc, 7:2) gave **136** (274 mg, 38%) and **137** (96 mg, 14%).



4-*O*-(2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyl)-2,3,6-tri-*O*-benzoyl-1-thio-β-D-galactopyranose (136)

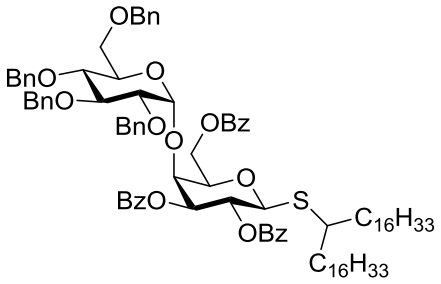
136: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (overlapping signals, 3H, aromatic H), 8.97 (overlapping signals, 5H, aromatic H), 7.60 (overlapping signals, 16H, aromatic H), 7.49 (overlapping signals, 6H, aromatic H), 7.27 (overlapping signals, 28H, aromatic H), 5.68 (t, *J* = 9.9 Hz, 1H, H-2), 5.32 (dd, *J* = 10.3, 2.9 Hz, 1H, H-3), 5.03 (d, *J* = 11.0 Hz, 1H, Bn-C*H*), 4.97 (overlapping signals, 2H, H-1', Bn-C*H*), 4.83 (overlapping signals, 2H, Bn-C*H* x2), 4.78 (overlapping signals, 2H, H-1, H6a), 4.71 (overlapping signals, 2H, H-6b, Bn-C*H*), 4.47 (d, *J* = 3.4 Hz, 1H, H-4), 4.41 (overlapping signals, 2H, Bn-C*H* x2), 4.16 (t, *J* = 9.6 Hz, 1H, H-3'), 4.10 (overlapping signals, 3H, H-5, H-5', Bn-C*H*), 3.76 (t, *J* = 9.5 Hz, 1H, H-4'), 3.57 (dd, *J* = 9.9, 3.5 Hz, 1H, H-2'), 3.43 (dd, *J* = 11.0, 2.1 Hz, 1H, H-6'a), 3.04 (dd, *J* = 11.0, 2.1 Hz, 1H, H-6'b), 2.51 (d, *J* = 14.5 Hz, 1H, S*H*). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.1 (C=O), 166.1 (C=O), 165.5 (C=O), 138.8 (C), 138.5 (C), 137.9 (C), 137.9 (C), 133.4 (C), 133.3 (C), 133.2 (C), 130.0 (CH), 129.8 (CH), 129.7 (CH), 129.7 (CH), 129.3 (CH), 129.2 (CH), 128.5 (CH), 128.5 (CH), 128.4 (CH), 128.4 (CH), 128.3 (CH), 128.1 (CH), 127.9 (CH), 127.8 (CH), 127.7 (CH), 127.6 (CH), 127.5 (CH), 127.5 (CH), 100.5 (C-1'), 81.7 (C-3'), 79.8 (C-2'), 79.4 (C-1), 77.6 (C-4'), 77.3 (C-5), 76.2 (C-4), 75.6 (Bn-*C*H_2), 74.9 (Bn-*C*H_2), 74.7 (C-3), 74.0 (Bn-*C*H_2), 73.4 (Bn-*C*H_2), 72.1 (C-2), 71.5 (C-5'), 67.8 (C-6'), 62.9 (C-6). ESI-HRMS calcd for $C_{61}H_{58}O_{13}SNa$ 1053.3496, found *m/z*. 1053.3496 $[M+Na]^+$.



4-*O*-(2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyl)-2,3,6-tri-*O*-benzoyl-1-thio-α-D-galactopyranose (137)

137: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (overlapping signals, 3H, aromatic H), 8.95 (overlapping signals, 5H, aromatic H), 7.59 (m, 1H, aromatic H), 7.48 (overlapping signals, 5H, aromatic H), 7.19 (overlapping signals, 28H, aromatic H), 6.22 (t, *J* = 5.3 Hz, 1H, H-1),

5.79 (dd, *J* = 10.8, 5.5 Hz, 1H, H-2), 5.61 (dd, *J* = 10.8, 3.0 Hz, 1H, H-3), 5.02 (m, 1H, Bn-C*H*), 4.93 (overlapping signals, 2H, Bn-C*H*, H-1'), 4.73 (overlapping signals, 6H, Bn-C*H* x3, H5, H6a, H6b), 4.47 (d, *J* = 3.1 Hz, 1H, H-4), 4.39 (overlapping signals, 2H, Bn-C*H* x2), 4.10 (overlapping signals, 3H, H-3', H-5', Bn-C*H*), 3.70 (t, *J* = 9.5 Hz, 1H, H-4'), 3.55 (dd, *J* = 9.9, 3.4 Hz, 1H, H-2'), 3.28 (dd, *J* = 11.0, 2.5 Hz, 1H, H-6'a), 2.91 (dd, *J* = 11.0, 2.0 Hz, 1H, H-6'b), 1.88 (d, *J* = 4.9 Hz, 1H, S*H*). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.0 (C=O), 166.0 (C=O), 165.3 (C=O), 138.8 (C), 138.3 (C), 137.8 (C), 137.7 (C), 133.4 (C), 133.4 (C), 133.2 (C), 129.9 (CH), 129.8 (CH), 129.8 (CH), 129.7 (CH), 129.3 (CH), 129.0 (CH), 128.5 (CH), 128.4 (CH), 128.4 (CH), 128.4 (CH), 128.4 (CH), 128.2 (CH), 128.2 (CH), 128.2 (CH), 128.1 (CH), 127.9 (CH), 127.9 (CH), 127.9 (CH), 127.9 (CH), 127.8 (CH), 127.8 (CH), 127.7 (CH), 127.7 (CH), 127.7 (CH), 127.6 (CH), 127.5 (CH), 127.5 (CH), 127.3 (CH) (aromatic carbons), 100.1 (C-1'), 81.8 (C-3'), 79.6 (C-2'), 78.2 (C-1), 77.6 (C-4'), 76.0 (C-4), 75.6 (Bn-*C*H_2), 74.9 (Bn-*C*H_2), 74.2 (Bn-*C*H_2), 73.4 (Bn-*C*H_2), 71.3 (C-5'), 70.5 (C-3), 69.6 (C-5), 68.4 (C-2), 67.7 (C-6'), 62.5 (C-6). ESI-HRMS calcd for $C_{61}H_{58}O_{13}SNa$ 1053.3496, found *m/z*. 1053.3503 $[M+Na]^+$.

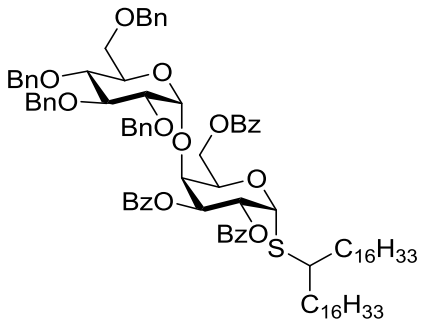


17-Tritriacontyl 4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-2,3,6-tri-*O*-benzoyl-1-thio-β-D-galactopyranoside (138)

Compound **138**, a new compound, was prepared by nucleophile substitution of **136** and **116** using reagents and conditions reported previously[1].

Compound **136** (100 mg, 0.27 mmol) was dissolved in DMF (5 mL) and cooled to 0 °C. NaH (5 mg, 1.2 equiv.) was then added and the reaction was stirred for 5 min, and a solution of **116** (115 mg, 2 equiv.) in DMF (5 mL) was then added. The mixture was stirred at room temperature for 3 h. It was then diluted with Et_2O, and the organic phase was washed with water and brine, dried over Na_2SO_4, filtered and the solvent removed under reduced pressure. Chromatography (cyclohexane-EtOAc, 15:1) gave **138** (88 mg, 61%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (overlapping signals, 2H, aromatic H), 7.93 (overlapping signals, 5H, aromatic H), 7.57 (overlapping signals, 2H, aromatic H), 7.45 (overlapping signals, 6H, aromatic H), 7.29 (overlapping signals, 26H, aromatic H), 7.15 (overlapping signals, 8H,

aromatic H), 5.70 (t, *J* = 10.0 Hz, 1H, H-2), 5.32 (dd, *J* = 10.2, 3.0 Hz, 1H, H-3), 5.00 (d, *J* = 10.9 Hz, 1H, Bn-C*H*), 4.92 (d, *J* = 11.0 Hz, 1H, Bn-C*H*), 4.89 (d, *J* = 3.5 Hz, 1H, H-1'), 4.81 (overlapping signals, 2H, Bn-C*H* x2), 4.76 (m, 1H, H-1), 4.73 (overlapping signals, 2H, H-6a, H-6b), 4.69 (t, *J* = 11.7 Hz, 1H, Bn-C*H*), 4.44 (overlapping signals, 2H, H-4, Bn-C*H*), 4.37 (d, *J* = 12.1 Hz, 1H, Bn-C*H*), 4.14 (t, *J* = 9.5 Hz, 1H, H-3'), 4.08 (overlapping signals, 3H, H-5, H-5', Bn-C*H*), 3.73 (t, *J* = 9.6 Hz, 1H, H-4'), 3.53 (m, 1H, H-2'), 3.39 (dd, *J* = 11.1, 2.1 Hz, 1H, H-6'a), 3.01 (dd, *J* = 11.1, 1.9 Hz, 1H, H-6'b), 2.85 (m, 1H, S-C*H* lipid), 1.53 (overlapping signals, 7H, lipid), 1.20 (overlapping signals, 72H, lipid), 0.88 (t, *J* = 6.8 Hz, 6H, lipid). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.1 (C=O), 165.0 (C=O), 164.2 (C=O), 137.8 (C), 137.6 (C), 137.0 (C), 136.9 (C), 132.2 (C), 132.1 (C), 132.0 (C), 129.2 (CH), 129.0 (CH), 128.8 (CH), 128.7 (CH), 128.6 (CH), 128.6 (CH), 128.3 (CH), 127.6 (CH), 127.4 (CH), 127.4 (CH), 127.3 (CH), 127.3 (CH), 127.3 (CH), 127.2 (CH), 127.2 (CH), 127.1 (CH), 127.0 (CH), 126.9 (CH), 126.9 (CH), 126.9 (CH), 126.7 (CH), 126.6 (CH), 126.6 (CH), 126.6 (CH), 126.5 (CH), 126.4 (CH), 126.4 (CH), 126.3 (CH), 99.5 (C-1'), 83.3 (C-1), 80.7 (C-3'), 78.7 (C-2'), 76.5 (C-4'), 75.6 (C-5), 75.3 (C-4), 74.6 (Bn-*C*H_2), 74.2 (C-3), 73.7 (Bn-*C*H_2), 72.8 (Bn-*C*H_2), 72.3 (Bn-*C*H_2), 70.5 (C-5'), 67.6 (C-2), 66.8 (C-6'), 62.1 (C-6), 45.8 (*C*H-S), 34.3, 34.2, 30.9, 28.7, 28.7, 28.6, 28.6, 28.6, 28.6, 28.6, 28.5, 28.5, 28.5, 28.3, 25.8, 25.3, 21.7, 13.1 (all lipid carbons). ESI-HRMS calcd for $C_{94}H_{124}O_{13}SNa$ 1515.8660, found *m/z*. 1515.8699 $[M+Na]^+$.

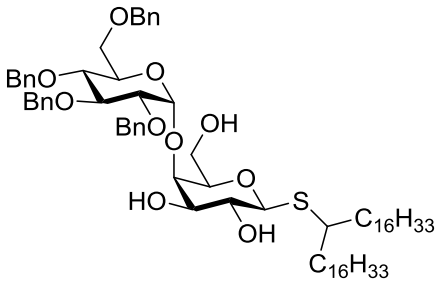


17-Tritriacontyl 4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-2,3,6-tri-*O*-benzoyl-1-thio-α-D-galactopyranoside (139)

Compound **139**, a new compound, was prepared by nucleophile substitution of **137** and **116** using reagents and conditions reported previously[1].

Compound **137** (100 mg, 0.27 mmol) was dissolved in DMF (5 mL) and cooled to 0 °C. NaH (5 mg, 1.2 equiv.) was then added and the reaction was stirred for 5 min, and a solution of **116** (115 mg, 2 equiv.) in DMF (5 mL) was then added. The mixture was stirred at room temperature for 3 h. It was then diluted with Et_2O, and the organic phase was washed with water and brine, dried over Na_2SO_4, filtered and the solvent removed under reduced pressure.

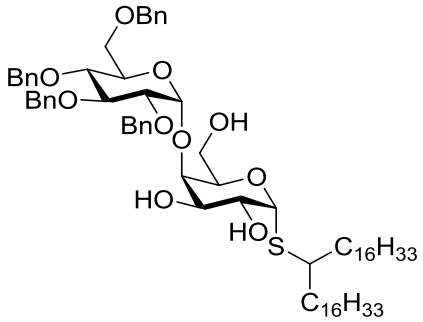
Chromatography (cyclohexane-EtOAc, 15:1) gave **139** (88 mg, 61%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (overlapping signals, 2H, aromatic H), 7.95 (overlapping signals, 4H, aromatic H), 7.57 (m, 1H, aromatic H), 7.46 (overlapping signals, 5H, aromatic H), 7.31 (overlapping signals, 19H, aromatic H), 7.20 (overlapping signals, 5H, aromatic H), 7.11 (overlapping signals, 6H, aromatic H), 5.96 (d, *J* = 5.7 Hz, 1H, H-1), 5.75 (dd, *J* = 11.0, 5.7 Hz, 1H, H-2), 5.56 (dd, *J* = 11.0, 2.9 Hz, 1H, H-3), 5.03 (d, *J* = 11.0 Hz, 1H, Bn-C*H*), 4.92 (d, *J* = 10.9 Hz, 1H, Bn-C*H*), 4.89 (d, *J* = 3.2 Hz, 1H, H-1'), 4.80 (overlapping signals, 2H, Bn-C*H* x2), 4.70 (overlapping signals, 4H, H-5, H-6a, H-6b, Bn-C*H*), 4.46 (d, *J* = 3.0 Hz, 1H, H-4), 4.37 (overlapping signals, 2H, Bn-C*H* x2), 4.12 (t, *J* = 9.5 Hz, 1H, H-3'), 4.05 (overlapping signals, 2H, H-5', Bn-C*H*), 3.69 (t, *J* = 9.7 Hz, 1H, C-4'), 3.54 (dd, *J* = 9.6, 3.4 Hz, 1H, C-2'), 3.22 (dd, *J* = 11.0, 2.3 Hz, 1H, H-6'a), 2.83 (d, *J* = 10.8 Hz, 1H, H-6'b), 2.73 (m, 1H, S-C*H* lipid), 1.46 (overlapping signals, 4H, lipid), 1.36 – 1.03 (overlapping signals, 56H, lipid), 0.88 (t, *J* = 6.7 Hz, 6H, lipid). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.0 (C=O), 165.9 (C=O), 165.6 (C=O), 138.9 (C), 138.4 (C), 137.8 (C), 137.7 (C), 133.2 (C), 133.2 (C), 133.1 (C), 129.9 (CH), 129.8 (CH), 129.8 (CH), 129.8 (CH), 129.7 (CH), 129.6 (CH), 129.4 (CH), 128.5 (CH), 128.4 (CH), 128.4 (CH), 128.4 (CH), 128.4 (CH), 128.3 (CH), 128.3 (CH), 128.3 (CH), 128.3 (CH), 128.2 (CH), 128.0 (CH), 127.9 (CH), 127.9 (CH), 127.9 (CH), 127.8 (CH), 127.8 (CH), 127.8 (CH), 127.7 (CH), 127.6 (CH), 127.5 (CH), 100.2 (C-1'), 81.9 (C-1), 81.8 (C-3'), 79.5 (C-2'), 77.6 (C-4'), 76.4 (C-4), 75.6 (Bn-*C*H$_2$), 74.9 (Bn-*C*H$_2$), 74.2 (Bn-*C*H$_2$), 73.3 (Bn-*C*H$_2$), 71.3 (C-3), 71.2 (C-5'), 69.0 (C-2), 69.0 (C-5), 67.7 (C-6'), 62.8 (C-6), 45.2 (*C*H-S), 35.8, 35.1, 34.6, 31.9, 29.7, 29.7, 29.7, 29.6, 29.6, 29.6, 29.5, 29.4, 27.1, 26.4, 22.7, 14.1 (all lipid carbons). ESI-HRMS calcd for $C_{94}H_{124}O_{13}SNa$ 1515.8660, found *m/z*. 1515.8619 $[M+Na]^+$.



17-Tritriacontyl 4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-1-thio-β-D-galactopyranoside (140)

Compound **138** (88 mg, 4.87 mmol) was reacted as described in the general procedure II.A to give **140** (66 mg, 94%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (overlapping signals, 20H, aromatic H), 7.18 (overlapping signals, 2H, aromatic H), 4.89 (s, 2H, Bn-C*H* x2), 4.84 (overlapping signals, 2H, Bn-C*H* x2), 4.75 (d, *J* = 3.6 Hz, 1H, H-1'), 4.63 (d, *J* = 11.9 Hz,

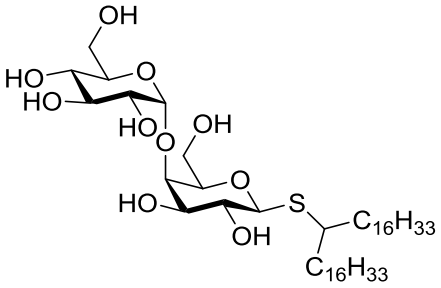
1H, Bn-C*H*), 4.53 (d, *J* = 11.9 Hz, 1H, Bn-C*H*), 4.48 (dd, *J* = 18.3, 12.0 Hz, 1H, Bn-C*H*), 4.43 (d, *J* = 12.0 Hz, 1H, Bn-C*H*), 4.28 (d, *J* = 8.9 Hz, 1H, H-1), 4.05 (overlapping signals, 2H, H-3', H-4'), 4.00 (m, 1H, H-4), 3.78 (dd, *J* = 9.3, 5.3 Hz, 1H, H-6'a), 3.66 (overlapping signals, 3H, H-5, H-6a, H-6'b), 3.55 (overlapping signals, 2H, H-2', H-6b), 3.46 (overlapping signals, 3H, H-2, H-3, H-5'), 2.85 (m, 1H, S-C*H*), 1.60 (overlapping signals, 4H, lipid), 1.47 – 1.14 (overlapping signals, 56H, lipid), 0.88 (t, *J* = 6.8 Hz, 6H, lipid). ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.2 (C), 137.8 (C), 137.5 (C), 136.8 (C), 128.8 (CH), 128.7 (CH), 128.6 (CH), 128.5 (CH), 128.5 (CH), 128.5 (CH), 128.4 (CH), 128.2 (CH), 128.1 (CH), 128.1 (CH), 128.0 (CH), 127.9 (CH), 127.9 (CH), 127.8 (CH), 127.8 (CH), 127.8 (CH), 127.7 (CH), 100.5 (C-1'), 86.4 (C-1), 81.8 (C-4'), 80.9 (C-4), 78.9 (C-2'), 78.1 (C-5'), 77.4 (C-5), 75.9 (Bn-*C*H_2), 75.2 (C-2), 75.1 (Bn-*C*H_2), 74.8 (Bn-*C*H_2), 73.6 (Bn-*C*H_2), 71.8 (C-3'), 71.3 (C-3), 68.5 (C-6), 60.3 (C-6'), 46.6 (*C*H-S), 35.3, 35.1, 31.9, 29.7, 29.6, 29.4, 26.6, 26.5, 22.7, 20.1, 14.1 (all lipid carbons). IR (film) cm^{-1}: 3457, 3017, 2971, 2918, 1455, 1366, 1229, 1217, 1092, 1019, 796.



17-Tritriacontyl 4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-1-thio-α-D-galactopyranoside (141)

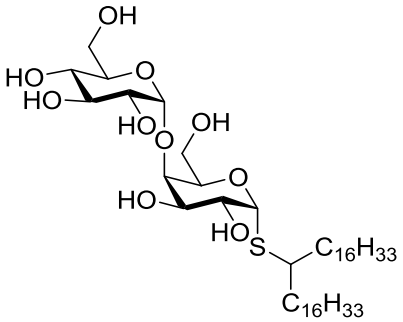
Compound **139** (88 mg, 4.87 mmol) was reacted as described in the general procedure II.A to give **141** (67 mg, 95%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (overlapping signals, 18H, aromatic H), 7.16 (d, *J* = 6.8 Hz, 2H, aromatic H), 5.42 (d, *J* = 5.4 Hz, 1H, H-1), 4.89 (overlapping signals, 2H, Bn-C*H* x2), 4.84 (overlapping signals, 2H, Bn-C*H* x2), 4.69 (d, *J* = 3.6 Hz, 1H, H-1'), 4.63 (d, *J* = 12.0 Hz, 1H, Bn-C*H*), 4.54 (d, *J* = 11.9 Hz, 1H, Bn-C*H*), 4.48 (d, *J* = 10.7 Hz, 1H, Bn-C*H*), 4.43 (d, *J* = 11.8 Hz, 1H, Bn-C*H*), 4.29 (t, *J* = 5.6 Hz, 1H, H-5), 4.03 (overlapping signals, 2H, H-3', H-5'), 3.96 (s, 1H, H-4), 3.91 (m, 1H, H-2), 3.78 (m, 1H, H-6a), 3.69 (m, 1H, H-6b), 3.63 (t, *J* = 10.3 Hz, 1H, H-6'a), 3.52 (overlapping signals, 4H, H-3, H-2', H-4', H-6'b), 2.72 (p, *J* = 6.5 Hz, 1H, S-C*H*), 2.13 (d, *J* = 6.0 Hz, 1H, OH), 1.58 (overlapping signals, 4H, lipid), 1.26 (overlapping signals, 56H, lipid), 0.88 (t, *J* = 6.8 Hz, 6H, lipid). ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.8 (C), 137.4 (C), 137.1 (C), 136.5 (C), 128.5 (CH), 128.3 (CH), 128.2 (CH), 128.2 (CH), 128.2 (CH), 128.1 (CH), 127.7 (CH), 127.7 (CH),

127.6 (CH), 127.6 (CH), 127.5 (CH), 127.5 (CH), 100.2 (C-1'), 85.7 (C-1), 82.4 (C-4), 81.5 (C-3'), 78.7 (C-2'), 77.7 (C-4'), 75.6 (Bn-*C*H$_2$), 74.8 (Bn-*C*H$_2$), 74.4 (Bn-*C*H$_2$), 73.3 (Bn-*C*H$_2$), 71.5 (C-3), 71.5 (C-5'), 69.7 (C-5), 69.4 (C-2), 68.2 (C-6'), 60.8 (C-6), 46.2 (*C*H-S), 35.2, 34.6, 31.6, 29.4, 29.4, 29.3, 29.3, 29.3, 29.0, 26.5, 26.4, 22.4, 13.8 (all lipid carbons). IR (film) cm^{-1}: 3450, 3033, 2922, 2852, 1720, 1455, 1066, 732, 969. ESI-HRMS calcd for $C_{73}H_{112}O_{10}SNa$ 1203.7874, found *m/z*. 1203.7833 $[M+Na]^+$.



17-Tritriacontyl 4-*O*-(α-D-glucopyranosyl)-1-thio-β-D-galactopyranoside (142)

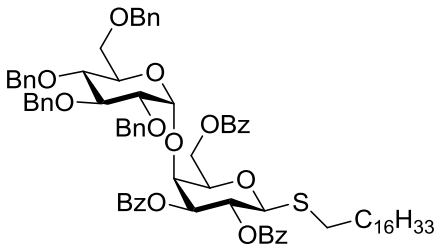
Compound **140** (20 mg, 0.017 mmol) was reacted as described in the general procedure II.M. Chromatography (CH_2Cl_2-MeOH 9:1) gave **142** (11 mg, 84%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$-CD_3OD, 1:1) δ 4.97 (d, *J* = 3.8 Hz, 1H, H-1'), 4.40 (d, *J* = 9.5 Hz, 1H, H-1), 4.08 (d, *J* = 2.9 Hz, 1H, H-4), 4.01 (ddd, *J* = 9.8, 6.6, 2.5 Hz, 1H, H-5'), 3.90 (m, 1H, H-6'a), 3.83 (dd, *J* = 11.0, 8.4 Hz, 1H, H-6a), 3.69 (overlapping signals, 4H, H-5, H-6b, H-3', H-6'b), 3.55 (dd, *J* = 9.6, 2.8 Hz, 1H, H-3), 3.47 (overlapping signals, 2H, H-2, H-2'), 3.29 (t, *J* = 9.5 Hz, 1H, H-4), 2.90 (m, 1H, S-C*H*), 1.62 (overlapping signals, 4H, lipid), 1.42 (overlapping signals, 4H, lipid), 1.27 (overlapping signals, 52H, lipid), 0.89 (t, *J* = 6.8 Hz, 6H, lipid). ^{13}C NMR (126 MHz, $CDCl_3$-CD_3OD, 1:1) δ 101.5 (C-1'), 86.8 (C-1), 79.2 (C-4), 78.2 (C-5), 75.2 (C-3), 73.9 (C-3'), 73.3 (C-5'), 72.9 (C-2), 71.1 (C-2'), 71.0 (C-4), 62.2 (C-6'), 59.8 (C-6), 46.7 (S-*C*H), 35.3, 35.3, 32.3, 30.0, 29.9, 29.7, 26.8, 23.0, 14.2 (all lipid carbons). IR (film) cm^{-1}: 3338, 2916, 2850, 1470, 1260, 1018, 797, 717. ESI-HRMS calcd for $C_{45}H_{87}O_{10}S$ 819.6020, found *m/z*. 819.6049 $[M-H]^-$.



17-Tritriacontyl 4-*O*-(α-D-glucopyranosyl)-1-thio-β-D-galactopyranoside (143)

Compound **141** (20 mg, 0.017 mmol) was reacted as described in the general procedure II.M. Chromatography (CH_2Cl_2-MeOH 9:1) gave **143** (12 mg, 87%) as a white solid.

143 was also synthesized from **148** (13 mg, 0.013 mmol) subjecting it to general procedure II.M. Chromatography (CH_2Cl_2-MeOH 9:1) gave **143** (9 mg, 85%). ^{1}H NMR (500 MHz, $CDCl_3$-CD_3OD 1:1) δ 5.41 (d, J = 5.4 Hz, 1H, H-1), 4.98 (d, J = 3.7 Hz, 1H, H-1'), 4.32 (dd, J = 8.0, 5.2 Hz, 1H, H-5), 4.09 (m, 1H, H-4), 4.04 (dd, J = 10.5, 5.4 Hz, 1H, H-2), 3.93 (dd, J = 10.0, 2.7 Hz, 1H, H-5'), 3.90 (d, J = 11.0 Hz, 1H, H-6'a), 3.86 (dd, J = 12.1, 8.8 Hz, 1H, H-6a), 3.68 (overlapping signals, 4H, H-3, H-3', H-6b, H-6'b), 3.50 (dd, J = 9.8, 3.8 Hz, 1H, H-2'), 3.29 (t, J = 9.5 Hz, 1H, H-4'), 2.76 (p, J = 6.5 Hz, 1H, CH-lipid), 1.61 (overlapping signals, 4H, lipid), 1.44 (overlapping signals, 9H), 1.29 (overlapping signals, 60H, lipid), 0.89 (t, J = 6.8 Hz, 7H). ^{13}C NMR (126 MHz, $CDCl_3$-CD_3OD 1:1) δ 102.0 (C-1'), 86.5 (C-1), 81.7 (C-4), 74.0 (C-5'), 74.0 (C-3'), 72.8 (C-2'), 71.8 (C-3), 71.1 (C-4'), 70.8 (C-5), 69.6 (C-2), 62.3 (C-6'), 60.7 (C-6), 46.2 (*C*H-lipid), 35.9, 35.3, 32.4, 30.2, 30.1, 30.1, 30.1, 29.8, 27.2, 23.1, 14.3 (all lipid carbons). IR (film) cm^{-1}: 3385, 2913, 2849, 1471, 1260, 1081, 1019, 799, 716. ESI-HRMS calcd for $C_{45}H_{87}O_{10}S$ 819.6020, found *m/z*. 819.6038 $[M-H]^-$.

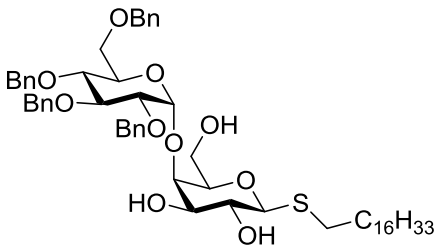


1-Heptadecanyl 4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-2,3,6-tri-*O*-benzoyl-1-thio-β-D-galactopyranoside (144)

Compound **144**, a new compound, was prepared by nucleophile substitution of **136** and **126** using reagents and conditions reported previously[1].

Compound **136** (100 mg, 0.27 mmol) was dissolved in DMF (5 mL) and cooled to 0 °C. NaH (5 mg, 1.2 equiv.) was then added and the reaction was stirred for 5 min, and a solution of **126**

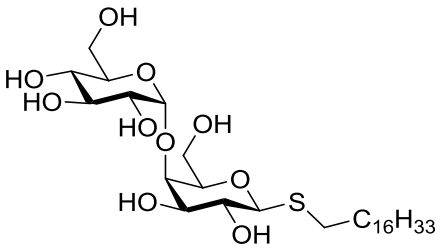
(71 mg, 2 equiv.) in DMF (5 mL) was then added. The mixture was stirred at room temperature for 3 h. It was then diluted with Et_2O, and the organic phase was washed with water and brine, dried over Na_2SO_4, filtered and the solvent removed under reduced pressure. Chromatography (cyclohexane-EtOAc, 14:1) gave **144** (53 mg, 43%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (overlapping signals, 2H, aromatic H), 7.94 (overlapping signals, 4H, aromatic H), 7.59 (overlapping signals, 2H, aromatic H), 7.47 (overlapping signals, 5H, aromatic H), 7.29 (overlapping signals, 18H, aromatic H), 7.16 (overlapping signals, 4H, aromatic H), 5.80 (t, *J* = 10.0 Hz, 1H, H-2), 5.34 (dd, *J* = 10.2, 2.9 Hz, 1H, H-3), 4.98 (d, *J* = 10.9 Hz, 1H, Bn-C*H*), 4.93 (overlapping signals, 2H, H-1', Bn-C*H*), 4.80 (overlapping signals, 2H, Bn-C*H* x2), 4.75 (overlapping signals, 2H, H-6a, H-6b), 4.71 (overlapping signals, 2H, H-1, Bn-C*H*), 4.46 (overlapping signals, 2H, H-4, Bn-C*H*), 4.37 (d, *J* = 12.1 Hz, 1H, Bn-C*H*), 4.10 (overlapping signals, 4H, H-5, H-3', H-5', Bn-C*H*), 3.73 (t, *J* = 9.6 Hz, 1H, H-4'), 3.56 (dt, *J* = 9.9, 3.0 Hz, 1H, H-2'), 3.34 (dd, *J* = 10.9, 2.1 Hz, 1H, H-6'a), 2.95 (dd, *J* = 11.0, 1.9 Hz, 1H, H-6'b), 2.82 (ddd, *J* = 12.5, 8.3, 6.3 Hz, 1H, butyl C*H*(H)O), 2.72 (dt, *J* = 12.5, 7.6 Hz, 1H, butyl C*H*(H)O), 1.61 (m, 2H, lipid), 1.25 (overlapping signals, 28H, lipid), 0.89 (m, 3H, lipid). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.1, 166.0, 165.3 (each C=O), 138.8 (C), 138.6 (C), 138.0 (C), 137.9 (C), 133.3 (C), 133.2 (C), 133.1 (C), 130.0 (CH), 129.7 (CH), 129.7 (CH), 129.5 (CH), 129.2 (CH), 128.6 (CH), 128.5 (CH), 128.4 (CH), 128.4 (CH), 128.4 (CH), 128.4 (CH), 128.3 (CH), 128.3 (CH), 128.3 (CH), 128.3 (CH), 128.2 (CH), 128.2 (CH), 128.1 (CH), 128.0 (CH), 127.9 (CH), 127.9 (CH), 127.7 (CH), 127.7 (CH), 127.6 (CH), 127.5 (CH), 127.5 (CH), 127.3 (CH), 100.2 (C-1'), 83.9 (C-1), 81.9 (C-3'), 79.7 (C-2'), 77.5 (C-4'), 76.5 (C-5), 75.7 (C-4), 75.6 (Bn-*C*H_2), 75.0 (C-3), 74.7 (Bn-*C*H_2), 73.9 (Bn-*C*H_2), 73.3 (Bn-*C*H_2), 71.5 (C-5'), 68.2 (C-2), 67.7 (C-6'), 62.7 (C-6), 29.8 (O-*C*H_2), 29.8, 29.7, 29.7, 29.7, 29.6, 29.6, 29.5, 29.5, 29.4, 29.2, 28.9, 26.9, 22.7, 14.1 (all lipid carbons). ESI-HRMS calcd for $C_{78}H_{92}O_{13}SNa$ 1286.6602, found *m/z*. 1286.6595 $[M+Na]^+$.



1-Heptadecanyl 4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-1-thio-β-D-galactopyranoside (145)

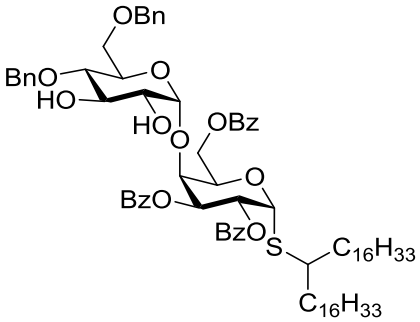
Compound **144** (53 mg, 0.042 mmol) was reacted as described in the general procedure II.A to give **145** (39 mg, 97%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (overlapping

signals, 18H, aromatic H), 7.18 (overlapping signals, 2H, aromatic H), 4.89 (s, 2H, Bn-C*H* x2), 4.84 (overlapping signals, 2H, Bn-C*H* x2), 4.73 (d, *J* = 3.6 Hz, 1H, H-1'), 4.62 (d, *J* = 11.9 Hz, 1H, Bn-C*H*), 4.51 (overlapping signals, 2H, Bn-C*H* x2), 4.43 (d, *J* = 11.8 Hz, 1H, Bn-C*H*), 4.28 (d, *J* = 8.5 Hz, 1H, H-1), 4.02 (overlapping signals, 3H, H-4, H-3', H-5'), 3.79 (overlapping signals, 2H, H-6a, H-6b), 3.70 (m, 1H, H-5), 3.64 (dd, *J* = 10.2, 1.8 Hz, 1H, H-6'a), 3.56 (d, *J* = 3.5 Hz, 1H, H-2'), 3.54 (m, 1H, H-6'b), 3.47 (overlapping signals, 3H, H-2, H-3, H-4'), 2.68 (t, *J* = 7.5 Hz, 2H, O-CH_2), 2.28 (s, 1H, OH), 1.62 (m, 2H, lipid), 1.37 (m, 2H, lipid), 1.25 (overlapping signals, 26H, lipid), 0.88 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.2 (C), 137.7 (C), 137.4 (C), 136.8 (C), 128.8 (CH), 128.7 (CH), 128.6 (CH), 128.5 (CH), 128.5 (CH), 128.5 (CH), 128.4 (CH), 128.2 (CH), 128.2 (CH), 128.1 (CH), 128.1 (CH), 128.0 (CH), 128.0 (CH), 127.9 (CH), 127.8 (CH), 127.8 (CH), 127.8 (CH), 127.7 (CH), 100.5 (C-1'), 86.5 (C-1), 81.8 (C-3'), 80.9 (C-4), 78.9 (C-2'), 78.2 (C-4'), 77.5 (C-5), 75.9 (Bn-*C*H_2), 75.3 (C-2), 75.1 (Bn-*C*H_2), 74.8 (Bn-*C*H_2), 73.6 (Bn-*C*H_2), 71.8 (C-5'), 71.2 (C-3), 68.7 (C-6'), 60.3 (C-6), 30.9 (O-*C*H_2), 30.5, 30.1, 29.7, 29.7, 29.7, 29.6, 29.6, 29.5, 29.4, 29.3, 29.2, 29.0, 28.9, 22.7, 14.1 (all lipid carbons). ESI-HRMS calcd for $C_{57}H_{80}O_{10}SNa$ 979.5370, found *m/z*. 979.5357 $[M+Na]^+$.



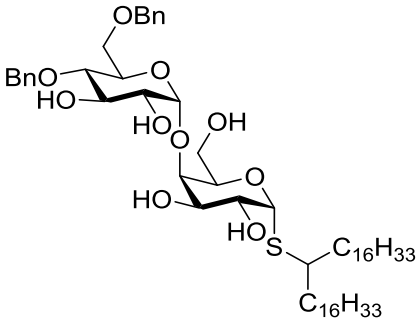
1-Heptadecanyl 4-*O*-(α-D-glucopyranosyl)-1-thio-β-D-galactopyranoside (146)

Compound **145** (39 mg, 0.017 mmol) was reacted as described in the general procedure II.M. Chromatography (CH_2Cl_2-MeOH 8:1) gave **146** (19 mg, 79%) as a white solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.86 (d, *J* = 3.9 Hz, 1H, H-1'), 4.28 (d, *J* = 9.3 Hz, 1H, H-1), 3.99 (overlapping signals, 2H, H-2, H-4), 3.91 (ddd, *J* = 12.6, 5.7, 2.5 Hz, 1H, H-5'), 3.80 (m, 1H, H-6a), 3.75 (overlapping signals, 2H, H-6'a, H-6'b), 3.70 (t, *J* = 6.5 Hz, 1H, H-5), 3.58 (overlapping signals, 3H, H-3, H-3', H-6b), 3.37 (dd, *J* = 9.9, 3.8 Hz, 1H, H-2'), 3.20 (t, *J* = 9.5 Hz, 1H, H-4'), 3.10 (m, 2H, O-CH_2-lipid), 1.73 (m, 2H, lipid), 1.45 (overlapping signals, 6H, lipid), 1.18 (overlapping signals, 28H, lipid), 0.79 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 100.4 (C-1'), 89.5 (C-1), 78.7 (C-5), 77.6 (C-4), 73.5 (C-3), 72.7 (C-3'), 72.3 (C-5'), 71.8 (C-2), 69.9 (C-4'), 65.9 (C-2), 60.9 (C-6'), 59.2 (C-6), 50.3 (S-CH_2), 31.1, 28.9, 28.8, 28.8, 28.7, 28.6, 28.5, 28.3, 28.0, 27.8, 27.7, 24.1, 21.9, 20.3, 12.9 (all lipid carbons).



17-Tritriacontyl 4-*O*-(4,6-di-*O*-benzyl-α-D-glucopyranosyl)-2,3,6-tri-*O*-benzoyl-1-thio-α-D-galactopyranoside (147)

Compound **138** (50 mg, 0.033) was reacted as described in the general procedure II.K using $TiCl_4$ (1 mol/L in CH_2Cl_2, 90 µL, 2.5 equiv.). Chromatography (cyclohexane-EtOAc, 6:1) gave the title compound (18 mg, 41%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (overlapping signals, 3H, aromatic H), 7.94 (overlapping signals, 4H, aromatic H), 7.58 (m, 1H, aromatic H), 7.47 (overlapping signals, 5H, aromatic H), 7.29 (overlapping signals, 13H, aromatic H), 7.15 (m 2H, aromatic H), 7.10 (overlapping signals, 3H, aromatic H), 5.94 (d, *J* = 6.0 Hz, 1H, H-1), 5.72 (dd, *J* = 11.1, 5.9 Hz, 1H, H-2), 5.57 (d, *J* = 11.0 Hz, 1H, H-3), 5.02 (d, *J* = 3.9 Hz, 1H, H-1'), 4.79 (m, 1H, H-5), 4.67 (overlapping signals, 3H, H-6a, H-6b, Bn-C*H*), 4.54 (d, *J* = 2.8 Hz, 1H, H-4), 4.42 (d, *J* = 11.5 Hz, 1H, Bn-C*H*), 4.35 (d, *J* = 12.1 Hz, 1H, Bn-C*H*), 4.03 (m, 1H, Bn-C*H*), 3.97 (overlapping signals, 2H, H-3', H-5'), 3.60 (s, 1H, H-2'), 3.55 (t, *J* = 9.8 Hz, 1H, H-4'), 2.99 (d, *J* = 11.3 Hz, 1H, H-6'a), 2.74 (m, 1H, S-C*H*), 2.63 (d, *J* = 11.2 Hz, 1H, H-6'b), 2.51 (s, 1H, OH), 2.47 (d, *J* = 8.1 Hz, 1H, OH), 1.63 (overlapping signals, 4H, lipid), 1.23 (overlapping signals, 54H, lipid), 0.88 (t, *J* = 6.9 Hz, 6H, lipid). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.9, 165.8, 165.6 (each C=O), 138.4 (C), 137.5 (C), 133.3 (C), 133.3 (C), 133.3 (C), 129.9 (CH), 129.8 (CH), 129.8 (CH), 129.5 (CH), 129.3 (CH), 129.2 (CH), 128.5 (CH), 128.4 (CH), 128.4 (CH), 128.2 (CH), 128.0 (CH), 127.9 (CH), 127.7 (CH), 127.7 (CH), 99.8 (C-1'), 82.1 (C-1), 76.9 (C-4'), 74.7 (C-4), 74.4 (benzyl *C*H_2), 74.3 (C-3'), 73.4 (Bn-*C*H_2), 72.6 (C-2), 71.0 (C-3), 70.9 (C-5'), 68.7 (C-2, C-5 (overlapping signals)), 67.3 (C-6'), 62.0 (C-6), 45.4 (*C*H-S), 35.0, 34.6, 31.9, 29.7, 29.7, 29.7, 29.6, 29.6, 29.6, 29.4, 27.1, 26.3, 22.7, 14.1 (all lipid carbons). IR (film) cm^{-1}: 3459, 2923, 2853, 1724, 1452, 1269, 1095, 1069, 1046, 1026, 708. ESI-HRMS calcd for $C_{80}H_{112}O_{13}SNa$ 1335.7721, found *m/z*. 1335.7678 $[M+Na]^+$.



17-Tritriacontyl 4-*O*-(4,6-di-*O*-benzyl-α-D-glucopyranosyl)-1-thio-α-D-galactopyranoside (148)

Compound **147** (18 mg, 0.014 mmol) was reacted as described in the general procedure II.A to give **148** (13 mg, 92%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (overlapping signals, 7H, aromatic H), 7.25 (overlapping signals, 3H, aromatic H), 5.42 (d, *J* = 5.4 Hz, 1H, H-1), 4.98 (s, 1H, H-1'), 4.77 (d, *J* = 11.2 Hz, 1H, Bn-C*H*), 4.58 (overlapping signals, 2H, Bn-C*H* x2), 4.50 (d, *J* = 11.7 Hz, 1H, Bn-C*H*), 4.26 (d, *J* = 6.1 Hz, 1H, H-5), 4.03 (overlapping signals, 2H, H-4, H-3'), 3.94 (s, 1H, H-2), 3.86 (overlapping signals, 2H, H-6a, H-5'), 3.73 (overlapping signals, 2H, H-6b, H-6'a), 3.61 (overlapping signals, 2H, H-2', H-6'b), 3.53 (d, *J* = 8.9 Hz, 1H, H-3), 3.39 (t, *J* = 9.3 Hz, 1H, H-4'), 2.72 (m, 1H, S-C*H*), 1.51 (overlapping signals, 4H, lipid), 1.25 (overlapping signals, 56H, lipid), 0.88 (t, *J* = 6.8 Hz, 6H, lipid). ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.9 (C), 137.4 (C), 128.6 (CH), 128.5 (CH), 128.1 (CH), 128.0 (CH), 128.0 (CH), 128.0 (CH), 101.3 (C-1'), 86.2 (C-1), 83.7 (C-4), 77.6 (C-4'), 74.8 (Bn-*C*H_2), 74.6 (C-5'), 73.7 (Bn-*C*H_2), 72.3 (C-2'), 71.7 (C-3), 71.6 (C-3'), 69.7 (C-5), 69.5 (C-2), 68.8 (C-6'), 61.9 (C-6), 46.5 (*C*H-S), 35.5, 34.9, 31.9, 29.7, 29.7, 29.7, 29.6, 29.6, 29.6, 29.4, 26.8, 26.7, 22.7, 14.1 (all lipid carbons). IR (film) cm^{-1}: 3431, 2921, 2852, 1733, 1455, 1055, 1027, 732, 697. ESI-HRMS calcd for $C_{59}H_{100}O_{10}SNa$ 1023.6911, found *m/z*. 1023.6910 $[M+Na]^+$.

IV. References

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